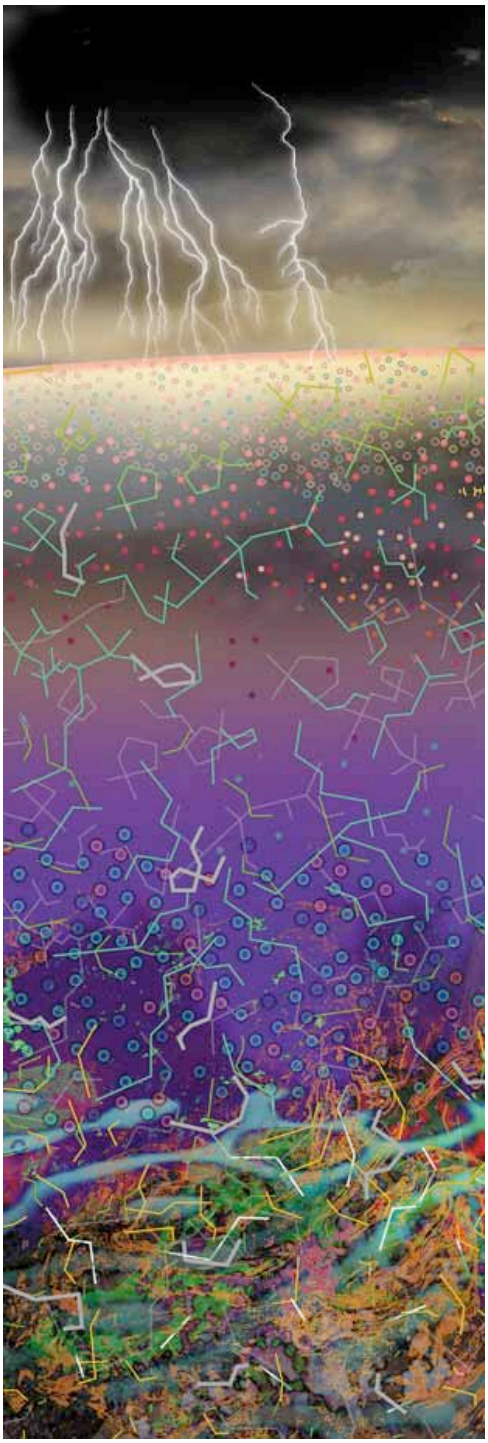
FEATURED STORY

February 2006

The Origins of Life

Have too many cooks spoiled the prebiotic soup?

By Antonio Lazcano



TWENTY-FIVE YEARS AGO, Francis Crick, who co-discovered the structure of DNA, published a provocative book titled *Life Itself: Its Origin and Nature.* Crick speculated that early in Earth's history a civilization from a distant planet had sent a spaceship to Earth bearing the seeds of life. Whether or not Crick was serious about his proposal, it dramatized the difficulties then plaguing the theory that life originated from chemical reactions on Earth. Crick noted two major questions for the theory. The first one—seemingly unanswerable at the time—was how genetic polymers such as RNA came to direct protein synthesis, a process fundamental to life. After all, in contemporary life-forms, RNA translates genetic information encoded by DNA into instructions for making proteins.

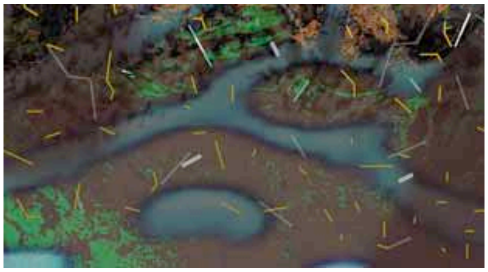
The second question was, What was the composition of Earth's early atmosphere? Many planetary scientists at the time viewed Earth's earliest atmosphere as rich in carbon dioxide. More important, they were also skeptical about a key assumption made by many chemists who were investigating life's origin—namely that Earth's early atmosphere was highly "reducing," or rich in methane, ammonia, and possibly even free hydrogen. In a widely publicized experiment done in 1953, the chemists Stanley L. Miller of the University of California, San Diego, and Harold C. Urey had demonstrated that in such an atmosphere, organic, or carbon-based, compounds could readily form and accumulate in a "prebiotic soup." But if a highly reducing atmosphere was destined for the scientific dustbin, so was the origin-of-life scenario to which it gave rise.

