The Mystery of Life's Origin

THE MYSTERY OF LIFE'S ORIGIN

THE CONTINUING CONTROVERSY

CHARLES B. THAXTON,
WALTER L. BRADLEY,
ROGER L. OLSEN, JAMES TOUR,
STEPHEN MEYER, JONATHAN WELLS,
GUILLERMO GONZALEZ,
BRIAN MILLER, DAVID KLINGHOFFER

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Description

The origin of life from non-life remains one of the most enduring mysteries of modern science. *The Mystery of Life's Origin: The Continuing Controversy* investigates how close scientists are to solving that mystery and explores what we are learning about the origin of life from current research in chemistry, physics, astrobiology, biochemistry, and more. The book includes an updated version of the classic text *The Mystery of Life's Origin* by Charles Thaxton, Walter Bradley, and Roger Olsen, and new chapters on the current state of the debate by chemist James Tour, physicist Brian Miller, astronomer Guillermo Gonzalez, biologist Jonathan Wells, and philosopher of science Stephen C. Meyer.

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Foreword

Robert Marks and John West

In 1984, three courageous scientists—Charles Thaxton, Walter Bradley, and Roger Olsen—published a rigorous reassessment of then-current scientific theories about the origin of life. Published by the Philosophical Library (the publisher of works by Albert Einstein, Werner Heisenberg, Max Planck, and many other eminent scientists and thinkers), *The Mystery of Life's Origins* challenged the scientific orthodoxy of the time and provoked significant interest in the scientific community. Long-time NASA scientist Robert Jastrow hailed the book as "a very well thought-out and clearly written analysis," while Robert Shapiro, Professor of Chemistry at New York University, lauded it as "an important contribution to the origin of life field."

The book's core message was startling: Current approaches to the origin of life were abysmal failures, and wholesale re-thinking was required. As the authors put it:

> the difficulty is fundamental. It applies equally to discarded, present, and possible future models of chemical evolution. We believe the problem is analogous to that of the medieval alchemist who was commissioned to change copper into gold… You can't get gold out of copper, apples out of oranges, or information out of negative thermal entropy. There does not seem to be any physical basis for the widespread assumption implicit in the idea that an open system is a sufficient explanation for the complexity of life.

At the end of the book, the authors suggested that the origin of life might have required what philosopher Michael Polanyi called "a profoundly informative intervention" or what they themselves called an "intelligent cause." Most scientists of the time did not want to hear that revolutionary proposal; but the authors' words inspired a new generation of scientists and scholars who were dedicated to seeking evidence of purpose and intelligent design throughout nature.

By republishing *The Mystery of Life's Origin* on the occasion of its 35th anniversary, we seek to recognize the signal accomplishment of its original authors, plus the hard work of Jon Buell of the Foundation for Thought and Ethics, who helped bring the book to reality. In the new introduction by David Klinghoffer, you will get to read the behind-the-scenes story of how the book came to be written—and the transformative impact it had on many. The original text has been lightly updated. The fact that only light updating was needed is a testament to the meticulous scholarship of the authors and to the enduring nature of the problem they identified in origin of life studies.

Although the text of the original *Mystery of Life's Origin* forms the first part of this volume, this book is much more than an historical appreciation. Its second half, "The State of the Debate," includes new chapters assessing the state of origin of life research today by chemist James Tour of Rice University, physicist Brian Miller, astronomer Guillermo Gonzalez, biologist Jonathan Wells, and philosopher of science Stephen C. Meyer. Those who want to understand not only the history of science's quest to understand the origin of life, but its current status, will find this book an invaluable guide.

We would like to thank the many people who made this new volume possible, including: Charles Garner of the University of Memphis, who reviewed the text of the original book for needed updates; Mike Perry of Inkling Books, who laid out and indexed the book; Brian Gage of Pipe & Tabor, who created the cover and produced the figures, tables, and equations; Iwan Sandjaja, who scanned the out-of-print original text and converted it into a digital format; Amanda Witt and others who copy-edited and proofed the volume; and of course, the original authors Charles Thaxton, Walter Bradley, and Roger Olsen, as well as the new contributing authors. Finally, we gratefully recognize the funding and support of the Walter Bradley Center for Natural and Artificial Intelligence at Discovery Institute, without which this new book couldn't have been published.

Robert J. Marks, PhD
Director, Walter Bradley Center for Natural and Artificial Intelligence
Discovery Institute

John G. West, PhD
Vice President
Discovery Institute
December, 2019

INTRODUCTION: INTELLIGENT DESIGN'S ORIGINAL EDITION

David Klinghoffer

How does life emerge from that which is not alive? This elicit mystery exercises a peculiar fascination, with the power to elicit remarkable feats of imagination. As the novelist Mary Shelley recalled, her invention of the story of Frankenstein traced back to conversations she witnessed between Lord Byron and her husband Percy Shelley. Holidaying in Switzerland in the summer of 1816, they spoke late into the night, past the "witching hour," about "the principle of life, and whether there was any probability of its ever being discovered and communicated." Up for discussion was gossip about "experiments of Dr. Darwin" (Erasmus, the grandfather of Charles) who "by some extraordinary means" produced "voluntary motion" in a length of spaghetti. The poets alluded to "galvanism," electrical experiments by Luigi Galvani, spurring thoughts that "a corpse would be reanimated."[1] Later, sleepless in her bed, Mrs. Shelley would experience a vision, receiving the seed for one of the great horror novels.

Less horrific but hardly less imaginative are scenarios of unguided "chemical evolution," or abiogenesis, featured in high school and college biology textbooks, taken as gospel by the media and preached as such by a range of authoritative popular and scholarly figures in the culture. Simple experimental work by Louis Pasteur in the early 1860s demonstrated that life does not spontaneously generate itself, not from spaghetti, not from anything. Instead, life comes from life. How then may science explain the origin of the very first life?

Charles Darwin in 1871 famously speculated in a letter to Joseph Hooker, "But if (and oh what a big if) we could conceive in some warm little pond with all sorts of ammonia and phosphoric salts, light, heat, electricity etcetera present, that a protein compound was chemically formed, ready to undergo still more complex changes."[2] The "warm little pond" generating "protein compounds" is not far off from textbook orthodoxy today. Students are taught that a prebiotic soup gave rise to key biotic chemicals, amino acids, stimulated by atmospheric electricity—galvanism in a modern guise—as demonstrated in the famed Miller-Urey experiment of 1952. One feat of imagination here lies in conceiving by what "extraordinary means" such building blocks came together, unguided, in precisely the right order to give rise to biological information, the digital code of DNA and RNA, that underlies all life on Earth.

In 1969, San Francisco State University biologist Dean Kenyon would give the theory of chemical evolution its then most up-to-date presentation, in an influential text, *Biochemical Predestination*. By 1984, Kenyon had abandoned the theory altogether in favor of what would later be called intelligent design. His public confession of apostasy came in the Foreword of a short yet remarkable book, *The Mystery of Life's Origin: Reassessing Current Theories*, by chemist Charles B. Thaxton, materials scientist Walter L. Bradley, and geochemist Roger L. Olsen. Discovery Institute Press is delighted to offer this new version of the book, the Ur-text or original edition of the modern theory of intelligent design, along with supplementary essays by scholars updating and extending the work. These new chapters, by synthetic organic chemist James Tour, physicist Brian Miller, astronomer Guillermo Gonzalez, biologist Jonathan Wells, and philosopher of biology Stephen Meyer, present the current state of the debate that Thaxton and his co-authors sparked in 1984. The enigma they identified remains, hardly resolved by further technical research amplified and distorted by press releases and hysterical headlines, but rather, if anything, compounded as science has advanced.

For anyone familiar with today's intelligent design theory, to read *The Mystery of Life's Origin* is to experience a powerful sense of déjà vu. Surely we have walked these halls before. Or rather, *Mystery* is the hall down which ID walked before it emerged into history as "intelligent design." The now familiar phrase appears nowhere in the text. But other phrases, persons, and motifs, the stock-in-trade of the modern ID theorist, are present. That is most notably, thickly so in the book's Epilogue, authored by Dr. Thaxton, where the technical details are left behind and a forthright argument for a design hypothesis is offered. Stephen Meyer has been forthcoming about his intellectual debt to Thaxton. In a sense, *Mystery* is a daring first draft of what would become Meyer's own work, especially in *Signature in the Cell*. Here we have the "principle of uniformity,"[3] "the present is a key to the past,"[4] adducing what "we know by experience" about how "intelligent investigators" act,[5] the role of the "idea of creation" in the "origin of modern science,"[6] the injunction to "follow the evidence where it leads,"[7] how "certain effects always have intelligent causes,"[8] Shannon information, Michael Polanyi, "specified complexity,"[9] taking Darwin himself as a historical precedent in one's argumentation, conceiving of the search for truth about biological origins as akin to the work of a detective in a murder mystery, and more.

A separate article could be written tracing the influence of such themes from Thaxton, Bradley, and Olsen on Meyer alone, reflected in his books including the forthcoming *The Return of the God Hypothesis*. That last formulation, the "God hypothesis," first used by Meyer in the title of a 1999 essay in the *Journal of Interdisciplinary Studies*, itself appears in the Epilogue of *Mystery*.[10] Thaxton uses it to contrast different theaters of scientific investigation, "operation science" versus "origin science," where consideration of a transcendent intelligent agent as being at work in causing certain events either doesn't belong at all, or might in fact be permissible. In *Signature in the Cell*, Meyer would later write that this "terminology" was "admittedly cumbersome."[11] For "origin science" he substitutes "historical science."

When I spoke to Thaxton recently, he explained that the "God hypothesis" was simply the shorthand way professors talked about the idea when Thaxton was a post-doctoral student at Harvard in the philosophy of science. Other key ID concepts and habits of thought came to him from this same period in his post-PhD studies. For example, looking to Darwin as a model or precedent for one's arguments, as Meyer does, was something he picked up from historian of science Reijer Hooykaas (1906–1994), whom he came to know at this time. "Uniformitarianism" is via the geologist Charles Lyell (1797–1875), but Hooykaas wrote a book about it in 1963, *The Principle of Uniformity in Geology, Biology, and Theology*. Shannon information was from information theorist Hubert Yockey (1916–2016), referring to mathematician Claude Shannon (1916–2001), and "specified complexity," now much associated with mathematician and intelligent design proponent William Dembski, from chemist Leslie Orgel (1927–2007). The advice to "follow the evidence where it leads," or as it is sometimes found, "We must follow the argument wherever it leads," a staple of writers on intelligent design, is a paraphrase from Socrates in Plato's *Republic*. In Allan Bloom's translation (394d), "[W]herever the argument, like a wind, tends, thither must we go."[12]

In other words, the interest of *The Mystery of Life's Origin* lies partly in the question of an *idea's* origin. Meyer and Thaxton form a link with scientific and philosophical investigations of the 20th century, the 19th century, and before, much as intelligent design more broadly connects Greek philosophy, especially Anaxagoras (5th century B.C.), with the thinking of Darwin's colleague turned rival, Alfred Russel Wallace (1823–1913). Without going into needless detail, or searching too far back into the past, this Introduction will sketch some of the immediate historical background behind the writing of *Mystery* and its subsequent influence on the evolution of the theory of ID.

It is impossible to fully disentangle the study of biological origins from reflections and speculations of a theological nature. Proponents of Darwinian evolution habitually advance arguments about God in support of their theory: "God, if he exists, and there seems to be no reason to think he does, surely wouldn't have done it *this* way." Much of the curiosity we feel about how life originated similarly derives from the observation that a purely naturalistic explanation is not what a theist would expect, and an explanation incorporating design or teleology is not what a materialist or an atheist would expect. Today, some of the most prominent exponents of neo-Darwinism are also outspoken and evangelizing atheists. Which is fair enough. That fact by itself does not invalidate their scientific thinking. So there is no shock or scandal in the fact that the idea for the book that became *The Mystery of Life's Origin* was first discussed among a group of friends and colleagues affiliated with Probe Ministries, operated by Jon Buell and his associate James Williams to advocate a Christian worldview. Buell would go on in 1981 to launch the Foundation for Thought and Ethics, in Dallas, Texas, publishing books on scientific, historical, and ethical subjects. This publishing work was absorbed in 2016 as an imprint of Discovery Institute Press.

Buell knew *Mystery* co-author Walter Bradley from Bradley's days as a PhD student at the University of Texas. In 1975, Buell was seeking an author for a rigorous book on evolution, and he proposed it to Bradley, then a professor at the Colorado School of Mines. Bradley wasn't interested in that focus, so he made a counter-proposal: a book on the origin of life. As he told Discovery Institute's John West in an interview, he suspected that could be the "ultimate barrier to this whole question of life and evolution," the "hardest step," "how you get started from scratch" —meaning, life from nonlife.[13] The study of the origin of life is by necessity multidisciplinary. It joins biology to fields with which Bradley's expertise, materials science, is more closely linked: biochemistry, physical chemistry, chemical kinetics, thermodynamics. "Interestingly enough," he says, "most of the people that I have met, who are doing work as biologists, seldom know very much about what I think of as more fundamental and theoretical chemistry. And so a lot of what they do is pretty qualitative."

Qualitative speculation was what Bradley wanted to avoid. Talking and teaching about the subject, including a 1974 guest lecture he gave on "Thermodynamics and the Origin of Life" at Colorado State University, convinced him he was onto something. One key question, the atmosphere of the early Earth, seemed to call for training in another field: geochemistry. For this, he sought out the collaboration of a co-author, Roger Olsen, then a PhD student in geochemistry at the Colorado School of Mines. "Some of the ideas of what people would want to believe about abiogenesis are very dependent on what the initial atmosphere was like," Bradley recalls of his thinking at the time. "For example, if you have too much oxygen, then there's no hope." Olsen's research could shed light on this. "Roger concluded that we never did have a reducing atmosphere," as the Miller-Urey experiment assumed, an assumption that "didn't have a snowball's chance in hell." An oxidizing atmosphere spelled doom for life's presumed chemical forerunners.

Bradley and Olsen had been working on their origin-of-life manuscript for six months when Charles Thaxton moved down to Dallas from Boston, where he had done post-doctoral studies at Harvard and Brandeis Universities, in the history of science and molecular biology, respectively. The text of *The Mystery of Life's Origin* furnishes a single brief autobiographical reference, in the Epilogue, but it is an intriguing one. It reflects Thaxton's experience: "When we are asked to consider 'far out' or 'strange' ideas such as Special Creation, as were the authors just a few years ago, typically the response is exactly that mentioned by [David] Bohm as cited earlier." This response is one of "violent disturbance." Moreover, "The process... can sometimes be painful (it was to one of the authors) but the quest for truth has never been easy, and has on more than a few occasions been known to make one unpopular."[14]

Thaxton, introduced to religious faith by his mother, had in college gone through a period of disbelief. Scientific knowledge seemed to crowd out any role for a deity. It was as a graduate student in physical chemistry at Iowa State that he first delved into the problem of abiogenesis. Until that point, he had thought that chemistry fully accounted for life's origins. The assumption turned out to be too simple. The pain and disturbance he referred to in the book was, first, the feeling of having betrayed his mother, and, second, the feeling of having betrayed those who looked to him as respectable materialist.

After moving to Dallas with his wife and first son, Thaxton went to work with Jon Buell. It was late 1975, and, as Thaxton told John West in an interview, "Buell came in one day and presented me with a manuscript that he'd had on his desk."[15] It was by Walter Bradley and Roger Olsen, the first draft of what would become *The Mystery of Life's Origin*. "So I read through it," Thaxton says, "and my first reaction was, wow, this is kind of interesting. But why is there not more chemistry in it?" He noted this objection to Buell, who invited him to come on a visit to meet with Bradley and Olsen in College Station, Texas, where by this time Bradley had moved to teach at Texas A&M. In Bradley's living room, they discussed the book, and Buell encouraged Thaxton to share his reservation about the dearth of chemistry. Bradley and Olsen both almost simultaneously spoke up and said, "Well, you're the chemist. You write it!"

And that is essentially what he did. Bradley was teaching and the now Dr. Olsen had switched to private industry. Thaxton was the "fresh man" on the project with the time to further develop the book. "I had a lot of studying to do, and I did," he says. "Night and day for weeks and weeks and months, and it turned into several years in fact, before it was all done." Olsen had written about the atmosphere of the early Earth in Chapter 5 ("Reassessing the Early Earth and Its Atmosphere"), while Bradley wrote Chapters 7, 8, and 9 ("Thermodynamics of Living Systems," "Thermodynamics and the Origin of Life," and "Specifying How Work Is to Be Done"). "Then Thaxton wrote the majority of the rest of it," according to Bradley, including the Epilogue which departs from pure scientific discussion and drew most of the fire once the book came out.

One problem was that the chapters seemed to reflect different voices, different terminologies and ways of arguing. As Thaxton recalls, it needed to be largely rewritten to sound "like a science book, not an engineering book." So, "I redid the whole manuscript, just started from scratch, just started over. And we completely went through that process at least two or three times." By 1978, it was done, and ready to be sent for scientific review, by a dozen or more scientists, some friendly to the thesis, others unfriendly.

One prominent scientist specializing in the origin-of-life field, presumed to be unfriendly but a fair critic nonetheless, was Dean Kenyon. Kenyon, exchanging letters with Thaxton in 1981, had read the book in its manuscript form and was interested enough to invite Buell and Thaxton to visit with him. They flew to San Francisco for the meeting. Thaxton did not know at the time that Kenyon had privately come to doubt his own chemical evolutionary theory.

"My stomach was all the way up in my throat as we sat in Kenyon's office that day," Thaxton recalls. "I remember asking him what he thought of the book." In response, Kenyon fixed him with a stern look, then smiled and said, "I thought it was terrific." This emboldened Thaxton, for he had come with an additional plan, beyond asking Kenyon for his view of their work. He was going to ask Kenyon to write the Foreword. He plunged in. "Well, then why don't you write the Foreword to the book?" Thaxton asked. "And he said, 'Well, I was hoping you would ask.'"

In the opinion of historian Ronald Numbers, in his book *The Creationists,* Kenyon's contribution, a leading origin-of-life theorist "confessing that he no longer believed in naturalistic evolution," was the "most striking feature of their book."[16] As Kenyon wrote, "It is very likely that research on life's origins will move in somewhat different directions once the professionals have read this important work." He concludes, "All scientists interested in the origin-of-life problem would do well to study this book carefully and to evaluate their own work in the light of its arguments."[17] Such an endorsement, for the three authors, was a coup that almost could not be topped.

The process of reviewing having been completed and needed changes having been made, it was time to seek a publisher. This task fell to Jon Buell. The goal was to reach a secular audience, not a religious one, and the style of the book indicates as much. To be strictly avoided, says Thaxton, was anything that sounded remotely "religious." He notes, "We wanted to make sure we weren't preaching." Yet finding a publisher was no simple matter. Then as now, the faintest hint of "creationism" was enough to set teeth on edge, even though the Thaxton book clearly did not support creationism in its most precise meaning of recruiting science on behalf of Biblical literalism. It probably did not help that a prominent Supreme Court case involving "creation science," *McLean v. Arkansas,* was being argued about this time, in 1981. The case was decided in January 1982, finding that teaching creationism in public schools violates the First Amendment's Establishment Clause.

As of late 1982, Buell was still in search of a publisher. Cornell University Press and MIT Press had both expressed initial interest, with "almost identical" final results, as Thaxton recalls. At Cornell, two internal reviewers read the book and delivered a split opinion, in favor and against. So a third was called in, a prominent scientist. Thaxton wonders if it was Carl Sagan. The acquisitions editor involved, Eric Halpern, wrote to Buell with the bad news, indicating that, "As you will see, the report falls far short of giving us the basis for a favorable recommendation to our faculty Board."[18] The "masked" report is indeed scathing, blasting the book for its "superficial" arguments, though interesting in how it shows how little has changed in conventional thinking about life's origin over the past four decades. The anonymous Cornell reviewer harrumphs, "Because the experiments have not yet produced a cell in the laboratory it is unrealistic to dismiss the effort." Researchers are still saying the same today, in very similar terms. Astronomer Abraham Loeb at Harvard, for one, writing in 2019 in *Scientific American,* considers the prospects of "produc[ing] synthetic life out of raw chemicals" in the lab, but concedes "even if we dismiss these prospects as unrealistic with our current technologies, another civilization that happened to be billions of years more technologically advanced than we are might have" done so.[19]

By return mail on Foundation for Thought and Ethics letterhead, Thaxton responded to Halpern, noting that while expert review was only to be expected from a university publisher, "it is difficult to escape the feeling that we have been sandbagged by someone who feels threatened by criticisms raised" in the book. He pointed out that their book had been sent accompanied by endorsements from "noted chemical evolution scholars," organic chemist Gordon Shaw at the University of Bradford in England, as well as Dean Kenyon. The reviewer had dismissed the manuscript as "a complete misrepresentation," lacking originality or comprehension. Yet Kenyon had called it "one of the best critical analyses of origin-of-life I have read to date." Thaxton asked why Halpern had not wondered at the stark discrepancy of views: "[C]onsider the implication of the allegations of your reader. To accept his word that we have submitted a shallow, often answered critique, is to charge the readers we cited in our Prospectus with having their critical faculties so numbed they could not detect superficial criticisms. And these are noted scholars."

Writing to Halpern at Cornell, Thaxton included an independent analysis from the editor at the MIT Press who had been "enthusiastic" about the book, only to lose his job because the publisher cut its division devoted to the life sciences. The editor, Grahame J. C. Smith, had particularly praised Walter Bradley's coverage of thermodynamic issues. These chapters were "so good that the rest of the book might be geared to cohesiveness with that part of the book."[20] He particularly liked Chapter 8, which he called "really excellent" and "Wonderful!" He had many helpful editorial suggestions and criticisms.

Thaxton had asked Halpern at Cornell to reconsider, but Halpern, in a final reply on December 23, 1982, courteously refused. With his masked "distinguished scholar in the field of chemical evolution" harshly opposed, he would have needed to seek additional support from Cornell scientists, and he did not want to take that course.

In the end, Buell and Thaxton went with an old and distinguished New York publisher, Philosophical Library, which while not a university or strictly scientific press could boast an impressive list of authors, prominent scientists and others. They have published a collection by Albert Einstein, *Out of My Later Years* (1950), and their backlist features books by Werner Heisenberg, Max Planck, Jean-Paul Sartre, Simone de Beauvoir, even Charles Darwin, including a range of Nobel Prize winners.[21] They also allowed the Foundation for Thought and Ethics to market the book. Far from a religious publisher, Philosophical Library was an appropriate choice for a scientific audience. A second edition of the book was published by Lewis and Stanley, in Dallas. The move was made, says Thaxton, simply because "we can do everything much faster, without having to have big turnarounds, and waits, and so on."

The book came trailing endorsements besides Kenyon's. The back-cover highlights praise from astronomer Robert Jastrow of NASA's Goddard Institute for Space Studies ("a very well thought-out and clearly written analysis") and from one of the best-known scholars on the origin of life, chemist Robert Shapiro at New York University ("an important contribution," "brings together the major scientific arguments that demonstrate the inadequacy of current theories," although "I do not share the final philosophical conclusion"). Shapiro published his own book on the topic two years later, *Origins: A Skeptic's Guide to the Creation of Life on Earth* (1986).

The subsequent reception by scientists helps to explain the spark that *The Mystery of Life's Origin* provided for a nascent intelligent design movement. The reception did not come immediately. In fact, the anxious authors were initially troubled by the lack of a response. "It was dead silence," says Thaxton. "Nobody said anything. And I was so dejected, and disappointed. It was like you drop it out there and — not a ripple. Nothing. No effect at all." The publisher was reassuring. "'Don't worry,' he said, 'it takes a year'" for a book like this to get its due.

So they waited. And while they did, we can pause briefly to remember how, for skeptics of evolution, whether chemical or biological, it was a different world from ours. In 1984, the full array of resources deployed today to intimidate dissenters didn't exist. There were no evolution professors speculating on their blogs about pre-publication books and poisoning the well against new ideas. Nor were there any pseudonymous Darwinist reviewers on Amazon posting enflamed reviews of books they hadn't purchased much less read. Everyone wrote under his own name, and named editors served in the role of gatekeeper, thus taking responsibility. It was a fine thing to be alive before the Internet. Interest had to build organically, more honestly, via typescripts and printed matter transiting through the U.S. mail. As a side benefit, there was no *Wikipedia* with its unknown yet wildly influential editors, many bearing fantastical pseudonyms instead of real names, disseminating misinformation about any controversial subject and on call 24/7, at a moment's notice, to undo an earnest effort to correct misstatements. As of 2017, Walter Bradley himself was among those ID scientists to have their *Wikipedia* entry disemboweled or erased by *Wiki* editors. Even *Wikipedia* co-founder Larry Sanger has called the encyclopedia's treatment of intelligent design "appallingly biased."[22] This is how opinions on profound subjects are developed and spread now.

Is what I have just recounted an irrelevant aside? No, it's not. I bring it up because, despite the aggravating interaction with Cornell University Press, the response from expert scientists to *The Mystery of Life's Origin* is impressive for how relatively relaxed, if not necessarily open-minded, the scientific establishment was. And in fact, the publisher's estimate of a year was about right. "So that was what happened," says Thaxton. "When the reviewers started, wow, it was like they all started coming at once."

Among the most significant voices to be raised was that of biochemist Sidney W. Fox at the University of Miami, a leading origin-of-life researcher. Thaxton calls him a "propagandist" for the naturalistic interpretation of abiogenesis. His June 1985 review in *The Quarterly Review of Biology* was loaded with ridicule, sniffing that of the writers, "Not one is listed in *American Men and Women of Science*, 14th edition."[23] Yet there is also a hint of grudging respect: "the authors of *The Mystery* present antievolutionary arguments with force."

Fox, as Thaxton recalls, was "more significant than Stanley Miller [of Miller-Urey fame] was, in the early days, in promoting all the origin-of-life materials in the high school textbooks and so on. In the late Fifties, early Sixties, it was all Sidney Fox. Everywhere. All the time." So despite the dyspeptic tenor of the review, it was an honor to get one from Fox at all. And despite the shot at their lack of status in the establishment pecking order, Thaxton notes the irony that they had a somewhat intimate connection: He inherited Fox's old office at Iowa State from when Fox was a postdoctoral student there. "In fact," Thaxton remembers, "I had to clean out a lot of stuff that it turns out was his."

The August 1985 *Yale Journal of Biology and Medicine* was another story. Professor James F. Jekel, in the Yale School of Medicine, was warmly congratulative. "To all who share the comfortable assumption that the scientific problems of abiogenesis are mostly resolved, this book will come as a real surprise," he wrote. He concluded: "The volume as a whole is devastating to a relaxed acceptance of current theories of abiogenesis. It is well written, and, though technical, much of the book is within the reach of the informed non-scientist." It is "strongly recommended to anyone interested in the problem of chemical and biological origins."[24]

An eminent scientist at Yale, biophysicist Harold J. Morowitz, had a fascinating mixed response. Morowitz testified in the 1981 *McLean v. Arkansas* "creation science" trial and was no friend of what would be come to be called intelligent design, writing in 2005 in the *Chronicle of Higher Education* that "Only creationists support the theory of intelligent design."[25] According to his *New York Times* obituary in 2016, "He was best known for applying thermodynamic theory to biology, exploring how "the energy that flows through a system acts to organize that system."[26] So he was in a strong position to evaluate the section of *The Mystery of Life's Origin*, authored by Walter Bradley, that dealt with that subject. Some years after *Mystery* was published, through a lucky personal connection, Charles Thaxton was able to get his book in front of the eminent Dr. Morowitz. "I contacted Morowitz about reading it," says Thaxton. "I thought, well, gee whiz here's a way to find out what he thinks about what Bradley has done. But I didn't tell him that that's what I was interested in."

Morowitz wrote a two-page private review.[27] He dismissed the Epilogue as "philosophically naïve," and "philosophically unfair," noting that it contains no mention of Bishop Berkeley or Benedict Spinoza. As to the science behind the book, however, he wrote, it is a "very substantial effort," a "scientifically useful critique of a very sizable literature," and "the authors have certainly succeeded in showing that we are very far from a convincing experimentally verifiable understanding of how something as complex as the simplest contemporary cells could have arisen." Yet the "assumption that the problem lies beyond present-day natural science seems premature."

There was one thing missing from the review, and it was odd given Morowitz's own expertise. Thaxton sought an opportunity to ask him about it by phone. Thaxton said, "I'm very curious. You said some positive things about our book. But you were the expert on thermodynamics at the Arkansas trial, and yet you had not one thing to say about our treatment of thermodynamics in *The Mystery of Life's Origin*. Can you tell me why?" As Thaxton remembers, over the telephone line, "There was a long, long pause. I mean, very disturbingly so. Long pause. And I said, 'Are you still there?' And he said, 'Yes. I'm just thinking.' And I said, 'Well, can you answer?' And he said, 'Well, I didn't see anything wrong with it, so I didn't say anything about it.'" Morowitz is still today held up as a champion against "misuses of the second law of thermodynamics," as the Darwin-lobbying National Center for Science Education puts it.[28] Yet Thaxton draws the evident conclusion from Morowitz's response: "That means he agreed with what Bradley said. Right?" It seems so.

More open praise rolled in from scientists in relevant fields.[29] "This is really a brilliant book," wrote chemist and origin-of-life researcher Clifford Matthews at the University of Illinois. "A superb re-evaluation, it's very fair and it's not a polemic." Molecular biologist Jay Roth at the University of Connecticut was "greatly impressed" and called *Mystery* a "fascinating scholarly work." Chemist Walter Thorson at the University of Alberta praised it as a "splendid book" offering "very careful and scientific argumentation." Physicist Graham Gutsche at the U.S. Naval Academy said it was "Outstanding!" and noted that he "used the information in my teaching." And so on.

As you would expect, there were attacks on the book's supposed "creationism," but also prominent rejoinders. *Chemical & Engineering News* gave the job of reviewing it to chemist Richard Lemmon at the Lawrence Berkeley National Laboratory. "Now this is the most widely read magazine by people in chemical engineering and chemistry in the world," says Walter Bradley. "But it normally has articles about new developments in science, in chemistry and chemical engineering and some industry-type things and so forth. So it has a very, very broad audience." Lemmon's review in the July 1, 1985, issue commences: "The only people to whom I can recommend *The Mystery of Life's Origin: Reassessing Current Theories* are the minuscule fraction of C&EN's readers who are religious creationists. These also are people who are prone to write letters to the editor whenever anything touching on creationism appears. I look forward to the forthcoming complaints about this review and, to help the complainers, aver that I am an agnostic, and proud of it."[30]

Under the headline, "Life's Origin and the Supernatural," Lemmon anathematizes the trio of authors over and over as "creationists" pushing "creationism." The best part may be his quoting H. L. Mencken at them: "If it could, science would explain the origin of life on Earth at once—and there is every reason to believe that it will do so on some not too remote tomorrow." Mencken wrote that in 1930, and science is hardly closer today to explaining life's origin, 90 years later.

In several subsequent issues, readers protested the style and content of Lemmon's review. Michael A. Beilstein at Oregon State University wrote that he had read the book and "found nothing inherently unscientific" in it but instead a "legitimate challenge" and an "excellent presentation" of problems in the field.[31] In the same issue, Eugene C. McKannan at NASA's Marshall Space Flight Center calculated that "57% of the review is about the reviewer's beliefs—not about the book" and skewered Lemmon's "circular logic" in appealing to Mencken, George Bernard Shaw, "and the federal courts, none of whom had any new data to present."[32] Among the most notable replies, Lemmon's U.C. Berkeley colleague Henry F. Schaeffer III, a chemist, regretted the "superficial review" and pointed out that he too had "read their book and found it to be both interesting and provocative."[33] He noted that the authors "are not 'creationists' in the sense popularized by recent court cases." Schaeffer has since gone on to fame. Identified by *Wikipedia* as "one of the most highly cited chemists in the world,"[34] he is also a signer of Discovery Institute's Scientific Dissent from Darwinism.[35] After moving to the University of Georgia, he invited Charles Thaxton to Athens for a visit with a few students and professors.[37] "So a bad review isn't all bad," says Thaxton.[36]

In fact, because of the book and its reception, Thaxton and Bradley became widely sought-after speakers for university audiences and other venues. Says Bradley, "Of the top 20 ranked universities in the United States, I have given lectures to 18." He lists Harvard, Yale, MIT, Cornell, the University of Pennsylvania, Stanford, UCLA, U.C. San Diego, the University of Texas, and others. His subjects are the origin of life as well as the origin of the universe. At U.C. Berkeley, he mentions having spoken to an audience of almost 2,000 people. On an occasion in Baltimore, he debated Robert Shapiro, the NYU chemist and origin-of-life skeptic. Though an atheist, Shapiro was friendly. According to Bradley, he apologized ahead of time to the audience: "This is not going to be a very good debate, because I've read the book that Dr. Bradley and his colleagues have written. And I agree with about 90 percent of it."

A "confidential report" by Jon Buell describes a 1988 visit and lecture by Thaxton at Princeton University. Though Buell asks in the memo, "I'd appreciate your helping us protect the anonymity of the various people mentioned," he writes of private meetings "instigated" by a Princeton alumnus, Thomas Woodward, and celebrates that "these science faculty had invited Charles to lecture because they had read *The Mystery of Life's Origin* (of which Charles is the major author) and were in agreement with his view!" At the public lecture by Thaxton at Princeton's Woodrow Wilson School, faculty members on hand included "Freeman Dyson, considered by many to be the premier physicist in the world today—the 'Albert Einstein' of the late 20th century."[37] Says Woodward, "Quite a flock of science and engineering professors attended, from the departments of chemistry, physics, geology, chemical engineering."[38]

Thaxton and Bradley describe origin-of-life conferences they attended about this time, including the select and private Gordon Research Conference. At a Gordon meeting in New Hampshire, Thaxton had a memorable conversation with James Ferris, the editor of an important academic journal, *Origins of Life and Evolution of Biospheres*. "Ferris was an experimental chemist at Rensselaer Polytechnic Institute. I sent him a copy of *Mystery*, and later met up with him at the conference in New Hampshire, where I asked if he had any comment after reading it. As I recall, what he said was to the effect of, 'Your book is too damn chemically sophisticated to be in support of those creationists.' He did say he thought many things we said are quite right, but that it takes things in the wrong direction." Meaning, the direction of intelligent design.

For measuring the impact of the book, one conference where Thaxton spoke, neither select nor private, was of significance for the future of the intelligent design movement. This was in Dallas, and it was the sort of event where a young geophysicist in the oil business, with no plans for the weekend, could wander in almost by chance. In his 2009 book *Signature in the Cell: DNA and the Evidence for Intelligent Design*, Stephen Meyer records the date, February 10, 1985, a Saturday, because what he heard "changed the course of my professional life. By the end of the year, I was preparing to move to the University of Cambridge in England, in part to investigate questions I first encountered on that day."[39] His three books, *Signature*, *Darwin's Doubt*, and the forthcoming *The Return of the*

God Hypothesis, all pay tribute to the work of Thaxton, Bradley, and Olsen.

Meyer wouldn't have met Thaxton, though, if he hadn't happened to attend another lecture the night before at Southern Methodist University. The speaker was Harvard astrophysicist Owen Gingerich on the Big Bang and what it suggested about divine purpose. Meyer heard that Gingerich would be speaking on the same subject the next day, at the old, historic Dallas Hilton, alongside Caltech astronomer Allan Sandage. Meyer was intrigued and decided to go.

The event featured theists and atheists, weighing what the Epilogue of *Mystery* calls the scientific "God hypothesis." There was a panel on the origin of life. The panel included Dean Kenyon, discussing his reasons for repudiating the scientific theory of unguided abiogenesis that he had previously championed, and Charles Thaxton arguing that the scientific evidence pointed to an "intelligent cause" behind the first life. At this, as Meyer writes in *Signature*, "Other scientists on the panel became uncharacteristically defensive and hostile. Dr. Russell Doolittle, of the University of California at San Diego, suggested that if the three authors were not satisfied with the progress of origin-of-life experiments, then they should 'do them.'"[40]

Meyer discovered that Thaxton was living in Dallas too, and he struck up a friendship. "I called him, and he offered to meet with me. We began to meet regularly and talk, often long after work hours."[41] Meyer was struck by Thaxton's "radical claim that an intelligent cause could be considered a legitimate *scientific* hypothesis for the origin of life." The claim, recognizing the "digital information" coded in DNA and inferring an author of the code, intersected with Meyer's own work which relied on computer imaging technology—coded, digital information, invariably tracing back to an author or authors—to locate oil in the ground. Understanding the origin of *biological* information, considering whether it must have an author, became the theme of Meyer's research down to today.

Meyer's career as a philosopher of science and an ID proponent got its start with hearing from Kenyon and Thaxton. Another leading intelligent design theorist, mathematician and philosopher William Dembski, had already reached conclusions in keeping with Thaxton, Bradley, and Olsen's argument. The book "came up in my personal readings about evolution and creation in the late 1980s," Dembski told me.[42] "This was before I got to know anyone in the emerging ID movement. I was a recent PhD in mathematics with an interest in reviving the design argument using probability theory. I went to the local public library in Evanston, Illinois, checked the book out, and read it. I came to the book already convinced that purely chemical processes, acting on non-living materials, were incapable of organizing anything that remotely deserved to be called a living form. This book, however, went much further in sealing the deal, in excruciating detail showing just how inadequate stochastic and mechanistic chemistry was in creating life."

In the late 1990s, Dembski would join Buell as academic editor for the Foundation for Thought and Ethics. He calls *Mystery* a "groundbreaker" not only for its scientific case ("its critique of chemical evolution still holds") but for "breaking into the secular academic market." Dembski, like Meyer, gives appropriate credit: "Although it's usually said that my book *The Design Inference* (Cambridge University Press, 1998) was the first book on intelligent design to be published by a major academic press, *The Mystery of Life's Origin,* as a book preparing the soil for intelligent design, can arguably be said to occupy that position instead, and 14 years earlier!"

Among proponents of intelligent design, Meyer and Dembski stand out as having had the most personal interaction with Charles Thaxton or Jon Buell. I have heard Discovery Institute philosopher of biology Paul Nelson speak in public, movingly, of his friendship with Walter Bradley, a mentor figure to him. Biochemist Michael Behe, author of *Darwin's Black Box* and other books, read *The Mystery of Life's Origin* in 1992 and told me, "It was the first book I encountered that made a positive case for the purposeful design of life—at least at its origin. It greatly strengthened my own conviction that design extends much deeper into biology."[43] Discovery Institute physicist Brian Miller recalls, "I read the book in the late 1990s when I was struggling to determine if I was a product of the blind forces of nature or the product of a Creator. The book demonstrated that life could not have originated through undirected natural processes, which moved me back towards believing in a Creator and therefore in the direction of ID."[44]

"Their book marked the beginning of interest in the theory of intelligent design in the United States," Stephen Meyer has written, "inspiring a generation of younger scholars."[45] Inspired, but sometimes more than just that. Thaxton remembers receiving a phone call in 1985 from a conflicted PhD student in anthropology at the University of Illinois, crying and grateful. The book had given him intellectual permission to believe that human life, and all life, had an intelligent source behind it. In the spiritually corrosive context of modern academia, such permission to believe is no small gift. "An anthropology student, of all things," says Thaxton. "Not origin of life, or anything like that. Anthropology. And he was in tears explaining to me that it was because of having read our book, that he was able to understand how he could stay in school."

In fact, though, like Darwin's *Origin of Species,* Thaxton's *Mystery of Life's Origin* has no doubt had its greatest, widest impact on the countless people who have never read it, and perhaps never heard of it. It is like that with many influential books, with notable exceptions such as the Bible. *Mystery,* as I said, doesn't use the term "intelligent design." However, the fact that intelligent design is a household phrase today can be, in no small part, credited to Charles Thaxton, Walter Bradley, and Roger Olsen. Every time an important intellectual is peeled away from Darwinian naturalism, from NYU atheist philosopher Thomas Nagel[46] to Yale computer scientist and polymath David Gelernter,[47] by reading Meyer and others, it is a tribute to them.

There is a much larger problem, though, than what intellectuals think. James Tour, the synthetic organic chemist at Rice University, well represented in this edition, is the leading scientific spokesman at the moment vigorously calling baloney on all too common media headlines about origin-of-life research ("Found: The Origin of Life,"[48] "Amazing Discovery May Hold Key to the Origins of Life,"[49] etc.) which, worse, proceed effortlessly from press releases from universities and research institutions, presumably approved by the research scientists themselves. I don't think anyone is deliberately setting out to fool the public. But the results, as Tour points out, are seriously misleading. He is rare in protesting this, and has taken abuse for it. That rarity is a serious problem. You can call it negligence, a failure to speak up, a failure to protest. Those are all possibilities.

This media misinformation is a stumbling block for many, rendering a false picture of the answer to an ultimate question. The authors of this book have inspired a defense of the truth. For ordinary, unnamed people, given hope of a purpose at work behind the veil of brute physical existence, to be recognized in the origin of life, the impact of *The Mystery of Life's Origin* is immeasurable.

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I. THE MYSTERY OF LIFE'S ORIGIN

FOREWORD

Dean Kenyon

The Mystery of Life's Origin presents an extraordinary new analysis of an age-old question: How did life start on Earth? The authors deal forthrightly and brilliantly with the major problems confronting scientists today in their search for life's origins. They understand the impasse in current laboratory and theoretical research and suggest a way around it. Their arguments are cogent, original, and compelling. This book is sure to stimulate much animated discussion among scientists and laymen. It is very likely that research on life's origins will move in somewhat different directions once the professionals have read this important work.

The modern experimental study of the origin of the first life on Earth is now entering its fourth decade, if we date the inception of this field of research to Stanley Miller's pioneering work in the early 1950s. Since Miller's identification of several (racemic) protein-forming amino acids in his electric discharge apparatus, numerous follow-up studies have been conducted. Conforming in varying degrees to the requirements of the so-called "simulation paradigm," these experiments have yielded detectable amounts of most of the major kinds of biochemical substance as well as a variety of organic microscopic structures suggested to be similar to the historical precursors of the first living cells.

This program of research can be regarded as a natural extension of Darwin's evolutionary views of the last century. The goal of the work is to find plausible uniformitarian mechanisms for the gradual spontaneous generation of living matter from relatively simple molecules thought to have been abundant on the surface of the primitive Earth.

The experimental results to date have apparently convinced many scientists that a naturalistic explanation for the origin of life will be found, but there are significant reasons for doubt. In the years since the publication of *Biochemical Predestination* I have been increasingly struck by a peculiar feature of many of the published experiments in the field. I am not referring to those studies conducted more or less along the lines of Miller's original work, although there are firm grounds for criticizing those studies as well. I am referring to those experiments designed to elucidate possible pathways of prebiotic synthesis of certain organic substances of biologic interest, such as purines and pyrimidines, or polypeptides.

In most cases the experimental conditions in such studies have been so artificially simplified as to have virtually no bearing on any actual processes that might have taken place on the primitive Earth. For example, if one wishes to find a possible prebiotic mechanism of condensation of free amino acids to polypeptides, it is not likely that sugars or aldehydes would be added to the reaction mixture. And yet, how likely is it that amino acids (or any other presumed precursor substance) occurred anywhere on the primitive Earth free from contamination substances, either in solution or the solid state? The difficulty is that if sugars or aldehydes were also present polypeptides would not form. Instead an *interfering cross-reaction* would occur between amino acids and sugars to give complex, insoluble polymeric material of very dubious relevance to chemical evolution. This problem of *potentially interfering cross-reactions* has been largely neglected in much of the published work on the chemical origins of life. The possible implications of such an omission merit careful study.

Other aspects of origin-of-life research have contributed to my growing uneasiness about the theory of chemical evolution. One of these is the enormous gap between the most complex "protocell" model systems produced in the laboratory and the simplest living cells. Anyone familiar with the ultrastructural and biochemical complexity of the genus *Myco-*

plasma, for example, should have serious doubts about the relevance of any of the various laboratory "protocols" to the actual historical origin of cells. In my view, the possibility of closing this gap by laboratory simulation of chemical events likely to have occurred on the primitive Earth is extremely remote.

Another intractable problem concerns the spontaneous origin of the optical isomer preferences found universally in living matter (e.g., L- rather than D-amino acids in proteins, D- rather than L- sugars in nucleic acids). After all the prodigious effort that has gone into attempts to solve this great question over the years, we are really no nearer to a solution today than we were thirty years ago.

Finally, in this brief summary of the reasons for my growing doubts that life on Earth could have begun spontaneously by purely chemical and physical means, there is the problem of the origin of genetic, i.e., *biologically relevant,* information in biopolymers. No experimental system yet devised has provided the slightest clue as to how biologically meaningful sequences of subunits might have originated in prebiotic polynucleotides or polypeptides. Evidence for some degree of spontaneous sequence ordering has been published, but there is no indication whatsoever that the non-randomness is biologically significant. Until such evidence is forthcoming one certainly cannot claim that the possibility of a naturalistic origin of life has been demonstrated.

In view of these and other vexing problems in origin-of-life research, there has been a need for some years now for a detailed, systematic analysis of all major aspects of the field. It is time to re-examine the foundations of this research in such a way that all the salient lines of criticism are simultaneously kept in view. *The Mystery of Life's Origin* admirably fills this need. The authors have addressed nearly all the problems enumerated above and several other important ones as well. They believe, and I now concur, that there is a fundamental flaw in all current theories of the chemical origins of life. Although the tone of the book is critical, the authors have written it in the positive hope that their analysis will help us find a better theory of origins. Such an approach is, of course, entirely consistent with the manner in which scientific advances have occurred in the past.

One of the uniquely valuable features of the book is its discussion (Chap. 6) of the relative geochemical plausibilities of the various types of simulation experiments reported in the literature. To my knowledge this is the first systematic attempt to devise formal criteria for acceptable degrees of interference by the investigator in such experiments. Another especially helpful feature is the detailed discussion of the implications of thermodynamics (Chaps. 7, 8, and 9) for the origin-of-life problem. This important topic is either omitted entirely or is treated superficially in most other books on the chemical origins of life. The authors might have included a more detailed discussion of the problem of optical isomer preferences, but this deficiency detracts in only a minor way from the overall strength of their argument.

If the authors' criticisms are valid, one might ask, why have they not been recognized or stressed by workers in the field? I suspect that part of the answer is that many scientists would hesitate to accept the authors' conclusion that it is fundamentally implausible that unassisted matter and energy organized themselves into living systems. Perhaps these scientists fear that acceptance of this conclusion would open the door to the possibility (or the necessity) of a supernatural origin of life. Faced with this prospect many investigators would prefer to continue in their search for a naturalistic explanation of the origin of life along the lines marked out over the last few decades, in spite of the many serious difficulties of which we are now aware. Perhaps the fallacy of scientism is more widespread than we like to think.

One's presuppositions about the origin of life, and especially the assumption that this problem will ultimately yield to a persistent application of current methodology, can certainly influence which lines of evidence and argument one chooses to stress, and which are played down or avoided altogether. What the authors have done is to place before us essentially all the pertinent lines of criticism in one continuous statement and to invite us to face them squarely.

All scientists interested in the origin-of-life problem would do well to study this book carefully and to evaluate their own work in the light of its arguments.

Dean H. Kenyon
Professor of Biology
San Francisco State University

PREFACE

Charles Thaxton, Walter Bradley, Roger Olsen

The Mystery of Life's Origin is a book that had to be written. There is a critical necessity in any developing scientific discipline to subject its ideas to test and to rigorously analyze its experimental procedures. It is an ill-fated science that doesn't do so. Yet, surprisingly, prebiotic or chemical evolution has never before been thoroughly evaluated. This book not only provides a comprehensive critique using established principles of physics and chemistry, it introduces some new analytical tools, particularly in chapters six and eight.

We do not want to suggest that scholars have offered no criticisms helpful to other workers in the field of origin-of-life studies. They have, of course, and scattered here and there in the chemical evolution literature these criticisms can be found. There is no comprehensive marshalling of these, however, no carefully ordered statement that brings them together in one volume to assess their combined import. That is a need that has existed now for several years, a need which, hopefully, this book helps remedy. It should not be thought that the authors cited as sources of specific criticism would be in agreement with the overall reassessment presented here. In most cases they would not.

The fact that chemical evolution has not received thorough evaluation to date does not mean it is false, only that it is unwise to build on it or extend it until we are satisfied it is sound. It is crucial to have a thorough critique of chemical evolution, especially since much of the optimism about finding life in space and the search for extraterrestrial intelligence (SETI) is based on it.

Workers who have come up within a discipline usually are the ones most qualified to administer criticism. There are times, however, when workers with specialized training in overlapping disciplines can bring new insights to an area of study, enabling them to make original contributions. The following chapters were produced by a chemist (CT), a materials scientist (WB), and a geochemist (RO). If there is validity to our reassessment it will mean that sizable re-adjustments in origin-of-life studies are in order. Even if our critique is shown to be deficient and the chemical evolution scenario is vindicated, perhaps the present work will have played a role in goading scientific workers into presenting a clearer and stronger defense in its behalf.

The authors would like to thank the following for permission to quote extracts or reproduce diagrams from their publications, as indicated in the text: Gordon and Breach, Science Publisher, Inc.: ed. Lynn Margulis, *Origins of Life: Proceedings of the First Conference*, 1970; Simon & Schuster, Inc.: F. Hoyle and N. C. Wickramasinghe, *Evolution from Space*, 1981; Marcel Dekker: S. Fox and K. Dose, *Molecular Evolution and the Origin of Life*, revised edition, 1977; Prof. A. E. Wilder-Smith, *The Creation of Life*, 1970; the MIT Press: ed. J. Neyman, *The Heritage of Copernicus*, 1974; and the American Chemical Society: S. W. Fox, K. Haxada, G. Krampitz, and G. Mueller, *Chemical Eng. News*, June 22, 1970.

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Finally, our heart-felt thanks go to our wives, Carole, Ann, and Candace, who endured through seven years of research, writing and revisions. It is to them whose loyalty and love never waned that we dedicate this book.

Dallas, Texas, Christmas, 1983
C. Thaxton, W. Bradley, and R. Olsen

1. CRISIS IN THE CHEMISTRY OF ORIGINS

Two monumental scientific reports appeared in 1953, both of which have subsequently received wide acceptance in the scientific community. One was the proposal by James Watson and Francis Crick[1] of their double helical model for deoxyribonucleic acid, or DNA. According to their now-famous model, hereditary information is transmitted from one generation to the next by means of a simple code resident in the specific sequence of certain constituents of the DNA molecule. It had previously been held that the spectacular diversity of life was due in part to some corresponding diversity of nuclear material. The breakthrough by Crick and Watson was their discovery of the specific key to life's diversity. It was the extraordinarily complex yet orderly architecture of the DNA molecule. They had discovered that there is in fact a code inscribed in this "coil of life," bringing a major advance in our understanding of life's remarkable structure.

Almost as if synchronized for the sake of irony, the other report in 1953, by Stanley Miller,[2] offered experimental support for what has become an increasingly apparent contradiction. Miller offered his work in support of the neo-Darwinian theory of prebiotic evolution. This notion suggested that the fantastic complexity in the molecular organization of living cells might somehow have resulted from nothing more than simple chemicals interacting at random in a primordial ocean.

In 1953, few if any were troubled by the tension between the new insights of Crick and Watson on the one hand and Miller's results on the other. Crick and Watson were concerned with life's *structure* and Miller was concerned with life's *origin*. Most observers had an unshakable confidence that these two investigative approaches would eventually converge. After all, young Miller's announcement of experimental success was just what was anticipated according to the general theory of evolution. Regardless of whether the particular theory of evolution is Darwinian, neo-Darwinian, or something else, an evolutionary preamble to the biological phase of evolution is clearly required. *Chemical evolution*, then, is the pre-biological phase of evolution in which the very earliest living things came into being. This monumental dawning of life occurred through the variation of natural forces acting on matter over long time spans, perhaps up to a thousand million years, or maybe longer.

In the decades since Miller's and Crick and Watson's reports, however, there have been indications that all is not well in the halls of biology. We have gained a far deeper appreciation of the extremely complex macromolecules such as proteins and nucleic acids. The enlarged understanding of these complexities has precipitated new suggestions that the DNA mechanism may be more complex and the molecular organization more intricate and information-filled than was previously thought.[3]

The impressive complexities of proteins, nucleic acids, and other biological molecules are presently developed in nature only in living things. Unless it is assumed such complexity has always been present in an infinitely old universe, there must have been a time in the past when life appeared *de novo* out of lifeless, inert matter. How can the mere interaction of simple chemicals in the primordial ocean have produced life as it is presently understood? That is the question. The signs do not bode well for the standard answers given, and some investigators are suggesting that our two approaches will not converge.

The Demise of the Role of Chance

By 1966 a major change in scientific thought was underway. In Philadelphia a symposium was held at the Wistar Institute to highlight these changes.[4] It was there that signs of an impending crisis first emerged.

Symposium participants came together to discuss the neo-Darwinian theory of evolution. One conclusion, expressed in the words of Murray Eden of MIT, was the need "to relegate the notion of randomness to a minor and non-crucial role"[5] in our theories of origins. This conclusion was based on probability theory, which shows mathematically the odds against the chance formation of the highly complex molecular structure required for life. With the help of high-speed computers, programs could be run which simulated the billions-of-years' process based on the neo-Darwinian model of evolution. The results showed that the complexity of the biochemical world could not have originated by chance even within a time span of ten billion years. Eden's conclusion was a reasonable if unsettling one.

Other symposium participants voiced similar views about chance or randomness. V. F. Weisskopf noted, "There is some suspicion that an essential point [about our theories of origins] is still missing."[6] Eden suggested "new laws" as the missing piece in the puzzle of life's origin.[7] In his opening remarks as chairman, Nobel Prize-winning biologist Sir Peter Medawar said, "There is a pretty widespread sense of dissatisfaction about what has come to be thought of as the accepted evolutionary theory in the English-speaking world, the so-called neo-Darwinian theory."[8] It was Marcel Schutzenberger of the University of Paris, however, who intimated the true extent of the developing crisis when he expressed his belief that the problem of origins *"cannot be bridged within the current conception of biology."*[9] (Emphasis added.)

These comments reflect the impotence of chance or randomness as a creative mechanism for life's origin. But there was dissent, too. Some symposium participants, C. H. Waddington for example, balked at this conclusion, saying that faulty programming was the problem, not chance.[10] Waddington's objection illustrates a basic dilemma that has always plagued probability calculations. Such calculations must first assume a plausible chemical pathway, or course of events, and then calculate the probability of this series of events, in the hopes that the answer will at least approximate the probability of the actual course of events.

Nevertheless, there is great uncertainty about the actual chemical pathway. As a consequence, calculations showing the extreme improbability that life began by chance usually have carried little weight with scientists.

Such probability calculations, however, have now been supplemented by a more definitive type of calculation which does not require a knowledge of the detailed process or exact path of events that led to life. Recent advances in the application of the first and second laws of thermodynamics to living systems provide the basis for these calculations. Through them, accurate probabilities for the spontaneous synthesis of complex chemicals can be calculated without regard to the path that led to their development. All that is needed is information about the initial chemical arrangement and the complex arrangement these chemicals are found to have in living things. These thermodynamic calculations have agreed in order of magnitude with earlier path-dependent probability calculations. For example, some investigators, including Ilya Prigogine, the Nobel Prize-winning thermodynamicist, have relied upon calculations based on equilibrium thermodynamics to show the probability that life occurred spontaneously. Prigogine et al. put it this way:

> The probability that at ordinary temperatures a macroscopic number of molecules is assembled to give rise to the highly ordered structures and to the coordinated functions characterizing living organisms is vanishingly small. The idea of spontaneous genesis of life in its present form is therefore highly improbable even on the scale of the billions of years during which prebiotic evolution occurred.[11]

The agreement between the two types of probability calculations has heightened the growing awareness of a crisis in the chemistry of origins.

Biochemical Predestination

Because of the increasing disillusionment with the role of chance, a shift took place in the late Sixties and the Seventies to the view that life was somehow the inevitable outcome of nature's laws at work over vast spans of time. Terms such as "directed chance" and "biochemical predestination" have entered the scientific literature to mean that life was somehow the result of the inherent properties of matter. The abundant use of these terms marks a shift in thinking. Many feel that bonding properties of atoms had a significant role in the origin of the complex molecular structures of life. Others, including M. Polanyi, however, have suggested that if atomic bonding properties accounted for the actual structure of DNA, including the distribution of bases, "then such a DNA molecule would have no information content. Its codelike character would be effaced by an overwhelming redundancy."[12] So the mystery behind life's origin continues in spite of the undaunted confidence of some that a solution is near. This is further illustrated by developments in the U.S. space program.

In 1974 Stanley Miller, who had continued in his efforts to put modern origin-of-life studies on a firm experimental footing, said that:

> We are confident that the basic process [of chemical evolution] is correct, so confident that it seems inevitable that a similar process has taken place on many other planets in the solar system... We are sufficiently confident of our ideas about the origin of life that in 1976 a spacecraft will be sent to Mars to land on the surface with the primary purpose of the experiments being a search for living organisms.[13]

In 1976, on the eve of the first Mars landing, NASA's chief biologist, Harold P. Klein, explained that if our theories of origins are correct, we should find corroborative evidence of it on Mars.[14] The theories of which he spoke had presupposed the same inexorable forces of chemistry and physics at work on Venus, Mars, and innumerable planets throughout the cosmos as on Earth. Although few space scientists actually expected to find life on Mars, there was wide agreement that organic chemicals in some stage of the life-forming process would likely be found there. And, of course, the cost of the Mars landing was a substantial pledge toward that confidence. A significant opportunity for confirmation had arrived. The origin-of-life experiments were disappointing, however, as an unexpected type of chemistry was found on Mars, which indicated environmental conditions unfavorable to chemical evolution.

In a detailed analysis of the Mars data as reported in the *Journal of Geophysical Research*, it was concluded that "the results of the organic analysis experiment... should not give encouragement to those who hope to find life on Mars."[15]

Results from the Voyager I fly-by of Jupiter (1979) and Saturn (1980) and the later Cassini-Huygens mission to Saturn have not given any additional encouragement to those hoping to discover life in the cosmos other than that on Earth.[16] One of Saturn's moons, Titan, was thought to be more hospitable toward life. It now appears that Titan is cold and dead, with a lower atmosphere about 94% nitrogen, 6% methane, and .1% hydrogen.[17]

The sticky question that remains unresolved is not merely whether objections raised at the Wistar Institute are correct, but, in light of current evidence, whether there is cause for optimism about the "directed chance" view of life's origin. What is responsible for the dashed expectations held about life first on the moon, then Venus, Mars, Jupiter, and now Saturn and its moon Titan?

It cannot be denied that the "pure chance" view of the origin of life is a position of extreme faith. The nagging difficulty, however, that faces us now is that the modified version of "directed chance" has not performed well to date. The question must be asked whether there is a flaw in our theory of chemical evolution—a flaw at such a fundamental level that it mars both theories, "pure chance" and "directed chance."

A flaw in our theory of origins need not be viewed with pessimism, however. H. R. Post, a philosopher of science, has suggested in an illuminating article that such a flaw might actually lead to a new even better theory, if we but learn to decipher properly the clues it can yield. Post said:

> The best workers [in scientific theory] are those who are best at noticing cracks, anomalies, in the existing structure of the old theory—not disagreement with (new) experimental data, but anomalies within the theory itself. These cracks are very strong hints that suggest the structure of the new theory: we infer, as it were, the nature of the new three-

> dimensional beast from its two-dimensional footprints. They are traces of the new theory in the old.[18]

So for now we assert there is a crack in all current theories of origins. We shall leave for the main body of the book the task of mapping out the contours of the crack, which we hope will further a better understanding of origins.

Speculative Reconstruction

Before coming to that, however, it will be valuable to consider how origin-of-life research relates to science as a whole. In the matter of origins, there were no observers present. For some this lack of observation entirely removes the question of life's origin from the domain of legitimate science. In another context, George Gaylord Simpson has observed that:

> It is inherent in any acceptable definition of science that statements that cannot be checked by observation are not really *about* anything—or at the very least they are not science.[19] (Emphasis his.)

It is primarily due to this lack of observational check on theories that science cannot provide any *empirical* knowledge about origins. It can only suggest plausible scenarios in an attempt to reconstruct the events that led to the appearance of life on Earth.

The strength of physical science lies in its ability to explain phenomena as well as make predictions based on observable, repeatable phenomena according to known laws. Science is particularly weak in examining unique, nonrepeatable events. Commenting on this inherent limitation of science, *Nature* magazine noted:

> Those who work on the origin of life must necessarily make bricks without very much straw, which goes a long way to explain why this field of study is so often regarded with deep suspicion. Speculation is bound to be rife, and it has also frequently been wild. Some attempts to account for the origin of life on the Earth, however ingenious, have shared much with imaginative literature and little with theoretical inference of the kind which can be confronted with observational evidence of some kind or another.[20]

Yes, naturalistic explanations of life's origin are speculative. But does this mean such inquiries are impotent or without value? The same criticism can be made of any attempt to reconstruct unique events in the past. This has not deterred Scotland Yard or the FBI, however, from employing, sometimes with dramatic success, the science of forensic medicine in some bizarre "whodunit." Blood stains and fingerprints are the data of the crime detector and constitute circumstantial evidence in a court of law. Blood stains and fingerprints do not tell their own story, so these data must be fitted into some speculative but plausible scenario to reconstruct what occurred in the past. This kind of scenario is nonetheless only speculation, and no matter how plausible it may be, the truth behind the blood stains and fingerprints may be entirely different from the story alleged. For this reason there is always an element of risk or uncertainty when a jury brings a conviction for a crime based on circumstantial evidence. Juries do bring convictions in such cases, however, and all that is required is that the case be made beyond reasonable doubt. Herein lies the value of the speculative reconstruction of some past event. Although such a speculative scenario may elicit a confession from the defendant, or lead to newly discovered eyewitnesses, its principal value comes from its use as a tool in the hands of a skillful lawyer to make a convincing appeal to the jury which must finally decide the matter.

The study of chemical evolution is strikingly similar to forensic science. Consistent with the uniformitarian view that life arose through processes still going on, numerous investigators have reported on laboratory observations and experiments which they offer as circumstantial evidence for the naturalistic origin of life. Though the conditions of the early Earth are assumed to have been different from today's conditions, the processes are assumed to have been the same. According to this uniformitarian thinking, if we can reproduce in our laboratories today conditions as they were in the remote past, we should expect to obtain the kinds of changes that occurred then. This is the basis of *prebiotic simulation experiments* reported in chemical evolution literature.

"Implicit in this [uniformitarian] assumption is the requirement that no supernatural agency 'entered nature' at the time of the origin, was crucial to it, and then withdrew from history."[21] (Actually all that is required for this assumption is that no intelligent-purposive interruption or manipulation of the workings of natural forces ever occurred at the time of life's origin or since.) The developers of chemical evolution theory acknowledge its speculative nature, but offer it as a highly plausible scenario for the origin of life. We agree that there is scientific value in the pursuit of such reconstructions that should not be dismissed out of hand.

Furthermore, the *source* of our initial assumptions is of little import. It is perfectly legitimate to derive our ideas about what conditions might have been like on the early Earth from backward inference from present conditions, intuition, or even from a religious holy book. The scientific criterion is whether this speculative scenario fits the data available and is plausible. Here some clarification is in order. In the familiar Popper[22] sense of what science is, a theory is deemed scientific if it can be checked or tested by experiment against observable, repeatable phenomena. On this basis, relativity theory, atomic theory, quantum theory, germ theory—all have been judged scientific. Since all these theories of science deal with various facets of the operation of the universe, let us call them operation theories of science. Our point of clarification notes the difference between operation theories and origin theories, such as theories about the origin of life. Although the various speculative origin scenarios may be tested against data collected in laboratory experiments, these models cannot be tested against the actual event in question, i.e., the origin. Such scenarios, then, must ever remain speculation, not knowledge. There is simply no way to know whether the results from these experiments tell anything about the way life itself originated. In a strict sense, these speculative reconstructions are not falsifiable; they may only be judged plausible or implausible. In fact, as with the speculative scenarios used in a courtroom, failure to render a scenario implausible lends support to its plausibility, its credibility, and enhances the possibility that the reconstruction has genuine explanatory value and is true.

This book is largely devoted to evaluating the speculative scenarios of chemical evolution in light of present and pertinent data. We will seek accurate readings on the progress of various investigative approaches. To set the stage, Chapter 2 will be devoted to a short account of the history and status of chemical evolution theory. Chapter 3 will review representative experiments to simulate chemical events at the monomer level. Chapter 4 begins the critique and main part of the book.

It is our opinion that modern chemical evolution theories of the origin of life are in a state of crisis. The reader will be in a better position to appreciate why we say this after having read the book. But be forewarned! If we are even partially correct, some notable changes are in store for chemical evolution theories. And if we are proven substantially correct, well... but for the time being let's pursue the topic at hand.

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2. THE THEORY OF BIOCHEMICAL EVOLUTION

Spontaneous generation has never enjoyed security in prevailing scientific thought. The theory has been alternately embraced, abandoned, and accepted but ignored. The principal reason is that at various times in history two quite distinct concepts have been termed "spontaneous generation." These are: (1) *abiogenesis*, the notion of life's first origin from inorganic matter, and (2) *heterogenesis*, the idea of life's arising from dead organic matter, such as the appearance of maggots from decaying meat.[1]

The concept of heterogenesis was the more conspicuous of the two, with its apparent observational basis. It was also the more important concept for early Western thinkers. Their Christianized world view seemed to answer the question of life's first origin. Moreover, the vitalistic notion that saw a dichotomy between organic and inorganic matter clearly ruled out the idea of abiogenesis. A long line of Western thinkers, however, including Newton, Harvey, Descartes, and van Helmont, accepted the occurrence of heterogenesis without question.

The intrigue of the story is that heterogenesis, on the surface a more facile speculation than life from brute chemistry, was put to rest almost simultaneously with the publication of *On the Origin of Species*. Francesco Redi had demonstrated that meat placed under a screen of muslin (so that flies could not lay their eggs) never developed maggots. Similarly, other examples of heterogenesis were systematically discredited. Schulze, Schwann, von Dusch, and Schroeder each contributed to the growing awareness that microscopic organisms were present in various organic substances.

It was the work of Louis Pasteur, however, which sounded the death knell of the theory of heterogenesis. He showed that air contains many microorganisms which can collect and multiply in water, giving the illusion of spontaneous generation. In 1864, Pasteur announced his results before the science faculty at the Sorbonne in Paris with the words "Never will the doctrine of spontaneous generation recover from the mortal blow of this simple experiment."[2]

The Emergence of Abiogenesis

But the sound of Pasteur's words had not yet stilled before some recognized that, if taken to its conclusion, Darwin's work required an even more difficult and remarkable form of spontaneous generation—abiogenesis. Even Darwin himself speculated in this regard. In 1871 he wrote in a letter:

> It is often said that all the conditions for the first production of a living organism are now present which could ever have been present. But if (and oh! what a big if!) we could conceive in some warm little pond, with all sorts of ammonia and phosphoric salts, light, heat, electricity, etc. present, that a protein compound was chemically formed ready to undergo still more complex changes, at the present day such matter would be instantly devoured or absorbed, which would not have been the case before living creatures were formed.[3]

The breakdown of the dichotomy of organic and inorganic matter had by this time occurred. The primary impetus in its demise was the Reductionist school of thought which maintained that living matter had no autonomous vital forces within. The reductionist school had drawn support from two important breakthroughs, one in the understanding of matter, the other in the understanding of energy. The first came with the synthesis of urea in 1828 by Wohler, this being the first of a variety of organic materials to be synthesized from strictly inorganic materials. It is evident that the assumed categorical barrier between the inorganic and organic worlds would be invalidated by such experimental results.

The second important occurrence in the turn toward reductionism was the development of the concept of the conservation of energy. If all energies in a reaction can be quantified with no remainder, then no vital force (which had been held to be a kind of energy) was required in the reaction. With these advances for the reductionist viewpoint, a major hurdle had been cleared for the concept of abiogenesis.

In Germany, the quest for a monistic world view (*Weltanschauung*), a consistent and comprehensive philosophical explanation of all things, demanded a lively debate about abiogenesis. Ernst Haeckel, the most influential of the German evolutionary monists in the two decades following the publication of *On the Origin of Species*, sought earnestly to ensure that the *Weltanschauung* was built around evolution. The dogmatic materialists added their zeal to the same effort.

In contrast, scientists in Britain refused to enter the discussion, at least for a time. British scientists not only resisted the ideas of the monists, but regarded themselves in the traditions of Newtonian science and J. S. Mill. The *London Times* captured their spirit well when it said, "We look to men of science rather for observation than for imagination."[4] World views to a British scientist were apt to be regarded as grandiose speculations, unbecoming to science.

By the 1870s, however, the rigidity of this approach was somewhat mitigated, and Henry Bastian, heavily influenced by Haeckel, argued for a continuous abiogenesis. Bastian saw protoplasm as a simple, undifferentiated substance, arising over relatively brief periods of time on many occasions. Huxley had linked biological evolution and the geological principle of uniformity, and Bastian's view seemed to make sense in that light. We should recognize that at the time, the Earth's atmosphere was considered to have been the same in the distant past as in the present. Bastian's notion seemed to be consistent with the principle of uniformity, which gave it added status to many. Indeed, by calling on the reductionist continuity of organic and inorganic matter, Bastian argued that evidence for heterogenesis (still lingering in his own experiments) was evidence for abiogenesis as well. Thus, until the discovery of heatresistant spores, it appeared that Bastian could actually offer experimental support for a continuous abiogenesis. But with the discovery of such spores, the case for abiogenesis was reduced to the argument of a few proponents.

By 1880, not only experiment but even most of the discussion about abiogenesis was abandoned. While subsequent thinkers were to speculate that living matter had greater complexity than Bastian's conception, it was not until the elemental nature of matter was understood that a modern theory of abiogenesis could be forged.

Then in 1924, after years of virtual silence, the Russian biochemist Alexander Ivanovich Oparin reopened the discussion by proposing that the complex molecular arrangements and functions of living systems evolved from simpler molecules that pre-existed on the lifeless, primitive Earth.[5] With this suggestion, the recognizably modern form of chemical evolution theory began to develop.

In 1928, the British biologist J. B. S. Haldane published a paper in the *Rationalist Annual* in which he speculated on the early conditions necessary for the emergence of terrestrial life.[6] Haldane pictured ultraviolet light acting upon the Earth's primitive atmosphere as the source of an increasing concentration of sugars and amino acids in the ocean. He believed that life eventually emerged from this primordial broth. Later, work by J. D. Bernal in 1947 elaborated this conception. Bernal suggested some possible mechanisms whereby biomonomers might accrue to concentrations sufficient to allow condensation reactions producing the macromolecules necessary for life.[7] Both marine and fresh-water clays were seen as instrumental in the synthesis of large macromolecules, as well as their protection from destruction by ultraviolet light.

A further critical contribution to the idea was made by Harold Urey. Urey observed that with the exception of the Earth and the minor planets, the solar system was reducing, being hydrogen-rich in all the planetary atmospheres. Urey suggested that perhaps the early Earth's atmosphere was reducing as well, and that only later in the Earth's evolution did it become an oxidizing atmosphere.[8] This concept provided for favorable conditions for the synthesis of organic compounds.

The Modern Theory of Chemical Evolution

The foundational suggestions of Oparin, Haldane, Bernal, and Urey have since been elaborated into what we shall call the modern theory of chemical evolution. This theory came to predominate the thinking of scientists in the latter half of the twentieth century. A well-established central core has become the basis for many variations as the theory has developed. In outline form, the general scheme is quite simple. It envisions that the atmosphere of the early Earth contained such gases as hydrogen, methane, carbon monoxide, carbon dioxide, ammonia, and nitrogen, but no free oxygen. While this atmosphere would be quite toxic to us, its reducing quality was hospitable to organic molecules. This atmosphere is the first of five stages in the schematic representation of chemical evolution shown in Figure 2-1.

Sometime close to 3.5 billion years ago, the Earth's surface had cooled to under 100°C. This allowed for the survival of various organic molecules that would have degraded in higher temperatures.

Various forms of energy bathed the primitive Earth. These energy sources—lightning, geothermal heat, shock waves, ultraviolet light from the sun, and others—drove reactions in the atmosphere and ocean to

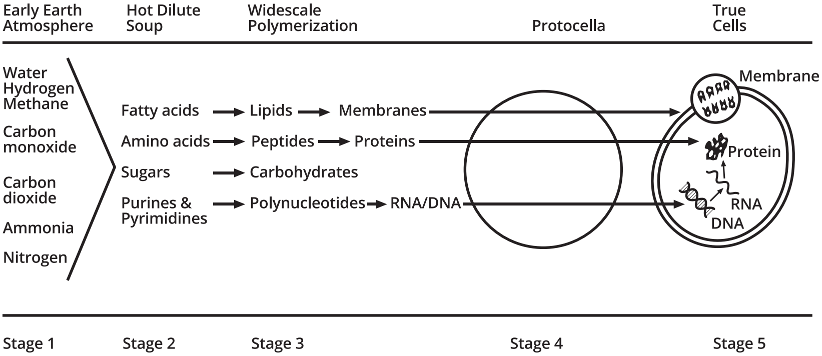

Figure 2-1. Major stages of chemical evolution.

form a wide variety of simple organic molecules. In the upper zones of this primitive atmosphere there would have been little, if any, free oxygen with which ultraviolet light could interact to produce an ozone layer such as presently protects all living things from lethal doses of ultraviolet. Instead, ultraviolet would irradiate the reducing atmosphere to form amino acids, formaldehyde, hydrogen cyanide, and many other compounds.

At lower altitudes these same organic compounds would result from the energy in electrical storms and thunder shock waves. Synthesis would be occasioned at the Earth's surface by wind blowing gases of the reduced atmosphere over hot lava flows near the sea.

The simple compounds formed in the atmosphere were washed down by rain into the oceans. Here they gathered with the products of ocean reactions as abundant organic material began to accumulate. Further reactions inevitably took place in this reservoir, and eventually the precursor chemicals reached the consistency of a "hot dilute soup." This is the second stage shown in Figure 2-1.

Innumerable smaller bodies of water provided a mechanism whereby the soup could be "thickened." In shallow pools, lakes, and shoreline lagoons, alternate flooding by the soup and evaporating of it resulted in a gradual concentration of organic chemicals. Further concentration occurred by adsorption of organic compounds on sinking clay particles in primordial water basins. The catalytic effect of these clays promoted polymerization on a wide scale. Polypeptides and polynucleotides were among the macromolecules produced. This is stage three as shown in Figure 2-1.

The conditions were now right for the development of protocells, stage four of Figure 2-1. Protocells were not true cells, but were coherent systems with a retaining membrane and sufficient functional capacity to survive an interim period. Over this period of time, their internal complexity increased. Polypeptides with suitable specificity to become enzymes developed. Additional characteristics of living cells emerged. When the nucleic acids—life's hereditary molecules—became sufficiently developed, they took control of these processes. Finally, life itself gained its critical first foothold, stage five of Figure 2-1.

This general outline has provided a rich basis for extensive study and numerous laboratory experiments. The theory maintains that natural processes alone operated to form life on this planet. No mysterious, divine, or vital forces had a part. As Cyril Ponnamperuma put it, "... life is only a special and complicated property of matter, and... *au fond* [basically] there is no difference between a living organism and lifeless matter..."[9] The question scientists have pursued, however, is, exactly what were the natural processes?

One view sees *extrinsic* forces bringing the increasing order as a result of their chance operation upon the chemical compounds involved. Another view sees matter's *intrinsic* properties as somehow responsible for its own increasing complexity. Life is seen as the inevitable result of the outworking of these intrinsic properties. This second view gradually gained ascendancy in the 1970s. Whether called "biochemical predestination" or some other name, it came to enjoy new prestige in the theoretical shift highlighted at the Wistar Institute, as mentioned in Chapter 1.

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8. H. C. Urey, *The Planets: Their Origin and Development* (New Haven: Yale University Press, 1952).
9. Cyril Ponnamperuma, "Chemical Evolution and the Origin of Life," *Nature* 201 (January 25, 1964): 337, doi: https://doi.org/10.1038/201337a0.

3. SIMULATION OF PREBIOTIC MONOMER SYNTHESIS

We may wish that a crack team of scientific observers had been present to record and detail the origin of life when it occurred. But since there were no observers, and since we can't go back to investigate the primitive Earth, we must do what we can to gain after-the-fact evidence of what may have occurred. We certainly can simulate in the laboratory what we postulate were the conditions of the early Earth and, using the uniformitarian principle, assume that the results will be similar to what actually occurred on the prebiotic Earth. With this expectation before us, the challenge is one of seeking to accurately identify and reproduce conditions of the prebiotic Earth for our experiments. Many noteworthy efforts have been made. But as we shall see, mimicking the early Earth is tricky business.

How to Run a Prebiotic Simulation Experiment

For example, we could run our simulation experiment simply by trying to reproduce early Earth conditions in a huge enclosed vat containing the suspected chemicals. The experiment would be conducted by passing various energy sources through a mixture of simple gases, liquid water, sand, clay, and other minerals, and just letting it go. Then at various times a portion could be withdrawn for analysis and the progress charted. Such a procedure—a "Synthesis in the Whole"—has on occasion been suggested.[1]

There are criticisms of this approach, however. First, if it truly simulated early Earth conditions and processes, we should not expect any meaningful results within laboratory time. Millions of years of simulation might be required for any detectable progress. Second, this method would obscure the complex chemical interactions sought for observation by allowing literally thousands of different reactions to go on simultaneously. This points out the need for a method of partitioning or isolating the various chemical reactions. Only through such partitioning can we gain clues as to the mechanisms involved in the production of life. So we would predictably learn nothing of consequence from a "Synthesis in the Whole" approach.

What we need is some technique which allows us to single out individual reaction processes in our simulated "prebiotic soup" and thus follow their progress. Such an approach would allow us to say something meaningful about the mechanisms that might have been involved in the pathway to life, and also about the validity of the proposed scheme itself.

In addition, for a laboratory simulation experiment to be of practical value, some technique must be used to overcome the factor of millions of years of time. Somehow we must speed up the process so that, like time-lapse photography, we are able to effectively compress the happenings of a long time-span into manageable laboratory time, yet without distortion.

In fact it is widely accepted today that a technique is available for simulating the extended time factor and for charting the progress of individual chemical reactions. The technique consists of carefully selecting and purifying chemicals conceived to have been the probable precursors of life and subjecting them in mixture to geologically plausible conditions of heat, light, temperature, concentration, pH, etc. An experiment is said to be geochemically plausible when the conditions used reproduce to a substantial degree the conditions alleged for the primitive Earth. These experiments are deemed successful if biologically significant molecules or their precursors are found among the products.[2]

In this way, an initial experiment can be run to produce amino acids. Then after isolating, purifying, and concentrating them, the next stage can be simulated, reacting the amino acids together to form polymers.

After a similar process of isolating, purifying, and concentrating these polypeptides, the next stage could be simulated in a third experiment to see what is produced. By following this procedure, products such as polysaccharides, lipids, polynucleotides, and protocells might all conceivably result. In time it is hoped that through the right experimental conditions in appropriate prebiotic simulation techniques, a living entity will be produced. Such an accomplishment, it is widely regarded, would lend a great deal of support to the view that life occurred on this planet by natural means. In this chapter we will give a representative review of the kind of simulation experiments at the monomer stage that have been done, and their results.

Table 3-1 shows the relative abundances of present sources of energy averaged over the Earth. We shall use this as a guide for the availability of energy sources on the early Earth. In the experiments discussed, five energy sources will be considered: electrical discharges, heat, ultraviolet light, shock waves, and high-energy compounds. There are a number of comprehensive reviews of prebiotic simulation experiments.[3] Readers are directed to them for more details.

Table 3-1. Sources of energy on the contemporary Earth.

Source	Energy (cal cm^{-2} yr^{-1})
Total radiation from sun	260,000
Ultraviolet light	
$\lambda < 3000$ Å	3,400
$\lambda < 2500$ Å	563
$\lambda < 2000$ Å	41
$\lambda < 1500$ Å	1.7
Electric discharges	4
Cosmic rays	0.0015
Radioactivity (to 1.0 km depth)	0.8
Volcanoes	0.13
Shock waves	1.1
Solar wind	0.2

Source: S. Miller, H. Urey, and J. Oro, "Origin of Organic Compounds on the Primitive Earth and in Meteorites," *J. Mol. Evol.* 9 (1976), 59.

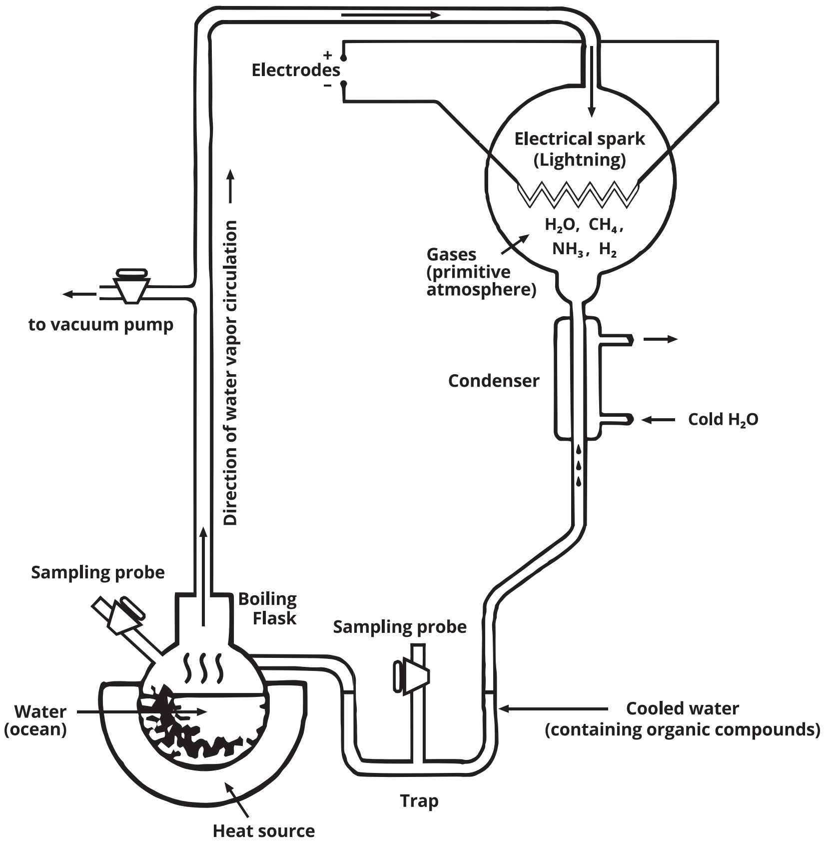


Figure 3-1. Apparatus used in Miller's electrical discharge experiments to form amino acids.

Survey of Prebiotic Simulation Experiments

Electrical Discharge Experiments

At the University of Chicago in December 1952, Stanley Miller provided the first experimental test of the Oparin-Haldane hypothesis of abiogenesis.[4] As a graduate student working in the laboratory of Nobel Laureate Harold Urey, Miller devised an experimental approach to simulate the formation of biomonomers on the early Earth. The simulated atmosphere consisted of methane, ammonia, hydrogen, and water vapor.

The pyrex apparatus for Miller's experiment (Figure 3-1) consisted of a small boiling flask containing water, a spark discharge chamber with tungsten electrodes, a condenser, and a water trap to collect the products. Although the early Earth is not considered to have had a boiling ocean, the boiling action of Miller's apparatus provided a convenient means of circulating gases past the spark discharge.

In most other ways, Miller's apparatus simulated the events on the primitive Earth. The spark simulated the action of lightning, which presumably would have been accompanied by the action of rain washing into the ocean nonvolatile compounds formed in the atmosphere. And the water trap (as well as the boiling flask) simulated the oceans, pools, and lakes which collected the compounds synthesized.

In 1974 Miller gave an account of "the first laboratory synthesis of organic compounds under primitive Earth conditions."[5] In his reminiscence we learn something of the prebiotic simulation technique he used. Describing his second attempt with the same apparatus, he recounts:

> Again after about a week's work getting everything ready, I filled up the apparatus with the same mixture of gases and turned the spark on, keeping the heating coil on the 500-ml flask at low heat... After two days I decided to see what had been produced. This time there were no visible hydrocarbons, but the solution was a pale yellow. I concentrated the solution and ran a paper chromatogram. This time I found a small purple spot on spraying with ninhydrin that moved at the same rate as glycine, the simplest amino acid.[6]

As he continues, we pick up some of the drama of those early experiments late in 1952:

> I set the apparatus up again and this time boiled the water more vigorously... In the morning when I looked at the apparatus the solution looked distinctly pink... My immediate thought was porphyrins... and I rushed over to Urey and brought him back to see the color, which he viewed with as much excitement as I did.
>
> At the end of the week, I removed the solution and did a little processing on it and then ran a two-dimensional paper chromatogram... This time seven purple spots showed up on spraying with ninhydrin. Three

of these amino acids were strong enough and in the correct position to be identified as glycine, α-alanine, and β-alanine.[7]

Since those early days of groundbreaking in the history of simulating prebiotic events, electrical discharge experiments have been repeated many times using a variety of atmospheric compositions. These have included mixtures of two or more of the following gases: methane, ethane, ammonia, nitrogen, water vapor, hydrogen, carbon monoxide, carbon dioxide, and hydrogen sulfide. By and large these experiments follow the same general technique used by Miller, although a number of modifications have been employed. As long as oxygen has been excluded from the mixture, amino acids and other organic compounds have resulted.

