# Making headway with the mysteries of life's origins

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In 1863, Charles Darwin opined in a letter to a friend that contemplating the origin of life was "mere rubbish thinking" and that "one might as well think of [the] origin of matter." Many researchers today would agree with Darwin. And yet, whereas cosmologists know how particles, elements, and many molecules formed after the big bang, biologists still struggle to explain how inorganic molecules turned into the stuff of life.

That's partly because no one researcher or laboratory can tackle all aspects of the problem. But recent experiments and simulations—studying planetary habitability, the conditions needed to produce biomolecules in the ratios and concentrations for self-sustaining metabolism, and the ways in which the precursors to DNA and RNA might have assembled and replicated—are beginning to answer some fundamental questions about the origin of life.

Multiple labs are tackling these interdisciplinary challenges with myriad approaches. At least one team believes they might be on track to learn how life got a start on our planet. "For years, people working on the origin of life had many ideas but nothing that fell into place as a single working pathway," says astronomer Dimitar Sasselov of Harvard University in Cambridge, MA. "In the last two or three years, we have the outline of that pathway. If it works, we will soon have the equivalent of a living thing in the lab at the chemical level."

## Soup of Life

Some of the earliest insights into life's origins came from the classic experiments conducted by Stanley

**Natural lakes with relatively high concentrations of phosphorous compounds, such as Mono Lake in California, may have been commonplace in the prebiotic Earth, providing the phosphorus-rich environments for biology and life to take hold. Image credit: Shutterstock/Radoslaw Lecyk.**



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**While seeking signs of fossilized microbial life in Mars' Jezero crater, once home to a river delta, NASA's Perseverance rover could uncover evidence of ferrocyanide derivatives, which would favor a hypothesis about how life started—one in which hydrogen cyanide reacts with the abundant iron dissolved in the waters of a lake, forming ferrocyanide, and causing cyanide salts to accumulate and react with flowing water. Image credit: NASA/JPL-Caltech.**

Miller and Harold Urey at the University of Chicago in the 1950s. The two chemists placed simple molecules such as water, ammonia, methane, and hydrogen in a flask and zapped them with heat and electricity (1). The setup was meant to simulate conditions on the early Earth, when our warm planet was bathed in gases and crackled with lightning. The crucible could induce reactions to form fairly complex molecules, including a number of amino acids, the building blocks of proteins.

Since then, researchers have discovered that the chemical precursors of life are common throughout the cosmos and can arise even in non-terrestrial environments. Radio telescopes have spotted the simplest amino acid, glycine, in interstellar dust clouds, and many meteorites that fall to Earth are packed with biomolecules.

To figure out how such organic chemicals might have formed, astrochemist Karin Öberg has simulated some aspects of outer space in her lab at Harvard. The gas and dust clouds surrounding nascent stars are known to contain tiny dust grains encrusted with ice. Starting in 2004, Öberg began simulating some of these environments. She and her colleagues placed dust grains coated with frozen carbon monoxide, molecular oxygen, methane, and other ices in a layer 10 to 100 molecules thick in high-vacuum chambers at extremely low temperatures. They then exposed the setup to ultraviolet radiation and electrons to mimic the environment near a young star. Under such conditions, methane ($CH_4$) and molecular oxygen ($O_2$) will transform into methanol ($CH_3OH$), whereas other organics can arise from the carbon monoxide (2). "You can form rather complex things, including amino acids, without too much trouble," Öberg says.

Peering into the vast cosmic wilderness, Öberg and others have detected simple biomolecules in young stellar disks at different distances from their central star, using the Atacama Large Millimeter/submillimeter Array (ALMA) and other radio telescopes. Dust grains encrusted with biomolecules could end up in Earth-like rocky planets that coalesce in the stellar disk relatively close to the parent star.

## Possible Pathway

But life needs more than just a broth of biomolecules; these chemicals need to be of specific kinds and present in specific amounts. So Sasselov—who, like Öberg, is one of 26 researchers working with an initiative called the Simons Collaboration on the Origins of Life (SCOL)—looked to see whether ultraviolet light helps create the right chemical conditions for life to originate. He focused his attention on the effect of UV light on nucleic acids, the building blocks of DNA and RNA.

Like all molecules, nucleic acids come in different isomers, which are different arrangements of the same atomic components. Isomers can differ in their functionality. Only one isomer of each of the canonical nucleic acids that constitute DNA and RNA—adenine, guanine, cytosine, thymine, and uracil—can be used to make self-replicating genetic material. Yet natural processes produce many different nucleic acid isomers. Building on previous work, Sasselov has shown that exposing the various isomers to ultraviolet light preferentially destroys the non-useful ones, leaving behind those relevant for life (3). The results imply that the origin of life might have happened in shallow water exposed to sunlight, rather than near deep-sea hydrothermal vents, as some researchers have previously hypothesized.

Getting the right chemicals, however, is not sufficient. The chemicals also need to be present in high enough concentrations in a particular environment to become incorporated into biomolecules. Take, for example, the case of phosphorus, an essential component of life on Earth. Phosphorus helps form the backbone of DNA and RNA, as well as adenosine triphosphate (ATP), which cells use to exchange energy. Yet in nature, phosphorus tends to be locked away, combining with atoms such as calcium to form minerals like apatite that make it unavailable to biomolecules.