The inventory of current views on life's origin range from the suggestion that life originated on Mars and came to Earth aboard meteorites, to the idea that life emerged from "metabolic" molecular networks, fueled by hydrogen released during the formation of minerals in hot volcanic settings.

In Crick's mind, the most inventive way to solve both problems was to assume that life had not evolved on Earth, but had come here from some other location—a view that still begs the question of how life evolved elsewhere.

Crick was neither the first nor the last to try to explain life's origin with creative speculation. Given so many difficult and unanswered questions about life's earthly origin, one can easily understand why so many investigators become frustrated and give in to speculative fantasies. But even the most sober attempts to reconstruct how life evolved on Earth is a scientific exercise fraught with guesswork. The evidence required to understand our planet's prebiotic environment, and the events that led to the first living systems, is scant and hard to decipher. Few geological traces of Earth's conditions at the time of life's origin remain today. Nor is there any fossil record of the evolutionary processes preceding the first cells. Yet, despite such seemingly insurmountable obstacles, heated debates persist over how life emerged. The inventory of current views on life's origin reveals a broad assortment of opposing positions. They range from the suggestion that life originated on Mars and came to Earth aboard meteorites, to the idea that life emerged from "metabolic" molecular networks, fueled by hydrogen released during the formation of minerals in hot volcanic settings.

This flurry of popular ideas has often distracted attention from what is still the most scientifically plausible theory of life's origin, the "heterotrophic" theory. The theory holds that the first living entities evolved "abiotically"—or from systems of nonliving organic molecules present on the primitive Earth. (The term



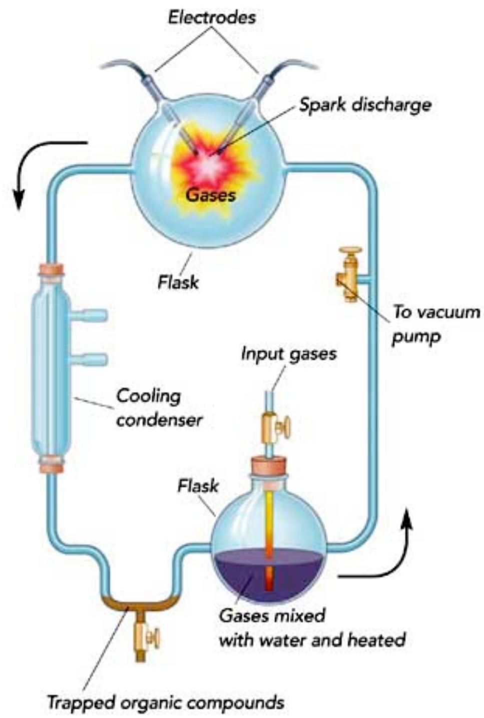
Jac Depczyk (jacdepczyk.com; netcells.net)

"heterotrophic" was originally coined to describe a kind of metabolism in which "nutrients" such as carbon and nitrogen must be obtained from nature as complex organic molecules such as amino acids, rather than from extremely simple compounds such as carbon dioxide.) According to the theory, organic molecules such as amino acids were chemically combined in a prebiotic soup and "cooked" by various sources of energy. True, some of the details of Miller and Urey's recipe for prebiotic soup presented difficulties, such as the ones Crick highlighted. But abandoning the premise of a prebiotic soup when new findings largely support its account of life's origin is to "throw the baby out with the bathwater."