In 1974, Miller reported the amino acids he had obtained in his original electrical discharge experiments.[8] These are listed in Table 3-2. In addition, asparagine,[9] lysine,[10] and phenylalanine[11] have been reported by others but disputed by Miller.[12]

Table 3-2. Yields of amino acids obtained from sparking a mixture of CH_4, NH_3, H_20, and H_2.

Compound	Yield (μM)
Glycine	630
Glycolic acid	560
Sarcosine	50
Alanine	340
Lactic acid	310
N-Methylalanine	10
α-Amino-n-butyric acid	50
α-Aminoisobutyric acid	1
α-Hydroxybutyric acid	50
β-Alanine	150
Succinic acid	40
Aspartic acid	4
Glutamic acid	6
Iminodiacetic acid	55
Iminoaceticpropionic acid	15
Formic acid	2,330
Acetic acid	150
Propionic acid	130
Urea	20
N-Methyl urea	15

Source: S. Miller and L. Orgel, *The Origins of Life on the Earth* (Englewood Cliffs: Prentice-Hall, 1974), Table 7-1, 85.

In all, ten of the twenty proteinous amino acids have been positively identified among the products of electrical discharge experiments, as well as about thirty non-proteinous amino acids. Both tert-leucine and N-ethylalanine have been reported but not definitely confirmed. When more than trace amounts of ammonia have been used, iminodiacetic acid and iminoaceticpropionic acid have resulted. When hydrogen sulfide is added to the gaseous mixture methionine is formed.

In 1963, it was found that a gaseous mixture of methane, ammonia, water vapor, and hydrogen irradiated by an electron beam yielded the heterocyclic base, adenine.[13] In 1983, however, C. Ponnamperuma reported that all five nucleic acid bases found in DNA and RNA had been formed in a single simulated primitive atmosphere experiment.[14]

In addition, the Miller experiment has shown that formaldehyde and "possibly" some sugars are produced.[15] Experiments by Ponnamperuma have shown that both ribose and deoxyribose can be produced during electron irradiation of methane, ammonia, and water.[16] Table 3-3 (below) shows the relative abundance of the various organic compounds produced in electrical discharge simulation. Note that much more has been done in synthesizing amino acids than other biologically significant molecules, which reflects the relative ease of their production compared to the production of heterocyclic bases, sugars, etc.

Now that many different experiments have been evaluated by scientists, it is widely acknowledged that spark discharge is the most efficient energy source for making HCN and amino acids. However, sparks have been used in laboratory experiments primarily for their convenience. But results to date suggest that spark discharge would not have been an effective energy source for the synthesis of pyrimidines and aldehydes (especially sugars) on the early Earth.

Heat Experiments

The heat energy produced today by volcanic activity is about an order of magnitude less than the energy produced by all electrical discharges (Table 3-1) and about the same amount of energy as that produced by

Table 3-3. Yields of organic compounds obtained from sparking a mixture of CH_4, NH_3, H_2O, and H_2.

Compound	Relative Yield*
Formic acid	1000
Glycine	270
Glycolic acid	240
Alanine	146
Lactic acid	133
β-Alanine	64
Acetic acid	64
Propionic acid	56
Iminodiacetic acid	24
Sarcosine	21
α-Amino-n-butyric acid	21
α-Hydroxybutyric acid	21
Succinic acid	17
Urea	9
Iminoaceticpropionic acid	6
N-Methyl urea	6
N-Methylalanine	4
Glutamic acid	3
Aspartic acid	2
α-Aminoisobutyric acid	0.4

Biologically relevant amino acids are written in italics. *Yields are relative to formic acid and presented in descending order.

Source: Authors' calculations based on data presented in S. Miller and L. Orgel, *The Origins of Life on the Earth* (Englewood Cliffs: Prentice-Hall, 1974), Table 7-1, 85.

lightning. Consequently, a number of workers, the most famous being Sidney Fox, have devised laboratory techniques to simulate "the flow of volcanic gases through fissures or 'pipes' of hot igneous rocks of lava."[17] These experiments are known as thermal synthesis or pyrosynthesis.

The apparatus used in these heat experiments is a modification of the spark apparatus used by Miller. The principal difference is that the spark electrodes have been replaced by a furnace (Figure 3-2). Various "primitive atmosphere" gases are allowed to flow over solid silica gel, alumina, or quartz sand in a furnace kept at 900–1100°C. Customarily, the gases remain in the hot zone for only a fraction of a second, and are then cooled quickly. The products are collected in the trap and then flow into the boiling flask. Table 3-4 (below) shows the results of heating methane, ammonia, and water at 950°C using quartz sand catalyst. Note that twelve proteinous amino acids were reported as dominant products in this experiment by Harada and Fox[18] in 1964. These scientists accounted for the large number of biological amino acids found in terms of a gratuitous role played by heat as an energy source. "According to these [thermal synthesis] results, the contents of unnatural amino acids are depressed and the contents of the natural amino acids enhanced by the use of thermal energy."[19] In addition, four other amino acids found in proteins have subsequently been reported by this heating technique: lysine, tryptophan, histidine, and arginine. Efforts have been made to

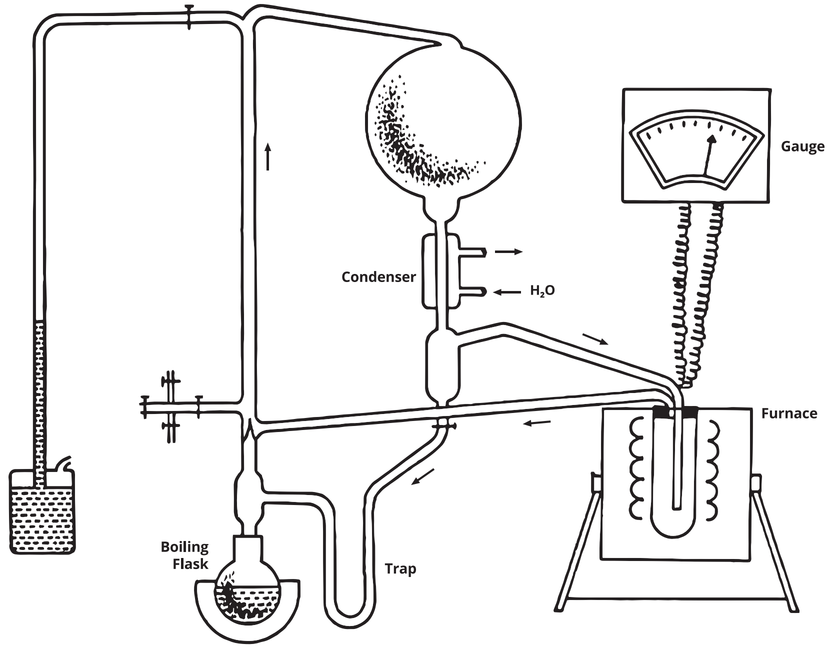


Figure 3-2. Apparatus used for the thermal synthesis of amino acids from simple gases.

Source: Harada and Fox, "The Thermal Synthesis of Amino Acids from a Hypothetically Primitive Terrestrial Atmosphere," in Sydney Fox, editor, *The Origins of Prebiological Systems and of Their Molecular Machines* (New York: Academic Press, 1965), 190.

produce the sulfur-bearing amino acids methionine and cysteine by adding hydrogen sulfide, but so far, these attempts have failed.

The reported results of thermal synthesis of amino acids from a simulated primitive atmosphere have been challenged. Lawless and Boynton[20] repeated the experimental procedure described by Harada and Fox, and identified the products by more sophisticated means. As Table 3-5 shows, only six amino acids were unequivocally identified, of which only glycine, alanine, and aspartic acid were types found in proteins. It is significant that Fox himself now regards low-temperature (i.e., < 120°C) routes to amino acids "as the most plausible."[21]

One important variation of thermal syntheses has been the Fischer-Tropsch type of technique.[22] In a typical synthesis, carbon monoxide, hydrogen, and ammonia flow through a vycor tube filled with metal or clay catalysts. When heated to 500–700°C for about 1.2 minutes, the

Table 3-4. Harada and Fox results of heating CH_4, NH_3, and H_2O at 950°C in the presence of quartz sand catalyst.

Amino Acid*	Percent Yield
Aspartic acid	3.4
Threonine	0.9
Serine	2.0
Glutamic acid	4.8
Proline	2.3
Glycine	60.3
Alanine	18.0
Valine	2.3
Alloisoleucine	0.3
Isoleucine	1.1
Leucine	2.4
Tyrosine	0.8
Phenylalanine	0.8
α-Aminobutyric acid	0.6
β-Alanine	?
Sarcosine	
N-Methylalanine	

Biologically relevant amino acids are written in italics. *Basic amino acids were not fully studied, and therefore were not listed. Yield is based on percent of total amino acid product.

Source: K. Harada and S. W. Fox, "Thermal Synthesis of Natural Amino-Acids from a Postulated Primitive Terrestrial Atmosphere," *Nature* 201 (1964), 335.

Table 3-5. Lawless and Boynton results of heating CH_4, NH_4, and H_2O at various temperatures using quartz sand catalyst.

Compound*	Percent Yield$^+$		
	1060°	980°	930°
Alanine	1	12	4
Glycine	1	59	96
α-Alanine	90	28	
N-Methyl-β-alanine	1.5	1	
Succinic acid	1.5		
β-Amino-n-butyric	1		
Aspartic acid	3		

Biologically relevant amino acids are written in italics. *Compounds identified by gas chromatography and gas chromatography combined with mass spectrometry. $^+$Yields were determined by amino acid analyzer and gas chromatography response.

Source: J. Lawless and C. Boynton, "Thermal Synthesis of Amino Acids from a Simulated Primitive Atmosphere," *Nature* 243 (1973), 406.

residence time in the tube, they react to yield a variety of amino acids. The usual Fischer-Tropsch synthesis is used industrially to make hydrocarbons from carbon monoxide and hydrogen.

Another version, a "no-flow" or static synthesis, consist of simply heating the gases in a vycor flask at 200–1000°C for 15–16 minutes, followed by sustained heating at lower temperatures (50–100°C for 15–183 hours).

Proteinous amino acids definitely confirmed[23] in Fischer-Tropsch type syntheses include glycine, alanine, aspartic acid, glutamic acid, tyrosine, lysine, histidine, and arginine.

Ultraviolet Experiments

As pointed out earlier, solar ultraviolet radiation is considered to have been a major energy source on the primitive Earth (see Table 3-1). Accordingly, some investigators have sought to use ultraviolet radiation in their simulation experiments. However, the major candidates for constituents of the primitive atmosphere (CH_4, CO, N_2, CO_2, H_2S, NH_3,

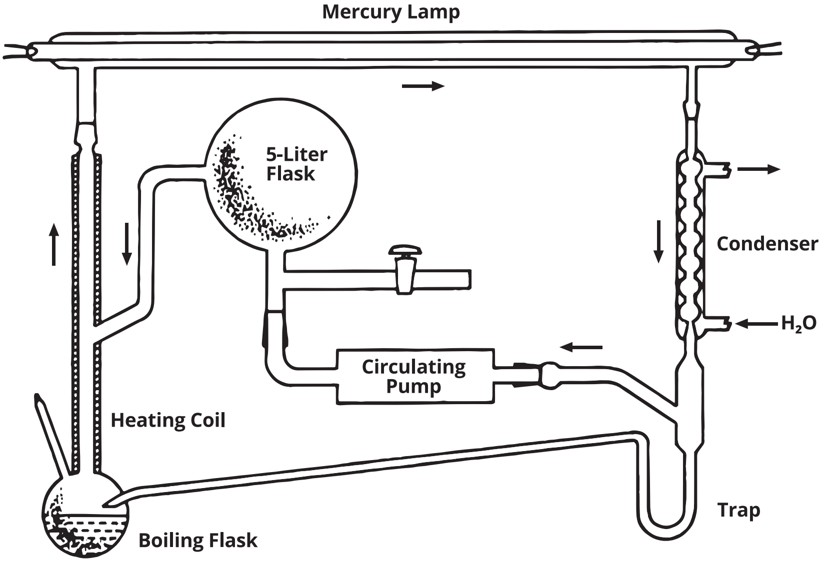


Figure 3-3. Apparatus used for the mercury-sensitized ultraviolet synthesis of amino acids.

Source: Adapted from Kenyon and Steinman, *Biochemical Predestination* (New York: McGraw Hill, 1969), 135.

H_2O, and H_2) absorb sunlight almost exclusively at wavelengths below 2000 Å. Yet only a minor fraction (0.015%)[24] of incident solar energy occurs at wavelengths this short.[25] Since these constituents absorb only trivial amounts of energy in the necessary wavelengths, little photochemical reaction occurs. However, this is conceptually not a serious limitation. There would have been many millions of years for the small amount of energy available from sunlight to have had its cumulative effect.

In laboratory simulation experiments the simple "primitive" gases are subjected to short wavelength ultraviolet (< 2000 Å) which is derived from the resonance lines of high-intensity emission sources. The simulation apparatus employed is similar to the electrical discharge apparatus used by Miller. The principal difference is that the ultraviolet source replaces the electrodes (Figure 3-3). Results of three such experiments are given in Table 3-6,[26] showing noteworthy products.

Table 3-6. Summary of various simulated atmosphere experiments using ultraviolet light as the energy source to produce amino acids.

Workers	Reactants	Wavelength	Products
Groth and v. Weyssenhoff	Methane, ethane, ammonia, and water vapor	1296 Å and 1470 Å; 1165 Å and 1235 Å	Glycine, alanine, α-amino-butyric acid
Terenin	Methane, ammonia, and water	Continuous UV spectrum	Alanine
Dodonova and Sidorova	Methane, carbon monoxide, ammonia, and water	1450 Å-1800 Å	Glycine, alanine, valine, and norleucine; methylamine, ethylamine, hydrazine, urea, and formaldehyde

In addition to these amino acids, Ponnamperuma has shown that ribose and deoxyribose are produced during ultraviolet irradiation of formaldehyde.[27]

Ultraviolet light would have been the most abundant energy source for the primitive Earth (Table 3-1). In simulation experiments, however, it has generally given low yields of amino acids. This has been interpreted as related to the fact that ultraviolet is not a good source for HCN, a principal intermediate to amino acids through the Strecker synthesis (see below). Ultraviolet light, however, may be the best source for aldehydes, which are also essential intermediates to amino acids by the Strecker mechanism. These results support the widely held belief that a variety of energy sources was responsible for the buildup of concentrations of essential biological precursor chemicals in the primitive oceans.

Photosensitization

Photosensitization provides a means of overcoming the scarcity of usable ultraviolet light in the early atmosphere. Through this ingenious technique it is possible to get the "primitive" atmospheric gases to undergo photochemical reaction by essentially "repackaging" the energy of

Table 3-7. Summary of simulated atmosphere experiments using ultraviolet light as the energy source and various photosensitizing agents to produce amino acids.

Workers	Reactants	Wavelength	Photosensitizer	Products
Groth and v. Weyssenhoff	Methane, ethane, ammonia, and water vapor	2537 Å	Mercury vapor	Glycine, alanine
Khare and Sagan	Methane, ethane, ammonia, and water	2537 Å	Hydrogen sulfide	Alanine, glycine, serine, glutamic acid, aspartic acid, cystine
Khare and Sagan			Formaldehyde	
Hong, Hong, and Becker	Ammonia, ethanol	2200-2800 Å Max 2520 Å	Hydrogen sulfide	Serine (or threonine), glycine, alanine, aspartic acid, valine, glutamic acid, leucine, isoleucine proline

the longer ultraviolet wavelengths of 2000–3000 Å where sunlight is plentiful. Using a photosensitizing agent, such as mercury vapor, formaldehyde, or hydrogen sulfide gas, experimenters have induced the absorption and transfer of energy to the primitive atmosphere gases, thus enabling reactions to take place in the longer spectral region. Representative examples of this experimental technique are summarized in Table 3-7.[28]

Shock Wave Experiments

According to chemical evolution scenarios, shock waves from thunder and meteorite impact in the atmosphere would have made a small but definite contribution as an energy source on the prebiotic Earth. Investigations have shown that shock waves are very efficient in the synthesis of amino acids from the simple gases of methane, ethane, ammonia, and water vapor. This means that although the overall energy contribution from shock waves may have been small (Table 3-1), they could have been a major source of these biomonomers on the early Earth.[29]

Shock wave synthesis works by subjecting the gases to a high temperature (2000–6000°K) for a small fraction of a second followed by rapid cooling.[30] Thus far this technique has resulted in the following amino acids: glycine, alanine, valine, and leucine.

High-Energy Chemicals

Most of the amino acids found in proteins have been identified as products in experiments using aqueous solutions to simulate the primordial ocean. Although many of these experiments still use heat or ultraviolet light, most do not require an additional outside energy source. Instead, reactions are found to go spontaneously by the use of high-energy chemicals such as hydrocyanic acid, cyanate, cyanoacetylene, formaldehyde, hydroxylamine, or hydrazine. The warrant for their use in ocean simulations is their presence among the products of atmosphere experiments.

Many of these high-energy compounds would have had double- or triple-bonded carbon atoms. Common examples would be the ethylenes ($> C{=}C <$), acetylenes ($-C{\equiv}C-$), aldehydes ($RCH{=}O$), ketones ($R_1R_2C{=}O$), carboxylic acids ($RCOOH$), and nitriles ($RC{\equiv}N$). These compounds would enter into reactions directly by using the energy released by their double and triple bonds. In general they simply add other chemical constituents to their structures by addition across the double or triple bond. For example, ethylene and acetylene will both add water to their structures:

$$\underset{\text{Ethylene}}{CH_2{=}CH_2} + H_2O \rightleftharpoons \underset{\text{Ethyl alcohol}}{CH_3CH_2OH}$$

$$\underset{\text{Acetylene}}{HC{\equiv}CH} + H_2O \rightleftharpoons \underset{\text{Acetaldehyde}}{CH_3CH{=}O}$$

Addition reactions have usually been held to lead to a build-up of a wide assortment of organic compounds in the early ocean. In turn there would have been interaction among these compounds to produce still more complex chemical constituents. For example, two molecules of acetaldehyde could react in aqueous solution to produce acetic acid and ethyl alcohol, as follows:

$$\underset{\text{Acetaldehyde}}{2\,CH_3CH{=}O} + H_2O \rightleftharpoons \underset{\text{Acetic acid}}{CH_3COOH} + \underset{\text{Ethyl alcohol}}{CH_3CH_2OH}$$

These products could then react to yield ethyl acetate:

$$\underset{\text{Acetic acid}}{CH_3COOH} + \underset{\text{Ethyl alcohol}}{CH_3CH_2OH} \rightleftharpoons \underset{\text{Ethyl alcohol}}{CH_3COOH_2CH_3} + H_2O$$

Addition reactions can be envisioned as playing a major role in the production of amino acids. First, two molecules of formaldehyde could react to give glycolaldehyde:

$$\underset{\text{Formaldehyde}}{2\,HCHO} \rightleftharpoons \underset{\text{Glycolaldehyde}}{CH_2OHCH{=}O}$$

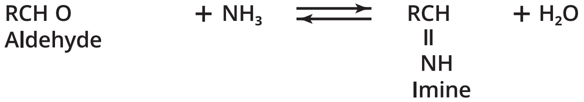
Then, two molecules of glycolaldehyde could react with water to yield glycol and glycolic acid:

$$\underset{\text{Glycolaldehyde}}{2\,CH_2OHCHO} + H_2O \rightleftharpoons \underset{\text{Glycol}}{CH_2OHCH_2OH} + \underset{\text{Glycolic acid}}{CH_2OHCOOH}$$

Finally, glycolic acid could react with ammonia to give glycine:

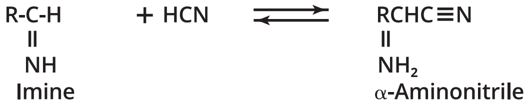
$$\underset{\text{Glycolic acid}}{CH_2OHCOOH} + NH_3 \rightleftharpoons \underset{\text{Glycine}}{CH_2NH_2COOH} + H_2O$$

It has also been suggested that a major synthetic pathway for the formation of amino acids in the primitive ocean would have been the well-known Strecker synthesis. In this synthesis ammonia would be added to an aldehyde carbonyl group to give an imine:



$$\underset{\text{Aldehyde}}{RCH\ O} + NH_3 \rightleftharpoons \underset{\text{Imine}}{\overset{RCH}{\underset{NH}{\|}}} + H_2O$$

Then hydrogen cyanide (HCN) adds to the imine to form an α-aminonitrile.



$$\begin{array}{c}\text{R-C-H}\\ \Vert\\ \text{NH}\\ \text{Imine}\end{array} + \text{HCN} \rightleftharpoons \begin{array}{c}\text{RCHC}\equiv\text{N}\\ \Vert\\ \text{NH}_2\\ \alpha\text{-Aminonitrile}\end{array}$$

Finally the synthesis is completed by the irreversible addition of water to the nitrile to form an α-amino acid:

$$\begin{array}{c}\text{RCHC}\equiv\text{N}\\ \vert\\ \text{NH}_2\end{array} + H_2O \longrightarrow \begin{array}{c}\text{RCHCOOH}\\ \vert\\ \text{NH}_2\\ \alpha\text{-Amino acid}\end{array}$$

This is a general synthesis where the amino acid produced depends on the initial aldehyde. For example, by starting with formaldehyde, acetaldehyde, or glycolaldehyde, the amino acids glycine, alanine, or serine, respectively, are produced. Miller and Orgel have shown that many of the 20 amino acids found in proteins could have been formed by the Strecker pathway.[31]

Examples of successful laboratory synthesis are given in Table 3-8.[32] Notice that the experiment done by Matthews and Moser produced no fewer than twelve proteinous amino acids.

All of the five bases have been synthesized in solutions which presumably depict oceans and other bodies of water that might have been found on the primitive Earth. Adenine was found after aqueous cyanide solutions were heated at 90°C for several days.[33] Both adenine and guanine have been synthesized by the action of ultraviolet light on dilute solutions of hydrocyanic acid.[34]

Of the pyrimidines, cytosine is produced by heating aqueous cyanoacetylene with cyanate for one day at 100°C, or by allowing it to stand at room temperature for seven days.[35] Uracil is formed by heating a solution of malic acid, urea, and polyphosphoric acid to 130°C for one hour.[36] It has also been formed by heating acrylonitrile with urea to 135°C in aqueous solution.[37] This synthesis of uracil has also been successful when using β-aminopropionitrile or β-amino propionamide instead of acrylonitrile. In addition, it has been found that thymine can

Table 3-8. Summary of simulated ocean experiments using high-energy compounds to yield amino acids.

Workers	High-Energy Compound	Medium	Products
Oro and Kamat	Ammonium cyanide	Alkaline aqueous solution	Alanine, glycine, aspartic acid
Lowe, Rees, and Markham	Ammonium cyanide	Alkaline aqueous solution	Glutamic acid, aspartic acid, theronine, serine, glycine, alanine, isoleucine, leucine
Friedmann, Haverland, and Miller	Hydrogen cyanide and acetone	Aqueous ammonia	Valine
Abelson	Hydrogen cyanide	Aqueous	Glycine, alanine, serine, aspartic acid, glutamic acid.
Matthews and Moser	Hydrogen cyanide	Anhydrous liquid ammonia	Lysine, histidine, arginine, aspartic acid, threonine, serine, glutamic acid, glycine, alanine, valine, isoleucine, leucine
Pavolovskaya and Pasynskii	Formaldehyde liquid	Aqueous solution ammonium salts	Serine, glycine, alanine, glutamic acid, valine, phenylalanine, isoleucine, (the latter only from ammonium nitrate)
Van Trump and Miller	Hyrocyanic acid, acrolein	Aqueous ammonia methylated hydrogen sulfide ammonium chloride	Methionine, glutamic acid
Sanchez, Ferris, and Orgel	Cyanoacetylene, hydrocyanic acid	Aqueous ammonia	Aspartic acid, asparagine
Friedmann, Haverland, and Miller	Hydrocyanic acid, phenylacetylene	Aqueous ammonia, hydrogen sulfide	Phenylalanine
Fox, Windsor Wolman, Miller, and Oro	Formaldehyde	Aqueous ammonia	Aspartic acid, serine, glutamic acid, proline, glycine, and alanine

be formed by heating uracil with formaldehyde and hydrazine in aqueous ammonia solution for three days.[38]

It would appear from the foregoing experimental evidence that it is fairly easy to form adenine and possibly the other heterocyclic bases. Since adenine is easiest to form and the most stable, we would expect to find it playing important roles in living systems. That is indeed what we find. Some of the most biologically important molecules in living system are those which contain adenine: DNA, RNA, ATP, ADP, NAD, NADP, FAD, and coenzyme A.

High-energy compounds have also been instrumental in the synthesis of sugars. As early as 1861, it was known that sugars could be produced from formaldehyde in dilute aqueous alkaline solutions.[39] Since then the method has yielded many different sugars. Examples include: fructose, cellobiose, xylulose, galactose, mannose, arabinose, ribose, xylose, lyxose, and ribulose. Other organic chemicals such as glycolaldehyde, glyceraldehyde, dihydroxyacetone, and a number of tetroses also have been formed by this method.[40] Deoxyribose was produced when solutions of formaldehyde and acetaldehyde were allowed to react to 50°C or less. The base for these solutions was calcium oxide or ammonia.[41] Ribose also has been produced by refluxing formaldehyde solution over the clay mineral kaolinite (a hydrated aluminum silicate).[42]

Summary

As this review demonstrates, there have been many biomonomers produced in these prebiotic experiments. These impressive achievements have included synthesis of nineteen of the twenty proteinous amino acids, all five heterocyclic bases found in nucleic acids, and several essential sugars, including glucose, ribose, and deoxyribose. Other likely constituents of the prebiotic soup have been produced as well. Taken together, this is a substantial body of experimental work, and provides the major source of support for chemical evolution theory. These laboratory results have been the basis for much optimism concerning chemical evolution, and many scientists have been virtually assured that the primitive ocean was full of organic compounds. For example, John Koesian said:

> Backed by all the recent experimental evidence, it is now safe to take for granted the existence of a great variety of organic compounds in prebiological times from which to start reconstructing the origin of the first living things.[43]

In a similar vein, Richard Lemmon remarked:

> This research has made it clear that these compounds would have accumulated on the primitive (prebiotic) Earth—that their formation is the inevitable result of the action of available high energies on the Earth's early atmosphere.[44]

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4. THE MYTH OF THE PREBIOTIC SOUP

According to Chapter 3 there is a great deal of experimental support for the early stages of chemical evolution. Yet in contrast to the conclusion usually drawn from these experiments, a credible alternative scenario can be presented which argues strongly against chemical evolution.

Although this chapter is essentially critical, our intent is positive. It is not out of malice that a sample of alleged gold is subjected to the refiner's fire. It is done to test the claim of purity, and to burn off dross that precious metal might shine even brighter. Similarly, any good theory should withstand the fires of criticism and be the better for it. In this spirit, we will look at several kinds of difficulty that have persisted for the chemical evolution theory of life's origin. Our purpose is not only to reveal cracks in present origin theories but also to point in the direction of a better theory, i.e., a theory which is in better accord with the data. In general the critique argues that, in the atmosphere and in the ocean, dilution processes would dominate, making concentrations of essential ingredients too small for chemical evolution rates to be significant. Dilution results from the destruction of organic compounds or diminishing the important chemicals for productive interaction. In this chapter we first survey various dilution processes. Then, as an example, we estimate how dilute the oceanic soup could have been in essential amino acids. Finally, we consider various mechanisms suggested as means to concentrate the chemical soup.

A Survey of Dilution Processes

According to the original Oparin-Haldane hypothesis from which arose the modern chemical soup theory of origins, ultraviolet light from the sun bathed the prebiotic Earth. Together with other sources of energy (e.g., lightning, thunder shock waves, tidal forces, volcanic heat) it would have been sufficient to drive reactions forward.

Simple gaseous molecules of the primitive atmosphere would react to form intermediates and biomonomers. This would be accomplished through the direct absorption of energy. Energy is seen as the means by which molecules can be organized into more complex arrangements, according to the theory.

But energy alone may not be sufficient to increase the complexity or organization of a system. A bull in a china shop does release a great deal of energy, but the effects are mostly destructive. In fact it can be plausibly argued that the energy effects on the early Earth would have been very much like the proverbial bull in a china shop. This predominately destructive feature of unbridled solar and other forms of energy is the first of the several areas of difficulty for the chemical soup theory of life's origin.

Destruction of Organic Compounds by Energy

Solar Ultraviolet Destruction of Atmosphere Constituents

Concentrations of some of the most important early atmosphere components would have been diminished by short-wavelength (i.e., < 2000 Å) ultraviolet photodissociation. Atmospheric methane would have polymerized and fallen into the ocean as more complicated hydrocarbons,[1] perhaps forming an oil slick 1–10 m deep over the surface of the Earth.[2] If this occurred, very small concentrations of methane would predictably have remained in the atmosphere. About 99% of the atmospheric formaldehyde would have been quickly degraded to carbon monoxide and hydrogen by photolysis.[3] Carbon monoxide concentrations in the atmosphere would have been small, however. Carbon monoxide would have been quickly and irreversibly converted to formate in an alkaline ocean.[4] Ammonia photolysis to nitrogen and hydrogen would have occurred very quickly, reducing its atmospheric concentration to so small a value that it could have played no important role in chemical evolution.[5] If all the nitrogen in the contemporary atmosphere had existed in the form of ammonia in the early atmosphere it would have been degraded by ultraviolet light in somewhere between 100,000 and 1,000,000 years.[6] If the ammonia surface mixing ratio were on the order of 10^{-5} as Sagan has estimated,[7] then the atmospheric lifetime of ammonia would have been a mere 10 years.[8] It would also have been difficult to maintain substantial levels of hydrogen sulfide in the atmosphere. Hydrogen sulfide would have been photolyzed to free sulfur and hydrogen in no more than 10,000 years.[9] The concentration of hydrogen sulfide in the ocean would have been further attenuated by the formation of metal sulfides with their notoriously low solubilities.[10] The same photodissociation process would have applied to water to yield hydrogen and oxygen. Some recent studies suggest that, through ultraviolet photolysis of water vapor, atmospheric oxygen did reach an appreciable fraction of today's concentration in early Earth times.[11] Naval Research Laboratory results of ultraviolet experiments aboard Apollo 16 suggested that "solar effects on the Earth's water may provide our primary supply of oxygen, and not photosynthesis as is generally believed."[12] The principal author of this research, G. R. Carruthers, has, however, declared that this news release was "inaccurate" and that photodissociative processes do not rival plant photosynthesis in the production of oxygen.[13] Nevertheless Carruthers is of the opinion that photodissociation of water may have produced perhaps as much as 1% oxygen gas, versus 21% now, in the primitive atmosphere of the first billion years.

Had the primitive oxygen level been even a thousandth part of the present level, it might have been sufficient for an effective ozone screen to form 3–4 billion years ago.[14] If it did, then effectively all ultraviolet wavelengths less than 3000 Å would have been screened from the Earth. Such an ozone screen would have deprived the early atmospheric gases of a major energy source. These short ultraviolet wavelengths are lethal to living organisms but are widely considered to have been essential for the origin of life. The issue of oxygen on the early Earth is controversial and very important. If the early Earth had strongly oxidizing conditions with molecular oxygen present, then spontaneous chemical evolution was impossible.[15]

Methane would absorb 1450 Å solar radiation totally by about 30 km altitude, even if its concentration in the primitive atmosphere were no greater than it is today.[16] Yet theories of life's origin usually allow a substantial methane concentration in the primitive atmosphere. Consequently, syntheses involving the photolysis of methane must have occurred at high altitudes. Amino acids could have been photoproduced at high altitudes from primitive atmospheric gases. Being produced so high, they would require perhaps three years (based on fall-out data) to reach the ocean.[17] During this lengthy transport amino acids and other organic compounds would be exposed to the destructive long-wavelength (i.e., > 2000 Å) ultraviolet radiation.[18] This long-wavelength UV is more intense than the short-wavelength (i.e., < 2000 Å) ultraviolet used in synthesis. It has been estimated that perhaps no more than 3% of the amino acids produced in the upper atmosphere could have survived passage to the ocean.[19] Ultraviolet light would also destroy many organic compounds in the ocean, since it would penetrate some tens of meters beneath the ocean surface.[20] Ocean currents periodically would bring to the surface even the deep water, thus exposing its organic content, too, to destructive ultraviolet light.

Pringle first raised this objection against the effectiveness of primordial synthesis of organic compounds by ultraviolet light in 1954.[21] It has been remarked on many times and continues to be a major objection.

Thermal Decay in Oceans

Organic compounds would have been subject to thermal degradation in the ocean. Based on the thermal half-lives of various organic soup constituents, Miller and Orgel have shown that chemical evolution could not occur if the ocean were warmer than about 25°C, since important intermediates would be destroyed by heat.[22] It is widely held, however, that the average surface temperature of the early Earth would have been some 20°C lower than today. This is due to the astronomical theory which says that only about 60% of the total solar energy striking Earth today would have been available 4 billion years ago. Miller and Orgel have pointed out that although 0°C would give a better chance for the accumulation of sufficient concentrations of organic compounds in the ocean, -21°C would be ideal for chemical evolution to occur. At -21°C, however, it is not unlikely that the ocean would be frozen. It is true that such low temperatures would give significantly longer half-lives to organic compounds, but a solid reaction medium is much less favorable for synthesis than a liquid one, which could only have prevailed in equatorial regions.

Temperatures would have been some 20°C lower than today unless the "Greenhouse Effect" of the primitive atmosphere were much more efficient than the present one.[23] According to the Greenhouse Effect water vapor in the atmosphere transmits most of the solar energy to the Earth's surface, which then re-emits energy at a longer wavelength in the infrared region of the spectrum. Instead of radiating off the planet, however, the re-emitted energy is absorbed by the water vapor, thus causing an elevated temperature. A lower temperature at the Earth's surface would mean less water vapor in the atmosphere, hence a reduced Greenhouse Effect. Unless greater quantities of some other infrared absorbing material (such as methane and especially ammonia) were present in the early atmosphere, surely the average temperature of the Earth would have been even more than 20°C lower than now, perhaps allowing a completely frozen ocean.[24] This prospect would seem probable because of the objection raised earlier against a substantial methane-ammonia primitive atmosphere.

The idea of a frozen ocean, which stems from astronomy, is not compatible with the view from geology that the Earth was too hot 3.98 billion years ago and earlier to support life. Neither of these views can be held without some mechanism to account for a geologically rapid (less than 200 million years) decrease in temperature. This figure of less than 200 million years is based on the date of 3.81×10^9 years for the first fossil evidence of life, as cited by Brooks and Shaw.[25]

Lightning

It has usually been assumed that electrical activity on the primitive Earth would have been comparable to that of today. If the early Earth were some 20°C cooler than today because of less solar luminosity, however, it would significantly reduce thunderstorms on the Earth, perhaps by a factor of 100 or more.[26] Atmospheric electrical storms arise under conditions which require minimally that water be evaporated and transported upward, an energy-consuming process. For thunderstorms to occur the air must be warm and humid below, and cold and dry above. It follows that at 20°C or more below present surface temperatures thunderstorm activity will be less, which is illustrated by the fact that not many thunderstorms occur in the Arctic, where less thermal energy is available to evaporate the water. With fewer electrical storms, lightning would be a far less abundant energy source than is generally believed, and it is generally believed anyway to have been a minor energy source. Sparks have been used as an energy source in laboratory experiments primarily as a matter of convenience.

Shock Waves

If there had been substantially fewer electrical storms due to a lower temperature on the early Earth, it follows that thunder shock waves were less frequent as well. Shock waves would also result, however, from the impact of meteors passing through the atmosphere. Nevertheless, as Table 3-1 shows, the meteorite contribution to the energy supply was less than a tenth of the energy supplied by electrical discharges. Total energy available from shock waves in any event was more than a thousand times less abundant than ultraviolet light. However, the optimism over shock waves as a candidate for a major energy source arises not from its abundance but from its efficiency. Shock waves are considered more than a million times more efficient than ultraviolet in producing amino acids.[27] Thus the "unexpected conclusion" is reached that shock waves may very well have been the principal energy source for prebiotic synthesis on the early Earth by a factor of a thousand.[28] Such optimism regarding possible shock-wave synthesis should be tempered by what we shall call the "Concerto Effect." This term means that all the energy sources (and chemicals) act together or in concert in the natural situation—both in synthesis and in destruction of organic compounds. One energy source destroys what another source produces. Since these sources are quite generally more effective in destruction than in synthesis, this amounts to a preponderance of destruction. Amino acids produced in the atmosphere by electrical discharges or shock waves, for example, would be vulnerable to long-wavelength (> 2000 Å) ultraviolet photodissociation, which we mentioned earlier. This is a major objection to the accumulation of amino acids in the primitive ocean. The problem posed by the Concerto Effect will remain even if the dispute concerning the temperature history of the Earth is resolved. Synthesized organic molecules are quite defenseless and vulnerable to destruction by all the energy sources.

Hydrolysis of HCN and Nitriles (RCN)

According to Ponnamperuma, hydrogen cyanide may be "the most important intermediate leading to the origin of life."[29] It is an ingredient for the production of amino acids in the Strecker synthesis (see Chapter 3). It also is considered a starting material in the synthesis of adenine and a host of other biomolecules, as shown in Figure 4-1.

The value of HCN in the chemical evolution scenario is enhanced by the fact that it escapes rapid destruction in the atmosphere by ultraviolet irradiation.[30] Hydrogen cyanide would have been generated in the atmosphere primarily by electrical discharges and collected in the ocean. It is the ubiquitous water molecule, however, that is the main obstacle to the reaction involving HCN and its nitrile derivatives.[31] For example, HCN adds water to its triple bond to form formamide, which, upon further hydrolysis, produces formic acid.

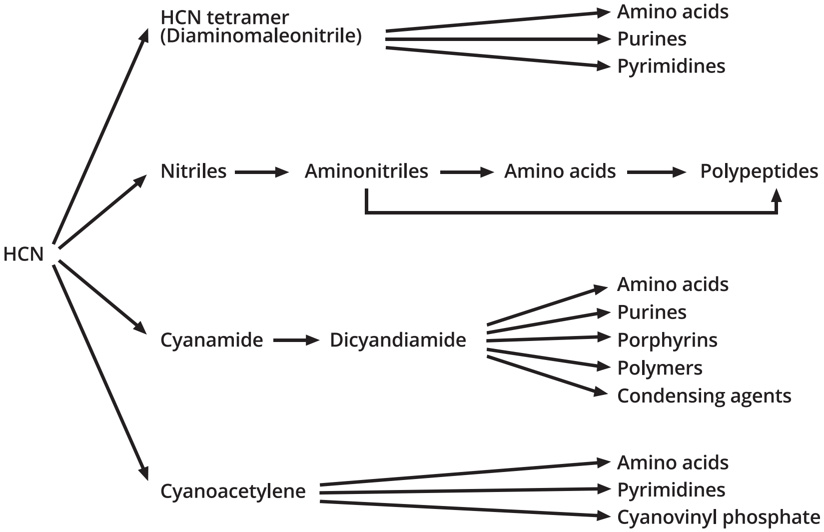
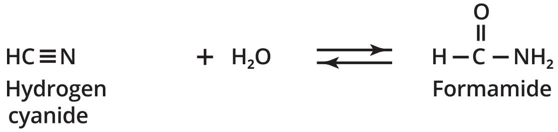
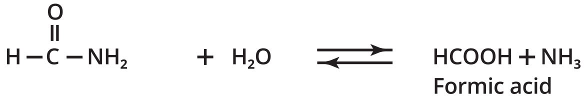


Figure 4-1. Chemical evolution of biomolecules from HCN.



$$HC{\equiv}N + H_2O \rightleftharpoons H{-}\overset{\overset{O}{\|}}{C}{-}NH_2$$

4-1



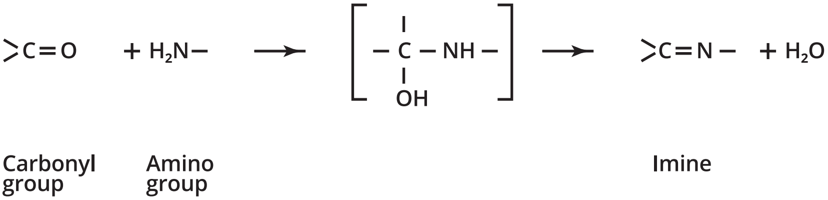
$$H{-}\overset{\overset{O}{\|}}{C}{-}NH_2 + H_2O \rightleftharpoons HCOOH + NH_3$$

4-2

Formic acid is the major product in electrical discharge experiments, and this reaction probably accounts for that fact. As long as HCN concentrations are 0.01M or less, hydrolysis predominates. As we shall discuss later, HCN polymerization will predominate in more concentrated solutions. But there are problems. "Such a high steady state concentration in an extended water mass does not seem likely since the hydrolysis to formic acid requires at most a very few years at reasonable pH's and temperature."[32] The highest average concentration of HCN would have been 10^{-6}M.[33] In other words, it is very unlikely that HCN could have played a significant role in the synthesis of biologically meaningful molecules in an oceanic chemical soup. This is significant since many recent scenarios give HCN a prominent place. Also, a variety of HCN-derived nitriles have been suggested as having an important role as condensing agents in the synthesis of biologically significant polymers.[34] Examples of condensing agents include cyanogen, cyanamide, dicyanamide, and cyanoacetylene. Some of these were mentioned in the review of ocean experiments in Chapter 3. The ease with which these cyano- compounds enter into reaction with water is, however, a major barrier to their usefulness in synthesis. It is, of course, the ability of these cyano- compounds to react with water that makes them attractive candidates as condensing agents. The role of a condensing agent is to remove the water that is spilt out or produced as a byproduct in polymer formation. For example, when two amino acids react to form a dipeptide, a water molecule is released. Although dimer formation is thermodynamically unfavorable, it can be made favorable simply by removing the water; hence the value of the condensing agent. A water solution, however, is a poor place for a condensing agent to perform its role. The condensing agent simply has no ability to discriminate between water molecules and will react with water from any source. Figure 4-2 shows a number of the reactions to be expected in the primitive ocean.

Reaction of Carbonyl Group with Amino Group

The reaction of compounds containing a free amino group (-NH_2) with compounds containing a carbonyl group (>C=O) would have been a very important destructive process. This reaction would vastly diminish concentrations of important organic compounds in the primitive ocean. It can be written generally as follows:



$$>C=O \quad + H_2N- \longrightarrow \left[-\underset{\substack{| \\ OH}}{\overset{|}{C}} - NH - \right] \longrightarrow \quad >C=N- \quad + H_2O$$

4-3

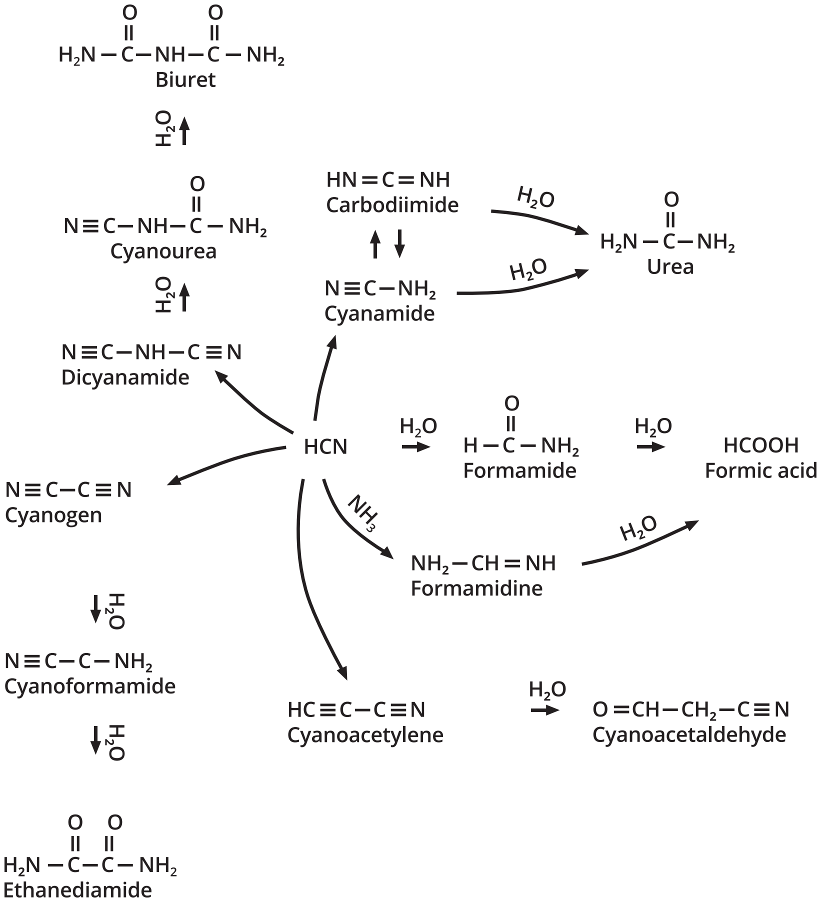


Figure 4-2. Hydrolysis of HCN and derivatives.

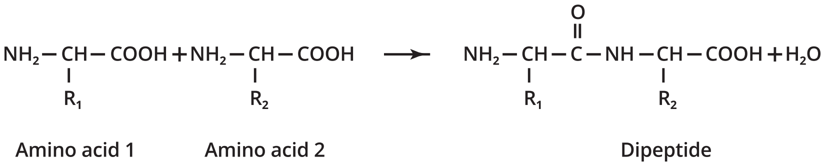
Since the addition product (in brackets) is often unstable and loses water, this reaction is frequently called a *dehydration-condensation* reaction.

Many substances used in prebiotic simulation experiments (see Chapter 3) presumably would have been present in the oceanic soup. According to the general equation above, the amino group ($-NH_2$) of amines (including the free amino group in purines and pyrimidines) and amino acids would combine with the carbonyl group ($>C=O$) of reducing sugars, aldehydes, and a few ketones. Huge amounts of essential organic compounds would thus be removed from the soup by these reactions.[35]

These reactions would have greatly diminished not only amino acid concentration but also the concentration of aldehydes. Buildup of concentrations of aldehydes, especially formaldehyde, would have been important in the primordial synthesis of sugars. Polymerization of formaldehyde in alkaline solution has given a variety of sugars vital to life, including glucose, ribose, and deoxyribose. Studies of thermodynamic and kinetic stability of the important sugars suggest, however, that only insignificant amounts of them could have existed in the primordial ocean.[36] Add to this the chemical reality of reactions of sugars with amino compounds and the problem is seen as acute. Such low sugar concentrations argue strongly against formation of nucleic acids, since they contain sugar.

Indiscriminate Amide Synthesis in Making Polypeptides

In the amide synthesis reaction the amino group (-NH_2) of amino acids would displace the hydroxyl group (-OH) from carboxylic acids (RCOOH), including amino acids. This is the reaction which occurs between amino acids to produce polypeptides and proteins. For example, two amino acids may react to form a dipeptide:



$$\mathrm{NH_2-\underset{\underset{R_1}{|}}{CH}-COOH+NH_2-\underset{\underset{R_2}{|}}{CH}-COOH \longrightarrow NH_2-\underset{\underset{R_1}{|}}{CH}-\overset{\overset{O}{\|}}{C}-NH-\underset{\underset{R_2}{|}}{CH}-COOH+H_2O}$$

4-4

Because two molecules are combined with the release of water this is also called a *dehydration-condensation* reaction. According to most chemical evolution scenarios this reaction probably accounted for the primordial synthesis of polypeptides and proteins. There would, however, have been many different kinds of amino acid in the soup available for

Table 4-1. Yields of amino acids obtained from sparking a mixture of CH_4, N_2, H_2O, and traces of NH_3.

Compound	Relative Yield	Empirical Formula
Alanine	1000	$C_3H_7NO_2$ (1/3)
Glycine	557	$C_2H_5NO_2$ (1/1)
α-Amino-n-butyric acid	342	$C_4H_9NO_2$ (1/8)
α-Hydroxy-γ-aminobutyric acid	94	$C_4H_9NO_3$ (1/3)
Norvaline	77	$C_5H_{11}NO_2$ (1/7)
Sarcosine	70	$C_3H_7NO_2$ (2/3)
Aspartic acid	43	$C_4H_7NO_4$ (1/1)
α, γ-Diaminobutyric acid	42	$C_4H_{10}N_2O_2$ (1/1)
N-Ethylglycine	38	$C_4H_9NO_2$ (2/8)
α-Aminoisobutyric acid	38	$C_4H_9NO_2$ (3/8)
Valine	25	$C_5H_{11}NO_2$ (2/7)
β-Alanine	24	$C_3H_7NO_2$ (3/3)
N-Methylalanine	19	$C_4H_9NO_2$ (4/8)
Leucine	14	$C_6H_{13}NO_2$ (1/5)
Glutatamic acid	10	$C_5H_9NO_4$ (1/1)
α, β-Diaminopropionic acid	8	$C_3H_8N_2O_2$ (1/1)
Norleucine	8	$C_6H_{13}NO_2$ (2/5)
Isoserine	7	$C_3H_7NO_3$ (1/2)
Alloisoleucine	6	$C_6H_{13}NO_2$ (3/5)
Serine	6	$C_3H_7NO_3$ (2/2)
Isovaline	6	$C_5H_{11}NO_2$ (3/7)
N-Methyl-β-alanine	6	$C_4H_9NO_2$ (5/8)
Isoleucine	6	$C_6H_{13}NO_2$ (4/5)
γ-Aminobutyric acid	3	$C_4H_9NO_2$ (6/8)
N-Propylglycine	~3	$C_5H_{11}NO_2$ (4/7)
N-Isopropyglycine	~3	$C_5H_{11}NO_2$ (5/7)
N-Ethyl-β-alanine	~3	$C_5H_{11}NO_2$ (6/7)
Proline	2	$C_5H_9NO_2$ (1/1)
Threonine	~1	$C_4H_9NO_3$ (2/3)
Allothreonine	~1	$C_4H_9NO_3$ (3/3)
β-Amino-n-butyric acid	~0.4	$C_4H_9NO_2$ (7/8)
β-Amino-isobutyric acid	~0.4	$C_4H_9NO_2$ (8/8)
N-Ethylalanine	<0.3	$C_5H_{11}NO_2$ (7/7)
Pipecolic acid	~0.06	$C_6H_{11}NO_2$ (1/1)
tert-Leucine	<0.03	$C_6H_{13}NO_2$ (5/5)

Yields are relative to alanine and presented in descending order. Numbers in parentheses indicate the comparative abundance of each compound among its isomers. For example, alanine is the most abundant of three isomers with the empirical formula $C_3H_7NO_2$. Biologically relevant amino acids are written in italics

Source: Authors' calculations based on data presented in S. Miller and L. Orgel, *The Origins of Life on the Earth* (Englewood Cliffs: Prentice-Hall, 1974), Table 7-2, 87.

reaction. Most of these would have been non-proteinous. For example, results from Miller's later spark discharge experiments (Table 4-1) show many more non-proteinous than proteinous amino acids. In most cases more than one isomer (molecules with the same number of atoms but different geometry) is found for a given empirical formula. For example, three amino acid isomers are formed with formula $C_4H_9NO_3$, two of which are non-proteinous. All eight isomers of formula $C_4H_9NO_2$ are non-proteinous (Figure 4-3). It is obvious that something other than

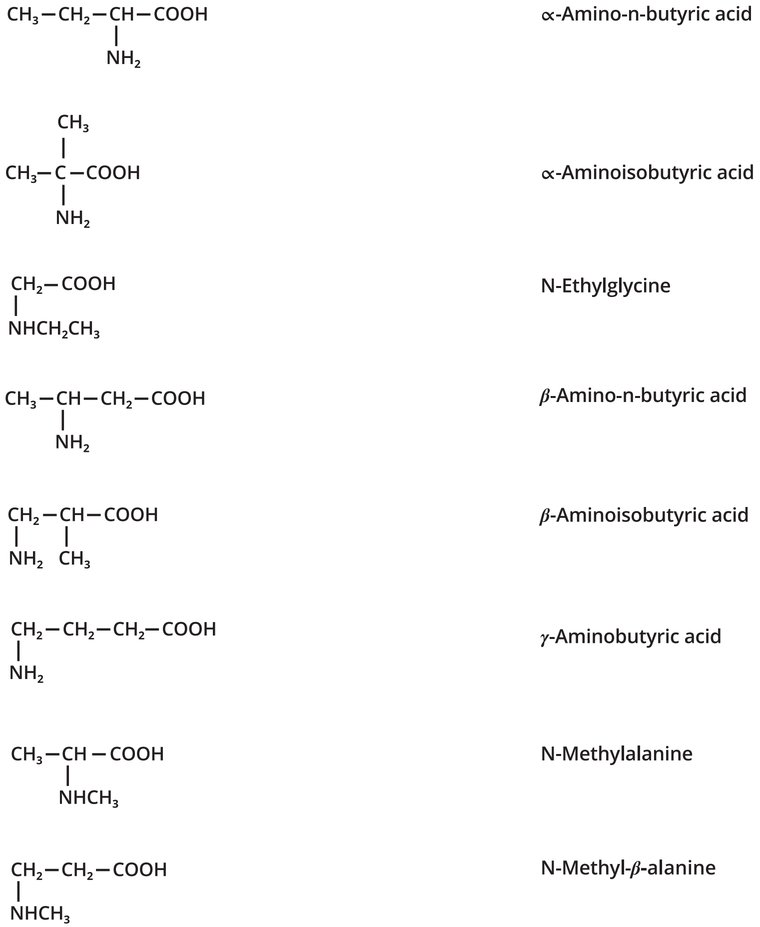


Figure 4-3. Structural isomers of amino acids with empirical formula $C_4H_9NO_2$ found in Miller experiment. None are found in proteins.

availability determines the selection of the set of 20 amino acids used in contemporary proteins. In addition, the amino acids produced in these experiments form a racemic mixture—an equal amount of both D- and L-amino acids. Proteinous and non-proteinous amino acids, both D- and L-, would lead to an indiscriminate production of polypeptides. These polypeptides would have scarce resemblance to protein. Protein not only requires exclusive use of L-amino acids, but also the use of a particular subset of only 20 amino acids. In addition, a biofunctional protein requires a precise sequence of the amino acids. The important fact that amino acids do not combine spontaneously, but require an input of energy, is a special problem discussed in detail in Chapters 8 and 9.

Termination of Polypeptides and Polynucleotides

If the various dilution processes considered so far did not prevent formation of polypeptides and polynucleotides, these macromolecules, once formed, would certainly have been vulnerable to degradation by chemical interaction with a variety of substances in the ocean. We have already seen how amino acids in the oceanic chemical soup would be expected to react with a variety of chemicals. In a similar fashion, growing polypeptides would be terminated by reactions with amines, aldehydes, ketones, reducing sugars,[37] or carboxylic acids. If by some remote chance a true protein did develop in the ocean, its viability would be predictably of short duration. For example, formaldehyde would readily react with free amino groups to form methylene cross-linkages between proteins.[38] This would tie up certain reactive sites, and retard the reaction of protein with other chemical agents. To illustrate, "irreversible combination of formaldehyde with asparagine amide groups" would result in a compound which is "stable to dilute boiling phosphoric acid."[39] This tying-up process is the principle of the well-known tanning reaction, and is used similarly to retard cadaver decay. "In general, reaction with formaldehyde hardens proteins, decreases their water-sensitivity, and increases their resistance to the action of chemical reagents and enzymes."[40] Survival of proteins in the soup would have been difficult indeed.

If we assume that some small number of nucleic acids formed in the primitive ocean, they too would be vulnerable to immediate attack by formaldehyde, particularly at the free amino groups of adenine, guanine, and cytosine. Some of the bonds formed with nucleic acids would be so stable that hydrolysis to liberate free formaldehyde would take place only by boiling with concentrated sulfuric acid.[41] As with proteins, it is difficult to conceive of a viable nucleic acid existing in the primordial soup for more than a very brief period of time.

Hydrolysis of Amino Acids and Polypeptides

But what if polypeptides and other biopolymers had formed in the prebiotic soup? What would their fate have been? In general the half-lives of these polymers in contact with water are on the order of days and months—time spans which are surely geologically insignificant.[42]

Besides breaking up polypeptides, hydrolysis would have destroyed many amino acids.[43] In acid solution hydrolysis would consume most of the tryptophan, and some of the serine and threonine. Further, acid hydrolysis would convert cysteine to cystine, and would deamidate glutamine and asparagine. On the other hand, hydrolysis would destroy serine, threonine, cystine, cysteine, and arginine in the alkaline solution generally regarded to have characterized the early ocean. An alkaline solution would also have caused several deamidations.

Precipitation of Fatty Acids and Phosphate with Calcium and Magnesium Salts

We have already discussed how attenuated concentrations of the nucleic acids in the primitive ocean would have been. Another reason for this is the severe restriction caused by the poor solubility of phosphate, an essential ingredient of nucleic acids. No soluble phosphates are known that could plausibly have existed in the primitive ocean.[44] They would be expected to precipitate out of the soup by forming insoluble salts with calcium and magnesium ions.[45] For example, hydroxyapatite,

$Ca_5(PO_4)_3OH$, has a solubility product of about 10^{-57}. Since there would have been ample amounts of dissolved calcium in the soup, it is difficult to imagine a phosphate concentration greater than $3 \times 10^{-6}M$.[46] As Griffith et al. have noted, "the primitive seas were probably severely deficient in phosphorus."[47] In addition, fatty acids which are essential ingredients for synthesis of cell membranes would have precipitated out of the soup by forming insoluble salts with magnesium and calcium ions.[48]

Adsorption of Hydrocarbons and Organic Nitrogen-Containing Compounds on Sinking Clay Particles

If there is any merit in the view that methane was an important constituent of the primitive atmosphere, hydrocarbons surely must have formed in the atmosphere under the influence of ultraviolet irradiation and fallen into the ocean.[49] Hydrocarbons would then be brought to rest on the ocean bottom by adsorption on sedimenting clays. The earliest Precambrian deposits would be expected to contain unusually large proportions of hydrocarbon material or its carbon remains. They do not, however.[50]

Nitrogen-containing organic compounds would also be expected to have been removed from the ocean by adsorption on clay particles. As Nissenbaum has noted, "We have also no reason to doubt that... adsorption on mineral surfaces, and especially clays, was operative in those remote times."[51] Brooks and Shaw have said in *Origin and Development of Living Systems*:

> If there ever was a primitive soup, then we would expect to find at least somewhere on this planet either massive sediments containing enormous amounts of the various nitrogenous organic compounds, amino acids, purines, pyrimidines, and the like, or alternatively in much-metamorphosed sediments we should find vast amounts of nitrogenous cokes [graphite-like nitrogen-containing materials]. In fact *no such materials have been found anywhere on Earth.*[52] (Emphasis added.)

In summary, the above dilution processes operating in both the atmosphere and in the ocean would have greatly diminished concentrations of essential precursor chemicals. Although these processes have been identified and discussed individually, they would have worked syn-

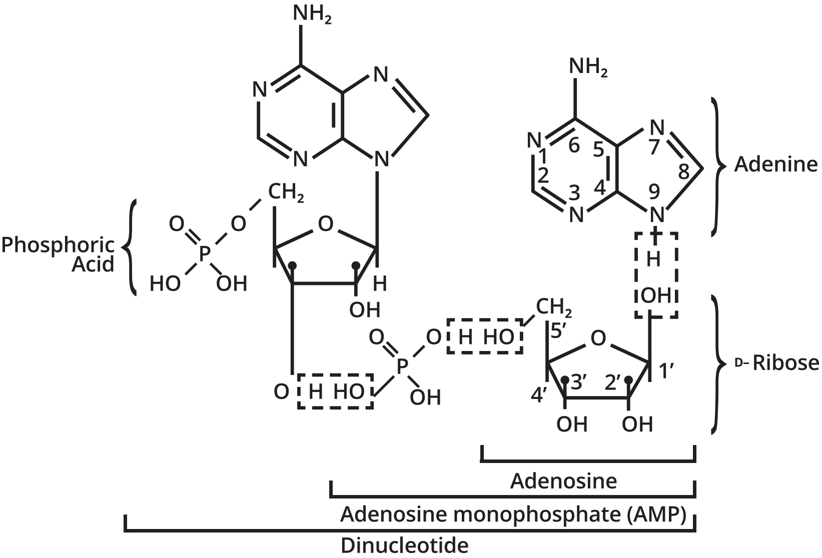


Figure 4-4. The role of the Concerto Effect in the formation of dinucleotide in the prebiotic soup.

ergistically, or in concert. Figure 4-4 summarizes the Concerto Effect by using many of the individual reactions discussed in this chapter. It seems probable that in an oceanic chemical soup the synthesis of RNA and other essential biomolecules would have been short-circuited at nearly every turn by many cross-reactions. The overall result would be very small, steady-state concentrations of important soup ingredients.

Assume initially an aqueous soup consisting of adenine, D-ribose, and phosphoric acid. There are 3 sites on adenine (N7, N9, and NH_2 attached to C6) which can react with hydroxyl at 5 sites on D-ribose (C1'α, C1'β, C2', C3', and C5') which gives rise to 15 structural isomers of adenosine. Only one of these, i.e., 9 (1 -β-D-ribofuranosyl) adenine, is found in living things. Proceeding to the level of AMP (adenosine monophosphate) there are 3 possible sites of attachment of phosphate to D-ribose (C2', C3', and C5'). Consequently the number of structural isomers of AMP (adenosine monophosphate) are the number for adenosine times 3, or 45. At the dinucleotide level, since there are still 2 free -OH groups on D-ribose, the number of possible isomers would be that of AMP times 2, or 90.

Although C2' and C3' of ribose are chiral carbons, and the hydroxyls attached to them may be conceived to be in four different arrangements, note that by definition only one of these is called ribose. The other sugar arrangements are given different names, i.e., lyxose, xylose, and arabinose. In general, then, the pentose sugars have 8 isomers (D- and L-). Consequently, the total number of dinucleotide isomers would be determined as:

3 (sites on adenine) x 5 (sites on D-ribose)
x 8 (pentoses) x 3 (sites left on pentose for phosphate links)
x 2 (sites left on pentose for dinucleotide links) = 720.

Also observe that aminopurines can form with the $-NH_2$ at C2 or C8 as well as at the C6 position for adenine: The number of possible isomers of dinucleotide would now be as previously determined times 3, or 2160.

The large number of possible isomers for dinucleotide suggests how difficult it would be for meaningful concentrations to develop. The role of the Concerto Effect becomes more pronounced when we consider the soup to contain aldehydes and other sugars which could react with the free amino group of adenine (purines). Phosphates would precipitate by reaction with calcium and magnesium salts. Pentoses would react with amines and amino acids. Adsorption of adenine (purine), adenosine, AMP, and dinucleotide on sinking clays would remove them from the soup. Ultraviolet light would destroy adenine, adenosine, AMP, and dinucleotides in the upper surface waters; the developing polymers being even more vulnerable to ultraviolet decay than the monomers. Many interfering cross-reactions would occur among the nucleotides and dinucleotides to terminate their growth. And of course all the substituent organic molecules would be subject to hydrolysis and thermal decay. Thus, extremely small amounts of dinucleotide would be expected.

Concentration of Essential Chemicals in the Prebiotic Soup: The Example of Amino Acids

The picture emerges of a primitive Earth with oceans much more dilute in organic material than is often assumed. How dilute would the early oceans have been? We shall now develop a more quantitative estimate of the concentration of important ingredients in the primitive oceanic soup.

It is a widely held view that the early oceans would have contained huge quantities of organic material. Urey theorized the primitive ocean was rich in organic compounds, containing enough dissolved carbon compounds to make perhaps a 10% solution.[53] This is equivalent to a concentration of 10^{-3}M for each of 1000 chemical compounds in a soup, with an average molecular weight of 100 for each compound.

More recent estimates have revised Urey's estimate downward. Sagan suggests that a 0.3% to 3% solution would result from dissolving in the oceans the organic matter produced by ultraviolet irradiation of a primitive atmosphere for a billion years.[54] Based on data from electric discharge experiments, Wolman et al. have estimated that the oceans of the primitive Earth would have been about 2 x 10^{-3}M in amino acids.[55] Both of these revised estimates are extremely optimistic, however. Sagan's estimate acknowledges "no destruction of synthesized material,"[56] and Wolman et al. "assume... that decomposition of amino acids after synthesis was minimal."[57] To the contrary, as much of this chapter has shown, any realistic assessment of the fate of chemicals such as amino acids on the early Earth *cannot ignore* their very considerable destruction either by energy sources or by chemical interaction in the soup.

The effectiveness of these various natural processes to degrade organic products suggests that the steady-state concentration of amino acids in the primitive oceans would have been quite low. Just how low can only be estimated in ways involving much uncertainty. Nevertheless, plausible estimates which take into account the destructive processes have been made. One estimate by Dose considers ultraviolet destructive effects in the ocean, but ignores both ultraviolet destruction of amino acids in the atmosphere and the destructive interaction between amino acids and other chemicals in the ocean.[58] Dose arrives at an *upper limit* estimate of amino acid concentration in the primitive ocean of 10^{-7}M, some 10,000 times more dilute than the optimistic estimates reported above. As it turns out, the present-day average concentration of amino acids in the North Atlantic Ocean is also about 10^{-7}M.[59]

A second estimate which gives a similar result considers the destructive interaction between amino acids and various soup ingredients, especially sugars, but ignores the ultraviolet destruction process entirely.[60] This estimate is based on a process of scavenging amino acids from the soup followed by polymerization. After a complicated polymerization reaction, the polymer is removed by sedimentation. The first step of the polymerization process involves a dehydration-condensation reaction between the amino group ($-NH_2$) of amino acids and the carbonyl group ($>C=O$) of reducing sugars, as previously discussed. In this manner the oceans of today are scavenged of their sugars and amino acids which come indirectly from the decay of more complex organic matter of previously living things. The early ocean, on the other hand, would have been directly supplied with abiotically derived amino acids and sugars. There is no reason to doubt the operation of the scavenging process in the early oceans.

Since this process is geologically instantaneous (1000–3500 years) it is difficult to imagine the primitive soup ever more concentrated than 10^{-7}M with amino acids.[61] Nissenbaum et al. have summed up the importance of the scavenging process by observing:

> This scavenging of dissolved organic matter from the oceans by polymerization and sedimentation would have left the oceans much more depleted in abiotically formed organic material than is usually assumed. It is difficult to see how, under such conditions, the "primordial soup" could have existed at all.[62]

A third estimate of amino acid concentration in the early oceans considers ultraviolet destruction both in the atmosphere and in the oceans, but ignores the destructive reactions of amino acids with other soup ingredients.[63] This estimate is based on a comparison of rates of formation of amino acids versus their decomposition by ultraviolet. It shows that only about 3% of the amino acids produced in the upper atmosphere (where most UV-promoted amino acid synthesis would have occurred) could have safely passed to the ocean. This would yield a maximum steady-state amino acid concentration of 10^{-12}M in the primitive ocean.

A truly realistic estimate must combine these factors and other destructive processes, and consider the effects of all the energy sources as well. It would be a very difficult estimate to make. Even so, the above estimates are sufficient to suggest that the primordial ocean would have been an extremely dilute "soup," much too dilute to reasonably expect the spontaneous formation of proteins.[64] Although the notion persists at the popular level that life began in the ocean, among scholars and researchers in the field, "it is now generally accepted that the concentration of the soup was probably too small for efficient synthesis, particularly of biopolymers."[65]

We conclude that if there ever was a prebiotic oceanic soup of chemicals, it would have been too dilute for chemical evolution rates to have been significant.

Concentrating Little Ponds

The realization that an organic soup would have been too dilute for direct formation of polymers may seem devastating to chemical evolution views. However, as Bernal has written, "The original concept of the primitive soup must be rejected only in so far as it applies to oceans or large volumes of water, and interest must be transferred to reactions *in more limited zones*."[66] (Emphasis added.) By this he meant lakes, pools, lagoons, and the like. These more limited zones might then have been the locus of life's origin rather than the ocean. The significance of these local places is their associated mechanisms for concentrating essential chemicals. By concentrating the monomers, the probability of their molecular interaction would have been increased, thus increasing reaction rates according to the law of mass action. This law states that the rate of a chemical reaction is directly proportional to the concentration of the reacting substances. Hence in concentrated ponds the probability of polymer formation would have been considerably enhanced.

Even phosphate, which was previously mentioned as limited to a concentration of about 10^{-6}M in the ocean, might conceivably be concentrated in a pool deficient in calcium and magnesium salts. A means to increased phosphate concentration seems essential, since the phosphorylating process to activate amino acids for further reaction assumes those conditions. The suggestion is made plausible since natural deposits of $NaBePO_4$, a highly soluble phosphate, and even deposits of monosodium phosphate, NaH_2PO_4, have been found, probably arising from non-biological processes.[67]

Two mechanisms for concentrating organic chemicals in lakes, pools, lagoons, etc. have been suggested. These are (1) simple evaporation and (2) freezing the body of water. Both of these concentrating mechanisms have been suggested as playing a significant role in enhancing chemical evolution rates.

Evaporation[68]

As a hypothetical evaporation mechanism (see Figure 4-5), let us picture a small pool in a cave (so the accumulating organic compounds are protected from ultraviolet light) located near a fumarole (so there is a heat source for evaporating the water) and so situated at the coast that at high tide the ocean soup will overflow into the pool to supply organic compounds without washing away the concentrated organics in the same action. Between high tides evaporation slightly increases the concentration of organic compounds. After many iterations of this cyclic process a reservoir of concentrated organic compounds is developed.

Although this hypothetical evaporation scheme is only one of many that can be envisioned, we shall use it to illustrate several facets of the mechanism. Whatever the details of the specific evaporating pool, lake, or lagoon, it must include:

1. A suitable reservoir for concentrating organic compounds.
2. A heat source for evaporating water.
3. The repeated admission of oceanic soup into the reservoir.
4. Some means to protect the organic compounds from ultraviolet light.

Figure 4-5. A hypothetical evaporation mechanism.

A small pond in a cave protects accumulating organic compounds from ultraviolet light. Located nearby is a fumarole which evaporates the water between high tides. During high tides dilute organic soup refills the pond, but without flooding away material.

If such evaporating pools existed they would surely have tended to concentrate non-volatile substances such as amino acids, purines, etc. But evaporating pools would have been inadequate for concentrating volatile substances such as aldehydes and HCN. Instead of becoming more concentrated upon evaporation of the pool, such volatile substances would simply evaporate and redissolve in more dilute water bodies. This is particularly important since, as we noted earlier, HCN will significantly polymerize only if it can be concentrated to more than 0.01M. Since HCN in the open ocean would have been on the order of 10^{-6}M,[69] it is clear that some other concentrating mechanism must have been involved if HCN were significant in chemical evolution.

Freezing

If the solar luminosity on the early Earth was less than today, as previously discussed, then many of the water bodies of Earth would have been covered with ice, if not completely frozen. In certain equatorial regions (where liquid water could have persisted) the water bodies might have alternately frozen and thawed with the seasons. In this setting Orgel has shown that dilute solutions of HCN at 10^{-5}M from the ocean might run into a localized pool in summer and collect there. As the water freezes over in winter, the HCN concentrates in the solution beneath the ice. A 10% conversion to organic material might occur. As this cyclic process continued, material of sufficient concentration might accumulate every million years.[70]

Critique of Concentrating Mechanism

There is no known geological evidence for organic pools, concentrated by these or other mechanisms, ever existing on this planet.[71] In contrast, much evidence is available that inorganic pools existed in early times. Such inorganic pools can be seen today at Yellowstone National Park.

It is not too significant, however, that evidence for isolated reservoirs of organic compounds has not been located. They would undoubtedly have been fewer in number, since requirements for an organic pool would have been more stringent. If evidence is available for such organic pools it may take some time to locate.

More significant is the fact mentioned earlier that geological evidence for the oceanic soup has not been located. If there ever was a dilute ocean that fed organic compounds into these smaller pools, there should be abundant evidence for it in the lower Precambrian sediments. None has been located, however. Remember, if the soup were as massive as the theory suggests, organic remains should be literally all over the Earth in deep sediments of great age. Scientists have looked but have not found organic compounds.

Further, if by some means concentrated pools did develop, not only would the desired materials concentrate, but also the undesirable impurities. For example, an evaporating pond concentrating non-volatiles such as amino acids would also concentrate sea salts such as NaCl.[72] A freezing pond concentrating volatile substances such as HCN would do the same. If such salts were in great excess (which is not unlikely), then organic compounds in the pond could not have been significantly concentrated as a result of the "salting-out effect." This effect assumes the NaCl and other sea salts compete for the water molecules in the solution of organic compounds such as amino acids. Salt has greater affinity for water than do these organic compounds. Therefore, in order for the salt to be dissolved the organic compounds must precipitate out of solution.

It is another type of "impurity," however, that would have been the greatest obstacle to the successful concentration of organic compounds in limited zones. This would be the host of oceanic organic compounds such as amines, amino acids, aldehydes, ketones, sugars, carboxylic acids, etc. that would have destructively interacted in the ocean.[73] The usual consequences of concentrating these would be, according to the law of mass action, merely an acceleration of the many destructive reactions (as well as the constructive reactions) that would also occur at slower rates in the more dilute ocean, as already discussed.

Hydrogen cyanide would seem to be an exception, since on concentration, polymerization tends to predominate. Hydrolysis of HCN would predominate in the dilute ocean. Polymers of HCN, however, would yield the vulnerable amino acids upon hydrolysis.[74] If peptides formed directly from HCN polymerized in the atmosphere and fell into the ocean,[75] these would be terminated by reacting with amines, carboxylic acids, etc., as discussed earlier.

Concentrating mechanisms have occupied the attention of some investigators. Stemming from this discussion, however, it is our observation that what is needed is a natural *sorting* mechanism. The problem demands a means of selecting organic compounds and isolating them from other chemicals with which they could destructively interact. Yet there is nothing (but the need) to suggest that such a sorting mechanism ever existed on this planet.

In other words, for these more limited zones (e.g., lakes, pools, lagoons), as for the ocean itself, it is difficult to imagine significant concentrations of essential organic compounds ever accumulating. As we have seen, degradative forces need to be taken into account in realistic estimates of concentrations, and they have frequently been ignored.

Conclusion

Based on the foregoing geochemical assessment, we conclude that both in the atmosphere and in the various water basins of the primitive Earth, many destructive interactions would have so vastly diminished, if not altogether consumed, essential precursor chemicals, that chemical evolution rates would have been negligible. The soup would have been too dilute for direct polymerization to occur. Even local ponds for concentrating soup ingredients would have met with the same problem.

Furthermore, no geological evidence indicates that an organic soup, even a small organic pond, ever existed on this planet. It is becoming clear that however life began on Earth, the usually conceived notion that life emerged from a soup of organic chemicals is a most implausible hypothesis. We may therefore with fairness call this scenario "the myth of the prebiotic soup."

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5. THE EARLY EARTH AND ITS ATMOSPHERE

Over the past several decades, our growing understanding of the early Earth has added crucial insight to theories of chemical evolution. In this chapter, three relevant points will be discussed. First, the time frame or the time available for chemical evolution will be established. Second, we will examine the chemical composition of the atmosphere on the primitive Earth to determine if it was conducive to abiogenesis. Third, we will examine the important question of oxygen content on the early Earth and in its atmosphere. This evaluation of plausible atmospheric conditions will help to establish constraints on the next generation of prebiotic simulation experiments.

Establishing the Time Frame

One of the most dramatic changes in evolutionary theory since the 1960s has been in understanding the sharp reduction of the time available for abiogenic synthesis. As Richard E. Dickerson states, "Perhaps the most striking aspect of the evolution of life on the Earth is that it happened so fast."[1] In fact, Cyril Ponnamperuma of the University of Maryland and Carl Woese of the University of Illinois have suggested that life may be as old as the Earth and that its origin may have virtually coincided with the birth of the planet.[2] In this section the data used to support such statements will be examined.

From radiometric dating techniques, the ages of stony meteorites have been set at 4.6 billion years.[3] If the sun, the planets, the meteorites, and other solar debris all formed from the same primordial dust cloud at about the same time, the Earth would be approximately 4.6 billion years old. There exists a tremendous gap, however, in information about the Earth from this date through the Precambrian until about 0.6 billion years ago.[4] This is especially so with respect to information about chemical evolution.[5] Until the late 1960s, the oldest suspected evidence for life was the occurrence of fossil stromatolites (photosynthesizing algae) in 2.7-billion-year-old limestone located in Southern Rhodesia.[6] However, in the late 1960s several scientists investigating very old rocks (3.2 billion years old) found evidence of molecular fossils and microfossils indicating past life.

Molecular Fossils

Molecular fossils (or chemical fossils) are actually chemical compounds found in the rocks and suspected of being the remains of once-living matter. The types of chemical that may indicate life are quite diverse. However, there are two different ways in which the compounds found may indicate an association with living organisms:

1. The compounds could be degradation products of chemicals found in living organisms. For example, isoprenoid alkanes (such as pristane and phytane) are assumed to result from the breakdown of chlorophyll. Isoprenoids found in ancient rocks could therefore be a record of living organisms. Many other chemicals associated with living organisms, such as porphyrins and steranes, may be found in very old rocks as well.
2. During their metabolic processes, organisms selectively use carbon-12 over carbon-13. Thus, chemicals with a high carbon-12-to-carbon-13 ratio may indicate the occurrence of living processes.

Microfossils

Microfossils may also indicate past life. Microfossils are microscopic outlines in rocks indicating past life forms. Usually these are very simple algae-like spheroids or filaments found in carbon-rich rocks. It would be nice if some detail beyond their morphological characteristics were preserved for our inspection. This is rarely the case, however. Still, through the chemical analysis and microscopic examination of very old organic-rich rocks,[7] the whole field of chemical evolution has been changed dramatically. That is, before the identification of microfossils and molecular fossils, most scientists thought that perhaps as much as 2 billion years were available for chemical evolution to occur.

The Evidence

Since the 1960s, the following evidence has become available to support the view that life originated on the Earth soon after its formation:

1. 1967: Micropaleontological studies of carbonaceous chert of the Fig Tree Series of South Africa (greater than 3.1 billion years old) indicated the presence of spheroidal microspheres. The photosynthetic nature of these primitive microorganisms was corroborated by organic geochemical and carbon isotopic studies.[8]
2. 1977: A population of organic walled microstructures from the Swaziland System of South Africa was identified as the morphological remains of primitive prokaryotes. The rocks were dated at 3.4 billion years old.[9]
3. 1979: Cell-like inclusions detected in the cherty layers of a quartzite, which is part of the Isua series in Southwest Greenland, consisted of biological materials. High carbon-12-to-carbon-13 ratios were found in the hydrocarbons. The age of the sequence is approximately 3.8 billion years.[10]
4. 1980: Researchers found biological-like cells in rocks from the "North Pole" region of Australia. The rocks were dated at 3.5 billion years old. Even more amazing was the fact that five different types of cell could be identified. "This tells us that life was diverse, abundant, and judging from the chemistry, really quite advanced."[11]
5. 1980: A fossilized mat of filamentous microorganisms called stromatolites were found preserved in ferruginous dolomitic

> chert of the Pilbara Block of Western Australia. They are estimated to be 3.4 to 3.5 billion years old.[12]

Until recently, "yeast-like microfossils" from the Isua belt in Southwest Greenland were regarded as evidence of living structures. Now, however, some researchers have raised questions about this interpretation,[13] suggesting that they are not the remains of early Archean life forms. Thus, the Australian deposits dating back to 3.5 billion years are currently considered the oldest sediments containing convincing evidence for biological activity. Even so, many scientists believe that life existed over 3.8 billion years ago.

The Time Available for Evolution

Brooks and Shaw state that the oldest rocks on Earth are probably about 3.98 billion years old.[14] However, the oldest age confirmed by dating techniques is 3.8 billion years for the rocks from the Isua series in Greenland.[15] In either case, the surprising implication is that we may almost say that life has always existed on Earth. Before 3.98 billion years ago (from 4.6 to 3.98 billion years), the Earth was probably too hot to support life.[16] Then life appeared about 3.81 billion years ago. That is, only 0.170 billion (170 million) years were available for the abiotic emergence of life. Indeed, according to Brooks and Shaw, this amount of time for abiogenic synthesis of essential precursors, let alone chemical evolution, is "very small."[17] The discovery of microfossils has confirmed this conclusion. As a result, the thinking of scientists has undergone dramatic change. In the words of Miller, "If the origin of life took only 10^6 years [0.001 billion], I would not be surprised."[18] Other scientists suspect a period of 10^7 to 10^8 years or less following the time after the Earth cooled. For instance, "If higher surface temperatures persisted until 4000 Ma [4 billion years] ago, then life probably originated about 3900 Ma ago."[19] The search is underway for mechanisms that could account for the "geologically instantaneous" origin of life.

The Composition of Earth's Primitive Atmosphere

During the past several years, space probes have examined the atmospheres of several planets in our solar system. These probes have included investigations of the following planets:

1. Mars (Viking Missions);
2. Venus (Pioneer and Venera Missions);
3. Jupiter (Voyager Missions);
4. Saturn (Voyager Missions).

The data collected by these space probes have resulted in the reexamination of scientific theories concerning the formation of planets and their atmospheres. For example, the Pioneer Venus argon-neon measurements provided much-needed constraints on models of how modern atmospheres were generated. James B. Pollock of NASA-Ames has suggested three logical possibilities:[20]

1. The Primary Atmosphere Hypothesis

   The gases in the modern atmosphere could be residuals from the pre-solar nebula. But if this were the case, the argon-neon ratios on Venus, the Earth, and Mars would be quite similar to the original ratio in the nebula and the contemporary ratio on the sun. However, the ratios of these planetary atmospheres are very different from that of the sun.

2. The External Source Hypothesis

   The gases could have been brought in on volatile-rich comets and asteroids in the post-T-tauri wind era while the planets were sweeping up the last pieces of matter from the solar system. These comets and asteroids must have bombarded all the inner planets at about the same rate; therefore, we would expect the planets to contain similar concentrations of the rare gases. However, this is not the case.

3. The Grain Accretion Hypothesis

   The modern planetary atmosphere could have resulted from outgassing of volatiles trapped in the original rocks.

According to Pollock, the last hypothesis is the only one not contradicted by the data. The term "grain accretion" is used because grains of material containing potential volatiles were accumulated into planetesimals that subsequently accreted to form planets.[21] Later, as a result of internal heating, volatiles reached the surface. Since the original volatile atmosphere of the Earth escaped its gravitational field during accretion, the Earth's primitive atmosphere was in fact a secondary atmosphere that resulted from gases issuing forth from the interior of the Earth by means of volcanoes or by means of diffusion through the mantle. This secondary atmosphere theory has been the most accepted theory for over a decade, even with the influx of new information from Venus, Mars, and other planets.

Despite wide acceptance of the outgassing model, other sources of gases have been suggested to supplement it. For example, interstellar cloud material could be responsible for much of the neon in the Earth's atmosphere.[22] Comets also may have supplied some of the volatiles.[23] Oro has estimated that 1,000 meteorites may have accounted for the volatiles on the Earth.[24]

Various Models for the Earth's Primitive Atmosphere

In contrast to the wide acceptance enjoyed by the outgassing model for the formation of the atmosphere, opinions about the composition of the atmosphere have varied greatly over the years. Some examples of compositions postulated over the past 30 years follow:

The CO_2-H_2O Atmosphere. Assuming the volcanic exhalations to be the same on the primitive Earth as today, the primitive atmosphere would be composed of carbon dioxide and water vapor with minor amounts of H_2S, SO_2, and N_2. This view was expressed by Fox and Dose,[25] Revelle,[26] Abelson,[27] and Brooks and Shaw.[28]

The CH_4-NH_3-H_2O Atmosphere. An opposing view was held by Oparin,[29] Urey,[30] and Miller and Urey.[31] These scientists reasoned that a small but significant level of H_2 remained in the atmosphere of the forming Earth so that at least 10^{-3} atmosphere was present (there is about 10^{-6}

atmosphere of H_2 today). The hydrogen would have reacted with any carbon, nitrogen, or oxygen present to form an atmosphere rich in methane (CH_4), ammonia (NH_3), and water (H_2O). Of course, scientists of the first view disagreed with this conclusion, stating that the atmospheric H_2 level was insignificant and that there is no geologic evidence for a primitive atmosphere containing CH_4.[32]

The Three-Stage Atmosphere. A third view, held by Holland,[33] was really the synthesis of the first two views. Holland disagreed with the basic assumption of the first view, stating that the composition of gaseous mixtures from volcanoes of the primitive Earth *was not* similar to that of present-day volcanic exhalations. This came from the hypothesis that primitive volcanic exhalations, unlike their present counterparts, were in equilibrium with hot molten rock containing large amounts of elemental iron. This led to a first stage rich in methane (CH_4) followed closely by a second stage rich in N_2. The present-day atmosphere is the third stage.

