Stanley L. Miller

1930–2007

BIOGRAPHICAL *Memoirs*

A Biographical Memoir by
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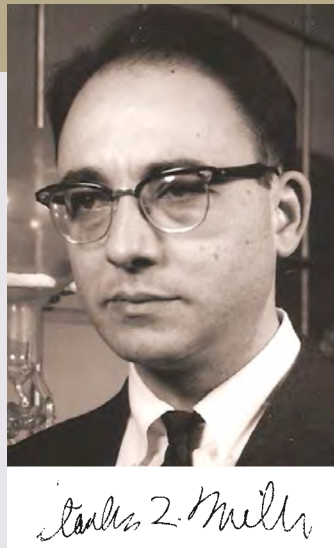
and Antonio Lazcano

NATIONAL ACADEMY OF SCIENCES

STANLEY L. **MILLER**

March 7, 1930–May 20, 2007

Elected to the NAS, 1973



From negavtive in The Register of Stanley Miller Papers, the Mandeville Special Collection Library at the Geisel Library, University of California at San Diego; MSS 642, box 163, file 5.

By Jeffrey L. Bada
and Antonio Lazcano

Stanley l. Miller, who was considered to be the father of prebiotic chemistry—the synthetic organic chemistry that takes place under natural conditions in geocosmochemical environments—passed away on May 20, 2007, at age 77 after a lengthy illness. Stanley was known worldwide for his 1950s demonstration of the prebiotic synthesis of organic compounds, such as amino acids, under simulated primitive Earth conditions in the context of the origin of life. On May 15, 1953, while Miller was a graduate student of Harold C. Urey at the University of Chicago, he published a short paper in *Science* on the synthesis of amino acids under simulated early Earth conditions. This paper and the experiment it described had a tremendous impact and immediately transformed the study of the origin of life into a respectable field of inquiry.

Stanley Lloyd Miller was born in March 7, 1930, in Oakland, California, the second child (the first was his brother, Donald) of Nathan and Edith Miller, descendants of Jewish immigrants from the eastern European countries of Belarus and Latvia. Both parents attended the University of California, Berkeley, where they met. Stanley's father became a very successful attorney who was appointed a deputy district attorney in 1927 by Earl Warren, then the district attorney in Alameda County and who eventually became the 30th governor of California and the 14th chief justice of the U.S. Supreme Court. The Miller and Warren families were close friends, and as a young boy, Stanley played with the Warren children.

Stanley's mother had been a teacher and thus education was highly emphasized in the Miller family. From an early age Stanley was an eager learner and avid reader. He easily advanced through Oakland High School, where he was known as "a chem whiz." He also had an interest in the natural world and became involved in the Boy Scouts, achieving the level of Eagle Scout. Stanley particularly liked Boy Scout summer camp because he could get away from people, enjoy the beauty of nature, and read undisturbed. After he returned to California in 1960 as a faculty member of the new University of California campus in San Diego, he often spent summers in the Sierra Nevada Mountains.

Both Miller sons were expected not only to excel in their studies and go to college but also to extend their education beyond a bachelor's degree. Like his parents before him, Stanley as well as his brother Donald, went to UC Berkeley for their undergraduate studies. Because his brother had chosen to study chemistry, Stanley decided to follow in his footsteps, mainly because he knew his brother would help him if he had trouble with his courses. He had taken most of the undergraduate chemistry classes by the end of his junior year and as a senior took graduate courses and carried out a senior thesis research project. Stanley obviously did extremely well at Berkeley and his first two published papers were based on his undergraduate research.

When it came time to think about graduate schools, Stanley consulted with several of his professors and he came up with a short list of schools they recommended. One of the concerns Stanley had was financial support. His father had died in 1946 and the family was not able to pay for graduate school. The only type of funding support available at the time was from teaching assistantships. Of the universities recommended by the Berkeley faculty, only the University of Chicago and the Massachusetts Institute of Technology offered teaching assistantships. Stanley put the University of Chicago at the top of his list, and was thrilled when he received a telegram in February 1951 notifying him of his acceptance, including an offer of a teaching assistantship. Stanley graduated from Berkeley in June 1951 and headed for Chicago.

The experiment of a lifetime

Stanley arrived at the University of Chicago in September 1951 and, besides enrolling in required courses, started to look around for a possible thesis project. At first he was not inclined to do an experimental thesis. He claimed experiments tended to be "time-consuming, messy and not as important" as theoretical research (1974). It is interesting to note that Stanley's first published paper, derived from his senior undergraduate research, was a single-authored theoretical paper on polarographic currents. As he discussed topics with various professors, the one that initially caught his interest was one suggested by Edward Teller on how the elements were synthesized in stars. Stanley started to investigate the topic and eventually after about six months finally began to understand the scope of the project.