One strong argument in favor of the heterotrophic theory is the surprising variety of biochemical constituents that emerge in laboratory simulations of Earth's prebiotic environment, and the remarkable similarity between them and the constituents of some carbon-rich meteorites. On September 28, 1969, for instance, a meteorite landed in Murchison, Australia, carrying nearly eighty kinds of amino acids. Among them were several amino acids that occur in proteins. Also embedded in the Murchison meteorite were purines, pyrimidines, carboxylic acids, and compounds derived from ribose and deoxyribose, the sugars present in RNA and DNA. (In fact, ribose is the "R" of RNA, deoxyribose the "D" of DNA.) Such relics of the early solar system provide insight into the kind of organic chemistry that took place some 4.6 billion years ago.

The similarity between the products of laboratory synthesis and the components of the meteorite seems more than accidental. In fact, it offers strong justification for bringing the study of the possible reaction pathways of prebiological molecules into the laboratory. Perhaps reactions such as the ones Miller and Urey simulated were common throughout the solar system, or at least in a prebiotic soup on Earth.

What about the criticisms that the highly reducing atmosphere in the Miller-Urey experiment was unrealistic? The hydrogen in such an atmosphere, according to the critics, would have escaped into space too quickly to have played any role in atmospheric chemistry. But the critics may have overstated their case. Recent theoretical models by Feng Tian, an atmospheric chemist at the University of Colorado, Boulder, and his colleagues suggest that hydrogen in the atmosphere of the early Earth may have escaped more slowly than planetary scientists previously assumed. So although Earth's primitive atmosphere may not have been as strongly reducing as Miller, Urey, and their followers have assumed, it may not have been lacking in hydrogen, either. The hydrogen would have coexisted with carbon dioxide. The presence of both gases would have helped forge hydrogen-rich molecules, which would have transformed into organic compounds.



Stanley L. Miller sought to simulate Earth's primordial conditions during life's molecular evolution. His apparatus, shown here schematically, blended ammonia, hydrogen, methane, and water—thought at the time of the experiment to be the primary constituents of Earth's early atmosphere—inside a sealed loop of glass tubes and flasks. The gases, mixed with water vapor in the lower flask, flowed into the upper flask, where electrodes, simulating lightning, sparked the vapor. The circulating vapor then condensed and trickled into a collecting trap. After one week, Miller and Urey found that between 10 percent and 15 percent of the system's carbon had formed organic compounds, including many of the amino acids needed to make proteins.

Illustration, courtesy Stanley L. Miller, by Ian Worpole

Certainly, the classical recipe for prebiotic soup requires updating. It must take into account such additional, newly recognized factors as extraterrestrial organic compounds, minerals such as combinations of iron and nickel with sulfur that act as chemical catalysts, and organic molecules synthesized in hydrothermal vents. None of those factors threatens the plausibility of a heterotrophic theory as an explanation for the origin of life.

The heterotrophic theory has also gained support from studies of the capabilities of RNA, which have shown that RNA may have played a far broader role during life's evolution than it does in life today. In 1982 the molecular biologists Thomas R. Cech, now at the Howard Hughes Research Institute in Chevy Chase, Maryland, and Sidney Altman of Yale University independently discovered that RNA molecules can act not only as messengers and repositories of information, but also as enzymes, which catalyze chemical reactions. The discovery of such "ribozymes" gave strong support to the idea that RNA might have both stored information and catalyzed reactions in the first living organisms—a hypothesis first put forth independently in the late 1960s by Carl R. Woese of the University of Illinois at Urbana–Champaign, Leslie Orgel of the Salk Institute for Biological Studies in La Jolla, California, and Crick himself.

If true, the hypothesis suggests that an "RNA world" may have preceded life as it occurs today. In such a world, RNA would have performed many functions that other molecules, including DNA and proteins, have now assumed. If such an RNA world preceded life's development, it would help explain how such biological functions as protein

An "RNA world" may have preceded life as it occurs today; in such a world, RNA would have performed many functions that other molecules, including DNA and proteins, have now assumed.