The CO_2-N_2 Atmosphere. Walker[34] has done an extensive study on the evolution of the atmosphere and concludes that the primitive atmosphere contained H_2O, CO_2, N_2, and 1% H_2. The 1% H_2 was emitted from volcanoes, and therefore he assumed that the volcanic source of hydrogen gas was larger in the past than today. Large quantities of the CO_2 emitted formed carbonates in oceans while large amounts of the H_2O condensed.

According to this view, the prebiological atmosphere contained no large amounts of reduced gases like methane and ammonia.[35] Recent photochemical calculations indicate that a heavily reducing atmosphere of methane and ammonia was extremely short-lived, if such a prebiological atmosphere existed at all.[36] The conclusion that the primitive atmosphere had little or no methane or ammonia has also won agreement from Holland.[37]

The notion that the primitive atmosphere was not highly reducing is a dramatic change from the previously held hypothesis. Various reports have elaborated on this shift in theories. For example:

> Now, for the first time in 30 years, the widely accepted recipe for primordial soup is changing from one rich in hydrogen—composed primarily of methane (CH_4) and ammonia (NH_3)—to a hydrogen-poor atmosphere similar to today's *sans* the oxygen.[38]
>
> No geological or geochemical evidence collected in the last 30 years favors a strongly reducing primitive atmosphere... Only the success of the laboratory experiments recommends it.[39]
>
> Scientists are having to rethink some of their assumptions. Chemists liked the old reducing atmosphere, for it was conducive to evolutionary experiments.[40]

Sherwood Chang of NASA-Ames Research Center has observed that prebiotic simulation experiments using a neutral atmosphere of water, nitrogen, and carbon dioxide produce only such chemicals as ammonia and nitric acid.[41] However, Joseph Pinto of the Goddard Institute for Space Studies synthesized formaldehyde in a primitive atmosphere poor in hydrogen.[42] Other simulation experiments using hydrogen-poor atmospheres have also produced abiotic organic molecules.[43] As reported in 1951, Melvin Calvin of the University of California at Berkeley synthesized organic compounds by irradiating a mixture of water and carbon dioxide with a beam of alpha particles.[44]

Oxygen Content of the Early Earth and Its Atmosphere

All Models Exclude O_2

Models for the primitive atmosphere are many and diverse. Each scientist uses one of these atmospheric models to demonstrate that the chemical building blocks of life could be formed under the chosen conditions. However, an interesting pattern emerges from these experimental studies which suggests that, within limits, the syntheses of amino acids and other essential organic molecules are unexpectedly independent of the specific details of the experimental conditions. As discussed in Chapter 3, reactions that begin with an atmosphere of CH_4 and NH_3 or of CO_2 and N_2 as the carbon and nitrogen sources respectively are likely to result in similar products. Therefore, while a detailed evaluation of the primitive atmosphere is fascinating, it may not be necessary except for one point. That point, central to the theory of chemical evolution, is that the primitive atmosphere could not contain any but the smallest amount of free (molecular) oxygen (O_2).

It is necessary to exclude oxygen for two reasons. First, all organic compounds (such as the essential precursor chemicals or basic building blocks that must have accumulated for chemical evolution to proceed) are decomposed rather quickly in the presence of oxygen. Second, if even trace quantities of molecular oxygen were present, organic molecules could not be formed at all. In the words of Shklovskii and Sagan, "As soon as the net [laboratory] conditions become oxidizing, the organic syntheses effectively turn off."[45] All the simulation experiments reviewed in Chapter 3 are largely inhibited by oxygen. None of the essential molecules of life, e.g. amino acids, could even be formed under oxidizing conditions, and if by some chance they were, they would decompose quickly. Chemical evolution would be impossible. This point is also made by Fox and Dose,[46] who list six reasons why the primordial atmosphere contained no significant amount of oxygen. Two of their reasons are worthy of note: (1) "laboratory experiments show that chemical evolution... would be largely inhibited by oxygen";[47] and (2) "organic compounds that... have accumulated on the surface of the Earth in the course of chemical evolution, are not stable over geologic time in the presence of oxygen."[48]

Fox and Dose hold the conviction that chemical evolution did occur, and list these points along with others as evidence for a reducing atmosphere. They reason that since chemical evolution requires it, free oxygen in the primitive atmosphere must have been negligible.

Fox and Dose are not the only ones who reason in this way. Walker[49] also concludes that the "strongest evidence" for an atmosphere without oxygen is that we know chemical evolution took place. While this may be an appropriate consideration for framing a hypothesis, it does not properly constitute evidence for the hypothesis.

We will discount this "strongest" evidence for an anoxic (no free oxygen) atmosphere since it is based on a circular argument. Such logic is hardly scientific, and simply assumes as true the hypothesis to be established. Without assuming in advance a reducing atmosphere, we will examine evidence concerning the oxygen content of the early Earth's atmosphere. We will first consider sources of oxygen, and then examine mineralogical evidence during the time period over which oxygen has been present in the atmosphere. This, in turn, will help us determine when and for how long the Earth's atmosphere was void of oxygen.

Sources of Free Oxygen for the Earth's Atmosphere

There are at least three possible sources of free oxygen for the Earth's early atmosphere: volcanic exhalations (and comets/meteorites), photodissociation of H_2O, and the oxygen-generating photosynthesis which is associated with living organisms. We will consider each of these sources in terms of the amount of oxygen produced and its probable date of appearance in geological history.

1. Volcanic Exhalation as a Possible Source of Free Oxygen. It has previously been suggested that the Earth's atmosphere was produced by vol-

Table 5-1. Estimates of Oxygen in the Early Atmosphere Due to Photodissociation.

Author	Year	Concentration	Note
Berkner and Marshall	1965	10^{-3} PAL	1
Brinkmann	1969	0.25 PAL	
Walker	1978	10^{-13} MR	
Kasting et al.	1979	10^{-12} PAL	2
VanderWood and Thiemens	1980	10^{-10} MR	
Kasting and Walker	1981	10^{-8} PAL	3
Carver	1981	10^{-1} PAL	
Levine	1982	10^{-15} PAL	4
Canuto et al.	1982	10^{-11} to 10^{-9} MR	

(1) 1.0 PAL O_2 = 0.21 Mixing Ratio (MR).
(2) 10^{-12} PAL at surface, increases to 10^{-5} PAL at 60 Km.
(3) 10^{-14} when reaction of O_2 and H_2 included.
(4) 10^{-15} PAL at surface, increases to 10^{-5} PAL at 50 km altitude (a strong altitude dependence).

canic eruptions which might have included free oxygen (O_2) among the various gases. Gases from volcanic eruptions today contain mainly CO_2, H_2O, and minor amounts of H_2S, SO_2, and N_2, but no free oxygen. Given the high temperatures in volcanoes and the highly reactive nature of oxygen, this is not surprising. At elevated temperatures (600–800°C), oxygen would react with minerals in the Earth, resulting in nonoxidizing gases. We are thus left with neither a theoretical nor an experimental basis for expecting the early volcanic emissions to have supplied any significant amount of free oxygen to the primitive atmosphere.[50]

2. *Photodissociation of Water as a Possible Source of Free Oxygen.* Another possible source of free oxygen to the early atmosphere is the photodissociation of water in the atmosphere due to ultraviolet light:

$$2H_2O + (h\nu) \text{ ultraviolet light energy } = 2H_2 + O_2$$

Since the 1960s, estimates of the amount of free oxygen in the prebiological atmosphere from photodissociation of water have ranged from 10^{-15} of present atmospheric level (PAL) to 0.25 PAL. The various estimates are provided in Table 5-1[51] and summarized briefly below. It will be helpful to keep in mind that Table 5-1 includes some entries listed as PAL and others as mixing ratio, where 1.0 PAL of oxygen is equivalent to a 0.21 mixing ratio (MR).

Berkner and Marshall[52] were the first to provide quantitative estimates of the concentration of oxygen in the early atmosphere resulting from photodissociation of water vapor. They concluded that concentrations of 10^{-3} PAL would have resulted.

Brinkmann[53] calculated the amount of O_2 generated from photodissociation and consumed in oxidation of rock, etc. He concluded that a minimum of 25% of the present level (0.25 PAL) of oxygen existed over 99% of geologic time. Therefore, he reasoned, "It does not seem that early [chemical] evolution could have proceeded in such an atmosphere."[54] Proponents of a neutral or reducing early atmosphere do not agree that such high O_2 levels resulted from photodissociation of H_2O. For example, Walker[55] contends that Brinkmann erred in assuming that the rate of hydrogen escape from the Earth is equal to the rate of photolysis of water. Walker, however, must assume that the volcanic source of hydrogen was considerably larger than the amount of hydrogen escaping into space after water was photolyzed. For this to have been true, volcanic sources of gases must have been much larger in the past than they are today. Van Valen[56] also objected to Brinkmann's study but failed to produce an alternative answer, offering only that there are serious and unresolved problems concerning the buildup of oxygen in the atmosphere.

Because of the importance of the question, Carver[57] recalculated the quantity of oxygen produced by photodissociation in Precambrian times using a larger water vapor mixing ratio than did previous studies. This study supports a warmer and more humid climate in the Precambrian. It also suggests that the free oxygen concentration could have reached 10% of the present level (0.1 PAL). If the surface oxidation rates were substantially greater in Precambrian times than at present, oxygen levels were probably 0.01 to 0.1 PAL.

Holland[58] has stated that a few percent of the present atmospheric level of oxygen was certainly present by 2.9×10^9 years ago. However, as shown in Table 5-1, the estimates cover too broad a range to draw definite conclusions. Additional estimates not discussed here have been included in Table 5-1 to illustrate the uncertainty in oxygen estimates.[59] The only trend in the recent literature is the suggestion of far more oxygen in the early atmosphere than anyone imagined. A significant part of this trend is due to measurements which suggest that stars resembling the sun at a few million years of age emit up to 10^4 times more UV light than the present sun.[60] This increase in UV could increase the O_2 surface mixing ratio by a factor of 10^4 to 10^6 over the standard value of 10^{-15}, thus affecting all the oxygen level estimates.[61]

Support for large estimates of O_2 is found in data from Apollo 16—data which suggest that a large amount of free oxygen does result from upper atmosphere photodissociation of water vapor. The Apollo 16's ultraviolet camera/spectrograph revealed a massive cloud of atomic hydrogen enveloping the Earth and extending outward some 40,000 miles. This hydrogen apparently resulted from the photodissociation of water vapor. An early report of these results noted that this lends "substantial support" to "the theory that solar separation of water vapor provides our primary oxygen source" today and not photosynthesis as is usually supposed.[62]

George Carruthers,[63] principal investigator for the Apollo 16 camera/spectrograph experiment, has subsequently noted that the amount of oxygen due to photodissociation was originally overestimated. That is, photodissociation was not the primary source of oxygen as originally stated. (More details concerning the results of the measurements by Apollo 16 can be found in a report by Carruthers et al.[64]) Carruthers agrees with other workers that little free oxygen was present in the Earth's primitive secondary atmosphere. However, without free oxygen (and therefore without ozone) solar ultraviolet radiation could penetrate to much lower water-rich layers of the atmosphere than is the case at present. Therefore, the water dissociation rate could have been much higher and the production rate of oxygen would have been considerably greater than at present. Thus, one may reasonably infer that the water vapor photodissociation process could have provided a sufficient amount of oxygen in the primitive atmosphere (perhaps as much as 1% of the atmosphere or 0.05 PAL) so that an ozone layer could have formed. An effective ozone screen would have allowed living organisms to proliferate by reducing the adverse effects of the solar UV radiation penetrating to ground level.

When asked about oxygen destroying organic molecules, Carruthers acknowledged it would, but not as rapidly as present-day oxidation because oxygen would have been more dilute and would not have been assisted by bacterial decay.[65] However, considering the long time postulated for chemical evolution to occur, even a small amount of oxygen would have been very detrimental. Most likely, if a small amount of O_2 were present, important precursor molecules would have been destroyed (oxidized) or their formation prevented in the first place.

Since living organisms and organic molecules need the protection from ultraviolet radiation provided by an ozone screen, yet the presence of oxygen prevents the development of such living systems and biological molecules, this would seem to constitute a catch-22 in the model. How much oxygen is required to produce the ozone screen and what maximum amount of oxygen can be tolerated in the synthesis of the molecular precursors to life? These two questions will be considered next.

Berkner and Marshall[66] were among the first scientists to evaluate the relationship of O_2 to O_3 as it pertains to chemical evolution. They suggested that when the O_2 concentration reached 10^{-2} PAL, the resulting concentration of O_3 was sufficient to restrict the penetration of lethal UV to a thin layer of the ocean. When the O_2 level reached 10^{-1} PAL, the O_3 concentration was sufficient to absorb all UV radiation less than 3000 Å. At these levels, life was able to migrate from the oceans to land masses for the first time. Since this initial evaluation by Berkner and Marshall, other scientists have investigated the origin and evolution of ozone.[67]

The suggestion has been made that very little atmospheric oxygen (possibly 10^{-3} PAL), is required to produce a biologically effective ozone screen. However, when several additional factors are taken into account it becomes apparent that perhaps as much as 0.1 PAL oxygen would have been required. Carver,[68] in reviewing the available data, concluded that a biologically effective ozone screen would be established once the oxygen content exceeded 0.01 PAL.

In summary, the development of an ozone screen apparently requires a higher oxygen concentration (0.01 to 0.1 PAL) than the original suggestion of 10^{-3} PAL. Whether such a free oxygen concentration developed by photodissociation of water alone, or eventually by the combined action of photodissociation and photosynthesis in algae, etc., is difficult to establish. It is not yet known at what rate free oxygen is removed by reaction with reducing gases such as methane or reduced minerals such as Fe_3O_4. In any case, it seems evident that free oxygen was being produced by photodissociation from earliest times and that this source of free oxygen would have continued until a significant free oxygen concentration developed, allowing an ozone screen to form, filter the short wavelengths (i.e., < 3000 Å) of ultraviolet light, and effectively turn off this mechanism of oxygen production in the atmosphere beneath the ozone screen.

Because only low levels of oxygen are needed, the Earth may have had an effective ozone screen since before life began. Such a prospect makes this area of research quite controversial. Two consequences of an early ozone screen are:

1. The requirement that sources of energy other than UV light would need to be postulated for prebiotic synthesis of organic molecules, and
2. The necessity of alternative scenarios which would allow substantial synthesis of organic molecules and their subsequent protection in an oxidizing milieu.

3. *Living Organisms as a Source of Free Oxygen.* Since volcanic eruptions apparently would not supply free atmospheric oxygen and photodissociation would supply free oxygen only until an ozone layer developed (apparently between 0.01 and 0.1 PAL of oxygen), it is generally assumed that our present 21% of free atmospheric oxygen was and is the result of photosynthesis by living plants. This transition from the *assumed* anoxic conditions to our present 21% free oxygen is usually thought to have occurred about 1 to 2 billion years ago. Figure 5-1 below illustrates estimates by several scientists of the increase in O_2 with time.

However, recent paleontological evidence suggests an advent of a more highly oxidizing atmosphere earlier than 1 to 2 billion years ago. At the beginning of this chapter, we discussed the age of the first life on Earth. Some of these life forms would have produced oxygen. Still, the level of O_2 production remains in doubt. The organisms could have been anaerobic bacteria, in which case the atmosphere could have been anoxic. Walker[69] dates autotrophic organisms at 3.5 billion years ago, bacterial photosynthesis at 3 billion years ago, and the advent of green-plant photosynthesis at about 2.5 billion years ago. Thus, oxygen-producing organisms (cyanobacteria/blue-green algae) certainly existed by 2.8 x 10^9 years ago and perhaps much earlier (probably 2.9–3.1 billion years

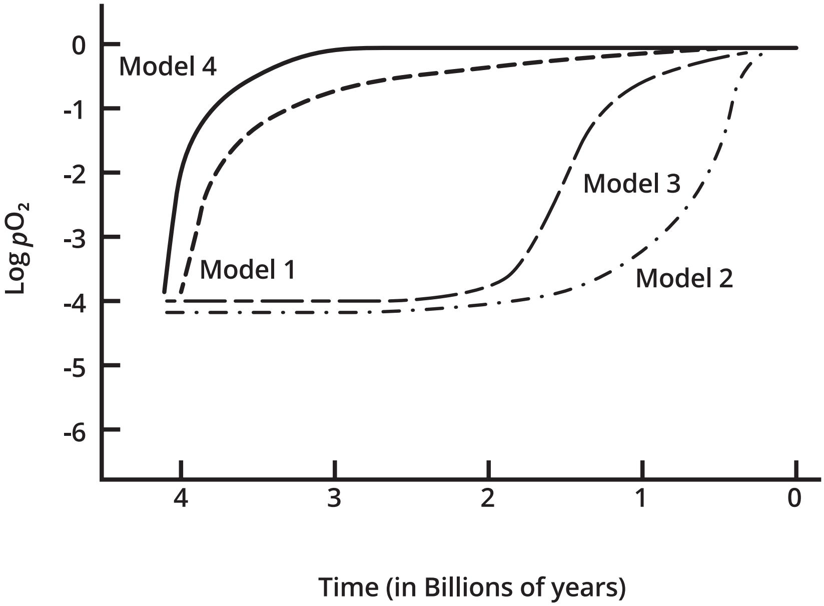

Figure 5-1. Estimates of Oxygen levels in the Earth's Atmosphere.

Source: D. E. Grandstaff, *Precambrian Research*, 13 (1980), 21.

ago). According to Schopf[70] these organisms would have produced fluctuating levels of free oxygen. At first, the oxygen would have been consumed by exposed reduced-mineral species (mainly ferrous iron). Then the quantity of oxygen would have varied depending on the exposure of more reduced minerals, the amount of volcanic emissions, etc., until the concentration reached fairly constant levels about 2 billion years ago. Until recently, however, most scientists thought that little oxygen existed before 2 billion years ago. Walker mused, "... it is hard to explain why oxygen pressures should have remained low for almost 2 billion years after the introduction of green plant photosynthesis."[71]

Based on the growing body of evidence, Walker has concluded that oxygen-evolving photosynthesis appeared prior to 3.8 billion years ago and that the lifetime of the prebiological atmosphere must have been "quite short in geologic terms."[72]

From the available data on isotopic sulfur composition of Precambrian minerals, Chukhrov et al. have concluded "the existence of sulfate-reducing organisms and the presence of substantial amounts of oxygen in the terrestrial atmosphere 3000 m.y. ago or earlier."[73] Likewise, from carbon isotope studies, Eichmann and Schidlowski have shown that more than 3 billion years ago "photosynthesis [had] produced already a large fraction of all the oxygen ever released and now fixed primarily in Fe_2O_3 and SO_4^{2-} with only 5% present as free oxygen in the atmosphere."[74] The data of Schidlowski et al.[75] also show no secular change in the isotopic composition of carbonates dating back more than 3 billion years ago. Even more recently Schidlowski has indicated that "the constancy of the isotopic fractionation observed between reduced and oxidized carbon throughout the record is best interpreted as the signature of biological activity during the past 3.5×10^9 yr. (or possibly 3.8×10^9 yr.)."[76] Broecker[77] considers such constancy of $^{13}C/^{12}C$ ratios in Phanerozoic (younger than 0.6 billion years) marine carbonates as indicative that the oxygen content must have been comparable to its present value. If this principle is valid for Phanerozoic carbonates, it should also be valid for carbonates 3 billion years ago. That is, we must conclude that the present level of oxygen also existed 3 billion years ago. Based on Schidlowski's data, other scientists have concluded that 80% of the present levels of oxygen have existed for the past 3.0 billion years.[78]

Oxygen-producing organisms probably formed very old limestone deposits (e.g., Bulawayan, 2.7–3.0 billion years) in the same manner as do the present-day limestone-depositing algae. Judging from the amount of limestone in ancient deposits, significant levels of O_2 would have been present. However, Rutten[79] disagrees with this conclusion and contends that since the O_2 concentration 2.7 billion years ago was only 1% of the present level, the metabolism of limestone-depositing organisms must have been different in the past from that of present algae. But we must ask, why infer a change in the metabolism of the algae? Surely the desire for a prebiotic Earth without free oxygen is not a compelling reason. It would have been just as easy (or easier?) to adjust the O_2 level to account for the limestone.

In summarizing this section on sources of free atmospheric oxygen, the most likely scenario is as follows. The early secondary atmosphere contained mainly N_2, H_2O, and CO_2. Photodissociation then produced an indeterminate free-oxygen concentration which was later supplemented by photosynthesis. Once the oxygen level reached a concentration of 0.01 to 0.1 PAL (by photodissociation alone or in combination with photosynthesis), an effective ozone layer formed and photodissociation ceased in the lower atmosphere. The remaining increase in oxygen concentration to present levels occurred by photosynthesis alone. Recent paleontological data combined with occurrence of living organisms 3.5 billion years ago indicate that these increases in oxygen levels may have occurred very early in geological history (over 3 billion years ago).

This scenario raises two very significant questions. First, what free oxygen concentration level was produced by photodissociation acting alone before the origin of life? And second, would this level of free oxygen adversely affect the formation or continuance of organic biomonomers? We have already addressed the first question and found that current estimates of O_2 in the early atmosphere resulting from photodissociation range from 10^{-15} PAL to 10^{-1} PAL. Levine states, "This is a wide range, even for studies of the paleoatmosphere. Additional research in this area is indicated."[80] The second question is equally difficult to answer in a precise manner. Only qualitative statements have been made. For example:

> Even at low levels of O_2, there is a slow oxidation of most organic compounds, and the rate is greatly enhanced in the presence of ultraviolet light. These and related arguments are so compelling that it does not seem possible that organic compounds remained in the primitive ocean for any length of time after O_2 entered the Earth's atmosphere.[81]

We can only say, based on current models for ozone formation, that the upper limit of free oxygen concentration resulting from photodissociation alone would be 0.01 to 0.1 PAL. As indicated, there is considerable controversy concerning whether this upper limit of oxygen concentration could have been reached by photodissociation alone. Current estimates of 10^{-15} PAL surely are too low for production of an ozone screen, while 10^{-1} PAL is the upper limit itself. One thing is clear: If further research confirms that photodissociation alone could have produced a biologically effective ozone screen, a second problem is inescapable. Enough oxygen would then have been present in the early atmosphere to effectively shut off any production and/or accumulation of biomonomers, thus preventing chemical evolution.

Mineral Evidence Pertinent to Defining Free Oxygen Content in the Atmosphere during Various Stages of Geological History

The results from atmospheric physics, while not conclusive about the oxidation state of the early atmosphere, do at least leave open the possibility the early Earth was oxidizing. This possibility is in conflict with the usual picture of the early Earth as reducing. Therefore, we shall reexamine the data and usual arguments supporting the notion of a reducing early Earth and atmosphere.

The interpretation of the mineral evidence pertinent to atmospheric free oxygen in geologic history depends on the oxidation states of elements in mineral deposits that were formed during the various geological periods. For example, in the reaction

$$2H_2O + (h\nu)\text{ ultraviolet light energy } = 2H_2 + O_2$$

at 25°C, the equilibrium pressure of O_2 for the oxidation of PbS to $PbSO_4$ is 10^{-63} atm. This equilibrium pressure is so small that if any oxygen were present PbS would be converted to $PbSO_4$. Therefore, if rocks can be found to contain PbS versus $PbSO_4$, it would seem reasonable to conclude they formed in an anoxic environment. Likewise, if $PbSO_4$ is more abundant than PbS, oxygen may be inferred to have been present at its formation. It is instructive to note that other minerals show a similar relationship in Table 5-2 below.

The thermodynamic data indicate that the equilibrium oxygen pressures for the oxidation of the sulfides (PbS, ZnS, and FeS) to the cor-

Table 5-2.

Reduced Form (formed under anoxic conditions)		*Oxidized Form* (formed under oxygenic conditions)
Fe_3O_4	(Magnetite)	Fe_2O_3 (Hematite)
$UO_2 — U_3O_8$	(Uraninite)	UO_3
PbS	(Galena)	$PbSO_4$
ZnS	(Wurtzite)	$ZnSO_4$ or $ZnSO_4 \cdot 7H_2O$
$Fe_{1-x}S$	(Pyrrhotite)	$FeSO_4 \cdot 7H_2O$

responding sulfates (SO_4^{2-}) are lower than the equilibrium pressure for the conversion

$U_3O_8 - UO_2$ to UO_3 ($pO_2 = 10^{-21} - 10^{-23}$ atm.)

The equilibrium O_2 pressure for the conversion of Fe_3O_4 to Fe_2O_3 ($pO_2 = 10^{-72}$ atm.) is even less than the values for sulfide oxidations. A comprehensive review of the various elements and the oxidation states used in this type of study has been summarized by Rutten.[82]

Basic Assumptions. Interpretation of mineral data involves two basic questions. First, how long does it take for a given mineral to oxidize? And second, how long was the mineral in question exposed to the atmosphere during formation or exposed thereafter during transportation and deposition? It is usually assumed that a reduced or only partially oxidized mineral was formed when the atmosphere was anoxic, but this is not necessarily the case. We must also consider the rate of the reaction (kinetics). The predictions of equilibrium thermodynamic data are only significant if given enough time. If the mineral is not in contact with the atmosphere or water saturated with the atmospheric gases for sufficient time during transportation and deposition, it will not come to equilibrium. Since some of these reactions are very sluggish at ambient temperatures, the presence of a reduced mineral or absence of a fully oxidized mineral does not necessarily mean that the atmosphere was anoxic. Several examples are offered by way of illustration in the following paragraphs.

Specific Examples of Mineral Assemblages: Iron and Uranium Oxides

1. Iron Oxides

It is by no means unequivocal that iron oxides indicate ancient O_2 levels. This is best demonstrated by examining the stability fields of different iron minerals under varying natural conditions of pH and oxidation/reduction potential. When the O_2 level is changed from the present level to 0.01 PAL, the stability fields change very little. That is, the stability and depositional conditions of the iron oxides are hardly affected. Rutten concluded, "It follows that arguments in favor of an anoxygenic atmosphere cannot be based on the equilibria of mineral reactions... but on their kinetics,"[83] or the rate at which oxidation occurs.

According to Fox and Dose[84] no agreement has been reached concerning the equilibrium between FeO, Fe_3O_4, and Fe_2O_3 as a function of O_2 level. Holland[85] points out that Fe_2O_3 would be stable under extremely low O_2 levels, which explains its existence in sediments greater than 2.5 billion years old when the atmosphere was thought to have contained no oxygen. But other geologists use the occurrence of Fe_2O_3 to indicate significant levels of O_2 in the primitive atmosphere. Davidson[86] states that such immense hematite (Fe_2O_3) deposits (as far back as 3.4 billion years ago) are only compatible with the presence of free oxygen in surface waters at this very early date. The fact that all oxidation states of iron, from FeO to Fe_2O_3 to FeS_2, have been found in sediments of all ages probably indicates that local conditions and not the overall conditions determine which particular mineral is present. For example, as recently as 0.4 to 0.5 billion years ago (when O_2 was at its present level), reduced minerals were being deposited in oxygen-free waters (a local anoxic environment) much like the Indian Ocean today, which has practically no free oxygen below 150 meters. By looking at these deposits, one would erroneously conclude that the atmosphere was anoxic at that time. Such data led Krejci-Graf to conclude that geological evidence cannot be used to make general deductions concerning the Earth's atmosphere.[87] Another explanation of the observed variation of oxidation states of iron is that the levels of oxygen fluctuated in the ancient atmosphere. Schopf indicates that such conditions probably existed over 3.0 billion years ago.[88]

Despite the inconclusive nature of oxygen levels and iron formations, the customary interpretation has been that red beds (Fe_2O_3) provide the best indication of the first appearance of oxygen.[89] Walker disagrees, however, stating, "The presence of banded iron formation in the Isua rocks of West Greenland therefore implies that oxygen-evolving photosynthesis appeared on Earth prior to 3.8 billion years ago."[90] Walker's reasoning assumes that many metabolic processes capable of affecting the atmosphere (e.g., fermentation, bacterial photosynthesis, and sulfate reduction) must have originated before oxygen-evolving photosynthesis. Therefore, the life-time of the prebiological atmosphere of nitrogen, carbon dioxide, and water vapor must have been quite short in geological terms.

2. Uranium Oxides

A somewhat clearer picture emerges from UO_2 - UO_3 deposits of the Dominion Reef and Witwatersrand system in South Africa. The mineral deposits contain uraninite (UO_2), galena (PbS), pyrite (FeS_2), and gold. The deposits are all sedimentary. The minerals were derived from weathering a granite source rock and carried by high-energy (steep, fast-flowing) rivers to a lower-energy (flat, slow) fan-delta system where the minerals were deposited. This is evidenced by the well-rounded, coarse-silt-sized (0.0655mm) uraninite grains in the deposit. This type of deposit is called a detrital or placer deposit and the environment in which it was deposited is called a fluvial fan-delta or a braided alluvial plain. The minerals were definitely in contact with the atmosphere as they were weathered and deposited, some 2.5–2.75 billion years ago. Because the reduced forms of the minerals are present, it is usually concluded that the deposits were formed under an anoxic environment. However, as Miller and Orgel point out, "... these minerals may have been deposited under local reducing conditions, or failed to have reached equilibrium with the atmosphere at the time they were laid down."[91] Most geologists, however, would readily conclude that the minerals were in equilibrium due to the river transport as detailed above. However, this too is a matter of kinetics. If the minerals were transported and deposited very rapidly, for example, they may not have had time to reach equilibrium with the atmosphere. If this were the case, the reduced UO_2 would still be deposited in the presence of significant levels of O_2. But rapid deposition may not have occurred, given that the individual mineral grains are well-rounded and sorted.

Another possibility is that these deposits were transported during glacial periods. The very cold environment would lower the rate of reaction of UO_2 with O_2. Therefore, UO_2 would be deposited in the presence of O_2. Some evidence exists of glaciers in South Africa 2.5 billion years ago, and present-day evidence indicates that UO_2 deposits are now being formed in cold environments. In fact there is evidence that detrital uraninite exists in the present-day Indus River of Pakistan.[92] This further illustrates the fact that the rates of reactions must be known before definite conclusions can be made.

Trow has proposed a mechanism for deposition of the Witwatersrand and Elliot Lake uranium deposits in an oxygenated atmosphere during glacial, CO_2-impoverished episodes. He states that "apparently an anoxic atmosphere did not exist at these times [2.25–2.5 billion years ago]."[93]

We agree with Walker[94] that the evidence for an anoxic atmosphere provided by the detrital uraninite and pyrite in the Witwatersrand is not strong. This is based upon work by Holland[95] that shows that an upper limit of about 1% of the oxygen-mixing ratio is consistent with the existence of detrital uraninite. Also, according to Muir,[96] detrital pyrite (a reduced mineral) is common even today. In summarizing the various contributions at the U.S. Geological Survey Quartz-Pebble Workshop, Skinner[97] stated that current theories on atmospheric control for such ores as the Witwatersrand are not well-established. He further remarked that the current thinking is not correct and the absence of atmospheric oxygen cannot be counted upon with certainty to explain uraniferous quartz-pebble conglomerates. He suggested a more neutral atmosphere as an alternative to either a reducing or oxidizing atmosphere.

Much of the ambiguity about mineral assemblages has been resolved by D. E. Grandstaff,[98] who made a kinetic analysis of the oxidation of U^{4+} to U^{6+}. Uraninite (UO_2-U^{4+}) is thermodynamically unstable at oxygen pressures greater than approximately 10^{-21} atmospheres. Yet Grandstaff's kinetic analysis indicates that uraninite may have survived without being oxidized at oxygen pressures as high as 0.01 PAL. Thus, deposition of uraniferous conglomerates

> does not require an essentially anoxic atmosphere as previously proposed, but may have occurred under an atmosphere containing small amounts of oxygen consistent with photodissociation of water vapor and limited aerobic photosynthesis.[99]

The important conclusion from Grandstaff's kinetic analysis is that the formation of a reduced mineral such as UO_2 or Fe_3O_4 need not have required the absence of free oxygen in the atmosphere at the time the mineral was formed. Thus, traditional arguments for a reducing atmosphere based on reduced minerals are unconvincing. At least a mildly oxidizing atmosphere of up to 0.01 PAL is possible without oxidizing U^{4+}. It has long been known that the proper understanding of a thermodynamically favorable reaction is simply a reaction that is permitted. It need not occur. Only by kinetic analysis can details be obtained of whether a reaction occurred, and at what rate.

Summary of Mineral Data. We have examined in detail the evidence from uranium and iron minerals concerning the existence of a reducing primitive atmosphere. Because of the uncertainty in the kinetics of oxidation of these minerals, it is difficult to conclude with confidence that there has ever been a time when the Earth's atmosphere was devoid of free oxygen. Erich Dimroth and Michael Kimberley have evaluated minerals besides uranium and iron, and have drawn a similar conclusion:

> In general, we find no evidence in the sedimentary distribution of carbon, sulfur, uranium, or iron that an oxygen-free atmosphere has

existed at any time during the span of geological history recorded in well-preserved sedimentary rock.[100]

Chapter Summary and Conclusions

Three relevant questions have been considered in this chapter. First, we considered the time available for chemical evolution. It was determined on the basis of evidence from molecular fossils and microfossils that the origin of life occurred almost instantaneously (geologically speaking), just after the Earth's crust cooled and stabilized about 4.0 billion years ago. This leaves little more than 100 million years (if that) for any chemical evolution to occur. Second, the early atmosphere of the Earth was examined and found not to be the strongly reducing atmosphere popularized for the past thirty years. Instead, the consensus of scientists about the early atmosphere is shifting. At the time of this writing, there is wide agreement in adopting a more neutral primitive atmosphere consisting of CO_2, N_2, H_2O, and perhaps 1% H_2. There is a current controversy concerning whether the early Earth and its atmosphere might actually have been oxidizing. Third, we examined the important question of the oxygen content of the early Earth.

Three lines of evidence have been evaluated that indicate the existence of free oxygen in the Earth's primitive atmosphere: (1) data showing oxygen-producing life forms in rocks older than 3.5×10^9 years; (2) data showing oxidized mineral species in rocks older than 3.5×10^9 years; and (3) calculations indicating that up to 0.1 PAL of O_2 could have been produced by photodissociation of water. Although no precise conclusions can be made concerning the levels of oxygen in the Earth's early atmosphere, these results are quite suggestive.

The accumulating evidence for an oxygenic early Earth and atmosphere heightens the mystery of life's origin. If this type of evidence continues to accumulate, chemical evolution theories may have to appeal to the random occurrence of fluctuating or localized reducing environments on the primitive Earth. Such micro-environments could have been present (as shown by reduced minerals), but were they suitable or maintained long enough for the formation of life? The odds of finding such a suitable niche on the primitive Earth for a sufficient length of time are extremely small.

The monomer experiments reviewed in Chapter 3 largely assumed a strongly reducing atmosphere. These experiments covered the period from Miller's classic experiment reported in 1953 to the mid-1970s. In fact, one can mark the shift to a less-reducing atmosphere with the Viking Mission to Mars. Although, as Chapter 5 has shown, considerable evidence of an oxidizing early Earth was available before 1976, the discovery of an oxidizing Mars void of life served to focus attention on the question of the oxygen history of Earth.

As might be expected, then, primitive atmosphere experiments will need to be reassessed in the light of evidence that the early Earth and its atmosphere were probably less reducing than first suspected, and possibly even oxidizing. There are signs that this important process of redoing experiments with more plausible atmospheres is underway. A few experiments using more neutral to mildly oxidizing atmospheres were mentioned earlier in this chapter. These experiments have generally yielded products in smaller quantities and less diversity than comparable experiments under more reducing conditions. However, there seems to be no less optimism regarding the prospects that chemical evolution was a near-certain occurrence on this planet.

Endnotes

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6. PLAUSIBILITY AND INVESTIGATOR INTERFERENCE

Destruction of essential chemicals dominated our discussion of the prebiotic soup in Chapter 4. Re-examination of the early Earth and its atmosphere in Chapter 5 shows it would have been far less reducing in character, and less conducive to abiogenic synthesis than previously imagined. If the theory of abiogenesis is to have any support, then *the burden to demonstrate such support rests squarely with the prebiotic simulation experiments.* And seemingly, reported results from simulation experiments suggest that a wide variety of important precursor chemicals would have existed in substantial concentrations in primitive water basins. Yet this contrasts sharply with the view presented in Chapter 4. Why the discrepancy? The answer becomes clear upon examining the details of prebiotic simulation experiments.

We propose in this chapter to evaluate various kinds of prebiotic simulation experiments (Chapter 3) and their associated techniques. Each of these techniques will be briefly discussed and for each some assessment of its geochemical plausibility will be offered. We provide this to point out the need for criteria for the acceptable role of the investigator in prebiotic simulation experiments. We will then arrange these experimental techniques on a scale of increasing geochemical implausibility. This ordering necessarily involves questions of judgment and may be revised as time goes on.

Evaluation of Various Types of Simulation Experiments and Techniques

Simulation Experiments Using Ultraviolet Light

The successful synthesis of amino acids and other organic compounds using ultraviolet light has been reported in laboratory simulation experiments. These experiments used short-wavelength (i.e., < 2000 Å) ultraviolet light but excluded the long-wavelength (i.e., > 2000 Å)[1] UV which is so effective in destruction.[2] Although this practice is effective, it is dubious as a prebiotic simulation procedure, since the full solar spectrum would have irradiated the primitive Earth.

Photosensitization

As we discussed in Chapter 3, photosensitization provides a means of using the plentiful longer-wavelength ultraviolet light (2000–3000 Å) to bring about photochemical reaction of the "primitive" reducing atmospheric gases. Mercury vapor, formaldehyde, and hydrogen sulfide gas all have served as photosensitizing agents, absorbing energy and transferring it to these primitive gases, thus enabling reactions to take place in the longer spectral region.[3]

A photosensitizer with an appropriate absorption spectrum can provide further benefits, too. For example, hydrogen sulfide can provide a protective shield against long-wavelength photodestruction of amino acids, as well as other biomonomers and essential intermediates produced in the atmosphere.[4] This protective shield operates because light in the range 2000–2600 Å is absorbed by hydrogen sulfide when it is present in sufficient concentration. Vulnerable organic molecules which otherwise would absorb below 2600 Å are thus protected.[5] Such a process operating in the primitive reducing atmosphere would have promoted the production and accumulation of vital precursors.

It is doubtful, however, that formaldehyde or hydrogen sulfide could have reached levels of concentration required to serve as early Earth photosensitizers or to protect organic products from photodecomposition. For as it turns out, formaldehyde and hydrogen sulfide are themselves vulnerable to photodestruction, as previously mentioned, and no suitable shield appears to exist for them.

Of the two, hydrogen sulfide would be the most attractive candidate to serve the dual role of photosensitizer and shield. It would, however, have been photolyzed to free sulfur and hydrogen in only 10,000 years,[6] so there would need to be a mechanism for replenishing hydrogen sulfide. (Volcanoes do produce this gas, but whether the quantities would have been sufficient has not been determined.)

The search for a suitable photosensitizer continues, but the field of candidates is limited. It must be assumed that such an agent was one of the simple gaseous components of the primitive atmosphere, or a derivative from it. Thus, mercury vapor could not possibly have served generally as a photosensitizer on the early Earth, although it might have had some localized application for short periods, as an effluent gas of volcanoes.[7] Photosensitization itself is not called into question, for photosynthesis uses chlorophyll as a photosensitizer, enabling plants to utilize sunlight. But the use of this technique as a simulation procedure depends on geochemically implausible conditions. The pivotal question concerns whether system conditions necessary for photosensitization and shielding could reasonably obtain on an early Earth.

Other Energy Sources: Heat

Experiments using heat, electrical discharge, and shock waves are also subject to criticism. Serious questions must be raised about the geological relevance of the heat experiments. For example, we do not find local high-temperature (> 150°C) regions on Earth except for geologically brief periods of time. Volcanoes, fumaroles, steam spouts, etc. have been cited as heat energy sources, but they are generally too far apart geographically, and do not last over geologically significant times.[8] Scientists who accept heat as a legitimate source have usually argued that protocells at least originated very quickly and so brief geologic periods of energy input are all that are required. A continuous supply of intermediate chemicals was needed, however, until photosynthesis developed.[9] For this reason, it is believed by most scientists that only general sources of energy (e.g., ultraviolet light) could have been effective for the origin of life.

It has also been suggested that wind blowing the primitive gases over hot lava (500–1000°C) would subject them to high temperatures for brief periods. In the unconfined, natural situation, however, slightly warmed gases would rise quickly away from the hot lava, and thus never approach the temperature needed for reaction.[10] In more confined settings, such as pipes or fissures in rocks, the objection is that any organic molecules formed there would remain in the heat, and such sustained heating of organic materials would destroy them.[11]

Lightning

Electrical discharge experiments have attempted to simulate lightning on the early Earth. The actual lightning leader is much too hot (i.e., 20,000°K) for effective synthesis, however, immediately destroying any products.[12] Much milder electrical discharges, the so-called corona discharges from pointed objects, have also been simulated in experiments. The energy density used in these experiments is, however, nine orders of magnitude too great to be called a simulation of natural phenomena.[13] In more imaginable terms, the Miller spark experiment adds so much energy that "two days of sparking represent an energy input into the system comparable to some 40 million years on the surface of the primitive Earth."[14] Another geologically implausible feature of electrical discharge experiments is the fact that they are closed systems containing as much as 75% hydrogen.[15] (While they are begun with more plausible hydrogen concentrations, hydrogen is generated in the reaction and not allowed to escape as it would from an open system.)

Traps

All prebiotic heat,[16] electrical discharge,[17] and ultraviolet light[18] (including photosensitization) experiments use traps. Traps allow for greater yields of product from equilibrium reactions in which dissolution would otherwise far outweigh synthesis (i.e., $K_{eq} << 1$).[19] Traps function by continually removing the small fraction of product formed by the reactions. As products are removed from the zone of their formation, additional reaction is continuously required to reestablish equilibrium. In this way, reactions can be productively prolonged until one of the reactants is finally consumed.

This technique functions in accordance with Le Chatelier's Principle, which states that when a stress is applied to a chemical reaction at equilibrium, in this case by the trap, the reaction will shift in the direction that relieves the stress and reestablishes equilibrium. Like the practice of concentrating chemical reactants, this technique is a legitimate means of collapsing time to manageable amounts.

This removal process also shields the products from subsequent destruction by the energy source which produced them. However, Carl Sagan has aptly commented on this shielding effect in the experiments:

> The problem we're discussing is a very general one. We use energy sources to make organic molecules. It is found that the same energy sources can destroy these organic molecules. The organic chemist has an understandable preference for removing the reaction products from the energy source before they are destroyed. But when we talk of the origin of life, I think we should not neglect the fact that degradation occurs as well as synthesis, and that the course of reaction may be different if the products are not preferentially removed. In reconstructing the origin of life, we have to *imagine reasonable scenarios which somehow avoid this difficulty.*[20] [emphasis added]

But even a brief scanning of published papers and symposium addresses on the topic demonstrates that there is no unanimity concerning such "reasonable scenarios." Instead, rebuttals and rejoinders to proposed solutions abound. Without reviewing the particulars of this dispute we simply note that it has been suggested that traps simulate a natural mechanism whereby rain washed these vital precursor heat, shock-wave, photo- and electro-products down to the ocean, where they were protected from the destructive rays of solar ultraviolet. How were these chemicals transported safely to the sea? It has been hypothesized that hydrogen sulfide gas, formaldehyde, mercury vapor, or some other photosensitizer was present in sufficient quantities in the primitive atmosphere (despite criticisms of photosensitizers discussed earlier) to allow substantial long-wavelength ultraviolet synthesis. Since long-wavelength UV could penetrate to great atmospheric depths, this shifts the zone of synthesis for amino acids and other vulnerable organic molecules closer to the ocean surface. From there they would not have had far to flee to the ocean's protection.[21] Heat, electrical discharge, and shock-wave syntheses would also have been operative at lower altitudes. Thus, transport time would already be short for organic compounds produced by these sources. If appropriate photosensitizers were present to intercept the destructive ultraviolet, as the hypothesis suggests, organic compounds synthesized in the atmosphere would be further protected, giving them an even greater chance for survival.

In spite of these factors it is not at all clear that the ocean would have provided the shielding function of a trap. Laboratory traps are not usually exposed to long-wavelength ultraviolet light, which would be the case for the ocean, where UV light would penetrate some tens of meters beneath the surface.[22] Furthermore, ocean currents periodically bring to the surface even the deep water, thus exposing its organic contents to destructive ultraviolet light. Because of this it would seem that the ocean would have had much less in common with a trap than is usually suggested.

The Concerto Effect

Laboratory simulation experiments are usually carried out by employing one of various energy sources in isolation. This is a legitimate procedure, since what is sought is the relative effect of each energy source. It is true, too, that the total effect is merely the sum of the effects of isolated energy sources. What often gets ignored, however, is that not only are the synthetic effects summed, but the destructive effects also. As we saw in Chapter 4, these energy sources act together or in concert in the natural situation, both in synthesis and destruction of organic compounds.

One energy source destroys what another source produces. Destruction predominates!

Protection from energy sources is not the only concern. Many laboratory experiments use carefully selected, highly purified, and often concentrated reactants in solutions isolated from other constituents of the soup mixture. The practice of using concentrated chemicals is based on the well-known "law of mass action," which simply states that the rate of a chemical reaction is proportional to the concentration of the reacting substances. In other words, if a chemical reaction occurs slowly in dilute solution (viz., the primitive ocean), it will occur much more rapidly in concentrated solution (viz., the investigator's flask). In this way, investigators seek to compress into manageable laboratory time chemical reactions that normally would have taken millions of years.[23] The reactions are not thereby altered, but only hastened. There is merit to this practice, then, even if natural concentrating mechanisms were not effective on the early Earth. Many other features of laboratory simulation techniques, however, are suspect when viewed against the backdrop of Chapter 4.

Isolated Reactants

Practically all simulated ocean experiments reported in the scientific literature have been based on the assumption that if two or three chemicals react when isolated from the soup mixture, they will also react in the same way in the presence of diverse chemicals in the soup.

This assumption is seen in part of a discussion recorded in the *Proceedings of the First Conference on Origins of Life*, a meeting held in 1967.[24] Alex Rich asked Leslie Orgel whether he or others had "tried what I have called syntheses in the whole: That is to say, you have a spark discharge, a handful of sand, and lots of miscellaneous debris, and then you look for the production of cytosine, uracil, and so on."[25] Orgel responded: "This is the opposite of what we are trying to do. We believe you should learn the kinetics of each step, and when you think you understand it adequately, then try to put the thing together. We have not really gone to this later stage yet. We can get as far as purines quite easily. Sooner or later someone should do a giant experiment to try to do all the syntheses simultaneously, but I think it would be foolish to start that way."[26]

As we saw in Chapter 3, it is part of a general operating procedure to perform lab experiments which give some fair chance of disentangling the many individual reactions that would occur in the soup, to provide a reasonable way to discover reaction mechanisms and pathways.

In spite of the fact that the procedure of isolating reactants is almost universally used and assumed to be valid, for all practical purposes this assumption is false in the general case. It is false because it overlooks the synergism of multiple reactions, the Concerto Effect. A mixture has a characteristic behavior of its own; it is not the simple sum of its individual components.[27] All components in a mixture have definite affinities for reacting with each other. Consequently, *soup mixture reactions do not equal the sum of the individual isolated reactions.* This has been seen in a great deal of the discussion in Chapter 4 about destructive interactions in the soup, and the scavenging mechanisms that "sweep clean" water basins of essential organic compounds. To state the case in general terms, substance A might react with substance B when isolated from substances C, D, and E. When all these substances are mixed together, however, competing reactions can be envisioned which assure that virtually no product accumulates from the reaction between A and B. Also, the reaction between A and B may begin as it would in isolation, only to be interrupted at some later step. Simulation experiments have thus produced some products which conceivably would never occur in the primitive soup.

To illustrate, consider whether freon (e.g., dichlorodifluoromethane) ever existed on this planet before a chemist synthesized it in a laboratory in the twentieth century. It was of course possible, and a few molecules conceivably formed sometime in terrestrial history. In the practical sense, however, freon owes its existence to investigator intervention—the careful guidance of reactions down a specified chemical pathway.

Furthermore, on a primitive Earth many chemicals would have been present that are usually absent in primitive atmosphere experiments. For

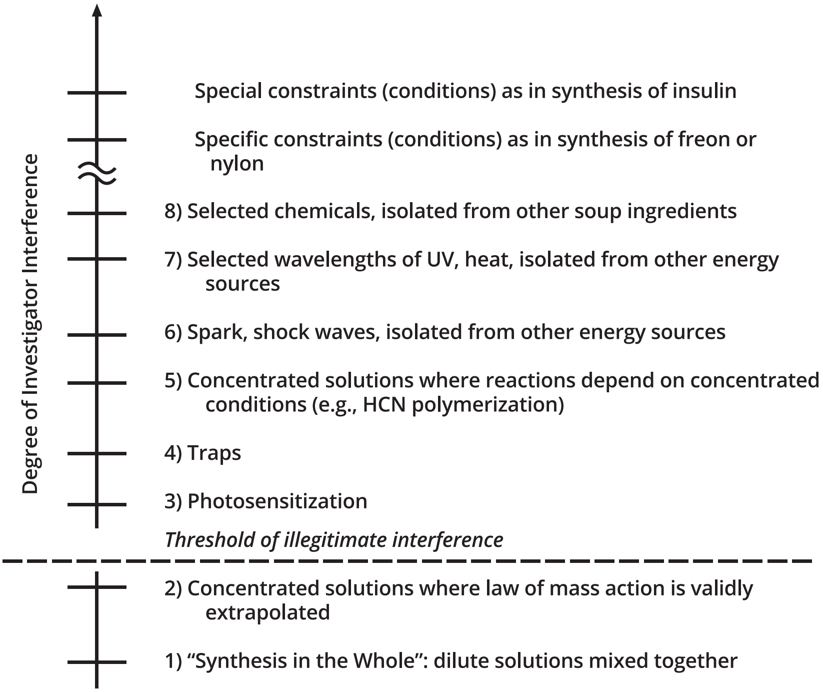

Figure 6-1. Geochemical plausibility scale for evaluating prebiotic simulation experiments.

Experimental techniques (conditions) are arranged according to the degree of investigator interference. At some point along the scale investigator involvement reaches a threshold, beyond which investigator interference is illegitimate.

example, aldehydes, including reducing sugars, would have been present, but these are not identified as products in primitive atmosphere simulation experiments. As a result, destructive interactions with amino acids are obviated and amino acids accumulate.[28] This use of selected chemicals in simulation experiments is highly artificial, and creates a certain unrealism in our expectations of the early Earth. In other words, when considering whether the ocean could have served as a trap, we must take into account the Concerto Effect, according to which the interaction of matter and energy must be considered synergistically.

Developing a Scale of Geochemical Plausibility

On the basis of the discussion here and in Chapter 4, we infer that the various simulation experiments can be ranked according to their geochemical plausibility (see Figure 6-1). We begin with the experimental reaction system of dilute solutions mixed together for a "synthesis in the whole" where the Concerto Effect is operative. This should form the basement of the scale, indicating the greatest geochemical plausibility of the various experiments examined. Next, the use of more concentrated solutions where the law of mass action would apply by extrapolation is only slightly less plausible than "Synthesis in the Whole."

Since it is conceivable that some as yet undiscovered mechanism worked to maintain hydrogen sulfide concentrations in the atmosphere, and since that alone would render photosensitization plausible, we place photosensitization next on the scale. It is certainly more plausible than using traps, for example, which would have required several gratuitous factors working simultaneously on the early Earth. More implausible still are those experiments which depend on conditions of higher concentration of reacting substances, e.g., HCN polymerization experiments, since there is greater question as to the existence of natural concentrating mechanisms.

Continuing up the scale, we come to spark and shock-wave experiments, each used in isolation from other energy sources. We rank these experiments more implausible than those whose success is dependent on higher concentration of chemicals, because no conceivable natural means for isolating energy sources is known. Use of both heat and selected wavelengths of UV light is more implausible still. Not only is there the lack of means for isolating them from other energy sources, but greater doubt arises about their geochemical plausibility. It may be argued that using energy in spark experiments several orders of magnitude greater than could have existed on the early Earth merely "speeds up" the process. No comparable argument applies for heat. For example, increasing temperature to 1000°C not only accelerates reaction rates, but destroys organic products. In the case of ultraviolet light, there is no natural filter known that would justify use of selected wavelengths (i.e., < 2000 Å) of light while excluding the longer wavelengths more destructive to some essential organic compounds.

Finally, to indicate greatest geochemical implausibility, we put experiments using selected chemicals, isolated from other soup ingredients, at the top of the scale. It is difficult to tell whether use of selected wavelengths of UV is more plausible than the use of isolated chemicals. In any case, we believe both are very implausible conditions. It does seem fairly clear that experiments number 1 and 2 are definitely acceptable prebiotic experiments, experiments number 3 through 6 probably unacceptable, and experiments number 7 and 8 definitely unacceptable.

Determining Acceptable Investigator Involvement

When does experimenter interference become illegitimate? As basic as this question is to the discussion of simulation experiments, it is very seldom mentioned as a problem. (A happy exception is Orgel and Lohrmann.[29]) Even when it is recognized, as with the use of high temperature and exotic chemicals, the discussion proceeds without any agreed-on criteria about what constitutes a legitimate simulation experiment. As a result, the discussion is surrounded by controversy. Throughout Chapter 4 we saw data showing that a wide discrepancy exists between plausible geochemical conditions and the conditions used in prebiotic simulation experiments. It is too radical to suggest that such experiments are without value. Their true value is difficult to assess, however.

Since all experiments are performed by an experimenter, they must involve *investigator intervention*. Yet experiments must be disqualified as prebiotic simulations when a certain class of investigator influence is *crucial* to their success. This is seen by analogy to the generally held requirement that no outside or supernatural agency was allowed to enter nature at the time of life's origin, was crucial to it, and then withdrew from history.[30] We can apply this principle through a careful extension of the analogy. In the preparation of a prebiotic simulation experiment, the investigator creates the setting, supplies the aqueous medium, the energy, and the chemicals, and establishes the boundary conditions. This activity produces the general background conditions for the experiment, and while it is crucial to the success of the experiment, it is *quite legitimate* because it simulates plausible early Earth conditions. The interference of the investigator becomes *crucial in an illegitimate sense*, however, wherever laboratory conditions are not warranted by analogy to reliably plausible features of the early Earth itself.

Thus the illegitimate intervention of the investigator is directly proportional to the geochemical implausibility of the condition arising from experimental design and/or the investigator's procedure, the illegitimate interference being greatest when such plausibility is missing altogether.

With this in mind, it seems reasonable to suggest that permissible interference by the investigator would include developing plausible design features of the experiment, adjusting the initial reaction mixture, beginning the input of free energy to drive the reaction at the outset, and performing whatever minimal disturbance to the system is necessary to withdraw portions of the reaction products at various stages for analysis.

Usually, in laboratory experiments, an experimenter employs a host of manipulative interventions in an effort to guide natural processes down specific, nonrandom chemical pathways. In other words it is the character of the constraint that determines the result. In some chemical syntheses, for example, it may be necessary to combine reactants in a particular order, or vary the rates of addition in order to control temperature, to adjust pH at a crucial color change, to remove products of reaction after ten minutes instead of twenty minutes, etc., etc. Such manipulations are the hallmark of intelligent, exogenous interference and *should not be employed in any prebiotic experiment.*

The arrangement of experimental techniques (conditions) in Figure 6-1 represents a scale or continuum of investigator interference. At some point on the scale, a degree of implausibility is reached where the experiment can no longer be considered acceptable. Beyond that point, there is no analogy between the techniques and reliably plausible prebiotic conditions. The experimenter who deviates from plausible conditions is like an actor who has forgotten his lines and begins to *ad lib*. Such techniques constitute illegitimate interference, and cannot be given the same status as those lying within the threshold of acceptability.

In light of our study, we draw the line of legitimate interference between 2 and 3, i.e., between experiments using concentrated chemicals where the law of mass action is validly extrapolated and experiments using photosensitization. Both the relative ordering and the drawing of the line of acceptable interference are tentative. The principal purpose in presenting this scale, however, is to emphasize how important it is that criteria for experiment acceptability be established.

Summary and Conclusion

Summarizing the above discussion, we state our view that for each of the experimental techniques (conditions) listed as being above the line of crucial but acceptable interference, the investigator has played a highly significant but illegitimate role in experimental success. Brooks and Shaw have commented on this after a review of abiotic experiments:

> These experiments... claim abiotic synthesis for what has in fact been produced and designed by highly intelligent and very much biotic man.[31]

In other words, for each of the unacceptable experimental techniques, the investigator has established experimental constraints, imposing intelligent influence upon a supposedly "prebiotic Earth." Where this informative intervention of the investigator is ignored, the illusion of prebiotic simulation is fostered. This unfortunate state of affairs will continue until the community of origin-of-life researchers agree on criteria for experiment acceptability.

If the techniques representing investigator interference are to be afforded the status of valid simulation, the burden must remain with the investigators to demonstrate their plausibility. This is nothing more than the demand of good science.

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7. THERMODYNAMICS OF LIVING SYSTEMS

It is widely held that in the physical sciences the laws of thermodynamics have had a unifying effect similar to that of the theory of evolution in the biological sciences. What is intriguing is that the predictions of one seem to contradict the predictions of the other. The second law of thermodynamics suggests a progression from order to disorder, from complexity to simplicity, in the physical universe. Yet biological evolution involves a hierarchical progression to increasingly complex forms of living systems, seemingly in contradiction to the second law of thermodynamics. Whether this discrepancy between the two theories is only apparent or real is the question to be considered in the next three chapters. The controversy, which is evident in an article published in the *American Scientist*[1] along with the replies it provoked, demonstrates that the question is still a timely one.

The First Law of Thermodynamics

Thermodynamics is an exact science which deals with energy. Our world seethes with transformations of matter and energy. Be these mechanical or chemical, the first law of thermodynamics—the principle of the Conservation of Energy—tells us that the total energy of the universe or any isolated part of it will be the same after any such transformation as it was before. A major part of the science of thermodynamics is accounting—giving an account of the energy of a system that has undergone some sort of transformation. Thus, we derive from the first law of thermodynamics that the change in the energy of a system (ΔE) is equal to the work done on (or by) the system (ΔW) and the heat flow into (or out of) the system (ΔQ). Mechanical work and energy are interchangeable, i.e., energy may be converted into mechanical work as in a steam engine, or mechanical work can be converted into energy as in the heating of a cannon which occurs as its barrel is bored. In mathematical terms (where the terms are as previously defined):

$$\Delta E = \Delta Q + \Delta W \qquad 7\text{-}1$$

The Second Law of Thermodynamics

The second law of thermodynamics describes the flow of energy in nature in processes which are irreversible. The physical significance of the second law of thermodynamics is that the energy flow in such processes is always toward a more uniform distribution of the energy of the universe. Anyone who has had to pay utility bills for long has become aware that too much of the warm air in his or her home during winter escapes to the outside. This flow of energy from the house to the cold outside in winter, or the flow of energy from the hot outdoors into the air-conditioned home in the summer, is a process described by the second law of thermodynamics. The burning of gasoline, converting energy-"rich" compounds (hydrocarbons) into energy-"lean" compounds, carbon dioxide (CO_2) and water (H_2O), is a second illustration of this principle.

The concept of entropy (S) gives us a more quantitative way to describe the tendency for energy to flow in a particular direction. The entropy change for a system is defined mathematically as the flow of energy divided by the temperature, or

$$\Delta S \geqslant \frac{\Delta Q}{T} \qquad 7\text{-}2$$

where ΔS is the change in entropy, ΔQ is the heat flow into or out of a system, and T is the absolute temperature in degrees Kelvin (K).[2]

A Driving Force

If we consider heat flow from a warm house to the outdoors on a cold winter night, we may apply Equation 7-2 as follows:

$$\Delta S_T = \Delta S_{house} + \Delta S_{outdoors} \geqslant -\frac{\Delta Q}{T_1} + \frac{\Delta Q}{T_2} \qquad 7\text{-}3$$

where ΔS_T is the total entropy change associated with this irreversible heat flow, T_1 is the temperature inside the house, and T_2 is the temperature outdoors. The negative sign of the first term notes loss of heat from the house, while the positive sign on the second term recognizes heat gained by the outdoors. Since it is warmer in the house than outdoors ($T_1 > T_2$), the total entropy will increase ($\Delta S_T > 0$) as a result of this heat flow. If we turn off the heater in the house, it will gradually cool until the temperature approaches that of the outdoors, i.e., $T_1 = T_2$. When this occurs, the entropy change (ΔS) associated with heat flow (ΔQ) goes to zero. Since there is no further driving force for heat flow to the outdoors, it ceases; equilibrium conditions have been established.

As this simple example shows, energy flow occurs in a direction that causes the total energy to be more uniformly distributed. If we think about it, we can also see that the entropy increase associated with such energy flow is proportional to the driving force for such energy flow to occur. The second law of thermodynamics says that the entropy of the universe (or any isolated system therein) is increasing; i.e., the energy of the universe is becoming more uniformly distributed.

It is often noted that the second law indicates that nature tends to go from order to disorder, from complexity to simplicity. If the most random arrangement of energy is a uniform distribution, then the present arrangement of the energy in the universe is nonrandom, since some matter is very rich in chemical energy, some in thermal energy, etc., and other matter is very poor in these kinds of energy. In a similar way, the arrangements of mass in the universe tend to go from order to disorder due to the random motion on an atomic scale produced by thermal energy. The diffusional processes in the solid, liquid, or gaseous states are examples of increasing entropy due to random atomic movements. Thus, increasing entropy in a system corresponds to increasingly random arrangements of mass and/or energy.

Entropy and Probability

There is another way to view entropy. The entropy of a system is a measure of the probability of a given arrangement of mass and energy within it. A statistical thermodynamic approach can be used to further quantify the system entropy. High entropy corresponds to high probability. As a random arrangement is highly probable, it would also be characterized by a large entropy. On the other hand, a highly ordered arrangement, being less probable, would represent a lower entropy configuration. The second law would tell us then that events which increase the entropy of the system require a change from more order to less order, or from less random states to more random states. We will find this concept helpful in Chapter 9 when we analyze condensation reactions for DNA and protein.

Clausius,[3] who formulated the second law of thermodynamics, summarizes the laws of thermodynamics in his famous concise statement: "The energy of the universe is constant; the entropy of the universe tends toward a maximum." The universe moves from its less probable current arrangement, one of low entropy, toward its most probable arrangement, one in which the energy of the universe will be more uniformly distributed.

Life and the Second Law of Thermodynamics

How does all of this relate to chemical evolution? Since the important macromolecules of living systems (DNA, protein, etc.) are more energy-rich than their precursors (amino acids, heterocyclic bases, phosphates, and sugars), classical thermodynamics would predict that such macromolecules will not spontaneously form. Roger Caillois has recently drawn this conclusion in saying, "Clausius and Darwin cannot both be right."[4] This prediction of classical thermodynamics has, however, merely set the stage for refined efforts to understand life's origin.

Harold Morowitz[5] and others have suggested that the Earth is not an isolated system, since it is open to energy flow from the sun. Nevertheless, one cannot simply dismiss the problem of the origin of organization and complexity in biological systems by a vague appeal to open-system, non-equilibrium thermodynamics. The mechanisms responsible for the emergence and maintenance of coherent (organized) states must be defined.

To clarify the role of mass and energy flow through a system as a *possible* solution to this problem, we will look in turn at the thermodynamics of (1) an isolated system, (2) a closed system, and (3) an open system. We will then discuss the application of open-system thermodynamics to living systems. In Chapter 8 we will apply the thermodynamic concepts presented in this chapter to the prebiotic synthesis of DNA and protein. In Chapter 9 this theoretical analysis will be used to interpret the various prebiotic synthesis experiments for DNA and protein, suggesting a physical basis for the uniform lack of success in synthesizing these crucial components for living cells.

Isolated Systems

An isolated system is one in which neither mass nor energy flows in or out. To illustrate such a system, think of a perfectly insulated thermos bottle (no heat loss) filled initially with hot tea and ice cubes. The total energy in this isolated system remains constant but the distribution of the energy changes with time. The ice melts and the energy becomes more uniformly distributed in the system. The initial distribution of energy into hot regions (the tea) and cold regions (the ice) is an ordered, nonrandom arrangement of energy, one not likely to be maintained for very long. By our previous definition, then, we may say that the entropy of the system is initially low but gradually increases with time. Furthermore, the second law of thermodynamics says the entropy of the system will continue to increase until it attains some maximum value, which corresponds to the most probable state for the system, usually called equilibrium.

In summary, isolated systems always maintain constant total energy while tending toward maximum entropy, or disorder. In mathematical terms

$$\frac{\Delta E}{\Delta t} = 0$$

(isolated system)

$$\frac{\Delta S}{\Delta t} \geqslant 0 \tag{7-4}$$

where ΔE and ΔS are the changes in the system energy and system entropy respectively, for a time interval Δt. Clearly the emergence of order of any kind in an isolated system is not possible. The second law of thermodynamics says that an isolated system always moves in the direction of maximum entropy and, therefore, disorder.

It should be noted that the process just described is irreversible in the sense that once the ice is melted, it will not reform in the thermos. As a matter of fact, natural decay and the general tendency toward greater disorder are so universal that the second law of thermodynamics has been appropriately dubbed "time's arrow."[6]

Closed Systems Near Equilibrium

A closed system is one in which the exchange of energy with the outside world is permitted but the exchange of mass is not. Along the boundary between the closed system and the surroundings, the temperature may be different from the system temperature, allowing energy flow into or out of the system as it moves toward equilibrium. If the temperature along the boundary is variable (in position but not time), then energy will flow through the system, maintaining it some distance from equilibrium. We will discuss closed systems near equilibrium first, followed by a discussion of closed systems removed from equilibrium next.

If we combine the first and second laws as expressed in Equations 7-1 and 7-2 and replace the mechanical work term W by $-P\Delta V$,[7] where P is pressure and ΔV is volume change, we obtain

$$\Delta S \geqslant \frac{\Delta E + P\Delta V}{T} \tag{7-5}$$

Algebraic manipulation gives

$$\Delta E + P\Delta V - T\Delta S \leqslant 0 \text{ or } \Delta G \leqslant 0$$

where

$$\Delta G = \Delta E + P\Delta S - T\Delta S \qquad 7\text{-}6$$

The term on the left side of the inequality in Equation 7-6 is called the change in the Gibbs free energy (ΔG). It may be thought of as a thermodynamic potential which describes the tendency of a system to change—e.g., the tendency for phase changes, heat conduction, etc. to occur. If a reaction occurs spontaneously, it is because it brings a decrease in the Gibbs free energy ($\Delta G < 0$). This requirement is equivalent to the requirement that the entropy of the universe increase. Thus, like an increase in entropy, a decrease in Gibbs free energy simply means that a system and its surroundings are changing in such a way that the energy of the universe is becoming more uniformly distributed.

We may summarize, then, by noting that the second law of thermodynamics requires

$$\frac{\Delta G}{\Delta t} \leqslant 0 \qquad \text{(closed system)} \qquad 7\text{-}7$$

where Δt indicates the time period during which the Gibbs free energy changed.

The approach to equilibrium is characterized by

$$\frac{\Delta G}{\Delta t} \longrightarrow 0 \qquad \text{(closed system)} \qquad 7\text{-}8$$

The physical significance of Equation 7-7 can be understood by rewriting Equations 7-6 and 7-7 in the following form:

$$\frac{\Delta S}{\Delta t} - \left[\frac{1}{T}\left(\frac{\Delta E}{\Delta t} + \frac{P\Delta V}{\Delta t}\right)\right] \geqslant 0$$

or

$$\frac{\Delta S}{\Delta t} - \frac{1}{T}\frac{\Delta H}{\Delta t} \geqslant 0 \qquad 7\text{-}9$$

and noting that the first term represents the entropy change due to processes going on within the system and the second term represents the entropy change due to exchange of mechanical and/or thermal energy with the surroundings. This simply guarantees that the sum of the entropy change in the system and the entropy change in the surroundings will be greater than zero; i.e., the entropy of the universe must increase. For the isolated system, $\Delta E + P\Delta V = 0$ and Equation 7-9 reduces to Equation 7-4.

A simple illustration of this principle is seen in phase changes such as water transforming into ice. As ice forms, energy (80 calories/gram) is liberated to the surroundings. The change in the entropy of the system as the amorphous water becomes crystalline ice is -0.293 entropy units (eu) per degree Kelvin (K). The entropy change is negative because the thermal and configuration[8] entropy (or disorder) of water is greater than that of ice, which is a highly ordered crystal. Thus, the thermodynamic conditions under which water will transform to ice are seen from Equation 7-9 to be:

$$-0.293 - \left(\frac{-80}{T}\right) > 0 \tag{7-10a}$$

or

$$T \leqslant 273K \tag{7-10b}$$

For condition of $T < 273°K$ energy is removed from water to produce ice, and the aggregate disordering of the surroundings is greater than the ordering of the water into ice crystals. This gives a net increase in the entropy of the universe, as predicted by the second law of thermodynamics.

It has often been argued by analogy to water crystallizing to ice that simple monomers may polymerize into complex molecules such as protein and DNA. The analogy is clearly inappropriate, however. The $\Delta E + P\Delta V$ term (Equation 7-9) in the polymerization of important organic molecules is generally positive (5 to 8 kcal/mole), indicating the reaction can never spontaneously occur at or near equilibrium.[9] By contrast the $\Delta E + P\Delta V$ term in water changing to ice is a negative, -1.44 kcal/mole, indicating the phase change is spontaneous as long as $T < 273°K$, as previously noted. The atomic bonding forces draw water molecules into an orderly crystalline array when the thermal agitation (or entropy driving force, $T\Delta S$) is made sufficiently small by lowering the temperature. Organic monomers such as amino acids resist combining at all at any temperature, however, much less in some orderly arrangement.

Morowitz[10] has estimated the increase in the chemical bonding energy as one forms the bacterium *Escherichia coli* from simple precursors to be an average of 0.27 eV/atom for the 2×10^{10} atoms in a single bacterial cell. This would be thermodynamically equivalent to having water in your bathtub spontaneously heat up to 360°C, happily a most unlikely event. He goes on to estimate the probability of the spontaneous formation of one such bacterium in the entire universe in five billion years *under equilibrium conditions* to be $10^{-10^{11}}$. Morowitz summarizes the significance of this result by saying that "if equilibrium processes alone were at work, the largest possible fluctuation in the history of the universe is likely to have been no larger than a small peptide."[11] Nobel Laureate I. Prigogine et al. have stated, with reference to the same problem:

> The probability that at ordinary temperatures a macroscopic number of molecules is assembled to give rise to the highly ordered structures and to the coordinated functions characterizing living organisms is vanishingly small. The idea of spontaneous genesis of life in its present form is therefore highly improbable, even on the scale of billions of years during which prebiotic evolution occurred.[12]

It seems safe to conclude that systems near equilibrium (whether isolated or closed) can *never* produce the degree of complexity intrinsic in living systems. Instead, they will move spontaneously toward maximizing entropy, or randomness. Even the postulate of long time-periods does not solve the problem, as "time's arrow" (the second law of thermodynamics) points in the wrong direction; i.e., toward equilibrium. In this regard, H. F. Blum has observed:

> The second law of thermodynamics would have been a dominant directing factor in this case [of chemical evolution]; the reactions involved tending always toward equilibrium, that is, toward less free energy, and, in an inclusive sense, greater entropy. From this point of view the lavish amount of time available should only have provided opportunity for *movement in the direction of equilibrium*.[13] (Emphasis added.)

Thus, reversing "time's arrow" is what chemical evolution is all about, and this will not occur in isolated or closed systems near equilibrium.

The possibilities are potentially more promising, however, if one considers a system subjected to energy flow which may maintain it far from equilibrium, and its associated disorder. Such a system is said to be a *constrained* system, in contrast to a system at or near equilibrium which is unconstrained. The possibilities for ordering in such a system will be considered next.

Closed Systems Far from Equilibrium

Energy flow through a system is the equivalent to doing work continuously on the system to maintain it some distance from equilibrium. Nicolis and Prigogine[14] have suggested that the entropy change (ΔS) in a system for a time interval (Δt) may be divided into two components.

$$\Delta S = \Delta S_e + \Delta S_i \qquad 7\text{-}11$$

where ΔS_e is the entropy flux due to energy flow through the system, and ΔS_i is the entropy production inside the system due to irreversible processes such as diffusion, heat conduction, heat production, and chemical reactions. We will note when we discuss open systems in the next section that ΔS_e includes the entropy flux due to mass flow through the system as well. The second law of thermodynamics requires

$$\Delta S_i \geqslant 0 \qquad 7\text{-}12$$

In an isolated system, $\Delta S_e = 0$ and Equations 7-11 and 7-12 give

$$\Delta S = \Delta S_i \geqslant 0 \qquad 7\text{-}13$$

Unlike ΔS_i, ΔS_e in a closed system does not have a definite sign, but depends entirely on the boundary constraints imposed on the system.

The total entropy change in the system can be negative (i.e., ordering within system) when

$$\Delta S_e \leqslant 0 \text{ and } | \Delta S_e | > \Delta S_i \qquad \text{7-14}$$

Under such conditions a state that would normally be highly improbable under equilibrium conditions can be maintained indefinitely. It would be highly unlikely (i.e., statistically just short of impossible) for a disconnected water heater to produce hot water. Yet when the gas is connected and the burner lit, the system is constrained by energy flow and hot water is produced and maintained indefinitely as long as energy flows through the system.

An open system offers an additional possibility for ordering—that of maintaining a system far from equilibrium via mass flow through the system—which will be discussed in the next section.

Open Systems

An open system is one which exchanges both energy and mass with the surroundings. It is well illustrated by the familiar internal combustion engine. Gasoline and oxygen are passed through the system, combusted, and then released as carbon dioxide and water. The energy released by this mass flow through the system is converted into useful work; namely, torque supplied to the wheels of the automobile. A coupling mechanism is necessary, however, to allow the released energy to be converted into a particular kind of work. In an analogous way the dissipative (or disordering) processes (ΔS_i) within an open system can be offset by a steady supply of energy to provide for ΔS_e type of work. Equation 7-11, applied earlier to closed systems far from equilibrium, may also be applied to open systems. In this case, the ΔS_e term represents the negative entropy, or organizing work done on the system as a result of both energy and mass flow through the system. This work done to the system can move it far from equilibrium, maintaining it there as long as the mass and/or energy flow are not interrupted. This is an essential characteristic of living systems, as will be seen in what follows.

Thermodynamics of Living Systems

Living systems are composed of complex molecular configurations whose total bonding energy is less negative than that of their chemical precursors (e.g., Morowitz's estimate of $\Delta E = 0.27$ eV/atom) and whose thermal and configurational entropies are also less than that of their chemical precursors. Thus, the Gibbs free energy of living systems (see Equation 7-6) is quite high relative to the simple compounds from which they are formed. The formation and maintenance of living systems at energy levels well removed from equilibrium requires continuous work to be done on the system, even as maintenance of hot water in a water heater requires that continuous work be done on the system. Securing this continuous work requires energy and/or mass flow through the system, apart from which the system will return to an equilibrium condition (lowest Gibbs free energy, see Equations 7-7 and 7-8) with the decomposition of complex molecules into simple ones, just as the hot water in our water heater returns to room temperature once the gas is shut off.

In living plants, the energy flow through the system is supplied principally by solar radiation. In fact, leaves provide relatively large surface areas per unit volume for most plants, allowing them to "capture" the necessary solar energy to maintain themselves far from equilibrium. This solar energy is converted into the necessary useful work (negative ΔS_e in Equation 7-11) to maintain the plant in its complex, high-energy configuration by a complicated process called photosynthesis. Mass, such as water and carbon dioxide, also flows through plants, providing necessary raw materials, but not energy. In collecting and storing useful energy, plants serve the entire biological world.

For animals, energy flow through the system is provided by eating high-energy biomass, either plant or animal. The breaking down of this energy-rich biomass, and the subsequent oxidation of part of it (e.g., carbohydrates), provides a continuous source of energy as well as raw materials. If plants are deprived of sunlight or animals of food, dissipation within the system will surely bring death. Maintenance of the complex, high-energy condition associated with life is not possible apart from a continuous source of energy. A source of energy alone is not sufficient, however, to explain the origin or maintenance of living systems. The additional crucial factor is *a means of converting this energy* into the necessary useful work to build and maintain complex living systems from the simple biomonomers that constitute their molecular building blocks.

An automobile with an internal combustion engine, transmission, and drive chain provides the necessary mechanism for converting the energy in gasoline into comfortable transportation. Without such an "energy converter," however, obtaining transportation from gasoline would be impossible. In a similar way, food would do little for a man whose stomach, intestines, liver, or pancreas were removed. Without these, he would surely die even though he continued to eat. Apart from a mechanism to couple the available energy to the necessary work, high-energy biomass is insufficient to sustain a living system far from equilibrium. In the case of living systems such a coupling mechanism channels the energy along specific chemical pathways to accomplish a very specific type of work. We therefore conclude that, given the availability of energy and an appropriate coupling mechanism, the maintenance of a living system far from equilibrium presents no thermodynamic problems.

In mathematical formalism, these concepts may be summarized as follows:

1. The second law of thermodynamics requires only that the entropy production due to irreversible processes within the system be greater than zero; i.e.,

$$\Delta S_i > 0 \qquad 7\text{-}15$$

2. The maintenance of living systems requires that the energy flow through the system be of sufficient magnitude that the negative entropy production rate (i.e., useful work rate) that results be greater than the rate of dissipation that results from irreversible processes going on within the system; i.e.,

$$|\Delta S_e| > \Delta S_i \qquad 7\text{-}16$$

3. The negative entropy generation must be coupled into the system in such a way that the resultant work done is directed toward restoration of the system from the disintegration that occurs naturally and is described by the second law of thermodynamics; i.e.,

$$-\Delta S_e = \Delta S_i \qquad 7\text{-}17$$

where ΔS_e and ΔS_i refer not only to the magnitude of entropy change but also to the specific changes that occur in the system associated with this change in entropy. The coupling must produce not just any kind of ordering but the specific kind required by the system.

While the maintenance of living systems is easily rationalized in terms of thermodynamics, the *origin* of such living systems is quite another matter. Though the Earth is open to energy flow from the sun, the means of converting this energy into the necessary work to build up living systems from simple precursors remains at present unspecified (see Equation 7-17). The "evolution" from biomonomers to fully functioning cells is the issue. Can one make the incredible jump in energy and organization from raw material and raw energy, apart from some means of directing the energy flow through the system? In Chapters 8 and 9 we will consider this question, limiting our discussion to two small but crucial steps in the proposed evolutionary scheme, namely, the formation of protein and DNA from their precursors.

It is widely agreed that both protein and DNA are essential for living systems and indispensable components of every living cell today.[15] Yet they are only produced by living cells. Both types of molecule are much more energy- and information-rich than the biomonomers from which they form. Can one reasonably predict their occurrence given the necessary biomonomers and an energy source? Has this been verified experimentally? These questions will be considered in Chapters 8 and 9.

Endnotes

1. Victor F. Weisskopf, "Views: The Frontiers and Limits of Science: Modern Science is a Powerful Tool for Acquiring Deeper Insights into the World around Us, but We Must Also Follow Other Avenues toward Reality," *American Scientist* 65, no. 4 (1977): 405–411, https://www.jstor.org/stable/27847961?seq=1#page_scan_tab_contents.
2. For a reversible flow of energy such as occurs under equilibrium conditions, the equality sign applies. For irreversible energy flow, the inequality applies.
3. Rudolf Clausius, "Ueber die bewegende Kraft der Wärme und die Gesetze, welche sich daraus für die Wärmelehre selbst ableiten lassen," *Annalen der Physik* 79, no. 4 (1850): 368–397, 500–524, doi:10.1002/andp.18501550403. See English Translation: "On the Moving Force of Heat, and the Laws Regarding the Nature of Heat Itself Which Are Deducible Therefrom," *Philosophical Magazine: Series 4* 2 (1851): 1–21, 102–119. See also Rudolf Clausius, "Über verschiedene für die Anwendung bequeme Formen der Hauptgleichungen der mechanischen Wärmetheorie," *Annalen der Physik* 201, no. 7 (1865): 353–400.
4. R. Caillois, *Coherences Aventureuses* (Paris: Gallimard, 1976).
5. H. J. Morowitz, *Energy Flow in Biology* (New York and London: Academic Press, 1968), 2–3.
6. H. F. Blum, *Time's Arrow and Evolution* (Princeton: Princeton University Press, 1951).
7. Volume expansion ($\Delta V > 0$) corresponds to the system doing work, and therefore losing energy. Volume contraction ($\Delta V < 0$) corresponds to work being done on the system.
8. Configurational entropy measures randomness in the distribution of matter in much the same way that thermal entropy measures randomness in the distribution of energy.
9. If $\Delta E + P\Delta V$ is positive, the entropy term in Eq. 7-9 must be negative due to the negative sign which precedes it. The inequality can only be satisfied by ΔS being sufficiently positive, which implies disordering.
10. Morowitz, *Energy Flow in Biology*, 67.
11. Morowitz, *Energy Flow in Biology*, 68.
12. Ilya Prigogine, Gregoire Nicolis, and Agnes Babloyantz, "Thermodynamics of Evolution," *Physics Today* 25, no. 11 (1972): 23, doi: 10.1063/1.3071090.
13. H. F. Blum, "Perspectives in Evolution," *American Scientist* 43 (1955): 595–610, https://www.jstor.org/stable/27826702.
14. G. Nicolis and I. Prigogine, *Self-Organization in Nonequilibrium Systems* (New York: John Wiley, 1977), 24.
15. S. L. Miller and L. E. Orgel, *The Origins of Life on the Earth* (Englewood Cliffs, New Jersey: Prentice-Hall, 1974), 162–3.

8. Thermodynamics and the Origin of Life

Peter Molton has defined life as "regions of order which use energy to maintain their organization against the disruptive force of entropy."[1] In Chapter 7 it has been shown that energy and/or mass flow through a system can constrain it far from equilibrium, resulting in an increase in order. Thus, it is thermodynamically possible to develop complex living forms, assuming the energy flow through the system can somehow be effective in organizing the simple chemicals into the complex arrangements associated with life.

In existing living systems, the coupling of the energy flow to the organizing "work" occurs through the metabolic motor of DNA, enzymes, etc. This is analogous to an automobile converting the chemical energy in gasoline into mechanical torque on the wheels. We can give a thermodynamic account of how life's metabolic motor works. The origin of the metabolic motor (DNA, enzymes, etc.) itself, however, is more difficult to explain thermodynamically, since a mechanism of coupling the energy flow to the organizing work is unknown for prebiological systems. Nicolis and Prigogine summarize the problem in this way:

> Needless to say, these simple remarks cannot suffice to solve the problem of biological order. One would like not only to establish that the second law ($dS_i \geq 0$) is compatible with a decrease in overall entropy ($dS < O$), but also to indicate the mechanisms responsible for the emergence and maintenance of coherent states.[2]

Without a doubt, the atoms and molecules which compose living cells individually obey the laws of chemistry and physics, including the laws of thermodynamics. The enigma is the origin of so unlikely an organization of these atoms and molecules. The electronic computer provides a striking analogy to the living cell. Each component in a computer obeys the laws of electronics and mechanics. The key to the computer's marvel lies, however, in the highly unlikely organization of the parts which harness the laws of electronics and mechanics. In the computer, this organization was specially arranged by the designers and builders and continues to operate (with occasional frustrating lapses) through the periodic maintenance of service engineers.