There are, however, some natural lakes in the United States, Canada, India, and parts of Africa that have relatively high concentrations of phosphorous compounds. The lakes are found in low-lying, dry places and contain carbon-rich minerals that form when dissolved carbon dioxide from the atmosphere interacts with calcium to form calcium carbonate, thereby freeing the phosphorus. Planetary researcher David Catling of the University of Washington in Seattle, another SCOL collaborator, speculates that on the prebiotic Earth, which had relatively high amounts of carbon dioxide in its atmosphere, such lakes might have been common and provided the phosphorus-rich environments for biology to take hold (4).

These lakes possibly also contained dissolved hydrogen cyanide, which likely either formed in our planet's early atmosphere or fell to Earth via comet impacts. Chemist John Sutherland of the Medical Research Council in Cambridge, England, who currently co-leads SCOL, has helped develop a model in which this hydrogen cyanide would have reacted with the abundant iron dissolved in the waters, forming ferrocyanide. Through cycles of evaporation and refilling of the shallow lakes, this ferrocyanide would cause cyanide salts to accumulate in the ground. If streams later flowed over these deposits, they could have facilitated chemical reactions and built up large concentrations of various important molecules suspended in an aquatic environment. "You can get really interesting ways of mimicking what a chemist does in a laboratory on a planetary surface," Sutherland says.

Given such findings, researchers now have an idea for how the compounds of prebiotic chemistry might have been stockpiled on our planet. Early on, the Earth's atmosphere might have mainly contained simple molecules, including carbon dioxide, hydrogen cyanide, and molecular nitrogen. Lakes containing carbon minerals could have accumulated phosphorous in their depths. Dissolved hydrogen cyanide would have created ferrocyanide salts. Evaporation cycles could then repeatedly dry the lakes out and concentrate all these materials during wetter seasons. Volcanoes and meteorite impacts might add additional necessary metals, such as magnesium and potassium, to the mix.

If such a rich body of water were exposed to sulfur dioxide and ultraviolet radiation, the resulting chemical reactions would produce a wide diversity of organic molecules. The stuff of biochemistry—nucleotides, amino acids, and lipids, which help form cell membranes —would have all sprung up in this fertile environment in the specific forms needed for cells. Additional organics might have occasionally rained down from space via asteroid and comet impacts (5).

The journey from such organic chemicals to self-replicating biomolecules and cells was still a long way off, but a number of researchers believe it may have involved strands of RNA. Nearly 40 years ago, biochemists noticed that at the core of ribosomes, the organelles that synthesize proteins, is an enzyme called a ribozyme (6). Ribozymes are strands of RNA capable of catalyzing reactions on other RNA strands, cleaving and splicing the genetic material. According to one scenario, known as the RNA-world hypothesis, life got going when ribozymes appeared on the scene. These ribozymes might have gotten encapsulated in lipids by chance, forming a compartment in which biochemical reactions could take place. Perhaps another RNA strand encountered a ribozyme and set off a reaction that made more copies of the RNA strand. The RNA would fill the compartment, eventually stretching and splitting the vesicle into two. "They'd be like floppy fluctuating bags," says biophysicist Irene Chen of the University of California, Los Angeles, who works on the RNA-world hypothesis for SCOL.

Such steps are plausible given what researchers know about RNA and other organics. Yet even here, many gaps remain before researchers can see their way to creating life. "The dot, dot, dot happens when you get to inventing proteins," Chen says. Those gaps have yet to be filled.

## Different Roads to Life

The scenario for the origin of life outlined by the Simons collaboration, however, is not the only one. Other collaborations, including the Origins Center in The Netherlands, the Earth-Life Science Institute in Japan, and CRC 235 Emergence of Life in Germany, have tackled some of the same fundamental questions. Often, this has focused less on the creation of specific molecules and the still-controversial RNA-world hypothesis and more on how metabolic cycles, such as the Krebs cycle—which organisms use to derive energy from fats, proteins, and carbohydrates—might have arisen as a whole.

"You can take all the molecules you have in the biochemical database and stir them with a spoon, and life will not happen," says prebiotic chemist Kamila Muchowska of the University of Strasbourg in France, who is not a SCOL member. "Life is a process; it's not a frozen fixture."

Although she favors the idea that key processes rather than self-replicated molecules emerged first, Muchowska has worked with others to bridge the gap between the two different approaches (7). Even those within the SCOL collaboration recognize that theirs is merely one hypothesis among many and that it's possible life could have emerged in multiple ways. Sutherland is looking forward to data from NASA's Perseverance rover, which landed on Mars on February 18. The rover will explore the Jezero crater, thought to be the site of a former shallow lake much like the one in his models. If the probe were to, for instance, find evidence of ferrocyanide derivatives, that would favor his hypothesis. But should future exploration of unlit ocean moons in the outer solar system discover life beneath their icy shells, it would suggest that life's origins did not rely on ultraviolet energy for life's creation (8). Even the smallest unequivocal evidence could have huge consequences for answering questions about the origin of life. "If you find life there," says Öberg, "then that would suggest it's probably super abundant in the universe."


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