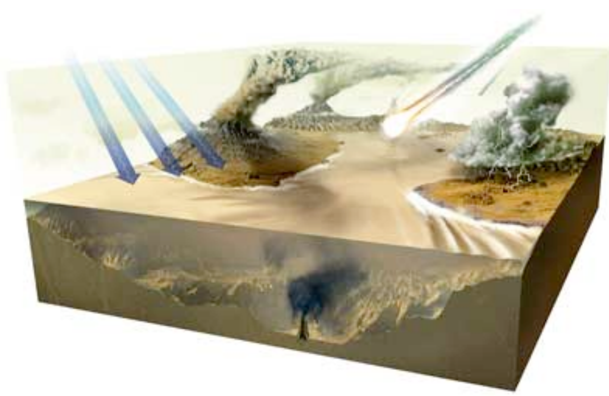
synthesis and genetic information storage and replication may have begun.

The history of modern thinking about the origins of life begins with the eighteenth-century naturalist Jean-Baptiste de Monet, chevalier de Lamarck, Charles Darwin's most distinguished predecessor. Darwin himself was reluctant publically to address the question of life's origin. But the idea that living organisms evolved from lifeless matter became widespread soon after the publication of Darwin's *Origin of Species* in 1859. Darwin expressed his private views on the matter in 1871, in a letter to the English botanist J.D. Hooker. Life, Darwin famously wrote, may have started in "a warm little pond, with all sorts of ammonia and phosphoric salts, light, heat, electricity, etc. present, that a proteine compound was chemically formed ready to undergo still more complex changes."

The nineteenth-century German zoologist and evolutionist Ernst Haeckel perhaps best epitomized the leading scientific beliefs after Darwin. The first life-forms, he contended, had been plantlike microorganisms, capable of photosynthesis, that had evolved directly out of nonliving matter according to physical laws.

In 1924, the Russian plant biochemist and evolutionary biologist Aleksandr I. Oparin questioned Haeckel's scheme. Oparin could not reconcile his Darwinian view—that simple organisms had gradually evolved into more complex ones—with the prevalent belief that life had suddenly appeared on Earth with a self-sustaining metabolism. So he proposed an alternative scenario. He posited that a long period of abiotic synthesis on early Earth had caused organic compounds to accumulate in a prebiotic soup, which had preceded life. Oparin then described how organic molecules could have evolved, via simple, ubiquitous fermentation reactions, into precellular systems on the primitive Earth. Such systems, he maintained, could then have led to cells that survived without oxygen and fed on the prebiotic soup.

Not too surprisingly, that line of thinking has sparked disagreement. As recently as 1988, the German chemist Günter Wächtershäuser, now a patent attorney in Munich, proposed an alternative "iron-sulfur" hypothesis. Wächtershäuser's core insight was that when iron sulfide (FeS) mixes with hydrogen sulfide (H_2S) to form pyrite (FeS_2), the reaction releases copious quantities of hydrogen gas (H_2). With the release of the hydrogen, on Wächtershäuser's view, organic compounds could form from carbon dioxide in the atmosphere. Life began when self-catalyzing molecular systems emerged from the organic compounds. Experiments confirm that the formation of pyrite can indirectly yield a few organic compounds as well as ammonia (NH_3).



Primitive terrain of the early Earth set the stage for life's evolution. Fueled by raw materials from volcanoes, meteorites, and undersea thermal vents, and energized by lightning, cosmic rays, and the planet's own internal heat, life's precursor molecules probably formed in a "soup" of prebiotic organic compounds about 4 billion years ago.

Illustration by [Advanced Illustrations Ltd]

But compared with the variety of biochemical compounds synthesized in simulations such as Miller and Urey's, the process Wächtershäuser described gives rise to only a limited range of molecules. Moreover, the Miller-Urey apparatus sought to simulate Earth's real environment shortly after our planet formed from the primordial solar nebula. In contrast, there is little empirical support for Wächtershäuser's hypothesis.

Unfortunately, since the Earth's geologic record from those early times is so sparse, the rocks cannot answer the kinds of questions raised by the Miller-Urey and Wächtershäuser experiments. Most rocks that are more than three billion years old have so thoroughly metamorphosed that life's precursor molecules are no longer detectable. There is no direct evidence of Earth's environmental conditions at the time of life's origin, either. No one knows the temperature of the early Earth, its ocean acidity, the composition of its atmosphere, or any other factors that may have substantially affected early life. Nor is there any fossil record of entities predating the first cells.