Living systems have even greater organization. The problem, then, that molecular biologists and theoretical physicists are addressing is how the organization of living systems could have arisen spontaneously. Prigogine et al. have noted:

> All these features bring the scientist a wealth of new problems. In the first place, one has systems that have evolved spontaneously to extremely organized and complex forms. Coherent behavior is really the characteristic feature of biological systems.[3]

In this chapter we will consider only the problem of the *origin* of living systems. Specifically, we will discuss the arduous task of using simple biomonomers to construct complex polymers such as DNA and protein by means of thermal, electrical, chemical, or solar energy. We will specify the nature and magnitude of the "work"[4] to be done in building DNA and enzymes. In Chapter 9, we will (1) describe the various theoretical models which attempt to explain how the undirected flow of energy through simple chemicals can accomplish the work necessary to produce complex polymers, (2) review the experimental studies that have been conducted to test these models, and (3) summarize the current understanding of this subject.

How can we specify in a more precise way the work to be done by energy flow through the system to synthesize DNA and protein from simple biomonomers? While the origin of living systems involves more than the genesis of enzymes and DNA, these components are essential to any system if replication is to occur. It is generally agreed that natural selection can act only on systems capable of replication. This being the case, the formation of a DNA/enzyme system by processes other than natural selection is a necessary (though not sufficient) part of a naturalistic explanation for the origin of life.[5]

Order vs. Complexity in the Question of Information

Only recently has it been appreciated that the distinguishing feature of living systems is complexity rather than order.[6] This distinction has come from the observation that the essential ingredients for a replicating system—enzymes and nucleic acids—are all information-bearing molecules. In contrast, consider crystals. They are very orderly, spatially periodic arrangements of atoms (or molecules), but they carry very little information. Nylon is another example of an orderly, periodic polymer (a polyamide) which carries little information. Nucleic acids and protein are aperiodic polymers, and this aperiodicity is what makes them able to carry much more information. By definition, then, *a periodic structure has order; an aperiodic structure has complexity*. In terms of information, periodic polymers (like nylon) and crystals are analogous to a book in which the same word or sentence is repeated throughout. The arrangement of "letters" in the book is highly ordered, but the book contains little information, since the information presented—the single word or sentence—is highly redundant.

It should be noted that aperiodic polypeptides or polynucleotides do not necessarily represent meaningful information or biologically useful functions. A random arrangement of letters in a book is aperiodic but contains little if any useful information, since it is devoid of meaning.[7] Only certain sequences of letters correspond to sentences, and only certain sequences of sentences correspond to paragraphs, etc. In the same way only certain sequences of amino acids in polypeptides and bases along polynucleotide chains correspond to useful biological functions.

Thus, informational macromolecules may be described as being aperiodic and in a specified sequence.[8] Orgel notes:

> Living organisms are distinguished by their *specified* complexity. Crystals fail to qualify as living because they lack complexity; mixtures of random polymers fail to qualify because they lack specificity.[9]

Three sets of letter arrangements show nicely the difference between order and complexity in relation to information:

1. An ordered (periodic) and therefore specified arrangement:
THE END THE END THE END THE END[10]
Example: Nylon, or a crystal.

2. A complex (aperiodic) unspecified arrangement:
AGDCBFE GBCAFED ACEDFBG
Example: Random polymers (polypeptides).

3. A complex (aperiodic) specified arrangement:
THIS SEQUENCE OF LETTERS CONTAINS A MESSAGE!
Example: DNA, protein.

Yockey[11] and Wickens[12] develop the same distinction, explaining that "order" is a statistical concept referring to regularity such as might characterize a series of digits in a number, or the ions of an inorganic crystal. On the other hand, "organization" refers to physical systems and the specific set of spatio-temporal and functional relationships among their parts. Yockey and Wickens note that informational macromolecules have a low degree of order but a high degree of specified complexity. In short, the redundant order of crystals cannot give rise to specified complexity of the kind or magnitude found in biological organization; attempts to relate the two have little future.

Information and Entropy

There is a general relationship between information and entropy. This is fortunate because it allows an analysis to be developed in the formalism of classical thermodynamics, giving us a powerful tool for calculating the work to be done by energy flow through the system to synthesize protein and DNA (if indeed energy flow is capable of producing information). The information content in a given sequence of units, be they digits in a number, letters in a sentence, or amino acids in a polypeptide or protein, depends on the minimum number of instructions needed to specify or describe the structure. Many instructions are needed to specify a complex, information-bearing structure such as DNA. Only a few instructions are needed to specify an ordered structure such as a crystal. In this case we have a description of the initial sequence or unit arrangement which is then repeated *ad infinitum* according to the packing instructions.

Orgel[13] illustrates the concept in the following way. To describe a crystal, one would need only to specify the substance to be used and the way in which the molecules were to be packed together. A couple of sentences would suffice, followed by the instructions "and keep on doing the same," since the packing sequence in a crystal is regular. The description would be about as brief as specifying a DNA-like polynucleotide with a random sequence. Here one would need only to specify the proportions of the four nucleotides in the final product, along with instructions to assemble them randomly. The chemist could then make the polymer with the proper composition but with a random sequence.

It would be quite impossible to produce a correspondingly simple set of instructions that would enable a chemist to synthesize the DNA of an *E. coli* bacterium. In this case the sequence matters. Only by specifying the sequence letter-by-letter (about 4,600,000 instructions) could we tell a chemist what to make. Our instructions would occupy not a few short sentences, but a large book instead!

Brillouin,[14] Schrodinger,[15] and others[16] have developed both qualitative and quantitative relationships between information and entropy. Brillouin[17] states that the entropy of a system is given by

$$S = k \ln \Omega \qquad 8\text{-}1$$

where S is the entropy of the system, k is Boltzmann's constant, and Ω corresponds to the number of ways the energy and mass in a system may be arranged.

We will use S_{th} and S_c to refer to the thermal and configurational entropies, respectively. Thermal entropy, S_{th}, is associated with the distribution of energy in the system. Configurational entropy, S_c, is concerned only with the arrangement of mass in the system, and, for our purposes, we shall be especially interested in the sequencing of amino acids in polypeptides (or proteins) or of nucleotides in polynucleotides (e.g., DNA). The symbols Ω_{th} and Ω_c refer to the number of ways energy and mass, respectively, may be arranged in a system. Thus, we may be more precise by writing:

$$S = k \ln \Omega_{th}\Omega_c = k \ln \Omega_{th} + k \ln \Omega_c = S_{th} + S_c \qquad \text{8-2a}$$

where $$S_{th} = k \ln \Omega_{th} \qquad \text{8-2b}$$

and $$S_c = k \ln \Omega_c \qquad \text{8-2c}$$

Determining Information: From a Random Polymer to an Informed Polymer

If we want to convert a random polymer into an informational molecule, we can determine the increase in information (as defined by Brillouin) by finding the difference between the negatives of the entropy states for the initial random polymer and the informational molecule:

$$I = -(S_{cm} - S_{cr}) \qquad \text{8-3a}$$

$$I = S_{cr} - S_{cm} \qquad \text{8-3b}$$

$$= k \ln \Omega_{cr} - k \ln \Omega_{cm} \qquad \text{8-3c}$$

In this equation, I is a measure of the information content of an aperiodic (complex) polymer with a specified sequence, S_{cm} represents the configurational "coding" entropy of this polymer informed with a given message, and S_{cr} represents the configurational entropy of the same polymer for an unspecified or random sequence.[18]

Note that the information in a sequence-specified polymer is maximized when the mass in the molecule could be arranged in many different ways, only one of which communicates the intended message. (There is a large S_{cr} from Equation 8-2c since Ω_{cr} is large, yet $S_{cm} = 0$ from Equation 8-2c since $\Omega_{cm} = 1$.) The information carried in a crystal is small because S_c is small (Equation 8-2c) for a crystal. There simply is very little potential for information in a crystal because its matter can be distributed in so few ways. The random polymer provides an even starker contrast. It bears *no* information because S_{cr}, although large, is equal to S_{cm} (see Equation 8-3b).

In summary, Equations 8-2c and 8-3c quantify the notion that only specified, aperiodic macromolecules are capable of carrying the large amounts of information characteristic of living systems. Later we will calculate "Ω_c" for both random and specified polymers so that the configurational entropy change required to go from a random to a specified polymer can be determined. In the next section we will consider the various components of the total work required in the formation of macromolecules such as DNA and protein.

DNA and Protein Formation

Defining the Work

There are three distinct components of work to be done in assembling simple biomonomers into a complex (or aperiodic) linear polymer with a specified sequence as we find in DNA or protein. The change in the Gibbs free energy, ΔG, of the system during polymerization defines the total work that must be accomplished by energy flow through the system. The change in Gibbs free energy has previously been shown to be

$$\Delta G = \Delta E - P\Delta V - T\Delta S \quad \text{8-4a}$$

or

$$\Delta G = \Delta H - T\Delta S \quad \text{8-4b}$$

where a decrease in Gibbs free energy for a given chemical reaction near equilibrium guarantees an increase in the entropy of the universe as demanded by the second law of thermodynamics.

Now consider the components of the Gibbs free energy (Equation 8-4b) where the change in enthalpy (ΔH) is principally the result of changes in the total bonding energy (ΔE), with the $P\Delta V$ term assumed to be negligible. We will refer to this enthalpy component (ΔH) as the *chemical work*. A further distinction will be helpful. The change in the entropy (ΔS) that accompanies the polymerization reaction may be divided into two distinct components which correspond to the changes in the thermal energy distribution (ΔS_{th}) and the mass distribution (ΔS_c). (See Equation 8-2.) So we can rewrite Equation 8-4b as follows:

$$\underset{\substack{\text{Gibbs}\\ \text{free energy}}}{\Delta G} \quad = \quad \underset{\substack{\text{Chemical}\\ \text{work}}}{\Delta H} \quad - \quad \underset{\substack{\text{Thermal}\\ \text{entropy work}}}{T\Delta S_{th}} \quad - \quad \underset{\substack{\text{Configurational}\\ \text{entropy work}}}{T\Delta S_c} \tag{8-5}$$

It will be shown that polymerization of macromolecules results in a decrease in the thermal and configurational entropies ($\Delta S_{th} < 0$, $\Delta S_c < 0$). These terms effectively increase ΔG, and thus represent additional components of work to be done beyond the chemical work.

Consider the case of the formation of protein or DNA from biomonomers in a chemical soup. For computational purposes it may be thought of as requiring two steps: (1) polymerization to form a chain molecule with an aperiodic but near-random sequence,[19] and (2) rearrangement to an aperiodic, specified information-bearing sequence. The entropy change (ΔS) associated with the first step is essentially all thermal entropy change (ΔS_{th}), as discussed above. The entropy change of the second step is essentially all configurational entropy change (ΔS_c). In fact, as previously noted, the change in configurational entropy "coding" as one goes from a random arrangement (S_{cr}) to a specified sequence (S_{cm}) in a macromolecule is numerically equal to the negative of the information content of the molecule as defined by Brillouin (see Equation 8-3a).

In summary, the formation of complex biological polymers such as DNA and protein involves changes in the chemical energy, ΔH, the thermal entropy, ΔS_{th}, and the configurational entropy, ΔS_c, of the system. Determining the magnitudes of these individual changes using experimental data and a few calculations will allow us to quantify the magnitude of the required work potentially to be done by energy flow through the system in synthesizing macromolecules such as DNA and protein.

Quantifying the Various Components of Work

1. Chemical Work

The polymerization of amino acids to polypeptides (protein) or of nucleotides to polynucleotides (DNA) occurs through condensation reactions. One may calculate the enthalpy change in the formation of a dipeptide from amino acids to be 5–8 kcal/mole for a variety of amino acids, using data compiled by Hutchens.[20] Thus, chemical work must be done on the system to get polymerization to occur. Morowitz[21] has estimated more generally that the chemical work, or average increase in enthalpy, for macromolecule formation in living systems is 16.4 cal/g. Elsewhere in the same book he says that the average increase in bonding energy in going from simple compounds to an *E. coli* bacterium is 0.27 eV/atom. One can easily see that chemical work must be done on the biomonomers to bring about the formation of macromolecules like those that are essential to living systems. By contrast, amino acid formation from simple reducing atmosphere gases (methane, ammonia, water) has an associated enthalpy change (ΔH) of -50 kcal/mole to -250 kcal/mole,[22] which means energy is released rather than consumed. This explains why amino acids form with relative ease in prebiotic simulation experiments. On the other hand, forming amino acids from less-reducing conditions (i.e., carbon dioxide, nitrogen, and water) is known to be far more difficult experimentally. This is because the enthalpy change (ΔH) is positive, meaning energy is required to drive the energetically unfavorable chemical reaction forward.

2. Thermal Entropy Work

Wickens[23] has noted that polymerization reactions will reduce the number of ways the translational energy may be distributed, while generally increasing the possibilities for vibrational and rotational energy. A net decrease results in the number of ways the thermal energy may be distributed, giving a decrease in the thermal entropy according to Equation 8-2b (i.e., $\Delta S_{th} < 0$). Quantifying the magnitude of this decrease in thermal entropy (ΔS_{th}) associated with the formation of a polypeptide or a polynucleotide is best accomplished using experimental results.

Morowitz[24] has estimated that the average decrease in thermal entropy that occurs during the formation of macromolecules of living systems is 0.218 cal/deg-g or 65 cal/g at 298°K. Recent work by Armstrong et al.[25] for nucleotide oligomerization of up to a pentamer indicates ΔH and $-T\Delta S_{th}$ values of 11.8 kcal/mole and 15.6 kcal/mole respectively, at 294°K. Thus the decrease in thermal entropy during the polymerization of the macromolecules of life increases the Gibbs free energy and the work required to make these molecules, i.e., $-T\Delta S_{th} > 0$.

3. Configurational Entropy Work

Finally, we need to quantify the configurational entropy change (ΔS_c) that accompanies the formation of DNA and protein. Here we will not get much help from standard experiments in which the equilibrium constants are determined for a polymerization reaction at various temperatures. Such experiments do not consider whether a specific sequence is achieved in the resultant polymers, but only the concentrations of randomly sequenced polymers (i.e., polypeptides) formed. Consequently, they do not measure the configurational entropy (ΔS_c) contribution to the total entropy change (ΔS). However, the magnitude of the configurational entropy change associated with sequencing the polymers can be calculated.

Using the definition for configurational "coding" entropy given in Equation 8-2c, it is quite straightforward to calculate the configurational entropy change for a given polymer. The number of ways the mass of the linear system may be arranged (Ω_c) can be calculated using statistics. Brillouin[26] has shown that the number of distinct sequences one can make using N different symbols and Fermi-Dirac statistics is given by

$$\Omega_c = N! \qquad 8\text{-}6$$

If some of these symbols are redundant (or identical), then the number of unique or distinguishable sequences that can be made is reduced to

$$\Omega_c = \frac{N!}{n_1!\, n_2! \ldots n_i!} \qquad 8\text{-}7$$

where $n_1 + n_2 + \ldots + n_i = N$, and i defines the number of distinct symbols. For a protein, it is i = 20, since a subset of twenty distinctive types of amino acids is found in living things, while in DNA it is i = 4 for the subset of four distinctive nucleotides. A typical protein would have 100 to 300 amino acids in a specific sequence, or N = 100 to 300. For DNA of the bacterium *E. coli,* N = 4,600,000. In Appendix 1, alternative approaches to calculating Ω_c are considered and Equation 8-7 is shown to be a lower bound to the actual value.

For a random polypeptide of 100 amino acids, the configurational entropy S_{cr} may be calculated using Equation 8-2c and Equation 8-7 as follows:

$$S_{cr} = k \ln \Omega_{cr}$$

$$\text{since } \Omega_c = \frac{N!}{n_1!\, n_2! \ldots n_{20}!} = \frac{100!}{5!5! \ldots 5!} = \frac{100!}{(5!)^{20}}$$

$$= 1.28 \times 10^{115} \qquad 8\text{-}8a$$

The calculation of Equation 8-8a assumes that an equal number of each type of amino acid, namely 5, are contained in the polypeptide. Since k, or Boltzmann's constant, equals 1.38×10^{-16} erg/deg, and ln $(1.28 \times 10^{115}) = 265$,

$$S_{cr} = 1.38 \times 10^{-16} \times 265 = 3.66 \times 10^{-14} \text{ erg/deg-polypeptide} \qquad 8\text{-}8b$$

If only *one* specific sequence of amino acids could give the proper function, then the configurational entropy for the protein or specified, aperiodic polypeptide would be given by

$$\begin{aligned} S_{cm} &= k \ln \Omega_{cm} \\ &= k \ln 1 \\ &= 0 \end{aligned} \qquad 8\text{-}9$$

Determining ΔSc in Going from a Random Polymer to an Informed Polymer

The change in configurational entropy (ΔS_c) as one goes from a random polypeptide of 100 amino acids with an equal number of each amino acid type to a polypeptide with a specific message or sequence is:

$$\begin{aligned} &= 0 - 3.66 \times 10^{-14} \text{ erg/deg-polypeptide} \\ &= -3.66 \times 10^{-14} \text{ erg/deg-polypeptide} \end{aligned} \qquad 8\text{-}10$$

The configurational entropy work ($-T\Delta S_c$) at ambient temperatures is given by

$$\begin{aligned} -T\Delta S_c &= -(298\text{K}) \times (-3.66 \times 10^{-14}) \text{ erg/deg-polypeptide} \\ &= 1.1 \times 10^{-11} \text{ erg/deg-polypeptide} \\ &= 1.1 \times 10^{-11} \text{ erg/deg-polypeptide} \times \frac{6.023 \times 10^{23} \text{ molecules/mole}}{10{,}000 \text{ gms/mole}} \\ &\quad \times \frac{1 \text{ cal}}{4.184 \times 10^{7} \text{ ergs}} \\ &= 15.8 \text{ cal/gm} \end{aligned}$$

8-11

where the protein mass of 10,000 amu was estimated by assuming an average amino acid weight of 100 amu after the removal of the water molecule. Determination of the configurational entropy work for a protein containing 300 amino acids equally divided among the twenty types gives a similar result of 16.8 cal/g.

In like manner, the configurational entropy work for a DNA molecule, e.g., in the *E. coli* bacterium, may be calculated assuming 4×10^{6}

nucleotides in the chain with 1 x 10^6 each of the four distinctive nucleotides, each distinguished by the type of base attached, and each nucleotide assumed to have an average mass of 339 amu. At 298°K:

$$\begin{aligned} T\Delta S_c &= -T\,(S_{cm} - S_{cr}) \\ &= T\,(S_{cr} - S_{cm}) \\ &= kT\ln\,(\Omega_{cr} - \ln\Omega_{cm}) \\ &= kT\ln\left[\frac{(4\times10^6)!}{(10^6)!\,(10^6)!\,(10^6)!\,(10^6)!}\right] - kT\ln 1 \\ &= 2.26\times10^{-7}\ \text{erg/polynucleotide} \\ &= 2.39\ \text{cal/gm} \end{aligned} \tag{8-12}$$

It is interesting to note that, while the work to code the DNA molecule with 4 million nucleotides is much greater than the work required to code a protein of 100 amino acids (2.26 x 10^{-7} erg/DNA vs. 1.10 x 10^{-11} erg/protein), the work per gram to code such molecules is actually less in DNA. There are two reasons for this perhaps unexpected result: first, the nucleotide is more massive than the amino acid (339 amu vs. 100 amu); and second, the alphabet is more limited, with only four useful nucleotide "letters" as compared to twenty useful amino acid letters. Nevertheless, it is the total work that is important, which means that synthesizing DNA is much more difficult than synthesizing protein.

It should be emphasized that these estimates of the magnitude of the configurational entropy work required are conservatively small. As a practical matter, our calculations have ignored the configurational entropy work involved in the selection of monomers. Thus, we have assumed that only the proper subset of 20 biologically significant amino acids was available in a prebiotic oceanic soup to form a biofunctional protein. The same is true of DNA. We have assumed that in the soup only the proper subset of 4 nucleotides was present and that these nucleotides do not interact with amino acids or other soup ingredients. As we discussed in Chapter 4, many varieties of amino acids and nucleotides would have been present in a real ocean—varieties which have been ignored in our calculations of configurational entropy work. In addition, the soup would have contained many other kinds of molecules which could have reacted with amino acids and nucleotides. The problem of using only the appropriate optical isomer has also been ignored. A random chemical soup would have contained a 50/50 mixture of D- and L-amino acids, from which a true protein could incorporate only the L-enantiomer. Similarly, DNA uses exclusively the optically active sugar D-deoxyribose. Finally, we have ignored the problem of forming unnatural links, assuming for the calculations that only α-links occurred between amino acids in making polypeptides, and that only correct linking at the 3',5'-position of sugar occurred in forming polynucleotides. A quantification of these problems of specificity has recently been made by Yockey.[27]

The dual problem of selecting the proper composition of matter and then coding or rearranging it into the proper sequence is analogous to writing a story using letters drawn from a pot containing many duplicates of each of the 22 Hebrew consonants and 24 Greek and 26 English letters all mixed together. To write in English the message

HOW DID I GET HERE?

we must first draw from the pot 2 Hs, 2 Is, 3 Es, 2 Ds, and one each of the letters W, O, G, T, and R. Drawing or selecting this specific set of letters would be a most unlikely event itself. The work of selecting just these 14 letters would certainly be far greater than arranging them in the correct sequence. Our calculations only considered the easier step of coding while ignoring the greater problem of selecting the correct set of letters to be coded. We thereby greatly underestimate the actual configurational entropy work to be done.

In Chapter 6 we developed a scale showing degrees of investigator interference in prebiotic simulation experiments. In discussing this scale it was noted that very often in reported experiments the experimenter has actually played a crucial but *illegitimate* role in the success of the experiment. It becomes clear at this point that one illegitimate role of the investigator is that of providing a portion of the configurational entropy work, i.e., the "selecting" work portion of the total $-T\Delta S_c$ work.

It is sometimes argued that the type of amino acid that is present in a protein is critical only at certain positions—active sites—along the chain, but not at every position. If this is so, it means that the same message (i.e., function) can be produced with more than one sequence of amino acids.

This would reduce the coding work by making the number of permissible arrangements Ω_{cm} in Equations 8-9 and 8-10 for S_{cm} greater than 1. The effect of overlooking this in our calculations, however, would be negligible compared to the effect of overlooking the "selecting" work and only considering the "coding" work, as previously discussed. So we are led to the conclusion that our estimate for ΔS_c is very conservatively low.

Calculating the Total Work: Polymerization of Biomacromolecules

It is now possible to estimate the total work required to combine biomonomers into the appropriate polymers essential to living systems. This calculation, using Equation 8-5, might be thought of as occurring in two steps. First, amino acids polymerize into a polypeptide, with the chemical and thermal entropy work being accomplished ($\Delta H - T\Delta S_{th}$). Next, the random polymer is rearranged into a specific sequence which constitutes doing configurational entropy work ($-T\Delta S_c$). For example, the total work as expressed by the change in Gibbs free energy to make a specified sequence is

$$\Delta G = \Delta H - T\Delta S_{th} - T\Delta S_c \qquad \text{8-13}$$

where $\Delta H - T\Delta S_{th}$ may be assumed to be 300 kcal/mole to form a random polypeptide of 101 amino acids (100 links). The work to code this random polypeptide into a useful sequence so that it may function as a protein involves the additional component of $-T\Delta S_c$ "coding" work, which has been estimated previously to be 15.9 cal/g, or approximately 159 kcal/mole for our protein of 100 links with an estimated mass of

10,000 amu per mole. Thus, the total work (neglecting the "sorting and selecting" work) is approximately

$$\Delta G = (300 + 159) \text{ kcal/mole} = 459 \text{ kcal/mole} \qquad 8\text{-}14$$

with the coding work representing 159/459 or 35% of the total work.

In a similar way, the polymerization of 4 x 10^6 nucleotides into a random polynucleotide would require approximately 27 x 10^6 kcal/mole. The coding of this random polynucleotide into the specified, aperiodic sequence of a DNA molecule would require an additional 3.2 x 10^6 kcal/mole of work. Thus, the fraction of the total work that is required to code the polymerized DNA is seen to be 8.5%, again neglecting the "sorting and selecting" work.

The Impossibility of Protein Formation under Equilibrium Conditions

It was noted in Chapter 7 that because macromolecule formation (such as amino acids polymerizing to form protein) goes uphill energetically, work must be done on the system via energy flow through the system. We can readily see the difficulty in getting polymerization reactions to occur under equilibrium conditions, i.e., in the absence of such an energy flow.

Under equilibrium conditions the concentration of protein one would obtain from a solution of 1 M concentration in each amino acid is given by:

$$K = \frac{[\text{protein}] \times [H_2O]}{[\text{glycine}]\,[\text{alanine}]\ldots} \qquad 8\text{-}15$$

where K is the equilibrium constant and is calculated by

$$K = \exp\left(\frac{-\Delta G}{RT}\right) \qquad 8\text{-}16$$

An equivalent form is

$$\Delta G = -RT \ln K \qquad 8\text{-}17$$

We noted earlier that ΔG = 459 kcal/mole for our protein of 101 amino acids. The gas constant R = 1.9872 cal/deg-mole, and T is assumed to be 298°K. Substituting these values into Equations 8-15 and 8-16 gives

$$\text{protein concentration} = 10^{-338}\text{M} \qquad 8\text{-}18$$

This trivial yield emphasizes the futility of protein formation under equilibrium conditions. In the next chapter we will consider various theoretical models attempting to show how energy flow through the system can be useful in doing the work quantified in this chapter for the polymerization of DNA and protein, and we will examine experimental efforts to accomplish biomacromolecule synthesis.

Endnotes

1. Peter M. Molton, "On the Likelihood of a Human Interstellar Civilization," *Journal of the British Interplanetary Soc*iety 31 (1978): 203–8.
2. G. Nicolis and I. Prigogine, *Self-Organization in Nonequilibrium Systems* (New York: John Wiley, 1977), 25.
3. Ilya Prigogine, Gregoire Nicolis, and Agnes Babloyantz, "Thermodynamics of Evolution," *Physics Today* 25, no. 11 (1972): 23, doi: 10.1063/1.3071090.
4. "Work" in physics normally refers to force times displacement. In this chapter it refers in a more general way to the change in Gibbs free energy of the system that accompanies the polymerization of monomers into polymers.
5. A sufficient explanation for the origin of life would also require a model for the formation of other critical cellular components, including membranes, and their assembly.
6. L. E. Orgel, *The Origins of Life* (New York: John Wiley, 1973), 189ff; Michael Polanyi, "Life's Irreducible Structure," *Science* 160, no. 3834 (1968): 1308–1312, doi: 10.1126/science.160.3834.1308; Hubert P. Yockey, "A Calculation of the Probability of Spontaneous Biogenesis by Information Theory," *Journal of Theoretical Biology* 67, no. 3 (1977): 377–398, https://doi.org/10.1016/0022-5193(77)90044-3; Jeffrey S. Wicken, "Information Transformations in Molecular Evolution," *Journal of Theoretical Biology* 72, no. 1 (1978): 191–204, https://doi.org/10.1016/0022-5193(78)90025-5.
7. H. P. Yockey, personal communication, 9/29/82. Meaning is extraneous to the sequence, arbitrary, and depends on some symbol convention. For example, the word "gift," which in English means "a present" and in German "poison," in French is meaningless.
8. Yockey, "A Calculation of the Probability," 383.
9. Orgel, *The Origins of Life*, 189.
10. Here we use "THE END" even though there is no reason to suspect that nylon or a crystal would carry even this much information. Our point, of course, is that even if they did, the bit of information would be drowned in a sea of redundancy.
11. Yockey, "A Calculation of the Probability," 579.
12. Wicken, "Information Transformations," 191.
13. Orgel, *The Origins of Life*, 190.

14. Leon Brillouin, "Maxwell's Demon Cannot Operate: Information and Entropy. I." *Journal of Applied Physics* 22, no. 3 (1951): 334–337, https://doi.org/10.1063/1.1699951. Brillouin, "Thermodynamics and Information Theory," *American Scientist* 38, no. 4 (1950): 594–599, https://www.jstor.org/stable/27826339; Brillouin, "Life, Thermodynamics, and Cybernetics," *American Scientist* 37, no. 4 (1949): 554–568, https://www.jstor.org/stable/29773671.
15. E. Schrodinger, *What is Life?* (London: Cambridge University Press, 1945).
16. Werner Ehrenberg, "Maxwell's Demon," *Scientific American* 217, no. 5 (1967): 103–111, https://www.jstor.org/stable/24926178; Myron Tribus and Edward C. McIrvine, "Energy and Information," *Scientific American* 225, no. 3 (1971): 179–190, http://www.esalq.usp.br/lepse/imgs/conteudo_thumb/mini/Energy-and-Information.pdf.
17. Brillouin, "Maxwell's Demon Cannot Operate," 335.
18. Yockey and Wicken define information slightly differently from Brillouin, whose definition we use in our analysis. The difference is unimportant insofar as our analysis here is concerned.
19. Some intersymbol influence arising from differential atomic bonding properties makes the distribution of matter not quite random. See Hubert P. Yockey, "Self Organization Origin of Life Scenarios and Information Theory," *Journal of Theoretical Biology* 91, no. 1 (1981): 13–31, https://doi.org/10.1016/0022-5193(81)90370-2.
20. In *Handbook of Biochemistry and Molecular Biology, Physical and Chemical Data*, 3rd edition, ed. Gerald D. Fasman (Cleveland: CRC Press, 1976).
21. H. Morowitz, *Energy Flow in Biology* (New York: Academic Press, 1968), 98.
22. H. Borsook and H. M. Huffman, *Chemistry of Amino Acids and Proteins*, ed. C. L. A. Schmidt (Springfield, Mass.: Charles C. Thomas Co., 1944), 822.
23. Wicken, "Information Transformations," 191.
24. Morowitz, *Energy Flow in Biology*, 98, 112.
25. D. W. Armstrong, F. Nome, J. H. Fendler, and J. Nagyvary, "Novel Prebiotic Systems: Nucleotide Oligomerization in Surfactant Entrapped Water Pools," *Journal of Molecular Evolution* 9, no. 3 (1977): 213–223, https://doi.org/10.1007/BF01796110.
26. Brillouin, "Maxwell's Demon," 338.
27. Yockey, "Self Organization," 13.

9. SPECIFYING HOW WORK IS TO BE DONE

In Chapter 7 we saw that the work necessary to polymerize DNA and protein molecules from simple biomonomers could potentially be accomplished by energy flow through the system. Still, we know that such energy flow is a necessary but not sufficient condition for polymerization of the macromolecules of life. Arranging a pile of bricks into the configuration of a house requires work. One would hardly expect to accomplish this work with dynamite, however. Not only must energy flow through the system; it must be coupled in some specific way to the work to be done. This being so, we devoted Chapter 8 to identifying various components of work in typical polymerization reactions. In reviewing those individual work components, one thing became clear. The coupling of energy flow to the specific work requirements in the formation of DNA and protein is particularly important, since the required configurational entropy work of coding is substantial.

Theoretical Models for the Origin of DNA and Protein

A mere appeal to open-system thermodynamics does little good. What must be done is to advance a workable theoretical model of *how* the available energy can be coupled to do the required work. In this chapter various theoretical models for the origin of DNA and protein will be evaluated. Specifically, we will discuss how each model proposes to couple the available energy to the required work, particularly the configurational entropy work of coding.

Chance

Before the specified complexity of living systems began to be appreciated, it was thought that, given enough time, "chance" would explain the origin of living systems. In fact, most textbooks state that chance is the basic explanation for the origin of life. For example, Lehninger in his classic textbook *Biochemistry* states:

> We now come to the critical moment in evolution in which the first semblance of "life" appeared, through the chance association of a number of abiotically formed macromolecular components, to yield a unique system of greatly enhanced survival value.[1]

More recently the viability of "chance" as a mechanism for the origin of life has been severely challenged.[2] The explanatory power of "chance" is no longer universally granted. A fresh analysis would therefore be helpful.

We are now ready to analyze the "chance" origin of life using the approach developed in the last chapter. This view usually assumes that energy flow through the system is capable of doing the chemical and the thermal entropy work, while the configurational entropy work of both selecting and coding is the fortuitous product of chance.

To illustrate, assume that we are trying to synthesize a protein containing 101 amino acids. In Equation 8-14 we estimated that the total free energy increase (ΔG) or work required to make a random polypeptide from previously selected amino acids was 300 kcal/mole. An additional 159 kcal/mole is needed to code the polypeptide into a protein. Since the "chance" model assumes no coupling between energy flow and sequencing, the fraction of the polypeptide that has the correct sequence may be calculated (Equation 8-16) using equilibrium thermodynamics; i.e.,

$$\frac{[\text{protein concentration}]}{[\text{polypeptide concentration}]} = \exp\left(\frac{-\Delta G}{RT}\right) \qquad \text{9-1a}$$

$$= \exp\left(\frac{-159{,}000}{1.9872 \times 298}\right)$$

$$\cong 1 \times 10^{-117}* \qquad 9\text{-}1b$$

* This is essentially the inverse of the estimate for the number of ways one can arrange 101 amino acids in a sequence (i.e., $1/\Omega_c$ in Equation 8-7).

This answer, converted into a ratio, i.e., $1/10^{117}$, gives the fraction of polypeptides. that have the right sequence to be a protein.

Eigen[3] has estimated the number of polypeptides of molecular weight 10^4 (the same weight used in our earlier calculations) that would be found in a layer 1 meter thick covering the surface of the entire Earth. He found it to be 10^{41}. If these polypeptides reformed with new sequences at the maximum rate at which chemical reactions may occur, namely 10^{14}/s, for 5×10^9 years (1.6×10^{17}s), the total number of polypeptides that would be formed during the assumed history of the Earth would be

$$10^{41} \times 10^{14}/\text{s} \times 1.6 \times 10^{17}\text{s} = 10^{72} \qquad 9\text{-}2$$

Combining the results of Equation 9-1 and 9-2, we find that the probability of producing one protein of 101 amino acids in five billion years is only $1/10^{45}$. Using somewhat different illustrations, Steinman[4] and Cairns-Smith[5] also come to the conclusion that chance is insufficient.

It is apparent that "chance" should be abandoned as an acceptable model for coding of the macromolecules essential in living systems. In fact, it has been, except in introductory texts and popularizations.

Neo-Darwinian Natural Selection

The widespread recognition of the severe improbability that self-replicating organisms could have formed from purely random interactions has led to a great deal of speculation—speculation that some organizing principle must have been involved. In the company of many others, Crick[6] has considered that the neo-Darwinian mechanism of natural selection might provide the answer. An entity capable of self-replication is necessary, however, before natural selection can operate. Only then could changes result via mutations and environmental pressures which might in turn bring about the dominance of entities with the greatest probabilities of survival and reproduction. The weakest point in this explanation of life's origin is the great complexity of the initial entity which must form, apparently by random fluctuations, before natural selection can take over. In essence this theory postulates the chance formation of the "metabolic motor" which will subsequently be capable of channeling energy flow through the system. Thus harnessed by coupling through the metabolic motor, the energy flow is imagined to supply not only chemical and thermal entropy work, but also the configurational entropy work of selecting the appropriate chemicals and then coding the resultant polymer into an aperiodic, specified, biofunctioning polymer. As a minimum, this system must carry in its structure the information for its own synthesis, and control the machinery which will fabricate any desired copy. It is widely agreed that such a system requires both protein and nucleic acid.[7] This view is not unanimous, however. A few have suggested that a short peptide would be sufficient.[8]

One way out of the problem would be to extend the concept of natural selection to the pre-living world of molecules. A number of authors have entertained this possibility, although no reasonable explanation has made the suggestion plausible. Natural selection is a recognized principle of differential reproduction which presupposes the existence of at least two distinct types of self-replicating molecules. Dobzhansky appealed to those doing origin-of-life research not to tamper with the definition of natural selection when he said:

> I would like to plead with you, simply, please realize you cannot use the words "natural selection" loosely. Prebiological natural selection is a contradiction in terms.[9]

Bertalanffy made the point even more cogently:

> Selection, i.e., favored survival of "better" precursors of life, already presupposes self-maintaining, complex, open systems which may compete; therefore selection cannot account for the origin of such systems.[10]

Inherent Self-ordering Tendencies in Matter

How could energy flow through the system be sufficiently coupled to do the chemical and thermal entropy work to form a nontrivial yield of polypeptides (as previously assumed in the "chance" model)? One answer has been the suggestion that configurational entropy work, especially the coding work, could occur as a consequence of the self-ordering tendencies in matter. The experimental work of Steinman and Cole[11] in the late 1960s is still widely cited in support of this model.[12] The polymerization of protein is hypothesized to be a nonrandom process, the coding of the protein resulting from differences in the chemical bonding forces. For example, if amino acids A and B react chemically with one another more readily than with amino acids C, D, and E, we should expect to see a greater frequency of AB peptide bonds in protein than of AC, AD, AE, BC, BD, or BE bonds.

Together with our colleague Randall Kok, we have recently analyzed the ten proteins originally analyzed by Steinman and Cole,[13] as well as fifteen additional proteins whose structures (except for hemoglobin) have been determined since their work was first published in 1967. Our expectation in this study was that one would only get agreement between the dipeptide bond frequencies from Steinman and Cole's work and those observed in actual proteins if one considered a large number of proteins averaged together. The distinctive structures of individual proteins would cause them to vary greatly from Steinman and Cole's data, so only when these distinctives are averaged out could one expect to approach Steinman and Cole's dipeptide bond frequency results. The reduced data presented in Table 9-1 below[14] shows that Steinman and Cole's dipeptide bond frequencies do not correlate well with the observed peptide bond frequencies for one, ten, or twenty-five proteins. It is a simple matter to make such calculations on an electronic digital computer. We surmise that additional assumptions not stated in their paper were used to achieve the better agreements.

Table 9-1. Comparison of Steinman and Cole's experimentally determined dipeptide bond frequencies, and frequencies calculated by Steinman and Cole, and by Kok and Bradley from known protein sequences.

Dipeptide	Values (relative to Gly-Gly)			
	S/C		K/B	
	exp	cal	cal-wa	cal-woa
Gly-Gly	1.0	1.0	1.0 (1.0) [1.0]	1.0 (1.0) [1.0]
Gly-Ala	0.8	0.7	1.1 (1.1) [2.0]	2.0 (1.2) [1.0]
Ala-Gly	0.8	0.6	1.0 (1.1) [2.2]	1.5 (1.2) [0.0]
Ala-Ala	0.7	0.6	1.3 (1.5) [4.4]	2.8 (1.5) [0.0]
Gly-Val	0.5	0.2	0.2 (0.3) [0.4]	1.5 (1.2) [1.0]
Val-Gly	0.5	0.3	0.3 (0.3) [0.6]	0.8 (0.6) [0.0]
Gly-Leu	0.5	0.3	0.3 (0.3) [0.2]	1.3 (0.7) [1.0]
Leu-Gly	0.5	0.2	0.3 (0.3) [0.8]	1.3 (1.0) [1.0]
Gly-Ile	0.3	0.1	0.1 (0.2) [0.6]	1.0 (0.8) [0.0]
Ile-Gly	0.3	0.1	0.1 (0.2) [0.2]	0.0 (0.4) [0.0]
Gly-Phe	0.1	0.1	0.1 (0.2) [0.4]	0.5 (0.5) [0.0]
Phe-Gly	0.1	0.1	0.1 (0.1) [0.6]	1.0 (0.5) [1.0]

Source: Adapted from G. Steinman and M. V. Cole, *Proc. Nat. Acad. Sci. U.S.* 58 (1967), 735.

Furthermore, the peptide bond frequencies for the twenty-five proteins approach a distribution predicted by random statistics rather than the dipeptide bond frequency measured by Steinman and Cole. This observation means that bonding preferences between various amino acids play no significant role in coding protein. Finally, if chemical bonding forces were influential in amino acid sequencing, one would expect to get a single sequence (as in ice crystals) or no more than a few sequences, instead of the large variety we observe in living systems. Yockey, with a different analysis, comes to essentially the same conclusion.[15]

A similar conclusion may be drawn for DNA synthesis. No one to date has published data indicating that bonding preferences could have had any role in coding the DNA molecules. Chemical bonding forces apparently have minimal effect on the sequence of nucleotides in a polynucleotide.

Mineral Catalysis

Mineral catalysis is often suggested as being significant in prebiotic evolution. In the experimental investigations reported in the early 1970s,[16] mineral catalysis in polymerization reactions was found to operate by adsorption of biomonomers on the surface or between layers of clay. Monomers were effectively concentrated and protected from rehydration so that condensation polymerization could occur. There does not appear to be any additional effect. In considering this catalytic effect of clay, Hulett has advised, "It must be remembered that the surface cannot change the free energy relationships between reactants and products, but only the speed with which equilibrium is reached."[17]

Is mineral catalysis capable of doing the chemical work and/or thermal entropy work? The answer is a qualified no. While it should assist in doing the thermal entropy work, it is incapable of doing the chemical work since clays do not supply energy. This is why successful mineral catalysis experiments invariably use energy-rich precursors such as aminoacyl adenylates rather than amino acids.[18]

Is there a real prospect that mineral catalysis may somehow accomplish the configurational entropy work, particularly the coding of polypeptides or polynucleotides? Here the answer is clearly no. In all experimental work to date, only random polymers have been condensed from solutions of selected ingredients. Furthermore, there is no theoretical basis for the notion that mineral catalysis could impart any significant degree of information content to polypeptides or polynucleotides. As has been noted by Wilder-Smith,[19] there is really no reason to expect the low-grade order resident on minerals to impart any high degree of coding to polymers that condense while adsorbed on the mineral's surface. To put it another way, one cannot get a complex, aperiodic-sequenced polymer using a very periodic (or crystalline) template.

In summary, mineral catalysis must be rejected as a mechanism for doing either the chemical or configurational entropy work required to polymerize the macromolecules of life. It can only assist in polymerizing short, random chains of polymers from selected high-energy biomonomers by assisting in doing the thermal entropy work.

Nonlinear, Nonequilibrium Processes

1. Ilya Prigogine

Prigogine has developed a more general formulation of the laws of thermodynamics which includes nonlinear, irreversible processes such as autocatalytic activity. In his book *Self-Organization in Nonequilibrium Systems* (1977)[20] co-authored with Nicolis, he summarized this work and its application to the organization and maintenance of highly complex structures in living things. The basic thesis in the book is that there are some systems which obey non-linear laws—laws that produce two distinct kinds of behavior. In the neighborhood of thermodynamic equilibrium, destruction of order prevails (entropy achieves a maximum value consistent with the system constraints). If these same systems are driven sufficiently far from equilibrium, however, ordering may appear spontaneously.

Heat flow by convection is an example of this type of behavior. Heat conduction in gases normally occurs by the random collision of gas molecules. Under certain conditions, however, heat conduction may occur by a heat-convection current—the coordinated movement of many gas molecules. In a similar way, water flow out of a bathtub may occur by random movement of the water molecules under the influence of gravity. Under certain conditions, however, this random movement of water down the drain is replaced by the familiar soapy swirl—the highly coordinated flow of the vortex. In each case random movements of molecules in a fluid are spontaneously replaced by a highly ordered behavior. Prigogine et al.,[21] Eigen,[22] and others have suggested that a similar sort of self-organization may be intrinsic in organic chemistry and can potentially account for the highly complex macromolecules essential for living systems.

But such analogies have scant relevance to the origin-of-life question. A major reason is that they fail to distinguish between order and complexity. The highly ordered movement of energy through a system as in convection or vortices suffers from the same shortcoming as the analogies to the static, periodic order of crystals. Regularity or order cannot serve to store the large amount of information required by living systems. A highly irregular, but specified, structure is required rather than an ordered structure. This is a serious flaw in the analogy offered. There is no apparent connection between the kind of spontaneous ordering that occurs from energy flow through such systems and the work required to build aperiodic information-intensive macromolecules like DNA and protein. Prigogine et al.[23] suggest that the energy flow through the system decreases the system entropy, leading potentially to the highly organized structure of DNA and protein. Yet they offer no suggestion as to how the decrease in thermal entropy from energy flow through the system could be coupled to do the configurational entropy work required.

A second reason for skepticism about the relevance of the models developed by Prigogine and others[24] is that ordering produced within the system arises through constraints imposed in an implicit way at the system boundary. Thus, the system order, and more importantly the system complexity, cannot exceed that of the environment.

Walton[25] illustrates this concept in the following way. A container of gas placed in contact with a heat source on one side and a heat sink on the opposite side is an open system. The flow of energy through the system from the heat source to the heat sink forms a concentration relative to the gas in the cooler region. The order in this system is established by the structure: source-intermediate systems-sink. If this structure is removed, allowing the heat source to come into contact with the heat sink, the system decays back to equilibrium. We should note that the information induced in an open system doesn't exceed the amount of information built into the structural environment, which is its source.

Condensation of nucleotides to give polynucleotides or nucleic acids can be brought about with the appropriate apparatus (i.e., structure) and supplies of energy and matter. Just as in Walton's illustration, however, Mora[26] has shown that the amount of order (not to mention specified complexity) in the final product is no greater than the amount of information introduced in the physical structure of the experiment or chemical structure of the reactants. Non-equilibrium thermodynamics does not account for this structure, but assumes it and then shows the kind of organization which it produces. The origin and maintenance of the structure are not explained, and as Harrison[27] correctly notes, this question leads back to the origin of structure in the universe. Science offers us no satisfactory answer to this problem at present.

Nicolis and Prigogine[28] offer their trimolecular model as an example of a chemical system with the required nonlinearity to produce self-ordering. They are able to demonstrate mathematically that within a system that was initially homogeneous, there may subsequently arise a periodic, spatial variation of concentration. To achieve this low degree of ordering, however, they must require boundary conditions that could only be met at cell walls (i.e., at membranes), relative reaction rates that are atypical of those observed in condensation reactions, a rapid removal of reaction products, and a trimolecular reaction (the highly unlikely simultaneous collision of three atoms). Furthermore the trimolecular model requires chemical reactions that are essentially irreversible. But condensation reactions for polypeptides or polynucleotides are highly reversible unless all water is removed from the system.

They speculate that the low degree of spatial ordering achieved in the simple trimolecular model could potentially be orders of magnitude greater for the more complex reactions one might observe leading up to a fully replicating cell. The list of boundary constraints, relative reaction rates, etc. would, however, also be orders of magnitude larger. As a matter of fact, one is left with so constraining the system at the boundaries that ordering is inevitable from the structuring of the environment by the chemist. The fortuitous satisfaction of all of these boundary constraints simultaneously would be a miracle in its own right.

It is possible at present to synthesize a few proteins such as insulin in the laboratory. The chemist supplies not only energy to do the chemical and thermal entropy work, however, but also the necessary chemical manipulations to accomplish the configurational entropy work. Without this, the selection of the proper composition and the coding for the right sequence of amino acids would not occur. The success of the experiment is fundamentally dependent on the chemist.

Finally, Nicolis and Prigogine have postulated that a system of chemical reactions which explicitly shows autocatalytic activity may ultimately be able to circumvent the problems now associated with synthesis of prebiotic DNA and protein. It remains to be demonstrated *experimentally,* however, that these models have any real correspondence to prebiotic condensation reactions. At best, these models predict higher yields without any mechanism to control sequencing. Accordingly, no experimental evidence has been reported to show how such models could have produced any significant degree of coding. No, the models of Prigogine et al., based on non-equilibrium thermodynamics, do not at present offer an explanation as to how the configurational entropy work is accomplished under prebiotic conditions. The problem of how to couple energy flow through the system to do the required configurational entropy work remains.

2. Manfred Eigen

In his comprehensive application of nonequilibrium thermodynamics to the evolution of biological systems, Eigen[29] has shown that selection could produce no evolutionary development in an open system unless the system were maintained far from equilibrium. The reaction must be autocatalytic but capable of self-replication. He develops an argument to show that in order to produce a truly self-replicating system the complementary base-pairing instruction potential of nucleic acids must be combined with the catalytic coupling function of proteins. Kaplan[30] has suggested a minimum of 20 to 40 functional proteins of 70 to 100 amino acids each, and a similar number of nucleic acids would be required by such a system. More recent research has shown that the minimum is likely much higher, running into hundreds of proteins.[31]

Yet, as has previously been noted, the chance origin of even one protein of 100 amino acids is essentially zero.

The shortcoming of this model is the same as for those previously discussed; namely, no way is presented to couple the energy flow through the system to achieve the configurational entropy work required to create a system capable of replicating itself.

Periodically we see reversions (perhaps inadvertent ones) to chance in the theoretical models advanced to solve the problem. Eigen's model illustrates this well. The model he sets forth must necessarily arise from chance events and is nearly as incredible as the chance origin of life itself. The fact that generally chance has to be invoked many times in the abiotic sequence has been called by Brooks and Shaw "a major weakness in the whole chemical evolutionary theory."[32]

Experimental Results in Synthesis of Protein and DNA

Thus far we have reviewed the various theoretical models proposed to explain how energy flow through a system might accomplish the work of synthesizing protein and DNA macromolecules, but found them wanting. Nevertheless, it is conceivable that experimental support for a spontaneous origin of life can be found in advance of the theoretical explanation for how this occurs. What then can be said of the experimental efforts to synthesize protein and DNA macromolecules? Experimental efforts to this end have been enthusiastically pursued for the past thirty years. In this section, we will review efforts toward the prebiotic synthesis of both protein and DNA, considering the three forms of energy flow most commonly thought to have been available on the early Earth. These are thermal energy (volcanoes), radiant energy (sun), and chemical energy in the form of either condensing agents or energy-rich precursors. (Electrical energy is excluded at this stage of evolution as being too "violent," destroying rather than joining the biomonomers.)

Thermal Synthesis

Sidney Fox[33] has pioneered the thermal synthesis of polypeptides, naming the products of his synthesis proteinoids. Beginning with either an aqueous solution of amino acids or dry ones, he heats his material at 200°C[34] for 6–7 hours. All initial solvent water, plus water produced during polymerization, is effectively eliminated through vaporization. This elimination of the water makes possible a small but significant yield of polypeptides, some with as many as 200 amino acid units. Heat is introduced into the system by conduction and convection and leaves in the form of steam. The reason for the success of the polypeptide formation is readily seen by examining again Equations 8-15 and 8-16. Note that increasing the temperature would increase the product yield through increasing the value of exp ($-\Delta G/RT$). But more importantly, eliminating the water makes the reaction irreversible, giving an enormous increase in yield over that observed under equilibrium conditions by the application of the law of mass action.

Thermal syntheses of polypeptides fail, however, for at least four reasons. First, studies using nuclear magnetic resonance (NMR) have shown that thermal proteinoids "have scarce resemblance to natural peptidic material because β, γ, and ε peptide bonds largely predominate over α-peptide bonds."[35] Second, thermal proteinoids are composed of approximately equal numbers of L- and D-amino acids, in contrast to viable proteins with all L-amino acids. Third, there is no evidence that proteinoids differ significantly from a random sequence[36] of amino acids, with little or no catalytic activity. Miller and Orgel have made the following observation with regard to Fox's claim that proteinoids resemble proteins:

> The degree of nonrandomness in thermal polypeptides so far demonstrated is minute compared to nonrandomness of proteins. It is deceptive, then, to suggest that thermal polypeptides are similar to proteins in their nonrandomness.[37]

Fourth, the geological conditions indicated are too unreasonable to be taken seriously. As Folsome has commented, "The central question [concerning Fox's proteinoids] is where did all those pure, dry, concentrated, and optically active amino acids come from in the real, abiological world?"[38]

There is no question that thermal energy flow through the system, including the removal of water, is accomplishing the thermal entropy and chemical work required to form a polypeptide (300 kcal/ mole in our earlier example). The fact that polypeptides are formed is evidence of the work done. It is equally clear that the additional configurational entropy work required to convert an aperiodic unspecified polypeptide into a specified, aperiodic polypeptide which is a functional protein has not been done (159 kcal/mole in our earlier example).

It should be remembered that this 159 kcal/mole of configurational entropy work was calculated assuming the sequencing of the amino acids was the only additional work to be done. Yet the experimental results of Temussi et al.[39] indicate that obtaining all L-amino acids from a racemic mixture and getting α-linking between the amino acids are quite difficult. This requirement further increases the configurational entropy work needed over that estimated to do the coding work (159 kcal/mole). We may estimate the magnitude of this increase in the configurational entropy work term by returning to our original calculations (Equation 8-7 and 8-8).

In our original calculation for a hypothetical protein of 100 amino acid units, we assumed the amino acids were equally divided among the twenty types. We calculated the number of possible amino acid sequences as follows:

$$\Omega_{cr} = \frac{100!}{5!5!5!\ldots5!} = \frac{100!}{(5!)^{20}} = 1.28 \times 10^{115} \qquad 9\text{-}3$$

If we note that at each site the probability of having an L-amino acid is 50%, and make the generous assumption[40] that there is a 50% probability that a given link will be of the α-type observed in true proteins, then the number of ways the system can be arranged in a random chemical reaction is given by

$$\Omega_{cr} = 1.28 \text{ x } 10^{115} \text{ x } 2^{100} \text{ x } 2^{99} = 10^{175} \qquad 9\text{-}4$$

where 2^{100} refers to the number of additional arrangements possible, given that each site could contain an L- or D-amino acid, and 2^{99} assumes the 99 links between the 100 amino acids in general are equally divided between the natural α-links and the unnatural β-, γ-, or ε-links.

The requirements for a biologically functional protein molecule are: (1) all L-amino acids, (2) all α-links, and (3) a specified sequence. This being so, the calculation of the configurational entropy of the protein molecule using Equation 8-8 is unchanged except that the number of ways the system can be arranged, Ω_{cr}, is increased from 1.28 x 10^{115} to 1.0 x 10^{175} as shown in Equations 9-3 and 9-4. We may use the relationships of Equations 8-7 and 8-8 but with the number of permutations modified as shown here to find a total configurational entropy work. When we do, we get a total configurational entropy work of 195 kcal/mole, of which 159 kcal/mole is for sequencing and 36 kcal/mole to attain all L-amino acids and all α-links. Finally, it should be recognized that Fox and others who use his approach avoid a much larger configurational entropy work term by beginning with only amino acids, i.e., excluding other organic chemicals and thereby eliminating the "selecting work" which is not accounted for in the 195 kcal/mole calculated above.

In summary, undirected thermal energy is only able to do the chemical and thermal entropy work in polypeptide synthesis, but not the coding (or sequencing) portion of the configurational entropy work. Proteinoids are just globs of random polymers. That a polymer composed exclusively of amino acids (but without exclusively peptide bonds) was formed is a result of the fact that only amino acids were used in the experiment. Thus, the portion of the configurational entropy work that was done—the selecting work—was accomplished not by natural forces but by illegitimate investigator interference. It is difficult to imagine how one could ever couple random thermal energy flow through the system to do the required configurational entropy work of selecting and sequencing. Finally, this approach is of very questionable geological significance, given the many fortuitous events that are required, as others have noted.

Solar Energy

Direct photochemical (UV) polymerization reactions to form polypeptides and polynucleotides have occasionally been discussed in the literature. The idea is to drive forward the otherwise thermodynamically unfavorable polymerization reaction by allowing solar energy to flow through the aqueous system to do the necessary work. It is worth noting that minor yields of small peptides can be expected to form spontaneously, even though the reaction is unfavorable (see Equation 8-16), but that greater yields of larger peptides can be expected only if energy is somehow coupled to the reaction. Fox and Dose have examined the peptide results of Bahadur and Ranganayaki[41] and concluded that UV irradiation did not couple with the reaction. They comment, "The authors do not show that they have done more than accelerate an approach to an unfavorable equilibrium. They may merely have reaffirmed the second law of thermodynamics."[42] Other attempts to form polymers directly under the influence of UV light have not been encouraging because of this lack of coupling. Neither the chemical nor the thermal entropy work, and definitely not any configurational entropy work, has been accomplished using solar energy.

Chemical Energy (Energy-Rich Condensing Agents)

Through the use of condensing agents, the energetically unfavorable dipeptide reaction (ΔG_1 = +3000 cal/mole) is made energetically favorable ($\Delta G_3 < 0$) by coupling it with a second reaction which is sufficiently favorable energetically ($\Delta G_2 < 0$), to offset the energy requirement of the dipeptide reaction:

dipeptide reaction

$$\text{A-OH} + \text{H-B} \longrightarrow \text{A-B} + H_2O \qquad \Delta G_1 > 0 \tag{9-5}$$

condensing agent reaction

$$\text{C} + H_2O \longrightarrow \text{D} \qquad \Delta G_2 < 0 \tag{9-6}$$

coupled reaction

$$\text{A-OH} + \text{H-B} + \text{C} \longrightarrow \text{A-B} + \text{D} \qquad \Delta G_3 < 0 \qquad 9\text{-}7$$

As in thermal proteinoid formation, the free water is removed. However, in this case, it is removed by chemical reaction with a suitable condensing agent—one which has a sufficient decrease in Gibbs free energy to drive the reaction forward (i.e., $\Delta G_2 < 0$ and $|\Delta G_2| \geq |\Delta G_1|$ so that $\Delta G_1 + \Delta G_2 = \Delta G_3 \leq 0$).

Unfortunately, it has proved difficult to find condensing agents for these macromolecule syntheses that could have originated on the primitive Earth and functioned properly under mild conditions in an alkaline aqueous environment.[43] Meanwhile, other condensing agents which are not prebiotically significant (e.g., polymetaphosphates) are used in experiments. The plausible cyanide derivative candidates for condensing agents on the early Earth hydrolyze readily in aqueous solutions (see Chapter 4). In the process, they do not couple preferentially with the H_2O from the condensation-dehydration reaction. Condensing agents observed in living systems today are produced only by living systems, and thus are not prebiotically significant. Moreover, enzyme activity in living systems first activates amino acids and then brings about condensation of these activated species, thus avoiding the problem of indiscriminate reaction with water.

Notice that if we could solve the very significant problems associated with the prebiotic synthesis of polypeptides by using condensing agents, we would still succeed only in polymerizing random polypeptides. Only the chemical and thermal entropy work would be accomplished by an appropriate coupling of the condensing agent hydrolysis to the condensation reaction. There is no reason to believe that condensing agents could have any effect on the selecting or sequencing of the amino acids. Thus, condensing agents are eliminated as a possible means of doing the configurational entropy work of coding a protein or DNA.

Chemical Energy (Energy-Rich Precursors)

Because the formation of even random polypeptides from amino acids is so energetically unfavorable ($\Delta G = 300$ kcal/mole for 100 amino acids), some investigators have attempted to begin with energy-rich precursors such as HCN and form polypeptides directly, a scheme which is "downhill" energetically, i.e., $\Delta G < 0$. There are advantages to such an approach; namely, there is no chemical work to be done since the bonding energy actually decreases as the energy-rich precursors react to form more complex molecules. This decrease in bonding energy will drive the reaction forward, effectively doing the thermal entropy work as well. The fly in the ointment, however, is that the configurational entropy work is enormous in going from simple molecules (e.g., HCN) directly to complex polymers in a single step (without forming intermediate biomonomers).

The stepwise scheme of experiments is to react gases such as methane, ammonia, and carbon dioxide to form amino acids and other compounds and then to react these to form polymers in a subsequent experiment. In these experiments the very considerable selecting-work component of the configurational entropy work is essentially done by the investigator who separates, purifies, and concentrates the amino acids before attempting to polymerize them. Matthews[44] and co-workers, however, have undertaken experiments where this intermediate step is missing and the investigator has no opportunity to contribute even obliquely to the success of the experiment by assisting in doing the selecting part of the configurational entropy work. In such experiments—undoubtedly more plausible as true prebiotic simulations—the probability of success is, however, further reduced from the already small probabilities previously mentioned. Using HCN as an energy-rich precursor, and ammonia as a catalyst, Matthews and Moser[45] have claimed direct synthesis of a large variety of chemicals under anhydrous conditions. After treating the polymer with water, even peptides are said to be among the products obtained. But as Ferris et al.[46] have shown, the HCN polymer does not release amino acids upon treatment with proteolytic (protein-splitting) enzymes; nor does it give a positive biuret reaction (color test for peptides). In short, it is very hard to reconcile these results with a peptidic structure.

Ferris[47] and Matthews[48] have agreed that direct synthesis of polypeptides has not yet been demonstrated. While some peptide bonds may form directly, it would be quite surprising to find them in significant numbers. Since HCN gives rise to other organic compounds, and various kinds of links are possible, the formation of polypeptides with exclusively α-links is most unlikely. Furthermore, no sequencing would be expected from this reaction, which is driven forward and "guided" only by chemical energy.

While we do not believe Matthews or others will be successful in demonstrating a single-step synthesis of polypeptides from HCN, this approach does involve the least investigator interference, and thus represents a very plausible prebiotic simulation experiment. The approach of Fox and others, which involves reacting gases to form many organic compounds, separating out amino acids, purifying, and finally polymerizing them, is more successful because it involves a greater measure of investigator interference. The selecting portion of the configurational entropy work is being supplied by the scientist. Matthews's lack of demonstrable success in producing polypeptides is a predictable indication of the enormity of the problem of prebiotic synthesis when it is not overcome by illegitimate investigator interference.

Mineral Catalysis

A novel synthesis of polypeptides has been reported[49] which employs mineral catalysis. An aqueous solution of energy-rich aminoacyl adenylates (rather than amino acids) is used in the presence of certain layered clays such as those known as montmorillonites. Large amounts of the energy-rich reactants are adsorbed both on the surface and between the layers of clay. The catalytic effect of the clay may result primarily from the removal of reactants from the solution by adsorption between the layers of clay. This technique has resulted in polypeptides of up to 50 units or more. Although polymerization definitely occurs in these reactions, the energy-rich aminoacyl adenylate (Figure 9-1 below) is of very doubtful prebiotic significance per the discussion of competing reactions

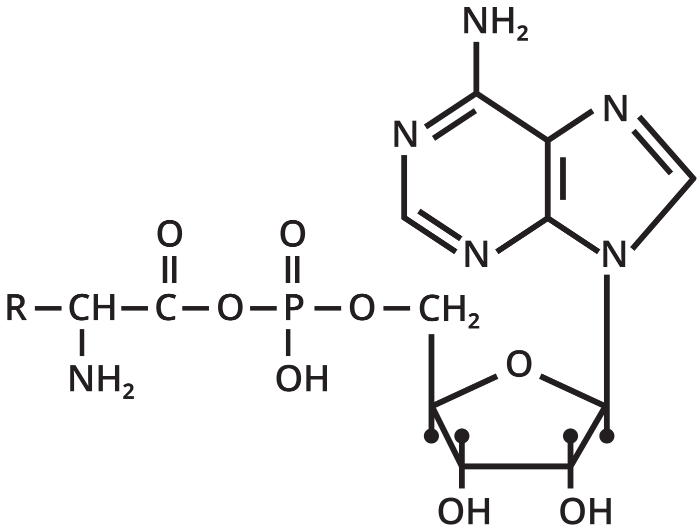

Figure 9-1. Aminoacyl adenylate.

in Chapter 4. Furthermore, the use of clay with free amino acids will not give a successful synthesis of polypeptides. The energy-rich aminoacyl adenylates lower their chemical or bonding energy as they polymerize, driving the reaction forward, and effectively doing the thermal entropy work as well. The role of the clay is to concentrate the reactants and possibly to catalyze the reactions. Once again, we are left with no apparent means to couple the energy flow, in this case in the form of prebiotically questionable energy-rich precursors, to the configurational entropy work of selecting and sequencing required in the formation of specified aperiodic polypeptides, or proteins.

Summary of Experimental Results on Prebiotic Synthesis of Protein

In summary, we have seen that it is possible to do the thermal entropy work and chemical work necessary to form random polypeptides, e.g., Fox's proteinoids. In no case, though, has anyone been successful in doing the additional configurational entropy work of coding necessary to convert random polypeptides into proteins. Virtually no mechanism with any promise for coupling the random flow of energy through the system to do this very specific work has come to light. The prebiotic plausibility of the successful synthesis of polypeptides must be questioned because of the considerable configurational entropy work of selecting done by the investigator prior to the polymer synthesis. Surely no suggestion is forthcoming that the right composition of just the subset of amino acids found in living things was "selected" by natural means, or that this subset consists only of L-α-amino acids. This is precisely why a large measure of the credit in forming proteinoids must go to Fox and others rather than nature.

Summary of Experimental Results on Prebiotic Synthesis of DNA

The prebiotic synthesis of DNA has proved to be even more difficult than that of protein. The problems that beset protein synthesis apply with greater force to DNA synthesis. Energy flow through the system may cause the nucleotides to chemically react and form a polymer chain, but it is very difficult to get them to attach themselves together in a specified way. For example, 3'-5' links on the sugar are necessary for the DNA to form a helical structure (see Figure 9-2 below). Yet 2'-5' links predominate in most prebiotic simulation experiments.[50] The sequencing of the bases in DNA is also crucial, as is the amino acid sequence in proteins. Both of these requirements are problems in doing the configurational entropy work. It is one thing to get molecules to chemically react; it is quite another to get them to link up in the right arrangement. To date, researchers have only succeeded in making oligonucleotides, or relatively short chains of nucleotides, with neither consistent 3'-5' links nor specific base sequencing.

Miller and Orgel summarized their chapter on prebiotic condensation reactions by saying:

> This chapter has probably been confusing to the reader. We believe that is because of the limited progress that has been made in the study of prebiotic condensation. Many interesting scraps of information are available, but no correct pathways have yet been discovered.[51]

The situation is much the same today.

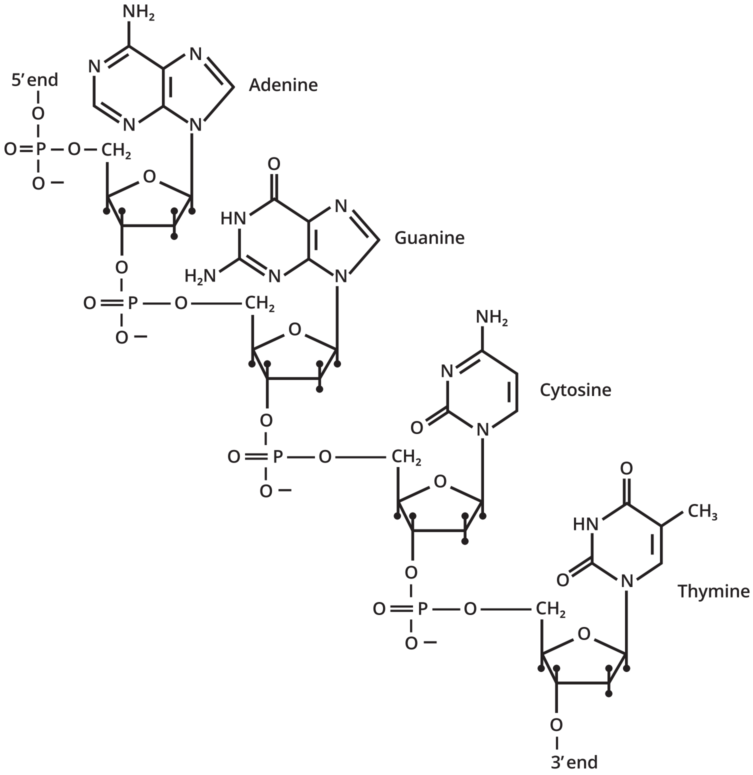

Figure 9-2. A section from a DNA chain showing the sequence AGCT.

Summary Discussion of Experimental Results

There is an impressive contrast between the considerable success in synthesizing amino acids and the consistent failure to synthesize protein and DNA. We believe the reason is the large difference in the magnitude of the configurational entropy work required. Amino acids are quite simple compared to protein, and one might reasonably expect to get some yield of amino acids, even where the chemical reactions that occur do so in a rather random fashion. The same approach will obviously be far less successful in reproducing complex protein and DNA molecules where the configurational entropy work term is a nontrivial portion of the whole. Coupling the energy flow through the system to do the chemical and thermal entropy work is much easier than doing the configurational entropy work. The uniform failure in literally thousands of experimental attempts to synthesize protein or DNA under even questionable prebiotic conditions is a monument to the difficulty in achieving a high degree of information content or specified complexity from the *undirected* flow of energy through a system.

We must not forget that the total work to create a living system goes far beyond the work to create DNA and protein discussed in this chapter. As we stated before, an estimated minimum of 20 to hundreds of proteins as well as DNA and RNA are required to make even a simple replicating system. The lack of known energy-coupling means to do the configurational entropy work required to make DNA and protein is many times more crucial in making a living system. As a result, appeals to chance for this most difficult problem still appear in the literature in spite of the fact that calculations give staggeringly low probabilities, even on the scale of 5 billion years. Either the work—especially the organizational work—was coupled to the flow of energy in some way not yet understood, or else it truly was a miracle.

Summary of Thermodynamics Discussion

Throughout Chapters 7–9 we have analyzed the problems of complexity and the origin of life from a thermodynamic point of view. Our reason for doing this is the common notion in the scientific literature today on the origin of life that an open system with energy and mass flow is *a priori* a sufficient explanation for the complexity of life. We have examined the validity of such an open and constrained system. We found it to be a reasonable explanation for doing the chemical and thermal entropy work, but clearly inadequate to account for the configurational entropy work of coding (not to mention the sorting and selecting work). We have noted the need for some sort of coupling mechanism. Without it, there is no way to convert the negative entropy associated with energy flow into negative entropy associated with configurational entropy and the corresponding information. Is it reasonable to believe such a "hidden" coupling mechanism will be found in the future that can play this crucial role of a template, metabolic motor, etc., directing the flow of energy in such a way as to create new information?

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14. The dipeptides are listed in terms of increasing volume of the side chains of the constituent residues. Gly = glycine, Ala = alanine, Val = valine, Leu = leucine, Ile = isoleucine, and Phe = phenylalanine. Example: Gly-Ala = glycylalanine.

Steinman and Cole's (S/C) experimentally determined dipeptide bond frequencies were normalized and compared to the calculated frequencies obtained by counting actual peptide bond frequencies in ten proteins, assuming all seryl and threonyl residues are counted as glycine and all aspartyl and glutamyl residues are counted as alanine. The ten proteins used were: egg lysozyme, ribonuclease, sheep insulin, whale myoglobin, yeast cytochrome c, tobacco mosaic virus, β-corticotropin, glucagon, melanocyte-stimulating hormone, and chymotrypsinogen. Because of ambiguity regarding sequences used by S/C, all sequences are those shown in *Atlas of Protein Sequence and Structure*, volume V, ed. M. O. Dayhoff (National Biomedical Research Foundation, Georgetown University Medical Center, Washington, D.C., 1972). The experimentally determined dipeptide frequencies were obtained with aqueous solutions containing 0.01 M each amino acid, 0.125 N HCl, 0.1 M sodium dicyanamide.

Kok and Bradley's (K/B) calculated dipeptide frequencies were obtained by counting actual peptide bond frequencies for the same ten proteins with (wa) and without (woa) SIC assumptions. The numbers in brackets are for one protein, enterotoxin B, with (wa) and without (woa) S/C assumptions. The numbers in parentheses are for twenty-five proteins with (wa) and without (woa) S/C assumptions. The twenty-five proteins are the ten used by S/C and alpha S1 Casein (bovine); azurin (bordetella bronchiseptica); carboxypeptidase A (bovine); cytochrome b5 (bovine); enterotoxin B; elastase (pig); glyceraldehyde 3-phosphate dehydrogenase (lobster); human growth hormone; human hemoglobin beta chain; histone IIB2 (bovine); immunoglobulin gamma-chain 1, V-I (human EU); penicillinase (bacillus licheniformis 749/c); sheep prolactin; subtilisin (bacillus amyloliquefaciens); and tryptophan synthetase alpha chain (*E-coli* K-12). Sequences are those shown in *Atlas of Protein Sequence and Structure*, vol. V, ed. Dayhoff (1972). Note disagreement between S/C and K/B calculated results. Also K/B calculated results are at variance with S/C experimental values for one, ten, or twenty-five proteins, with (wa) or without (woa) S/C assumptions.

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36. It is noted, however, that Fox has long disputed this.
37. Miller and Orgel, *The Origins of Life on the Earth*, 144.
38. Folsome, *The Origin of Life*, 87.
39. Temussi, Paolillo, Ferrera, Benedetti, and Andini, "Structural Characterization," 105.

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10. PROTOCELLS

A summary of the overall theory of biochemical evolution was given in Chapter 2. Stage 4 of biochemical evolution is the development of protocells, presented in Figure 2-1. Protocells represent the link between the synthesis of macromolecules and the appearance of the first living cells. That is, they bridge the gap between the nonliving and the living. It is usually agreed in evolutionary theory that the bridge over this gap is the least understood aspect of the origin of life. William Day has summarized the bridging in the following way:

> In some manner the macromolecules that had condensed from the building blocks managed to associate and pass over the threshold to become life. They assembled into a coordinated arrangement that looked like and functioned as a cell. This was a quantum jump in the events leading to the formation of life and has, of course, because of its spectacular feature, received particular attention.[1]

Types of Protocells

The great chasm in our knowledge of the molecule-to-cell transition means we are free to speculate in many directions. It is not surprising, then, to see a wide variety of candidates for protocell systems. Some of these are:

1. Microspheres (Fox and Dose[2]);
2. Coacervates (Oparin[3]);
3. "Jeewanu" (Bahadur[4]);
4. NH_4CN microspherules (Labadie et al.[5]);
5. "Sulphobes" (Herrera[6]) or "plasmogeny" (Herrera[7]);

6. NH_4SCN-HCHO microstructures (Smith et al.[8]);
7. Organic microstructures (Folsome et al.[9]);
8. Melanoidin and aldocyanoin microspheres (Kenyon and Nissenbaum[10]);
9. Lipid vesicles (Deamer and Oro,[11] Stillwell[12]).

In 1976, Kenyon and Nissenbaum[13] listed the protocells known at that time (numbers 1–7) and then commented:

> Although each of the proposed model systems exhibits some rudimentary properties of chemical evolutionary interest, it must be emphasized that a very large gap separates the most complex model systems from the simplest contemporary living cells. Moreover, the geochemical plausibility of many of these "protocell" models is open to serious question.[14]

Geochemical Plausibility

Kenyon and Nissenbaum's comment is especially appropriate in view of the evidence cited in the previous chapters. In Chapter 4 we saw that the essential precursor chemicals would probably have been vastly diminished in their concentrations. This conclusion is particularly relevant to the production of protocells, for in all the nine systems proposed above, the organic chemicals must exist in fairly concentrated solutions. That is, the protocell systems proposed are essentially encapsulating mechanisms, and therefore substantial quantities of macromolecules must have existed in close proximity to be enclosed in some primitive membrane. The existence of sufficient concentrations is doubtful, and the lack of geological evidence for a chemical soup or organic ponds supports this pessimistic picture.

The use of high concentrations of selected organic chemicals in the laboratory production of protocells versus the greatly diminished concentrations expected in the ancient geological setting prompted Kenyon and Nissenbaum to comment that "... the geochemical plausibility of many of these 'protocell' models is open to serious question."[15] Several examples will illustrate the implausibility concerning concentrations necessary to form protocells.

Folsome[16] points out that Fox used 15 grams total weight of amino acids in 375 ml of artificial seawater to produce proteinoid microspheres. Therefore, the amino acid concentration would be approximately 0.4 M. Calculations regarding formation rates, concentration rates, and thermal and photochemical decomposition rates point to an abundance of amino acids in seawater of no more than about 10^{-7} M (see Chapter 4). Thus Fox's synthesis uses a molar ratio of amino acids to salts that is "10 million times less in the geologically plausible world."[17]

In more recent experiments, Fox has used concentrations of 6.0 mg of proteinoid per ml of reaction solution.[18] This synthesis would result in proteinoid concentrations of approximately 10^{-3} M, which corresponds to amino acid concentrations of approximately 0.05 M, a figure that is still more than ten thousand times too high to be plausible.

Deamer and Oro state that vesicles of single chain amphiphiles "... require relatively high concentrations [in the millimolar range] of substrate in order to be formed."[19] According to Day, "coacervation can take place in extremely dilute solutions—in concentrations as low as 0.001 percent..."[20] As coacervates are usually formed from relatively high molecular weight compounds (i.e., gum arabic and histone) the molar concentration is also extremely low. The corresponding concentration of the component amino acids would be approximately 10^{-4} M for a 0.001 percent solution. According to Folsome, however, "To make coacervates in the laboratory requires quite high concentrations of polymers."[21] That is, when compared to the primeval ponds of "dilute soup of small organic molecules," Folsome says that a "concentration gap" must be crossed to arrive at the concentration of polymers necessary for coacervation to occur.[22]

The concentrations of amino acids discussed above are typical for the various proposed protocell models. Although the range in concentrations is extremely wide (from 1 to 10^{-4} M), all organic molecules must exist in fairly concentrated solutions relative to geologically plausible concentrations.

In light of the necessary requirements and the conclusions of the previous chapters, it is difficult to imagine that all the correct chemicals or circumstances to form protocells existed on the early Earth. Even if the chemicals did occur, large quantities of configurational entropy work would have to be supplied to form biopolymers and then to organize these into a functional cell. As shown in Chapters 8 and 9, unless some hitherto unknown principle operated, the availability of such work would have been negligible.

Groups of Protocells

Historically, the two best-known protocell models are the coacervates of Oparin and the proteinoid microspheres of Fox. Lately, Folsome's microstructures and Stillwell's lipid vesicles have also received considerable attention. These models will, therefore, be discussed in more detail.

Stillwell[23] has recently divided the types of protocell models into three groups:

1. Inorganic spheres (Herrera,[24] 1942; Smith et al.,[25] 1968; Grossenbacher and Knight,[26] 1965).
2. Phase-separated polyanions and cations, e.g., Jeewanu (Bahadur,[27] 1972; Bahadur,[28] 1973), coacervates (Oparin,[29] 1968), proteinoid microspheres (Fox and Dose,[30] 1972), and most recently, melanoidin (Kenyon and Nissenbaum,[31] 1976).
3. Lipid vesicles (Goldacre,[32] 1958; Hargreaves and Deamer,[33] 1978).

Stillwell's classification emphasizes the similarity of many of the proposed protocell models. Therefore, although we will not discuss all the models in detail, comments concerning one particular model will typically apply to the whole group. Stillwell's groupings are also relevant, as the following discussions emphasize the actual formation mechanisms of coacervates, microspheres, lipid vesicles, and organic microstructures. By understanding the actual formation processes, the protocell models can be more thoroughly evaluated and the relations among and within groups perceived. The following discussions will focus on Groups 2 and 3, as the vast majority of experimental research has been performed on these types of protocell systems.

Coacervates

Coacervates were first noticed by H. G. Bungenberg de Jong in 1932.[34] When nucleic acids, proteins, and other molecules are put into water under certain conditions, spherical droplets 2–670 microns in diameter form. These droplets have higher concentrations of proteins and nucleic acids (compared to the water) and are called coacervates. Oparin realized that coacervates were a potential method to get proteins and nucleic acids together in a concentrated form.

Proteins and nucleic acids have both hydrophilic and hydrophobic parts. Proteins and nucleic acids can also be positively or negatively charged in solution (the charge depending on the pH). The proteins are attracted to the water as are the nucleic acids. If ions (of Na^+, Cl^-, etc.) are added to the solution, they also attract water to themselves. This attraction of water to the ions is usually stronger than the proteins' attraction to the water. Therefore, the water is stripped from the proteins and nucleic acids, making them less soluble. The opposite charges of the nucleic acids and proteins plus the lateral cohesion forces attract the nucleic acids and proteins together to form coacervates. This is why Stillwell groups coacervates as "phase separated" polyanions and cations.[35] This process is sometimes called "salting out" because a salt (Na^+, Cl^-, etc.) is added. The process is based on physical, attractive, and repulsive forces.

Some of the similarities between coacervates and cells noted by Oparin[36] and others are their tendency to form spherical structures, their boundaries, and their ability to absorb selectively. Coacervates are not self-organizing units, however, and they do not contain the structural regularities or selective metabolic processes found in living cells. No matter how large a list of cell-like properties is amassed, the coacervates are simply the result of physical forces of attraction,[37] and their

Table 10-1. Proteinoid microparticles possess many properties similar to contemporary cells.

Stability (to standing, centrifugation, sectioning)
Microscopic size
Variability in shape but uniform in size
Numerousness
Stainability
Producibility as gram-positive or gram-negative
Osmotic type of property in atonic solutions
Ultrastructure (electron microscope)
Double-layered boundary
Selective passage of molecules through boundary
Catalytic activities
Patterns of association
Propagation by "budding" and fission
Growth by accretion
Motility
Selective inclusion of polynucleotides with basic proteinoids (particles are composed of nucleoproteinoid not proteinoid)

Source: S. W. Fox, K. Harada, G. Krampitz, and G. Mueller, *Chem. Eng. News*, June 22, 1970, 90.

resemblance to complex living cells is only superficial. We must note, too, that coacervates are formed under very defined conditions of pH, temperature, and ionic strength. They are readily dissolved with dilution, pH change, or heat, and are easily broken up by agitation. In fact, this instability is cited by Fox et al.[38] and Fox and Dose[39] as evidence that coacervates could have played no major role as intermediate protocells. Coacervates probably would not have existed for any length of time in the primitive environment.

Wilder-Smith, in his evaluation of coacervates' ability to absorb molecules and increase their mass, states:

> The vital point for us in this whole matter is whether, by means of coacervate formation, we have found any parallel or even insight into biological cell formation, or into the mechanism by which cells increase their mass. That is, whether coacervate formation gives us insight into abiogenesis or into cell metabolism resulting in growth. It is our view that there is absolutely no parallel in the formation of coacervates and protocells. We risk this rather categorical statement on the grounds that there is no evidence that salting-out processes could ever produce

> anything resembling the inner structure of the true biological cell. For the true biological cell is always, in our experience, so structured and complex that it may be classed as almost one large code in its sequences and specificity. On theoretical grounds alone we do not see any possibility of such structures arising by mere salting-out mechanisms.[40]

He goes on to conclude that:

> It is obvious that coacervate mass increase does not occur by metabolic processes but by purely physical absorption… In reality, any fundamental likenesses between even the simplest living cells and coacervates are conspicuous by their absence.[41]

The above discussion by Wilder-Smith focused on the ability of coacervates to absorb molecules and increase their mass (growth). In the following section, many cell-like properties attributed to proteinoid microspheres will be examined in detail. As shall be observed, many of Wilder-Smith's comments above could also apply to proteinoid microspheres.

Microspheres

Microspheres form when solutions of proteinoids cool. A "remarkable" list of cell-like properties has been assembled by Fox and Dose,[42] and Fox et al.,[43] (provided in Table 10-1) and most recently by Fox and Nakashima.[44]

Because of the many similar properties between microspheres and contemporary cells, microspheres were confidently called protocells, the link between the living and nonliving in evolution. Similar structures were given the names plasmogeny[45] (plasma of life) and Jeewanu[46] (Sanskrit for "particles of life").

Essentially, microspheres result when small "protein-like" substances (proteinoids) are placed in water. As previously stated, proteinoids have both hydrophilic and hydrophobic parts. When the concentration of the proteinoids is increased, the lateral forces of cohesion between the proteinoids bring them together into a spherical particle (technically called an association colloid). These particles can also form micelles, structural aggregates in which the hydrophilic part of the protein extends outward into the water and the hydrophobic part inward.

Kenyon and Steinman also emphasize the role of micelles:

> Large molecules with both polar and nonpolar regions have the ability to form micelles in aqueous solutions. This phenomenon results from the nonpolar regions of several such molecules coming close enough together to mutually exclude much of the water in their immediate vicinity. At the same time the polar ends face outwards to the aqueous environment.[47]

Likewise, microspheres are simply proteinoids attracted together (by physical forces) into a somewhat ordered spherical structure. Here too, the structure is due to the attraction of the hydrophilic parts of the proteinoids to water and of the hydrophobic parts to each other.

We will examine in detail some of the "cell-like" properties of microspheres. Fox et al. state that "microparticles possess in large degree the rate enhancing activities of the polymer of which they are composed."[48] These are microspheres' "catalytic activities" listed in Table 10-1. If the protein by itself has a catalytic property, it seems very logical that the protein would retain that property when put in a micelle. The catalytic activity of the microsphere is not due to any special structure that the microsphere possesses. The increase in reaction rate observed in microspheres is very small by comparison to the rate increase seen in true enzymes (where rate increase factors are in the billions—10^9). Furthermore, much of the rate increase seen in proteinoids is due to the amino acids themselves, not the proteinoid.

Another "cell-like" property cited is the selective passage of certain molecules. Fox et al. explain that "Polymers that are similar in composition to those inside the microspheres can selectively diffuse through the boundary."[49] It is to be expected that similar molecules (the hydrophobic ones) would be incorporated into the micelle by the physical forces of attraction present.

Microspheres also "grow by accretion"[50]. This, however, is the attraction of like molecules to the micelle by simple physical forces. The process of microsphere "growth" has little if any similarity to the process by which contemporary cells grow. True cells grow through a metabolic process involving many chemical reactions. In microspheres no chemical reactions are taking place, only accumulation through physical forces of attraction.