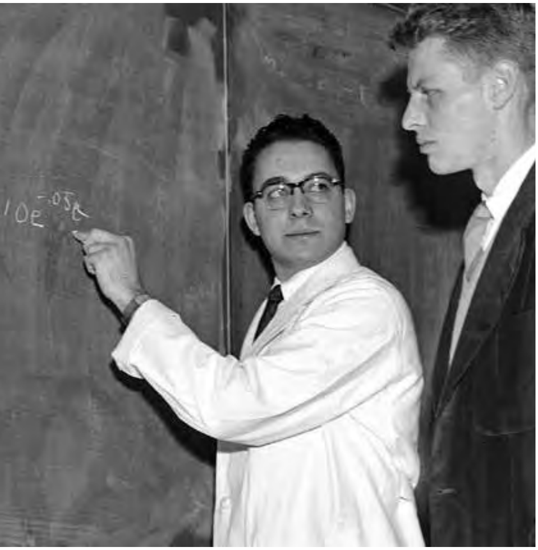
As was customary, graduate students were expected to attend seminars presented in the Chemistry Department. During his first semester in the fall of 1951, Stanley went to a seminar in which the Nobel laureate and University of Chicago chemistry professor Harold C. Urey presented his ideas about the origin of the solar system and the chemical events associated with this process. One of the points that Urey made was that the atmosphere of primitive Earth was much different from the modern atmosphere and likely consisted of a highly reducing gas mixture of methane, ammonia, hydrogen sulfide, and hydrogen. Urey further suggested that with such an atmosphere it might be possible to synthesize organic compounds that in turn could have provided the raw materials needed for the emergence of life.

The concept of prebiotic synthesis was originally proposed in 1924 by a pioneer in the origin-of-life field, Aleksandr Ivanovich Oparin.[1] Oparin suggested that collections of molecules synthesized by natural processes were continually reacting with each other in a prebiotic soup, and that the ones persisting the longest would come to predominate. This process of chemical evolution led to the first self-replicating entities, and once this had happened biological evolution took over.

As Urey pointed out in his lecture, up until that time few experiments had been conducted to mimic prebiotic organic synthesis and suggested that someone needed to try to synthesize organic compounds using reducing conditions, The next year, in 1952, Urey published a paper in the *Proceedings of the National Academy of Sciences* that detailed his model of Earth's primitive atmosphere and its role in the origin of life. Stanley was obviously taken with Urey's lecture and ideas because he could remember in great detail its content even decades later.

After working on the origins-of-elements problem with Teller for nearly a year and making little progress, Stanley was confronted with a dilemma when Teller announced he was leaving Chicago to start a weapons laboratory at the Lawrence Livermore National Laboratory. Although Teller offered to continue to supervise Miller's thesis work from afar, several professors, in particular Willard Libby, thought this was a bad idea. So Stanley was left to search for another thesis topic. In retrospect, Teller did Stanley a huge favor because the origin of the elements was soon to be elucidated in elegant detail by Margaret and Geoffrey Burbidge, William Fowler, and Fred Hoyle in classic papers published in 1956-1957.[2]

At this point Stanley began to think again about Urey's talk. He approached Urey in September 1952 about the possibility of doing a prebiotic synthesis experiment using a reducing gas mixture. Urey was not very enthusiastic. He felt, with some justification, that graduate students should only do experiments that had a reasonable chance of working, rather than taking a leap into the unknown. He suggested instead that Miller work on determining the amount of the element thallium in meteorites, a safe and pedestrian topic. The reasoning for the project was that the abundances of thallium seemed higher in the crust when compared with its abundance in meteorites, but Urey felt the data were too inadequate to confirm this and the issue could only be resolved with further careful analyses. But Miller was persistent about the prebiotic synthesis project. Urey finally relented and agreed to let him try some experiments, but specified that there must be signs of success within a year or the project should be abandoned.



Stanley Miller at the University of Chicago in 1953 explaining an equation to a fellow student. (© Bettmann/CORBIS)

The first challenge was to design an apparatus for the experiment. The mixture of water and gases that Urey wanted Miller to try was unlikely to do anything interesting if it just sat there in a flask. Some sort of high-energy input to induce chemical reactions would be required. Miller knew that chemists had been experimenting with electric sparks in gas mixtures since the pioneering work in the 18th century by Lord Cavendish, who showed that the action of a spark discharge in air resulted in the production of nitrous acid (Cavendish, 1788). It appeared that no one had thought about how this might relate to prebiotic syntheses and the origin of life. He realized that such discharges were probably common on early Earth. The atmosphere at the time must have been subject to extensive lightning along with corona discharges, and lightning would also have been associated with volcanic eruptions that were also likely to have been common on primitive Earth. In the laboratory a spark discharge simulating these processes could easily be made by using a simple commercial Tesla coil.