In a sense, Miller and Urey were also heirs to a second tradition of scientific thought, distinct from that of Darwin, whose aim can be understood today as an attempt to synthesize molecules of prebiotic significance. Such experiments date back as far as 1807, with the work of the French chemist Joseph Louis Proust, as well subsequent chemists, including the Swede Jöns Jacob Berzelius, the Germans Friedrich Wöhler and Adolph Strecker, and the Russian Aleksandr Mikhaylovich Butlerov. All of them attempted to synthesize biologically related molecules under what today would be called primitive conditions—though they were not the conditions Darwin imagined in his "warm little pond."

True prebiotic simulations began with Miller and Urey, and others have followed in their wake. All of them confirmed that amino acids, purines, and pyrimidines—all molecules of biological significance—readily formed under atmospheric conditions thought to be similar to the ones present on the early Earth. Most likely, those molecules would also have formed in the prebiotic soup, along with many other biologically related compounds: urea and carboxylic acids, sugars formed from formaldehyde, and various hydrocarbons, alcohols, and fatty acids, including some known to develop into bilayered membranes—the probable precursors of cell membranes. In addition to all those molecules, other, extraterrestrial

Life's precursor molecules built up over at most a few hundred million years. The schematic diagram indicates several kinds of molecules may have spiced the prebiotic soup. They would have arrived on Earth aboard fragments of comets, meteorites, and interplanetary dust, as the chemist Juan Oró of the University of Houston first suggested in 1961.

Yet exactly how those simple organic compounds assembled themselves into more complex molecules, or polymers, and then into the first living entities remains one of the most tantalizing questions in science. Earth's primitive broth must have included a bewildering array of organic compounds, a virtual chemical wonderland that synthesized, disintegrated, and absorbed a wide variety of molecules, in ongoing cycles of transformation.

One feature of life, though, remains certain: Life could not have evolved without a genetic mechanism—one able to store, replicate, and transmit to its progeny information that can change with time. That condition, of course, does not imply that nucleic acids (the stuff of RNA and DNA) wriggled in the primitive oceans, ready to serve as primordial genes. Nor does it suggest that RNA arose completely assembled from simple precursors in a prebiotic soup. Rather, precellular evolution likely resembled a branching tree of chemical transformations. Some of the branches would have become evolutionary dead ends. Others would have grown in fits and starts toward the earliest living entities. It is also likely that Darwinian-style natural selection winnowed entire populations of molecules and chemical systems. From that perspective, the first entities that could replicate, catalyze, and multiply would have truly marked the origin of life and its evolution.

Surely, RNA meets all those requirements. But RNA is also highly unstable. A self-catalyzing, self-replicating RNA molecule is unlikely to have arisen spontaneously. So where did it come from?

