Stanley L. Miller

10 The First Laboratory Synthesis of Organic Compounds under Primitive Earth Conditions

It is now generally accepted by scientists that life arose on the earth early in its history. The sequence of events started with the synthesis of simple organic compounds by various processes. These simple organic compounds reacted to form polymers,[1] which in turn reacted to form structures of greater and greater complexity, until one was formed that could be called living.

This is a relatively new idea, first expressed clearly by A. I. Oparin in 1938 [2] (a Russian version of his book appeared in 1924 but received little notice). The first synthesis of organic compounds under primitive earth conditions was not done until 1953. There had been a great deal of speculation prior to this on the origin of life, but much of it was incorrect, incomplete, or not convincing. An example of an incorrect hypothesis was the proposal that a living organism arose spontaneously by an extremely improbable event while the atmosphere of the earth was essentially the same as now; such an organism would have had to be like an alga and to be able to synthesize all its constituents from carbon dioxide, water, and light. The reason for making such a proposal was that there was no known mechanism for making organic compounds in the earth's atmosphere except by photosynthetic organisms. When a mechanism became available for synthesizing organic compounds in the atmosphere of the primitive earth, proposals of this type involving extremely improbable events were no longer seriously considered.

It is not strictly correct to say that the 1953 experiments were the first organic compound synthesis under primitive earth conditions. Many of the reactions previously studied by organic chemists have turned out to be important primitive earth synthetic reactions. This includes the first synthesis of an organic compound from inorganic materials,[3] the synthesis of urea from ammonium cyanate by F. Wöhler in 1828. But the motivation of such studies was to synthesize organic compounds and not to understand what happened on the primitive earth. In addition, a number of scientists had attempted to produce organic compounds under primitive earth conditions, but they had assumed the wrong primitive atmosphere and they obtained no organic compounds at all or in extremely small yield. So the first successful prebiotic synthesis experiment was done in 1953, and I will explain how these experiments came about.

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At the beginning of my senior year (1950) at the Berkeley campus of the University of California, I made the rounds of the professors I knew to find out which graduate schools in chemistry were the good ones. Perhaps this was earlier than necessary, but the choice of a graduate school is an important one. I received some frank evaluations of various graduate schools and was advised to go to the best all-around chemistry department unless I was interested in a particular field of chemistry or professor. But there was also the essential factor of financial support. At that time, almost the only source of support for graduate students was a teaching assistantship. Of the universities with good chemistry departments, only the University of Chicago and the Massachusetts Institute of Technology had an adequate teaching assistantship. I applied to both these places, with the University of Chicago being my first choice, and I was very pleased when a telegram arrived in February 1951 saying I was accepted there.

I arrived in Chicago in September 1951, registered for the usual courses, and naturally attended the chemistry department seminars. About the middle of the fall semester, Urey gave a seminar on the origin of the solar system, in which he pointed out that the solar system is reducing (that is, there is an excess of molecular hydrogen) except for the earth and the minor planets (Mars, Venus, and Mercury), which are more oxidized, with the earth's atmosphere being highly oxidized. The earth's atmosphere contains carbon dioxide (CO_2), molecular nitrogen (N_2), water (H_2O), and molecular oxygen (O_2); it is highly oxidized because of the presence of molecular oxygen. It seemed very likely to Urey that the earth was also reducing when it was first formed. A reducing atmosphere would contain methane (CH_4), ammonia (NH_3), water (H_2O), and molecular hydrogen (H_2); this is just the atmosphere present on Jupiter and Saturn, except that the water has been frozen out, and on Uranus and Neptune, where both the water and ammonia have been frozen out.

A reducing atmosphere would be a favorable place to synthesize organic compounds, Urey thought, and the organic compounds synthesized would form the basis to make the first living organism on the earth. The present oxidizing atmosphere is not a favorable place to synthesize organic compounds, and a number of experiments in other laboratories which attempted to synthesize organic compounds from the constituents of the earth's atmo-

sphere (usually from carbon dioxide and water) were total failures or gave very disappointing results. Urey suggested that someone should do an experiment to test the feasibility of organic compound synthesis in a reducing atmosphere.