The apparatus Miller and Urey designed was meant to simulate the ocean-atmosphere system on primitive Earth. This apparatus configuration, now referred to as the classic apparatus, was the one most extensively used in the original experiments, and is the one most widely known today. The apparatus consisted of two glass flasks connected by glass tubing (see Figure 1a in Lazcano and Bada, 2003). One flask contained water, while the other had electrodes and contained the reduced gases methane, ammonia, and hydrogen to be tested in the experiment (most of the ammonia gas dissolved into the water flask during the experiment). One tube directly connected the water flask to the gas/electrode flask. The other tube was U shaped and connected the two flasks. At the top of the U tube was a condenser that acted to condense water from the gas flask, allowing it to flow back into the water flask. Water vapor produced by heating the water flask would be like evaporation from the oceans, and as it mixed with the reduced gases, it would mimic a water-vaporsaturated primitive atmosphere. The condenser returned any compounds produced in the gas phase back into the water, much like rain and river discharge transport compounds from the atmosphere into the oceans.

The "volcanic" apparatus showing the jet of steam into the spark flask. (Courtesy David Brigg BBC Scotland)

During the course of Miller's thesis work, he constructed two other apparatus designs. One apparatus (now referred to as the volcanic apparatus) had an aspirating nozzle that attached the water-containing flask directly to the one with the electrodes and gas, so that it injected a jet of steam and gas into the spark (see Figure 1c in Lazcano and Bada, 2003), possibly mimicking a steam-rich volcanic plume. The third apparatus used a so-called silent discharge instead of a spark (see Figure 1d in Lazcano and Bada, 2003), a concept that had been used previously in attempts to make organic compounds from carbon dioxide in order to try to understand photosynthesis.

Results with the classic apparatus were produced almost as soon as Stanley began the experiments in the fall of 1952. Although the methods available to Stanley were crude in comparison with contemporary analytical tools,[3] he was able to demonstrate that glycine could be detected after only two days of sparking the gaseous mixture. After repeating the experiment and sparking the gas mixture for a whole week, he noticed that the inside of the sparking flask was coated with a dark, oily material and the water had a yellow-brown color.[3] When two-dimensional paper chromatography with ninhydrin detection was used to analyze the water solution, the glycine spot was much more than intense and spots corresponding to several other amino acids were also detected.[4]

When Miller showed the results to Urey, they decided that it was time to write a manuscript describing the experiment and submit for publication, preferably in a leading journal. Stanley completed a draft of the manuscript and asked Urey for his comments, which he promptly gave. Urey declined Stanley's offer to be coauthor because Stanley would receive little or no credit. Urey then contacted the editors of *Science* and asked them to quickly review the manuscript and publish it as soon as possible.

The manuscript with Stanley as the single author was mailed to *Science* on February 10, 1953, and was received at the editorial office on February 14 (a detailed record of the submission and subsequent correspondence with *Science* is in the Urey papers in the Mandeville Special Collection in the library at the University of California, San Diego). On February 27, 1953, Urey wrote Howard Meyerhoff, chair of the Editorial Board, complaining about the lack of progress in publication of the manuscript.[5] After another month went by with still no decision from *Science*, Urey was infuriated and sent Meyerhoff a telegram on March 10 asking that *Science* return the paper. Urey then submitted the manuscript on Stanley's behalf to the *Journal of the American Chemical Society* on March 13. In the meantime, Meyerhoff, obviously frustrated with what he considered to be Urey's interference with the publication process, wrote directly to Stanley on March 11 telling him that he wanted to publish the manuscript. Stanley promptly accepted Meyerhoff 's offer to publish the manuscript and telegraphed the editor of the *Journal of the American Chemical Society* asking that the manuscript be returned, stating, "A mistake was made in sending this to you." The paper appeared two months later in the May 15 issue of *Science* (1953).

Interestingly, while Stanley's manuscript was under review at *Science*, another paper by Kenneth Wilde and coworkers on the attempted electric arc synthesis of organic compounds using carbon dioxide and water was also under review. This manuscript was received on December 15, 1952, two months before Stanley's was submitted. In the Wilde et al. manuscript, it was reported that no interesting products, such as formaldehyde, were synthesized using the carbon dioxide and water mixture. This result nicely supported the surmise of Miller and Urey that reducing conditions were needed in order for effective organic syntheses to take place. The Wilde et al. paper was published in *Science* on July 10, 1953, and made no mention of Stanley's paper although they did mention that their experiments had "implications with respect to the origin of living matter on earth."

Although Stanley's experiments and publication of the *Science* paper laid the foundation for the field of prebiotic synthesis, further work was needed to validate the results. Thus, Miller started to refine the details and the analytical aspects of the experiment. The first order of business was to identify the amino acids more rigorously. He used melting-point determinations, which at that time were considered to be the most conclusive way to identify organic compounds.[6] These tests confirmed the identities of the amino acids Miller had found earlier, and also showed that an even wider variety of amino acids had been made than he had first thought. At the end of all this painstaking work, nine different amino acids had been positively identified, and a host of others whose identity was uncertain were also shown to be present. Some of the ones that had been identified—such as glycine, alanine, and glutamic acid—are found in proteins, but others, such as β-alanine, are not.