"Propagation by budding"[51] also has no connection to the present-day cell process of reproduction, which requires enzymes, DNA, energy, and many reactions coupled together precisely. By contrast, the "budding" illustrated in microspheres is merely a breaking up of the microsphere due to heat or pH changes.

Oparin further criticizes microspheres by saying,

> Fox's microspheres, since they are obtained thermally, do not present very promising results from this view [i.e., evolving to include metabolic processes]. Their structure is static. This... creates difficulties when it comes to converting them into dynamic systems which could be used for modeling the evolution of metabolism.[52]

Miller and Orgel also criticize Fox's statements relating microspheres to living cells. They state that the microsphere's bilayer membranes "... are not 'biological-like' membranes since they do not contain lipids or carry out any of the functions of biological membranes."[53] They conclude, "It seems unlikely... that the division of microspheres is related to the origin of cell division."[54]

One of the most important aspects of any cell is its chemical composition. As mentioned in Chapter 9, proteinoids (from which microspheres are formed) contain many nonbiological features. In fact, Temussi refers to proteinoids as "the preferential formation of unnatural peptide bonds."[55]

Folsome criticizes microspheres in that they possess a "grossly thick" boundary layer that more closely resembles a nearly impermeable cell wall or spore coat than a cell membrane.[56]

In the present-day cell, there are thousands of different chemical reactions taking place. Not even one chemical reaction takes place in microspheres, only mechanical and physical processes due to simple attractive forces. We question listing these purely physical forces as resemblances to true cell processes. In truth, they have scant relation to actual processes in living cells. Actually, microspheres possess only outward likenesses and nothing of the inward structure and function of a true cell. They contain no information content, no energy-utilizing system, no enzymes, no nucleic acid, no genetic code, and no replication system. They contain only a mixture of polymers of amino acids, the so-called proteinoids. Microspheres cannot be said to be living in any sense of the word, and it is questionable whether they should even be given the name "protocell." They are merely an aggregation of polymers, and do not help to bridge the gap between life and non-life.

Also mentioned previously are the unlikely geological conditions that would be necessary to form microspheres. The requirement of implausible conditions has been emphasized by Miller and Urey[57] and Miller and Orgel.[58] In reference to Fox's method of microsphere preparation, Folsome asks, "The central question is where did all these pure, dry, concentrated, and optically active amino acids come from in the real, abiological world?"[59]

William Day reflects similar views concerning microspheres, coacervates, and Jeewanu when he states, "There have been similar efforts to create models of the primal cell where a greater regard was given to the gross morphology than chemical functionality."[60] But, says Day, "No matter how you look at it, this is scientific nonsense."[61] Finally, Day concludes:

> These pseudo-cellular models, like clay, soap bubbles, or any other inanimate objects, have neither the mechanism nor the potential of becoming anything beyond what they are... But the most serious fault of models from particles held together by ionic forces is that they would have been continually periled with dissolution. Coacervates are notoriously unstable and microspheres exist only in saturated solutions. Their existence in Archean lakes or oceans would have been short-lived.[62]

In his critique of microspheres and coacervates, Folsome emphasizes that these models "... suffer from the same practical problems of the concentration gap."[63] That is, the formation of microspheres and coacervates requires quite high concentrations of polymers not present in the primeval ponds. Folsome goes on to say, "Hypothetically, there are ways to circumvent the concentration gap, but all appear to be more wishful thinking than plausible facets of reality."[64]

Overall, it appears that coacervates, microspheres, and all the "phase-separated polyanion and cation" models of Group 2 have serious deficiencies that disqualify them as protocell systems. That is, they cannot be considered forerunners to the modern cell.

Lipid Vesicles

The interest in lipids stems from their functionality in modern membranes. Here they have a primary role, and it is not surprising they should be used in developing protocell systems. Bangham and Horne[65] originally demonstrated that phospholipid molecules will self-assemble into closed vesicles. Phospholipids are fatty acid derivatives of glycerophosphoric acid. The hydrocarbon chain of the fatty acid is hydrophobic, whereas the phosphate end of the molecule is hydrophilic. Therefore, the phospholipids align themselves when surrounded by water to form spherical shapes. If a single layer of phospholipid molecules forms, a micelle results. If a bimolecular layer creates a sphere, the particle is a liposome or vesicle.

Simple fatty acids with hydrocarbon chains of eight or more carbons can also form structured vesicles or micelles, depending on the pH of the solution.[66] Compared to liposomes, however, the structures are relatively unstable, and quite sensitive to ionic environment and temperature. They also require relatively high concentrations (in the millimolar range) in order to form.[67] Contemporary phospholipids can form vesicles at lower concentration, and are not so sensitive to the environment. Such vesicles have been criticized as being composed of highly evolved phospholipids.[68] Stillwell[69] states that phospholipids were probably not present in the early ocean, while Deamer and Oro[70] claim that phospholipids can be formed under plausible prebiotic conditions. In the opinion of the authors, however, several nongeological (i.e., implausible) chemical components have been used in the synthesis. In particular, soluble phosphate compounds were used as reactants. It is doubtful, however, that soluble phosphate concentration exceeded 10^{-6} M in the primitive ocean, due to precipitation by calcium and magnesium salts. The fatty acids needed for phospholipid formation would also predictably have been in short supply in the oceanic soup, having precipitated with calcium and magnesium salts. (See Chapter 4.)

The synthesis of complex lipids, such as the phospholipids, probably also suffered from the concentration gap discussed earlier. The precursors of the complex lipids include fatty acids, glycerol, and glycerol phosphate.[71] These compounds, if they existed at all in the prebiotic soup, would have been present in dilute concentrations, since they would have been subject to many competing reactions. In view of this, the formation of more complex lipids necessary for stable vesicles is dubious.

Note that in Stillwell's[72] review of lipid membranes in protocells, he criticizes microspheres and coacervates as being too "leaky" to be protocells. That is, the molecules encapsulated in the structure can easily leak through the boundary. Interestingly, the lipid vesicles may be too "tight." They do not readily transport molecules through their membranes. Contemporary cells contain both lipids and proteins in their membranes, enabling a complex, selective transport mechanism to operate. Several transport mechanisms have been proposed for the vesicle protocells.[73] The facilitated diffusion of molecules through the boundary may be one of the few function-like properties of vesicles. Nevertheless, the mechanisms are nowhere comparable to those in contemporary cells. In summary, the vesicle protocells bear only superficial resemblance to true cells.

Organic Microstructures

Folsome[74] has been the main proponent of the organic microstructure protocell system. Microstructures are formed during Miller-Urey electrical discharge experiments. They resemble (morphologically) microfossils found in ancient rocks and are thought to consist of cross-linked kerogenous polymer structures.

Fox has criticized Folsome's experiments as being nongeological—"without terrestrial counterpart."[75] Furthermore, Fox states that the alleged potential of microstructures as a protocell model is poorly supported because the microstructures have not demonstrated any cellular function. The microstructures are also basically uncharacterized and have not been shown to contain polymers.

Fox's criticisms appear valid. A strength of Folsome's structures which must be acknowledged, however, is that they do not require the usual stepwise approach. That is, the organic microstructures form directly in spark discharge simulation experiments. This is in contrast to the formation of most protocell models, which require intermediate steps. For example, coacervates are formed from relatively high molecular weight polymers such as histones and gum arabic, and microspheres are formed from pure amino acids. In view of the discussion in Chapter 5, however, concerning the composition of the primitive Earth and atmosphere, the geological plausibility of Folsome's highly reducing, closed-flask experiments should be questioned. The limited evidence (first-order kinetics and self-assembly) given by Folsome in support of the organic microstructure's biogenicity suffers from the same problems as other proposed protocell systems. That is, purely physical and morphological properties are being dressed up to resemble present-day cellular processes when no true functional similarity exists. In fact, the morphology of organic microstructures is very diverse and sometimes irregular. Present-day cells are typically spherical with smooth, regular boundaries. Organic microstructures possess few, if any, properties of present-day cells and must therefore be questioned as forerunners of true cells.

Conclusion

In light of the conclusions from the previous chapters (especially Chapters 4, 5, 8, and 9), it seems doubtful that the macromolecules necessary for living cells existed on the early Earth. Even if the molecules were present in substantial quantities, the encapsulating protocell systems reviewed in this chapter appear to be highly tenuous as true protocells. In most cases, the only resemblance that the proposed models have to contemporary cells is their size and morphology (spherical shape).

Cellular functions claimed for the protocell system are the result of simple physical forces. Similarities to present-day cell processes are superficial. In all cases, the protocell systems are only conglomerations of organic molecules that provide no genuine steps to bridge the gap between living and nonliving. Furthermore, most protocells are highly unstable and have been formed under nongeological conditions. In summary, the assessment of Green and Goldberger is still appropriate:

> … the macromolecule-to-cell transition is a jump of fantastic dimensions… The available facts do not provide a basis for postulating that cells arose on this planet.[76]

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    1, Hydrogen bonding.

    2. One dipole attracting another dipole (dipole-dipole forces are weak electrostatic attractions).

    3. Lateral forces of cohesion (weak forces between like molecules which probably consist of Van der Waals forces).

    4. Hydrophilicity and hydrophobicity (result of previous three forces).

    These physical forces of attraction are contrasted with forces that form chemical bonds:

    1. Sharing of electrons (covalent bonding).

    2. Transfer of electrons (ionic bonds).

    3. Metallic bonding.

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11. SUMMARY AND CONCLUSION

Summary

Chemical evolution is broadly regarded as a highly plausible scenario for how life on Earth might have begun. It has received support from many competent theorists and experimentalists. Ideas of chemical evolution have been modified and refined considerably through their capable efforts. Many of the findings of these workers, however, have not supported the scenario of chemical evolution. In fact, what has emerged over the last three decades, as we have shown in the present critical analysis, is an alternative scenario which is characterized by destruction, and not the synthesis of life.

This alternative scheme envisions a primitive Earth with an oxidizing atmosphere. A growing body of evidence supports the view that substantial quantities of molecular oxygen existed very early in Earth history before life appeared. If the early atmosphere was strongly oxidizing, as we find on Mars today, then no chemical evolution ever occurred. Even if the primitive atmosphere was reducing or only mildly oxidizing, then degradative processes predominated over synthesis. Furthermore, macromolecule polymerization would be subjected to countless competing reactions. Small steady-state concentrations (no greater than 10^{-7} M for amino acids, for example) of essential precursor chemicals would fill the Earth's water basins. Because of such small concentrations, the rates of chemical evolution in the ocean were never more than negligible. This follows from the law of mass action. The same law also predicts that any concentrating mechanisms (such as freezing or evaporating ponds) would merely have served to accelerate both destructive and synthetic processes already going on at slower rates in the dilute seas. In the end there would have been no discernible chemical evolutionary benefit from these small concentrating ponds. An idea of how dilute in biomonomers these seas must have been comes from the fact that the prebiotic chemical soup, presumably a world-wide phenomenon, left no known trace in the geological record.

Since monomer concentrations were so low, polymerizations by spontaneous means were made all the more difficult. The primary difficulty was not lack of suitable energy sources. Rather, it was both a lack of sufficient energy-mobilizing means to harness the energy to the specific task of building biopolymers and a lack of means to generate the proper sequence (of, say, amino acids in a polypeptide) to get biological function. We have identified this latter problem as one of doing the configurational entropy work. Here the difficulty is fundamental. It applies equally to discarded, present, and possible future models of chemical evolution. We believe the problem is analogous to that of the medieval alchemist who was commissioned to change copper into gold. Energy flow through a system can do chemical work and produce an otherwise improbable distribution of energy in the system (as, e.g., in a water heater). Thermal entropy, however, seems to be physically independent from the information content of living systems which we have analyzed and called configurational entropy. As was pointed out, Yockey has noted that negative thermodynamic entropy (thermal entropy) has nothing to do with information, and no amount of energy flow through the system and negative thermal entropy generation can produce even a small amount of information. You can't get gold out of copper, apples out of oranges, or information out of negative thermal entropy. There does not seem to be any physical basis for the widespread assumption implicit in the idea that an open system is a sufficient explanation for the complexity of life. As we have previously noted, there is neither a theoretical nor an experimental basis for this hypothesis. There is no hint in our experience of any mechanistic means of supplying the necessary configurational entropy work. Enzymes and human intelligence, however, do it routinely.

Actually the configurational entropy work is of two types. The job of selecting or sorting the appropriate chemical composition out of a random soup mixture we have referred to as the "selecting" work. The task of arranging these selected monomers in the proper sequence in a polymer for biological function is the "coding" work. The early Earth conditions appear to offer no intrinsic means of supplying either of these indispensable components of the configurational entropy work necessary to make the macromolecules of life.

It is this unmet configurational entropy work requirement which is the central problem in developing essential macromolecules such as DNA and protein, let alone the more complex cellular structures.

So-called protocells have been produced in the laboratory in an attempt to bridge the gap between the nonliving and the living. Such structures do have a crude resemblance to true cells but none of the internal cellular machinery, such as enzymes, DNA, or phospholipid cell membranes. The few "cell" functions manifested by protocell systems typically arise from simple physical forces. Any similarity to true cellular processes is highly superficial.

The usual interpretation of chemical evolution derives a great deal of apparent plausibility from reports of laboratory prebiotic simulation experiments. In fact, most of these experiments are probably invalid. Unlike other established experimental disciplines, "prebiotic chemistry" has no generally accepted criteria for what constitutes a valid prebiotic simulation experiment. Consequently, many incredible experiments have been published as "simulation" experiments.

As a meager step toward remedying this situation, we have offered a tentative definition of a valid prebiotic simulation experiment. Based on the widely held view that life was not the result of the *crucial* involvement of the supernatural, we have carefully extended this to show that a valid prebiotic simulation experiment must not have crucial investigator interference in any *illegitimate* sense. By definition there are numerous *legitimate* activities of the investigator. Simply stated, an investigator may appropriately adjust conditions of the experiment that are deemed analogous to the primitive Earth situation. But such conditions must be plausible.

To help evaluate the degree of interference by the investigator, we devised a scale on which we placed the various common experimental procedures. To the degree a lab experiment deviates from plausible early Earth conditions, to that degree it is an illegitimate interference by the experimenter. This view assumes that we need to take into account only *probable* conditions. With the help of this scale we have judged the conditions of most simulation experiments to be implausible, and therefore excluded them as legitimate simulation experiments. This is a severe judgment. But it should be recognized that part of the deep suspicion that has surrounded prebiotic chemistry from its beginning has been over precisely this matter, that ill-defined experimental criteria have been used. As one scoffer was heard to remark in a scientific meeting, "In prebiotic chemistry anything counts." It is up to the investigators in this field to come to grips with the problem of what is a valid simulation experiment, and what is not.

One characteristic feature of the above critique needs to be emphasized. We have not simply picked out a number of details within chemical evolution theory that are weak, or without adequate explanation for the moment. For the most part this critique is based on crucial weaknesses intrinsic to the theory itself. Often it is contended that criticism focuses on present ignorance. "Give us more time to solve the problems" is the plea. After all, the pursuit of abiogenesis is young as a scientific enterprise. It will be claimed that many of these problems are mere state-of-the-art gaps. And, surely, some of them are. Notice, however, that the sharp edge of this critique is not what we *do not* know, but what we *do* know. Many facts have come to light in the past three decades of experimental inquiry into life's beginning. With each passing year the criticism has become stronger. The advance of science itself is what is challenging the notion that life arose on Earth by spontaneous (in a thermodynamic sense) chemical reactions.

Over the years a slowly emerging line or boundary has appeared which shows observationally the limits of what can be expected from matter and energy left to themselves, and what can be accomplished only through what Michael Polanyi has called "a profoundly informative intervention."[1] When it is acknowledged that most so-called prebiotic simulation experiments actually owe their success to the crucial but *illegitimate* role of the investigator, a new and fresh phase of the experimental approach to life's origin can then be entered. Until then, however, the literature of chemical evolution will probably continue to be dominated by reports of experiments in which the investigator, like a metabolizing Maxwell Demon, will have performed work on the system through intelligent, exogenous intervention. Such work establishes experimental boundary conditions, and imposes intelligent influence or control over a supposedly "prebiotic" Earth. As long as this informative interference of the investigator is ignored, the illusion of prebiotic simulation will be fostered. We would predict that this practice will prove to be a barrier to solving the mystery of life's origin.

Conclusion

A major conclusion to be drawn from this work is that the undirected flow of energy through a primordial atmosphere and ocean is at present a woefully inadequate explanation for the incredible complexity associated with even simple living systems, and is probably wrong.

Many will find this critique "interesting" but will not draw the same conclusions we have. Why will many predictably persist in their acceptance of some version of chemical evolution? Quite simply, because chemical evolution has not been *falsified*. One would be irrational to adhere to a falsified hypothesis. We have only presented a case that chemical evolution is highly implausible. By the nature of the case that is all one can do. In a strict, technical sense, chemical evolution *cannot* be falsified because it is not falsifiable. Chemical evolution is a speculative reconstruction of a unique past event, and cannot therefore be tested against recurring nature. As Pirie remarked, "Now we have little expectation of being able to conclude a discussion with the statement 'This is how life did arise'; the best we can hope for is 'This is one of the ways life could have arisen.'"[2]

Some will immediately conclude that if Pirie is right, then chemical evolution is not science and it should be consigned to the rubbish heap. This seems to have been the conclusion of Mora when he said, "[As for] how life originated, I am afraid that, since Pasteur, this question is not within the scientific domain."[3]

But this conclusion is too hasty. It must be realized, as we pointed out in Chapter 1, that the speculative nature of chemical evolution does not mean that it is without value. In forensic medicine, a speculative scenario in the hands of a skillful lawyer can be used to persuade a jury of the guilt or innocence of a defendant. So it is with chemical evolution scenarios.

In the persuading process there is always the risk that partial truth will be viewed as the whole truth and mislead a jury. To minimize the risks of convicting the innocent and freeing the guilty, the court in the U.S.A. uses an adversarial approach, which means the jury gets to hear likely scenarios from attorneys for both prosecution and defense. In addition, attorneys from both sides can cross-examine witnesses. When a jury weighs the evidence, it is hoped the evidence in hand is a fair sampling so that justice is served. For a jury to render a guilty verdict for a capital offense the case must be established beyond reasonable doubt.

To be sure, the case for the origin of life via chemical evolution as usually presented sounds plausible, and has been accepted very widely, if not generally, by the scientific community. Furthermore, popularizations have carried the case to millions in a persuasive manner. Because of the fact that chemical evolution cannot be falsified, however, its apparent plausibility can easily be exaggerated, and it tends to move beyond its true status as speculation and to be regarded instead as knowledge.

Perhaps this is always a danger with speculative approaches, but it would seem to be particularly likely here, since the substantial case questioning the plausibility of chemical evolution has been all but muted. Our chapters, we believe, have shown that reasonable doubt exists concerning whether simple chemicals on a primitive Earth did spontaneously evolve (or organize themselves) into the first life. Now we leave it to you—the jury—to decide.

> That's the worst of circumstantial evidence. The prosecuting attorney has at his command all the facilities of organized investigation. He uncovers facts. He selects only those which, in his opinion, are significant. Once he's come to the conclusion the defendant is guilty, the only facts he considers significant are those which point to the guilt of the defendant. That's why circumstantial evidence is such a liar. Facts themselves are meaningless. It's only the interpretation we give those facts which counts.—"Perry Mason" in *The Case of the Perjured Parrot.*[4]

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12. EPILOGUE

In the introductory chapter we stated our hope that criticism of current theories of the origin of life would prove to be a first step toward a more satisfactory theory of origins. No consideration, however, was given to alternatives. So, in this epilogue, we will consider five alternative views which have been mentioned in the literature on the origin of life. These are:

1. New natural laws
2. Panspermia
3. Directed Panspermia
4. Special Creation by a creator within the cosmos
5. Special Creation by a Creator beyond the cosmos

We foresee that the major theories of origins for the future are listed here. Before considering these, however, let us enumerate some notable results from our analysis of origin of life research. Any satisfactory alternative should account for these factors:

1. There is accumulating evidence for an oxidizing early earth and atmosphere.
2. Destructive processes would have predominated over synthesis in the atmosphere and ocean in the prebiotic world.
3. There is continued shortening of the time interval (now less than 170 million years) between earth's cooling and the first appearance of life.
4. Geochemical analysis shows that the composition of Precambrian deposits is short of nitrogen.

5. There is an observational limit or boundary between what has been accomplished in the laboratory by natural processes left to themselves and what is done through investigator interference.
6. In our experience only two things, biotic processes (carried out by enzymes, DNA, etc.) and investigator interference, are able to couple energy flow to the task of constructing biospecific macromolecules.
7. True living cells are extraordinarily complex, well-orchestrated dynamic structures containing enzymes, DNA, phospholipids, carbohydrates, etc., to which so-called protocells bear only a superficial resemblance.

New Natural Laws[1]

We have seen the failure, perhaps the impotence, of presently known fundamental physical and chemical laws to explain the origin of biological structures. This has given renewed inspiration to the idea that new principles of physics must be discovered to adequately explain this phenomenon. Elsasser[2] has argued that classes of living structures are too few to be subject to the statistical averaging procedures of physics, suggesting that new natural laws must be identified instead. Recall from Chapter 1 that this was also the suggestion of Murray Eden at the Wistar Institute Symposium. In the same vein Garstens[3] postulated that the application of statistical mechanics to biological systems requires a new set of auxiliary assumptions different from those traditionally used in physics. Mora[4] concurs that new laws are essential, pointing out that it is impossible to reconcile statistical and thermodynamic constraints with the formation of living systems.

Using the quantum mechanical method, Wigner[5] calculated the probability of a living organism interacting with nutrients to produce another identical organism, assuming that this interaction is governed by a random symmetric Hamiltonian matrix. This is the same assumption employed by von Neumann[6] to prove that the Second Law of Thermodynamics is a consequence of quantum mechanics. On counting up the number of equations describing the interactions, Wigner found they greatly exceeded the number of unknowns which described the final state of the nutrient plus two organisms. Wigner's analysis showed a zero probability that there would be any state of the nutrient which would allow multiplication of the organism. He says: "It would be a miracle" and would imply the interaction of the organism with the nutrient had been deliberately "tailored" so as to make the lesser number of unknowns satisfy the greater number of equations.[7] Of course the interaction between living systems and nutrients is not random, but directed by the DNA molecule. Prebiotic systems, on the other hand, have no such endowment, and are subject to the problem of randomness alluded to by Wigner.

Landsberg[8] also used quantum mechanics to examine the question of spontaneous generation and reproduction of organisms. He found that by broadening Wigner's analysis to include nonequilibrium systems, the probabilities were greater than zero, though still very small. Based on the work of Wigner and Landsberg, we may conclude that quantum mechanics does not forbid the origin of life, but does suggest that life could not arise as a result of random interactions encountered in inanimate matter. The implication is that some hitherto little-understood "principle of organization" must be responsible for the necessary "instructed" interaction of chemicals leading to the formation of living systems. This conclusion drawn from quantum mechanics is in agreement with the earlier observation from thermodynamics (Chapter 8) that a coupling of the energy flow through the system to the required work, especially configurational entropy work, is essential for the formation of life.

Polanyi[9] has emphasized that the mechanism and design in living organisms is irreducible to the laws of inanimate matter. He notes that the laws of chemistry and physics are expressed mathematically in terms of differential equations. The existence of living systems may only be understood, however, in the fixing of the boundary conditions that determine the form which both the equations and nature take. He leaves unanswered the question of how the "fixing" of the boundary conditions occurred, implying again the need for new laws.

In a similar way, Longuet-Higgins[10] affirms that physics and chemistry are conceptually inadequate as a theoretical framework for biology, and recommends more serious consideration of biological problems in terms of design, construction, and function.

The need for new laws is further underscored in the paradox seen by Schrodinger[11] in 1944. In inanimate matter, regular, orderly behavior is always the averaged result of the collective behavior of a large number of molecules acted on by particular constraints. In living systems, however, orderly behavior appears to result from the activity of single molecules or very small collections of molecules, in spite of the fact that fundamental physical laws lead us to believe that single molecules should behave in a random manner. Pattee[12] and Bohm[13] both have discussed this problem but have found no satisfactory solution. Bohm stresses that it is virtually certain that fundamental theory will not explain even the accurate transmission of genetic information, much less its origin. He further notes the ironic twist that just when physics and chemistry are abandoning mechanistic interpretations for probabilistic ones, biology is adopting them.

In summary, those who suggest new natural laws do not show it is reasonable to believe that energy flow through a system would be coupled to accomplish the required work to produce the first protein, DNA, and ultimately, the first living cell. They simply point out that new organizing principles are *needed* as present ones are clearly inadequate. The mere need of new laws is a legitimate reason for seeking them, but only evidence can legitimately establish and sustain them. Intelligent contrivances harness a portion of the energy flow for work in the human world. How some energy converting/coupling means might arise without intelligence in the inorganic world before life is difficult to say.

Panspermia

Panspermia is the classical extraterrestrial view which originated after Pasteur's disproof of spontaneous generation in the 19th century, and was popularized early in the 20th century by S. Arrhenius.[14] According to this view, a life spore was driven to earth from somewhere else in the cosmos by electromagnetic radiation pressure. The idea is sometimes called radiopanspermia.

Arrhenius calculated that if a particle were in the size range of 0.1–3 microns it could escape solar gravity and be pushed along in space by the pressure of light waves. Although panspermia was an ingenious idea, it failed to account for three significant factors:

1. Panspermia did not really answer the question of origins; it merely pushed the problem to some other planet or place in the cosmos.
2. Panspermia offered no way to protect life spores from the lethal effects of intense radiation in space.
3. Panspermia offered no mechanism for safe entry through the earth's atmosphere. Arrhenius calculated that any life spore larger than 1 micron in diameter would burn up on entry. Most plant and animal cells, however, are 10–40 microns in diameter.

These problems were seen as severe, and most people dismissed panspermia as nonviable. Any flickering interest in panspermia seemed to fade in the mid-1950s with the emergence of the modern view of terrestrial abiogenesis.

Revived Interest in Panspermia

More recently, however, major objections to terrestrial chemical evolution scenarios, surveyed in the main body of the book, have caused some to reconsider panspermia, even though it does not purport to be an account of life's origin. Why persist in looking to the earth for the answer to life's origin, especially since the evidence questioning terrestrial chemical evolution is quite substantial? As Brooks and Shaw noted, "We must be interested in the truths of matters and must not modify truths so that we can conveniently express our origins in ways which for some reason or other give us maximum satisfaction."[15]

Fred Hoyle and N. C. Wickramasinghe[16] have revived interest in panspermia. They have offered calculations showing that particles up to 60 microns in size (which includes most living cells) could reach the earth, make "soft" landings, and neither burn up on entry in the atmosphere nor be obliterated on impact.

The problem of preserving life in space might not be as severe as Arrhenius thought. Through radio astronomy, organic molecules have been discovered in space, including some that are usually considered as precursors to life (e.g., formaldehyde, methanol), suggesting that some method of preservation is operative. Apparently these molecules are protected by thin layers of graphite dust a few tenths of a micron thick, which provide a shield from the destructive rays of ultraviolet light.

Added to this is the suggestive discovery of amino acids in meteorites, including some that are important in proteins. The Murchison meteorite, which fell in Australia in 1969, contained DL-amino acids,[17] including some proteinous ones. The presence of DL-amino acids was considered proof of extraterrestrial origin, and evidence that the meteorite was free of contamination from earth life. This is significant because the meteorite fell on a sheep farm, where remaining uncontaminated would be no trifling feat!

Perhaps more significant is the discovery of amino acids in another meteorite, said to be 3.83 billion years old, in the deep freeze of Antarctica. It was hailed as proof that the amino acids were of extraterrestrial origin. According to Cyril Ponnamperuma, who conducted much of the investigation:

> The processes of chemical evolution appear to be common in the solar system... Nobody has found life beyond the earth, but all of the evidence we are finding seems to point in that direction. I am certain that it is there.[18]

In spite of the optimism of Ponnamperuma and others, the relevance of these molecules from (and in) space is far from clear. Perhaps a story will put the issue in perspective. It is said that a little boy asked his mother whether it was true that we come from dust and at death we return to dust. After an affirmative reply from his mother, the boy exclaimed, "Well, somebody is under my bed, but I can't tell if he's coming or going!" Only by a mistaken presupposition did the boy infer "somebody" from the presence of dust under his bed. The situation of the molecules in space seems remarkably parallel to this story. Clearly what is guiding some scientists to infer life in space from the mere presence of organic molecules is their hypothesis that life is rather common in the cosmos, being merely a stage in the development of matter. What else could have informed Ponnamperuma when he said concerning the possibility of life in space, "I am certain that it is there"? But surely the question is whether this hypothesis is correct; it is not an axiom for making a deduction.

We cannot disagree that there is need for an alternative to chemical evolution. In recognition of the fact that panspermia offers no theory of origins, it must implicitly assume chemical evolution in some other locale in the cosmos, where conditions are more favorable than on earth. Many of the objections raised concerning terrestrial chemical evolution must, however, apply to other planets by the principle of uniformity. In any setting it comes down to the fact that natural forces acting alone must be capable of supplying the necessary configurational entropy work of building the protein, DNA, etc., and then assembling the cell. We know by experience that intelligent investigators can synthesize proteins and build genes. We still have no evidence it can be done by unassisted abiotic means.

If one takes the view that only the organic materials from which to assemble life, and not life itself, came from space, then the next step must be faced. The assembly of life under these circumstances must occur in spite of the destructive forces discussed in Chapter 4. Space-incident organic molecules do little to solve the mystery of life's origin. As was pointed out in Chapter 4, two great conditions for assembly of life are:

(1) a source of precursor molecules; and (2) protection of these till assembly occurs.

In spite of the problems with panspermia, the number of scientists ready to defend it is growing.

Directed Panspermia

Also to be considered is an enterprising variation of panspermia called directed panspermia.[19] Suggested by Francis Crick and Leslie Orgel, this hypothesis purports that life spores were sent to earth in some kind of rocket ship by some extraterrestrial intelligence (ETI), most likely from some other galaxy. Speculations have been numerous. Perhaps extraterrestrial beings purposefully sent life spores to earth to make it a "wilderness area or zoo,"[20] or perhaps a cosmic dump site.[21] It is even possible life spores were left here inadvertently "on some ancient astronaut's boot."[22]

As in the case of panspermia, few scientists have considered directed panspermia worthy of pursuit. According to A. Dauvillier (who wrote prior to the notion of directed panspermia, but whose words are still appropriate):

> The doctrine of cosmic Panspermia can only be conceived if one accepts the idea of the carriage of live germs by foreign astronauts. This, to all intents and purposes, is a facile hypothesis, a subterfuge which seeks to avoid the fundamental problem of the origin of life.[23]

Most scientists probably agree with Dauvillier that the notion of panspermia directed by ETI is fantasy. There is some limited circumstantial evidence, however, that enhances its appeal over panspermia. Like panspermia, this view notes that there are some significant problems with terrestrial chemical evolution, such as the accumulating evidence for an oxidizing early atmosphere in contrast to the expected reducing condition. As Crick has mentioned, if it were really true that the primitive atmosphere contained a significant amount of oxygen, it would be difficult to imagine chemical evolution. In such a case, reasons Crick, "it would support the idea of Directed panspermia."[24]

A fact that has enamored Crick is that in the fossil record, the earliest organisms appear suddenly without any evidence of a prebiotic soup or simple precursors.[25] For Crick this too is good evidence for directed panspermia. There is no compelling evidence that Crick and others can cite for this view, however. In fact the evidence cited above for directed panspermia would also apply to panspermia. It is not surprising then to hear Crick lament, "Every time I write a paper on the origin of life, I swear I will never write another one, because there is too much speculation running after too few facts..."[26]

An additional form of "evidence" that is often used to support ideas about the existence of ETI in the cosmos is the Green Bank-Drake equation.[27] This equation gives the value of N, the number of advanced civilizations which are presently (presumably) communicating in the galaxy, to be

$$N = Rf_p n_e f_l f_i f_c f_d L \qquad 12\text{-}1$$

where R is the rate of star formation; f_p, the probability that a star will have planets; n_e, the number of planets per star with environments favorable to life; f_l, the probability that life will develop; f_i, the probability that intelligent life will develop; f_c, the probability that intelligent beings attempt interstellar communication; f_d, the probability that such beings desire to communicate; and L, the lifetime of a civilization after it reaches the interstellar communication stage.

Various estimates have been reached using the Green Bank-Drake equation. They range from $N = 1$ (even this value is assigned on the nearly universal assumption that spontaneous chemical evolution occurred once) to $N = 10^8$ or more. The wide spectrum of numbers cited in the literature for N reflects the room for individual subjectivity by those doing the estimating. Many enthusiasts consider it reasonable to conclude that perhaps a million advanced societies inhabit the cosmos. Several federally-funded projects, such as Project OZMA, have been undertaken to search for extraterrestrial intelligence (SETI). There is a growing body of literature critical of the ETI concept, however. For example, Frank Tipler has thoroughly examined the arguments for ETI, and notes, "the problem with the Drake equation is that only f_p, and to a lesser degree n_e, are subject to experimental determination."[28] Even when assigning to each term the value usually given in discussions of interstellar communities, the conclusion is reached that "we are alone."[29]

Directed panspermia, like panspermia itself, fails to give an account of the origin of life. It merely assumes that spontaneous generation must have occurred in some favored environment somewhere in the cosmos. Directed panspermia is primarily a suggested mechanism to get life safely to earth. Surely intelligent beings could design an appropriate spaceship.

Thus, in spite of the lack of any real evidence for the existence of ETI, there appears to be growing interest in directed panspermia among some scientists.

Special Creation by a Creator Within the Cosmos

Hoyle and Wickramasinghe[30] have developed a novel and creative argument, which we shall present in some detail. As will be seen, the view of intelligence creating biological specificity comes in not one, but two types: (1) a creating intelligence within the cosmos; (2) a creating intelligence beyond the cosmos. In arguing for the former, Hoyle and Wickramasinghe contend that Darwinism has failed to account for the origin of life and the development of terrestrial biology:

> No matter how large the environment one considers, life cannot have had a random beginning... there are about two thousand enzymes, and the chance of obtaining them all in a random trial is only one part in $(10^{20})^{2000} = 10^{40,000}$, an outrageously small probability that could not be faced even if the whole universe consisted of organic soup.
>
> If one is not prejudiced either by social beliefs or by a scientific training into the conviction that life originated on the Earth, this simple calculation wipes the idea entirely out of court... the enormous information content of even the simplest living systems... cannot in our view be generated by what are often called "natural" processes, as for instance through meteorological and chemical processes occurring at the surface of a lifeless planet... For life to have originated on the Earth

> it would be necessary that quite explicit instruction should have been provided for its assembly... There is no way in which we can expect to avoid the need for information, no way in which we can simply get by with a bigger and better organic soup, as we ourselves hoped might be possible a year or two ago.[31]

The logic so far is that the customary notion of life originating by chemical evolution in an organic chemical soup is too improbable. The information content of living cells is too great to expect it to have arrived by "natural" means.

An adequate theory of origins requires an information source capable of generating chemical complexity. Hoyle and Wickramasinghe argue that the evidence is overwhelming that intelligence provided the information and produced life:

> The correct position we think is... an intelligence, which designed the biochemicals and gave rise to the origin of carbonaceous life... Given an atlas showing the amino acid sequences of all the enzymes, human biochemists could construct them with complete accuracy, thereby demonstrating the enormous superiority of intelligence allied to knowledge over blind random processes... Any theory with a probability of being correct that is larger than one part in $10^{40,000}$ must be judged superior to random shuffling. The theory that life was assembled by an intelligence has, we believe, a probability vastly higher than one part in $10^{40,000}$ of being the correct explanation of the many curious facts discussed in preceding chapters... Paley likened the precision of the living world to a beautifully made watch. He then argued that, just as a watch owes its origin to a watchmaker, the world of Nature must owe its origin to a Creator, God... The speculations of *The Origin of Species* turned out to be wrong... It is ironic that the scientific facts throw Darwin out, but leave William Paley, a figure of fun to the scientific world for more than a century, still in the tournament with a chance of being the ultimate winner... Indeed, such a theory is so obvious that one wonders why it is not widely accepted as being self-evident. The reasons are psychological rather than scientific.[32]

To be sure, such a creative view entails purpose, a point which Hoyle and Wickramasinghe address:

> The revulsion which biologists feel to the thought that purpose might have a place in the structure of biology is therefore revulsion to the concept that biology might have a connection to an intelligence higher than our own.[33]

By this time surely every schoolboy has figured out that Hoyle and Wickramasinghe are offering to the world the traditional view of Special Creation. But every schoolboy would be wrong! Hoyle and Wickramasinghe deny that the creator is the traditional supernatural God. They envision a creator within the total cosmos. They contend that a flaw in logic kept generations of scientists from seeing the truth that intelligence is the authentic source of the information in the biological world:

> The whole of the special creation theory was thought to be wrong and there was a general revulsion among scientists against it. In effect, because the details were seen to be incorrect, the fundamental idea that life was created by an intelligence was also rejected... If we define "creation" to mean arrival at the Earth from outside, the unit of creation in our picture is the gene, not the working assembly of genes that we call a species.[34]

The novelty of this suggestion is that is seems to solve the major problem of the origin of life that both panspermias merely skirted. A real origin is suggested, primarily of genes but also of some bacterial cells. The implication is that the mechanism of panspermia can be used to safely transport these genes to earth without having to resort to anything as elaborate as a spaceship. Since genes or gene fragments would be within the size range of 0.1–3 microns, light waves could easily move them across the solar system. Furthermore, they could be protected from intense radiation in space by a thin sheath of graphite. Finally, they would be well within the 60-micron limit for safe entry into our atmosphere without burning up.

Such a process as this would operate not only at the beginning; Hoyle and Wickramasinghe suggest it is a continuous process through history even to this day:

> In our view the arrival at the Earth of living cells, and of fragments of [created] genetic material more generally, is a continuing ongoing process that directs the main feature of biological evolution. It is this process which does the job that is usually attributed to Darwinism.[35]

In addition to the origin of life, Hoyle and Wickramasinghe account for the whole of biology by these falling genes. The gaps in the fossil record are real; there never were transitional forms, because the genetic information necessary for the jumps in species came continuously to earth by cosmic means.

If the cosmic intelligence responsible for the creation of genes and bacteria is not God, then who or what is it?

> The advantage of looking to the whole universe is rather that it offers a staggering range of possibilities which are not available here on the Earth. For one thing it offers the possibility of high intelligence within the universe that is not God. It offers many levels of intelligence rising upwards from ourselves... To be consistent logically, we have to say that the intelligence which assembled the enzymes did not itself contain them. This is tantamount to arguing that carbonaceous life was invented by a noncarbonaceous intelligence, which by no means need be *God*, however.[36]

What other kind of high intelligence is also free of enzymes? Hoyle and Wickramasinghe point us to ancient and medieval schemes in which there were intelligent agencies in the universe higher than man, but lower than God.[37]

Hoyle and Wickramasinghe speculate further that the intelligence may not have simply remained in the outer regions of the cosmos, but may have in fact become incarnate on earth in a sort of "invasion from space":

> We come now to what for us is a strong argument for the existence of an overt plan of planetary invasion... we have so far been unable to exterminate a single insect species. Not even one species among millions![38]

And what do we learn from this curious fact? Hoyle and Wickramasinghe write:

> The situation points clearly to one of two possibilities. Either we are dealing with an overt plan invented by an intelligence considerably higher than our own... or the insects have already experienced selection pressure against intelligences of at least our level in many other environments elsewhere in the universe.[39]

The moment of truth finally arrives when we learn the identity of the superintelligence. Hoyle and Wickramasinghe ask, "Could the insects themselves be the intelligence higher than our own?"[40] If anyone wonders why we are so long in discovering their true identity, Hoyle and Wickramasinghe suggest it is because they do not wish to be known:

> Perhaps concealment is an essential tactic. Perhaps the intelligence is static because it understands the dictum of sagacious lawyers: "When your case is going well, say nothing."[41]

We suspect that few will find Hoyle and Wickramasinghe's hypothesis of falling genes acceptable as a genuine contribution of science. Although their criticism of chemical evolution is cogent, the novel notion of cosmically created genes falling to the earth does not realistically take into account the fate of genes once they reach the earth (Chapter 4); nor does it heed the fact that genes need a proper cellular context in which to work, or allow that the configurational entropy work requirement applies to cell assembly too.

Genes are complex segments of DNA. As we saw in Chapter 4, they are extremely vulnerable to a host of chemicals that surely would have been present under reducing conditions. On the other hand, oxidizing conditions would have been even worse for gene survival. Genes are wonderful templates for building enzymes, but without a cellular host endowed with the appropriate enzymes they are powerless to do synthesis. One could perhaps so contrive the surrounding milieu in a laboratory setting that cellular conditions were mimicked to bring about replication and enzyme-building. Such a possibility is extremely doubtful in the prebiotic world—even one rained upon by cosmic genes from above.

Special Creation by a Creator Beyond the Cosmos

In agreement with views of abiogenesis, and the foregoing view of Hoyle and Wickramasinghe, Special Creation by a Creator beyond the cosmos holds there was once a time in the past when matter was in a simple arrangement, inert and lifeless. Then at a later time matter was in the state of biological specificity sufficient for bearing and sustaining life. Special Creation (whether from within the cosmos or beyond it) differs from abiogenesis in holding that the *source which produced* life was intelligent.

Throughout history, many writers have attempted to describe the work of the Creator. What they all seem to hold in common is the idea that an intelligent Creator *informed* inert[42] matter by shaping it as a potter fashions clay. Some representations are quite anthropomorphic, others less so. But there is considerable agreement that somehow an active intellect produced life.

In 1967 J. D. Bernal, a leading developer of the chemical evolution scenario, issued a challenge to divine creationists. He said:

> Now that we are embarking on a serious scientific discussion on the origin of life, it is time... we were furnished with a more precise, complete and self-consistent account of the spiritual or divine origin of life than any that have been produced as an alternative to the mechanistic one. Such an argument... should provide us with *a clearer path to further scientific advance*, even if it does not reach the end.[43] (Emphasis added.)

We do not believe there has been any significant response to Bernal's challenge that would "provide us with a clearer path to further scientific advance." In fact, what follows should be viewed as only introductory to that end.

What Concerns Scientists about Creation?

Scientists have three major concerns about the idea of creation:

(1) Creation involves the supernatural. It is common knowledge that the claim that an active intellect informed nature has been on uneasy terms with the mainstream of science. To anyone trained in science, the reason is no mystery. It involves the supernatural. The objection is ex-

pressed well by the recognized science writer, J. W. N. Sullivan. Upon his death Sullivan was described by *Time* magazine as "one of the world's four or five most brilliant interpreters of physics to the world of common men."[44] He showed the concern most scientists have in considering a theistic explanation of the origin of life. Sullivan said (in 1933, but the statement is still cogent today):

> The beginning of the evolutionary process raises a question which is as yet unanswerable. What was the origin of life on this planet? Until fairly recent times there was a pretty general belief in the occurrence of "spontaneous generation."... But careful experiments, notably those of Pasteur, showed that this conclusion was due to imperfect observation, and it became an accepted doctrine that life never arises except from life. So far as actual evidence goes, this is still the only possible conclusion. But since it is a conclusion that seems to lead back to some supernatural creative act, it is a conclusion that scientific men find very difficult of acceptance.[45] (Emphasis added.)

So it is the supernatural that concerns many scientists. But what is it about the supernatural that troubles them? Why is creation difficult to accept?

(2) Creation entails discontinuity. A major concern of many scientists is that to allow supernatural involvement is to introduce *discontinuity* into science. Continuing to quote Sullivan:

> It carries with it what are felt to be, in the present mental climate, undesirable philosophic implications, and it is opposed to the scientific desire for continuity. *It introduces an unaccountable break in the chain of causation,* and therefore cannot be admitted as part of science unless it is quite impossible to reject it. For that reason most scientific men prefer to believe that life arose in accordance with the laws of physics and chemistry.[46] (Emphasis added.)

Here is the vision of nature as a seamless web of causal connections, an idea dominant in science for more than 250 years. As Einstein wrote, "The scientist is possessed by the sense of universal causation."[47] And, of course, creation would be a discontinuity. Hans Gaffron also expressed this concern in his address to the Darwin Centennial Celebration in 1959. Regarding chemical evolution Gaffron said:

> [It] is a nice theory, but no shred of evidence, no single fact whatever, forces us to believe it. What exists is only the scientist's wish not to admit a discontinuity in nature and not to assume a creative act forever beyond comprehension.[48] (Emphasis added.)

Notice, however, that in the above quotations of Sullivan, Einstein, and Gaffron there is only a *desire, sense, preference,* and *wish* that nature be continuous. This is important to understand because the wish went unfulfilled. The great quantum revolution has banished the notion of continuity as a necessity in science. According to de Broglie, one of the pioneers of the new physics, "on the day when quanta, surreptitiously, were introduced the vast and grandiose edifice of classical physics found itself shaken to its very foundation."[49] In addition advances in astronomy, as chronicled by Robert Jastrow,[50] have made it clear there was also a discontinuity at the beginning of the world. In fact there seems to be no good reason to suppose an original discontinuity would undermine a scientific understanding of the functioning of the world. For science in this sense is not concerned with the origin but with the operation of the world. It is clear from these developments in science that discontinuity is not the whole reason that creation is difficult for many scientists to accept.

(3) Creation might destroy the scientific quest for knowledge. Even though the structure of science and scientists themselves have survived the news that at bottom reality is discontinuous, there is no less suspicion that creation would stifle the quest for knowledge. But would creation necessarily destroy the scientific quest and hence bring an end to science?

In giving an answer to this question it will be necessary to briefly consider the nature of science.

Operation Science and the God Hypothesis

It is widely appreciated that from its beginning modern science has been concerned with finding and describing orderly patterns in the recurring events of nature. To do this a well-defined method is used. Data are gathered through observation and experimentation. As data are gathered, theories are proposed to explain the behavior or operation of the phenomena investigated. According to wide usage, a valid theory of science must pass a three-fold test:[51]

1. Its ability to explain what has been observed.
2. Its ability to explain what has not yet been observed.
3. Its ability to be tested by further experimentation and to be modified as required by the gathering of new data.

Notice, however, that this approach to testing theories only works if there is some pattern of recurring events against which theories can be checked and falsified if they are false. Through repeated observation attention is focused on a class of events, each of which is similar. The equations describing the behavior of the class would be applicable to any of its individual members. Let us say, for example, we have a theory about earth orbiting the sun and we propose to test it by predicting a solar eclipse. Although a particular eclipse would be the focus of the experiment, the result would apply to solar eclipses as a general class. Because there are recurring patterns of celestial movements we can test the theory. Such theories are operation theories. That is, they refer to the ongoing operation of the universe. We shall call the domain of operation theories "operation science," for these theories are concerned with the recurring phenomena of nature. Examples of operation science include the recurring motion of planets about the sun, the swinging of a pendulum, the parabolic trajectory of a cannonball, a single cell turning by stages into a fully formed organism, the recurrent cubic structure of table salt crystallizing out of water solution, and the migration of a Monarch butterfly. These and many other phenomena have been accounted for in the language of operation science. Because of its familiarity and long, successful history, it is surely what most people think of when they think about science.

Here in operation science the appeal to God is quite illegitimate, since by definition God's supernatural action would be willed at His pleasure and not in a recurring manner. Yet it is true that on numerous occasions throughout the history of science there have been those who have appealed to the "God hypothesis" to "solve" some knotty problem of the ongoing operation of the universe instead of grappling with it and searching for natural causes to explain it.

Basically the idea of the God hypothesis is that whenever there is a gap in our knowledge, we run God in as a "bit-player," so to speak, to fill the gap. This view is known fittingly as the God-of-the-gaps. There is legitimate concern about this means of solving problems in operation science.

A classic example of this approach to scientific problem-solving is seen in the life of the great Isaac Newton, who appealed to the God hypothesis to account for certain anomalies in the heavens. (Note that an anomaly was defined by reference to Newton's own view of things.) Later, Laplace accounted for such discrepancies in a perfectly lawful manner. This was an important but painful lesson for scientists to learn. The illustration is sharpened by the story of the French Emperor Napoleon who asked Laplace where God fit in his equations, to which Laplace responded, "Sire, I have no need of that hypothesis."[52] Although some have misunderstood Laplace's reply in this instance as being anti-God, it was quite appropriate.

Origin Science

On the other hand, an understanding of the universe includes some singular events, such as origins. Unlike the recurrent operation of the universe, origins cannot be repeated for experimental test. The beginning of life, for example, just won't repeat itself so we can test our theories. In the customary language of science, theories of origins (origin science) cannot be falsified by empirical test if they are false, as can theories of operation science.

How then are origins investigated? The method of approach is appropriately modified to deal with unrepeatable singular events. The investigation of origins may be compared to sleuthing an unwitnessed murder, as discussed in Chapter 11. Such scenarios of reconstruction may be deemed plausible or implausible. Hypotheses of origin science, however, are not empirically testable or falsifiable, since the datum needed for experimental test (namely, the origin) is unavailable. In contrast to operation science, where the focus is on a class of many events, origin science is concerned with a particular event, i.e., a class of one.

When Galileo's ideas on acceleration (operation science) were presented, observers were not limited to mere plausibility. They could actually empirically falsify the claims of Galileo had they been false. Indeed, Pasteur's falsification of spontaneous generation was possible only because it was said to recur in the domain of operation science. Appropriate testing against nature falsified the notion of spontaneous generation. But the best we can ever hope to achieve with wrong ideas about origins is to render them *implausible*. By the nature of the case, true falsification is out of the question.

In spite of this fundamental difference between origin science and operation science, there is today very little recognition of it, and an almost universal convention of excluding the divine from origin science as well as from operation science. This has occurred without any careful prior analysis of the problem to see if the exclusion is valid in the case of origin science. It seems to have been merely assumed.

An example of this exclusion by assumption instead of valid argument comes from this statement by Orgel:

> Any "living" system must come into existence either as a consequence of a long evolutionary process or a miracle... Since, as scientists, we must not postulate miracles, we must suppose that the appearance of "life" is necessarily preceded by a period of evolution.[53]

We agree with Orgel that miracles must not be posited for operation science.[54] We disagree with Orgel, however, and others, when it is merely assumed that the exclusion of the divine from origin science is valid. This has not been demonstrated.

There are significant and far-ranging consequences in the failure to perceive the legitimate distinction between origin science and operation science. Without the distinction we inevitably lump origin and operation questions together as if answers to both are sought in the same manner and can be equally known. Then, following the accepted practice of omitting appeals to divine action in recurrent nature, we extend it to origin questions too. The blurring of these two categories partially explains the widely held view that a divine origin of life must not be admitted into the scientific discussion, lest it undermine the motive to inquire and thus imperil the scientific enterprise. This is what Preston Cloud meant when he noted, "The most serious threat of creationism is that, if successful, it would stifle inquiry."[55] One can also see the same concern echoed by Stansfield:

> ... the creationist can easily explain any phenomenon by simply saying "God did it." This approach, though it may be perfectly correct in an absolute sense, does not foster further inquiry and is therefore intellectually emasculated.[56]

The perception of a threat to scientific inquiry and the possible end of science are legitimate concerns. But we question whether the God hypothesis in origin science would necessarily have this disastrous effect. Just a little reflection on the history of science brings out the irony in the current state of affairs. For there is a rather impressive reason to doubt that science (i.e., operation science) would suffer much by positing Special Creation by a Creator beyond the cosmos. On the contrary, it turns out that this very idea of creation played a significant role in the origin of modern science. Speaking with one voice on this point are such diverse authors as Alfred N. Whitehead,[57] Melvin Calvin,[58] Michael B. Foster,[59] R. Hooykaas,[60] Loren Eiseley,[61] C. F. von Weizsacker,[62] Stanley Jaki,[63] J. Robert Oppenheimer,[64] and Langdon Gilkey.[65] For example, Eiseley said the birth of modern science was due to "[t]he sheer act of faith that the universe possessed order and could be interpreted by rational minds," and in the same passage elaborated as follows:

> The philosophy of experimental science… began its discoveries and made use of its method in the faith, not the knowledge, that it was dealing with a rational universe controlled by *a Creator who did not act upon whim nor interfere with the forces He had set in operation*. The experimental method succeeded beyond man's wildest dreams but the faith that brought it into being owes something to the Christian conception of the nature of God. It is surely one of the curious paradoxes of history that science, which professionally has little to do with faith, owes its origins to an act of faith that the universe can be rationally interpreted, and that science today is sustained by that assumption.[66] (Emphasis added.)

Notice that while Eiseley does not identify the distinction between operation science and origin science, the distinction is implicit in his explanation that a great deal of good science was done by early modern scientists who allowed at least a few discontinuities, i.e., the origin of matter, the universe, and life.

It would be quite ironic if the very idea of creation which provided much of the energy and impetus to launch modern natural science (and did so without noticeable lethargy) should lead to the demise of this same science. In our view, as long as one acknowledges and abides by the above distinction between origin science and operation science, there is no *necessary* reason that Special Creation would have the disastrous effects predicted for it. One must be careful, however, to follow the tradition of early modern scientists and *disallow* any divine intervention in operation science.

Why then is Special Creation so summarily dismissed by nearly all writers, especially since it is typically listed as a theoretical alternative for the origin of life? Our analysis suggests that failure to properly distinguish origin science and operation science has led many to dismiss creation. Also we believe another factor is involved, and is worthy of discussing in some detail. To be sure, the matter of discontinuity, and the possible demise of science discussed above, are part of the reason. But we should not ignore our own humanness, and the role of metaphysical thinking in the origin of life question.

Metaphysics and the Origin of Life

Hilde Hein, in her book *On the Nature and Origin of Life*, says that "a metaphysical position... makes a claim about reality which is somehow prior to or more fundamental than our scientific or common-sense observations."[67] How we happen to come by these metaphysical positions is of no concern to us here. However, as Hein continues,

> once it is adopted, it will shape, rather than be shaped by, our scientific and common-sense observations. This is to say that, on the whole our metaphysical commitment has priority over our scientific and common-sense beliefs such that, if challenged, they will yield to it rather than the reverse.[68]

It might appear that if metaphysical views have such control over us, the best approach would be simply to look at reality straight-on without any metaphysical lens at all. This, however, is not an option that is open to us. The grand old days of positivism, when people actually thought this possible, are over.

Scientific developments of the twentieth century, particularly in the area of relativity and quantum physics, have shown presuppositionless science to be a myth. The powerful writings of Polanyi,[69] Popper,[70] Kuhn,[71] Toulmin,[72] and others have strictly shown that because of the role of the observer (e.g., actually disturbing the object during the act of observing) it is difficult for objective reality to be objectively known.

Old myths die hard, however. Although news of these advances in science and philosophy are filtering through society, their effect in some quarters is minimal and there are dangerous consequences as a result. As David Bohm has written:

> It seems clear that everybody has got some kind of metaphysics, even if he thinks he hasn't got any. Indeed, the practical "hard-headed" in-

> dividual who "only goes by what he sees" generally has a very dangerous kind of metaphysics, i.e., the kind of which he is unaware… Such metaphysics is dangerous because, in it, assumptions and inferences are being mistaken for directly observed facts, with the result that they are effectively riveted in an almost unchangeable way into the structure of thought.[73]

Bohm then adds some practical advice:

> One of the best ways of a person becoming aware of his own tacit metaphysical assumptions is to be confronted by several other kinds. His first reaction is often of violent disturbance, as views that are very dear are questioned or thrown to the ground. Nevertheless, if he will "stay with it" rather than escape into anger and unjustified rejection of contrary ideas, he will discover that this disturbance is very beneficial. For now he becomes aware of the assumptive character of a great many previously unquestioned features of his own thinking.[74]

We believe Bohm is quite right. It is in the interest of science to have the metaphysical assumptions out on the table. Just what are the fundamental metaphysical alternatives in the question of the origin of life? Historically, they have been called theism and naturalism. For simplicity, we will note that theism affirms a fundamental distinction between the Creator and the creature, while naturalism denies this absolute distinction and defines all of reality in terms of what theists see as some aspect of the created world.[75]

The origin perspective of metaphysical naturalism is spontaneous generation (abiogenesis), and of theism[76] it is Special Creation. It follows from what Bohm has said that a great deal of practical self-awareness of our individual views would probably emerge if we allowed ourselves to be confronted with both theism and naturalism in the area of origins. Very often the debate between theism and naturalism is cast as a conflict between religion (i.e., the supernatural) and science. However, as Ian Barbour has pointed out, this is a mistake. It is "a conflict between two metaphysical interpretations of the nature of reality and the significance of human life."[77]

Metaphysical Commitment vs. Unreason

If metaphysical positions have such a controlling influence as Hein has indicated, this raises a practical question. In the face of contradictory evidence, when is one to be praised for metaphysical commitment, and chided for unreasonable faith? The answer one gives to this question depends in large measure on the metaphysical stance already adopted. To illustrate, consider George Wald's discussion of how biologists responded after Pasteur's refutation of spontaneous generation. Says Wald:

> We tell this story [of Pasteur's experiments] to beginning students of biology as though it represents a triumph of reason over mysticism. In fact it is very nearly the opposite. The reasonable view was to believe in spontaneous generation; the only alternative, to believe in a single, primary act of supernatural creation. There is no third position.[78]

Wald is saying that there are times when it is clearly unreasonable to follow the evidence where it leads. When? Those times when following the evidence would lead one to the supernatural. This is an example of metaphysical commitment to naturalism in the face of contradictory evidence. Clair E. Folsome[79] represents another example of commitment to metaphysical naturalism in spite of contradictory evidence. Folsome critiqued the abiogenesis that Wald had upheld. Folsome pointed out the extreme dilution of the primitive soup, the scarcity of organic nitrogen in the early sediments, and the grave deficiencies in the concentration mechanism proposed for the primitive water basins. He then noted: "Every time we examine the specifics of the theories presented by Oparin and Bernal, current information seems to contradict them."[80] Does Folsome then entertain doubt as to the plausibility of the Oparin-Bernal hypothesis? No.

This also is apparently a time when it would be unreasonable to follow the evidence where it leads. Instead, Folsome expresses his commitment: "... yet, in the main, they were right [in postulating that some sort of chemical evolution had occurred]... their models were wrong, but the central theme they pursued seems even more right now than before."[81] (Emphasis added.)

Of course, creationists also manifest a similar commitment to theism, even if like Wald and Folsome they remain silent about their metaphysical stance. We have not bothered to document this for theism, since it is generally acknowledged.

Special Creation and the Evidence

Special Creation by a Creator beyond the cosmos envisions a prepared earth with oxidizing conditions, an earth ready to receive life. It is suggestive then that there has been accumulating evidence for an oxidizing early earth and atmosphere. If the early earth were really oxidizing it would not only support creation; it would also be difficult to even imagine chemical evolution. Similarly, the short time interval (< 170 million years) between earth's cooling and the earliest evidence of life supports the notion of creation. And, of course, if life were really created it would account for there being so little nitrogen in Precambrian sediments (i.e., there never was a prebiotic soup). In addition, Special Creation accords well with the observed boundary between what has been done in the laboratory by abiotic means and what has been done only through interference by the experimenter. If an intelligent Creator produced the first life, then it may well be true that this observed boundary in the laboratory is real, and will persist independent of experimental progress or new discoveries about natural processes. Also, an intelligent Creator could conceivably accomplish the quite considerable configurational entropy work necessary to build informational macromolecules and construct true cells. As Fong has said:

> The question of the ultimate source of information is not trivial. In fact it is the basic and central philosophical and theoretical problem. The essence of the theory of Divine Creation is that the ultimate source of information has a separate, independent existence beyond and before the material system, this being the main point of the Johannine Prologue.[82]

It is doubtful that any would deny that an intelligent Creator could conceivably prepare earth with oxidizing conditions and create life. And, of course, the data discussed above are consistent (and compatible) with this view of Special Creation. What we would like to know, of course, is whether an intelligent Creator *did* create life. The question, unfortunately, is beyond the power of science to answer. Another question which can be answered, however, is whether such a view as Special Creation is plausible.

Plausibility and Creation

On several occasions we have indicated that hypotheses of origin science may be evaluated in terms of their plausibility, but falsification, the language of operation science, will not apply. How then does one determine whether an origin science scenario is plausible? The principles of causality and uniformity are used. *Cause* means that necessary and sufficient condition that alone can explain the occurrence of a given event. By the principle of *uniformity* is meant that the causes we observe producing certain effects today can be counted on to have produced similar effects in the past. We can go back into the past with some measure of plausibility only by assuming the kind of cause needed to produce that kind of effect in the present was also needed to produce it in the past. In other words, "the present is a key to the past."

As we saw, this is how scientists have arrived at the reconstructed scenario of a prebiotic earth. What makes views of abiogenesis legitimate as origin science, then, is the assumed legitimacy of cause-effect reasoning and the principle of uniformity.

The problem for chemical evolutionary theory, however, has been its failure to identify any contemporary example of specified complexity (as distinct from order, see Chapter 8) arising by abiotic causes. What is needed is to identify in the *present* an abiotic cause of specified complexity. This would then provide a basis for extrapolating its use into the past as a conceivable abiotic cause for supplying the configuration entropy work in the synthesis of primitive DNA, protein, and cells. The failure to identify such a contemporary abiotic cause of specified complexity is yet another way to support our conclusion that chemical evolution is an implausible hypothesis.

But does creation employ cause-effect and the principle of uniformity? Yes. In fact, it appeals to them as the only way we can plausibly reconstruct the past. Consider, for example, the matter of accounting for the informational molecule, DNA. We have observational evidence in the present that intelligent investigators can (and do) build contrivances to channel energy down nonrandom chemical pathways to bring about some complex chemical synthesis, even gene-building. May not the principle of uniformity then be used in a broader frame of consideration to suggest that DNA had an intelligent cause at the beginning? Usually the answer given is "No." But theoretically, at least, it would seem the answer should be "Yes," in order to avoid the charge that the deck is stacked in favor of naturalism.

We know that in numerous cases certain effects always have intelligent causes, such as dictionaries, sculptures, machines, and paintings. We reason by analogy that similar effects also have intelligent causes. For example, after looking up to see "BUY FORD" spelled out in smoke across the sky we infer the presence of a skywriter even if we have heard or seen no airplane. We would similarly conclude the presence of intelligent activity were we to come upon an elephant-shaped topiary in a cedar forest.

In like manner an intelligible communication via radio signal from some distant galaxy would be widely hailed as evidence of an intelligent source. Why then doesn't the message sequence on the DNA molecule also constitute *prima facie* evidence for an intelligent source? After all, DNA information is not just *analogous to* a message sequence such as Morse code; it *is* such a message sequence.[83] The so-called Shannon information laws apply equally to the genetic code and to the Morse code. True, our knowledge of intelligence has been restricted to biology-based advanced organisms, but it is currently argued by some that intelligence exists in complex non-biological computer circuitry. If our minds are capable of imagining intelligence freed from biology in this sense, then why not in the sense of an intelligent being before biological life existed?[84]

We believe that if this question is considered, it will be seen that most often it is answered in the negative simply because it is thought to be inappropriate to bring a Creator into science.

The above discussion is not meant as a scientific proof of a Creator, but is merely a line of reasoning to show that Special Creation by a Creator beyond the cosmos is a plausible view within origin science.

Metaphysical Tolerance: A Discipline for Progress

To be sure, there are sensitive issues involved when we begin to explore the metaphysical questions surrounding the origin of life. However, there is no easy way to resolve these issues. The only sure path is difficult. It demands the discipline required to temporarily table our personal tastes and preferences and humble ourselves in order to give serious consideration to how the data can be viewed from the other metaphysical position. We must do so recognizing that the truth of origins surely remains the truth regardless of which metaphysical position we individually adopt. As Melvin Calvin has observed, "The true student will seek evidence to establish fact rather than confirm his own concept of truth, for truth exists whether it is discovered or not."[85]

The difficulty in pursuing these metaphysical matters is that scientists on the whole have seen so little value in this pursuit. After the birth of modern science in the 17th century it became increasingly common, and by the end of the 19th century the accepted procedure, to separate science and metaphysics into isolated, thought-tight compartments. This seemed to work well in practice, for after science got started the practitioners of science could function without even being aware of the metaphysical basis on which they operated. The modern scientific tradition has largely developed within the area we have called operation science, with its emphasis on recurring phenomena and testable hypotheses. Because of the inertia of heritage, the practice of science continued with only a few practicing scientists apparently aware of its metaphysical basis. As a result, now that we need to negotiate metaphysical terrain for proper understanding of origin science, few in science are equipped with the requisite skills. We believe this is a major reason creation in the area of origin science is viewed with such deep suspicion by many and frequently simply dismissed.

When we are asked to consider "far out" or "strange" ideas such as Special Creation, as were the authors just a few years ago, typically the response is exactly that mentioned by Bohm as cited earlier: "His first reaction is often of violent disturbance." This was our reaction, too. However, as Bohm goes on to say, if one is willing to "stick with the inquiry rather than escape into anger or unjustified rejection of contrary ideas... he becomes aware of the assumptive character of a great many previously unquestioned features of his own thinking."

The process as Bohm described it can sometimes be painful (it was to one of the present authors) but the quest for truth has never been easy, and has on more than a few occasions been known to make one unpopular.

To be sure, not everyone who goes into the matter will reach the creationist conclusion that we have. Even so, in the words of Davis and Solomon, as expressed in their book *World of Biology*:

> We cannot imagine that the cause of truth is served by keeping unpopular or minority ideas under wraps... Specious arguments can be exposed only by examining them. Nothing is so unscientific as the inquisition mentality that served, as it thought, the truth, by seeking to suppress or conceal dissent rather than by grappling with it.[86]

As with the trial by jury analogy discussed in Chapter 11, we believe both sides[87] of the origins issue (i.e., representatives of both metaphysical positions) must be considered, precisely because there is no way to test origins ideas in origin science against recurring phenomena (origins by definition do not recur). The issue will be decided on the basis of plausibility, not falsifiability. There is good historical precedent for this approach. Charles Darwin in his introduction to *The Origin of Species* said:

> For I am well aware that scarcely a single point is discussed in this volume on which facts cannot be adduced, often apparently leading to conclusions directly opposite to those at which I have arrived. *A fair result can be obtained only by fully stating and balancing the facts and arguments on both sides of each question,* and this is here impossible.[88] (Emphasis added.)

Presenting origin science ideas from both metaphysical positions—theism and naturalism—in addition to giving an opportunity to choose the most plausible view from the total theoretical spectrum, will also help us become aware of:

1. Our own position and why we hold it;
2. The weaknesses and disadvantages of our position;
3. The need for tolerance of others' positions;
4. The limitations of science.

Our purpose in this epilogue has been to shed light on the issues and to avoid heat as much as possible. Only the reader can judge how successful we have been. If there is but one thing our acquaintance with the history of science has taught us, it is that unless some progress is made in recognizing the role of metaphysical thinking and properly using it, the origins debate will simply rage on, much as it has in the past, with representatives of each side of the dispute failing to hear or understand the other. Consequently, such scientists who go along blithely oblivious to the role of metaphysical thinking will simply act as if data really are observed and comprehended as neutral fact. Hopefully the lion of positivism has made its last roar and we can learn from advances in philosophy and science since the time of Darwin. If we can learn from our mistakes, we may expect more productive interchanges in the future. Toward that end we reach.

Endnotes

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APPENDIX 1: AN ALTERNATIVE CALCULATION

In Chapter 8 the number of unique or distinguishable polymer sequences, Ω_c, was calculated using Equation 8-7. An alternative but equivalent approach presented by Brillouin[1] and Yockey[2] is to consider the number of different symbols that might be incorporated into each position, with the total number of sequences being the product of the number of symbols times the number of positions in the sequence. The result then is

$$\Omega_c = i^N \qquad \text{App 1-1}$$

where typical values for i and N have previously been given (Chapter 8).

This relationship requires the assumption that each of the i symbols is equally probable. A similar relationship can be derived which allows for symbols of different rather than equal probability.[3] The number of sequences predicted by Equation Appendix-1 will always be larger than that predicted by Equation 8-7, since it allows for many different sets of $n_1 + n_2 + n_3 ... + n_i = N$ rather than a given set of n_i values which one could substitute in Equation 8-7. In fact, it can be shown that if one were to evaluate Equation 8-7 for each possible set of $n_1 + n_2 + n_3 ... + n_i = N$ values and sum these results, the total would be identical to that given directly by Equation Appendix-1.

Consider a hypothetical protein of 100 amino acids of 20 types (N = 100, i = 20) and assume that an equal number of each of the 20, i.e., 5, are present in this protein. Using Equation 8-7 we may calculate the number of distinctive sequences for this set of amino acids to be 1.28

x 10^{115}. If we allow the number of each type of amino acid to assume any value in the range of 0-100, as long as the sum $20n_i = 100$ $(i = 1)$ is retained, additional distinctive sequences are possible. The 1.28 x 10^{115} sequences possible for $n_1 = n_2 = \ldots n_{20} = 5$ would be added to additional distinctive sequences—for example, for $n_1 = 3$, $n_2 = 7$, $n_3 = n_4 \ldots n_{20} = 5$, and all other possible combinations of n_i. The sum of all these distinctive sequences is calculated using Equation Appendix-1, which gives

$$\Omega_c = i^N = 20^{100} = 1.26 \times 10^{130} \qquad \text{App 1-2}$$

Yockey[4] has done a more rigorous analysis for cytochrome c, a protein found in different animals (with somewhat different structures for each cytochrome c, we might add). He modifies Equation 8-7 to allow for an unequal probability of occurrence of each amino acid, based on observed frequencies of appearance in actual proteins. He calculates the number of distinctive sequences of 101 amino acids to be 1.8 x 10^{126}, a number which is bracketed by our two previous estimates of 1.28 x 10^{115} using Equation 8-7 and 1.26 x 10^{130} using Equation App. 1-1. We may be sure that Equation 8-7 gives a lower bound to the number of distinctive sequences observed in a given polypeptide, given that it restricts consideration to the set of n_i values observed in the specified-sequence polypeptide, or protein. Therefore, Equation 8-7 has been used from Chapter 8 through the remainder of this book as a lower bound estimate of Ω_c.

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APPENDIX 2: 1997 UPDATE

Charles Thaxton

Editor's Note: The following chapter was written as an update for the Hungarian edition of The Mystery of Life's Origin, published in 1997.

Since the publication of *The Mystery of Life's Origin*, additional results have been reported that make our case even stronger. Yet most review articles and popular expositions continue to portray origin-of-life research as a vibrant and flourishing field of inquiry, with much progress being made.[1] The optimistic state of affairs is precisely what led us to write our critical assessment. In our opinion nothing has happened in this field to upset our original position; therefore, we are adding this update material instead of offering a new edition.

In general the published results on the origin of life continue to ignore two important factors, thereby giving the illusion of progress. First is the problem of interfering cross-reactions, i.e., what we called the "concerto effect." (See Chapter 4.) Second is the problem of information, i.e., specified complexity, which is supplied by doing the necessary configurational entropy work (Chapter 8).

We will organize our presentation under the following headings:

- RNA World
- Hydrothermal Sea Floor Vents and Pyrite Formation
- Clay Life
- Order, Complexity, and Information
- Intelligent Design

RNA World

For generations the uneducated and scholars alike have puzzled over a fundamental question, Which came first, the chicken or the egg? In the origin-of-life discussion that question has been asked in a different form, Which came first, protein or nucleic acid, particularly DNA? For decades origin-of-life research has been divided into two competing camps, one advocating protein-first and the other, DNAfirst. Both sides have operated within the reigning paradigm of the Oparin Hypothesis, with its characteristic feature of an organic chemical soup. This is the paradigm analyzed in the preceding chapters.

The conundrum faced by these two sides is that living organisms require both DNA and protein for the life process. It takes DNA to make proteins, and proteins (enzymes) are required to make DNA.

An apparent way around the impasse came with the discovery that RNA plays both the role of information storage and the catalytic role of enzymes.[2] Such RNA enzymes, or ribozymes, did not come as a total surprise, however. Crick had suggested in 1968 that "possibly the first 'enzyme' was an RNA molecule with replicase properties."[3] This discovery led some to think a pathway might have existed that led from the primordial soup to the first living organism. This is the "RNA world," where it has been proposed that the first self-replicating system did not depend on the catalytic activity of proteins (enzymes), but instead on the preenzyme activity of RNA (ribozymes).[4]

Although the RNA world designation was not known at the time of our book's publication, one may easily see a critique of it within its pages. Specifically, the text accompanying Figure 4-4 applies to the RNA world. Supplementing the overall critique of Chapter 4, "The Myth of the Prebiotic Soup," is the following. RNA consists of four smaller components: the sugar ribose, purine bases (adenine, guanine), pyrimidine bases (uracil and cytosine), and phosphate. According to the RNA world scenario, these components and many other chemical substances would have been available in the prebiotic soup. Realistically, however, instead of these constituents chemically reacting to produce polynucleotides, these and many additional ingredients in the soup would likely have been involved in interfering cross-reactions. It is highly improbable in such an environment that nucleotides and polynucleotides would be produced.

The problem raised by interfering cross-reactions applies also to the production of the ingredients themselves. How realistic is it to think that the primitive water basins contained substantial concentrations of ribose, purines (e.g. adenine), pyrimidines, and phosphate? The literature has many optimistic suggestions that these ingredients would have been readily available. R. E. Dickerson, for example, wrote: "It is not difficult to account for the appearance of the bases and sugars of nucleic acids on the primitive earth... current knowledge of the chemistry by which amino acids, bases, sugars and other monomers of life could have been synthesized on the primitive earth is really rather impressive."[5]

Ribose

Let us consider the production of two organic constituents of RNA, ribose and adenine. Would they plausibly have been available on the primitive earth? We begin with ribose.[6] Throughout origin-of-life literature, one chemical reaction is cited in support of the claim that ribose would have been available on the early earth. That is the formose reaction initially described in 1861 whereby formaldehyde reacts in alkaline medium to produce a host of sugars, including ribose. Usually textbooks mention this reaction in order to justify its presence on the prebiotic earth. For example, Lehninger's biochemistry text says: "Formaldehyde, also readily formed in simulated primitive-earth experiments, yields a variety of sugars when heated with limestone (calcium carbonate)."[7]

This formose reaction yields a host of different sugars, and it requires strongly alkaline conditions in order to work. In addition there is an optimum time period for the reaction to give its best yields, beyond which the sugars begin to decompose.

After reviewing the formose reaction, Reid and Orgel summarized: "We do not believe that the formose reaction as we and others have carried it out is a plausible model for the prebiotic accumulation of sugars.... The formation of sugars in plausible conditions and their incorporation into nucleosides have not been achieved. Until the problem is solved or by-passed, it remains a weakness in theories of abiotic nucleic-acid synthesis."[8] In the nearly thirty years since that report, little has happened to change their judgment. After his review of the availability of ribose, Shapiro concluded: "The evidence that is currently available does not support the availability of ribose on the prebiotic earth, except perhaps for brief periods of time, in low concentration, as part of a complex mixture, under circumstances that are unsuitable for nucleotide synthesis."[9]

Adenine

Adenine is essential for both nucleic acids, RNA and DNA. It is an important component also in many other biomolecules, including ATP and coenzyme A. Because of this, much experimental effort has been devoted to finding prebiotically plausible routes to adenine. As discussed in Chapter 4, HCN is one of the molecules that could have formed in the prebiotic atmosphere and then escaped destruction by ultraviolet light. Figure 4-1 gives a general pathway from HCN to numerous compounds, including purines. Figure App 2-1 presents one specific prebiotic pathway to adenine:

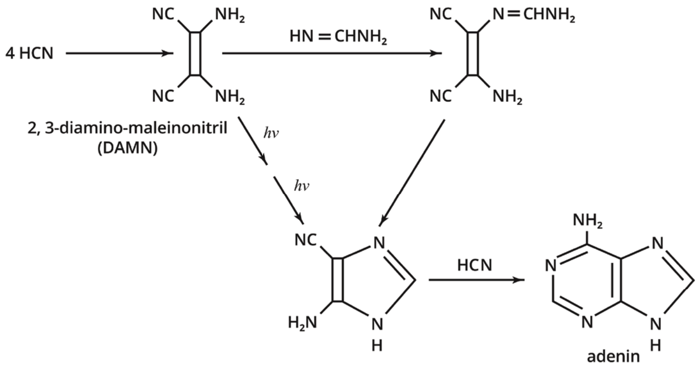

Figure App 2-1

In addition to the general criticism given in Chapter 4, let us consider the availability of adenine on the prebiotic earth. Would that be a plausible ingredient from which to realistically expect RNA synthesis to take place on the early earth? From the enthusiasm given to the RNA world hypothesis in some quarters, one would naturally expect adenine to be prebiotically available. Gerald Joyce has stated: "The self-condensation of HCN to produce purines is such a remarkably simple and efficient reaction that it would be surprising if it did not have some relevance to the early history of life."[10] And Joyce and Orgel added: "The synthesis of the nucleoside bases is one of the success stories of prebiotic chemistry. Adenine is formed with remarkable ease from ammonia and hydrogen cyanide."[11]

Despite the optimism for finding satisfactory amounts of adenine on the prebiotic earth for synthesis of RNA and other important biomolecules, it has not been demonstrated.[12] Experimentally we know that unless the concentration of HCN exceeds 0.01 M, the condensation reactions leading to adenine will not take place.

As Sanchez et al. have reported, "The yield of purines formed from HCN would fall off very rapidly at cyanide concentrations less than 0.01 M."[13] Most of the studies carried out and reported in the origin-of-life literature have been in the 1-15 M range, far too high to be considered prebiotically plausible. In addition to estimates of HCN concentration given in Chapter 4, Stribling and Miller have reported that under the most favorable circumstances of O °C and pH of 7, the HCN concentration would be 4×10^{-5} M.[14] This is a thousand times too dilute to expect condensation.

Most of the reported adenine syntheses have incorporated ammonia concentrations at least half that of the HCN concentration. Miller and Orgel reviewed the adenine synthesis and commented: "The chemistry described above does not easily describe the synthesis of purines under prebiotic conditions because useful yields of adenine cannot be obtained except in the presence of 1.0 M or stronger ammonia. The highest reasonable concentration of ammonia or ammonium ion that can be postulated in oceans and lakes on the primitive earth is about 0.01 M."[15] A more recent estimate of the ammonia concentration placed concentrations at no more than 7 x 10^{-5} M.[16]

Adenine is a reactive molecule that would have found many available substances with which to react. The accumulative effect of interfering cross-reactions would have been to make concentrations realistically smaller than the estimates cited above.

Orgel analyzed the problem of synthesizing the very first information system, and concluded that "its monomeric components must have been abundant components of a prebiotic mixture of organic compounds."[17] From the criticisms offered here, there is considerable basis to doubt that prebiotic supplies of adenine were abundant.

Including various lines of evidence, and much of what was discussed above, Joyce reviewed the case for the RNA world. His conclusion was that "RNA is not a plausible prebiotic molecule."[18] What happens then to the RNA world? Joyce concluded, "The most reasonable interpretation is that life did not start with RNA."[19] For the optimist who believes that life started in a primordial soup, there must have been "a simpler genetic system, or systems, that preceded RNA" that possibly "carried over to the RNA world."[20] The inquiry merely shifts to consider possible pre-RNA scenarios.

Hydrothermal Sea Floor Vents and Pyrite Formation

Hydrothermal Vents

Although some investigators are beginning to explore possible pre-RNA world scenarios, these remain mostly theoretical, and no substantial body of experimental work has yet appeared. Most efforts continue to be devoted to finding a pathway to life that follows the traditional thinking of the organic chemical soup. What seemed at first a major obstacle in principle to the chemical soup approach was the discovery in the 1980s that prior to 3.8 x 10^9 (billion) years ago, the earth underwent periodic intense meteoritic bombardment. Under such heavy impacts the temperature reached levels that would destroy all incipient life and degrade all complex chemicals.[21]

A discovery of the late 1970s was thus thrust into prominence. Scientists had discovered several submarine hot springs or vents, which support thriving colonies of living organisms such as bacteria, clams, and tube worms.[22] The primary source of energy for these creatures is not sunlight, being too far below the surface, but sulfur compounds coming out of the vents. Some researchers, such as John B. Corliss of NASA's Goddard Space Flight Center, have developed a hydrothermal vent hypothesis for the origin of life.[23] Corliss believes that life might have originated and been sustained by the energy and reduced chemicals, including ammonia, methane, hydrogen sulfide, and hot water, supplied by these sea floor vents. According to the hypothesis, complex organic compounds would be synthesized in underwater hot springs and then protected by rapid quenching to deep ocean temperatures. Such a scenario obviates difficulties maintaining sufficient concentrations of reduced chemicals for polymerizations to occur in a prebiotic soup. The dilution of chemicals has always been a significant drawback to the chemical soup hypothesis. Any life formed near the vents and remaining there would receive some protection from cometary and meteoritic bombardment by 2 km or more of sea water above.

There was still the thermodynamic problem of how to carry out the polymerization reaction in the presence of so much water, since for every peptide bond formed, a molecule of water must be expelled (see Chapter 8). The vent hypothesis does not solve that problem directly, being primarily a novel source of energy and of the necessary ingredients for life. Even if the polymerization problem were solved, the synthesized complex organic chemicals would eventually (in about 107 years)[24] be cycled back through the vents, with temperatures above 350 °C.[25] For this reason, Miller and Bada maintain that organic compounds such as sugars and peptides should not be expected in the vent waters. Under such harsh conditions of temperature and pressure, rapid decomposition of complex organic chemicals, not their synthesis, would be expected.[26]

Based on arguments such as these, Miller has estimated the upper limit of amino acid concentrations in the ocean to be 3 x 10^{-4} M.[27]

Pyrite Formation

A variation of the vent hypothesis and an ingenious solution to the thermodynamic problem of synthesizing complex organic compounds in water (as discussed above and in Chapters 8 and 9) was proffered by Günter Wächtershäuser, a German patent attorney.[28] The traditional chemical soup approach is an heterotrophic hypothesis, one that requires an outside source of energy to carry out the chemical reactions. In discussing equations 9-5 to 9-7 we showed how condensing agents were coupled to achieve dipeptide synthesis. In the terminology of thermodynamics a combined change of Gibbs free energy must be less than zero, i.e., $\Delta G < 0$, in order to drive the synthesis forward. Wächtershäuser suggested an autotrophic hypothesis, where the Gibbs free energy for synthesis is supplied by the chemical reaction. The hypothesis involves the fixation of carbon (reducing CO_2) directly on certain iron minerals that are found in the vicinity of hydrothermal vents, giving iron pyrite, FeS_2, as a product. An example of a productive carbon fixation reaction is the following, for pH zero:

$$4CO_2 + 7H_2S + 7FeS \text{-->} (CH_2\text{-}COOH)_2 + 4H_2O + 7FeS_2$$
$$\Delta G^0 = -420\text{kJ/mol}$$

An advantage of this proposal is that organic compounds are produced locally and ready for immediate use directly from chemicals readily found at the vents, thus avoiding the need for a separate step to concentrate precursors. The reactions yield the energy for carbon fixation and, with the production of iron pyrite, provide a mineral surface to which the newly formed organic compounds may adsorb. Thus held in place for further reaction, the organic compounds are not lost by dissolution in the ocean. Adsorption on the mineral surface also reduces the tendency for the organic compounds to degrade in the elevated temperature of the vent waters.

Wächtershäuser's proposal also includes the production of lipid membranes and anionic amino acids. The positively charged pyrite provides for surface-bonding of these amino acids, holding them in place for polymerization. The promise in this innovative proposal needs to be tempered by Wächtershäuser's own admission that, so far, the model remains for the most part "pure speculation."[29]

Some evidence for the vent hypothesis comes from the work of Carl Woese, who discovered a fourth living kingdom, the archaebacteria, that thrives in hot temperatures.[30] Some bacteria can thrive at temperatures of 120 °C or more. An observation that makes the vent hypothesis attractive to some origin-of-life researchers is that some bacterial species thrive in a hot acidic environment without oxygen, with a continuous supply of sulfur, just the conditions that prevail at sea floor hydrothermal vents.

As suggestive as the pyrite and hydrothermal vent hypotheses are in solving an important aspect of the energy problem for polymerizations in a water world, a proper assessment of these scenarios must consider the question of generating proper sequences of monomers for biological function. This is the information problem, or, as we called it, specified complexity. (See Chapters 8 and 9.) We shall postpone consideration of this important aspect of the problem of life's origin until after a brief discussion of the clay life hypothesis.

Clay Life

Perhaps the most unusual and novel approach to the origin-of-life problem has come from the hypothesis of A. G. Cairns-Smith, a University of Glasgow chemist, in *Genetic Takeover and the Mineral Origins of Life*.[31] For readers unfamiliar with his general ideas, we present the following analogy, developed by Cairns-Smith, as an introduction.