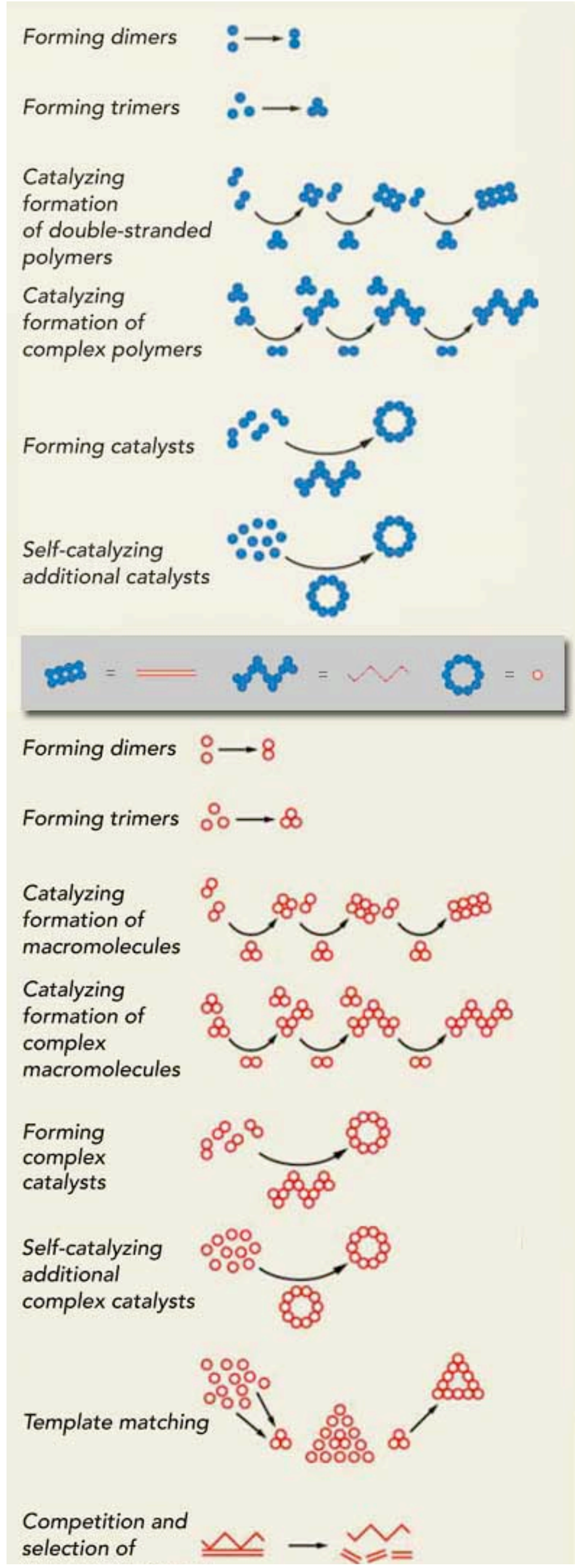
The answer is not so clear. This difficulty has led to the suggestion that a pre-RNA world of primordial living systems predated and gave rise to the RNA world. Such a pre-RNA world would have spawned the first "genetic polymers" capable of encoding and perhaps transmitting information. If that view is correct, the denizens of a pre-RNA world may actually have initiated what is now called heredity. They, in turn, would have subsequently evolved through natural selection toward RNA.

To explore the possibilities of such reactions, Albert Eschenmoser, an organic chemist at the Eidgenössische Technische Hochschule in Zur-ich, and his colleagues have modified nucleic acids to include various versions of ribose and other simple sugars. Still other investigators have synthesized similar polymers without ribose or phosphate. Did systems of such polymers predate the RNA world? The answer to that question remains unknown.

Precisely how the first genetic machinery evolved also persists as an unresolved issue. The hypothesis of a pre-RNA world does not presume that genetic polymers could evolve only from simpler genetic polymers, in a never-ending succession of molecular takeovers. But it does point toward a need to simulate, under plausible prebiotic conditions, the pathways that simple monomers and genetic polymers might have taken to become evolutionary precursors of RNA. Perhaps the best way to comprehend life's emergence is through the molecular dynamics, and evolution, of systems with "replicating entities," endowed with polymers that can store genetic information and replicate differentially.

Whether or not membranes enclosed such entities is also not yet clear. But as I mentioned earlier, lipids and other fatty acids were almost certainly present in the prebiotic soup. Thus cell-like enclosures may have been present as well. Nevertheless, it is reasonable to assume

chemical reactions that led, over perhaps several "generations" (blue, red, and green, respectively) to increasingly elaborate molecular complexes. (As the keys in the two small boxes below indicate, the products of one generation become the building blocks for the next.) Among those complexes, some began to carry out functions associated with the basic molecules of life.