Amino acids were not the only compounds produced in the discharge apparatus. Miller found another class of closely related compounds called hydroxy acids. The simplest of these was glycolic acid, the hydroxy acid analog of glycine. The hydroxy acid relative of alanine, lactic acid, was also found, as were the hydroxy acids corresponding to many of the other amino acids that had been produced in the experiment (1955). This led Stanley to suggest that the amino acids had been synthesized by the Strecker reaction (Strecker, 1850). In this synthesis hydrogen cyanide reacted with aldehydes and ketones in the presence of ammonia to first form amino nitriles, which when hydrolyzed yielded amino acids. By painstakingly carrying out a time-series sampling of the spark-discharge-apparatus water solution, Stanley was able to demonstrate cyanide and aldehydes were produced during the course of the experiment, thus supporting the surmise of a Strecker-based synthesis (1957).

Two years later, an English research group reported first repetition of Miller's experiment and confirmed his results (Hough and Rogers, 1956). Soon afterwards, other laboratories repeated Miller's experiments, using a variety of conditions and energy sources. Their results demonstrated the importance of using reducing gases in the "atmosphere" flask of the experiment; if methane were replaced with carbon dioxide and ammonia with nitrogen, only very low amounts of amino acids were apparently produced. Other energy sources such as ultraviolet light gave similar results, though the yields of amino acids were in general lower than those obtained with a spark discharge. However, in the absence of an energy source, even if the atmosphere was reducing, nothing would happen.

The Miller experiment made headlines of major newspapers and periodicals around the world, attracting the attention of both researchers and the public.

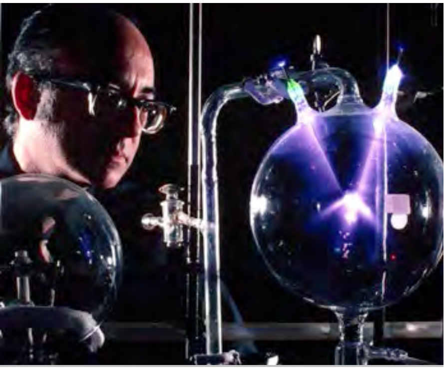
After Miller earned his Ph.D. in chemistry in 1954, he moved to the California Institute of Technology, where he was an F. B. Jewett Fellow in 1954-1955. During this period, he worked on determining the mechanism involved in the amino and hydroxy acid synthesis (1957). Stanley then joined the Department of Biochemistry at the College of Physicians and Surgeons, Columbia University, where he stayed until 1960 when he was appointed the first assistant professor in the Department of Chemistry at the new University of California, San Diego.

The Miller experiment made headlines of major newspapers and periodicals around the world, attracting the attention of both researchers and the public. When Oparin heard the news of Stanley's experiment, he supposedly commented that he did not believe the results.[7] Nevertheless, in 1957 Oparin invited Miller to visit the Soviet Union and take part in the first international meeting devoted fully to the origin of life to be held in Moscow (see Lazcano and Bada, 2008). But this was at the height of the cold war, and Miller was hesitant to go. He rapidly wrote to Urey asking for advice. Urey's letter in response ends with a very revealing paragraph:

> *I do not know how to advise you. I think each of us must make up his own mind about this. The nuclear scientists went some time ago, and if they will let nuclear scientists go in the United States without stigmatizing them, I should think that innocent people like us might also go, but one never knows what a McCarthy will do in the future. It is a very sad situation.*

Stanley decided to take his chances and accepted Oparin's invitation and started the paperwork to obtain travel funds. Before he departed, he was approached by American intelligence officers and asked to report to them any "interesting information" that he may have the chance to see. When he returned home he was interrogated by the agents; thirty years later he would chuckle describing how he had played the naïve young scientist overwhelmed by the hot weather in Moscow and the lack of air conditioning in Soviet buildings (Lazcano and Bada, 2008).

In the early 1970s Miller and his collaborators repeated the 1953 experiment and used the now available automatic amino acid analyzer to detect the amino acids that were produced (Ring et al, 1972). This time they found 33 different amino acids, including over half of the 20 that are commonly found in proteins. As they expected, amino acids that had the most carbons in their side chains were the least abundant. In addition, a comparison of the amino acid abundances detected in the Murchison carbonaceous chondrite was found to be similar to that produced in the spark discharge experiments, suggesting that the meteorite amino acids were produced by the Strecker reaction that took place somewhere in the early solar system (Ring et al., 1972).



Stanley Miller with a spark discharge apparatus 1994. (© Roger Ressmeyer/CORBIS)

Miller continued to carry out research in various aspects of prebiotic chemistry and the origin of life for the rest of his career. His main interest was not only the synthesis of key biochemical components under plausible conditions on early Earth and elsewhere but also on the stability of these compounds in geocosmochemical environments. Miller was particularly interested in how the transition from simple abiotic chemistry to biochemistry took place and the nature of the first entity that could undergo imperfect self-sustaining replication. This was reflected in his experimental analysis of the stability of RNA components (1998); the prebiotic synthesis of alternative nucleobases that could substitute for those present in present-day RNA and DNA (1995); and the synthesis under possible prebiotic conditions of the subunits of peptide nucleic acids, which is considered by some to be the prototype molecular entity capable of self-sustained imperfect self-replication (2000).