Urey's point immediately seemed valid to me. For the nonchemist the justification for this might be explained as follows: it is easier to synthesize an organic compound of biological interest from the reducing atmosphere constituents because less chemical bonds need to be broken and put together than is the case with the constituents of an oxidizing atmosphere. Alternatively one can say that methane is already an organic compound; therefore, it should be easier to synthesize a larger organic compound from methane in most, but not all, cases than to synthesize it from carbon dioxide, which is inorganic, as a starting material. This point is very obvious today, but it was not so clear then.

After this seminar someone pointed out to Urey that in his book Oparin had discussed the origin of life and the possibility of synthesis of organic compounds in a reducing atmosphere. Urey's discussion of the reducing atmosphere was more thorough and convincing than Oparin's; but it is still surprising that no one had by then done an experiment based on Oparin's ideas.

It was about this time that I was thinking about what type of chemistry I would do for my dissertation. As an undergraduate I had done an experimental senior research project and found experiments to be time-consuming, messy, and not as important, I then thought, as theoretical work. The synthesis of organic compounds from the reducing atmosphere constituents promised to be a very messy and time-consuming experiment. So I decided to look for a theoretical thesis topic.

I went around to the professors doing theoretical work and listened to a great many interesting projects, but the one that seemed most attractive and fundamental was suggested by Edward Teller. This was to figure out how the elements could be synthesized in very hot stars. After about six months of looking at this problem and just as I was beginning to understand it and make a little progress, Teller announced to me one day that he was leaving the University of Chicago to set up a laboratory in Livermore, California. Although Teller said I could continue the project in Chicago while he was

in California, this did not seem a good way to do things, and the chemistry department advised against this. Subsequently others worked on the problem of element synthesis in stars, and the generally accepted method for their synthesis is along the lines of the project I had just started.

It was now September 1952, and I was confronted with the problem of finding a new thesis topic. I now remembered Urey's seminar and the more I thought about it, the more reasonable it seemed, and the more fundamental. The problem was not just how to synthesize organic compounds on the primitive earth, it was the first step in understanding how life started on the earth. This was every bit as fundamental as the origin of the elements. So I went to Urey's office and said that I wanted to do an experiment on organic synthesis in a reducing atmosphere.

Urey seemed reluctant to go along with this and suggested that measuring the amount of the element thallium in meteorites, which was important for reasons I can no longer remember, would be a good thesis topic. I explained that thallium was very nice, but I was more interested in organic compound synthesis and hinted that it was either organic compound synthesis or I would go to another professor for a thesis project. Urey realized I was determined and then explained his reservations about the project I wanted to do. It was not that he did not believe in it, the problem was that it was an unusual project, and the chances for success were quite small. A professor has the responsibility to give a student a project that can be finished in a reasonable length of time (two to four years) so that he can finish his Ph.D. He then agreed that I could try the organic compound synthesis for six months or a year. If nothing came of the project by this time, I would have to switch to a more conventional project with a greater probability of success.

He suggested that I read the paper on which his lecture had been based,[4] Oparin's book, and a book on biochemistry of which I knew next to nothing. A few weeks later I went back to Urey to discuss what to do next, and we quickly decided that ultraviolet light and electric discharges must have been the most abundant energy sources on the primitive earth, and that an electric discharge would be best to try for the first experiments. So I repaired to the library to find out what was known about electric discharge reactions. I found considerable work had been done on electric discharge reactions of

methane alone, but little had been done on mixtures of methane with nitrogen or oxygen compounds. Some work had been done producing hydrogen cyanide from the methane and ammonia and from methane and nitrogen, but this did not make an impression on me then.[5] The action of electric discharges on methane seemed to give a random mixture of hydrocarbons, so I was convinced that I would at least get hydrocarbons as products and probably a random mixture of organic compounds containing nitrogen and/or oxygen; and this random mixture of organic compounds would contain, hopefully, a trace of amino acids and other compounds of biological interest.

I went back to Urey and reported what I had found in the literature and my feelings about a random buildup of amino acids. We decided that amino acids were the best group of compounds to look for first, since they were the building blocks of proteins and since the analytical methods were at that time relatively well developed. We then designed a glass apparatus that contained a model ocean, an atmosphere, and a condenser to produce the rain. We finished our conversation by reassuring each other that we ought to be able to find at least traces of amino acids from the action of the electric discharge on the model primitive atmosphere.