Have you ever seen a wooden bead in a pocket calculator? Sounds ludicrous, doesn't it? But calculators have not always contained such "high tech" components as silicon and plastic. The primitive abacus relied on racks of wooden beads to perform mathematical calculations. Of course our modern version retains none of the wooden components of its "low tech" precursor.

So it is with life, according to Cairns-Smith, who has offered a bold conjecture.

Life, just like the calculator, started in a "low tech" model, but of clay instead of wood. The clay was eventually taken over by organic matter to produce the "high tech" life with its biochemical components of protein and DNA.[32]

The clay hypothesis maintains that life arose on solid substrates, probably crystalline clays with enough complexity to mutate and evolve in a lifelike way. Cairns-Smith argued that some clays might have become better breeders by developing the ability to attract or synthesize organic compounds such as nucleic acids or proteins. Eventually the organic compounds might have become sophisticated enough to begin replicating and evolving on their own.

Cairns-Smith's clay genes hypothesis was offered as a way to bypass the usual chemical problems with a prebiotic soup. The hypothesis, at least in the refined form presented in *Genetic Takeover*, claims not to require a primordial soup, although it is likely that something like a soup was needed in the final stages to provide the organic materials needed for "genetic takeover."

There are difficulties, however. No evidence indicates that a "low tech" clay life ever existed or was transformed into organic-based substances. According to science writer John Horgan, "Cairns-Smith cheerfully admits the failings of his pet hypothesis: no one has been able to coax clay into something resembling evolution in a laboratory; nor has anyone found anything resembling a clay-based organism in nature."[33] The reason for this singular lack of success, we believe, is related to the central problem plaguing all origin-of-life scenarios so far, namely, how to account for and generate INFORMATION.

Order, Complexity, and Information

Getting the Right Arrangement of Building Blocks

In Chapter 8 we reviewed the thermodynamic difficulty of carrying out condensation reactions in the various water basins presumably available on the prebiotic earth. The difficulty arises in trying to get amino acids to join in the very specific ways required to provide functional protein. And of course the problem also applies to synthesizing nucleic acids.

The universal thermodynamic equation that must be satisfied in any chemical reaction, repeating equation 8-5, is:

ΔG	=	ΔH	−	$T\Delta S_{th}$	−	$T\Delta S_c$
Gibbs free energy		**Chemical work**		**Thermal entropy work**		**Configurational entropy work**

Assuming that the monomer units have been successfully reacted to form a polymer, according to the discussion in Chapter 8, we can be assured that both chemical work and thermal entropy work have been accomplished. The central problem in nearly all origin-of-life discussions published to date is that no provision has been taken into account for abiotically supplying the configurational entropy work, which is quite substantial in the synthesis of macromolecules. As a result, ALL models and scenarios of the origin of life that have been reviewed in this book and update chapter are, as we said in Chapter 11, "woefully inadequate," carrying with them a fundamental incompleteness.

Supplementing the discussion in Chapters 8 and 9, we note for protein formation, though it applies also for nucleic acids, that configurational entropy is made up of several parts: $\Delta S_{1c} = \Delta S_{1c} + \Delta S_{2c} + \Delta S_{3c} + \Delta S_{4c.}$

The configurational entropy work associated with obtaining only L-amino acids in the protein chain is called $-T\Delta S_{1c}$. The configurational entropy work required to obtain only peptide bonds between two amino acids is called $-T\Delta S_{2c}$. The $-T\Delta S_{3c}$ term refers to additional configurational entropy work to get the proper sequencing of the twenty amino acids in the polymer chain. Finally, $-T\Delta S_{4c}$ refers to the sorting and selecting configurational entropy work, or the work to get only the required subset of amino acids that appear in the protein, from the "prebiotic soup," which contains many different kinds of organic molecules.

In summary, primarily chemical work (ΔH) and thermal entropy work($-T\Delta S_{th}$) is being done, and it is sufficient to get some amino acids and nucleotides to chemically react to form polymers. In order for these polymers to possess biological activity, however, the full complement of configurational entropy work ($-T\Delta S_c$) must also be supplied. As we pointed out in Chapter 6, and identified in Chapter 9, it is the investigator who supplies this configurational entropy work through illegitimate manipulation of conditions in prebiotic simulation experiments.

Order, Complexity, and Information

How to get proper arrangement of amino acids to make a biofunctional protein or of nucleotides to make RNA or DNA is an information problem, or, as we called it in Chapter 8, specified complexity. Information is an important and often ignored aspect of the modern origin-of-life discussion. Therefore we shall devote this section to the subject of information.

Information theory is a special branch of mathematics that has developed a way to measure information.[34] In brief, the information content of a structure is the minimum number of instructions required to describe or specify it, whether that structure is a rock or a rocket ship, a pile of leaves or a living organism. The more complex a structure is, the more instructions are needed to describe it.[35] Clear discussions of information theory and how it provides a mathematical definition of, and distinction between, order and complexity can be found in Yockey[36] and also in Wicken.[37]

Order: Periodic and Specified

The development of information theory provides a tool for distinguishing between order and complexity. Examples of ordered structures are a repeating wallpaper or floor tile pattern, the single structure repeated over and over in a crystal, the repeating pattern of monomeric units in polyurethane, and a sequence of alphabetical letters ABABABABAB.... The characteristic feature of an ordered structure is the PERIODIC AND SPECIFIED arrangement of its constituent parts. That means the parts are arranged in a highly repetitious and specific fashion. Such structures have a low information content and require only a few instructions to specify them. As an example, in telling a chemist how to make a crystal, you need only two instructions. First, specify the substance you want and the way you want the molecules packed together. Second, tell the chemist, "Now do it again." Repeat until the crystal is made. The structural information has to be given only once because a crystal has a regular pattern. To tell your computer's printer to make a page of "Hello Bob!" will take only two instructions, (1) "Print 'H-e-1-1-o B-o-b-!,'" and (2) "Do it again," until the page is filled.

Complexity: Aperiodic and Unspecified

On the other hand, aperiodic structures or structures that lack periodicity are called "complex." Complex structures are of two types. The simplest type of complexity is a random structure. A random structure has no order, but, like an ordered structure, it has little information because few instructions are needed to specify it. By definition random structures are APERIODIC AND UNSPECIFIED, such as a lump of granite, a pile of leaves, a random polymer, or a sequence of letters drawn at random. A pile of leaves is random and can be described with just two instructions: (1) "Select any type of leaf and drop it on the pile," and (2) "Do it again." To write a series of random letters, you also need only two instructions: (1) "Select at random a letter from A to Z and write it down," and (2) "Do it again." This way you can make as long a random sequence as you want.

Information: Aperiodic and Specified

It is the second type of complexity that is the most relevant for biology. Written messages, artifacts, DNA, and proteins are all examples of *specified* complexity. By definition structures characterized by specified complexity are those with constituent parts arranged in an APERIODIC

AND SPECIFIED manner. Such structures have a high information content, which means that many instructions are needed to specify them. As an example, if you wanted to print out a copy of Lincoln's Gettysburg Address, which begins "Four score and seven years ago," you could not find any brief set of instructions to give your computer. Your instructions would be as long as the famous address itself. You must specify every letter, one at a time, in the correct sequence. There are no shortcuts.

It would be quite impossible to give a chemist a set of few instructions to synthesize the DNA of even the simplest bacterium. The instructions would have to include every chemical letter, one by one. That would be several million of them. Rather than a few sentences of instructions, there would be enough to fill a large book.

With a clear and mathematically defined distinction between order and complexity, we can continue to analyze origin-of-life scenarios.

Critique

These scenarios do not make a clear distinction between order and complexity, as defined above. Also these scenarios focus on energetics and tend to ignore configurational entropy work that is required if biological function is to be achieved.

We shall first consider Cairns-Smith's suggestion that the information we see today in carbon-based living organisms first resided in a pattern of imperfections that existed in crystalline clays. Then through a complex and unknown natural mechanism, the information was supposedly transferred to, or "taken over" by, organic macromolecules, perhaps protein or RNA.

The problem that arises immediately with this hypothesis is that a crystal is orderly. "If we could shrink ourselves to the atomic scale," as Richard Dawkins colorfully describes, "we would see almost endless rows of atoms stretching to the horizon in straight lines—galleries of geometric repetition."[38] If the nucleotides were arranged in DNA, like atoms or molecules in a crystal, the resulting pattern would be repetitive, orderly, everywhere the same, and it would be incapable of storing and transmitting information. How, then, do the defect patterns give rise to information?

Imagine a situation created by certain mixed layer clays such as kaolinite, which might possess two or a few different types of layers characterized by distinguishing defect structures. If we envision each layer as a page in a book, then "the information is simply in the order in which these pages are stacked."[39] Instead of information being conveyed by a linear sequence of alphabetical letters, according to linguistic conventions of spelling, grammar, and word choice, the information rests in the sequence of clay layers in the crystal. Instead of a linear sequence, we have a stack of two-dimensional surfaces.

There is, however, no code that relates the pattern of imperfections on stacked crystal surfaces to the sequences of monomers in macromolecules. Herein lies the great difficulty in Cairns-Smith's hypothesis. According to Hubert Yockey, "The transfer of information from clay surfaces to organic macromolecules... is mathematically *impossible,* not just unlikely"![40] (Emphasis his.) Of course it is the operation of the genetic code in living organisms that makes possible the transfer of information from the four-letter DNA alphabet to the twenty-letter protein alphabet. It is the failure to distinguish between order and complexity that makes the faulty analogy that order in a crystal is like the "order" of informational macromolecules.

Some scientists have turned to a new analogy, developed by physicist Ilya Prigogine.[41] When you pull the plug on a bathtub, the water running down the drain forms a whirlpool. By slowly heating oil on a well-regulated hot plate, at a certain temperature hexagonal patterns spontaneously form on the surface. These are called nonequilibrium systems, and Prigogine developed a set of mathematical equations for describing them.[42] His work is often touted as new evidence for the power of self-organization in nature. Mechanistic accounts of life's origin are likely to appeal to Prigogine's work for analogies of spontaneous ordering. Agnesa Babloyantz, a close associate of Prigogine's, has written an excellent and clear introduction to Prigogine's views. She is enthusiastic about the powers of selforganizing systems, adopting the "bold and audacious hypothesis which assumes that life has been created as a result of the self-organization of matter."[43]

Prigogine's new examples, however, are not essentially different from the old example of crystals. The order represented by a bathtub whirlpool or hexagonal patterns in oil is similar to the order in a crystal. As a consequence these analogies have no relevance to the central problem of how to produce information, i.e., specified complexity. We showed earlier that configurational entropy work is required to produce information. Prigogine has shown how to pass energy through chemical and physical systems in the production of order, not complexity, and certainly not specified complexity.

Prebiotic simulation experiments made famous by Miller, Fox, Oro, Sagan, Ponnamperuma, Orgel, etc., are providing mainly chemical and thermal entropy work. Thus they succeed in getting chemical reactions that yield polymers. These experiments, however, cannot *in principle* be expected to produce materials with biological function because the configurational entropy work is not being *abiotically* supplied. It is the configurational entropy work that supplies the specified complexity, or information. Robert Woodward justifiably received the Nobel Prize for his synthesis of chlorophyll and other natural products, but the experiments were not abiotic. The configurational entropy work was supplied by Woodward in the constraints and specialized conditions placed on the experiment. Woodward received the Nobel Prize because *he*, not natural processes, supplied the configurational entropy work.

Many of the prebiotic simulation experiments reviewed in Chapter 6, as we stated in Chapter 11, "owe their success to the crucial but *illegitimate* role of the investigator," who supplies some measure of the configurational entropy work by imposing boundary conditions and experimental constraints. It is likely that the "illusion of prebiotic simulation," (Chapter 11) continues to be a problem because workers have not addressed the problem of how to provide a natural cause mechanism for accomplishing the configurational entropy work.

No one has shown how to produce informational patterns of sequences by the natural processes of chemistry and physics without the illegitimate role of an investigator. This important result is what led us, in the Epilogue, to consider anew the intelligent design hypothesis that had been scorned for over a century. We propose to reexamine this ancient hypothesis in the light of modern knowledge.

Intelligent Design

In the Epilogue we considered various alternatives to the dominant paradigm of the Oparin Hypothesis. It was clear to the authors that there is something odd and unusual about the informational molecules, nucleic acids and proteins. They are in a class by themselves among molecules. No other molecules possess the characteristic of storing and transmitting information. So striking was this feature to us that we eventually concluded that the structure of these molecules fits the pattern that our experience shows resulted only from intelligence.

Heresy it might be called, but it was not a conclusion that we had imposed upon the data. We drew the conclusion that DNA had an intelligent source from the striking pattern within the DNA itself. In presenting our case about an intelligent cause, we introduced a distinction between origin science and operation science, a distinction that is unnecessary to present the case for intelligent design.

We now make the case directly for intelligent design, without a distinction between origin science and operation science. In order to show the legitimacy of intelligent design, we review first some relevant episodes in the history of science.

History

For generations theologians and philosophers had argued that order requires an ordering intelligence, which they called God. Over the course of the development of modern experimental science, western culture learned to rely on sensory experience to gain knowledge about natural phenomena.[44] By following experience scientists learned to infer causes from effects, i.e., to work backward from the character of the effect to the cause. A cause is that necessary and sufficient condition that alone can explain the occurrence of a given event. And it does not matter if the cause is natural or intelligent. In the words of David Hume, who gave a formal analysis of this approach, "From causes which appear *similar* we expect similar effects." (Emphasis his.) Later in the same book he added, "the same rule holds, whether the cause assigned be brute unconscious matter, or a rational intelligent being."[45]

Let us now apply the method of inferring causes from experience to a few examples. Strolling along a wave-swept beach we notice ripple patterns in the sand. The first time it may seem mysterious, but after repeated experiences, we associate the ripple patterns and the waves. We are so accustomed to making this assignment of cause that if we saw photographs of similar ripple patterns in sediments that geologists had dated as three billion years old, we would infer water as the natural cause. Likewise deep channels or rills on the Martian surface are so similar to what we know by experience to be the result of running water, that we would associate the natural cause of the channels with water—even if there is no water on Mars today. Thus scientists at NASA (National Aeronautics and Space Administration) have concluded that water must have been on Mars sometime in the past.[46]

On the other hand, were we to hike in the Black Hills of South Dakota and come upon granite cliffs bearing the likenesses of four United States Presidents, we would quickly identify Mount Rushmore as the work of artisans instead of a product of wind and erosion. Our accumulated reservoir of experience enables us to discriminate types of effects we see and to distinguish a natural process from an intelligent cause. Walking farther along and finding "John loves Mary" etched on a rock, what do we conclude? Again from experience, we infer that someone, perhaps John or Mary, left this sign of his affection. We would not conclude it to be the work of erosional forces, since we are able to discriminate causes. This ability is what led anthropologists to eventually change their judgment regarding eoliths.

Eoliths are chipped flints that, for a time, had been considered indicators of early man. Later it was discovered that such chips and scars on rocks can result from tumbling in a stream. This change in the assignment of cause was on the basis of additional experience.[47]

Following the method of experience gives us a way to approach phenomena without a prior assumption of the nature of the cause. It is a method that is completely open to either natural or intelligent causes. The assignment of causal category depends on the character of the effects. To illustrate the method, suppose we are detectives investigating someone's death. Is this a case of death by natural causes (accident) or death by design (murder or suicide)? We do not know the answer in advance. We must investigate to find out. If we announced before beginning our investigation that death must have been accidental (natural), others would be justified in objecting that we had illegitimately restricted the field of possible causes. An important purpose of the investigation is to determine whether this was a case of intelligent cause (murder or suicide) or natural death. We need a method that is open to either possibility. Experience gives us the greatest probability of determining which category of cause it was, whether natural or intelligent.

Despite the above explanation, many scientists suggest that science may not entertain intelligent causes. This notion is certainly mistaken. The reasoning involved in the application of the method of experience is analogical, and is very much at home in modern science. Analogical reasoning is routinely used by NASA scientists as they explore the heavens looking for signs of intelligence in their SETI (Search for Extra-Terrestrial Intelligence) program. If signals from space conveyed artificial electromagnetic pulses sent in code to give, for example, the first thousand digits in the transcendental number π (3.14159...), this would be considered so improbable an occurrence that we concur that intelligence had sent it. If scientists ever receive radio signals that are distinguished from noise and have the indicia of intelligence, we can surely expect a jubilant announcement from Washington.

The Planetary Society has initiated its Billion Channel Extraterrestrial Assay (BETA) scan of the heavens using the world's largest receiver, an 84-foot radio telescope set up in Harvard, Massachusetts.[48] The goal of this heavenly scan is to receive intelligent messages that some advanced civilization could be beaming our way. It is a program going on within the borders of legitimate science. It is safe to put the objection aside that modern science is opposed *in principle* to the notion of intelligent cause.

What Experience Shows About Natural Phenomena

Why then do scientists no longer accept intelligent design in nature? The short answer is that science can show many examples of natural processes producing order in addition to that displayed in the regular course of the planets, which was a primary concern of scientists in the early development of modern science. Many natural processes have been discovered, and their amazing power catalogued.

Whether the beautiful patterns in crystals, the soapy swirl down the drain, or the order evident in a spiral nebula, the forces of physics have been demonstrated which produce order.

According to the scientific picture, even if we consider the total universe as a thermodynamically isolated system, one where energy will eventually run down, there are still pockets within the total system of the universe where energy flow may sustain order over long periods. That is all the defense that materialists needed in order to satisfy themselves against the classic order-means-design and design-meansa-designer argument.

For nineteen hundred years of western history, the presence of order was held to require an ordering intelligence to account for it. The dominant view of the twentieth century in scientific cultures is that an ordering intelligence is no longer needed. Natural processes have been demonstrated to account for many types of order in the world, and it is assumed that natural processes will be found to account for all the remaining examples of unexplained order.

Throughout the last four hundred years orderly phenomena of nature have been accounted for by inferential linking of the observed phenomena to natural causes.

Because so many examples of orderly pattern had been investigated and shown to be the result of natural causes, the notion of an ordering intelligence was recognized as not needed, except possibly in the remote sense of an intelligence standing behind the natural process, as many theists believe. But with the discovery of informational molecules, DNA and protein, which are characterized by specified complexity instead of order, the situation has changed dramatically.

DNA is called an informational molecule because its unique structure functions as the central part of an elaborate communication system within the cell. This code aspect was hinted at by Francis Crick and James Watson in their modest announcement of the famous double helix structure of DNA.[49] An early written statement of this idea was recorded in a letter that Crick wrote on March 19, 1953 to his son Michael: "Now we believe that the D.N.A *is* a code. That is, the order of bases (the letters) makes one gene different from another gene (just as one page of print is different from another)."[50]

The second group of informational molecules is proteins. They are long chain-like molecules composed of amino acids linked together end to end, which fold up into very complicated shapes. The specific sequence of amino acids *in* a protein is what determines its overall three-dimensional shape and function.

DNA, with its alphabet of four bases, and protein, with an alphabet of twenty amino acids, represent two different languages related by a code. When the cell constructs proteins, a translation takes place between one language and the other; the sequence in DNA codes for and determines the sequence in protein.

DNA and proteins, and, of course, living organisms, are rich in information.

Other structures that are characterized by specified complexity, or high information content, are linguistic messages, bridges, paintings, computer programs, and other human artifacts.

Molecular biology has discovered a structural identity between the genetic messages on DNA and the written messages of a human language. This discovery opened the way for the application of information theory to biology. Information theory applies to any symbol system, regardless of the elements of that system. The so-called Shannon information laws apply equally well to human language, Morse code, and the genetic code. Hubert P. Yockey notes in the *Journal of Theoretical Biology:*

> It is important to understand that we are not reasoning by analogy. The sequence hypothesis [that the exact order of symbols records the information] applies directly to the protein and the genetic text as well as to written language and therefore the treatment is mathematically identical.[51]

There is an identity of structure between DNA (and protein) and written linguistic messages. Since we know by experience that intelligence produces written messages, the implication, according to established experimental method of inferring causes from effects, is that an intelligent cause most probably produced the informational pattern in DNA and protein. The significance of this inference lies in the security of it, for it is much stronger than if the structures were merely similar.

We are not dealing with anything like a superficial resemblance between DNA and a written text. We are not saying DNA is *like* a message. Rather, DNA *is* a message. Even though logic indicates a message sender, a result that has obvious philosophical and spiritual implications, it is important to note that it was not reached by philosophical or spiritual presuppositions.[52] It may be an unwanted or unpopular result in some quarters, but scientists do not have a reputation of advocating only what is wanted or popular. We seek the truth.

As we come to the close of this update chapter for *The Mystery of Life's Origin,* it is well to remember that for centuries it seemed to be an obvious fact to many that life resulted from spontaneous generation. Today we no longer accept spontaneous generation. For many today, however, it is considered an equally obvious fact that life resulted by the quite natural outcome of chemical and physical processes, either on this planet or somewhere else before it came to earth. Without direct evidence, all such cases are based on circumstantial evidence. Even though many cases have been settled on this basis, let us recall what that venerable detective Sherlock Holmes noted in another baffling mystery. "'Circumstantial evidence is a very tricky thing,' answered Holmes thoughtfully, 'it may seem to point very straight to one thing, but if you shift your own point of view a little, you may find it pointing in an equally uncompromising manner to something entirely different... There is nothing more deceptive than an obvious fact.'"[53]

Endnotes

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II. The State of the Debate

13. WE'RE STILL CLUELESS ABOUT THE ORIGIN OF LIFE

James M. Tour

Organisms have well-defined molecular assemblies, redox potentials across membranes, and metabolic pathways—all operating in exquisite states that we call "life."

Chemistry, by contrast, is utterly indifferent to whether anything is alive or not. Without a biologically derived entity acting upon them, molecules have never been shown to "evolve" toward life. Never.[1]

While organisms exploit chemistry for their own ends, chemicals have never been seen to assemble themselves into an organism. Origin-of-life research keeps attempting to make the chemicals needed for life, and then to have those assemble toward something to which they are inherently indifferent. But try as they might, without preexisting life no researchers have ever seen molecules assemble into a living cell, or anything even remotely resembling a living cell. Contrary to the hyperbole of press reports, any synthetic molecularly derived structures that have been touted as being cell-like are in reality far from it. This situation might change in the future, but it is unlikely to change under the current course of research. Scientists have no data to support molecular "evolution" leading to life. The research community remains clueless.

Many scientists and professors who are outside boutique origin-of-life circles have been led astray by researchers' claims and the subsequent press, thinking that far more is known about life's origin than really is known. This has affected the highest seats in the academy where even some science professors confuse origin of life with biological evolution. Like a muddy prebiotic cesspool, confusion abounds in the academy.

Two-thirds of a century since the 1952 Miller-Urey experiment, where some racemic amino acids were formed from small molecules and an electrical discharge, the world is no closer to generating life from small molecules—or any molecules for that matter—than it was in 1952.[2] One could argue that origin-of-life research is even more befuddled now than it was in 1952 since more questions have evolved than answers, and the voluminous new data regarding the complexity within a cell makes the target much more daunting than it used to be.[3]

Consider what has occurred in other fields in the past sixty-seven years since Miller-Urey performed their experiments: human space travel, satellite interconnectivity, unlocking DNA's code and its precise genetic manipulation, biomedical imaging, automated peptide and nucleotide synthesis, molecular structure determination, silicon device fabrication, integrated circuits, and the internet, to name just a few.

By comparison, origin-of-life research has not made any progress whatsoever in addressing the fundamental questions of life's origin. Two-thirds of a century and all that has been generated are more suggestions on how life *might* have formed—suggestions that really show how life *probably did not* form. Nothing even resembling a synthetic cellular structure has arisen from its independent components, let alone a living cell. Not even close.

In 1775, the French Academy in Paris refused to entertain any further proposals for perpetual motion machines; the devices just did not work as advertised.[4] No one knew why not—the mature science of thermodynamics, which gave us a theoretical account for *why* the *perpetuum mobile* schemes failed, lay nearly one hundred years in the future—but the machines clearly failed. Today we need a French Academy-like directive toward origin-of-life proposals; for, like perpetual motion machines, such proposals just do not work as advertised. Instead we should explore why scientists have failed to produce life. Clearly life can exist—unlike perpetual motion machines, we have the ubiquity of life surrounding us on this planet. But there needs to be a wholly different scientific approach to reveal life's origin.

This is an appeal to the origin-of-life research community: Step back and consider the claims within the research, the true state of the field, the retarded state of the science relative to other research areas, and the confusion or delusion of the public regarding life's origin. Many researchers in origin-of-life organic synthesis are superb scientists. However, overly confident assertions, exaggerated and spread by the over-zealous press, have led to gross public misconceptions regarding what is and is not known concerning the beginning of life.

We will now turn to an exploration of the two main classes of origin-of-life science: chemical synthesis and molecular assembly. After a brief summary of each, the two classes of experiments will be considered separately in depth.

First, the chemical synthesis of the four molecule types for life: nucleotides, carbohydrates, proteins, and lipids. Nucleotides are composed of a trimeric nucleobase-carbohydrate-phosphate combination, and once polymerized, constitute DNA and RNA. Five different nucleobases comprise the entire alphabet for DNA and RNA. The nucleotides and their subsequent DNA and RNA structures are homochiral, meaning that they exist as one mirror image form and not the other, yielding one of two possible enantiomers.

Amino acids are most often homochiral. When amino acids are polymerized, they form proteins and enzymes, the latter being nature's nanomachines that build the biological system. Like DNA and RNA, proteins and enzymes also have a tertiary homochirality based upon their coiling and folding.

Lipids are dipolar molecules having a polar water-soluble head and a non-polar water-insoluble tail. They too are most often homochiral.

Carbohydrates, in addition to being part of the backbone of DNA and RNA using their 5-carbon containing versions, also use 6-carbon containing structures. Cells live on carbohydrates for energy, and carbo-

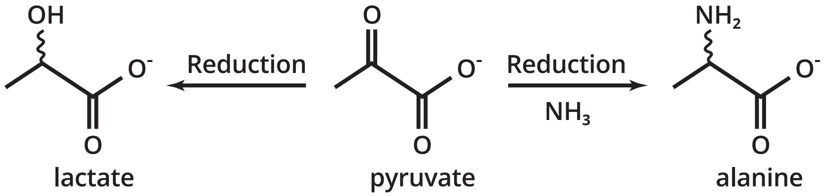

Figure 13-1. The reduction and reductive amination of pyruvate to lactate and alanine.
This was described in the NASA press release as "NASA Study Reproduces Origins of Life on Ocean Floor."

hydrates, along with proteins, are identification-receptors wherein some regulation on and within cells is controlled. Carbohydrates are also homochiral, and their polymeric forms take on tertiary homochiral shapes.

Origin-of-life efforts have spent much time trying to make these four classes of molecules and their polymers, starting from simple chemicals that were presumed to be available on the prebiotic earth, such as formaldehyde, hydrogen cyanide, and carbonates.

The second class of experiments that are performed in origin-of-life research deal with the assembly of the molecules. For example, when lipids are added to water and subjected to shear forces, they can form spherical bilayer vesicles. These vesicles have the lipid polar ends pointing inward and outward toward the water on the inside and outside of the vesicle, respectively, and the nonpolar tails pointing toward each other and away from the water phases. Sometimes researchers will add other compounds to the water that become engulfed when the bilayer vesicles form. In order to obtain a cell, molecules must precisely assemble into many higher-order structures.

Chemical Synthesis Experiments

Chemical synthesis experiments in origin of life can be summed up by a protocol analogous to this:

- Purchase some chemicals, generally in high purity, from a chemical company.

- Mix those chemicals together in water in high concentrations and a specific order under some set of carefully devised conditions in a modern laboratory—sets of conditions that often would be difficult to replicate in a non-laboratory environment on early earth.
- Obtain a mixture of compounds that have a resemblance to one or more of the basic four classes of chemicals needed for life: carbohydrates, nucleotides, amino acids, or lipids. Most of the time they are synthesized in racemic (both mirror images) or near racemic form, not in homochiral form.
- Identify the desired compound in a mixture of many other isomers and products. Then buy (or make, using modern non-abiotic methods) a purified version of that desired compound and proceed to the next step.
- Publish a paper making bold extrapolations about origin of life from these functionless crude mixtures of stereochemically scrambled intermediates.
- Engage with the often over-zealous press to dial up the knob of unjustified origin-of-life projections.
- Watch the misled and mesmerized layperson exclaim, "You see, scientists understand how life formed!"
- Accept a generation of science textbooks yielding colorful, deceptive cartoons of raw chemicals assembling into cells, which then emerge as slithering creatures from a prehistoric pond.

Even professors have been misled by this. Nor do the scientists themselves understand anything more about life's origin than they did before they performed their experiments, because their experiments offer no solution to the fundamental questions needed for a path to life.

How can the results be published if there is nothing new regarding life's origin? Because this becomes the norm in the field—there are no expectations of addressing grander questions. Reviewers are of the same mind, believing this is the best that can be done. Journal editors have been numbed to believe the same, and to ignore unjustified claims regarding the origin-of-life implications. Some published work contains chemistry which is pedestrian, while other papers show remarkably ingenious routes to these molecular classes starting from simple chemicals—but in every case, fundamental questions of life are not addressed. Thus the field stagnates for two-thirds of a century while other areas of research make quantum leaps that advance humankind.

Here is a recent example of such a scenario of simple chemistry and the hyperbole that follows. In 2019, Laura Barge and coworkers at NASA Jet Propulsion Laboratory, the California Institute of Technology, and the Oak Crest Institute of Science simulated an undersea hydrothermal vent. Heating an aqueous solution of pyruvate to 70°C and introducing ammonia and iron hydroxides while limiting oxygen, they observed simple reduction and reductive amination to stereo-scrambled lactate and alanine, respectively.

Those are such simple reducing reactions that the chemistry is certain and therefore wholly unremarkable. Yet the authors write, "This shows that aqueous, partially reducing iron mineral systems (which would have been common in early-Earth seafloor/vent environments) could have facilitated synthesis and concentration of prebiotic organic molecules relevant for the emergence of life."[5]

The NASA press office then had a field day with this result, titling their article "NASA Study Reproduces Origins of Life on Ocean Floor" and writing, further, "Scientists have reproduced in the lab how the ingredients for life could have formed deep in the ocean 4 billion years ago. The results of the new study offer clues to how life started on Earth and where else in the cosmos we might find it."[6] The press cut and pasted from the NASA press release, resulting in a blitzkrieg of deeply misleading news.

Although the chemistry of this experiment is less complex and less interesting than that of the 1952 Miller-Urey experiment, it was published in the *Proceedings of the National Academy of Sciences*, a superb scientific journal. This underscores that journals themselves are complicit in continuing this sort of rudimentary experiment claiming to be suggestive of life's origin. Unlike the far more sophisticated synthetic chemistry of origin-of-life leaders like John D. Sutherland, the work by NASA is nonsensically simple—so in that sense, much like the prebiotic earth would have been.

Unlike the artless 2019 NASA experiment, most origin-of-life researchers today put far more precision into their protocols to make more elaborate arrays of stereo-scrambled intermediates. One could easily argue, therefore, that the researchers are moving further from the heart of abiogenesis since they are filling the protocols with the best of their intellectual training to coax molecules into the form that the researcher desires. Yet even with all that intellectual input, the origin-of-life researchers overcome few if any of the hurdles noted below that need to be considered when dealing with chemical synthesis experiments common to all origin-of-life protocols that are being published.

Hurdle 1: Homochirality

Molecules that compose living systems almost always show homochirality. So one particular enantiomer, selected from the many possible stereoisomers, needs synthesizing. Generally there are 2^n possible stereoisomers where *n* is the number of stereocenters in the molecule. If discussing carbohydrates, there are eight possibilities among the abundant 5-carbon carbohydrate and sixteen possibilities from the 6-carbon-long carbohydrates. Claims that these structures could be prepared under prebiotic conditions in high enantiomeric purity using inorganic templates, or any presumed templates, have never been realized even with the advanced designs of the origin-of-life researchers. How much less could homochiral compounds have been obtained in a mindless prebiotic environment?

In addition, this would have to happen repeatedly for all the varying carbohydrates. Nobody has ever offered a demonstrative solution.

Moreover, each class of compound, the carbohydrates, the amino acids, and the lipids, and further each compound within each of those classes, would require its own separate methodology to control its specific regiochemistry and stereochemistry. To merely say that all the diverse stereochemistries form and the required one preferentially reacts (kinetic resolution) repeatedly over its enantiomer or diastereomers negates what is known about the difficulties of selective synthesis, especially when envisioned in a mindless prebiotic system where no enzymes yet exist. The differences in reaction rates often require chiral systems acting upon chiral molecules.

If this can be done sufficiently well in a mindless prebiotic puddle, why cannot the experts in research repeatedly replicate it in sixty-seven years of trying while using their sophisticated modes of synthetic ingenuity?

Hurdle 2: Pre-DNA and -RNA

Abiogenesis starts long before DNA and RNA are formed. So en route to those compounds, one would have to select the 5-carbon carbohydrate for its backbone over the 6-carbon structure, and all this in homochiral form. Further, for DNA, it has to be one hydroxyl group deficient, or deoxyribose. If it is not, then it will be suitable for RNA, but far less stable. Prebiotic systems never knew any of this.

Hurdle 3: Selectors

In choosing the molecule types to go forward, there are no chemical selectors yet formed in a prebiotic system, or if there are selectors, they generally need to be more complex than the molecule that they are selecting. What is the origin of the selector in a prebiotic system?

Hurdle 4: Redesigns

When building molecular systems, constant redesigns are needed which take the synthesis back to step one. It is often impossible to remove a moiety once it has been added to a molecule. So if a prebiotic and mindless reaction makes one small mistake, the synthesis has to go back to the beginning—but that could mean sending it back a hundred million years, and it will likely make the same mistake again since it has no memory to prevent its repeated mistake. Plus it has no impetus to start over, because chemistry is indifferent to moving toward life. It is chaos.

Hurdle 5: Stopping Point

The synthetic reactions do not know how to stop their current course of progression, or why to stop. The prebiotic system will continue to make derivatives. Time, although claimed to be the great savior of abiogenesis, can actually be the enemy. Time works against obtaining desired chemicals, particularly when the needed target is a kinetic product. For example, carbohydrate prebiotic synthesis is generally conducted through the formose reaction, but then one gets aldol reactions in equilibrium with retro-aldol reactions, and Cannizzaro reactions, which, taken together over time, favor the branched and "caramelized" polymeric products. How does the system know when or how to stop if reaction times can be in the thousands of years or longer? Routes to carbohydrates from presumed prebiotic molecules are an all-around mess.

Hurdle 6: Purification

A prebiotic system does not have the ability to easily purify the structures. Sometimes selective crystallization can occur with the designed input of a synthetic chemist, but most often not. And the impurities contaminate and inhibit subsequent steps. Separations have to be done repeatedly across broad arrays of the four classes of compounds or else the impurities withdraw the resources from the chemical pools. Most origin-of-life researchers do not even purify the desired products. They simply identify the desired product in a morass of other isomers or related molecules, and then purchase a pure sample for the next step. That's cheating when it comes to total synthesis, but it's a cheat rarely acknowledged by the researchers.

Hurdle 7: Order

Reagent addition-order is essential. One cannot add the icing to a cake at the stage of mixing the flour and eggs. Chemistry is even more demanding with its sequences throughout multiple steps, each requiring their own reaction conditions. To claim that compound A spilled in from one pool, and then another pool dumped its contents of compound B, seems far-fetched when such sequences are repeatedly required with specific timings.

Hurdle 8: Activation Steps

The making of the amino acid monomers is hard enough, but the synthesis of a single dipeptide bond generally requires activation steps that are complex if they are to be performed cleanly and repeatedly. Automated systems today require multiple individual steps to cleanly prepare a single amide bond. Likewise, nucleotide polymerization can be terribly messy unless proper activators (leaving groups) and blocking chemistry is exploited. No general solution to this problem has been offered.

Hurdle 9: Environmental Factors

The parameters of temperature, pressure, solvent, light, pH, and atmospheric gases have to be carefully controlled in order to build complex molecular structures. Ultraviolet light in particular is highly degrading to organic compounds. Some origin-of-life researchers use these wavelengths of light to make their compounds, and as soon as those compounds are synthesized, the lights are removed to prevent further rapid degradation. That is convenient in a lab, but how is that done outside the laboratory, such as at the edge of a volcano, and repeatedly? The ultraviolet light that is present in the atmosphere will severely degrade the molecules if left even for days or months.

Hurdle 10: Molecular Characterization

Molecular characterization at each step is essential. If the chemist doesn't know the molecular structure or at least the gross composition of the intermediates, the process is doomed for failure. So how might this be done in a prebiotic milieu? A prebiotic system knows nothing of molecular structure. It is mindless.

Hurdle 11: Isolation

Each organic reaction needs a carefully controlled work-up (isolation) protocol to prevent decomposition of the product. For example, nucleotides are sensitive compounds, and chemists today, even origin-of-life chemists, take great pains to work up these reactions very carefully.

Hurdle 12: Mass Transfer

The mass transfer problem will be the killer of all routes. How does one bring sufficient material through a complex multistep synthesis? If the route runs out of material after, say, 300 million years of progression, how does it go back to make more when nature has never kept a laboratory notebook of its former path?

In addition to origin-of-life researchers leaving this problem unaddressed, they exacerbate it. One origin-of-life research team will publish a paper where they make a trace amount of a stereochemically impure target, like a particular carbohydrate. And then the next researcher will use that formerly published carbohydrate as their starting point for the next synthetic step, claiming a protocol called "relay synthesis." But the new researcher will either buy the intermediate in large amounts and pure homochiral form or make it using purely advanced synthesis, separation, and characterization means. They will not use that former cumbersome proposed prebiotic route. So there is no accountability of mass transfer when going from one published work to the next; a prebiotic world would never have such a luxury.

And how many chemical steps are needed to make all the chemicals that compose a simple cell, and in sufficient quantities to build the higher-order structures within a cell? Nobody knows, but the number of steps must be enormous, regardless of whether the compounds are made by linear or convergent routes. Any synthetic chemist knows that the mass transfer would be daunting and impenetrable in their advanced laboratories. A typical thirty-step synthesis, using our most advanced methods, can often afford less than 1% overall yield of the final product in an optimized sequence.

How this could have been done with thousands of necessary steps to the thousands of requisite compounds in a prebiotic world is presently beyond our comprehension. So most researchers just bypass this difficulty by not mentioning it.

Furthermore, claims of "it only has to happen once" are incorrect. The chemistry would have to occur repeatedly, en masse, to produce the quantities needed to progress through a mindless and structurally blinded synthesis. Some might argue that higher molecular concentrations might have accumulated locally next to volcanoes where there is a heat source, or in gels, but how could this happen repeatedly through broad arrays of chemical classes? There is no reasonable explanation.

Elsewhere I have considered and discussed these deficiencies in synthesis in greater detail, presenting several examples from the recent literature.[7] When the obvious glaring problems are unaddressed, might this explain the arrested state of origin-of-life research when compared to the progress of other fields?

Molecular Assembly Experiments

In addition to chemical synthesis experiments that do not traverse the hurdles, there are origin-of-life experiments that deal with the assembly of chemicals into what researchers refer to as a "protocell," that is, "a self-organized, endogenously ordered, spherical collection of lipids proposed as a stepping-stone to the origin of life."[8]

Basically, if one takes a few drops of a lipid, adds them to water, and shakes, lamellae can form, which are lipid bilayer films. A small amount of spherical bilayer vesicles can break off from these lamellae, but much higher yields are realized if the lamellae are put through shear forces such as obtained during sonication. While origin-of-life researchers call the results "protocells," no life or pre-life exists. It remains lipid bilayer vesicles in water.

Most so-called protocell assembly experiments in origin-of-life research can be summed up by a protocol analogous to this:

- Purchase one homochiral lipid type from a chemical company or synthesize stereochemically scrambled lipids from smaller molecules. Add those lipids to water and observe the simple and expected thermodynamically driven assembly of those lipids into synthetic bilayer vesicles upon agitation. Sometimes the researchers will add other molecules, like nucleotides, that are engulfed by the vesicle as it forms.
- Publish a paper claiming that the synthetic vesicles are protocells and suggestive of early forms of cellular life.[9]
- Engage with the media to ramp up the hype.
- Watch the layperson being misled.

Here is one of many recent examples, published in 2017, of standard chemistry being portrayed as having something to do with the construction of a living cell.[10] A team from the *Origins of Life Initiative* at Harvard University performed a known type of polymerization reaction in water, called Reversible Addition-Fragmentation Chain Transfer (RAFT). This reaction type is not seen in nature—it is a purely synthetic process. The monomers that the research team chose are all synthetic and unnatural. This is standard chemistry used to make polymers wherein there is a controlled radical polymerization reaction that can afford a polymer chain bearing a hydrophobic block attached to a hydrophilic block when two different monomer types are used sequentially. The researchers observed these to form polymeric vesicles during the polymerization, which is interesting but surely not extraordinary.

While they kept the radical chain growing through ultraviolet light activation (a typical activating source) the vesicles grew, consuming monomer within the vesicles, to the point where the vesicles would burst. Again, nothing surprising; a critical vesicle size is reached and then the forces between the growing vesicle and the surrounding water dictate a critical growth volume before the vesicle ruptures. The vesicles move toward the ultraviolet light, likely by heating gradients induced by the light source or reaction thermodynamics.

Chemists like myself find this type of polymerization reaction to be interesting. It was a fine job by the researchers and well-worth publishing. The claims should have ended there. But here is how the work was portrayed in the published article:

> The observed net oscillatory vesicle population grows in a manner that reminds one of some elementary modes of sustainable (while there is available "food"!) population growth seen among living systems. The data supports an interpretation in terms of a micron scale self-assembled molecular system capable of embodying and mimicking some aspects of "simple" extant life, including self-assembly from a homogenous but active chemical medium, membrane formation, metabolism, a primitive form of self-replication, and hints of elementary system selection due to a spontaneous light triggered Marangoni instability [surface tension gradients].[11]

Was that statement justified? Just because A "reminds" me of B, it does not make A an "embodying" form of B—it is just my imagination. If the disc-shaped vesicle "reminds one" of a flying saucer, is it a "simple extant" flying saucer? No extant life, not even simple extant life, was demonstrated.

Following those excessive extrapolations by the authors, the claims were then rephrased and projected to the lay public by the *Harvard Gazette* and other news outlets: "A Harvard researcher seeking a model for the earliest cells has created a system that self-assembles from a chemical soup into cell-like structures that grow, move in response to light, replicate, and exhibit signs of rudimentary evolutionary selection."[12] Is that an accurate representation of the article? Surely not.

Here is a listing of a few of the challenges that need to be considered when dealing with lipid bilayer vesicle experiments common to most origin-of-life protocols that are being published.[13]

Challenge 1: Heterogeneity

Researchers have identified thousands of different lipid structures in modern cell membranes. These include glycerolipids, sphingolipids, sterols, prenols, saccharolipids, and polyketides. All are homochiral or sp^2-stereo-defined.

For this reason, the origin-of-life researchers' selection of simple one-component synthetic vesicle lipid bilayers is far from realistic. When making synthetic vesicles—synthetic lipid bilayer membranes—mixtures with monoacyl lipids can destabilize the system, so researchers conveniently avoid these mixtures, while a prebiotic earth would not have that option. The heterogeneity of lipid bilayer structure is essential for cellular function, yet very hard for the researcher to reproduce.

Challenge 2: Varying Lipid Composition

Lipid bilayers surround subcellular organelles, such as nuclei and mitochondria, which are themselves microsystem assemblies. Each of these has their own lipid composition, different from the host vesicle.

Challenge 3: Symmetry

Lipid bilayers have a non-symmetric distribution. The outer and inner faces of the lipid bilayer are chemically inequivalent and cannot be interchanged without flippase enzymes, yet origin-of-life bilayer membranes are homogeneous across the bilayer; hence, they do not resemble the lipid bilayer of a living cell.

Challenge 4: Gatekeepers

Protein–lipid complexes and ionophores are the required passive transport sites and active pumps for the passage of molecules and ions through bilayer membranes, often with high specificity. Some allow passage for substrates into the compartment, and others their exit—they are highly specialized gatekeepers composed of very intricate structures. These complexes are rarely addressed by researchers working on their so-called protocell assemblies, yet they are essential for cell function.

Challenge 5: Glycans

Most cellular lipid bilayers have vast numbers of polycarbohydrate appendages, known as glycans. These are essential for cell regulation. For example, just six repeat units of the carbohydrate D-pyranose can form more than one trillion different hexamers through branching (constitutional) and glycosidic (stereochemical) diversity. The diversity in branching patterns can store more information about the state of the cell than both DNA and RNA combined.[14]

Every cell membrane is coated with a complex array of glycans, and all cell-to-cell interactions take place through carbohydrate participation on the lipid bilayer membrane surface. Eliminating any class of carbohydrates from an organism results in its death, and almost every known cellular dysfunction involves carbohydrates.

Furthermore, in nature, these glycans are not made using a direct genetic template but result from the activity of several hundreds of enzymes organized in complex pathways—these are super-hard to construct and their structures selectively morph throughout cellular life changes.

So how do the origin-of-life researchers address the prebiotic synthesis of these complex lipid bilayers? They do not. Yet they claim a protocell through merely the formation of a homogeneous lipid bilayer vesicle. Might this retard the field?

Another example: Lipid bilayer assembly experiments were conducted by teams from the University of California at Santa Cruz and the University of New South Wales in Australia, and they disclosed a summary of the work in 2017.[15] These teams combined nucleotides and lipids in water to form lamellae with the nucleotides sandwiched between the layers. Recall that nucleotides are trimers of nucleobase-carbohydrate-phosphate, and in this case they were purchased in pure homochiral form—so already in a well-developed state. The lipids were also purchased in pure homochiral form.

The researchers showed that a condensation polymerization of the nucleotides via the pre-loaded phosphate with the purchased stereo-defined alcohol moiety on a neighboring nucleotide can take place within the lamella upon dehydration. They further demonstrated that similar reactions can occur at the edges of hydrothermal fields associated with volcanic landmasses to provide the heat needed for the reactions. The chemistry is indifferent to the heat source, whether a volcano, a Bunsen burner, or a laboratory heating oven; the nucleotide will polymerize upon reaching a critical concentration and temperature.

The chemistry is unremarkable since it is preloaded through the purchased derivatives. This work addresses the essential concentration needs by removing the water and driving the intermolecular reactions to form oligomers that resemble the nucleic acids. The problem with a condensation (step growth) polymerization is that any alcohol can compete for the reactive electrophilic site, but in the researchers' case, they conveniently added only nucleotides and no other alcohols. In other words, the system is stacked to work through its purity. Condensation polymerization reactions need to be very pure, free of competing nucleophilic and electrophilic components, as explained by the Carothers equation defining degrees of polymerization based upon monomer purity.[16] If there happen to be amino acids or carbohydrates with the nucleotides, these would terminate or interrupt the growth of the oligonucleotides.

Moreover, the researchers did not confirm the detailed integrity of the claimed structures, which, if carefully analyzed, would likely show attacks from unintended hydroxyl sites. Nonetheless, even when short oligonucleotides form, they are not a usable form of RNA, since they have no useful sequences. It would be like a book of random letters, or in this actual case a small book of all the same letters.

The authors suggest that the lamellae sandwiching oligonucleotides eventually break off to form lipid bilayer vesicles containing the oligonucleotide-within-vesicle constructs, which they call protocells. The conversion of planar lamellae into multilamellar vesicles (onion-like structures) as they hydrate is well-established, but these generally need shearing (extrusion-type mechanical) forces, sonication, or peptides in order to form the requisite lipid bilayer vesicle, so the researchers' yields of the desired vesicles were sure to be very low.[17]

The conditions used in this experiment are hard to fathom being found in the prebiotic earth: homochiral nucleotides in high chemical purity, trapped in a lamella composed of homochiral stereo- and regiochemically pure lipids. Even accepting that improbability, those obtained vesicle structures have almost no resemblance to cellular lipid bilayers that have a vastly more complex constitution. The authors are merely forming lipid bilayer balls made from purchased homochiral lipids containing some randomly sequenced oligonucleotides from purchased homochiral nucleotides.

While exciting chemistry to the origin-of-life researcher, nothing here is chemically remarkable and it has almost no resemblance to a real cell. Nonetheless, behold the claims in the published paper:

- "Then, in the gel phase, protocells pack together in a system called a progenote and exchange sets of polymers, selecting those that enhance survival during many cycles."[18] But chemicals know nothing of survival since they are indifferent to "survival." There is no mechanism shown for how their protocells would bear different sets of polymers or exchange their sets of polymers between them, or make a "selection" process. The researchers misappropriate terms from biology and use them in a prebiotic world in a manner that makes no chemical sense.
- "The best-adapted protocells spread to other pools or streams, moving by wind and water, and some develop the ability to use carbon dioxide for photosynthesis."[19] However, there is no suggestion regarding the meaning of "best-adapted." It is again a misuse of terminology. Photosynthesis is a highly precise process requiring many enzymes, a well-ordered electron pathway, and precisely defined distances between photon receptors and electron ejectors, with electron transfers traveling down defined homochiral polypeptide channels. The authors' statement not only blurs the line of realism, but is fallacious.
- "After much trial and error, one protocell assembles the complicated molecular machinery that enables it to divide into daughter cells. This paves the way for the first living microbial community."[20] However, there is neither a demonstration of

how "molecular machinery" is made, nor even a proposal. The mechanisms needed for cellular division are highly complex, requiring cascades of enzymes functioning in precise and timed manner. This is utterly inconceivable based on the demonstrated results, and nothing proposed, let alone demonstrated, "paves the way for the first living microbial community."

- And these "ultimately evolve into a primitive metabolism required by the earliest forms of life."[21] It seems to be commonplace for origin-of-life researchers to co-opt terms from biological evolution and move them into the prebiotic vocabulary. This is unhelpful. Molecules are indifferent to moving toward life. Furthermore, what is a "primitive metabolism"? There is nothing being metabolized. There is only a condensation polymerization, a simple chemical reaction based upon the addition of nucleophiles to electrophiles. Such a reaction is never referred to as a metabolism within synthetic chemistry.

Those origin-of-life assembly claims are akin to buying twenty pounds of sliced turkey meat, adding a gallon of turkey broth, warming, sticking in a few feathers and suggesting that a "prototurkey," "primitive turkey," or "extant turkey" had just been synthesized.

A book by the famous science writer Ed Regis, entitled *What is Life?: Investigating the Nature of Life in the Age of Synthetic Biology,* attempts to describe life's origin from molecules: "Life began with little bags of garbage, random assortments of molecules doing some crude kind of metabolism. That is stage one. The garbage bags grow and occasionally split in two, and the ones that grow and split fastest win."[22] Few origin-of-life researchers would state it so shamelessly; nonetheless, "little bags of garbage" are precisely what origin-of-life researchers have been making. Those "little bags of garbage" have no more resemblance to living cells than a big bag of garbage resembles a horse.

There is a highly complex non-covalent interactive connectivity within a functioning cell—just like the parts of a machine need to be fitted together—but with far more complexity in a biological organism. Nobody knows how a viable cell emerges from the massive combinatorial complexity of its molecular components. Of course, nobody has ever synthetically mimicked it either.

To begin to grasp the complexity involved, consider the interactome. An "interactome" is the whole set of molecular interactions in a particular cell.[23] Just as one sees the precise overlap and interconnectivity in human anatomical structures, in molecular biology the interconnectivity effects (through van der Waals interactions) are displayed trillions of times more abundantly than in gross human anatomy. The interactome can be protein-protein, gene-gene, or molecule-molecule interactions, and these greatly affect the function of the cellular system. It is through the molecular interactions that information is transferred. Electrostatic potentials permit information to flow through non-covalent molecular arrays, but these molecules need specific orientations relative to each other.[24] The interactome defines the intermolecular orientations, alignments that are unattainable through random mixing.

Peter Tompa of the University of Brussels and George Rose from Johns Hopkins University calculated that if one merely considers all protein-protein interactome combinations in just a single yeast cell, the result is an estimated $10^{79,000,000,000}$ combinations.[25] That is the number 1 followed by 79 billion zeros, a whoppingly large number. To put that in perspective, the number of elemental particles in the universe is estimated to be $\sim10^{90}$. These numbers are beyond the realm of human appreciation.

The authors understate the ramifications, writing that "the numbers preclude formation of a functional interactome by trial and error complex formation within any meaningful span of time." Thus, "a complicated cellular sorting/trafficking and assembly system, made up of membranous organelles, receptors, membrane translocation devices, cytoskeletal tracks, motor proteins, and accessory chaperones guides the proper compartmentalization, localization, and assembly of proteins in the cell." But even with all that sophisticated biochemical guidance and scaffolding, "in the absence of energy even this well developed infrastructure would be insufficient to account for the generation of the interactome, which requires a continuous expenditure of energy to maintain steady state." They conclude:

> The inability of the interactome to self-assemble de novo imposes limits on efforts to create artificial cells and organisms, that is, synthetic biology. In particular, the stunning experiment of 'creating' a viable bacterial cell by transplanting a synthetic chromosome into a host stripped of its own genetic material has been heralded as the generation of a synthetic cell (although not by the paper's authors). Such an interpretation is a misnomer, rather like stuffing a foreign engine into a Ford and declaring it to be a novel design. The success of the synthetic biology experiment relies on having a recipient interactome… that has high compatibility with donor genetic material. The ability to synthesize an actual artificial cell using designed components that can self-assemble spontaneously still remains a distant challenge.[26]

Regarding the ability to effect reactions through successive dehydration and rehydration steps as proposed by some researchers, Tompa and Rose write that "it is implausible that a completely 'denatured' cell could be reversibly renatured spontaneously, like a protein. Instead, new cells are generated by the division of pre-existing cells, an unbroken chain of renewal tracking back through contingent conditions and evolving responses to the origin of life on the prebiotic earth." Indeed, "all extant cells are generated by the division of preexisting cells that provide the necessary template for perpetuation of the interactome."[27]

Therefore, even if one were to try to simplify the problem with network connectivity theory, interactomes add a massive layer of complexity to all cellular structures. That further underscores the difference between a real cell and the so-called protocells or extant cells made by origin-of-life researchers. In fact, terms such as "protocells" or "extant cells" are misnomers that exacerbate the confusions.

So how close have researchers come to creating an artificial cell? In 2010, Craig Venter's team made a copy of a known bacterial genome and transplanted it into another cell.[28] In 2016 the Venter team did something related. They removed all but 473 genes from a natural genome, transplanting it into another cell.[29]

These are indeed exciting experiments, but the cells were already made, naturally, and alternate genomes were inserted. This is analogous to buying two Corvettes, removing one of the electronic engine control modules (ECUs) from the first Corvette, and swapping it as a substitute into the second Corvette; or copying the ECU in a fabrication facility and inserting the copied version into a car. One could not rightly claim the building of a Corvette; it is an exchange of parts, while the cars already existed.

More recently Henrike Niederholtmeyer, Cynthia Chaggan, and Neal K. Devaraj of the University of California at San Diego have made what they term "mimics of eukaryotic cells"[30]; the journal *Science* declared these "the most lifelike artificial cells yet."[31] In this experiment, semi-porous microcapsules made of *plastic* (from acrylate polymerization) containing *clay* were prepared using modern microfluidics techniques that are done within fabrication devices. Due to their inherent charges, these clays have a high affinity for binding DNA, so when DNA was then added to the solution, it diffused through the semi-porous plastic microcapsules and bound to the clay. The requisite RNA polymerases for mRNA transcription, ribosomes for polypeptide translation, tRNA, amino acids, enzymatic cofactors, energy sources, and cellular components essential for proper protein folding were similarly purchased or extracted from living systems, added to the medium, and permitted to diffuse into the plastic capsules.

The expected chemical reactions ensued, resulting in protein synthesis. The newly formed proteins could diffuse out of the plastic microcapsules to other nearby semi-porous plastic microcapsules that had been similarly prepared, and the nearer the neighboring plastic microcapsule was to the original microcapsule, the more exchange of reagents between them took place. Those neighboring plastic microcapsules could then similarly become production sites for proteins. This diffusion between nearby plastic microcapsules was termed "quorum sensing," relying on standard local concentration gradients where the nearer neighbors received more of the leached materials. The chemistry of the exogenously added reagents will work regardless of the container, whether it be a plastic semi-porous microcapsule, a test tube, or a large-scale industrial production tank.

While the experimental design is clever and exciting, the actual chemical synthesis is unremarkable, and it is—as expected—based upon the purchased bio-extracted chemicals that were added. Such use of known and commercially available cellular components to synthesize new proteins is done every day in laboratories around the world, and one can buy commercial kits to do this.[32]

So it is far from the embarrassing press-hyped claim of "gene expression and communication rivaling that of living cells."[33] There is no rivalry here. All of the active chemical components for the synthesis were extracted from living systems. Further, one might arguably agree that these are indeed "the most lifelike artificial cells yet,"[34] but that only serves to underscore the point: Nobody has ever yet come close to generating the workings of life.

There are further demonstrations of such over-extrapolations. In a 2018 article entitled "How Did Life Begin?" in the top-ranked scientific venue in the world, *Nature,* Nobel laureate Jack Szostak wrote a synopsis for the process of life's origin. (The article appeared in the journal's special report, "Innovations In: The Biggest Questions in Science.") Directing his message to the non-expert, Szostak explained:

> …iron-cyanide compounds accumulated over time, building up into a concentrated stew of reactive chemicals. Life as we know it requires RNA. Some scientists believe that RNA emerged directly from these reactive chemicals, nudged along by dynamic forces in the environment. Nucleotides, the building blocks of RNA, eventually formed, then joined together to make strands of RNA. Some stages in this process are still not well understood. Once RNA was made, some strands of it became enclosed within tiny vesicles formed by the spontaneous assembly of fatty acids (lipids) into membranes, creating the first protocells. As the membranes incorporated more fatty acids, they grew

> and divided; at the same time, internal chemical reactions drove replication of the encapsulated RNA.[35]

The descriptions listed here were derived from Szostak's earlier article in *Scientific American*,[36] and the presentation in *Nature* of Szostak's synopsis elevates its credibility in the eyes of the scientific community. But let us examine Szostak's claims.

First, Szostak's statement that "some scientists believe that RNA emerged directly from these reactive chemicals, nudged along by dynamic forces" is painful to a synthetic chemist because a complex pathway of reactions would be needed, along with all the steps of purification and then assembly, polymerization, and sequencing. All that is reduced to a simple passing sentence. For example, how could RNA emerge directly from iron cyanide? Iron cyanide is highly stable, and the concentration of free cyanide is minuscule. Nothing "emerges directly," let alone something as complex as RNA.

Further, words like "nudged along by dynamic forces" have no meaning in the realm of synthetic chemistry, though they seem acceptable to the layperson. That "nucleotides… eventually formed and then joined together to make strands of RNA," is an incredible statement for which there is no basis. Nucleotides do not merely join together with any significant precision without complex protection and deprotection steps.

In sum, Szostak's remark that "some stages in this process are still not well understood" would be more accurately phrased as "in almost all stages we remain clueless when it comes to the chemistry needed on a prebiotic earth."

Accompanying Szostak's article is a figure that purports to summarize the chemical process leading to the formation of RNA nucleotides.[37] However, the compounds listed in this figure as "simple sugars" are not sugars; they are glycerol and ethylene glycol. There are known routes to convert those to very simple sugars,[38] but only in gross relative and absolute stereochemically mixed states, and as a mixture of several different polyols—so separation problems abound that remain poorly delineated. Carbohydrate synthesis is a very difficult problem for a prebiotic earth.[39] Further, the carbohydrate, as shown, is devoid of stereochemistry, and therefore is not ribose. If it is not ribose, then it cannot be an RNA nucleotide as written. Moreover, the nucleotide as drawn is dehydrated, and the "cyanide derivatives" as shown in the figure are unrecognizable as cyanide derivatives.

In an act of grace, let us attribute these chemical structural errors to the faulty renderings of a staff artist. However, far more importantly, there is no way that heat and light can directly make a nucleotide, even if there were simple sugars and cyanide derivatives. The primary literature upon which this scheme is based shows the process as involving ten to twelve chemical steps. Many of those steps form vast and unusable mixtures of products. As has been mentioned previously, researchers do not then use the desired compounds formed in those various mixtures; instead they just identify the compounds' presence, and then buy pure versions of them from a chemical vendor or else make them using purely modern synthetic chemical methods.

Granted, it is difficult to explain origin-of-life chemistry to the layperson, but that is part of the problem. Its portrayal to those outside the field has been so oversimplified as to mislead even the academic community. Professors themselves are confused regarding the state of origin-of-life research.

Chasing Fool's Gold?

When origin-of-life researchers are confronted by skeptics regarding the weakness of the data on the fundamental questions of life's origin, they will sometimes quote the famous late origin-of-life researcher, Leslie Orgel: "Anybody who thinks they know the solution to this problem [of the origin of life] is deluded. But anybody who thinks this is an insoluble problem is also deluded."[40] The remark is a strawman—the skeptics would merely enjoy seeing some new results that move the field toward an explanation of life's origin. The direction of origin-of-life research is suspect and the petty dismissal of questioning is unhelpful to the field.

So is the current fixation on extraneous experimental results. Consider an analogy from history: Alchemists tried to convert inexpensive metals into gold. They discovered that metals could be treated with sulfur to make yellow solids, sometimes even with lustrous facets, like pyrite, "fool's gold." While it was clear to the alchemists that they had not formed gold, would not the alchemist community have viewed sulfur additives as "a step in the right direction"?[41] These are the dangers of building a field of study around minute experimental results that do not even attempt to tackle the fundamental questions; one might be chasing fool's gold.

One such fundamental question that must be addressed is the origin of the chemical code; this is likely the single-most significant hurdle in any approach to understanding life's origin. The information or coding within the DNA or RNA that corresponds to the sequence of the nucleotides is essential to the entire discussion of life's origin. Some would rightly argue that the information is even more fundamental than the matter (molecules) upon which it is encoded. Present origin-of-life research does not address this foundational issue, but rather merely demonstrates that the requisite molecules are unlikely to have occurred in the states and quantities needed, and any assembly into an organism is even more unlikely.

This is grossly insufficient. The sequence of the nucleotides is the blueprint upon which life is founded. It is that code that will be translated to the enzymes that build the organism. The code defines the operating system for cellular function. The code vs. the molecules is analogous to the difference between the Library of Congress and a box of alphabetic letters—the library (DNA or RNA) has a huge amount of embedded information while the random box of letters (molecules) has little. We know from computer science that one needs complex non-regular patterns for complex computation and processing. Accordingly, complex patterns constitute the molecular assemblies seen in all living systems, even in the simplest bacterium. The simple regular pattern of thermodynamically driven crystallization or self-assembly is actually antithetical to what is needed for organism function, even when considering a cellular lipid bilayer.

To demonstrate how far humankind is from generating life, if origin-of-life researchers were given all the molecules and their polymeric forms that they desperately seek, and all in 100% homochirality, and their advanced laboratories, and all the chemical literature, and the DNA and RNA in any sequence (code) that they wish, could they assemble even a simple cell? The answer is a resounding *No!* Moreover, there is not an origin-of-life researcher on earth that would claim differently. As with perpetual motion machines, the pieces just do not come together as advertised.

When all else fails for explanations, some call upon Father Time, suggesting that hundreds of millions of years solve their mysteries. No other field of chemistry would accept such a proposition. In chemical synthesis, as we have seen, time is often the enemy, especially when making kinetic products that constitute the requisite organic chemicals of life.

Interestingly, Edward Steele and his thirty-two co-authors, spread over eleven countries, in 2018 in *Progress in Biophysics and Molecular Biology* conceded the following:

> The transformation of an ensemble of appropriately chosen biological monomers (e.g., amino acids, nucleotides) into a primitive living cell capable of further evolution appears to require overcoming an information hurdle of superastronomical proportions, an event that could not have happened within the time frame of the Earth except, we believe, as a miracle. All laboratory experiments attempting to simulate such an event have so far led to dismal failure.[42]

Further, they add, "At this stage of our scientific understanding we need to *place on hold the issue of life's actual biochemical origins*—where, when and how may be too difficult to solve on the current evidence." [Italics added]

However, Steele and his co-workers then merely push back the problem by fancifully increasing the reaction space: "It would thus seem reasonable to go to the biggest available 'venue' in relation to space and time. A cosmological origin of life thus appears plausible and overwhelmingly likely to us…." They write: "It is many orders of magnitude more likely that it emerged in one of the trillions of comet-like incubators or water-bearing planets (cosmic-wide versions of Darwin's 'warm little ponds') at a very early time in the growth of this Universe, perhaps 12 billion years ago which then went on to infect via knock-on effects other life-favourable sites (planets, moons, comets) throughout that Galaxy and then in an interconnected and interactive way throughout the Cosmos as the Universe expanded."[43]

In other words, while conceding that origin-of-life research has been a "dismal failure" and the community should "place a hold" on it, Steele and his colleagues reveal their own cluelessness regarding any of the details in life generation by hoping for a gigantic reaction space to overcome the vanishingly small probabilities of life originating from anything observable through "current evidence."

This too would require its own miracle.

In Praise of Humility

I have had cordial discussions with biologist proponents of origin-of-life research on these issues, and I am amazed that they fail to appreciate the magnitude of the problem in building molecules. These biologists see little difficulty in accepting a chemical synthesis where a desired product is mixed with a large array of closely related yet undesired compounds—mixtures from which separations would be enormously complex, and subsequent reactions unavailing.

But chemists see the inherent problems, even in their own research. John Sutherland of the University of Cambridge, one of origin-of-life's giants and the most skilled synthetic chemist to engage in origin-of-life research, has recently proposed that "chemical determinism can no longer be relied on as a source of innovation, and further improvements have to be chanced upon instead."[44]

"Chanced upon"? Why? Could it be due to chemistry's indifference to life and the cluelessness of the researchers?

It appears that Sutherland is grappling with the perplexity of the origin-of-life problem. The befuddlement is greatest for the synthetic chemist because he appreciates what molecules will and will not do, whereas to the biologist, all seems possible because he is used to using biology's constructs, while glossing over the requirements of the chemistry.

Another example: In 2017, Ramanarayanan Krishnamurthy of the Scripps Research Institute and his team cleverly showed that diamidophosphate can phosphorylate nucleosides, nucleotides, and stereo-scrambled lipid precursors. These can further result in the formation of random oligonucleotides and oligopeptides. The fundamental challenges noted above for the synthesis and assembly experiments remain unaddressed, so Krishnamurthy was rightly measured in the claims within his publication, writing that "any comparison must be viewed with caution given the pitfalls of extrapolating extant biochemical pathways backwards all the way to prebiotic chemistry and vice versa."[45] More of these realistic conclusions are needed from the origin-of-life community.

Further refreshing comments are making their way into the primary literature. In a 2018 article in *Nature Communications*, Clement Richert describes prebiotic chemistry versus human intervention. He explains that "the ideal experiment does not involve any human intervention."[46] Further, he even reflects upon the pure chemicals used by the researchers as being unrealistically available but prebiotically necessary for the syntheses to have ensued.

Thus, there is a glimmer of hope. The origin-of-life community is taking heed of their own unrealistic protocols that have supposedly been simulating prebiotic conditions.

And none too soon. Claims that mislead the all-too-patient taxpayer are not only dishonest, but unhelpful; the public will eventually realize that they have been taken for fools, and their ensuing distrust of scientific claims will carry over into other fields of scientific endeavor. Uncorrected or unfounded assertions jeopardize science beyond a singular field, especially since there is mounting distrust of higher education in general.[47]

Going Forward

Bearing all this in mind, should origin-of-life research continue in the same vein as it has been practiced for the past two-thirds of a century? Does not the field's stagnation suggest that a dramatic change should be instituted?

The Defense Advanced Research Projects Agency (DARPA) presents challenges to shake the research and engineering community out of their stagnancy on topics related to technology, putting before them contests that demand proposals that are wholly unlike the status quo. DARPA mandates new fundamental ways to address problems, often embracing young nonconformist researchers who would not normally be funded by the seasoned research community of peers.

Origin-of-life research needs some such shake-up to do something beyond the making of yet another small chemical intermediate, *ad nauseam,* or forming suspensions of lipid bilayers, protocells as they call them, which have little resemblance to true cellular bylayer vesicles. Researchers must be challenged to address hurdles such as the origin of life's code, the complex assembly and interactomes that are essential to cellular functioning, and the mass-throughput in synthesis to provide the requisite quantities of molecules in their homochiral form. Alternatively, researchers must offer some conjectures, underpinned by experiments, to show that perhaps these features, such as the code or the interactomes, are irrelevant to life's origin from prebiotic chemicals.

Any moratorium needs to be initiated by the funding agencies and directed by the program managers. This starts with a thoughtful evaluation that compares origin-of-life progress to the progress in other fields of research over the past sixty-seven years. Are these current origin-of-life experiments taking us closer, or do the newer findings on cellular complexity drive the target further out of reach with each passing year?

Formulation of new programmatic goals should ensue, with those outside the mainstream origin-of-life community being encouraged to offer divergent thoughts. A moratorium is something that the scientific community might be obliged to request, because origin-of-life research uses taxpayer dollars, and its overexpressed assertions jeopardize trust in scientific claims in general.

As in any field, it is important to maintain engagement with the press so that the scientific message reaches the masses. The press has an essential role in the ecosystem of technical dissemination, and most science reporters will heed advice from the scientists whom they interview. We cannot continue to let them run unchecked. Their over-the-top claims jeopardize scientific credibility.

There also needs to be a cessation of the gross extrapolations and hyperbole within scientific publications themselves that give the impression that scientists are near to creating life. The field has migrated outside of the bounds of scientific credibility. Thus, journal editors should be held accountable to restrict grossly exaggerated claims and even terminology that is misleading. For example, when simply referring to a lipid bilayer vesicle, cavalier use of the term "protocell" should be discouraged; "lipid bilayer vesicle" or "liposome" is sufficient.

Therefore, I appeal to the research community and funding agencies to consider whether a moratorium on origin-of-life research is warranted.

This starts with a redefinition of targets that will address the fundamental questions: mass transfer of starting materials to the requisite four compound classes in high chemical and stereochemical purity, the origin of life's code, the massive combinatorial complexities present in any living system, and the precise non-regular assembly of required cellular components.

Without deliberate and widespread changes, origin-of-life progress will likely remain retarded.

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Endnotes

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14. THERMODYNAMIC CHALLENGES TO THE ORIGIN OF LIFE

Brian Miller

The thermodynamic barriers to the origin of life have become decidedly more well defined since this book's first publication. The initial challenges described in the original edition still stand. Namely, spontaneous natural processes always tend toward states of greater entropy, lower energy, or both. The change of entropy and energy are often combined into the change of free energy, and all spontaneous processes move toward lower free energy. However, the generation of a minimally functional cell on the ancient Earth required a local system of molecules to transition into a state of both lower entropy and higher energy. Therefore, it must move toward dramatically higher free energy. The chance of a system accomplishing this feat in a system near equilibrium is astronomically small.[1]

Many origin-of-life researchers have responded to this challenge by arguing that a system driven far from equilibrium could self-organize into a functional cell through processes which are connected to such monikers as complex systems,[2] emergence,[3] synergetics,[4] or nonequilibrium dissipative systems.[5] The basic hope is that some new physical principles could overcome the barriers to life's origin mandated by classical thermodynamics. However, advances in nonequilibrium thermodynamics have proven that the odds of a system driven far from equilibrium generating an autonomous cell are no greater than the odds for one near equilibrium.

Others have proposed that "natural engines" on the early Earth converted one form of energy into another which could drive a local system to sufficiently high free energy.[6] These approaches have proven equally disappointing. The only plausible explanation for the origin of life is intelligent agency.

Fluctuation Theorems and the Origin of Life

One of the greatest challenges in systems driven far from equilibrium was describing them quantitatively. Then a breakthrough came in the 1990s with the advent of the fluctuation theorems. The first derived theorem was the Evans-Searles fluctuation theorem (ESFT).[7] It demonstrated in dissipative systems[8] that entropy can run in reverse. But probabilities drop exponentially with the magnitude of the entropy decrease[9] (note that the entropy, S, is presented in the units of nats, so its value is dimensionless):

$$\frac{p\left(\mathrm{S} = \mathrm{A}\right)}{p\left(\mathrm{S} = -\mathrm{A}\right)} = e^{\mathrm{A}}$$

This theorem was used to solve the apparent contradiction of macroscopic processes progressing irreversibly toward greater entropy while the underlying physical dynamics are time-reversible. The ESFT demonstrated that the dynamics of individual particles in a given microstate (specific configuration of molecules) might be time-reversible, but the statistical tendency is for microstates to move in a direction which corresponds to an increase in entropy. Therefore, the average entropy production moving forward in time is always positive.[10]

In the context of the origin of life, the theorem demonstrates the implausibility of any realistic energy source, such as sunlight or heat from a thermal vent, driving a local system toward dramatically lower entropy.

As mentioned in Chapter 8 above, Harold Morowitz performed a crude estimate for the reduction of entropy in the formation of a cell associated with the generation of macromolecules (e.g. RNA, DNA, proteins). His approximation for the entropy reduction was on the order of .1 cal/deg-gm.[11] This quantity corresponds in a bacterium[12] to a reduction of greater than 10^{10} nats, which yields a probability from the ESFT for a bacterial cell spontaneously forming of less than 1 in 10^{10^9}, a clear impossibility even if the first cell were orders of magnitude smaller.

A second theorem, known as the Crooks Fluctuation Theorem, was derived to study systems acted upon by nondissipative fields or forces which transition a system from an initial state to a final state with a different equilibrium free energy. In classical thermodynamics the transition can often be assumed to proceed slowly enough for the process to remain close to equilibrium. The work, W, performed could then equal the change in free energy, ΔF.[13] However, if the transition occurs away from equilibrium, some of the applied work will typically be lost as heat.

Now let A and –A designate work performed in forward and time-reversed transitions. Crooks's theorem establishes that the ratio of probabilities over A and –A is

$$\frac{p_f\left(W = A\right)}{p_r\left(W = -A\right)} = e^{\beta(A-\Delta F)}$$

where β is the inverse of the initial temperature of the system and the thermal bath surrounding it times the Boltzmann constant, and $A - \Delta F$ is the heat released during the transition into the thermal bath.

Similar to the ESFT, the Crooks theorem shows that there is a finite probability that, while work is performed on the system, the increase in free energy can exceed the amount of applied work: A – ΔF is negative. As a result, heat will be *absorbed* from the bath and converted to free energy, thus gaining energy for free. However, the probability drops exponentially with the magnitude of the heat absorbed.[14]

The Crooks theorem can be used to calculate the probability for a driven system absorbing sufficient heat from the environment to provide the needed increase in free energy for the origin of life. As mentioned in Chapter 7, Morowitz estimated that the formation of a cell would require a collection of prebiotic molecules absorbing roughly 10^{-9} joules (10^{10} eV) of heat.[15] This value corresponds in the Crooks equation to a probability of occurring on the order of 1 in $10^{10^{11}}$ which is the same as in a system near equilibrium.

The odds do not improve if the process takes place in multiple steps separated by extended periods of time.[16] In fact, the challenges actually increase if each step towards life does not proceed immediately after the previous one, for the chances of the system moving toward higher entropy (or lower free energy) are far greater than moving in a life-friendly direction. Any progress could be completely squandered by a few deleterious thermal fluctuations or chemical interactions. Therefore, all origin-of-life scenarios appear thermodynamically implausible.

The Inadequacy of "Natural Engines"

The only way to overcome the free energy challenge is for some mechanism to apply work in such a manner as to raise a system's free energy. Modern cells accomplish this goal by employing complex molecular machinery and finely-tuned chemical networks to convert one form of energy from the environment into high-energy molecules. The energy from the breakdown of these energy-currency molecules is directed toward powering targeted chemical reactions and other processes.[17] However, no such machinery could be synthesized until after life originated.

Many proposals have been offered for how various natural mechanisms could impart the needed work. Examples include meteorite crashes,[18] moving mica sheets,[19] shock waves,[20] volcanic hot springs,[21] and proton gradients.[22] However, none of these sources could have generated more than a tiny fraction of the required free energy. They primarily produce energy in the form of heat or light, but such raw energy bursts increase the entropy of a system,[23] causing it to move in a direction opposite to that of life. Life requires a mechanism which can increase the free energy to allow for the energy of the system to increase while also decreasing the entropy.

To illustrate the challenge, the power production density (free energy increase per time per mass) of the simplest known cell for only maintenance[24] is on the order of 1 watt per gram (W/g), which is comparable to that of a high-performance sports car. A protocell would have to generate this amount in the latter stages[25] leading toward an autonomous cell just to overcome the thermodynamic drive back toward equilibrium, and even greater amounts would be required for replication.[26] For comparison, a leading proposal for energy production involves proton gradients in small crevices in hydrothermal vents powering life-friendly chemical reactions. However, experimental simulations of vents under ideal conditions only generate small quantities of formaldehyde,[27] which is believed to be a precursor to some of life's building blocks. The corresponding power production density is on the order of 1 nanowatt per gram (nW/g),[28] a billionth of what is needed. Moreover, the concentration of yielded formaldehyde is about a millionth of what would be required to drive any life-friendly reaction. As a result, alkaline vents could never supply even the smallest fraction of the power needed, and only minuscule amounts of the generated chemical energy[29] could be directed toward forming the first cell. Other scenarios perform no better.

Such an enormous disparity between the required and available energy production demonstrates the implausibility for a "natural engine" forming on the early Earth with sufficient capacity to support any origin-of-life scenario. Consequently, highly efficient molecular engines comparable to those in modern cells are needed from the very beginning to provide a continuous supply of energy-currency molecules capable of driving nonspontaneous cellular processes.

The Necessity of Proteins

An additional challenge is that a minimally functional metabolism requires directing a highly specific set of chemical reactions and preventing interfering cross-reactions. The chance of a randomly selected set of reactions meeting such exacting criteria is infinitesimally small.[30]

Compounding the difficulty, individual reactions in the chemical pathways to synthesize life's building blocks and other metabolic reactions require multiple, mutually exclusive reaction conditions,[31] so no environment could support more than a few of them. In addition, many of the reactions are energetically unfavorable, so energy from the breakdown of the energy-currency molecules must be directed toward enabling them to move in the required direction. And even energetically favorable reactions are typically too slow to drive cellular operations. As a consequence, special protein molecules known as enzymes, or their equivalent, are essential to support cellular life since only they could sufficiently accelerate a highly specific set of reactions.[32]

Enzymes are long chains of amino acids which fold into specific three-dimensional structures with crevices known as active sites. These sites accelerate specific reactions' turnover rates by factors typically between 10^8 and 10^{10}, and the increase in many cases could be significantly higher.[33] Without their presence, the concentration of a reactant would typically need to be at least millions of times greater to maintain a comparable reaction rate. Achieving such high concentrations for nearly every cellular metabolite[34] would be highly implausible. The active sites also create the necessary physical and chemical conditions to support their target reactions, so a multitude of diverse reactions can be maintained in the same cellular environment simultaneously. In addition, the enzymes couple the breakdown of the energy-currency molecules to energetically unfavorable chemical reactions and other processes, so the energy from the former can power the latter. As a consequence, a complete suite of enzymes must have existed at the very earliest stages of life's origin.

Yet the challenges faced in any origin-of-life scenario related to the formation of enzymes and other proteins are immense. First, any natural process which yielded amino acids would also have produced a myriad of other molecules which would have blocked the formation of long functional chains.[35] Second, the probability of amino acids forming a chain in even the most ideal conditions drops exponentially with its length, so none would likely have formed on the early Earth sufficiently long to correspond to nearly any of the essential proteins in a minimally functional cell.[36] Third, even if the probability for long-chain formation were significantly higher, all realistic processes on the early Earth would have yielded both left-handed and right-handed amino acids. However, functional proteins require amino acids of only one chirality. Even if some process could generate a solution of homochiral amino acids, it would spontaneously racemize (move toward equal quantities of both versions).[37] Every one of these hurdles appears insurmountable.

An additional challenge, which is rarely acknowledged, is the excessive time requirement for a protein and a cell membrane located in the same small pool of water to make contact through the random motion of diffusion. The main search mechanism would have to be diffusion, since water sufficiently agitated to mix molecules at microscales would likely eviscerate any cell membrane.[38] An estimate for the timescale begins by calculating the time required for an enzyme to traverse the diameter of a cell using the protein's diffusion coefficient (100 $\mu m^2/s$)[39] and the width of a bacterium (1 μm^3). The average time approximates to one millisecond. Therefore, an enzyme could only sample a volume of 1 μm^3 every millisecond, even ignoring the fact that diffusion would cause resampling of the same micro-volumes repeatedly. A lower estimate for enzyme-membrane contact would then be on the order of tens of millions of years.

Yet a protein's lifespan is on the order of weeks to years, based on the half-life of peptide bonds in water,[40] and the actual breakdown time measured in bacteria is typically considerably less, only on the order of hours.[41] Therefore, any protein formed on the early Earth would denature long before finding its way into a protocell. The problem for RNA is even greater since it is considerably less stable.[42]

The Information Challenge

An even greater challenge is that the protein molecules which compose the molecular engines and the enzymes consist of chains of amino acids in precise sequences, so a prerequisite for life is large quantities of functional information.[43] Specifically, the amino acids have to be arranged in the right order in the same way the letters in a sentence must be arranged properly to convey the intended meaning.[44] The sequential order is crucial for the chains to fold into the correct three-dimensional structures to properly perform their intended functions.

The centrality of information is becoming increasingly apparent with theoretical analyses on its role in enacting causal control over outcomes, such as a metabolic pathway synthesizing a specific amino acid at the correct time in the needed quantities.[45] The term "control information" has even been designated to those entities within cells (e.g. nucleotide sequences in DNA) which direct the acquisition and use of matter, energy, and information to enable biological functions. And the implementation of this information has been recognized as essential for maintaining a cell's highly specified low-entropy state.[46]

An extreme lower bound for the prerequisite information required for the origin of life can be calculated from the needed enzymes' *algorithmic specified complexity* (ASC). The ASC measure was developed to quantify the functional, semantic, or meaningful information in a pattern,[47] and it provides an upper limit on the probability for a pattern with a given ASC measure to occur by any undirected process: $P\ [ASC\ (X,C,P) \geq \alpha] \leq 2^{-\alpha}$.[48] The minimal information calculation proceeds by first estimating the minimal number of required enzymes in an autonomous cell and then estimating the ASC for a single enzyme. The product of these two numbers is the lower bound for the first cell.

Several research groups have attempted to identify for the simplest viable cell the minimal set of proteins. Removing just one of these essential proteins would result in the metabolism ceasing to function, and the cell would degrade irreversibly into simple chemicals. Similarly, systems engineers, such as those at NASA, have analyzed the minimal functional requirements for a self-replicating machine.[49] The results from both classes of studies converge on several essential functional components:

- Large repositories of information and information processing.
- Manufacturing centers that construct all of the essential pieces.
- Assembly and installation processes.
- Energy production and distribution machinery.
- Automated repair and replacement of parts.
- Global communication and coordination with feedback control systems.
- Sensing of environment and calculation of needed responses.
- Self-replication, which draws upon nearly all other essential functions.

In the context of a minimal cell, these requirements correspond to over 300 protein-coding genes in a parasite[50] and probably double that amount in a free-living prokaryote.[51]

The ASC associated with a single protein can be estimated from the probability for a random sequence of amino acids to properly fold into a structure which performs a specific cellular function. That value for only one portion of a relatively small protein was calculated to be on the order of 1 in 10^{77}.[52] This estimate equates to an ASC value of over 250 bits,[53] so the minimal ASC for one copy of the over 300 required proteins is over 75,000 bits. This value can be compared with the maximum ASC value that could have been generated from the total number of protein sequences which could have occurred in the entire history of the Earth. The most wildly optimistic estimates have assumed that all of the available atoms of nitrogen, carbon, and oxygen on the planet contributed to amino acid sequences of at least modest length.[54] The upper estimates are less than 10^{60}, which corresponds to a maximum ASC value of roughly 200 bits.[55]

Clearly, the required prerequisite information vastly exceeds what could have been generated by any undirected process. In fact, even if 1 in 10 amino acid sequences corresponded to a functional protein, the cumulative ASC value would still exceed the maximum limit.

In reality, the required information is significantly greater than the previous analysis suggests, for it does not include several other constraints and requirements.[56] For instance, the metabolism must start with sufficient numbers of enzymes, energy-currency molecules, and intermediate metabolites.[57] In addition, multiple copies of most proteins are needed,[58] such as those which are assembled into multiprotein complexes.[59]

Compounding the problem, proteins have a limited lifespan, so they must constantly be replaced. Proteins do not self-replicate, and RNAs are too unstable for long-term information storage.[60] Therefore, the minimal requirements for a cell must include the protein sequences being encoded into DNA, and the cell must possess the DNA-protein translational machinery to access the encoded information and implement it in the manufacture of new proteins. In addition, a functional metabolism requires the cell to tightly control each reaction using feedback loops, and this meticulous coordination is to a large extent accomplished through the regulation of the genes through gene-specific promoter, operator, and enhancer regions.[61] They direct the timing and quantities of proteins manufactured.