A series of strokes starting in November 1999 left him increasingly disabled.

Just prior to Miller's death on May 20, 2007, several boxes containing vials of dried residues were found among his laboratory materials at the University of California, San Diego. His notebooks (Mandeville Special Collections, Geisel Library, University of California, San Diego) indicated that the vials came from his 1952-1954 University of Chicago experiments that used the three different apparatus configurations, as well from a set of experiments conducted in 1958 while he was at Columbia University.

Although Miller repeated his experiment in the 1970s using a modified version of the original classic configuration, the other apparatus designs he made in his thesis work were never tested again. Finding dried portions of all three experiments from the 1952-1954 experiments meant that by reanalyzing the original residues, we could compare yields in the various designs in more detail than Miller had originally done. In addition, included were a set of preserved samples from experiments Miller had conducted in 1958 that had been generated using a mixture of CH_4, NH_3, H_2S, and CO_2, a gas mixture Miller had never tested before. The original dried residues from this experiment had been collected, catalogued, and stored by Miller. This experiment marks the first spark discharge experiment to which H_2S was added to the gas mixture that imitated the primordial atmosphere, but for unknown reasons, analyses of the residues from this experiment apparently were never analyzed or reported by Miller.

It was only logical that with his research into the origin of life that Stanley also was interested in the possibility of life beyond Earth, in particular on Mars.

These preserved samples presented a unique opportunity to reinvestigate Miller's pioneering experiments. We and our colleagues[8] carried out a series of analyses on these samples using state-of-the-art analytical methods in order to better understand the diversity of compounds produced (Johnson et al., 2008; Parker et al., 2011a,b,c). We found that with the "volcanic" apparatus a much wider variety of amino acids and amines, including many that had not been reported previously in spark discharge experiments, were produced. In the 1958 experiments with H_2S, besides an abundant mixture of various amino acids, seven organosulfur compounds were also detected. This experiment was the first synthesis of sulfur amino acids from spark discharge experiments designed to imitate primordial environments. These recent analyses of Miller's preserved experimental extracts once again demonstrate the breakthrough nature of his pioneering work.

Life on Mars?

It was only logical that with his research into the origin of life that Stanley also was interested in the possibility of life beyond Earth, in particular on Mars. This interest is reflected in the statement below (1959):

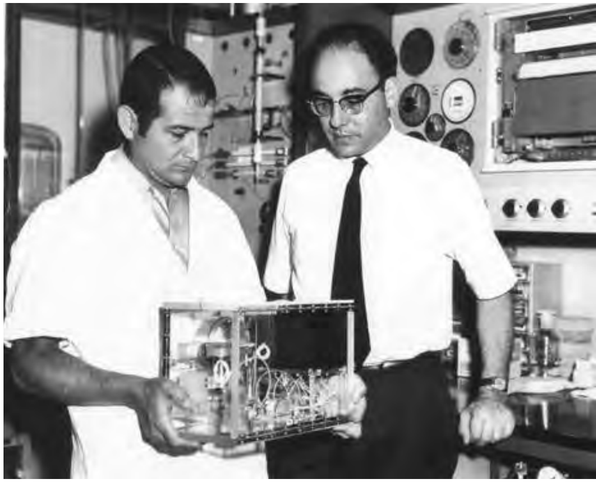
> *Surely one of the most marvelous feats of 20th-century science would be the firm proof that life exists on another planet. All the projected space flights and the high costs of such developments would be fully justified if they were able to establish the existence of life on either Mars or Venus. In that case, the thesis that life develops spontaneously when the conditions are favorable would be far more firmly established, and our whole view of the problem of the origin of life would be confirmed.*

Stanley further developed the idea of searching for evidence of life on Mars in a little-known paper (1963) where he summarized what was known about the evidence for life on Mars at that time. He was especially intrigued by the claim of William Sinton (1959) who had measured the reflectance spectra of Mars and concluded that this provided evidence for the presence of vegetation. Stanley expressed doubts about the validity of Sinton's claims,[9] but it likely motivated him to think about the possibility of the origin of life beyond Earth. In the 1963 paper Stanley suggested that the development of a "reliable experiment to determine whether life is actually present on Mars becomes even more urgent." Typical of Stanley, he turned his attention to doing just that.

Stanley considered amino acids to be the best compounds to search for on Mars because of their ubiquitous role in terrestrial biochemistry and the ease by which they could be synthesized under prebiotic conditions. He received a grant from NASA to develop a miniaturized extraction system and an amino acid analyzer that could be deployed on a future mission to the red planet. Stanley was able to construct a functioning prototype of the instrument that was about the size of a shoebox (compare this to the standard laboratory amino acid analyzer that at the time was about the size of a large refrigerator). He also worked with scientists at NASA Ames to construct a complementary gas chromatograph instrument that could separate amino acid enantiomers to help determine the origin of any detected amino acids,. The assumption was that life would be based only on one amino acid enantiomer, and thus life on Mars would be expected to be homochiral as on Earth, although it could be based on the opposite handedness compared to terrestrial life.