I went back to the lab and drew out the apparatus carefully enough for the glassblower to build it. The apparatus is shown in Figure 10.1. I then looked at the spark I was going to use—a Tesla coil used for detecting leaks in vacuum lines—and read the instructions that said it produced 60,000 volts of high-frequency current. As I looked at the glass apparatus I began to have second thoughts about its design. I felt that this high voltage in the presence of the water vapor might be dangerous and decided to interchange the condenser and spark from that shown in Figure 10.1. It took about a week to get everything ready. It was particularly important to make sure that there were no leaks in the apparatus because air and hydrogen or methane form explosive mixtures. I filled the apparatus with the postulated primitive atmosphere, water, methane, hydrogen, and ammonia, turned the spark on and let it run overnight. The next morning there was a thin layer of hydrocarbons on the surface of the water, and after several days the hydrocarbon layer was somewhat thicker. So I stopped the spark and looked for amino acids by one-dimensional paper chromatography (Figure 10.2a).

Paper chromatography is a simple technique for separating compounds by differences in the rate of migration of compounds, in this case amino

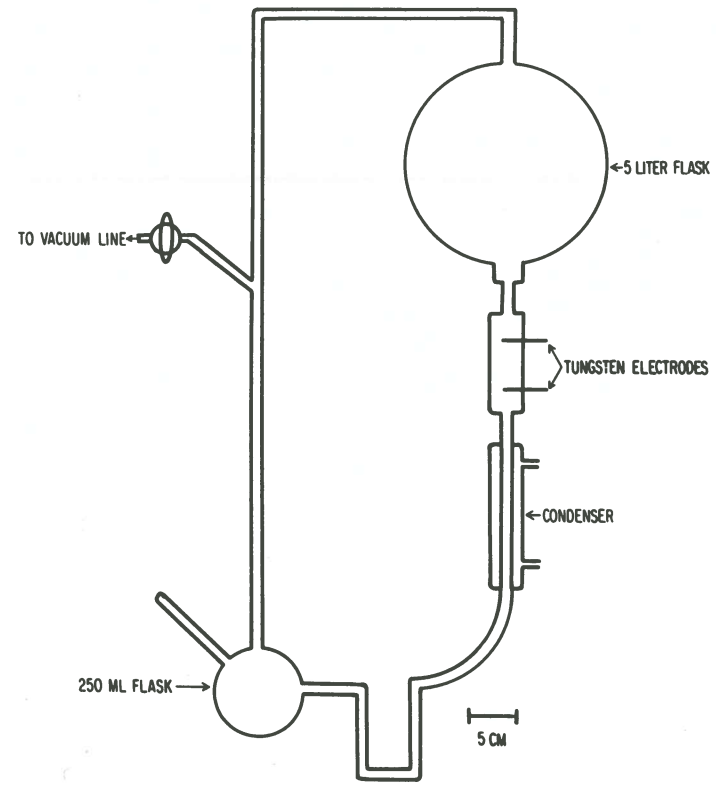

Figure 10.1. The apparatus used in the first electric discharge synthesis of amino acids. It is made entirely of glass except for the tungsten electrodes. (From S. L. Miller, "A Production of Amino Acids under Possible Primitive Earth Conditions." *Science*, Vol. *117*, 1953, p. 528.)

acids, on a piece of filter paper. The amino acids are colorless, but most of them give a purple color when they react with a compound called ninhydrin.

I was not particularly disappointed when no amino acids showed on the paper when sprayed with ninhydrin, since only traces at best were expected. I then thought about the interchanging of the spark and condenser and decided that this had been a mistake. The spark was not really dangerous. It has a high voltage but low current and can be held against one's finger with only a tingling sensation. So I took the apparatus back to the glassblower, and he put it back into its original design.