Studies on metabolic networks[62] have demonstrated that a functional metabolism requires an "intricate network of mutual interactions" which "depends crucially on the numerical values of kinetic parameters and regulatory interactions," so the additional information associated with these regulatory regions in DNA must be significant. Future studies will undoubtedly only increase the chasm between the information which could be produced by any natural process and that required in a minimally functional cell at its instantiation.

In summary, the formation of the original cell cannot plausibly be explained by any undirected process. In addition, its minimal requirements demonstrate unmistakable signs of intelligence. In any other context, the identification of a nanotechnology vessel capable of energy production, information processing, and the other identified requirements would immediately be recognized as a product of design by any reasonable criteria. In particular, cellular structures and operations demonstrate unmistakable evidence of foresight, coordination, and goal-directedness which are telltale signs of intelligent agency.

Endnotes

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8. Dissipative systems are driven by dissipative fields which do not change the ground state energy of the system. Instead, the energy which enters the system due to these fields can completely turn into heat and diffuse out into the surrounding environment. Examples include the application of an electric field to a resistor or of light to a solution of interacting chemicals. In contrast, the energy imparted due to the application of a nondissipative or elastic field can be stored in the system as potential energy. For instance, the application of an electric field to solid sodium chloride increases the potential energy corresponding to intermolecular forces between the constituent molecules. See Denis J. Evans, Debra J.

Searles, and Stephen R. Williams, *Fundamentals of Classical Statistical Thermodynamics: Dissipation, Relaxation, and Fluctuation Theorems* (Weinheim, Germany: Wiley-VCH, 2016), 23.

9. The probability density ratio for $p(S)/p(-S)$ can be converted to an upper bound for the probability of entropy, S, taking on the negative value of –A or less by recognizing that $p(S) < p(-S)e^{-A}$ for values of S less than –A. Therefore, $P(S < -A) < P(S > A)e^{-A} < e^{-A}$.

10. Some physicists have argued that the proposed solution is incomplete and must be combined with the fact that our universe started in a low entropy state. See P. C. W. Davies, "The Arrow of Time," *Astronomy and Geophysics* 46, no. 1 (February 1, 2005): 1.26–1.29, https://doi.org/10.1046/j.1468-4004.2003.46126.x.

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13. The change in the Helmholtz free energy (F) equals the change in the internal energy of a system (U) minus the temperature times the change in entropy (S): $\Delta F = \Delta U - T\Delta S$. In a system where the volume is held constant, ΔF for spontaneous processes is always negative. If the pressure is held constant, then spontaneous processes correspond to a negative change in the Gibbs free energy (G) which is equal to the change in enthalpy (H) minus the temperature times the change in entropy: $\Delta G = \Delta H - T\Delta S$. The change in enthalpy represents the change in energy of a transition adjusted for the work performed on the environment due to a change in volume: $\Delta H = \Delta U + P\Delta V$. Positive changes in enthalpy represent heat being absorbed from the environment and negative changes represent heat being released. Physicists and chemical engineers typically work with the Helmholtz free energy while chemists typically work with the Gibbs free energy.

14. The same general approach can be applied to the Crooks FT as was applied to the Evans-Searles FT to demonstrate that the probability for the heat being absorbed with a value of Q or greater drops exponentially with Q.

15. Morowitz, *Energy Flow in Biology*, 65. The estimate was performed by calculating the difference between the average bond energies in a bacterium and those in the molecules in the environment of the ancient Earth.

16. The entropy and the free energy are state functions, so they are path-independent. The probabilities are exponentials of those functions. To appreciate the significance, imagine breaking the path from nonlife to life into three steps which constantly move toward lower entropy (or higher free energy). Then, $-\Delta S = -\Delta S1 - \Delta S2 - \Delta S3$, and the probabilities associated with random fluctuations driving each step would be $e^{-\Delta S_1}$, $e^{-\Delta S_2}$, and $e^{-\Delta S_3}$. The chance for all three fluctuations taking place consecutively is then $e^{-\Delta S_1} \cdot e^{-\Delta S_2} \cdot e^{-\Delta S_3} = e^{-\Delta S_1-\Delta S_2-\Delta S_3} = e^{-\Delta S}$. The probability for the three steps is the same as for one combined step.

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Electrochemistry (Weinheim, Germany: Wiley-VCH, 2007), 78. The corresponding power generation density is on the order of 1 nW/g.

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15. What Astrobiology Teaches about the Origin of Life

Guillermo Gonzalez

The modern era of astrobiology research began in 1995–96 with two momentous events: the discovery of the first planet around another Sun-like star (October 1995) and the announcement of evidence of ancient Martian life in the meteorite ALH84001 (July 1996). To be sure, there were astrobiologists before astrobiology became a "thing." For example, as Jonathan Wells helpfully reviews in his chapter on the 1953 Miller-Urey experiment, geophysicists and geochemists chimed in on the composition of the early Earth's atmosphere to evaluate the plausibility of the experiment. But the field of astrobiology leapt into prominence after the discoveries of 1995–1996, as the exciting prospect of being able to address the topic of life in the universe scientifically caused many scientists—myself included—to bring their specialties to bear on this new field.[1]

One of the main areas of research within astrobiology is the problem of the origin of life. It attracts scientists with backgrounds in astronomy, biochemistry, chemistry, geology, and atmospheric physics. Most astrobiologists working in this area are focused on the more narrow question of the origin of life on Earth.

In the following I will explore the current state of origin-of-life research from the perspective of astrobiology. I will review recent literature on the time window available for the origin of life on Earth, examine proposed scenarios, discuss the origin of life on other worlds in the solar system, and then end with a discussion of panspermia.

Time Window for the Origin of Life on Earth

In 1953 Harold Urey and Stanley Miller sought to create some of the simplest building blocks of life from a mix of gases they believed to have dominated in the early Earth's atmosphere. The assumed setting was a "warm little pond" at some indeterminate time soon after Earth's formation. Geological dates were not well known at the time of the Miller-Urey experiment, but this situation has much improved in the intervening years.

The Age of the Solar System

The age of the solar system is well dated at 4.5682 +/- 0.0003 billion years from radiometric analyses of primitive meteorites.[2] Theoretical stellar evolutionary models of the Sun applied to its present observed properties yields an age of 4.569 to 4.587 billion years, depending on the model used.[3] These estimates set a hard limit on the earliest date for the origin of life in the solar system.

Evidence from Rocks on Earth

The oldest dated rocks on Earth are 4.03 billion years old.[4] Earth's active geological and hydrological cycles have severely altered rocks from the Hadean (the period prior to ~4 billion years ago). However, tiny but tough zircon crystals can survive the violent geologic upheavals that destroy other rocks and crystals. What's more, individual major geological events can cause zircons to grow rings, like a tree. Zircons have been described as "time capsules," preserving in a datable time-ordered manner some of the earliest geologic events in Earth's history. The oldest well-dated zircon crystal (from Western Australia) has an age of 4.374 +/- 0.006 billion years.[5]

The evidence from zircons has pushed back the period in the Hadean when Earth's surface was a hot molten magma sea to before ~4.4 billion years ago. Given this, the "cool early Earth" theory has displaced the earlier view that Earth could not have been habitable prior to about 3.8 billion years ago, after which the bombardment from asteroids and comets declined from its prior high rate.[6] The evidence from the zircons also implies the presence of continents and oceans as early as ~4.4 billion years ago.

The oldest undisputed fossil evidence for life dates to 3.47 billion years ago.[7] Less convincing fossil and isotopic evidence dates back to 3.7 billion years ago.[8] Given the extreme rarity and alteration of rocks from this period, it is difficult to place a firm date on the first life on Earth. It is possible that there is no surviving evidence anywhere on Earth of our planet's first life.

But there may be evidence on the Moon.

Evidence from the Moon

When you look up at the Moon you are looking at an ancient body. If you traveled in a time machine to visit Earth three billion years ago, the Moon would look very similar, except that it would appear larger in the sky. Since its formation, probably from a giant impact,[9] it has been slowly receding from Earth (presently at 3.82 cm/yr).[10]

Originally, planetary scientists studying the lunar cratering record and the returned Apollo lunar samples proposed the so-called *late heavy bombardment* to explain what appeared to be a late spike in lunar impactors, which peaked about 4.0 billion years ago.[11] Recently, new analyses of the Apollo rock samples and lunar meteorites have, instead, supported a monotonic decline in bombardment from 4 to 3 billion years ago, as remnants from the initial stages of planet formation were swept up.[12]

During the critical period for the origin of life from 4.4 to 3.5 billion years ago, the high bombardment rate on Earth and the close proximity of the Moon would have meant that large amounts of Terran impact ejecta would have landed on the Moon. Once arriving on "Earth's attic," Terran meteorites would have been buried with ejecta from subsequent lunar impacts and lava flows. The concentration of early terrestrial meteorites in the lunar regolith potentially containing preserved biological materials is high enough to warrant searches for it.[13] Searching for terrestrial meteorites on the Moon is now cited as one of the reasons for a return there.[14] In fact, about three grams of Terran material has already been found in the Apollo lunar samples.[15] Our closest celestial neighbor turns out to be the ideal storehouse for early life samples from Earth.[16]

The formation of the Moon is another useful time marker that can set the upper limit on the origin of life. The leading theory for the formation of the Moon is called the *giant-impact hypothesis,* which posits that a roughly Mars-size planetesimal impacted upon the still-forming Earth. The debris thrown off by the impact coalesced to form the Moon. The event has been dated a couple of ways, giving a consistent value of 4.47 billion years ago.[17]

Although there were likely oceans during a large portion of the Hadean, large and small impactors on the Earth would have been frequent during this period. The oceans would have been boiled away into a steam atmosphere multiple times.[18] At first these would seem to be effective sterilizing events, which would mean either that life began after the last large impactor, or that it restarted multiple times. The second option implies the origin of life is easy. However, there is good reason to doubt that these would be sterilizing events. It is possible for Earth to be reseeded by its own returning ejecta fragments after it cools down from a large impact.[19]

Previously, the consensus among origin-of-life researchers had been that life began almost immediately after the end of the late heavy bombardment 3.8 billion years ago. This conclusion was based on the now largely discarded theory of the late heavy bombardment and discredited evidence for fossils near 3.8 billion years ago. Given what we now know, the best current evidence and modeling indicates a single origin of life sometime between ~4.4 and ~3.7 billion years ago.

Proposed Origin-of-Life Scenarios on Earth

Many diverse scenarios have been proposed for the origin of life on Earth. They vary in their environmental settings, assumptions about pre-biotic chemistry, and the origin of the raw building materials (amino acids, nucleotides, lipids, and sugars) from basic feedstocks (carbon dioxide, water, nitrogen, methane, and possibly ammonia). But all scenarios must take into account that the early (Hadean) Earth was different in multiple important ways from the present Earth.

The sun was dimmer, though more active, producing frequent bursts of ionizing radiation. Ultraviolet radiation down to 200 nm would have reached the surface. While there were temporary hot spots from volcanism and impacts, cold conditions may have prevailed. The atmosphere lacked oxygen and was probably dominated by carbon dioxide. The ocean tides would have been larger due to the Moon's smaller distance from Earth. In addition, the days were shorter. Tides would have swept ocean water farther inland than they do today. Energetic impacts from asteroids and comets were orders of magnitude more frequent, and the bigger ones would have cracked the crust. The impacts into the oceans would also have created large tidal waves. The difference between these two types of flooding would have been one of regularity. The lunar high tides would have been periodic, occurring every half rotation.

Tidal Chain Reaction

In 2004 Richard Lathe of the University of Edinburgh proposed that these stronger tidal cycles were key to the origin of life.[20] Lathe argued that the repeated cycles of wetting (dilution and cooling) and drying (concentration and warming) with salty water from the oceans were analogous to the chemical reactions in the polymerase chain reaction (PCR). The PCR process is used in biomedical laboratories to greatly amplify the number of DNA molecules, starting even from a single molecule. The following year Lathe elaborated his model, calling it a "tidal chain reaction" (TCR).[21] In the TCR process polymerization would occur during the drying phase and dissociation during the wetting phase, together producing the amplification.

In 2006 Lathe was criticized for his assumptions about the lunar distance and length of the day at the time of the origin of life (then presumed to be 3.9 billion years ago). Instead of the day length being a few hours, as Lathe had assumed, it was more likely 15 to 17 hours, and the Moon was only about 20% closer.[22] In response, Lathe acknowledged his mistaken assumptions, but noted that regardless of the precise values of the lunar and terrestrial parameters at the origin of life, the length of day and the Moon's distance were both significantly smaller.[23] I would have to agree with Lathe; these criticisms were relatively minor, not affecting the overall plausibility of his model.

Even better for Lathe, recent thinking on the early Earth works in his favor. As I noted above, researchers no longer limit the origin of life to the period near 3.9 billion years ago. It could have occurred as early as ~4.4 billion years ago. This is within 100 million years of the formation of the Moon. Still, even during this brief interval, the Moon would have receded very quickly from its place of formation near the Earth, and the Earth's rotation would have slowed down quickly. So, maybe the Moon was about 50% closer and the length of the day about half its present value at the origin of life.[24] One possible problem is the paucity of dry land during the Hadean. While the evidence from the earliest zircons implies some continental crust was present then, it would have been much less than today, even including volcanic islands and impact crater rims.[25]

More serious criticisms of Lathe's TCR model were published in a 2007 study, which showed that the TCR process was unlikely to function because of a process the authors label the "elongation catastrophe."[26] The authors offer a possible way out of this conundrum in the last sentence of their paper, writing, "One proposed solution to the elongation problem is the early evolution of a minimal replicase ribozyme with restriction activity."[27] But unfortunately for the TCR model, as Finn Werner and Dina Grohmann point out, "no naturally occurring ribozyme RNA polymerases have been discovered yet."[28]

The TCR model is a part of the broader RNA world hypothesis. Steven Benner of the Foundation for Applied Molecular Evolution and his collaborators write, "Current experiments suggest that RNA molecules that catalyze the degradation of RNA are more likely to emerge from a library of random RNA molecules than RNA molecules that catalyze the template-directed synthesis of RNA, especially given cofactors (e.g., Mg^{2+}). This could, of course, be a serious (and possibly fatal) flaw to the RNA-first hypothesis for bio-origins."[29] Harold Bernhardt of the University of Otago reviews additional problems for the RNA world hypothesis.[30]

Even if true, the TCR model doesn't account for the origin of the organic feedstock monomer molecules (and, now, the replicase ribozyme).

Hydrothermal Vents

Perhaps the great abundance of water during the Hadean favors the *hydrothermal vent* setting for the origin of life. It is this setting that Günter Wächtershäuser proposed in 1990 as the origin of the first autocatalytic chemical cycle operating on the surface of iron sulfide minerals.[31] Wächtershäuser proposed this scenario as starting with the ubiquitous citric acid cycle that generates energy in extant aerobic organisms. This "metabolism first" scenario posits that something like the citric acid cycle came first, and genetic-capable molecules somehow grafted onto the chemical network and eventually took over.

The hydrothermal vent settings do have the advantage in that they exist today and very likely existed in the Hadean. However, experiments simulating aspects of hydrothermal vent chemistry have had only limited success in producing biologically relevant organics. Michael Russell's research group at the Jet Propulsion Laboratory built an artificial hydrothermal vent reactor and managed to produce one of the simplest amino acids, alanine, as well as lactate.[32]

Leading origin-of-life synthetic chemist John Sutherland of the Medical Research Council Laboratory of Molecular Biology in Cambridge has strong words about the vent setting for the origin of life:

> A requirement for ultraviolet irradiation to generate hydrated electrons would rule out deep sea environments. This, along with strong bioenergetic and structural arguments, suggests that the idea that life originated at vents should, like the vents themselves, remain 'In the deep bosom of the ocean buried'. The chemistry places certain demands on the environment of the early Earth: for example, the high concentrations of certain species through evaporation of solutions.[33]

In summarizing the work of organic chemists, Long-Fei Wu and Sutherland note that "15 simple to moderately complex building compounds would have been necessary to progress biology towards translation."[34] However, they add, "It is not possible to make everything in 'one pot' by one sequence of conditions, some degree of separation of the branches of each reaction network is necessary."[35]

In other words, while some biological precursors might be made in hydrothermal vents and others might be made on the surface via concentration by evaporation or UV radiation, no single setting is compatible with all the required precursors. In addition, some of the reactions produce intermediates that interfere with the production of other precursors.

Hydrogen Cyanide Chemistry

Sutherland advocates, instead, hydrogen cyanide (HCN) chemistry as the single starting point for life: "Hydrogen cyanide is a perfect feedstock to produce the palette of products necessary for the emergence of translation. It is a source of carbon and nitrogen and is constitutionally implicated in the purines (adenine is a pentamer of HCN), the amino acids (through Strecker-type syntheses), sugars and glycerol (through reductive homologation)."[36]

Stuart Harrison and Nick Lane of the Centre for Life's Origin and Evolution at University College London criticize Sutherland's position. They write, "Perhaps the biggest problem is that the chemistry involved in these clever syntheses does not narrow the gap between prebiotic chemistry and biochemistry—it does not resemble extant biochemistry in terms of substrates, reaction pathways, catalysts or energy coupling.

Does that matter? Those with chemical acuity claim to see 'strategic similarities' to biochemistry, but biochemists are apt to disagree."[37]

Instead, Harrison and Lane favor the hydrothermal vent setting, writing, "Alkaline hydrothermal vents present tantalising parallels to cells."[38]

Late Veneer

Some origin-of-life researchers suggest that delivery of meteoritic material may have produced a more reducing atmosphere early on. A reducing atmosphere favors production of several prebiotics.

Evidence from zircons suggests that the Hadean mantle was oxidizing as far back as ~4.4 billion years ago. Dustin Trail and collaborators write:

> If our deductions regarding the oxidation state of Hadean magmas are correct, then the speciation of gases emanating from the Earth at this time would have been dominated by CO_2, SO_2, H_2O and N_2. An atmosphere of this composition is known to yield a lower abundance of sugars and especially amino acids and nucleotides. If a highly reduced atmosphere is required for the origin of life, then it may have occurred exceptionally early on our planet. However, pre-4,400-Myr outgassing of H_2 coupled with slow escape may have resulted in an atmosphere out of equilibrium with Earth's interior. Alternatively, a "late veneer" may have served as a source of pre-biotic molecules.[39]

The idea of the late veneer is that Earth received a large helping of meteoritic material, including iron and compatible metals (siderophiles), after its core formed. Core formation is important to the oxidative state of the atmosphere; iron in the mantle keeps it reduced and the volcanically produced gases are thus reduced as well. However, the mantle contains abundances of highly siderophile elements that are too elevated in abundance to be consistent with core formation. A solution to this riddle is the late veneer of specifically chondritic meteoritic material.[40]

However, the required meteoritic material would have to be about 1% of Earth's mass. If it was in the form of many small objects impacting

Earth over some period, then both the Moon and Earth should show similar siderophile elemental abundances, but they don't.

One proposed solution is a glancing impact on the Earth by a single differentiated Moon-size object during the early Hadean.[41] This would cause the iron core of the impactor to be disrupted into many small pieces and thus prevent the iron from sinking into the core, which would have happened if the impact had not been glancing. The iron would have reacted with the oceans to produce large amounts of H_2 in the atmosphere, which would have lasted 100 to 200 million years, depending on the mass of the oceans at the time.[42] The timescale for the loss of the H_2 is set by the level of the Sun's activity, which was very high at this early time.[43] This story is still very new, and it may yet change.

Our understanding of the timing and relative importance of the late veneer and even the timing of the Moon's formation and differentiation is still in flux. One recent study pushes the Moon's formation earlier than the age I quoted above and also diminishes the importance of the late veneer.[44] Even if a reduced atmosphere had not been produced from the iron core of a large impactor in the Hadean, other sources are possible. In particular, shocks produced on the Earth's surface from the many small to modest-size impactors would have induced substantial NH_3 production.[45] In addition, impact by icy bodies (comets) probably produced racemic mixtures of the amino acid alanine.[46] Another shock synthesis experiment produced amino acids glycine, serine and alanine, the last of which had an L excess.[47]

In addition to impact shock synthesis of various simple prebiotic organics, the exogenous delivery of organics by numerous small meteorites would have been important during the Hadean. Carbonaceous chondrite meteorites are known to contain ammonia, which would have been produced in their asteroidal parent bodies.[48] They also contain amino acids, amphiphilic compounds, and purine nucleobases.[49] Aside from a few examples of slight enantiomeric excesses in meteorites, the various organics on the early Earth would have had racemic mixtures; life requires chiral amino acids and sugars. The question that still needs answering is whether meteorites delivered enough organics to make any difference.

Problem: The Water Paradox

One of the more serious problems that origin-of-life theories need to overcome is the Water Paradox. On the one hand, water quickly hydrolyzes biopolymers, including nucleic acids and proteins. On the other hand, water is also necessary for all life. Harvard Earth and planetary scientist Zachary Adam proposed a simple solution: Just provide a different solvent for some of the earliest reactions. Adam suggested formamide, which, like water, is a polar solvent.[50] Formamide is known to be a nucleobase precursor, and it has favorable properties for phosphorylation and polymerization. But creating significant concentrations of formamide under early Earth conditions has proven problematic.

Experiments show that high levels of gamma radiation can make formamide out of HCN via radiolysis much faster than it degrades,[51] as well as simple sugar precursors.[52] Where could that radiation come from? Adam proposed that natural fission reactors were common on the early Earth. There is one well-known example. The Oklo, Gabon reactors are a set of fossil natural fission reactors that were in operation about 1.7 billion years ago. They are located in a region with rich uranium ore that became flooded with water, which served as the neutron moderator. The Oklo region is the only place known to have natural fission reactors. The uranium in the Oklo region was deposited and concentrated when there was sufficient oxygen in the atmosphere for it to be water soluble. Oklo-like natural reactors are probably no longer possible, given the relatively short half-life of the fissile isotope, ^{235}U (0.7 billion years). Uranium could not have been concentrated in this way prior to the oxygenation of the atmosphere about 2.4 billion years ago. Still, the relative abundance of ^{235}U would have been much greater 4.4 billion years ago.

Adam also proposed placer deposits along beaches and rivers, as localities where radioactive minerals could be concentrated, though not nearly as much as in Oklo-like reactors.[53] Beaches would also have the advantage in that they would be subject to the wetting and drying cycles of the lunar tides.

These ideas are still relatively new and require considerable additional testing, given the complexities of the proposed mechanisms of formamide formation, concentration, and subsequent pre-biological reactions.

In summary, the early Hadean, ~4.4 billion years ago, was a period of extremes and extreme differences compared to the present Earth. Following the period shortly after the Moon's formation, the impact rate declined rapidly (episodically spiking) from a value near 10^4 times its present rate.[54] At the same time, residual primordial H_2 as well as any newly generated H_2 were being lost rapidly from the intense ionizing radiation from the Sun, which was also declining rapidly in intensity. The radiation produced by the fission of ^{235}U was declining by a factor of two every 0.7 billion years. As these rates declined, so did the rate of delivery and production of organics. Volcanism would have produced oxidized gases throughout this period. Given our limited understanding of the early Hadean, it seems safe to say that HCN and some of its reaction products and other organics were present on the Earth ~4.4 billion years ago during a short window.

Life from Beyond Earth

Concerned over the low probability of the origin of life on Earth, some scientists have expanded their explanatory horizons. *Panspermia* is the name given to the idea that life is transported through space between planetary bodies, and is usually discussed as an alternative to the origin of life on Earth. Svante Arrhenius proposed the first detailed scientific theory of panspermia, whereby individual living cells are moved through space by radiation pressure (*radiopanspermia*). However, we now know that unprotected spores cannot survive in the harsh radiation environment of space.

Lithopanspermia, the transport of life in rocks, has some potential, at least between close planetary neighbors.[55] This brings up the possibility of an exchange of living cells among Earth, Mars and Venus. We know life has existed on Earth for at least 3.5 and possibly 3.7 billion years. Earth has been spreading living cells around the solar system since then, though given the declining impact rate, very little has occurred for the last ~3 billion years. We know that intact pieces of planetary crust can be exchanged between planets, because we have meteorites from Mars.

A paradox for panspermia is that the period when the exchange of planetary materials is most frequent, the Hadean, is also the period when radiation levels are the highest. The early Sun's high activity is going to make the space journey far less survivable than present conditions; 4.5 billion years ago the overall galactic cosmic radiation level was also greater. What's more, radioactive isotopes with short half-lives, like ^{235}U, are going to produce a more harsh radiation environment for cells within rocks, even if they are protected from cosmic radiation.

The relevant question is: Can a relatively small number of surviving cells from Mars infect Earth with life? Any surviving cells arriving at Earth would have to make a living in the different environment they now found themselves in. Would all the nutrients be present in the minimum required abundances, and would toxic aspects of the environment be low enough? This seems unlikely. Going the other way, from Earth to Mars, is potentially testable. If we eventually find life on Mars, can we determine if it came from Earth? Maybe. Even better would be finding early Terran and Martian meteorites on the Moon. Then, we could better compare any Martian life to early Earth life.

At this time there isn't any convincing evidence for Martian life, extant or fossil. The take-home lesson from this is that although Earth sent some of its microbes to Mars, they didn't take. And, if panspermia didn't work out for Mars, our nearest, most Earth-like planetary neighbor, then it isn't going to work for more distant worlds. By similar logic, interstellar panspermia isn't going to seed early Earth with life.

Conclusions

What has astrobiology taught us about the origin of life?

It has shown that the conditions on Earth during the early Hadean probably provided avenues for the formation of significant amounts of HCN and possibly formamide, both of which are considered important precursors to biomolecules. This, however, is only a tiny factor in explaining the origin of life. Even granting that all the needed nucleic acids, lipids, carbohydrates, and amino acids could have been made on the early Earth, that is still a long way from life—never mind the homochirality problem. Further, due to the rapidly changing conditions on the Earth during this period, the window for the origin of life was short, probably 100–200 million years. This gives chance relatively little time to do its magic.

When we look beyond our planet, we see that the astronomical setting of the Earth was very important for the origin of life, including the Sun's ionizing radiation output, the Moon, and asteroid and comet impacts. We do not, however, see evidence of life originating elsewhere. And if we eventually do find life on another planet, would it show that the origin of life is an easy natural process? Not necessarily. It would only show that whatever or whoever made the origin of life occur on Earth did so elsewhere as well.

Astrobiology continues to make fascinating and potentially productive contributions to origin-of-life research; as of yet, however, we remain far from a definite answer as to how life originated.

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16. TEXTBOOKS STILL MISREPRESENT THE ORIGIN OF LIFE

Jonathan Wells

Discussed earlier in this book, the Miller-Urey experiment may well be called the poster child for origin-of-life research. Most modern biology students have seen some version of the drawing shown in Figure 16-1, which represents an experimental apparatus used in 1952 by University of Chicago graduate student Stanley L. Miller. Because Miller performed his experiment under the supervision of Nobel laureate Harold C. Urey, and the results were published in 1953, it became known as the "1953 Miller-Urey experiment." A cornerstone of textbook coverage of the origin of life, this famous experiment has been seriously misrepresented by textbook authors for decades, and as I will show here, the misrepresentations continue to this day.

An Icon of Evolution

In 2000, I published a book titled *Icons of Evolution: Why Much of What We Teach About Evolution Is Wrong*.[1] I described and analyzed ten images ("icons of evolution") commonly used in biology textbooks to teach high school and college students about evolutionary theory. I showed that all ten icons misrepresent the evidence—and that some scientists had known this for decades.

After 2000 some textbooks were corrected, but in many cases the corrections were minor and the books continued to perpetuate the misrepresentations. This prompted me to publish another book in 2017, titled *Zombie Science,* which included six more icons of evolution that I didn't have room to include in my 2000 book.[2] All sixteen icons misrepresented the evidence, but many were still being used in 2017. I called this "zombie science," because although the icons were empirically dead they continued to stalk our classrooms and research institutions.

I argued that this was not due simply to laziness or a reluctance to give up an attractive theory. It revealed something much deeper: a dogmatic commitment to materialistic philosophy. Biology courses were being misused to indoctrinate students in materialism, the view that only material objects and the forces among them are real. In this view free will, spirit, intelligent design, and God are mere illusions.

One of the icons of evolution was the Miller-Urey experiment. Although Charles Darwin did not mention the origin of life in his books, he speculated in his correspondence that life originated in a "warm little pond" when various chemicals spontaneously assembled themselves into living cells.[3] Darwinian evolution is often used to support a materialistic just-so story, but the story is not complete without an account of the origin of life. So textbook treatments of evolution generally include a materialistic story about the origin of life. And the Miller-Urey experiment is usually included to show that scientists have empirically demonstrated how some of life's most important building blocks formed spontaneously on the early Earth.

In what follows I begin with some historical background. Then I describe the experiment and its publication, subsequent doubts among geochemists about its relevance, a 1983 experiment that Miller performed in light of those doubts, and various later attempts to salvage his earlier experiments. I conclude by showing that biology textbooks are *still* misleading students about the Miller-Urey experiment.

Historical Background

In 1924, Russian biochemist Alexander I. Oparin wrote, "We have no reason to think of life as something which is completely different in principle from the rest of the world… Life is not characterized by any special properties but by a definite, specific combination" of properties. In the history of our planet, "the appropriate conditions must certainly have arisen" to enable the assembly of that specific combination, and "to discover these conditions would be to explain the origin of life."[4]

Oparin published a revised and expanded version of his ideas in 1936. He relied on James H. Jeans's 1917 theory that the solar system formed when a star almost collided with the Sun and pulled out of it a "tidal wave" of hot gases that later condensed into the planets. By the 1930s scientists had learned a lot about the composition of the Sun from analyses of the spectrum of light emitted by it. Oparin reasoned that the early Earth's atmosphere—like the Sun—was rich in hydrogen, and that free oxygen and oxidized gases such as carbon dioxide were absent. In other words, the primitive planet had a reducing atmosphere, and carbon "first appeared on the Earth's surface in the reduced form, particularly in the form of hydrocarbons," the simplest of which is methane.[5] Furthermore, it was probable that "nitrogen, like carbon, first appeared on the Earth's surface in its reduced state, in the form of ammonia."[6] From these molecules, Oparin believed, life evolved. (In 1929, British scientist J. B. S. Haldane had independently published a similar proposal. According to Haldane, organic molecules were synthesized in a reducing atmosphere and dissolved in the primitive oceans to form a "hot dilute soup" in which life evolved.[7])

In 1951, Harold Urey gave a seminar at the University of Chicago dealing with the origin of the solar system and the Earth. Like Oparin, Urey maintained that the early Earth probably had a reducing atmosphere. Miller, who had just started his PhD work with another scientist, attended Urey's seminar. The following year, Urey published his hypothesis in *Proceedings of the National Academy of Sciences USA*.

Urey's 1952 article was titled, "On the Early Chemical History of the Earth and the Origin of Life." He argued that the Earth's primitive atmosphere consisted mainly of methane (CH_4), hydrogen gas (H_2), ammonia (NH_3), and water vapor (H_2O). Urey recommended "experimentation on the production of organic compounds from water and methane in the presence of ultraviolet light" to investigate how life originated. He also recommended experimenting with "electric discharges" since "electric storms in the reducing atmosphere can be postulated reasonably."[8]

Miller's first year of graduate research produced no fruit, so in September 1952 he approached Urey about working with him and doing an experiment to test his origin-of-life hypothesis. Urey was unenthusiastic about the idea, because he felt it would be better for a PhD student to do research with a higher probability of success. Miller persisted, however, and Urey finally agreed.[9]

Together, Miller and Urey designed the now-famous apparatus (Figure 16-1) and had a glassblower make it for them. Then, in the fall of 1952, Miller performed the experiment.

Experiment and Publication

The caption for Figure 16-1 (below) describes how Miller conducted his experiment. In his first run, the heated water had become noticeably pink after only one day. On the second day, Miller removed the water and added a small amount of mercuric chloride to prevent the growth of microorganisms.

He analyzed the contents using paper chromatography, a crude technique by today's standards. Miller placed a drop of the sample on a piece of filter paper near one corner. He then suspended the paper over a container of solvent, with the sample near the lower edge and with that edge touching the solvent. The solvent moved upward by capillary action and carried soluble components of the sample with it. Since those components move at different rates, the process separated them on the filter paper. Then Miller turned the paper ninety degrees, placed another edge of the paper in a different solvent, and repeated the process.

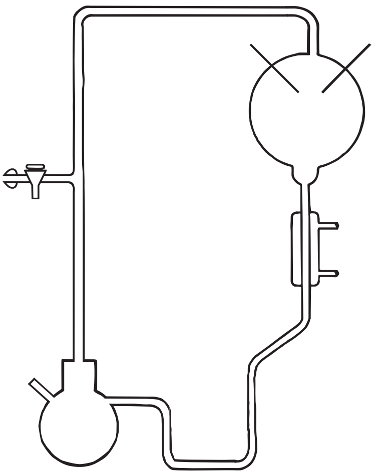

Figure 16-1. The iconic apparatus used by Stanley Miller in 1952.

After pumping all the air out of it, he heated some water in the small flask at the lower left. Then he introduced a mixture of gases (hydrogen, methane, and ammonia) through the valve midway up the glass tube above it. The mixture of gases and water vapor entered the five-liter flask at the upper right, where two electrodes produced a spark to simulate lightning. Miller liquefied some of the reaction products by running cold water through the condenser around the glass tube below the five-liter flask. The U-shaped trap at the bottom prevented fluids from backing up, and they accumulated in the small flask at the bottom left. Then Miller withdrew the water through the small tube extending upward from the left side of the small flask and analyzed it chemically.

Redrawn from Stanley L. Miller, "A Production of Organic Compounds Under Possible Primitive Earth Conditions" (PhD dissertation, University of Chicago, Chicago, 1954), 30.

After the sample's components had been spread out on the filter paper, Miller sprayed the paper with ninhydrin, a chemical that stains amino acids purple. Comparing the results with controls containing known amino acids, Miller identified a spot corresponding to glycine, the simplest amino acid found in living cells.

Urey was out of town during the week, but he was delighted to hear about the results when he returned. Miller repeated the experiment. This time he boiled the water instead of just heating it, and he let the experiment run for a week. By that time the water had turned deep red. Analyzing the water with paper chromatography again, Miller found spots corresponding to several amino acids: glycine, alanine, and possibly two others (though the spots for the latter were too weak for him to be sure).

Miller's results so impressed Urey that he called the editor of *Science,* who promised he would publish a paper reporting the experiment in about six weeks. Miller quickly wrote the paper, with himself as the sole author. (Urey did not put his name on it, afraid that if he did so Miller would not get enough credit for his work.) The paper was submitted in mid-December 1952.

After six weeks Miller had heard nothing from the editor of *Science,* and Urey was furious. He had Miller withdraw the paper and submit it to the *Journal of the American Chemical Society.* Then the editor of *Science* called, apologized, and promised to publish the paper as soon as possible. It turned out that one of the original reviewers for *Science* did not believe Miller's result and had simply set the paper aside.[10]

The paper was finally published in *Science* on May 15, 1953.[11] The drawing of the apparatus shown in the *Science* article was different from the drawings Miller later included in his PhD dissertation—though the general idea was the same.

Miller's 1953 paper was a model of brevity and clarity, unusual qualities in a technical scientific paper. In this sense it was in the same league as another groundbreaking scientific paper: James Watson and Francis Crick's 1953 *Nature* paper on "A Structure for Deoxyribose Nucleic Acid," which had been published just three weeks earlier.[12]

Unlike Watson and Crick's paper, however, Miller's eventually came under a cloud as scientists had growing doubts about it.

Growing Doubts

It was obvious that Miller's experiment did not "explain the origin of life," as Oparin had anticipated such an experiment might. First, the experiment produced not only amino acids, but also many toxic substances that would have to be removed or chemically modified before life could emerge. Second, the experiment did not explain how the amino acids would join together in long chains with the specific sequences needed to make proteins. Third, the experiment did not show how other molecules essential to life might have formed. And fourth, the experiment did not explain how proteins and those other molecules might assemble into a living cell.

But at least—or so it was thought at first—Miller had shown how amino acids could have formed prebiotically ("before life") under conditions that existed on the early Earth. Or had he? As more and more geochemical evidence accumulated, it became increasingly clear that the atmosphere of the early Earth was probably different from the atmosphere of methane, hydrogen gas, ammonia, and water vapor that Miller and Urey had assumed.

Scientists had already discovered in the 1920s that the inert gases (helium, neon, argon, krypton, xenon, and radon; now called "noble" gases) are a million times rarer on Earth than would be expected from their distribution elsewhere in the solar system.[13] In 1949, University of Chicago chemist Harrison Brown reviewed the evidence and concluded that virtually *all* of Earth's gases had been lost during its formation. The gases that now make up our atmosphere—nitrogen (N_2), water vapor (H_2O), oxygen (O_2), and carbon dioxide (CO_2)—must initially have been retained *chemically* in other compounds and then subsequently released as gases. Since the noble gases do not readily form chemical compounds, they were not retained in the first place and escaped into space.[14]

In 1962, Princeton geochemist Heinrich D. Holland wrote, "There seems little question now that the constituents of the Earth's atmosphere have been largely, if not wholly, evolved from the interior of the

Earth." According to Holland, volcanic gases ejected in the earliest stage of Earth's history "probably contained a large amount of hydrogen, and the atmosphere was highly reduced" at first.[15] But Holland wrote in 1984 that the "residence time of hydrogen in the atmosphere is geologically very short" because of its lightness. So this early hydrogen probably quickly escaped into space.[16]

Carnegie Institution geophysicist Philip H. Abelson agreed in 1966 that the scarcity of noble gases "suggests that the atmosphere evolved as a result of outgassing of the Earth." Water and carbon dioxide "are the major volatiles produced by outgassing," though they are accompanied by a significant amount of hydrogen. Nevertheless, Abelson wrote: "What is the evidence for a primitive methane-ammonia atmosphere on Earth? The answer is that there is no evidence for it, but much against it." For one thing, experiments had shown that ammonia is destroyed by ultraviolet radiation and would have disappeared from the atmosphere in about thirty thousand years. For another, if large amounts of methane had been present "the earliest rocks should contain an unusually large proportion of carbon or organic chemicals. This is not the case."[17]

In 1975, Belgian biochemist Marcel Florkin announced that "the concept of a reducing primitive atmosphere has been abandoned," and the Miller-Urey experiment is "not now considered geologically adequate."[18] Two years later, biochemists Sidney W. Fox and Klaus Dose wrote that a reducing atmosphere did "not seem to be geologically realistic" because evidence indicated that "most of the free hydrogen probably had disappeared into outer space and what was left of methane and ammonia was oxidized."[19]

According to Fox and Dose, not only did the Miller-Urey experiment start with the wrong gas mixture, but also it did "not satisfactorily represent early geological reality because no provisions [were] made to remove hydrogen." During a Miller-Urey experiment hydrogen gas accumulates, becoming up to 76 percent of the mixture, but on the early Earth it would have escaped into space. Fox and Dose concluded: "The inference that Miller's synthesis does not have a geological relevance has become increasingly widespread."[20]

Miller's 1983 Experiment

As more and more scientists accepted the view that the early Earth's atmosphere was neutral (consisting mostly of H_2O and CO_2) rather than reducing, Miller decided to perform additional spark discharge experiments to compare the amino acid yields obtained from different mixtures of hydrogen, methane, carbon dioxide, carbon monoxide (CO), and water vapor.

In 1983, Miller and Gordon Schlesinger published a paper in the *Journal of Molecular Evolution* titled "Prebiotic Synthesis in Atmospheres Containing CH_4, CO, and CO_2: I. Amino Acids." The authors reported that they could synthesize the simplest amino acid, glycine, in an atmosphere consisting of CO_2 and CO "as long as sufficient H_2 is present." What was "sufficient"? If the amount of H_2 was less than half that of CO_2, "the yields of amino acids are so low it is difficult to detect them," and such yields "might not permit sufficient accumulation of amino acids to make it possible for life to arise."[21] Adequate yields were obtained only when there was at least as much H_2 as there was CO_2, and at least as much H_2 as there was CO. But Miller and Schlesinger conceded that these ratios are "30 to 300 times those produced by modern volcanoes."[22]

But even if there were enough hydrogen, the authors wrote, "there is a problem with using CO and CO_2 atmospheres. From the standpoint of amino acid synthesis the results are quite disappointing—essentially only glycine is produced." So "CO and CO_2 containing atmospheres give a suite of amino acids that is apparently inadequate" for the origin of life.[23]

Only by including methane could Schlesinger and Miller produce significant amounts of amino acids more complex than glycine. So electric discharges in a primitive atmosphere lacking methane and an excess of hydrogen would not produce the amino acids needed for life. The abstract of the paper concluded: "If it is assumed that an abundance of amino acids more complex than glycine was required for the origin of life, then these results indicate the requirement for CH_4 in the primitive atmosphere."[24]

Note the logic. Schlesinger and Miller assumed that amino acids on the early Earth *must* have been produced the way the two had produced them in their spark discharge experiment. Since all living cells need amino acids more complex than glycine, the authors reasoned backwards to the presence of methane in the primitive atmosphere. But by 1983 the preponderance of geochemical evidence indicated that the primitive atmosphere *did not* contain a significant amount of methane. In effect, Schlesinger and Miller were assuming that their theory about the origin of life carried more weight than the geochemical evidence.

Such reasoning prompted chemist Robert Shapiro to write in 1986, "We have reached a situation where a theory has been accepted as fact by some, and possible contrary evidence is shunted aside." Shapiro concluded that this is "mythology rather than science."[25]

In 1999 physicist Freeman Dyson wrote, "Miller's beguiling picture of a pond full of dissolved amino acids under a reducing atmosphere has been discredited." His experiment "was supposed to be a true simulation of prebiotic chemistry on the primitive Earth. But now nobody believes this anymore."[26]

Dyson should have written "almost nobody." Some people continued to believe that the Miller-Urey experiment was a true simulation of prebiotic chemistry. In 2005, Chinese astrobiologist Feng Tian and his colleagues published calculations in *Science* to show that "hydrogen escape from early Earth's atmosphere was not as rapid as previously assumed."[27] If true, then a Miller-Urey-type scenario for the origin of life's building blocks might work.

Astrobiologist David C. Catling objected that the assumptions underlying their calculations were "too unrealistic," but Tian and his colleagues countered that Catling's objection was "speculative."[28] In 2013 three Japanese planetary scientists published calculations that contradicted Tian's but were "consistent with geological evidence implying low hydrogen in the early Earth atmosphere."[29] Since nobody has direct access to the actual conditions on the early Earth, the theoretical debate is likely to continue.

But against the disputed theoretical calculations of Tian and his colleagues stands the geochemical evidence. And that evidence implies that when life first appeared, the Earth did not have a hydrogen-rich methane-ammonia atmosphere. Instead, after Earth's initial gases were lost into space its atmosphere probably came from volcanoes, which emit predominantly water vapor and carbon dioxide.

Other Attempts to Salvage the Miller-Urey Experiment

In his 1952 experiments Miller used three different versions of his apparatus. Figure 16-1 shows the principal (and most famous) one. In a second version, Miller used an aspirating nozzle above the boiling water to inject steam into the circulating gases (Figure 16-2). In a third version (not shown here), Miller used a silent electric discharge instead of a spark.

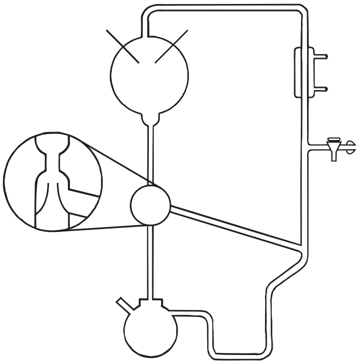

Figure 16-2. A second version of the apparatus used by Miller in 1952.

In this version of his apparatus, Miller routed the gases past an aspiration nozzle above the boiling water, shown in the magnified view on the left.

Adapted from Stanley L. Miller, "A Production of Organic Compounds Under Possible Primitive Earth Conditions" (PhD dissertation, University of Chicago, Chicago, 1954), 31.

After Miller passed away in 2007, his former graduate student Jeffery L. Bada and some colleagues re-analyzed some vials from the 1952 experiments. Using modern techniques that were not available to Miller, Bada and his colleagues identified many more amino acids than Miller had found, especially in the vials from the second apparatus. Bada and his colleagues were particularly interested in Miller's second apparatus "because it possibly simulates the spark discharge synthesis by lightning in a steam-rich volcanic eruption." In 2008 they published an article about their findings in *Science*, titled "The Miller Volcanic Spark Discharge Experiment."[30]

It has long been known that lightning is often associated with volcanic eruptions.[31] Bada and his colleagues justified their "volcanic" description of Miller's second apparatus by citing a 2000 report that volcanic lightning is probably due to "charge separation in the erupting ash column."[32] But passing the steam from the flask of boiling water through a nozzle and pointing out that lightning is often associated with volcanic eruptions does not transform the second apparatus into a "volcanic experiment." Miller did not call it a "volcanic experiment" in his published report. (His only reference to volcanoes was a speculation that they might have provided "local hot spots [that] synthesized other simple organic compounds."[33]) The gases Miller used in his so-called "volcanic experiment" were the same ones he used in his other 1952 experiments—methane (CH_4), hydrogen gas (H_2), ammonia (NH_3), and water vapor (H_2O). And the relevant reactions still occurred in the five-liter flask, not in the plume of steam near the nozzle.

The only thing in the 2008 paper that provided a rationale for the "volcanic" label was a claim by Bada and his colleagues that "the volcanic apparatus experiment suggests that, even if the overall atmosphere was not reducing, localized prebiotic synthesis could have been effective."[34] But the experiment did not provide any evidence for this. The experiment didn't even suggest it. The "localized prebiotic synthesis" was sheer speculation.

In another paper published in 2008, Bada and some colleagues attempted to meet head-on the objection that Earth's early atmosphere was not reducing but was dominated by volcanic gases. (Miller passed away in 2007, but since he had contributed to the work his name was added posthumously to the paper.) In 1983, Schlesinger and Miller had reported that in a CO_2 atmosphere "the yields of amino acids are so low it is difficult to detect them."[35] When Bada and his colleagues did some electric discharge experiments using carbon dioxide (CO_2), nitrogen (N_2), and water vapor (H_2O), they also obtained "only negligible yields of amino acids." But they reasoned that the low yields "were likely the result of oxidation" by nitrite and nitrate ions produced by the electric discharge. So they added ascorbic acid (Vitamin C) to inhibit oxidation. They acknowledged that Vitamin C is "an unlikely prebiotic anti-oxidant," but they argued that prebiotic iron-sulfur compounds could have done the job instead.[36]

Bada and his colleagues also discovered that nitrites and nitrates from the spark discharge make the liquid in the apparatus too acidic for amino acids to form. So they added excess calcium carbonate ($CaCO_3$) to keep the liquid close to a neutral pH (7.1). They concluded that "buffering the reaction solution with respect to pH and the addition of oxidation inhibitors" greatly increased the yield of amino acids from a neutral atmosphere.[37]

Of course, a good organic chemist with suitable methods and an adequate laboratory can synthesize all the amino acids found in living things from gases that contain the necessary elements: carbon, hydrogen, oxygen, and nitrogen (and sulfur and selenium for a few of them). The question is whether biologically important amino acids can be synthesized from gases containing these elements under realistic prebiotic conditions, before there were any chemists or laboratories.

In 2018, German organic chemist Clemens Richert wrote: "We do our best to perform experiments that we believe re-enact possible steps of prebiotic evolution, but we know that we need to intervene manually to obtain meaningful results. Simply mixing chemicals and watching for a living system to appear" has never worked. But human intervention must be kept to a minimum: "A reaction or a reaction network is allowed to unfold, and the sample is only broken up when the experiment has been finished. Perhaps, samples are drawn, as in the famous Miller experiment, but there is no addition of new chemicals or an artificial change in conditions."[38]

So the Miller-Urey experiment works with a realistic primitive atmosphere, but only with the addition of new chemicals and an artificial change in conditions. In other words, the 1983 results of Schlesinger and Miller are still valid: Without additional human intervention, sparking a predominantly CO_2 atmosphere does not produce amino acids adequate for the origin of life.

In 2011, Bada and some colleagues published analyses of samples that Miller had produced with his apparatus in a 1958 experiment that he never reported. In his 1958 experiment, Miller used a gaseous mixture of hydrogen sulfide (H_2S), methane (CH_4), ammonia (NH_3), and carbon dioxide (CO_2)—and of course water vapor (H_2O). The analyses identified "a large assortment of amino acids" in the samples, including some that (not surprisingly) contained sulfur. Since the gases emitted by modern volcanoes include small amounts of hydrogen sulfide, Bada and his colleagues concluded that "Miller's 1958 study could thus serve as a model for the chemistry that may have occurred in early volcanic plumes."[39]

But except for the addition of hydrogen sulfide and some carbon dioxide, Miller's 1958 experiment came no closer to simulating a volcanic eruption than what Bada called his "volcanic" experiment of 1952. The gases Miller used were still a highly reducing mixture dominated by methane and ammonia, not the neutral or slightly reducing mixtures of gases emitted by modern volcanoes.

Nevertheless, Bada and his associates have continued to promote the Miller-Urey experiment, including its so-called "volcanic" version.[40] They have even posted online instructions on how to re-enact the experiment in a science classroom.[41]

Recent Textbooks

Recent biology textbooks not only feature the Miller-Urey experiment, but also give students the false impression that it and its successors demonstrated how life's chemical building blocks could have formed under realistic prebiotic conditions on the early Earth.

Five such textbooks are reviewed here. They all acknowledge one or more problems with the Miller-Urey experiment, but they all conclude by defending it.

For example, the 2017 edition of Freeman's *Biological Science* reports:

> The production of more complex molecules from simple molecules in Miller's experiment supported his claim that the formation of a prebiotic soup was possible. The results came under fire, however, when other researchers pointed out that the early atmosphere was dominated by volcanic gases like CO, CO_2, and H_2, not the CH_4 and NH_3 used in Miller's experiment. This controversy stimulated a series of follow-up experiments, which showed that the assembly of small molecules into more complex molecules could also occur under more realistic early Earth conditions.[42]

But with a few exceptions (mentioned above) researchers do *not* think H_2 dominated the early atmosphere. And "the assembly of small molecules into more complex molecules" is inexcusably vague. Small molecules assemble into complex sodium aluminum silicates that make up much of the lava that flows from volcanoes. Yet they have nothing to do with the origin of life.

Freeman's *Biological Science* gets more specific a few pages later: "The early Earth simulations designed by Stanley Miller and others who followed up on his work sparked particular excitement for origin-of-life researchers, because the same molecules were repeatedly discovered among their products—amino acids."[43]

But this glosses over the fact (as we saw above) that without an excess of hydrogen, a Miller-Urey-type experiment using a realistic atmosphere of CO_2 and water vapor does not produce even the simplest amino acid (glycine).

According to the 2017 edition of Raven and Johnson's *Biology,* "Very few geochemists agree on the exact composition of the early atmosphere. One popular view is that it contained principally carbon dioxide (CO_2) and nitrogen gas (N_2), along with significant amounts of water vapor (H_2O). It is possible that the early atmosphere also contained hydrogen gas (H_2) … hydrogen sulfide (H_2S), ammonia (NH_3), and methane (CH_4)."[44]

Without further explanation, the textbook informs students: "We refer to such an atmosphere as a *reducing atmosphere* [emphasis in the original]." Raven and Johnson's *Biology* concludes that the Miller-Urey experiment and its successors showed that "the key molecules of life could have formed in the reducing atmosphere of the early Earth."[45]

Wait a minute! An atmosphere that contains principally carbon dioxide, nitrogen and water vapor—even if it also contains small amounts of hydrogen, hydrogen sulfide, ammonia and methane—is nearly neutral. It is not even close to being the "reducing atmosphere" that Miller used to synthesize "the key molecules of life." The textbook is misleading, to say the least.

The 2018 edition of Campbell's *Biology* has this to say about Miller's experiment and its successors:

> [Miller's] apparatus yielded a variety of amino acids found in organisms today, along with other organic compounds. Many laboratories have since repeated Miller's classic experiment using different recipes for the atmosphere, some of which also produced organic compounds. However, some evidence suggests that the early atmosphere was made up primarily of nitrogen and carbon dioxide and was neither reducing nor oxidizing (electron removing). Recent Miller/Urey-type experiments using such 'neutral' atmospheres have also produced organic molecules.[46]

So—like Freeman's inexcusably vague reference to "complex molecules" instead of amino acids—this textbook resorts to ambiguity. According to the *Encyclopedia Britannica,* an organic molecule is "any of a large class of chemical compounds in which one or more atoms of carbon are covalently linked to atoms of other elements, most commonly hydrogen, oxygen, or nitrogen. The few carbon-containing compounds not classified as organic include carbides, carbonates, and cyanides."[47]

Carbides are compounds of carbon with a less electronegative element (e.g., calcium carbide, CaC_2); carbonates are compounds containing CO_3 (e.g., sodium bicarbonate, $NaHCO_3$); and cyanides are compounds containing triple-bonded CN (e.g., hydrogen cyanide, HCN). Even with these classes of chemicals excluded, "organic molecules" could refer to a host of compounds unrelated to the origin of life, including crude oil and cellulose. The textbook's vagueness misleads students into believing that the Miller-Urey experiment still explains how life's building blocks formed on the early Earth.

Campbell's *Biology* also relies heavily on Bada's "volcanic" label for two of Miller's experiments: the unreported 1958 experiment in which Miller included H_2S among his reactants, and the 1952 experiment using an aspirating nozzle to inject steam into the other gases. According to the textbook, "since H_2S is released by volcanoes, the H_2S experiment was designed to mimic conditions near volcanoes on early Earth."[48] Yet Miller never published anything to suggest that. It was Bada and his colleagues who added that gloss to his work fifty years later.

The textbook also reports, "In addition to his classic [1952] study, Miller also conducted an experiment simulating a volcanic eruption."[49] Yet, again, Miller did not suggest that in his published report.[50] And again, it was a gloss added more than fifty years later by Bada and his colleagues.[51]

According to the 2019 edition of Mader and Windelspecht's *Biology*: "The Miller-Urey experiment has been tested and re-examined over the decades since it was first performed. Other investigators have achieved similar results as Miller by using other, less-reducing combinations of gases dissolved in water."[52]

As we saw above, this is inexcusably vague, if not downright false. The textbook concludes: "If early atmospheric gases did react with one another to produce small organic compounds, neither oxidation (no free oxygen was present) nor decay (no bacteria existed) would have destroyed these molecules, and rainfall would have washed them into the ocean, where they would have accumulated for hundreds of millions of years. Therefore, the oceans would have been a thick, warm organic soup."[53]

So like Campbell's *Biology*, Mader and Windelspecht's *Biology* uses the ambiguous and elusive term "organic compounds" to obscure what is a very misleading description of the current status of the Miller-Urey experiment.

The 2019 edition of a popular high school textbook, [Kenneth R.] Miller and Levine's *Biology*, describes how Miller performed his 1952 experiment and reports: "The results were spectacular. Miller and Urey's analysis revealed that 21 amino acids had been produced in their apparatus."[54]

Of course, Miller detected only two with certainty, and perhaps two more. So this description is highly exaggerated. But that's trivial compared to the textbook's now-familiar repetition of the false claim that a Miller-Urey-type experiment using a realistic atmosphere produces results similar to those using a reducing atmosphere:

> Miller and Urey's experiment suggests that organic compounds necessary for life could have arisen from simpler compounds on a primitive Earth. While Miller and Urey's hypotheses about the composition of the early atmosphere were incorrect, more recent experiments using current ideas about the early atmosphere have validated their conclusion: Organic compounds could have been produced on the early Earth.[55]

Once again, this textbook resorts to the ambiguous and elusive term "organic compounds."

Conclusions

It doesn't take an expert to see that biology textbooks are still obscuring the truth about the Miller-Urey experiment. There might be a legitimate place for drawings of their iconic apparatus, because it was a historic milestone in origin-of-life research. But there is no scientific justification for giving students the impression that the experiment works just fine with a realistic atmosphere.

Why do so many biology textbooks mislead students about the Miller-Urey experiment? One sometimes hears the excuse that textbooks are expensive to produce, and it is difficult to keep up with the latest in every area of research. But the Miller-Urey experiment was discredited among most scientists decades ago, despite the efforts of a few determined defenders. Surely two decades is enough time to remove the passages that continue to mislead students about its relevance!

The problem is exacerbated by the enormous financial burden placed on today's students, parents, and taxpayers. The five textbooks reviewed here cost an average of $97 each, and they are usually required, not optional. Surely at those prices students, parents, and taxpayers are entitled to the truth about the Miller-Urey experiment: that for good scientific reasons it is now widely thought to be irrelevant to the origin of life on Earth.

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17. EVIDENCE OF INTELLIGENT DESIGN IN THE ORIGIN OF LIFE

Stephen C. Meyer

Theories about the origin of life necessarily presuppose knowledge of the attributes of living cells. As historian of biology Harmke Kamminga has observed, "At the heart of the problem of the origin of life lies a fundamental question: What is it exactly that we are trying to explain the origin of?"[1] Or as the pioneering chemical evolutionary theorist Alexander Oparin put it, "The problem of the nature of life and the problem of its origin have become inseparable."[2] Origin-of-life researchers want to explain the origin of the first and presumably simplest—or, at least, minimally complex—living cell. As a result, developments in fields that explicate the nature of unicellular life have historically defined the questions that origin-of-life scenarios must answer.

Since the late 1950s and 1960s, origin-of-life researchers have increasingly recognized the complex and specific nature of unicellular life and the biomacromolecules on which such systems depend. Further, molecular biologists and origin-of-life researchers have characterized this complexity and specificity in informational terms. Molecular biologists routinely refer to DNA, RNA, and proteins as carriers or repositories of "information."[3] Many origin-of-life researchers now regard the origin of the information in these biomacromolecules as the central question facing their research. As Bernd-Olaf Kuppers has stated, "The problem of the origin of life is clearly basically equivalent to the problem of the origin of biological information."[4]

This chapter will evaluate competing explanations for the origin of the information necessary to build the first living cell. To do so will require determining what biologists have meant by the term information as it has been applied to biomacromolecules. As many have noted, "information" can denote several theoretically distinct concepts. This chapter will attempt to eliminate this ambiguity and to determine precisely what type of information origin-of-life researchers must explain "the origin of." What follows will first seek to characterize the information in DNA, RNA, and proteins as a fact in need of explanation; and, second, to evaluate the efficacy of competing classes of explanation for the origin of biological information.

Part I will seek to show that molecular biologists have used the term "information" consistently to refer to the joint properties of complexity and functional specificity or specification. Biological usage of the term will be contrasted with its classical information-theoretic usage to show that "biological information" entails a richer sense of information than the classical mathematical theory of Shannon and Wiener. Part I will also argue against attempts to treat biological "information" as a metaphor lacking empirical content and/or ontological status.[5] It will show that the term biological information refers to two real features of living systems, complexity and specificity, features that jointly do require explanation.

Part II will evaluate competing types of explanation for the origin of the specified biological information necessary to produce the first living system. From the 1920s to the mid-1960s, origin-of-life researchers relied heavily on theories emphasizing the creative role of random events—"chance"—often in tandem with some form of prebiotic natural selection. Since the late 1960s, theorists have instead emphasized deterministic self-organizational laws or properties—that is, physical-chemical "necessity." Part II will show the causal inadequacy of explanations involving "chance," "necessity," and the combination of the two.

Part III will suggest that the origin of biological information requires a radically different explanatory approach. It will argue that our present knowledge of causal powers suggests intelligent design as a better, more causally adequate explanation for the origin of the specified complexity (the information so defined) present in large biomolecules such as DNA, RNA, and proteins.

I.

A. The Growing Recognition of the Complexity of the Cell

After Darwin published the *Origin of Species* in 1859, many scientists began to think about a problem that Darwin had not addressed.[6] Although Darwin's theory purported to explain how life could have grown gradually more complex starting from "one or a few simple forms," it did not explain, or attempt to explain, how life had first originated. Yet in the 1870s and 1880s, evolutionary biologists like Ernst Haeckel and Thomas Huxley assumed that devising an explanation for the origin of life would be fairly easy, based on their assumption that life was, in essence, a chemically simple substance called "protoplasm" that could easily be constructed by combining and recombining simple chemicals such as carbon dioxide, oxygen, and nitrogen.

Over the next sixty years, biologists and biochemists gradually revised their view of the nature of life. During the 1860s and 1870s, biologists tended to see the cell, in Haeckel's words, as an undifferentiated and "homogeneous globule of plasm." By the 1930s, however, most biologists had come to see the cell as a complex metabolic system.[7] Origin-of-life theories reflected this increasing appreciation of cellular complexity. Whereas nineteenth-century theories of abiogenesis envisioned life arising almost instantaneously via a one- or two-step process of chemical "autogeny," early twentieth-century theories, such as Oparin's theory of evolutionary abiogenesis, envisioned a multibillion-year process of transformation from simple chemicals to a complex metabolic system.[8] Even so, most scientists during the 1920s and 1930s still vastly underestimated the complexity and specificity of the cell and its key functional components—as developments in molecular biology would soon make clear.

B. The Complexity and Specificity of Proteins

During the first half of the twentieth century, biochemists had come to recognize the centrality of proteins to the maintenance of life. However, they repeatedly underestimated the complexity of proteins. Beginning in the 1950s a series of discoveries caused this simplistic view of proteins to change. Researchers ultimately found that proteins exhibit an extraordinarily complex and irregular three-dimensional shape: a twisting, turning, tangle of amino acids. As John Kendrew explained in 1958, "The big surprise was that it was so irregular... the arrangement seems to be almost totally lacking in the kind of regularity one instinctively anticipates, and it is more complicated than has been predicted by any theory of protein structure."[9]

By the mid-1950s, biochemists recognized that proteins possess another remarkable property. In addition to their complexity, proteins also exhibit *specificity*. Whereas proteins are built from chemically rather simple amino acid "building blocks," their function (whether as enzymes, signal transducers, or structural components in the cell) depends crucially on a specific arrangement of those building blocks.[10] In particular, the specific sequence of amino acids in a chain and the resultant chemical interactions between amino acids largely determine the specific three-dimensional structure that the chain as a whole will adopt. Those structures or shapes in turn determine what function, if any, the amino acid chain can perform in the cell.

For a functioning protein, its three-dimensional shape gives it a hand-in-glove fit with other molecules, enabling it to catalyze specific chemical reactions or to build specific structures within the cell. Because of its three-dimensional specificity, one protein can usually no more substitute for another than one tool can substitute for another. A topoisomerase can no more perform the job of a polymerase than a hatchet can perform the function of a soldering iron. Instead, proteins perform functions only by virtue of their three-dimensional specificity of fit, either with other equally specified and complex molecules or with simpler substrates within the cell. Moreover, the three-dimensional specificity derives in large part from the one-dimensional sequence specificity in the arrangement of the amino acids that form proteins. Even slight alterations in sequence often result in the loss of protein function.

C. The Complexity and Sequence Specificity of DNA

During the early part of the twentieth century, researchers also vastly underestimated the complexity (and significance) of nucleic acids such as DNA and RNA. By then, scientists knew the chemical composition of DNA. Biologists and chemists knew that in addition to sugars (and later phosphates), DNA was composed of four different nucleotide bases, called adenine, thymine, cytosine, and guanine. In 1909, chemist P. A. Levene thought he had shown that the four different nucleotide bases always occurred in equal quantities within the DNA molecule.[11] He conjectured that the four nucleotide bases in DNA linked together in repeating sequences of the same four chemicals in the same sequential order. Yet if those sequential arrangements of nucleotides were repetitive and invariant, their potential for expressing any genetic diversity seemed inherently limited. To account for the heritable differences between species, biologists needed to discover some source of variable or irregular specificity, some source of information, within the germ lines of different organisms. Yet insofar as DNA was seen as an uninterestingly repetitive molecule, many biologists assumed that DNA could play little if any role in the transmission of heredity.

That view began to change in the mid-1940s for several reasons. Crucially, work by Erwin Chargaff of Columbia University in the late 1940s undermined Levene's "tetranucleotide hypothesis." Chargaff showed that nucleotide frequencies actually do differ between species, even if they often hold constant within the same species or within the same organs or tissues of a single organism.[12] More important, Chargaff recognized that even for nucleic acids of exactly "the same analytical composition"—meaning those with the same relative proportions of the four bases (abbreviated A, T, C, and G)—"enormous" numbers of variations in sequence were possible.[13] Thus, Chargaff showed that base sequencing in DNA might well display the high degree of variability and aperiodicity required by any potential carrier of heredity.

Eventually, elucidation of the three-dimensional structure of DNA by Watson and Crick in 1953 made clear that DNA could function as a carrier of hereditary information.[14] The model proposed by Watson and Crick envisioned a double-helix structure. According to the now well-known Watson and Crick model, the two strands of the helix were made of sugar and phosphate molecules linked by phosphodiester bonds. Nucleotide bases were linked horizontally to the sugars on each strand of the helix and to a complementary base on the other strand to form an internal "rung" on a twisting "ladder."

The Watson-Crick model made clear that DNA might possess an impressive chemical and structural complexity. The double-helix structure for DNA presupposed an extremely long and high-molecular-weight structure, possessing an impressive potential for variability and complexity in sequence. As Watson and Crick explained, "The phosphate-sugar backbone of our model is completely regular, but any sequence of the pairs of bases can fit into the structure. It follows that in a long molecule many different permutations are possible, and it therefore seems likely that the precise sequence of the bases is the code which carries the genetical information."[15]

The notion of a "code" was important. Discovery of the complexity and specificity of proteins had led researchers to suspect a functionally specific role for DNA. Molecular biologists assumed that proteins were much too complex to arise by chance *in vivo*. Moreover, given their irregularity, it seemed unlikely that a general chemical law or regularity could explain their assembly. Instead, molecular biologists had begun to look for some source of information or "specificity" within the cell that could direct the construction of such highly specific and complex structures. To explain the presence of the specificity and complexity in the protein, Monod would later insist, "you absolutely needed a code."[16]

The structure of DNA as elucidated by Watson and Crick suggested a means by which information or "specificity" might be encoded along the spine of DNA's sugar-phosphate backbone.[17] Their model suggested that variations in sequence of the nucleotide bases might find expression in the sequence of the amino acids that form proteins. In 1955, Crick proposed this idea as the so-called sequence hypothesis. According to Crick's hypothesis, the specificity of arrangement of amino acids in proteins derives from the specific arrangement of the nucleotide bases on the DNA molecule.[18] The sequence hypothesis suggested that the nucleotide bases in DNA functioned like letters in an alphabet or characters in a machine code. Just as alphabetic letters in a written language may perform a communication function depending on their sequence, so, too, might the nucleotide bases in DNA result in the production of a functional protein molecule depending on their precise sequential arrangement. In both cases, function depends crucially on sequence. The sequence hypothesis implied not only the complexity but also the functional specificity of DNA base sequences.

By the early 1960s, a series of experiments had confirmed that DNA base sequences play a critical role in determining amino acid sequence during protein synthesis.[19] By that time, the processes and mechanisms by which DNA sequences determine key stages of the process were known (at least in outline). Protein synthesis or "gene expression" proceeds as long chains of nucleotide bases are first copied during a process known as transcription. The resulting copy, a "transcript" made of single-stranded "messenger RNA," now contains a sequence of RNA bases precisely reflecting the sequence of bases on the original DNA strand. The transcript is then transported to a complex organelle called a ribosome. At the ribosome, the transcript is "translated" with the aid of highly specific adaptor molecules (called transfer-RNAs) and specific enzymes (called amino-acyl tRNA synthetases) to produce a growing amino acid chain.[20]

Whereas the function of the protein molecule derives from the specific arrangement of twenty different types of amino acids, the function of DNA depends on the arrangement of just four kinds of bases. This lack of a one-to-one correspondence means that a group of three DNA nucleotides (a triplet) is needed to specify a single amino acid. In any case, the sequential arrangement of the nucleotide bases determines (in large part) the one-dimensional sequential arrangement of amino acids during protein synthesis.[21] Since protein function depends critically on amino acid sequence and amino acid sequence depends critically on DNA base sequence, the sequences in the coding regions of DNA themselves possess a high degree of specificity relative to the requirements of protein (and cellular) function.

D. Information Theory and Molecular Biology

From the beginning of the molecular biological revolution, biologists have ascribed information-bearing properties to DNA, RNA, and proteins. In the parlance of molecular biology, DNA base sequences contain the "genetic information" or the "assembly instructions" necessary to direct protein synthesis. Yet the term "information" can denote several theoretically distinct concepts. Thus, one must ask which sense of "information" applies to these large biomacromolecules. In fact, molecular biologists employ a concept of information stronger than that of mathematicians and information theorists, but slightly weaker conception than that of linguists and ordinary users.

During the 1940s, Claude Shannon at Bell Laboratories developed a mathematical theory of information.[22] His theory equated the amount of information transmitted with the amount of uncertainty reduced or eliminated by a series of symbols or characters.[23] For example, before one rolls a six-sided die, there are six possible outcomes. Before one flips a coin, there are two. Rolling a die will thus eliminate more uncertainty and, on Shannon's theory, will convey more information than flipping a coin. Equating information with the reduction of uncertainty implied a mathematical relationship between information and probability (or its inverse, complexity). Note that for a die each possible outcome has only a one in six chance of occurring, compared to a one in two chance for each side of the coin. Thus, in Shannon's theory the occurrence of the more improbable event conveys more information. Shannon generalized this relationship by stating that the amount of information conveyed by an event is inversely proportional to the prior probability of its occurrence. The greater the number of possibilities, the greater the improbability of any one being actualized, and thus more information is transmitted when a particular possibility occurs.

Moreover, information increases as improbabilities multiply. The probability of getting four heads in a row when flipping a fair coin is $\frac{1}{2} \times \frac{1}{2} \times \frac{1}{2} \times \frac{1}{2}$, or $(\frac{1}{2})^4$. Thus, the probability of obtaining a specific sequence of heads and/or tails decreases exponentially as the number of trials increases. The quantity of information increases correspondingly. Even so, information theorists found it convenient to measure information additively rather than multiplicatively. Thus, the common mathematical expression ($I = -\log_2 p$) for calculating information converts probability values into informational measures through a negative logarithmic function, where the negative sign expresses an inverse relationship between information and probability.[24]

Shannon's theory applies most easily to sequences of alphabetic symbols or characters that function as such. Within any given alphabet of x possible characters, the placement of a specific character eliminates x-1 other possibilities and thus a corresponding amount of uncertainty. Or put differently, within any given alphabet or ensemble of x possible characters (where each character has an equi-probable chance of occurring), the probability of any one character occurring is $1/x$. The larger the value of x, the greater the amount of information that is conveyed by the occurrence of a specific character in a sequence. In systems where the value of x can be known (or estimated), as in a code or language, mathematicians can easily generate quantitative estimates of information-carrying capacity. The greater the number of possible characters at each site and the longer the sequence of characters, the greater is the information-carrying capacity—or Shannon information—associated with the sequence.

The essentially digital character of the nucleotide bases in DNA and of the amino acid residues in proteins enabled molecular biologists to calculate the information-carrying capacity (or syntactic information) of those molecules using the new formalism of Shannon's theory. Because at every site in a growing amino acid chain, for example, the chain may receive any one of twenty amino acids, placement of a single amino acid in the chain eliminates a quantifiable amount of uncertainty and increases the Shannon or syntactic information of a polypeptide by a corresponding amount. Similarly, since at any given site along the DNA backbone any one of four nucleotide bases may occur with equal probability, the p value for the occurrence of a specific nucleotide at that site equals 1/4, or .25.[25] The information-carrying capacity of a sequence of a specific length n can then be calculated using Shannon's familiar expression ($I = -\log_2 p$) once one computes a p value for the occurrence of a particular sequence n nucleotides long where $p = (1/4)^n$. The p value thus yields a corresponding measure of information-carrying capacity or syntactic information for a sequence of n nucleotide bases.[26]

E. Complexity, Specificity, and Biological Information

Though Shannon's theory and equations provided a powerful way to measure the amount of information that could be transmitted across a communication channel, it had important limits. In particular, it did not and could not distinguish merely improbable sequences of symbols from those that conveyed a message. As Warren Weaver made clear in 1949, "The word information in this theory is used in a special mathematical sense that must not be confused with its ordinary usage. In particular, information must not be confused with meaning."[27] Information theory could measure the information-carrying capacity or the syntactic information of a given sequence of symbols but could not distinguish the presence of a meaningful or functional arrangement of symbols from a random sequence (for example, "we hold these truths to be self-evident" versus "ntnyhiznlhteqkhgdsjh"). Thus, Shannon information theory could quantify the amount of functional or meaningful information that *might be present* in a given sequence of symbols or characters, but it could not distinguish the status of a functional or message-bearing text from gibberish. Thus, paradoxically, random sequences of letters often have more syntactic information (or information-carrying capacity), as measured by classical information theory, than do meaningful or functional sequences that happen to contain a certain amount of intentional redundancy or repetition. Thus, Shannon's theory remains silent on the important question of whether a sequence of symbols is functionally specific or meaningful.

In its application to molecular biology, Shannon information theory did succeed in rendering rough quantitative measures of the information-carrying capacity or syntactic information (where those terms correspond to measures of brute complexity),[28] establishing that DNA and proteins were highly complex, and quantifiably so; yet it could not establish whether base sequences in DNA or amino acid sequences in proteins possessed the property of functional specificity. Information theory helped establish that DNA and proteins *could* carry large amounts of functional information; it could not establish whether they *did*.

The ease with which information theory applied to molecular biology (to measure information-carrying capacity) has created considerable confusion about the sense in which DNA and proteins contain "information." Since as early as 1958, leading molecular biologists have defined biological information so as to incorporate the notion of specificity of function (as well as complexity).[29] Molecular biologists such as Monod and Crick recognized that sequences of nucleotides and amino acids in functioning biomacromolecules possessed a high degree of specificity relative to the maintenance of cellular function. As Crick explained in 1958, "By information I mean the specification of the amino acid sequence of the protein… Information means here the precise determination of sequence, either of bases in the nucleic acid or of amino acid residues in the protein."[30] Crick's "precise determination of sequence" is now equated with the extra-information-theoretic property of specificity or specification. Biologists have defined specificity tacitly as "necessary to achieve or maintain function." They have determined that DNA base sequences, for example, are specified not by applying information theory but by making experimental assessments of the function of those sequences within the overall apparatus of gene expression.[31] Similar experimental considerations have established the functional specificity of proteins.

Further, developments in complexity theory have now made possible a fully general theoretical account of specification, one that applies readily to biological systems. According to mathematician William Dembski, specification involves a match or correspondence between a physical system or sequence and an independently recognizable pattern or set of functional requirements.[32]

To illustrate Dembski's notion of specification, consider these two strings of characters:

"iuinsdysk]idfawqnzkl,mfdifhs"

"Time and tide wait for no man."

Given the number of possible ways of arranging the letters and punctuation marks of the English language for sequences of this length, both of these two sequences constitute highly improbable arrangements of characters. Thus, both have a considerable and quantifiable information-carrying capacity. Nevertheless, only the second of the two sequences exhibits a specification on Dembski's account.

The reason for this is that English has many functional requirements. For example, to convey meaning in English one must employ existing conventions of vocabulary (associations of symbol sequences with particular objects, concepts, or ideas) and existing conventions of syntax and grammar. When symbol arrangements "match" existing vocabulary and grammatical conventions (i.e., functional requirements), communication can occur. Such arrangements exhibit "specification." The sequence "Time and tide wait for no man" clearly exhibits such a match, and thus performs a communication function.

Biological organisms also exhibit specifications, though not necessarily semantic or subjectively "meaningful" ones. The nucleotide base sequences in the coding regions of DNA are highly specific relative to the independent functional requirements of protein function, protein synthesis, and cellular life. To maintain viability, the cell must regulate its metabolism, pass materials back and forth across its membranes, destroy waste materials, and do many other specific tasks. Each of these functional requirements in turn necessitates specific molecular constituents, machines, or systems (usually made of proteins) to accomplish these tasks. Building these proteins with their specific three-dimensional shapes requires specific arrangements of nucleotide bases on the DNA molecule.

Since the chemical properties of DNA allow a vast ensemble of combinatorially possible arrangements of nucleotide bases, any particular sequence will necessarily be highly improbable and rich in Shannon information or information-carrying capacity. Yet within that set of possible sequences a very few will, given the multimolecular system of gene expression within the cell, produce functional proteins.[33] Those that do are thus not only improbable but also functionally "specified" or "specific," as molecular biologists use the terms. Thus, the nucleotide sequences in the coding regions of DNA possess both syntactic information and "specified" information.

A note of definitional clarity must be offered about the relationship between "specified" information and "semantic" information. Though natural languages and DNA base sequences are both specified, only natural language conveys meaning. If one defines "semantic information" as "subjectively meaningful information that is conveyed syntactically (as a string of phonemes or characters) and is understood by a conscious agent," then clearly the information in DNA does not qualify as semantic. Rather, the coding regions of DNA function in much the same way as a software program or machine code, directing operations within a complex material system via highly complex yet specified sequences of characters. As Richard Dawkins has noted, "The machine code of the genes is uncannily computer-like."[34] Or as software developer Bill Gates has noted, "DNA is like a computer program, but far, far more advanced than any software we've ever created."[35] Just as the specific arrangement of two symbols (0 and 1) in a software program can perform a function within a machine environment, so, too, can the precise sequencing of the four nucleotide bases in DNA perform a function within the cell.

Since the late 1950s, the concept of information as employed by molecular biologists has conjoined the notions of complexity (or improbability) and specificity of function. The crucial biomolecular constituents of living organisms possess not only Shannon or syntactic information but also "specified information" or "specified complexity."[36] Biological information so defined, therefore, constitutes a salient feature of living systems that any origin-of-life scenario must explain "the origin of." Further, as we will see below, all naturalistic chemical evolutionary theories have encountered difficulty explaining the origin of such functionally "specified" biological information.

F. Information as Metaphor: Nothing to Explain?

Though most molecular biologists would see nothing controversial in characterizing DNA and proteins as "information-bearing" molecules, some historians and philosophers of biology have challenged that description. Before evaluating competing types of explanation for the origin of biological information, this challenge must be addressed. In 2000, the late historian of science Lily Kay characterized the application of information theory to biology as a failure, in particular because classical information theory could not capture the idea of meaning. She suggests, therefore, that the term information as used in biology constitutes nothing more than a metaphor. Since, in Kay's view, the term does not designate anything real, it follows that the origin of "biological information" does not require explanation. Instead, only the origin of the use of the term "information" within biology requires explanation. As a social constructivist, Kay explained this usage as the result of various social forces operating within the "Cold War Technoculture."[37] In a different but related vein, Sarkar has argued that the concept of information has little theoretical significance in biology because it lacks predictive or explanatory power.[38] He, like Kay, seems to regard the concept of information as a superfluous metaphor lacking empirical reference and ontological status.

Of course, insofar as the term "information" connotes semantic meaning, it does function as a metaphor within biology. That does not mean, however, that the term functions only metaphorically or that origin-of-life biologists have nothing to explain. Though information theory has a limited application in describing biological systems, it has succeeded in rendering quantitative assessments of the complexity of biomacromolecules. Further, experimental work established the functional specificity of the sequences of monomers in DNA and proteins. Thus, the term "information" as used in biology does refer to two real and contingent properties of living systems: complexity and specificity. Indeed, since scientists began to think seriously about what would be required to explain the phenomenon of heredity, they have recognized the need for some feature or substance in living organisms possessing precisely these two properties together. Thus, Schrödinger envisioned an "aperiodic crystal"; Chargaff perceived DNA's capacity for "complex sequencing"; Watson and Crick equated complex sequences with "information," which Crick in turn equated with "specificity"; Monod equated irregular specificity in proteins with the need for "a code"; and Orgel characterized life as a "specified complexity."[39] Further, Davies has recently argued that the "specific randomness" of DNA base sequences constitutes the central mystery surrounding the origin of life.[40] Whatever the terminology, scientists have recognized the need for, and now know the location of, a source of complex specificity in the cell to transmit heredity and maintain biological function. The incorrigibility of these descriptive concepts suggests that complexity and specificity constitute real properties of biomacromolecules—indeed, properties that could be otherwise, but only to the detriment of cellular life. As Orgel notes: "Living organisms are distinguished by their specified complexity. Crystals… fail to qualify as living because they lack complexity; mixtures of random polymers fail to qualify because they lack specificity."[41]

The origin of specificity and complexity (in combination), to which the term "information" in biology commonly refers, therefore does require explanation, even if the concept of information connotes only complexity in classical information theory and even if it has no explanatory or predictive value in itself. Instead, as a descriptive (rather than as an explanatory or predictive) concept, the term "information" helps to define (either in conjunction with the notion of "specificity" or by subsuming it) the effect that origin-of-life researchers must explain "the origin of." Thus, only where "information" connotes subjective meaning does it function as a metaphor in biology. Where it refers to an analog of meaning, namely, *functional* specificity and complexity, it defines an essential feature of living systems.

II.

A. Naturalistic Explanations for the Origin of Specified Biological Information

The discoveries of molecular biologists during the 1950s and 1960s raised the question of the ultimate origin of the specified complexity or specified information in both DNA and proteins. Since at least the mid-1960s, many scientists have regarded the origin of information (so defined) as the central question facing origin-of-life biology.[42] Accordingly, origin-of-life researchers have proposed three broad types of naturalistic explanation to explain the origin of specified genetic information: those emphasizing chance, necessity, or the combination of the two.

B. Beyond the Reach of Chance

Perhaps the most common popular naturalistic view about the origin of life is that it happened exclusively by chance. A few serious scientists have also voiced support for this view, at least, at various points in their careers. In 1954, biochemist George Wald, for example, argued for the causal efficacy of chance in conjunction with vast expanses of time. As he explained, "Time is in fact the hero of the plot... Given so much time, the impossible becomes possible, the possible probable, and the probable virtually certain."[43] Later, in 1968, Francis Crick would suggest that the origin of the genetic code—that is, the translation system—might be a "frozen accident."[44] Other theories have invoked chance as an explanation for the origin of genetic information, though often in conjunction with prebiotic natural selection (see part C below).

Almost all serious origin-of-life researchers now consider "chance" an inadequate causal explanation for the origin of biological information.[45] Since molecular biologists began to appreciate the sequence specificity of proteins and nucleic acids in the 1950s and 1960s, many calculations have been made to determine the probability of formulating functional proteins and nucleic acids at random. Various methods of calculating probabilities have been offered by Morowitz, Hoyle and Wickramasinghe, Cairns-Smith, Prigogine, Yockey, and, more recently, Robert Sauer.[46] For the sake of argument, these calculations have often assumed extremely favorable prebiotic conditions (whether realistic or not), much more time than was actually available on the early earth, and theoretically maximal reaction rates among constituent monomers (that is, the constituent parts of proteins, DNA, or RNA). Such calculations have invariably shown that the probability of obtaining functionally sequenced biomacromolecules at random is, in Prigogine's words, "vanishingly small... even on the scale of... billions of years."[47] As Cairns-Smith wrote in 1971: "Blind chance... is very limited. Low levels of cooperation [it] can produce exceedingly easily (the equivalent of letters and small words), but [it] becomes very quickly incompetent as the amount of organization increases. Very soon indeed long waiting periods and massive material resources become irrelevant."[48]

Functioning proteins require amino acids that link up in functionally specified sequential arrangements, like the arrangements required in meaningful sentences. In some cases, changing even one amino acid at a given site results in the loss of protein function. Moreover, because there are twenty biologically occurring amino acids, the probability of getting a specific amino acid at a given site is small—1/20. (Actually the probability is even lower because, in nature, there are also many non-protein-forming amino acids.) On the assumption that each site in a protein chain requires a particular amino acid, the probability of attaining a particular protein 150 amino acids long would be $(1/20)^{150}$ or roughly 1 chance in 10^{195}.