With prototype instrumentation in hand Stanley decided to try to use it to answer the question of life beyond Earth once and for all. He proposed the amino acid instruments as part of the experimental package for the NASA Viking missions that landed two spacecrafts on the surface of Mars in 1976. He was disappointed when he learned that the instrument was not selected; in his final report to NASA Stanley mentioned that he hoped that something along the lines of his proposed design might someday fly to Mars. NASA did obviously appreciate Stanley's interest in searching for organic compounds on Mars: he was personally invited to attend the 1976 Viking landings at the Jet Propulsion Laboratory in Pasadena.[10]

Stanley's dream of searching for amino acids on Mars and determining their chirality was resurrected two decades later. The detection of amino acids and their enantiomers was a central focus of the "Urey Mars Organic and Oxidant Detector" instrument that was selected as one of the instruments on the European Space Agency's ExoMars mission (Aubrey et al., 2008), although funding for the instrument was to be provided by NASA. Urey could detect amino acids at the part-pertrillion level, equivalent to the presence of only around 10^3 bacterial cells in a gram of soil. After several years of development, because of cost issues and concerns about complexity, the Urey instrument was eventually considered too risky to be included in the ExoMars instrument suite.



Stanley Miller with Fred Castillo in 1969 with a prototype of a minaturized amino acids analyzer developed to search for amino acids on Mars. The instrument in the backgorund was the commerical version of the automatic amino acid analyzer available at the time.
(From The Register of Stanley Miller Papers 1952 to 2010 in the Mandeville Special Collection Library at the Geisel Library, University of California at San Diego; MSS 642, box 133, file 3.)

The search for amino acids, however, may soon yield results. The Mars Science Laboratory that was launched on November 26, 2011, has as part of its instrument package, the Surface Analysis on Mars (SAM) instrument suite, which has the capability of possibly detecting amino acids in Martian

Stanley became intrigued with clathrates when he read about the problem that methane chlathrate formation posed in gas pipelines. The formation of the methane clathrates plugged the pipelines and impeded gas flow.

surface samples (Mahaffy, 2008). But whether any detected amino acids are abiotic or biotic in origin, which could be ascertained by their chirality, is beyond SAM's capabilities. Miller's dream of searching for amino acids possibly associated with life on Mars is still sometime in the future.

Clathrates and exploding ice

Although Stanley is best known for his work in prebiotic chemistry, he also made significant contributions to the understanding of gas clathrates (hydrates). Clathrates are icy solids made of water molecules that contain "cages" in which small gas molecules can be entrapped. They form at a pressure and temperature characteristic of the particular gas that is encapsulated.

Stanley became intrigued with clathrates when he read about the problem that methane chlathrate formation posed in gas pipelines. The formation of the methane clathrates plugged the pipelines and impeded gas flow. Stanley wondered if gas clathrate might form in natural environments and thus began investigating their possible geochemical and cosmochemical occurrence. This resulted in a 1961 *PNAS* paper on the presence of gas clathrates in the solar system.

At about the same time, Stanley became interested in the role of gas clathrates in anesthesia. He noted in a *PNAS* paper also published in 1961 that several anesthetic gases formed stable clathrates and perhaps these formed under physiological conditions and allowed the anesthetic gases to be transported in the blood stream. Interestingly, Linus Pauling published the same idea in a *Science* paper (1963), a couple of months prior to Stanley's publication.

Stanley's gas clathrate research led him in 1969 to predict the presence of the clathrate of air in the Antarctic ice sheet at the depth where gas bubbles had been found to disappear. He named this naturally occurring air clathrate "craigite" in honor of his friend and fellow Urey graduate student Harmon Craig (1969). It was soon jokingly noted by various colleagues that when craigite melts at atmospheric pressure it spontaneously explodes to hot gas and water, in reference to Craig's sometime volatile personality. Others soon confirmed the presence of craigite in Antarctic ice.

Another significant aspect of Stanley's clathrate research dealt with the occurrence of the carbon dioxide clathrate on Mars. The NASA Mariner Mars flybys in the 1960s provided confirmation of the temperature of the Martian ice caps and the partial pressure of carbon dioxide in the atmosphere that previously had been obtained only by Earth-based observations. Stanley took the Mariner information and predicted that the clathrate $CO_2 \bullet 6H_2O$ would be stable under the conditions at the poles of Mars and thus should be a significant component of the Martian polar ice (1970). This prediction was later confirmed by other observations.

The Stanley Steamer

As time went by Stanley stopped one of the customs he had followed his entire scientific career: he ceased to write down his name in books he purchased. The only exceptions were those books about railroad engines and steam-powered automobiles. His fascination with steam power took him in several directions, including a trip on the Trans-Siberian railroad pulled by a steam-powered locomotive in the early 1970s.