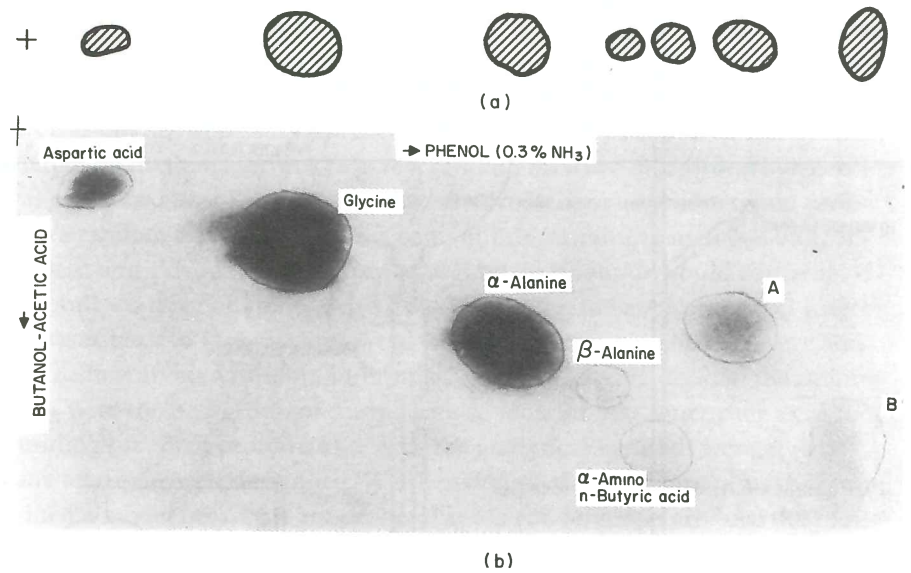

Figure 10.2. (a) Drawing of a one-dimensional paper chromatogram.

One-dimensional paper chromatography involves putting a drop of an amino acid solution at the origin (+). The solvent (phenol saturated with 0.3% aqueous ammonia in this case) is allowed to run down the strip of filter paper to the end. Different amino acids travel at different rates relative to the solvent, thereby separating them.

(b) Photograph of a two-dimensional paper chromatogram.

Two-dimensional paper chromatography involves putting a drop of amino acid solution at the origin (+) and allowing the solvent (butanol-acetic acid) to run down the sheet of filter paper as in one-dimensional paper chromatography. The paper is then dried, rotated clockwise through 90°, and the second solvent (phenol) is allowed to run down the paper, separating the amino acids over the sheet of paper. (From S. L. Miller, "A Production of Amino Acids under Possible Primitive Earth Conditions." *Science,* Vol. *117,* 1953, p. 528.)

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 a low heat. The reason for the low heating rate was that a closed system was being heated, which can build up dangerous pressures. 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.

The next day Urey returned from a lecture tour, and I went to him with the paper chromatogram. Before I could show him the chromatogram he told me about one of his lectures. He had described his ideas about the early solar system and the primitive reducing atmosphere and mentioned that I was doing an experiment. During the question period someone in the audience had asked him in a voice full of doubt, "and what do you expect to get?" Urey replied "Beilstein." *Beilstein's Handbuch der Organische Chemie,* now over 100 volumes, contains a list of properties and reactions of every organic compound that has ever been synthesized. Urey's reply meant that the electric discharge would be expected to produce a little of everything.

I then showed him the paper chromatogram with the faint glycine spot and commented that maybe I was doing better than "Beilstein" (a random mixture of organic compounds) although it was too early to tell. He was extremely pleased with this result. I said that I would repeat the experiment, this time letting the spark run for a week.

I set the apparatus up again and this time boiled the water more vigorously, making sure dangerous pressures did not build up, and started the spark. In the morning when I looked at the apparatus the solution looked distinctly pink. Then I noticed that the heater, which had an exposed coil, was glowing red and that the color probably came from the reflection of the coil. I removed the heater and the solution was still pink. My immediate thought was porphyrins (the red color in blood is due to an iron porphyrin), and I rushed over to Urey and brought him back to see the color, which he viewed with as much excitement as I did. As the sparking continued, the solution became at first a deeper red and then a yellow-brown which obscured somewhat the red color.

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 (Figure 10.2b). Two-dimensional paper chromatography involves letting one solvent separate the amino acids as in one-dimensional paper chromatography, followed by letting a second solvent run at right angles to spread the amino acids over the entire square sheet of filter paper. 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. Two spots were considerably weaker in color but corresponded to aspartic acid and α-amino-n-butyric acid. I was less confident of these identifications and decided to refer to them as tentatively identified. The two remaining spots did not correspond to any of the amino acids that occur in proteins or any known amino acids I then had on hand, so I simply referred to them as A and B.

Paper chromatography is not a very quantitative procedure, but I estimated that I had at least 10 mg of amino acids (subsequent quantitative experiments showed the presence of 110 mg of amino acids). To play it safe, I stated that the total yield of amino acids was estimated to be in the miligram range.