Molecular biologists have known for a while that most sites along the chain can tolerate several of the different twenty amino acids commonly found in proteins without destroying the function of the protein, though some cannot. This raised an important question: How rare, or common, are the *functional* sequences of amino acids among all the possible sequences of amino acids in a chain of any given length? In the late 1980s, several important studies were conducted in the laboratory of MIT biochemist, Robert Sauer, in order to investigate this question. His research team used a sampling technique known as "cassette mutagenesis" to determine how much variance among amino acids can be tolerated at any given site in several proteins. So what did they find? Their most clear-cut experiments[49] seemed to indicate that, even taking the possibility of variance into account, the probability of achieving a functional sequence of amino acids in several known (roughly 100-residue) proteins at random is still "exceedingly small," about 1 chance in 10^{63} (to put this in perspective, there are 10^{65} atoms in our galaxy).[50] Using a variety of mutagenesis techniques, they and other scientists showed that proteins (and thus the genes that produce them) are highly specified relative to biological function.[51] Earlier studies had shown that amino acid residues at many sites cannot vary without functional loss.[52] Now Sauer and others had shown that even for sites that do admit some variance, not just any amino acid will do. Instead, they showed that functional requirements place significant constraints on sequencing at sites where some variance is allowed. By quantifying that allowable variance, they made it possible to calculate the probability of finding a protein with a functional sequence among the larger ensemble of combinatorial possibilities.

Further work in this area has been done by Douglas Axe. He asked a question similar to that which had motivated Sauer: "How rare, or common, are the amino acid sequences that produce the stable folds that make it possible for proteins to perform their biological functions?" The results of his work were published in a series of papers between 1996 and 2004.

The results of a 2004 paper were particularly telling.[53] Axe performed a mutagenesis experiment, using his refined method, on a functionally significant 150-amino-acid section of a protein called beta-lactamase, an enzyme that confers antibiotic resistance upon bacteria. On the basis of his experiments, Axe was able to make a careful estimate of the ratio of (a) the number of 150-amino-acid sequences that could perform that function to (b) the whole set of possible amino acid sequences of this length. Based on his experiments, Axe estimated this ratio to be $1/10^{77}$.

This was a staggering number, and it suggested that a random process would have great difficulty generating a protein with that particular function by chance. But origin-of-life researchers didn't just want to know the likelihood of finding a protein with a particular function within a space of combinatorial possibilities. They wanted to know the odds of finding *any* functional protein whatsoever within such a space. That number would make it possible to evaluate chance-based origin-of-life scenarios, by assessing the probability that a single protein—*any working protein*—would have arisen by chance on the early Earth.

Fortunately, Axe's work provided this number as well. Axe knew that in nature proteins perform many specific functions. He also knew that in order to perform these functions their amino acids chains must first fold into stable three-dimensional structures. Thus, before he estimated the frequency of sequences performing a specific (beta-lactamase) function, he first performed experiments that enabled him to estimate the frequency of sequences that will produce stable folds. On the basis of his experimental results, he calculated the ratio of (a) the number of 150-amino-acid sequences capable of folding into stable "function-ready" structures to (b) the whole set of possible amino acid sequences of that length. He determined that ratio to be 1 in 10^{74}. Axe's ratio of 1 in 10^{74} implied that a random process producing amino acid chains of this length would stumble onto a functional protein only about once in every 10^{74} attempts.

Axe's improved estimate of how rare functional proteins are within "sequence space" has now made it possible to calculate the probability that a 150-amino-acid compound assembled by random interactions in a prebiotic soup would be a functional protein. This calculation can be made by multiplying three independent probabilities by one another: the probability of incorporating only peptide bonds (1 in 10^{45}), the probability of incorporating only left-handed amino acids (1 in 10^{45}) and the probability of achieving correct amino acid sequencing (using Axe's 1 in 10^{74} estimate). Making that calculation (multiplying the separate probabilities by adding their exponents: $10^{45+45+74}$) gives a dramatic answer. The odds of getting a functional protein of modest length (150 amino acids) by drawing a compound of that size from a prebiotic soup is no better than 1 chance in 10^{164}. In other words, the probability of constructing a rather short functional protein at random becomes so small (no more than 1 chance in 10^{164}) as to appear absurd on the chance hypothesis.

Yet the probabilities, as small as they are, are not by themselves conclusive. One also has to consider the number of opportunities that the event in question might have had to occur. That is, one has to take into account what William Dembski calls the *probabilistic resources*.

But what were those resources—how many opportunities did the necessary proteins or genes have to arise by chance? The advocates of the chance hypothesis envisioned amino acids, or nucleotide bases, phosphates and sugars, knocking into each other in an ocean-sized soup until the correct arrangements of these building blocks arose by chance somewhere. Surely, they think, such an environment would have generated many opportunities for the assembly of functional proteins and DNA molecules. But how many? And were there enough such opportunities to render these otherwise exceedingly improbable events probable?

In order to establish an upper bound on the probabilistic resources that might be available to produce functional proteins and DNA by chance,[54] Dembski calculated the maximum number of events that could actually have taken place during the history of the observable universe.[55] His calculation was elegantly simple and yet made a powerful point.

He noted that there were about 10^{80} elementary particles[56] in the observable universe.[57] He also noted that there had been roughly 10^{16} seconds since the Big Bang. He then introduced another parameter: the shortest time in which any physical event can occur. This unit of time is the Planck time of 10^{-43} seconds. Since elementary particles can only interact with each other so many times per second (at most 10^{43} times), and since there are a limited number (10^{80}) of elementary particles, and since there has been a limited amount of time since the Big Bang (10^{16} seconds), Dembski was able to calculate the total number of events that could have taken place in the observable universe since the origin of the universe. He obtained this number by simply multiplying the three relevant factors together: the number of elementary particles (10^{80}) times the number of seconds since the Big Bang (10^{16}) times the number of possible interactions per second (10^{43}). The product, i.e., 10^{139}, provided a measure of the probabilistic resources of the entire observable universe.[58] Other mathematicians and scientists have made similar calculations.[59]

Recall Axe's calculation that the probability of producing a single 150-amino acid functional protein by chance stands at about 1 in 10^{164}. Thus, for each functional sequence of 150 amino acids, there are 10^{164} other non-functional sequences of the same length. Therefore, to have a good (i.e., better than 50/50) chance of producing a single functional protein of this length by chance, a random process would have to generate (or sample) more than half of the 10^{164} non-functional sequences corresponding to each functional sequence of that length. Unfortunately, as we see from Dembski's calculation, that number vastly exceeds the most optimistic estimate of the probabilistic resources of the universe, i.e., 10^{139}.

It seems, then, that what Mora said in 1963 still holds: "Statistical considerations, probability, complexity, etc., followed to their logical implications suggest that the origin and continuance of life is not controlled by such principles. An admission of this is the use of a period of practically infinite time to obtain the derived result. Using such logic, however, we can prove anything."[60]

C. Prebiotic Natural Selection: A Contradiction in Terms

Of course, even many early theories of chemical evolution did not rely exclusively on chance as a causal mechanism. For example, Oparin's original theory of evolutionary abiogenesis, first published in the 1920s and 1930s, invoked prebiotic natural selection as a complement to chance interactions. Oparin's theory envisioned a series of chemical reactions that he thought would enable a complex cell to assemble itself gradually and naturalistically from simple chemical precursors.

Developments in molecular biology during the 1950s cast doubt on Oparin's scenario. Oparin originally invoked natural selection to explain how cells refined primitive metabolism once it had arisen. His scenario relied heavily on chance to explain the initial formation of the constituent biomacromolecules on which even primitive cellular metabolism would depend. Discovery during the 1950s of the extreme complexity and specificity of such molecules undermined the plausibility of his claim. For that and other reasons, Oparin published a revised version of his theory in 1968 that envisioned a role for natural selection earlier in the process of abiogenesis. His new theory claimed that natural selection acted on random polymers as they formed and changed within his coacervate protocells.[61] As more complex and efficient molecules accumulated, they would have survived and reproduced more prolifically.

Even so, Oparin's concept of prebiotic natural selection acting on initially unspecified biomacromolecules remained problematic. For one thing, it seemed to presuppose a preexisting mechanism of self-replication. Yet self-replication in all extant cells depends on functional and, therefore, (to a high degree) sequence-specific proteins and nucleic acids. Yet the origin of specificity in these molecules is precisely what Oparin needed to explain. As Christian de Duve has stated, theories of prebiotic natural selection "need information which implies they have to presuppose what is to be explained in the first place."[62] Oparin attempted to circumvent the problem by claiming that the first polymers need not have been highly sequence-specific. But that claim raised doubts about whether an accurate mechanism of self-replication (and thus natural selection) could have functioned at all.

Thus, the need to explain the origin of specified information created an intractable dilemma for Oparin. On the one hand, if he invoked natural selection late in his scenario, he would need to rely on chance alone to produce the highly complex and specified biomolecules necessary to self-replication. On the other hand, if Oparin invoked natural selection earlier in the process of chemical evolution, before functional specificity in biomacromolecules would have arisen, he could give no account of how such prebiotic natural selection could even function. Thus, Dobzhansky would insist that "prebiological natural selection is a contradiction in terms."[63]

Nevertheless, during the 1980s, Richard Dawkins and Bernd-Olaf Kuppers attempted to resuscitate prebiotic natural selection as an explanation for the origin of biological information.[64] Both accepted the futility of naked appeals to chance and invoke what Kuppers calls a "Darwinian optimization principle." Both used computers to demonstrate the efficacy of prebiotic natural selection. In these computer simulations, a target sequence is selected, to represent a desired functional polymer. After creating a crop of randomly constructed sequences and generating variations among them at random, the computers select those sequences that match the target sequence most closely. The computers then amplify the production of those sequences, eliminate the others (to simulate differential reproduction), and repeat the process. As Kuppers puts it, "Every mutant sequence that agrees one bit better with the meaningful or reference sequence… will be allowed to reproduce more rapidly."[65] In his case, after a mere thirty-five generations, his computer succeeded in spelling his target sequence, "NATURAL SELECTION."

Despite superficially impressive results, such "simulations" conceal an obvious flaw: Molecules *in situ* do not have a target sequence "in mind." Nor will they confer any selective advantage on a cell, and thus differentially reproduce, until they combine in a functionally advantageous arrangement. Thus, nothing in nature corresponds to the role that the computer plays in selecting functionally non-advantageous sequences that happen to agree "one bit better" than others with a target sequence. The sequence NORMAL ELECTION may agree more with NATURAL SELECTION than does the sequence MISTRESS DEFECTION, but neither of the two yields any advantage over the other in trying to communicate something about NATURAL SELECTION. If that is the goal, both are equally ineffectual. Even more to the point, a completely nonfunctional polypeptide would confer no selective advantage on a hypothetical protocell, even if its sequence happened to agree "one bit better" with an unrealized target protein than some other nonfunctional polypeptide.

Both Kuppers's and Dawkins's published results of their simulations show the early generations of variant phrases awash in nonfunctional gibberish.[66] In Dawkins's simulation, not a single functional English word appears until after the tenth iteration (unlike the more generous example above that starts with actual, albeit incorrect, words). To make distinctions on the basis of function among sequences that have no function is entirely unrealistic. Such determinations can be made only if considerations of *proximity to possible future function* are allowed, but that requires foresight, which natural selection does not have. A computer, programmed by a human being, can perform such functions. To imply that molecules can do so as well illicitly personifies nature. Thus, if these computer simulations demonstrate anything, they subtly demonstrate the need for intelligent agents to elect some options and exclude others; that is, to create information. In *Signature in the Cell*, I show that other, more recent genetic algorithms such as *Ev* and *Avida* demonstrate this same need.[67]

D. Self-Organizational Scenarios

Because of the difficulties with chance-based theories, including those relying on prebiotic natural selection, most origin-of-life theorists after the mid-1960s attempted to address the problem of the origin of biological information in a completely different way. Researchers began to look for self-organizational laws and properties of chemical attraction that might explain the origin of the specified information in DNA and proteins. Rather than invoking chance, such theories invoked necessity. Given a limited number of broad explanatory categories, the inadequacy of chance (with or without prebiotic natural selection) has, in the minds of many researchers, left only one option. Christian de Duve articulates the logic: "A string of improbable events—drawing the same lottery number twice, or the same bridge hand twice in a row—does not happen naturally. All of which lead me to conclude that life is an obligatory manifestation of matter, bound to arise where conditions are appropriate."[68]

When origin-of-life biologists began considering the self-organizational perspective that de Duve describes, several researchers proposed that deterministic forces (stereochemical "necessity") made the origin of life not just probable but inevitable. Some suggested that simple chemicals possessed "self-ordering properties" capable of organizing the constituent parts of proteins, DNA, and RNA into the specific arrangements they now possess.[69] Steinman and Cole, for example, suggested that differential bonding affinities or forces of chemical attraction between certain amino acids might account for the origin of the sequence specificity of proteins.[70] Just as electrostatic forces draw sodium (Na^+) and chloride (Cl^-) ions together into highly ordered patterns within a crystal of salt ($NaCl$), so, too, might amino acids with special affinities for each other arrange themselves to form proteins. A discussion of other self-organization scenarios can be found in my book *Signature in the Cell*.[71]

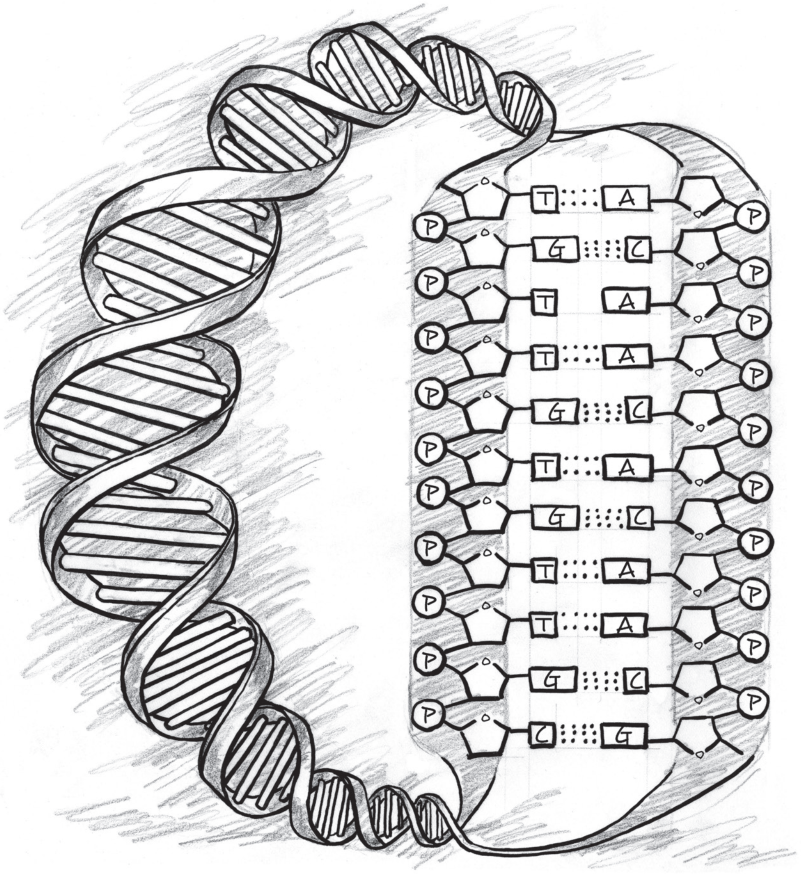

Figure 17-1. The bonding relationship between the chemical constituents of the DNA molecule.

Sugars (designated by the pentagons) and phosphates (designated by the circled Ps) are linked chemically. Nucleotide bases (A's, T's, G's and C's) are bonded to the sugar-phosphate backbones. Nucleotide bases are linked by hydrogen bonds (designated by dotted double or triple lines) across the double helix. But no chemical bonds exist between the nucleotide bases along the message-bearing spine of the helix.

Adapted by permission from an original drawing by Fred Hereen. Adaptation © 2009 by Ray Braun.

For many current origin-of-life scientists, self-organizational models now seem to offer the most promising approach to explaining the origin of specified biological information. Nevertheless, critics have called into question both the plausibility and the relevance of self-organizational models. Ironically, a prominent early advocate of self-organization, Dean Kenyon, later explicitly repudiated such theories as both incompatible with empirical findings and theoretically incoherent.[72] Kenyon voiced his doubts in his Foreword to *The Mystery of Life's Origin*, reprinted earlier in this volume.

It is true that empirical studies have shown that some differential affinities do exist between various amino acids; that is, certain amino acids do form linkages more readily with some amino acids than with others.[73] Nevertheless, such differences do not correlate to actual sequences in large classes of known proteins.[74] In short, differing chemical affinities do not explain the multiplicity of amino acid sequences existing in naturally occurring proteins or the sequential arrangement of amino acids in any particular protein.

In the case of DNA, this point can be made more dramatically. Figure 17-1 shows that the structure of DNA depends on several chemical bonds. There are bonds, for example, between the sugar and the phosphate molecules forming the two twisting backbones of the DNA molecule. There are bonds fixing individual (nucleotide) bases to the sugar-phosphate backbones on each side of the molecule. There are also hydrogen bonds stretching horizontally across the molecule between nucleotide bases, making so-called complementary pairs. The individually weak hydrogen bonds, which in concert hold two complementary copies of the DNA message text together, make replication of the genetic instructions possible. It is important to note, however, that there are no chemical bonds between the bases along the longitudinal axis in the center of the helix. Yet it is precisely along this axis of the DNA molecule that the genetic information is stored.

Just as magnetic letters can be combined and recombined in any way to form various sequences on a metal surface, so, too, can each of the four bases (A, T, G, and C) attach to any site on the DNA backbone with equal facility, making all sequences equally probable (or improbable). Indeed, there are no significant differential affinities between any of the four bases and the binding sites along the sugar-phosphate backbone. The same type of N-glycosidic bond occurs between the base and the backbone regardless of which base attaches. All four bases are acceptable; none is chemically favored. As Kuppers has noted, "The properties of nucleic acids indicate that all the combinatorially possible nucleotide patterns of a DNA are, from a chemical point of view, equivalent."[75]

Thus, "self-organizing" bonding affinities cannot explain the sequentially specific arrangement of nucleotide bases in DNA because (1) there are no bonds between bases along the information-bearing axis of the molecule, and (2) there are no differential affinities between the backbone and the specific bases that could account for variations in sequence. And because the same holds for RNA molecules, researchers who speculate that life began in an RNA world have also failed to solve the sequence specificity problem—that is, the problem of explaining how information in functioning RNA molecules could have arisen in the first place.

For those who want to explain the origin of life as the result of self-organizing properties intrinsic to the material constituents of living systems, these rather elementary facts of molecular biology have decisive implications. The most obvious place to look for self-organizing properties to explain the origin of genetic information is in the constituent parts of the molecules that carry that information. But biochemistry and molecular biology make clear that forces of attraction between the constituents in DNA, RNA, and proteins do not explain the sequence specificity of these large, information-bearing biomolecules.

The properties of the monomers constituting nucleic acids and proteins simply do not make a particular gene, let alone life as we know it, inevitable. Imagine a pool of all four DNA bases and all necessary sugars and phosphates; would any particular genetic sequence inevitably arise? Given all necessary monomers, would any particular functional protein or gene, let alone a specific genetic code, replication system, or signal transduction circuitry, inevitably arise? Clearly not. Yet de Duve has claimed that "the processes that generated life" were "highly deterministic," making life as we know it "inevitable" given "the conditions that existed on the prebiotic earth."[76]

In the parlance of origin-of-life research, monomers are "building blocks," and building blocks can be arranged and rearranged in innumerable ways. The properties of stone blocks do not determine their own arrangement in the construction of buildings. Similarly, the properties of biological building blocks do not determine the arrangement of functional polymers. Instead, the chemical properties of the monomers allow a vast ensemble of possible configurations, the overwhelming majority of which have no biological function whatsoever. Functional genes or proteins are no more inevitable, given the properties of their "building blocks," than, for example, the Palace of Versailles was inevitable, given the properties of the stone blocks that were used to construct it.

Significantly, information theory makes clear that there is a good reason for this. If chemical affinities between the constituents in the DNA determined the arrangement of the bases, such affinities would dramatically diminish the capacity of DNA to carry information. Recall that classical information theory equates the reduction of uncertainty with the transmission of information, whether specified or unspecified. The transmission of information, therefore, requires physical-chemical contingency. As Robert Stalnaker has noted, "[information] content requires contingency."[77] If, therefore, forces of chemical necessity completely determine the arrangement of constituents in a system, that arrangement will not exhibit complexity or convey information.

Consider, for example, what would happen if the individual nucleotide bases (A, C, G, and T) in the DNA molecule did interact by chemical necessity (along the information-bearing axis of DNA). Suppose that every time adenine (A) occurred in a growing genetic sequence, it attracted cytosine (C) to it.[78] Suppose every time guanine (G) appeared, thymine (T) followed. If this were the case, the longitudinal axis of

DNA would be peppered with repetitive sequences in which C followed A and T followed G. Rather than a genetic molecule capable of virtually unlimited novelty and characterized by unpredictable and aperiodic sequences, DNA would contain sequences awash in repetition or redundancy—much like the arrangement of atoms in crystals. In a crystal, the forces of mutual chemical attraction do determine, to a very considerable extent, the sequential arrangement of its constituent parts. Hence, sequencing in crystals is highly ordered and repetitive but neither complex nor informative. In DNA, however, where any nucleotide can follow any other, a vast array of novel sequences is possible, corresponding to a multiplicity of possible amino acid sequences and protein functions.

The forces of chemical necessity produce redundancy (roughly, law- or rule-generated repetition) or monotonous order but reduce the capacity to convey information and express novelty. Thus, as chemist Michael Polanyi noted:

> Suppose that the actual structure of a DNA molecule were due to the fact that the bindings of its bases were much stronger than the bindings would be for any other distribution of bases, then such a DNA molecule would have no information content. Its code-like character would be effaced by an overwhelming redundancy... Whatever may be the origin of a DNA configuration, it can function as a code only if its order is not due to the forces of potential energy. It *must be* as physically indeterminate as the sequence of words is on a printed page [emphasis added].[79]

Bonding affinities, to the extent they exist, inhibit the maximization of information because they determine that specific outcomes will follow specific conditions with high probability.[80] Yet information-carrying capacity is maximized when just the opposite situation obtains, namely, when antecedent conditions allow many improbable outcomes. Chemical affinities do not generate complex sequences. Thus, they cannot be invoked to explain the origin of information, whether specified or otherwise.

A tendency to conflate the qualitative distinctions between "order" and "complexity" has characterized self-organizational scenarios—whether those that invoke internal properties of chemical attraction or an external organizing force or source of energy. That tendency calls into question the relevance of these scenarios of the origin of life. What needs explaining in biology is not the origin of order (defined as symmetry or repetition) but of specified information—the highly complex, aperiodic, and specified sequences that make biological function possible. As Yockey warns: "Attempts to relate the idea of order… with biological organization or specificity must be regarded as a play on words that cannot stand careful scrutiny."[81]

In the face of these difficulties, some self-organizational theorists have claimed that we must await the discovery of new natural laws to explain the origin of biological information. As Manfred Eigen has argued, "our task is to find an algorithm, a natural law, that leads to the origin of information."[82] Such a suggestion betrays confusion on two counts. First, scientific laws don't generally produce or cause natural phenomena, they describe them. For example, Newton's law of gravitation described, but did not cause or explain, the attraction between planetary bodies. Second, laws necessarily describe highly deterministic or predictable relationships between antecedent conditions and consequent events. Laws describe highly repetitive patterns in which the probability of each successive event (given the previous event) approaches unity. Yet information sequences are complex, not repetitive—information mounts as improbabilities multiply. Thus, to say that scientific laws can produce information is essentially a contradiction in terms. Instead, scientific laws describe (almost by definition) highly predictable and regular phenomena—that is, redundant order, not complexity (whether specified or otherwise).

One could argue that we might someday discover a very particular configuration of initial conditions that routinely generates high informational states. Yet the statement of this hypothetical seems itself to beg the question of the ultimate origin of information, since "a very particular set of initial conditions" sounds precisely like an information-rich—a highly complex and specified—state. In any case, everything we know experientially suggests that the amount of specified information present in a set of antecedent conditions necessarily equals or exceeds that of any system produced from those conditions.

E. The RNA World Scenario and the Displacement of the Information Problem

In addition to the general categories of explanation already examined, origin-of-life researchers have proposed many more specific scenarios, each emphasizing random variations (chance), self-organizational laws (necessity), or both. Some of those scenarios purport to address the information problem; others attempt to bypass it altogether. Yet on closer examination, even scenarios that appear to alleviate the problem of the origin of specified biological information merely shift the problem elsewhere. Genetic algorithms can "solve" the information problem, but only if programmers provide informative target sequences and selection criteria. Simulation experiments can produce biologically relevant precursors and sequences, but only if experimentalists manipulate initial conditions or select and guide outcomes—that is, only if they add information themselves. As discussed in detail in my book *Signature in the Cell*, origin-of-life theories can leapfrog the problem altogether, but only by presupposing the presence of information in some other preexisting form.[83]

For example, some have claimed that the RNA-world scenario offers a promising approach to the origin-of-life problem and with it, presumably, the problem of the origin of the first genetic information. The RNA world was proposed as an explanation for the origin of the interdependence of nucleic acids and proteins in the cell's information-processing system. In extant cells, building proteins requires genetic information from DNA, but information in DNA cannot be processed without many specific proteins and protein complexes. This poses a chicken-or-egg problem. The discovery that RNA (a nucleic acid) possesses some limited catalytic properties similar to those of proteins suggested a way to solve that problem. "RNA-first" advocates proposed an early state in which RNA performed both the enzymatic functions of modern proteins and the information-storage function of modern DNA, thus allegedly making the interdependence of DNA and proteins unnecessary in the earliest living system.

Nevertheless, many fundamental difficulties with the RNA-world scenario have emerged. First, synthesizing (and/or maintaining) many essential building blocks of the RNA molecules under realistic conditions has proven either difficult or impossible.[84] Further, the chemical conditions required for the synthesis of ribose sugars are decidedly incompatible with the conditions required for synthesizing nucleotide bases.[85] Yet both are necessary constituents of RNA. Second, naturally occurring RNA possesses very few of the specific enzymatic properties of proteins necessary to extant cells. In fact, RNA catalysts do not function as true enzyme catalysts. Enzymes are capable of coupling energetically favorable and unfavorable reactions together. RNA catalysts, so-called "ribozymes," are not. Third, RNA-world advocates offer no plausible explanation for the transitions from (1) RNA-based RNA synthesis to (2) RNA-based protein synthesis to (3) the modern DNA, RNA *and* protein-based protein synthesis translation system used in cells today.[86] Fourth, attempts to enhance the limited catalytic properties of RNA molecules in so-called ribozyme engineering experiments have inevitably required extensive investigator manipulation, thus simulating, if anything, the need for intelligent design, not the efficacy of an undirected chemical evolutionary process.[87]

Most importantly for our present considerations, the RNA-world hypothesis presupposes, but does not explain, the origin of sequence specificity or information in the original functional RNA molecules. As noted, the RNA-world scenario was proposed as an explanation for the functional interdependence problem, not the information problem. Even so, some RNA-world advocates seem to envision leapfrogging the sequence-specificity problem. They imagine oligomers of RNA arising by chance on the prebiotic earth and then later acquiring an ability to polymerize copies of themselves—that is, to self-replicate. In such a scenario, the capacity to self-replicate would favor the survival of those RNA molecules that could do so and would thus favor the specific sequences that the first self-replicating molecules happened to have. Thus, sequences that originally arose by chance would subsequently acquire a functional significance as "an accidental choice remembered."

This suggestion, however, merely shifts the information problem out of view. To date, scientists have been able to design RNA catalysts that will copy only about 10% of themselves.[88] For strands of RNA to perform even this limited replicase (self-replication) function, they must, like proteins, have very specific arrangements of constituent building blocks (nucleotides in the RNA case). Further, the strands must be long enough to fold into complex three-dimensional shapes (to form so-called tertiary structures). Thus, any RNA molecule capable of even limited replicase function must have possessed considerable (specified) information[89]—information that, in the case of actual (partial) RNA replicators was produced by intelligent "ribozyme engineers."

Indeed, explaining how the building blocks of RNA arranged themselves into functionally specified sequences in a prebiotic environment has proven no easier than explaining how the constituent parts of DNA might have done so, especially given the high probability of destructive cross-reactions between desirable and undesirable molecules in any realistic pre-biotic soup. As de Duve noted in a critique of the RNA-world hypothesis, "hitching the components together in the right manner raises additional problems of such magnitude that no one has yet attempted to do so in a prebiotic context."[90]

Recently some have claimed that a scientific study by chemists Matthew Powner, Béatrice Gerland, and John Sutherland of the University of Manchester[91] has rendered the RNA scenario "eminently plausible,"[92] as Stephen Fletcher, a chemist from the University of Loughborough, has put it. Starting with several simple chemical compounds, Powner and his colleagues successfully synthesized a pyrimidine ribonucleotide, one of the two types of the four bases of the RNA molecule. (Of the four information-carrying nucleotide bases in DNA and RNA, chemists classify two as "pyrimidines" and two as "purines" due to differences in chemical structure.)

Nevertheless, this work did nothing to address the much more acute problem of explaining how the nucleotide bases in DNA or RNA acquired their specific information-rich arrangements. In effect, the Powner study putatively explains the origin of two of the "letters" in the genetic text, but not the specific arrangements of the four different "letters" into functional genetic "words" or "sentences."

Moreover, Powner and his colleagues only partially addressed the problem of generating the constituent building blocks of RNA under plausible pre-biotic conditions. The weakness in their demonstration, ironically, was their own skillful intervention. To ensure a biologically relevant outcome, they had to intervene—repeatedly and intelligently—in their experiment: first, by selecting only the "right-handed" versions of sugar that life requires (sugars, like amino acids, come in two mirror-image chemical structures called isomers); second, by purifying their reaction products at each step to prevent interfering cross-reactions; and third, by following a precise procedure in which they carefully selected chemically purified reagents and then choreographed the order in which those reagents were introduced into the reaction series. As my colleague David Berlinski pointed out, "They began with what they needed and purified what they got until they got what they wanted."

Thus, not only did this study *not* address the problem of getting nucleotide bases to arrange themselves into functionally specified sequences, but the extent to which it did succeed in producing biologically relevant chemical constituents of RNA actually illustrates the indispensable role of *intelligence* in generating such chemistry.

Proponents of chemical evolution have also cited the more recent work of Tracey Lincoln and Gerald Joyce,[93] who have ostensibly established the capacity of RNA to self-replicate as a way of demonstrating the plausibility of the RNA World. Nevertheless, their "self-replicating"

RNA molecules could not copy a template of genetic information from free-standing nucleotides as protein machines (called polymerases) do in actual cells. Instead, in the experiment, a pre-synthesized *specifically sequenced* RNA molecule merely catalyzed a single chemical bond, fusing together two other pre-synthesized partial RNA chains. Their version of "self-replication," therefore, amounted to nothing more than joining two sequence-specific pre-made halves together.

More significantly, Lincoln and Joyce themselves *intelligently arranged* the base sequences in these RNA chains. They generated the sequence-specific functional information that made even this limited form of "self-replication" possible. Thus, the experiment not only demonstrated that even a limited capacity for RNA self-replication depends upon information-rich RNA molecules, it also lent inadvertent support to the idea that intelligence is necessary to produce such functionally specified information. The Lincoln and Joyce experiment illustrates a well-known problem in origin-of-life research known as "investigator interference," wherein the "success" of the experiment invariably and crucially depends on the intervention, guidance, or choreography of *intelligent* chemists doing the organic synthesis experiments.

III.

A. The Return of the Design Hypothesis

If attempts to solve the information problem only relocate it, and if neither chance nor physical-chemical necessity, nor the two acting in combination, explains the ultimate origin of specified biological information, what does? Do we know of any entity that has the causal powers to create large amounts of specified information? We do. As Henry Quastler recognized, "creation of new information is habitually associated with conscious activity."[94]

Indeed, experience affirms that functionally specified information routinely arises from the activity of intelligent agents. A computer user who traces the information on a screen back to its source invariably comes to a mind, that of a software engineer or programmer. Similarly, the information in a book or newspaper column ultimately derives from a writer—from a mental, rather than a strictly material, cause.

But could this intuitive connection between information and the prior activity of a designing intelligence justify a rigorous scientific argument for intelligent design? I first began to consider this possibility during my PhD research at Cambridge University in the late 1980s, after reading *The Mystery of Life's Origin* and extensive discussions with Charles Thaxton during my last year in Dallas before leaving for England. During my PhD work, I began to examine how scientists investigating origins events developed and evaluated their hypotheses and arguments. Specifically, I examined the method of reasoning that historical scientists use to identify causes responsible for events in the remote past.

I discovered that historical scientists often make inferences with a distinctive logical form (known technically as *abductive inferences*).[95] Paleontologists, evolutionary biologists, and other historical scientists reason like detectives and infer *past* conditions or causes from *present* clues. As Stephen Jay Gould notes, historical scientists typically "infer history from its results."[96]

Nevertheless, as many philosophers have noted, there is a problem with this kind of historical reasoning, namely, there is often more than one cause that can explain the same effect. This makes reasoning from present clues (circumstantial evidence) tricky because the evidence can point to more than one causal explanation or hypothesis. To address this problem in geology, the nineteenth-century geologist Thomas Chamberlain delineated a method of reasoning he called "the method of multiple working hypotheses."[97]

Contemporary philosophers of science such as Peter Lipton have called this the method of "inference to the best explanation."[98] That is, when trying to explain the origin of an event or structure from the past, scientists often compare various hypotheses to see which would, if true, best explain it. They then provisionally affirm the hypothesis that best explains the data as the one that is most likely to be true. But that raises an important question: Exactly what makes an explanation best?

As it happens, historical scientists have developed criteria for deciding which cause, among a group of competing possible causes, provides the best explanation for some event in the remote past. The most important of these criteria is called "causal adequacy." This criterion requires that historical scientists, as a condition of a successful explanation, identify causes that are known to have the power to produce the kind of effect, feature or event that requires explanation. In making these determinations, historical scientists evaluate hypotheses against their present knowledge of cause and effect. Causes that are known to produce the effect in question are judged to be better candidates than those that are not. For instance, a volcanic eruption provides a better explanation for an ash layer in the earth than an earthquake because eruptions have been observed to produce ash layers, whereas earthquakes have not.

One of the first scientists to develop this principle was the geologist Charles Lyell who also influenced Charles Darwin. Darwin read Lyell's *magnum opus, The Principles of Geology,* on the voyage of the *Beagle* and employed its principles of reasoning in *The Origin of Species*. The subtitle of Lyell's *Principles* summarized the geologist's central methodological principle: *Being an Attempt to Explain the Former Changes of the Earth's Surface, by Reference to Causes Now in Operation.*[99] Lyell argued that when scientists seek to explain events in the past, they should not invoke unknown or exotic causes, the effects of which we do not know. Instead they should cite causes that are known from our uniform experience to have the power to produce the effect in question. Historical scientists should cite "causes now in operation" or presently acting causes. This was the idea behind his uniformitarian principle and the dictum: "The present is the key to the past." According to Lyell, our *present* experience of cause and effect should guide our reasoning about the causes of *past* events. Darwin himself adopted this methodological principle as he sought to demonstrate that natural selection qualified as a *vera causa*, that is, a true, known, or actual cause of significant biological change. He sought to show that natural selection was "causally adequate" to produce the effects he was trying to explain.[100]

Both philosophers of science and leading historical scientists have emphasized causal adequacy as the key criterion by which competing hypotheses are adjudicated. But philosophers of science also have noted that assessments of explanatory power lead to conclusive inferences only when it can be shown that there is *only one known cause* for the effect or evidence in question. Philosophers of science Michael Scriven and Elliot Sober, for example, have pointed out that historical scientists can make inferences about the past with confidence when they discover evidence or artifacts for which there is only one cause known to be capable of producing them.[101] Indeed, when scientists can infer a *uniquely* plausible cause, they can avoid the fallacy of affirming the consequent and the error of ignoring other possible causes with the power to produce the same effect.[102]

B. Intelligent Design as the Best Explanation?

What did all this have to do with the origin of the information necessary to produce the first life? As a PhD student I wondered if a case for an intelligent cause could be formulated and justified in the same way that historical scientists would justify any other causal claim about an event in the past. My study of historical scientific reasoning and origin-of-life research suggested to me that it was possible to formulate a rigorous scientific case for intelligent design as an inference to the best explanation, specifically, as the best explanation for the origin of biological information. The action of a conscious and intelligent agent clearly represents a known (presently acting) and adequate cause for the origin of information. Uniform and repeated experience affirms that intelligent agents produce information-rich systems, whether software programs, ancient inscriptions, or Shakespearean sonnets. Minds are clearly capable of generating functionally specified information.

Further, the functionally specified information in the cell also points to intelligent design as the *best* explanation for the ultimate origin of biological information. Why? Experience shows that large amounts[103] of such information (especially when digitally or alphabetically encoded) *invariably* originate from an intelligent source—from a mind or a personal agent. In other words, intelligent activity is *the only known cause* of the origin of functionally specified information (at least, starting from a non-living source, that is, from purely physical or chemical antecedents).[104] Since intelligence is the only known cause of specified information in such a context, the presence of functionally specified information sequences in even the simplest living systems points definitely to the past existence and activity of a designing intelligence.

Notice also that one can detect (or retrodict) the past action of a designing intelligence from an information-rich effect even if the cause itself cannot be directly observed.[105] For example, the information-rich inscriptions in the famed Rosetta Stone clearly allow archeologists to infer the activity of intelligent scribes even if they did not see such agents chisel the letters and hierogylphs into the stone. Similarly, the specified and complex arrangements of nucleotide bases in DNA imply the past action of intelligence, even if such activity cannot be directly observed.

Ironically, the generalization that intelligence is the only known cause of specified complexity or information (at least, starting from a nonbiological source) has received support from origin-of-life research itself. During the last fifty years, every naturalistic model proposed has failed to explain the origin of the specified genetic information required to build a living cell.[106] Instead, attempts to solve the origin-of-life problem with pre-biotic simulation experiments and computer simulations have invariably required inputs of functional information from intelligent agents, further confirming intelligence as the only known or "presently acting" cause of the origin of functionally specified information.

When I first noticed the subtitle of Lyell's book, referring us to "causes now in operation," a light came on for me. I immediately asked myself a question: "What causes 'now in operation' produce digital code or specified information?" Is there a known cause—a *vera causa*—of the origin of such information? What does our uniform experience tell us?

As I thought about this further, it occurred to me that by Lyell's and Darwin's own rule of reasoning and test of a sound scientific explanation, intelligent design must qualify as the currently best scientific explanation for the origin of biological information. Why? Because we have independent evidence—"uniform experience"—that intelligent agents are capable of producing specified information and, as origin-of-life research itself has helped to demonstrate, we know of no other cause capable of producing functional or specified information starting from a purely physical or chemical state.

Scientists in many fields recognize the connection between intelligence and specified information and make inferences accordingly. Anthropologists establish the intelligence of early hominids from chipped flints that are too improbably specified in form (and function) to have been produced by natural causes; NASA's search for extraterrestrial intelligence (SETI) presupposes that any information embedded in electromagnetic signals coming from space would indicate an intelligent source.[107] Astronomers have not found such information-rich signals coming from space, but closer to home, molecular biologists have identified information-rich sequences and systems in the cell, suggesting, by the same logic, an intelligent cause for those effects.

Indeed, our uniform experience affirms that specified information—whether inscribed in hieroglyphs, written in a book, encoded in a terrestrial radio signal, or produced in an RNA-world "ribozyme engineering" experiment—*always* arises from an intelligent source, from a mind and not a strictly material process. So the discovery of the functionally specified digital information in DNA and RNA provides strong grounds for inferring that intelligence played a role in the origin of these molecules. Whenever we find specified information and we know the causal story of how that information arose, we always find that it arose from an intelligent source. It follows that the best, most likely explanation for the origin of the specified, digitally encoded information in DNA and RNA is that it too had an intelligent source. Intelligent design best explains the specified genetic information necessary to produce the first living cell.

C. Argument from Ignorance? Or an Inference to the Best Explanation?

Objectors charge that this design argument constitutes an argument from ignorance. They say that design advocates use our present ignorance of any sufficient materialistic cause of specified information as the sole basis for inferring an intelligent cause of the information present in the cell. Since we don't yet know how specified biological information could have arisen, we invoke the mysterious notion of intelligent design. On this view, intelligent design functions not as an explanation but as a placeholder for ignorance.

My response is that arguments from ignorance occur when evidence against a proposition X is offered as the sole (and conclusive) grounds for accepting some alternative proposition Y. The inference to design as sketched above (see part III, sections A and B) does not commit this fallacy.

True, the previous part of this chapter (see part II, sections A–E) argued that at present all types of natural causes and mechanisms fail to account for the origin of biological information from a prebiotic state. And clearly, this lack of knowledge of any adequate natural cause does provide *part* of the grounds for inferring design from information in the cell; but our "ignorance" of any sufficient natural cause is only part of the basis for inferring design. We also *know* that intelligent agents can and do produce information-rich systems: we have positive experience-based knowledge of an alternative cause that is sufficient, namely, intelligence or "conscious activity."

For this reason, the design inference defended here does not constitute an argument from ignorance but an inference to the best explanation.[108] Inferences to the best explanation do not assert the adequacy of one causal explanation merely on the basis of the inadequacy of some other causal explanation. Instead, they compare the explanatory power of many competing hypotheses to determine which hypothesis would, if true, provide the best explanation for some set of relevant data based upon our *knowledge* of the causal powers of competing explanatory entities.[109]

This chapter has followed precisely this method to make a case for intelligent design as the best explanation for the origin of biological information. It has evaluated and compared the causal efficacy of four broad categories of explanation—chance, necessity, the combination of those two, and intelligent design—with respect to their ability to produce large amounts of specified complexity or information. As we have seen, neither scenarios based on chance nor those based on necessity (nor those that combine the two) can explain the origin of specified biological information in a prebiotic context. That result comports with our uniform human experience. Natural processes do not produce information-rich structures starting from purely physical or chemical antecedents. Nor does matter, whether acting at random or under the force of physical-chemical necessity, arrange itself into complex, information-rich sequences.

On the other hand, we know from experience that conscious intelligent agents can create informational sequences and systems. To quote Quastler, "creation of new information is habitually associated with conscious activity."[110] Further, experience teaches that whenever large amounts of specified complexity or information are present in an artifact or entity whose causal story is known, invariably creative intelligence—intelligent design—played a causal role in the origin of that entity. Thus, when we encounter such information in the biomacromolecules necessary to life, we may infer—based on our *knowledge* (not our ignorance) of established cause-effect relationships—that an intelligent cause operated in the past to produce the specified complexity or information necessary to the origin of life.

Insofar as the inference to design depends on present knowledge of the demonstrated causal powers of natural entities and intelligent agency, it no more constitutes an argument from ignorance than any other well-grounded inference in geology, archaeology, or paleontology—where present knowledge of cause-effect relationships guides the inferences that scientists make about the causal past.

Some objectors would characterize the design inference presented here as invalid or unscientific because it depends on a negative generalization—i.e., "purely physical and chemical causes do not generate large amounts of specified information"—which future discoveries may later falsify. We should "never say never," they say.

Yet science often says "never," even if it can't say so for sure. Negative or proscriptive generalizations often play an important role in science. As many scientists and philosophers of science have pointed out, scientific laws often tell us not only what does happen but also what does not happen.[111] The conservation laws in thermodynamics, for example, proscribe certain outcomes. The first law tells us that energy is never created or destroyed. The second tells us that the entropy of a closed system will never decrease over time. Those who claim that such "proscriptive laws" do not constitute knowledge, because they are based on past but not future experience, will not get very far if they try to use their skepticism to justify funding for research on, say, perpetual motion machines.

Further, without proscriptive generalizations, without knowledge about what various possible causes cannot or do not produce, historical scientists could not make determinations about the past. Reconstructing the past requires making abductive inferences from present effects back to past causal events.[112] Making such inferences requires a progressive elimination of competing causal hypotheses. Deciding which causes can be eliminated from consideration requires knowing what effects a given cause can—and cannot—produce. If historical scientists could never say that particular entities lack particular causal powers, they could never eliminate them, even provisionally, from consideration. Thus, they could never infer that a specific cause had acted in the past. Yet historical and forensic scientists make such inferences all the time, without worrying about committing fallacious arguments from ignorance. And for good reason. A vast amount of human experience shows that intelligent agents have unique causal powers that matter (especially nonliving matter) does not. When we observe features or effects that we know from experience only agents produce, we rightly infer the prior activity of intelligence.

To determine the best explanation, scientists do not need to say "never" with absolute certainty. They need only say that a postulated cause is best, given what we know at present about the demonstrated causal powers of competing entities or agencies. That cause C can produce effect E makes it a better explanation of E than some cause D that has never produced E (especially if D seems incapable of doing so on theoretical grounds), even if D might later demonstrate causal powers of which we are presently ignorant.[113]

Thus, the objection that the design inference constitutes an argument from ignorance reduces in essence to a restatement of the problem of induction. Yet one could make the same objection against any scientific law or explanation or against any historical inference that takes present, but not future, knowledge of natural laws and causal powers into account. Our knowledge of what can and cannot produce large amounts of specified information may later have to be revised, but so might the laws of thermodynamics. Inferences to design may later prove incorrect, as may other inferences implicating various natural causes. Such possibilities do not stop scientists from making generalizations about the causal powers of various entities or from using those generalizations to identify probable or most plausible causes in particular cases.

D. But Is It Science?

Of course, many simply refuse to consider the design hypothesis on grounds that it does not qualify as "scientific." Such critics affirm an extra-evidential principle known as methodological naturalism.[114] Methodological naturalism asserts that, as a matter of definition, for a hypothesis, theory, or explanation to qualify as "scientific," it must invoke only naturalistic or materialistic entities. On that definition, critics say, the intelligent design hypothesis does not qualify. Yet, even if one grants this definition, it does not follow that some nonscientific (as defined by methodological naturalism) or metaphysical hypothesis may not constitute a better, more causally adequate, explanation. This chapter has argued that, whatever its classification, the design hypothesis does constitute a better explanation than its materialistic or naturalistic rivals for the origin of specified biological information. Surely, simply classifying an argument as metaphysical does not refute it.

In any case, methodological naturalism now lacks justification as a normative definition of science. First, attempts to justify methodological naturalism by reference to metaphysically neutral (that is, non-question-begging) demarcation criteria have failed.[115] Second, to assert methodological naturalism as a normative principle for all of science has a negative effect on the practice of certain scientific disciplines, especially the historical sciences. In origin-of-life research, for example, methodological naturalism artificially restricts inquiry and prevents scientists from seeking some hypotheses that might provide the best, most causally adequate explanations. To be a truth-seeking endeavor, the question that origin-of-life research must address is not "Which materialistic scenario seems most adequate?" but rather "What actually caused life to arise on Earth?" Clearly, one possible answer to that latter question is this one: "Life was designed by an intelligent agent that existed before the advent of humans." If one accepts methodological naturalism as normative, however, scientists are not allowed to consider the design hypothesis as possibly true. Such an exclusionary logic diminishes the significance of any claim of theoretical superiority for non-design hypotheses and raises the possibility that the best "scientific" explanation (as defined by methodological naturalism) may not be the best in fact.

As many historians and philosophers of science now recognize, theory-evaluation is an inherently comparative enterprise. Theories that gain acceptance in artificially constrained competitions can claim to be neither "most probably true" nor "most empirically adequate." At best, such theories can be considered "the most probably true or adequate among an artificially limited set of options." Openness to the design hypothesis would seem necessary, therefore, to any fully rational historical biology—that is, to one that seeks the truth, "no holds barred."[116] A historical biology committed to following the evidence wherever it leads will not exclude hypotheses *a priori* on metaphysical grounds. Instead, it will employ only metaphysically neutral criteria—such as explanatory power and causal adequacy—to evaluate competing hypotheses. Yet this more open (and seemingly rational) approach to scientific theory evaluation would now suggest the theory of intelligent design as the best, most causally adequate explanation for the origin of the information necessary to build the first living organism.

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18. Judson, *Eighth Day*, 245–46, 335–36.
19. *Ibid*., 470–89; J. H. Matthei and M. W. Nirenberg, "Characteristics and Stabilization of DNAase-Sensitive Protein Synthesis in *E. coli* Extracts," *Proceedings of the National Academy of Sciences, USA* 47 (1961): 1580–88; J. H. Matthei and M. W. Nirenberg, "The Dependence of Cell-Free Protein Synthesis in *E. coli* upon Naturally Occurring or Synthetic Polyribonucleotides," *Proceedings of the National Academy of Sciences, USA* 47 (1961): 1588–1602.
20. Alberts et al., *Molecular Biology*, 106–8; S. L. Wolfe, *Molecular and Cellular Biology* (Belmont, CA: Wadsworth, 1993), 639–48.
21. We now know, of course, that in addition to the process of gene expression, specific enzymes must often modify amino acid chains after translation in order to achieve the precise sequencing necessary to allow correct folding into a functional protein. The amino acid chains produced by gene expression may also undergo further modification in sequence at the endoplasmic reticulum. Finally, even well-modified amino acid chains may require preexisting protein "chaperones" to help them fold into a functional three-dimensional configuration. All these factors make it impossible to predict a protein's final sequence from its corresponding gene sequence alone. See S. Sarkar, "Biological Information: A Skeptical Look at Some Central Dogmas of Molecular Biology," in *The Philosophy and History of Molecular Biology: New Perspectives*, ed. S. Sarkar (Dordrecht, Netherlands: Boston Studies in Philosophy of Science, 1996), 196, 199–202. Nevertheless, this unpredictability in no way undermines the claim that DNA exhibits the property of "sequence specificity," or the isomorphic claim that it contains "specified information" as argued here in part I, section E. Sarkar argues, for example, that the absence of such predictability renders the concept of information theoretically superfluous for molecular biology. Instead, this unpredictability shows that the sequence specificity of DNA base sequences constitutes a necessary, though not sufficient, condition of attaining proper protein folding; that is, DNA does contain specified information (part I, section E), but not enough to determine protein folding by itself. Instead, the presence of both post-translation processes of modification and pretranscriptional genomic editing (through exonucleases, endonucleases, spliceosomes, and other editing enzymes) only underscores the need for other preexisting, information-rich biomolecules in order to process genomic information in the cell. The presence of a complex and functionally integrated information-processing system does suggest that the informa-

tion on the DNA molecule is insufficient to produce proteins. It does not show that such information is unnecessary to produce proteins, nor does it invalidate the claim that DNA, therefore, stores and transmits specified genetic information.

22. C. Shannon, "A Mathematical Theory of Communication," *Bell System Technical Journal* 27 (1948): 379–423, 623–56.
23. F. Dretske, *Knowledge and the Flow of Information* (Cambridge: MIT Press, 1981), 6–10.
24. *Ibid.*; Shannon, "A Mathematical Theory."
25. B. Kuppers, "On the Prior Probability of the Existence of Life," in *The Probabilistic Revolution*, ed. Lorenz Kruger et al. (Cambridge: MIT Press, 1987), 355–69.
26. Schneider, "Information Content"; see also H. P. Yockey, *Information Theory and Molecular Biology* (Cambridge: Cambridge University Press, 1992), 246–58, for important refinements in the method of calculating the information-carrying capacity of proteins and DNA.
27. C. Shannon and W. Weaver, *The Mathematical Theory of Communication* (Urbana: University of Illinois Press, 1949), 8.
28. Schneider, "Information Content," 58–177; Yockey, *Information Theory*, 58–177.
29. Schneider, "Information Content"; Yockey, *Information Theory*; Sarkar, "Biological Information," 199–202, esp. 196; F. Crick, "On Protein Synthesis," *Symposium for the Society of Experimental Biology* 12 (1958): 138–63, esp. 144, 153.
30. Crick, "On Protein Synthesis," 144, 153.
31. Recall that the determination of the genetic code depended, for example, on observed correlations between changes in nucleotide base sequences and amino acid production in "cell-free systems." See Judson, *Eighth Day*, 470–87.
32. For a much more detailed discussion of specification, see W. A. Dembski, *The Design Inference: Eliminating Chance through Small Probabilities* (Cambridge: Cambridge University Press, 1998), 1–35, 136–74. The simplified discussion here draws in part on Stephen Meyer, "Yes, Intelligent Design Is Detectable by Science," *Evolution News*, April 24, 2018, https://evolutionnews.org/2018/04/yes-intelligent-design-is-detectable-by-science/.
33. J. Bowie and R. Sauer, "Identifying Determinants of Folding and Activity for a Protein of Unknown Sequences: Tolerance to Amino Acid Substitution," *Proceedings of the National Academy of Sciences, USA* 86 (1989): 2152–56; J. Reidhaar-Olson and R. Sauer, "Functionally Acceptable Solutions in Two Alpha-Helical Regions of Lambda Repressor," *Proteins, Structure, Function, and Genetics* 7 (1990): 306–10.
34. R. Dawkins, *River out of Eden* (New York: Basic Books, 1995), 11.
35. B. Gates, *The Road Ahead* (Boulder, CO: Blue Penguin, 1996), 228.
36. L. E. Orgel, *The Origins of Life* (New York: John Wiley, 1973), 189.
37. Kay, "Who Wrote the Book of Life?" 611–12, 629; Kay, "Cybernetics"; Kay, *Who Wrote the Book of Life?* (For full details for Kay references, see note 5 above.)
38. Sarkar, "Biological Information," 199–202.
39. E. Schrödinger, *What Is Life?* and *Mind and Matter* (Cambridge: Cambridge University Press, 1967), 82; Alberts et al., *Molecular Biology*, 21; Crick and Watson, "A Structure"; Crick and Watson, "Genetical Implications"; Crick, "On Protein"; Judson, *Eighth Day*, 611; Orgel, *Origins of Life*, 189.
40. P. Davies, *The Fifth Miracle* (New York: Simon and Schuster, 1998), 120.
41. Orgel, *Origins of Life*, 189.

42. Loewenstein, *Touchstone*; Davies, *Fifth Miracle*; Schneider, "Information Content"; C. Thaxton and W. Bradley, "Information and the Origin of Life," in The *Creation Hypothesis: Scientific Evidence for an Intelligent Designer*, ed. J. P. Moreland (Downers Grove, IL: InterVarsity Press, 1994), 173–210, esp. 190; S. Kauffman, *The Origins of Order* (Oxford: Oxford University Press, 1993), 287–340; Yockey, *Information Theory*, 178–293; Kuppers, *Information and Origin*, 170–72; F. Crick, *Life Itself* (New York: Simon and Schuster, 1981), 59–60, 88; J. Monod, *Chance and Necessity* (New York: Vintage Books, 1971), 97–98, 143; Orgel, *Origins*, 189; D. Kenyon and G. Steinman, *Biochemical Predestination* (New York: McGraw-Hill, 1969), 199–211, 263–66; Oparin, *Genesis*, 146–47; H. Quastler, *The Emergence of Biological Organization* (New Haven, CT: Yale University Press, 1964).

43. G. Wald, "The Origin of Life," *Scientific American* 191 (August 1954): 44–53; R. Shapiro, *Origins: A Skeptic's Guide to the Creation of Life on Earth* (New York: Summit Books, 1986), 121.

44. F. Crick, "The Origin of the Genetic Code," *Journal of Molecular Biology* 38 (1968): 367–79; H. Kamminga, "Studies in the History of Ideas on the Origin of Life from 1860" (PhD dissertation, Chelsea College, University of London, 1980), 303–4.

45. C. de Duve, "The Constraints of Chance," *Scientific American*, Jan. 1996, 112; Crick, *Life Itself*, 89–93; Quastler, *Emergence*, 7.

46. H. J. Morowitz, *Energy Flow in Biology* (New York: Academic Press, 1968), 5–12; F. Hoyle and C. Wickramasinghe, *Evolution from Space* (London: J. M. Dent, 1981), 24–27; A. G. Cairns-Smith, *The Life Puzzle* (Edinburgh: Oliver and Boyd, 1971), 91–96; I. Prigogine, G. Nicolis, and A. Babloyantz, "Thermodynamics of Evolution," *Physics Today* 23 (Nov. 1972); Yockey, *Information Theory*, 246–58; Yockey, "Self-Organization, Origin of Life Scenarios and Information Theory," *Journal of Theoretical Biology* 91 (1981): 13–31; Bowie and Sauer, "Identifying Determinants"; Reidhaar-Olson et al., *Proteins;* Shapiro, *Origins*, 117–31.

47. Prigogine, "Thermodynamics of Evolution."

48. Cairns-Smith, *The Life Puzzle*, 95.

49. John Reidhaar-Olson and Robert Sauer, "Functionally Acceptable Substitutions in Two Alpha-Helical Regions of Lambda Repressor," in *Proteins: Structure, Function, and Bioinformatics* 7, no. 4 (1990): 306–316; James Bowie and Robert Sauer, "Identifying the Determinants of Folding and Activity for a Protein of Unknown Structure," *Proceedings of the National Academy of Sciences USA* 86 (1989): 2152–2156.

50. Interestingly, their descriptions of their own results often downplay the rarity of functional sequences within sequence space. Instead, they often emphasize the tolerance for different amino acids that is allowable at each site. For example, the abstract of the paper reporting the figure of 1 in 10^{63} makes no mention of that figure or its potential significance, stating instead that their results "reveal the high level of degeneracy in the information that specifies a particular protein fold." Reidhaar-Olson and Sauer, "Functionally Acceptable Substitutions."

51. Bowie and Sauer, "Identifying the Determinants of Folding"; Reidhaar-Olson and Sauer, "Functionally Acceptable Substitutions"; Cyrus Chothia, Israel Gelfand, and Alexander Kister, "Structural Determinants in the Sequences of Immunoglobulin Variable *Acid* Domain," *Journal of Molecular Biology* 278 (1998), 457–479; Douglas Axe, "Extreme Functional Sensitivity to Conservative Amino Acid Changes on Enzyme Exteriors" *J. Mol. Biol.* 301 (2000), 585–595; Taylor, Sean V., Kai U. Walter, Peter Kast, and Donald Hilvert,

"Searching Sequence Space for Protein Catalysts," *Proceedings of the National Academy of Sciences USA* 98 (2001), 10596–10601.

52. See, for example, Max F. Perutz and Hermann Lehmann, "Molecular Pathology of Human Hemoglobin," *Nature* 219 (1968), 902–909.

53. Douglas Axe, "Estimating the Prevalence of Protein Sequences Adopting Functional Enzyme Folds" *J. Mol. Biol.* 341 (2004), 1295–1315.

54. For Dembski's treatment of probabilistic resources at the scale of the known universe, see Dembski's above-cited *Design Inference*, ch. 6.

55. The number of possible ways to combine elementary particles (and thus the number of combinatorial possible events) is actually much greater than the number of different events that could have taken place in the history of the universe. Why? Because the occurrence of each individual event precludes the occurrence of many other possible events within the larger combinatorial space. The number of combinatorial possible events represents the number of different events that might have occurred before the universe actually unfolded in the way that it did. Dembski correctly identifies the maximum number of events that could *actually* occur in any given history of the universe as the number that determines the probabilistic resources of the universe. This smaller number determines how many opportunities the universe has to produce a particular outcome by chance. As Dembski explains, it is not the total number of combinatorial possible events (or elementary particles) in the universe which determines the available probabilistic resources, but how many opportunities there are to "individuate" actual events. See *The Design Inference*, ch. 6, and in that chapter p. 209 n.15.

56. The elementary particles enumerated in this calculation include only protons, neutrons, and electrons (fermions), because only these particles have what physicists call "half-integral spin" which allows them to form material structures. This calculation does not count bosons, which cannot form material structures, but instead only transmit energy. Nor does this calculation count the quarks out of which protons and neutrons are made, because quarks are necessarily bound together within these particles. Even if quarks were counted, however, the total number of elementary particles would change by less than one order of magnitude, because there are only three quarks per proton or neutron.

57. Because there is an upper limit on the speed of light, only those parts of the universe that are observable to us can affect events on Earth. Thus, the observable universe is the only part of the universe with probabilistic resources relevant to explaining events on Earth.

58. To be safe, Dembski rounded the number that he had calculated up a few orders of magnitude to 10^{150}, though without any physical or mathematical justification. Since he didn't need to do this, I decided to use his more accurate, if less round, number as the actual measure of the probabilistic resources of the universe in my evaluations of the chance hypothesis.

59. See discussion and references in *Signature in the Cell*, 217.

60. P. T. Mora, "Urge and Molecular Biology," *Nature* 199 (1963): 212–19.

61. Oparin, *Genesis*, 146–47.

62. C. de Duve, *Blueprint for a Cell: The Nature and Origin of Life* (Burlington, NC: Neil Patterson, 1991), 187.

63. T. Dobzhansky, "Discussion of G. Schramm's Paper," in *The Origins of Prebiological Systems and of Their Molecular Matrices*, ed. S. W. Fox (New York: Academic Press, 1965), 310; H. H. Pattee, "The Problem of Biological Hierarchy," in C. H. Waddington, ed.,

Organization, Stability, & Process [vol. 3 of *Toward a Theoretical Biology*] (Piscataway, NJ: Transaction, 1970), 123.

64. Richard Dawkins, The *Blind Watchmaker: Why the Evidence Reveals a Universe Without Design* (New York: Norton, 1987), 47–49; Kuppers, "On the Prior Probability."

65. Kuppers, "On the Prior Probability," 366.

66. Dawkins, *Blind Watchmaker*, 47–49; P. Nelson, "Anatomy of a Still-Born Analogy," *Origins and Design* 17, no. 3 (1996): 12.

67. Stephen C. Meyer, *Signature in the Cell: DNA and the Evidence for Intelligent Design* (San Francisco: HarperOne, 2009), 283–291.

68. C. de Duve, "The Beginnings of Life on Earth," *American Scientist* 83 (1995), 437.

69. Morowitz, *Energy Flow*, 5–12.

70. G. Steinman and M. N. Cole, "Synthesis of Biologically Pertinent Peptides Under Possible Primordial Conditions," *Proceedings of the National Academy of Sciences USA* 58 (1967): 735–41; G. Steinman, "Sequence Generation in Prebiological Peptide Synthesis," *Archives of Biochemistry and Biophysics* 121 (1967): 533–39; R. A. Kok, J. A. Taylor, and W. L. Bradley, "A Statistical Examination of Self-Ordering of Amino Acids in Proteins," *Origins of Life and Evolution of the Biosphere* 18 (1988): 135–42.

71. Meyer, *Signature in the Cell*, 229–270.

72. C. Thaxton, W. Bradley, and R. Olsen, *The Mystery of Life's Origin: Reassessing Current Theories* (Dallas: Lewis and Stanley, 1992), v–viii; D. Kenyon and G. Mills, "The RNA World: A Critique," *Origins and Design* 17, no. 1 (1996): 9–16; D. Kenyon and P. W. Davis, *Of Pandas and People: The Central Question of Biological Origins* (Dallas: Haughton, 1993); S. C. Meyer, "A Scopes Trial for the '90s," *Wall Street Journal*, Dec. 6, 1993, A14; Kok et al., "Statistical Examination."

73. Steinman and Cole, "Synthesis"; Steinman, "Sequence Generation."

74. Kok et al., "Statistical Examination"; B. J. Strait and G. T. Dewey, "The Shannon Information Entropy of Biologically Pertinent Peptides," *Biophysical Journal* 71 (1996): 148–155.

75. Kuppers, "On the Prior Probability," 64.

76. C. de Duve, "Beginnings of Life," 437.

77. R. Stalnaker, *Inquiry* (Cambridge: MIT Press, 1984), 85.

78. This, in fact, happens where adenine and thymine do interact chemically in the complementary base-pairing across the information-bearing axis of the DNA molecule. Along the message-bearing axis, however, there are no chemical bonds or differential bonding affinities that determine sequencing.

79. M. Polanyi, "Life's Irreducible Structure," *Science* 160 (1968): 1308–12, esp. 1309.

80. Yockey, "Self-Organization," 18.

81. H. P. Yockey, "A Calculation of the Probability of Spontaneous Biogenesis by Information Theory," *Journal of Theoretical Biology* 67 (1977): 377–98, esp. 380.

82. M. Eigen, *Steps Toward Life* (Oxford: Oxford University Press, 1992), 12.

83. Meyer, *Signature in the Cell*, 267–268, 284–286, 288–290.

84. R. Shapiro, "Prebiotic Cytosine Synthesis: A Critical Analysis and Implications for the Origin of Life," *Proceedings of the National Academy of Sciences, USA* 96 (1999): 4396–

4401; M. M. Waldrop, "Did Life Really Start Out in an RNA World?" *Science* 246 (1989): 1248–49.

85. R. Shapiro, "Prebiotic Ribose Synthesis: A Critical Analysis," *Origins of Life and Evolution of the Biosphere* 18 (1988): 71–85; Kenyon and Mills, "RNA World."

86. G. F. Joyce, "RNA Evolution and the Origins of Life," *Nature* 338 (1989): 217–24. Yuri I. Wolf and Eugene V. Koonin, "On the Origin of the Translation System and the Genetic Code in the RNA World by means of Natural Selection, Exaptation, and Subfunctionalization," *Biology Direct* 2 (2007): 1–25.

87. A. J. Hager, J. D. Polland Jr., and J. W. Szostak, "Ribozymes: Aiming at RNA Replication and Protein Synthesis," *Chemistry and Biology* 3 (1996): 717–25.

88. Johnston et al, "RNA-Catalyzed RNA Polymerization: Accurate and General RNA-Templated Primer Extension," *Science* 292 (2001): 1319–25.

89. In addition, for a single-stranded RNA catalyst to self-replicate (the only function that could be selected in a prebiotic environment), it must find another catalytic RNA molecule in close vicinity to function as a template, since a single-stranded RNA cannot function as both enzyme and template. Thus, even if an originally unspecified RNA sequence might later acquire functional significance by chance, it could perform a function only if another RNA molecule—that is, one with a highly specific sequence relative to the original—arose in close vicinity to it. Thus, the attempt to bypass the need for specific sequencing in an original catalytic RNA only shifts the specificity problem elsewhere, namely, to a second and necessarily highly specific RNA sequence. Put differently, in addition to the specificity required to give the first RNA molecule self-replicating capability, a second RNA molecule with an extremely specific sequence—one with essentially the same sequence as the original—would also have to arise. Yet RNA-world theorists do not explain the origin of the requisite specificity in either the original molecule or its twin. Joyce and Orgel have calculated that to have a reasonable chance of finding two identical RNA molecules of a length sufficient to perform enzymatic functions would require an RNA library of some 10^{54} RNA molecules. The mass of such a library vastly exceeds the mass of the earth, suggesting the extreme implausibility of the chance origin of a primitive replicator system. Yet one cannot invoke natural selection to explain the origin of such primitive replicators, since natural selection only ensues once self-replication has arisen. Further, RNA bases, like DNA bases, do not manifest self-organizational bonding affinities that could explain their specific sequencing. In short, the same kind of evidentiary and theoretical problems emerge whether one proposes that genetic information arose first in RNA or DNA molecules. The attempt to leapfrog the sequencing problem by starting with RNA replicators only shifts the problem to the specific sequences that would make such replication possible.

90. Christian de Duve, *Vital Dust: The Origin and Evolution of Life on Earth* (New York: Basic Books, 1995), 23.

91. Matthew W. Powner, Béatrice Gerland, and John D. Sutherland, "Synthesis of Activated Pyrimidine Ribonucleotides in Prebiotically Plausible Conditions," *Nature* 459 (2009), 239–42.

92. Stephen Fletcher, *Times Literary Supplement*, Letters, 3 February, 2010.

93. Tracey A. Lincoln and Gerald F. Joyce, "Self-Sustained Replication of an RNA Enzyme," *Science* 323 (2009), 1229–32.

94. Quastler, *Emergence*, 16.

95. Charles Sanders Peirce, *Collected Papers*, vol. II, edited by Charles Hartshorne and Paul Weiss (Cambridge, MA: Harvard University Press, 1932), 372–78. Abductive reason-

ing was first described by the American philosopher and logician C. S. Peirce. He noted that, unlike inductive reasoning, in which a universal law or principle is established from repeated observations of the same phenomena, and unlike deductive reasoning, in which a particular fact is deduced by applying a general law or rule to another particular fact or case, scientists use abductive reasoning to infer unseen facts, events, or causes in the past from clues or facts in the present. As Peirce himself showed, however, there is a problem with abductive reasoning. Consider the following syllogism:

If it rains, the streets will get wet.

The streets are wet.

Therefore, it rained.

This syllogism affirms a past condition (i.e., that it rained) but it commits a logical fallacy known as *affirming the consequent*. Given that the street is wet (and without additional evidence to decide the matter), one can only conclude that *perhaps* it rained. Why? Because there are many other possible ways by which the street may have gotten wet. Rain may have caused the streets to get wet; a street cleaning machine might have caused them to get wet; or an uncapped fire hydrant might have done so. It can be difficult to infer the past from the present because there are many possible causes of a given effect.

Given that abductive inferences affirm the consequent, Peirce wondered how we can nevertheless frequently make reliable inferences about the past? He noted, for example, that no one doubts the existence of Napoleon. Yet we use abductive reasoning to infer Napoleon's existence. That is, we must infer his past existence from present effects. But despite our dependence on abductive reasoning to make this inference, no sane or educated person would doubt that Napoleon Bonaparte actually lived. How could this be if the problem of affirming the consequent bedevils our attempts to reason abductively? Peirce's answer was revealing: "Though we have not seen the man [Napoleon], yet we cannot explain what we have seen without [the hypothesis of his existence]." For Peirce, a particular abductive hypothesis can be reasonably believed (in practice) if it explains in a way that no other hypotheses do. In other words, an abductive inference is a strong one if it represents the best or the only adequate explanation of the effects in question.

96. Stephen Jay Gould, "Evolution and the Triumph of Homology: or, Why History Matters," *American Scientist* 74 (1986): 61.

97. Thomas Chamberlain, "The Method of Multiple Working Hypotheses," *Science* (old series) 15 (1890): 92–96. Reprinted in *Science* 148 (1965): 754–759.

98. P. Lipton, *Inference to the Best Explanation* (New York: Routledge, 1991).

99. Charles Lyell, *Principles of Geology: Being an Attempt to Explain the Former Changes of the Earth's Surface, by Reference to Causes Now in Operation,* three volumes (London: John Murray, 1830–1833).

100. V. Kavalovski, "The Vera Causa Principle: A Historico-Philosophical Study of a Meta-Theoretical Concept from Newton through Darwin" (PhD dissertation, University of Chicago, 1974), 78–103.

101. E. Sober, *Reconstructing the Past* (Cambridge, MA: MIT Press, 1988), 4–5; M. Scriven, "Causes, Connections, and Conditions in History," in *Philosophical Analysis and History,* ed. W. Dray (New York: Harper and Row, 1966), 238–64, esp. 249–50; Michael Scriven, "Explanation and Prediction in Evolutionary Theory," *Science* 130 (1959): 477–82, especially 480.

102. Meyer, "Of Clues," 96–108.

103. Of course, the phrase "large amounts of specified information" again begs a quantitative question, namely, "How much specified information or complexity would the minimally complex cell have to have before it implied design?" Recall that Dembski has calculated a universal probability bound of $1/10^{150}$ corresponding to the probabilistic/specificational resources of the known universe. Recall further that probability is inversely related to information by a logarithmic function. Thus, the universal small probability bound of $1/10^{150}$ translates into roughly 500 bits of information. Chance alone, therefore, does not constitute a sufficient explanation for the *de novo* origin of any specified sequence or system containing more than 500 bits of (specified) information. Further, since systems characterized by complexity (a lack of redundant order) defy explanation by self-organizational laws and since appeals to prebiotic natural selection presuppose but do not explain the origin of the specified information necessary to a minimally complex self-replicating system, intelligent design best explains the origin of the more than 500 bits of specified information required to produce the first minimally complex living system. Thus, assuming a nonbiological starting point, the *de novo* emergence of 500 or more bits of specified information will reliably indicate design. One gene capable of coding for one protein of average length easily exceeds this threshold.

104. A possible exception to this generalization might occur in biological evolution. If the Darwinian mechanism of natural selection acting on random variation can account for the emergence of all complex life, then a mechanism does exist that can produce large amounts of information—assuming, of course, a large amount of preexisting biological information in a self-replicating living system. Thus, even if one assumes that the selection/variation mechanism can produce all the information required for the macroevolution of complex life from simpler life, that mechanism will not suffice to account for the origin of the information necessary to produce life from nonliving chemicals. As we have seen, appeals to prebiotic natural selection only beg the question of the origin of specified information. Thus, based on experience, we can affirm the following generalization: "for all nonbiological systems, large amounts of specified complexity or information originate only from mental agency, conscious activity, or intelligent design." Strictly speaking, experience may even affirm a less qualified generalization (such as "large amounts of specified complexity invariably originate from an intelligent source"), since the claim that natural selection acting on random mutations can produce large amounts of novel genetic information depends on debatable theoretical arguments and extrapolation from observations of small scale microevolutionary changes that do not themselves manifest large gains in biological information. I have argued elsewhere (see Stephen. C. Meyer, "The Origin of Biological Information and the Higher Taxonomic Categories," in *Proceedings of the Biological Society of Washington* 117 (2004): 213–239; Stephen C. Meyer, *Darwin's Doubt: The Explosive Origin of Animal Life and the Case for Intelligent Design*, San Francisco: HarperOne, 2013), that neither the neo-Darwinian mechanism nor any other current naturalistic mechanism adequately accounts for the origin of the information required to build the novel protein folds and body plans that arise in the Cambrian explosion. In any case, the more qualified empirical generalization (stated above in this note) is sufficient to support the argument presented here, since this chapter seeks only to establish intelligent design as the best explanation for origin of the specified information necessary to the origin of the first life.

105. Meyer, "Of Clues," 77–140.

106. K. Dose, "The Origin of Life: More Questions Than Answers," *Interdisciplinary Science Reviews* 13 (1988): 348–56; Yockey, *Information Theory*, 259–93; Thaxton et al., *Mystery*, 42–172; Thaxton and Bradley, "Information and the Origin," 193–97; Shapiro, *Origins*.

107. Less exotic (and more successful) design detection occurs routinely in both science and industry. Fraud-detection, forensic science, and cryptography all depend on the application of probabilistic or information-theoretic criteria of intelligent design. See Dembski, *Design Inference*, 1–35. Many would admit that we may justifiably infer a past human intelligence operating (within the scope of human history) from an information-rich artifact or event, but only because we already know that human minds exist. But, they argue, since we do not know whether an intelligent agent or agents existed prior to humans, inferring the action of a designing agent that antedates humans cannot be justified, even if we observe an information-rich effect. Note, however, that SETI scientists do not already know whether an extraterrestrial intelligence exists. Yet they assume that the presence of a large amount of specified information (such as the first 100 prime numbers in sequence) would definitively establish the existence of one. Indeed, SETI seeks precisely to establish the existence of other intelligences in an unknown domain. Similarly, anthropologists have often revised their estimates for the beginning of human history or civilization because they discovered information-rich artifacts dating from times that antedate their previous estimates. Most inferences to design establish the existence or activity of a mental agent operating in a time or place where the presence of such agency was previously unknown. Thus, to infer the activity of a designing intelligence from a time prior to the advent of humans on Earth does not have a qualitatively different epistemological status than other design inferences that critics already accept as legitimate. See T. R. McDonough, *The Search for Extraterrestrial Intelligence: Listening for Life in the Cosmos* (New York: Wiley, 1987).

108. P. Lipton, *Inference to the Best Explanation*, 32–88.

109. *Ibid*.; S. C. Meyer, "The Scientific Status of Intelligent Design: The Methodological Equivalence of Naturalistic and Non-Naturalistic Origins Theories," in *Science and Evidence for Design in the Universe*, The Proceedings of the Wethersfield Institute, vol. 9 (San Francisco: Ignatius Press, 2000), 151–212; Meyer, "The Demarcation of Science and Religion," in *The History of Science and Religion in the Western Tradition: An Encyclopedia*, ed. G. B. Ferngren (New York: Garland, 2000), 17–23; E. Sober, *The Philosophy of Biology* (San Francisco: Westview Press, 1993); Meyer, "Of Clues," 77–140.

110. Quastler, *Emergence*, 16.

111. Oparin, *Origin of Life*, 28; M. Rothman, *The Science Gap* (Buffalo, NY: Prometheus, 1992), 65–92; K. Popper, *Conjectures and Refutations: The Growth of Scientific Knowledge* (London: Routledge and Kegan Paul, 1962), 35–37.

112. Meyer, "Of Clues," 77–140; Sober, *Reconstructing the Past*, 4–5; de Duve, "Beginnings of Life," 249–50.

113. R. Harré and E. H. Madden, *Causal Powers* (London: Basil Blackwell, 1975).

114. M. Ruse, "McLean v. Arkansas: Witness Testimony Sheet," in *But Is It Science?* ed. M. Ruse (Amherst, NY: Prometheus Books, 1988), 103; Meyer, "Scientific Status"; Meyer, "Demarcation."

115. Meyer, "Scientific Status"; Meyer, "Demarcation"; L. Laudan, "The Demise of the Demarcation Problem," in Ruse, *But Is It Science?* 337–50; L. Laudan, "Science at the Bar—Causes for Concern," in Ruse, *But Is It Science?* 351–55; A. Plantinga, "Methodological Naturalism?" *Origins and Design* 18, no. 1 (1986): 18–26; A. Plantinga, "Methodological Naturalism?" *Origins and Design* 18, no. 2 (1986): 22–34.

116. Bridgman, *Reflections of a Physicist*, 2nd ed. (New York: Philosophical Library, 1955), 535.

ABOUT THE AUTHORS

Charles B. Thaxton

Charles B. Thaxton is a Fellow of Discovery Institute's Center for Science and Culture. He received his PhD in physical chemistry from Iowa State University. He completed two post-doctoral programs, one in history of science at Harvard University and the second in the molecular biology laboratories of Brandeis University. He is co-author of *The Mystery of Life's Origin* and also *The Soul of Science* (with Nancy Pearcey). He has published technical articles in *Journal of Inorganic Chemistry, Journal of Scientific Instruments,* and *Journal of Cell Biology*. He has lectured widely at American universities, including Princeton, Yale, Vanderbilt, Johns Hopkins, University of Michigan, and Rice University. He has lectured internationally at the Korean Advanced Institute of Science, the Russian Academy of Science, and in various universities in Mongolia, Romania, Poland, Hungary, and the former Czechoslovakia. He has held appointments at Slovak Technical University, the Biomathematical Institute, and at Charles University in Prague, where he was a Templeton scholar in the department of natural sciences.

Walter L. Bradley

Walter L. Bradley is a Distinguished Fellow of the Walter Bradley Center for Natural and Artificial Intelligence at Discovery Institute and a Fellow of Discovery Institute's Center for Science and Culture. He received his BS in Engineering Physics and his PhD in Materials Science and Engineering, both at the University of Texas (Austin). He taught for eight years as an Assistant and Associate Professor of Metallurgical Engineering at the Colorado School of Mines, for 24 years as a Professor of Mechanical Engineering at Texas A&M University (TAMU), and for ten years as a Distinguished Professor of Mechanical Engineering at Baylor University. During his time at TAMU he served as the Director of the Polymer Technology Center, as Department Head of Mechanical Engineering, and as Division Head of Offshore Composite Materials in the National Science Foundation-sponsored Offshore Technology Research Center. He has published over 150 refereed journal articles. He has given invited lectures at Harvard, Dartmouth, Brown University, University of Wisconsin, and many other institutions.

Roger L. Olsen

Roger L. Olsen is a Senior Vice President in the Denver office of the global consulting, engineering, and construction firm CDM Smith Inc. He received his BS in Chemistry and PhD in Geochemistry from the Colorado School of Mines. He is a Board Certified Environmental Scientist by the American Academy of Engineers and Scientists, one of the first ten scientists to be so certified. He has served as an Instructor at the Colorado School of Mines, a Research Chemist at Rockwell International, and a Project Geochemist at D'Appolonia Consulting Engineers/International Technology Corporation. He is author of dozens of published scientific papers and routinely makes presentations at scientific and engineering conferences around the world. He is an internationally recognized expert in the fields of geochemistry and environmental chemistry and has testified as an expert witness.

David Klinghoffer

David Klinghoffer is a Senior Fellow at Discovery Institute and the Editor of *Evolution News & Science Today*, the daily voice of Discovery Institute's Center for Science and Culture. Klinghoffer is the author of six books, including *The Lord Will Gather Me In: My Journey to Jewish Orthodoxy*, *The Discovery of God: Abraham and the Birth of Monotheism*, *Why the Jews Rejected Jesus: The Turning Point in Western History,* and with Senator Joe Lieberman, *The Gift of Rest: Rediscovering the Beauty of the Sabbath.* A former Senior Editor and Literary Editor at *National Review* magazine, he has written for *The Los Angeles Times, The New York Times, The Wall Street Journal, The Washington Post, The Seattle Times, Commentary,* and other publications. He has been a feature reporter and movie and TV critic for *The Washington Times.* He is the editor of several books, including *Signature of Controversy, Debating Darwin's Doubt,* and *The Unofficial Guide to Cosmos.*

James Tour

James Tour is the T. T. and W. F. Chao Professor of Chemistry, Professor of Computer Science, and Professor of Materials Science and Nano-Engineering at Rice University. A synthetic organic chemist, he received his BS in Chemistry from Syracuse University, his PhD in synthetic organic and organometallic chemistry from Purdue University, and postdoctoral training in synthetic organic chemistry at the University of Wisconsin and Stanford University. He has served on the faculty of the University of South Carolina and as a visiting scholar at Harvard University. Tour has over 680 research publications and over 130 patent families. He was inducted into the National Academy of Inventors in 2015 and was listed in "The World's Most Influential Scientific Minds" by Thomson Reuters in 2014. He has been named "Scientist of the Year" by *R&D Magazine* and was ranked one of the Top 10 chemists in the world over the past decade by a Thomson Reuters citations per publication index survey in 2009. The same year he was elected a Fellow of the American Association for the Advancement of Science (AAAS). He won the Feynman Prize in Experimental Nanotechnology in 2008, the NASA Space Act Award in 2008 for his development of carbon nanotube reinforced elastomers, and the Arthur C. Cope Scholar Award from the American Chemical Society for his achievements in organic chemistry in 2007.

Brian Miller

Brian Miller is Research Coordinator for the Center for Science and Culture at Discovery Institute. He holds a BS in Physics with a minor in Engineering from MIT and a PhD in Physics from Duke University. He speaks internationally on the topics of intelligent design and the impact of worldviews on society. He also has consulted on organizational development and strategic planning, and he is a technical consultant for TheStartup, a virtual incubator dedicated to bringing innovation to the marketplace.

Guillermo Gonzalez

Guillermo Gonzalez is a Senior Fellow with the Center for Science and Culture at Discovery Institute and has served on the faculties of Iowa State University, Grove City College, and Ball State University. He received his PhD in Astronomy from the University of Washington, and he has done post-doctoral work at the University of Texas, Austin and the University of Washington. His work has received funding from both NASA and the National Science Foundation. Gonzalez is a world-class expert on the astrophysical requirements for habitability and a co-founder of the concept of the "Galactic Habitable Zone." Gonzalez has published nearly 90 articles in refereed astronomy and astrophysical journals. In 2004 he co-authored *The Privileged Planet: How Our Place in the Cosmos is Designed for Discovery* with Jay W. Richards. He also is co-author of the second edition of *Observational Astronomy*, published by Cambridge University Press.

Jonathan Wells

Jonathan Wells is a Senior Fellow at Discovery Institute's Center for Science and Culture. He previously worked as a postdoctoral research biologist at the University of California at Berkeley and the supervisor of a medical laboratory in Fairfield, California. He has earned two PhDs, one in Molecular and Cell Biology from the University of California at Berkeley, and one in Religious Studies from Yale University. He also taught biology at California State University in Hayward and lectured around the world. He has published articles in *Development, Proceedings of the National Academy of Sciences USA, BioSystems, The Scientist,* and *The American Biology Teacher*. His books include *Charles Hodge's Critique of Darwinism, Icons of Evolution: Why Much of What We Teach about Evolution Is Wrong, The Politically Incorrect Guide to Darwinism and Intelligent Design, The Myth of Junk DNA,* and *Zombie Science*. He is also co-author with William Dembski of *The Design of Life*.

Stephen C. Meyer

Stephen C. Meyer is Director and co-founder of the Center for Science and Culture at Discovery Institute. He previously served as a professor at Whitworth University and Palm Beach Atlantic University and as a geophysicist with ARCO in Texas. He received his PhD in the History and Philosophy of Science from the University of Cambridge. His books include *Darwin's Doubt: The Explosive Origin of Animal Life and the Case for Intelligent Design* (a *New York Times*-bestseller) and *Signature in the Cell: DNA and the Evidence for Intelligent Design* (named a Book of the Year by the *Times Literary Supplement*). Meyer's other books include *Darwinism, Design and Public Education* (co-editor, Michigan State University Press) and the textbook *Explore Evolution* (co-author, Hill House Publishers, 2007). He has published articles in *The Wall Street Journal, USA Today, The National Post, The Daily Telegraph,* and *The Los Angeles Times*. He has appeared on NBC, ABC, CBS, CNN, Fox News, and many other media outlets.

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