At about that time he mentioned his interest in steam power to a graduate student who had an office just down the hall from Stanley's laboratory at UCSD. As part of his Ph.D. thesis work, the graduate student, Ray Salemme, had helped set up a machine shop in collaboration with the Physics Department. After discussing their mutual interest in steam power, Stanley and Ray decided to recruit a team (eventually including a professor of engineering, Rod Burton, and about a half dozen assorted graduate and undergraduate students) to build a steam car to compete in the Intercollegiate Clean Air Car Race. The concept of an automobile powered by an alternative to the internal combustion engine was ahead of its time as were so many of Stanley's research ideas.

After numerous design exercises and experiments (including a few minor explosions), the final design incorporated a Harley-Davidson 74 cubic inch V2 motorcycle engine that received high-pressure steam from a Doble-inspired, coiled-monotube steam generator heated by propane. The drive train was mounted in an American Motors Javelin chassis that was donated to the project. The car was not completely finished in time for the race, so the team trucked the parts to a staging area in a garage in Cambridge, Massachusetts, to do the final assembly. Owing to a mishap while traveling across the country, many of the planned automatic control systems were not installed, so it took two operators to drive the car.

The 1970 Intercollegiate Clean Air Car Race featured 50 low-emission vehicles from 40 colleges and universities all over America. Electric cars, hybrid electric cars, steam cars, propane cars, and turbine cars were placed in five separate race divisions. The race started at the Massachusetts Institute of Technology in Cambridge on August 24, 1970, and ended at the California Institute of Technology in Pasadena, California on September 2, 1970.

The longest run attempted by Stanley's steam car entry was a few miles, which was probably not bad considering the car's early stage of development. After the race, the steam car was shown at several auto shows around the country. The car was ultimately sold at auction to a steam locomotion enthusiast.

Stanley Miller biking near Nuite St. George, France in 1985. (From The Register of Stanley Miller Papers 1952 to 2010 in the Mandeville Special Collection Library at the Geisel Library, University of California at San Diego; MSS 642, box 163, file 1.)

Activities beyond science

Although Miller was a dedicated scientist, he also had many outside interests and activities. He was an avid traveler, and he documented his travels with slides, which he eagerly showed to his friends when he returned home. His 1957 trip to Moscow to attend the First International Conference on the Origin of Life was his first trip to Europe (also probably the first on an airplane) and he kept a detailed account of the people he met, the food and the various places he visited.[11] Stanley was also a railroad enthusiast and especially liked steam locomotives (thus his interest in the steam car), which was perhaps a carryover from the times he traveled to Chicago and later New York when train transportation was often the only affordable means of travel. Miller frequently went on trips in Europe and elsewhere by train, including taking the Trans-Siberian railroad from Moscow to Vladivostok, as well as train trips across India and to various areas in Japan. After traveling in India, Miller took a bus through the Khyber Pass in the Hindu Kush Mountains between Pakistan and Afghanistan. He then traveled on to Iran and other places in the Middle East.

Miller especially enjoyed riding his bicycle and often rode from his home to UCSD, as well as to various regions of San Diego County. One of his favorite activities was to take bicycling tours in Europe that involved staying at hotels with outstanding restaurants nearby. He felt he could indulge himself with excellent meals because he would get plenty of exercise the next day. Miller often returned to the Evergreen Lodge just outside Yosemite National Park in the summer, where he would ride his bicycle to various places in the area.

Stanley Miller in his office at the University of California, San Diego in 2006.
(Courtesy Wes Newcome.)

Miller went on several expeditions with colleagues from the Scripps Institution of Oceanography. He traveled in 1966 and 1967 to Australia's Great Barrier Reef and the Brazilian Amazon River to take part in research onboard the RV *Alpha Helix*. He also traveled across South Africa, Kenya, and Tanzania with one of us (J. L. B.) during research trips to collect samples for the study of the geochemistry of amino acids in fossil bones. The places visited in Tanzania included Olduvai Gorge, where we were hosted by Mary Leakey.

Besides these activities Miller enjoyed opera. He read extensively on the history of World War II, possibly because part of his family suffered greatly during this period. He was an avid reader of books on Winston Churchill and maritime warfare.

Honors and awards

Miller was awarded numerous honors throughout his career. He was president of the International Society for the Study of the Origin of Life (1986-1989) and he was awarded the society's Oparin Medal in 1983 for his work in the field. He was selected as an honorary councilor of the Higher Council for Scientific Research of Spain in 1973. Miller was elected to the National Academy of Sciences in 1973. In 2009 his 1953 paper in *Science* was selected by the Division for the History of Chemistry of the American Chemical Society for one of their Citation for Chemical Breakthrough awards. Miller belonged to Sigma Xi and Phi Beta Kappa and was a member of the American Chemical Society, American Association for the Advancement of Science, and American Society of Biological Chemists.