I showed all this to Urey and said that I thought I had enough to write a short paper on the results and he agreed. It was now December 1952 and I had been working on the project only three and a half months. The results were strikingly successful, and there was no question about my being able to continue on the project and to write my dissertation on it. The experiment needed repetition at least once and preferably twice before publication, but I could do this during the writing and during the time between the submission of the paper and its appearance. So I wrote up a short paper putting Urey's name as a coauthor and brought it to him for approval. He first said that I should take his name off since I had done this work largely by myself, and if his name was on it I would receive little or no credit. This was extremely generous of him since in chemistry the research director almost always appears on the papers resulting from the student's thesis.

We then decided that *Science* would be the best journal for the paper rather than the *Journal of the American Chemical Society,* the most prestigious chemical journal, because of the paper's interest to several fields of

science. I made the necessary revisions of the paper and sent it off a few days later.

I had by this time repeated the experiment once and began the second repetition of the experiment. The results in both repetitions were the same as before, so I was extremely confident of the results. After four months the paper appeared in *Science* (May 15, 1953).[6]

I had expected that this paper would generate considerable interest, and that *Time* magazine would probably have a piece about it in their science section since they liked this sort of thing. But the reaction to the paper startled me. It began with an article by Earl Ubell in the *New York Herald Tribune* and an article and editorial by Walter Sullivan in the *New York Times,* and spread to most newspapers across the country, including considerable mention in the local Chicago newspapers. There was even a Gallup poll asking whether people thought it possible "to create life in a test tube." (The results were 9 percent yes, 78 percent no, and 13 percent no opinion. The results of a poll today would probably give a much higher percentage of yes.) After a while the furor died down and I was able to devote full time again to the experiments.

There was a lot to do, and I spent another year and a half at Chicago completing my dissertation and a year after that at Cal Tech finishing up the experiments. The story would be too long to go into complete detail on everything I did, but I will discuss some of the highlights.

The red color observed the first day of the "successful" experiment turned out to be elusive, and the color has never been identified. It is the only aspect of the experiment that has not proved reproducible. I was able to observe the color in about six experiments, but when I rebuilt the apparatus the color no longer appeared. The red color was adsorbed on the silica that was leached from the glass. The Pyrex glass of the first apparatus was particularly rich in trace elements, and this is apparently why the red color appeared only in the original apparatus. Professor Klüver at the University of Chicago looked for porphyrins in the discharge products, especially the red color, but he could not detect any.

One day Urey came to me and said that he was concerned that the amino acids may have been produced by bacteria. We had discussed this possibility before, but it was clear that someone had expressed his concern and doubts

to Urey about the experiment. Urey said that if I had made a mistake it would be far better for me to find this out and retract the *Science* paper than if someone else found this out.

I was not really concerned about bacteria since most of the apparatus was too hot for bacteria to live in, the amino acids were not the kind and distribution obtained from bacteria, and it was evident organic compounds were being made by the spark (some of the yellow color could be seen to be made on the tungsten electrodes). But it was best to settle the bacteria problem once and for all. I filled up the apparatus with the reduced gases, completely sealed the apparatus and heated it in an autoclave for 18 hours. I then ran the spark and showed the yield was the same as the runs where the apparatus was not autoclaved. Since 15 minutes heating in an autoclave is usually sufficient to kill all bacteria, the 18 hours was overdoing it a bit, but the bacteria issue has not been raised since.

It was important to obtain quantitative values for the amino acids as well as to find out what else was present in the mixture of organic compounds produced. To do this an elaborate separation scheme involving various ion exchange resins was developed. I was able to separate the different amino acids and was also able to separate out the aliphatic and hydroxy acids. The scheme was so thorough that I would have found any single compound present in greater than 0.5 percent yield (greater than about 10 mg).

The problem of positive identification of the compounds arose. Urey sent me to one of the professors of organic chemistry (Weldon Brown) to make sure I was doing things correctly. He approved of what I had done so far but inquired if I had obtained any melting points of my amino acids. At that time the usual method of positively identifying organic compounds was to obtain a melting point of the compound or a derivative of it, show that an authentic sample of the compound has the same melting point, and most important, that the unknown and authentic compound when mixed has the same melting point. (Two different compounds both melting at, for example, 130° will melt at a considerably lower temperature when mixed.) I replied that I had not done this and that it would be difficult because of the small amounts of material available. Professor Brown said that in spite of any difficulties I should get the melting points.