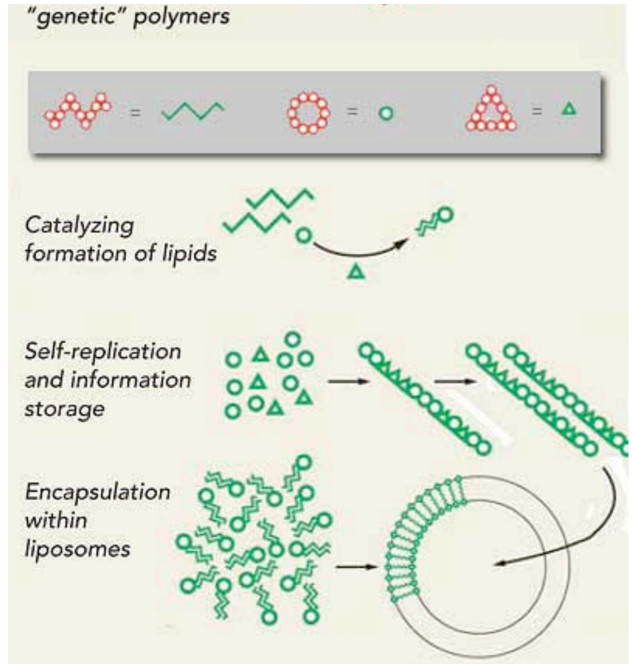


that protein synthesis and the encapsulation of machinery to replicate information did not originate until the RNA world emerged. As the molecular biologists Gerald Joyce of the Scripps Institute, Jack W. Szostak of the Howard Hughes Research Institute, and David Bartel of the Whitehead Institute for Biomedical Research in Cambridge, Massachusetts, among others, have shown, ribozymes alone can perform the reactions needed to construct key chemical bonds.

Taking into account the latest experimental evidence, it seems likely that abiotic synthesis generated the raw materials needed to assemble the first self-maintaining molecular systems capable of replicating. Even if the first living systems had little capacity to synthesize their own compounds, their primary sources of raw materials would have been organic molecules synthesized in the prebiotic soup. Perhaps the energy needed to enable these primitive systems to grow and reproduce came from cyanamide or other high-energy compounds.

Yet by the time RNA-based life appeared on Earth, the supply of raw materials needed to sustain life had probably become exhausted. This famine, so to speak, would have favored the natural selection of simple metabolic-like pathways that could supply materials needed to sustain simple living beings. Ribozymes may have helped maintain some metabolic pathways, until they eventually gave way to protein-based catalysts—that is, enzymes.

In spite of all of the scientific debates, the hypothesis that a prebiotic soup fostered an RNA world that then spawned life still offers the most coherent framework to explain life's evolution. The exact pathway for life's origin may never be known. Many gaps in understanding persist.



At some stage, complex polymers emerged that could store and transfer information via template matching. Such "genetic" polymers ultimately became encapsulated within cell-like membranes formed by lipid molecules. The resulting cell-like complexes thereby housed self-replicating molecules capable of multiplying—and hence evolving—genetic information. Many specialists consider the emergence of genetic replication to be the true origin of life.

Illustration by Advanced Illustrations Ltd

Yet, however imperfect it may be, today's evolutionary framework is rich enough not to require any appeal to the supernatural or to religious accounts such as those based on "intelligent design." Evidence of scientific incompleteness is not evidence for creationism. Although healthy disagreements on this subject will continue, scientists see such debates as challenges, not as reasons to abandon reason or data. The fact that people can reconstruct life's emergence at all, albeit with imperfect precision, should be cause for celebration: an intellectual achievement of the first rank in shedding so much light on one of the fundamental questions of existence.

Antonio Lazcano *was trained as both an undergraduate and a graduate student at the Universidad Nacional Autónoma de México in Mexico City, where he is now professor of the origins of life. After working for some time on the prebiotic synthesis of organic compounds and the role of extraterrestrial molecules in shaping the primitive environment on Earth, he has become increasingly engaged in comparative genomics as a tool for understanding the origin and early evolution of metabolic pathways. Lazcano has just been re-elected president of the International Society for the Study of the Origins of Life (ISSOL).*

Return to Web Site Archive