
Jim Sugar

Stanley Miller 1930–2007

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During the 1993 meeting of the International Society for the Study of the Origin of Life in Barcelona, Spain, a local newspaper proclaimed the attendance of *el padre de la química prebiòtica*—the father of prebiotic chemistry—referring to Stanley Lloyd Miller. The title was dramatic, but not inappropriate. Forty years earlier, as a 23-year-old graduate student, Miller had shocked both the scientific community and society as a whole with his demonstration that organic biomolecules could be synthesized in a laboratory simulation of the primitive Earth. In the years following his landmark experiment, Miller continued to be a leader and innovator in the study of the origin of life and surely had earned the venerable title.

Stanley Miller was born in Oakland, California, and earned his bachelor's degree in chemistry at the University of California, Berkeley, before attending the University of Chicago for his doctoral studies. It was in Chicago that Miller would perform the experiments that would shape his career, despite an initial preference for theory over 'messy' and 'time-consuming' experiments. Following a one-year postdoctoral fellowship at the California Institute of Technology, Miller joined the faculty of Columbia University in 1955. In 1960 he was recruited by his mentor Harold Urey to the brand-new San Diego campus of the University of California, where he spent the remainder of his career until his death on 20 May 2007.

The story of Miller's defining achievement begins in 1951, when, as a new graduate student at the University of Chicago, Miller attended a lecture given by Harold Urey on the subject of the origin of the solar system. Urey described the conditions under which Earth and the other planets would have formed and suggested an outline for the conditions under which life presumably had arisen. Theories for the origin of life, in 1951 and still today, can be partitioned into two broad competing philosophies: autotrophy and heterotrophy. An autotrophic organism is characterized by its ability to grow and reproduce by synthesizing everything it needs, requiring only the most basic inorganic materials and an energy source, such as sunlight or various gradients. In contrast, heterotrophic organisms are simpler because they do not rely on making all of their nutrients themselves, but instead must scavenge some of their complex organic building blocks from the environment. Heterotrophy, articulated most famously with Darwin's suggestion that life arose from a 'warm little pond', had long been a familiar concept, but this begged the question of where the building blocks for life—amino acids, nucleic acid bases and sugars, among others—would have come from. Urey believed that for the origin of life to be most plausible, these biological starting materials should have been formed as the result of relatively robust and likely natural processes. These ideas intrigued Miller, and he eventually approached Urey with the proposal of studying the abiotic synthesis of organic biomolecules under prebiotic conditions for his thesis project.

The now-famous Miller-Urey experiment was designed to simulate the conditions of the primitive Earth as they were understood at the time. A sealed glass apparatus was constructed with two hollow spheres in a closed circuit of tubing. One sphere contained water and could be heated to simulate the Earth's oceans. It was connected to a second sphere that represented the Earth's atmosphere, and in the original experiment was filled with a reducing mixture of gases based on Urey's model of the early Earth. The circuit was completed by a trap between the 'atmosphere' and the 'ocean' to condense volatile materials from the 'atmosphere' and 'rain' them into the 'ocean'. The experiment was initiated with the addition of an energy source in the form of a spark discharge between two electrodes in the 'atmosphere' to simulate lightning. When the 'lightning' was turned on in Miller's experiment, the colorless, gaseous starting materials, over the course of days, gave rise to a rich and complex mixture of organic molecules that turned the experiment's 'ocean' yellow and deposited a sticky, tar-like substance on the walls of the atmosphere flask. In Miller's analysis of the products, he found large amounts of several amino acids, one of the main types of building blocks for life. The experiment was a success beyond anyone's expectations, and the discovery, published in *Science* in 1953, was considered shocking and amazing. The implications were tremendous in the context of the heterotrophic model of life's origin because the fundamental components for the assembly of living systems, rather than being specialized, rare molecules, would have been produced in large quantities as a consequence of natural processes and, because of availability, would have promoted their assimilation into the substance of life. The discovery captivated the imaginations of scientists and nonscientists alike, and fueled a new era of origins-related research that continues to this day.

Miller continued for the rest of his career to contribute important advances along with a standard of careful research, insightful dialog and leadership in the field of prebiotic chemistry that he had helped create. He continued to investigate the prebiotic syntheses of amino acids and helped match the amino acid signatures found in fallen meteorites to that of spark-discharge experiments, showing that this prebiotic synthesis process had occurred at least somewhere in our own solar system. Miller also focused on the components of nucleic acids, vitamins and coenzymes, and placed constraints on the set of likely conditions at the origin of life by carefully studying the decomposition kinetics of biomolecules. And although origins research remained Miller's primary emphasis, he also made fundamental contributions to the study of clathrate hydrates and the mechanism of general anesthesia.

In recent years, the relevance of Miller's spark-discharge experiment has been questioned by some. Currently favored models for the composition of the primitive atmosphere predict a nearly neutral atmosphere rather than the highly reducing mix of gases used in the Miller-Urey experiment. Spark-discharge experiments performed in those types of neutral atmospheres have traditionally not produced many, if any, detectable amino acids, although a recent report suggests that simply buffering the 'ocean' is sufficient to rescue high levels of amino acid production. Although many questions remain to be answered, it appears that Miller's simulated prebiotic synthesis is robust and quite likely ubiquitous in the universe. But beyond the specific details of Miller's discovery, most importantly, it transformed origins-of-life research from a largely theoretical to an experimental science, and an explosion of data and ideas has blossomed in the decades that have followed. A humble and generous mentor, Stanley inspired those around him with his passion and dedication to his science, but those who knew him will also remember his kindness and sense of humor.

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