This was several months work, but it was worth the effort, since the identifications were then firmly established. In subsequent work by others in

this field such care in identifying compounds was not taken, and a number of embarrassing errors have been made.

I was able to prove unequivocally by melting point the presence of glycine, alanine, and β-alanine, which I had "identified" by paper chromatography. The α-amino-n-butyric acid, which I had tentatively identified in the *Science* paper, was proved to be present, but the spot I had tentatively identified as aspartic acid turned out to be iminodiacetic acid (aspartic acid was present, but in much smaller amounts). Compound A turned out to be sarcosine (N-methyl glycine), and compound B turned out to be, in part, N-methyl alanine.

During the isolation and attempt to crystallize a derivative of sarcosine, I ran into some trouble. A compound precipitated that was not the sarcosine derivative, even though I knew that the sample must have been relatively pure sarcosine. The sarcosine derivative was eventually induced to crystallize, but there was the problem of the first set of crystals. A look at the melting point tables and a good guess showed that these crystals might be α-aminoisobutyric acid, and I was able to prove this guess correct. So this amino acid was found by an accident during the crystallization process when I did not even suspect that it was present.

The search for amino acids was very thorough in terms of the techniques then available. Nine amino acids were identified, but about twenty-five others were shown to be present but not identified, mainly because the yields were too small to prepare derivatives for identification. Between 1957 when I reported the final details of these experiments[7] and 1972, the experiment was repeated many times by others using many variations. No one was able to find any amino acids that I had not found, with one exception (serine), although many invalid claims were made. One laboratory spent five years trying to find additional compounds without success. In 1972 I repeated the experiments and using more modern and sensitive techniques, it was possible to identify 33 of the amino acids produced by the spark discharge.[8] It was also surprising that the yields of amino acids from these first experiments are the highest so far reported in any prebiotic experiment of this type.

There was always the question of whether these experiments were an adequate model of the primitive earth. For example, one objection would be that the input of electrical energy was far higher than possible in the primi-

tive atmosphere. This is a complicated topic, but a striking confirmation of the general validity of these experiments came from the analysis of a meteorite.

On September 29, 1969, a meteorite fell in Murchison, Australia. This meteorite was a carbonaceous chondrite, a meteorite that contains organic compounds. Amino acids had previously been reported in other carbonaceous chondrites, but these amino acids were generally believed to be contamination. In the case of Murchison, the meteorite was a freshly fallen one, and the techniques used were the most modern and showed convincingly that the amino acids were indigenous.

The amino acids reported in Murchison in the first paper[9] were glycine, alanine, sarcosine, glutamic acid, α-aminoisobutyric acid, all of which I had found in the electric discharge, the α-aminoisobutyric acid by accident. Valine and proline, which I had not found among the electric discharge products, were also reported. In the second paper[10] on amino acids in Murchison, among the amino acids reported were N-methyl alanine, β-alanine, aspartic acid and α-amino-n-butyric acid. In other words, most of the amino acids I had found in the electric discharge synthesis were in the meteorite. I was stunned at this result. It looked as if the Murchison amino acids were produced by an electric discharge reaction. However, a number of amino acids were found in Murchison that I had not found in the discharge. But it was easy to show on repeating the discharge experiments and using modern analytical techniques that all the amino acids found in the meteorite could also be produced in the electric discharge apparatus.

The synthesis of organic compounds under primitive earth conditions is not, of course, the synthesis of a living organism. We are just beginning to understand how the simple organic compounds were converted to polymers on the primitive earth, but how these polymers organized into the first living organisms is completely unknown. Nevertheless we are confident that the basic process is correct, so confident that it seems inevitable that a similar process has taken place on many other planets in the solar system. The question that is discussed is whether millions of planets in our galaxy, as well as other galaxies, have some form of life on them, or whether it is just a few planets. It is to be expected if there are millions of planets with life that some of them will have civilizations more advanced than our own and may

be trying to communicate with us. Radio telescopes have been used to listen for such signals, so far without success, but this listening program is just beginning. 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.

Notes

1. An example of a polymer is Nylon, in which many molecules of an amino acid ε-amino caproic acid) are linked together forming long chains. Hemoglobin, the protein in blood that binds oxygen, is also an amino acid polymer, but there are twenty different amino acids in this polymer and they are linked together in an exactly specified sequence.