NOTES

1. The book titled *Proiskhozhdenie zhizny* was not widely available in English until 1967 when it was translated and published as part of a book by J. D. Bernal (*Origin of Life*, pp. 199-234. London: Weidenfeld & Nicolson). A copy of the original Oparin publication in Russian is in the Register of Stanley Miller Papers 1952-2010 (MSS 642, box 185, file 1).
2. See F. Hoyle, W. A. Fowler, E. M. Burbidge, and G. R. Burbidge. Origin of the elements in stars. *Science* 124(1956):611-614 and E. M. Burbidge, G. R. Burbidge, W. A. Fowler, and F. Hoyle. Synthesis of elements in stars. *Rev. Mod. Phys.* 29(1957):547-650.
3. Harmon Craig and Gerald Wasserburg were also graduate students in Urey's laboratory (both would also become members of the National Academy of Sciences) when Stanley did the first experiment. When Stanley showed them that the solution in the spark discharge experiment had turned brown after a couple of days of sparking the gas mixture, they started snickering. When Stanley asked them what they were laughing at, they told him he had a lot of fly excrement (they did not use that polite word) in his apparatus and that he should have cleaned it out better (personal communication to J. L. B., e-mail message, June 16, 2010, from G. Wasserburg).
4. At the time, amino acid separation by paper chromatography followed by detection of the separated amino acids by reaction with ninhydrin was the most readily available technique. The first stages of the development of the automatic amino acid analyzer were being carried out by Stanford Moore and William Stein (they were awarded the 1972 Nobel Prize in Chemistry for this work), but it would not be until the 1960s that these instruments became commercially available. Because of their cost, only a few laboratories could afford these, although by 1970 many major universities and research centers had acquired one.

5. On Sunday March 8, 1953, *The New York Times* published a short article titled "Looking back two billion years" that described the experiments by Wollman M. MacNevin and his associates at The Ohio State University. It was reported that MacNevin and his team had performed a number of experiments simulating the primitive Earth, including a discharge experiment in which a spark was sent through methane producing "resinous solids too complex for analysis." MacNevin also reported the production of porphyrin from the heating of a mixture of CO_2, H_2O, and NH_3. When Stanley read this, he was obviously concerned because the next day he sent Urey a copy of the clipping along with the following note: "I am not sure what should be done now, since their work [MacNevin and his group] is, in essence, my thesis. As of today, I have not received the proof from *Science*, and in the letter that was sent to you, Meyerhoff said that he had sent my note for review." Stanley was right to be concerned. MacKevin organized a symposium on prebiological chemistry that was held at The Ohio State University on April 25, 1953, less than a month before Stanley's *Science* paper appeared. Several of the papers presented discussed the synthesis of organic compounds under various conditions, although none of these were evidently ever published in scientific journals. A record of the correspondence associated with the manuscript can be found in the Register of the Harold Clayton Urey Papers 1929-1981 in the Mandeville Special Collection Library at the Geisel Library, University of California, San Diego (MSS 0044, box 58, file 18). The volume of the papers at the prebiological chemistry symposium is in the Register of Stanley Miller Papers (1952-2010) in the Mandeville Special Collection Library at the Geisel Library, University of California, San Diego (box 145, file 10).
6. Marcel Florkin, a Belgian biochemist interested in evolution, was having breakfast with Oparin the day Belgium newspapers carried a story about Stanley's experiment. When Florkin showed Oparin one of the newspapers, he immediately said he did not believe the results. Miller noted in 1994 that "perhaps this would explain why Oparin never did an experiment to test his theory of a reducing atmosphere." See the August 1994 comments attached to Miller (1974) available in the Register of Stanley Miller Papers (1952-2010) in the Mandeville Special Collection Library at the Geisel Library, University of California, San Diego (MSS 642, box 25, file 6).
7. To help with compound identification Urey referred Miller to another professor in the Chemistry Department at Chicago, Weldon Brown, who suggested that Miller should determine the melting points of the compounds he thought were present. At that time the melting point of an unknown compound if identical to that of an authentic compound was considered a strong positive identification. But this required long, dedicated work, and it took Miller several months to do this. The melting points eventually confirmed his identifications (1974).

8. The collaborators included two former Ph.D. students of Miller, Jason Dworkin and Henderson James Cleaves, as well as Daniel Glavin, a former Ph.D. student of one of us (J. L. B.).
9. The Sinton correspondence is available in the Register of Stanley Miller Papers (1952-2010) in the Mandeville Special Collection Library at the Geisel Library, University of California, San Diego (box 222, file 5).
10. As was typical, Stanley saved all the correspondence associated with the Viking landings including telegrams with information about delays in the landing date as well as decals commemorating the landings. In the Register of Stanley Miller Papers (1952-2010) in the Mandeville Special Collection Library at the Geisel Library, University of California, San Diego (MSS 642, box 83, file 9).
11. These notes as well as those from other trips are in the Register of Stanley Miller Papers 1952-2010 in the Mandeville Special Collection Library at the Geisel Library, University of California, San Diego (MSS 642, box 145, file 13). Also in the Stanley Miller Papers is his first passport that was issued in June 1957 (MSS 642, box 1, file 3). In this is stamped: "This passport is not valid for travel in Hungary," which may explain why Stanley may have had apprehensions about going to Russia. It was also not valid for "Albania, Bulgaria and those portions of China, Korea and Viet-Nam under Communist control."

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