2. A. I. Oparin, *The Origin of Life*. Macmillan, New York, 1938; reprinted by Dover, 1953. A translation of the 1924 pamphlet, *Proiskhozhdenie Zhizni, Moskovskii Rabochii,* Moscow, 1924, is in J. D. Bernal, *The Origin of Life*. Weidenfeld and Nicolson, London, 1967.

3. An organic compound means a compound containing carbon and usually hydrogen and may contain other elements as well. Diamond, carbon monoxide, and carbon dioxide are usually considered to be inorganic compounds. The word organic compound originally meant compounds that occur in living organisms or derived from them. It was thought that organic compounds were fundamentally different from inorganic compounds. Wöhler's synthesis of urea showed that there was no fundamental difference since an inorganic compound could be converted to an organic compound.

4. H. C. Urey, "On the Early Chemical History of the Earth and the Origin of Life." *Proceedings of the National Academy of Science* (U.S.), Vol. *38,* 1952, pp. 351–363.

5. A year later when I made a more thorough search of the literature I found a paper by Löb in 1913 (W. Löb, "Über das Verhalten des Formamids unter der Wirkung der stillen Entladung. Ein Beilrag zur Frage der Stickstoff-Assimilation." *Berichte der Deutschen Chemischen Gesellschaft,* Vol. *46,* 1913, pp. 684–697) that reported the synthesis of an amino acid (glycine) by sparking a mixture of carbon monoxide and hydrogen. This paper had been missed by workers in the field of electric discharge reactions.

6. S. L. Miller, "A Production of Amino Acids under Possible Primitive Earth Conditions." *Science,* Vol. *117,* 1953, pp. 528–529.

7. S. L. Miller, "Production of Some Organic Compounds under Possible Primitive Earth Conditions." *Journal of the American Chemical Society,* Vol. *77,* 1955, pp. 2351–2361. S. L. Miller, "The Mechanism of Synthesis of Amino Acids by Electric Discharges." *Biochimica et Biophysica Acta,* Vol. *23,* 1957, pp. 480–489. S. L. Miller, "The Formation of Organic Compounds on the Primitive Earth." *Annals of the New York Academy of Sciences,* Vol. *69,* 1957, pp. 260–274; also in *Proceedings of the First International Symposium on the Origin of Life on the Earth*. Edited by A. I. Oparin et al., Pergamon Press, New York, 1959, pp. 123–135.

8. D. Ring, Y. Wolman, N. Friedmann, and S. L. Miller, "Prebiotic Synthesis of Hydrophobic and Protein Amino Acids." *Proceedings of the National Academy of Sciences* (U.S.), Vol. *69,* 1972, pp. 765–768.
Y. Wolman, W. J. Haverland, and S. L. Miller, "Nonprotein Amino Acids from Spark Discharges and Their Comparison with the Murchison Meteorite Amino Acids." *Proceedings of the National Academy of Sciences* (U.S.), Vol. *69,* 1972, pp. 809–811.

9. K. Kvenvolden et al., "Evidence of Extraterrestrial Amino Acids and Hydrocarbons in the Murchison Meteorite." *Nature,* Vol. *228,* 1970, pp. 923–926.

10. K. A. Kvenvolden, J. G. Lawless, and C. Ponnamperuma, "Nonprotein Amino Acids in the Murchison Meteorite." *Proceedings of the National Academy of Sciences* (U.S.), Vol. *68,* 1971, pp. 486–490.

David Hubel

11 Neurobiology: A Science in Need of a Copernicus

The object of neurobiology is to understand the nervous system. For man, this amounts to asking what happens in our heads when we think, act, perceive, learn, or dream. In this essay I shall try to assess our present state of knowledge in neurobiology, in order to ask, at the end, whether anything like a Copernican revolution has occurred, is taking place, or is to be expected.

The two great interlocking branches of neurobiology are neuroanatomy and neurophysiology. Anatomy seeks to describe how the brain is put together, and physiology asks how the various parts work together. Though traditionally the two fields have tended to pursue separate courses, usually housed in separate departments at universities, in fact they are very much interdependent. Most modern neuroanatomists are not content with a simple description of spatial relationships for their own sake but soon go on to ask what the structures are for. A precise drawing of a watch, a printing press, or a television set has little interest in itself, especially if we do not know that the purpose is to tell time, print books, or entertain. Physiology, on the other hand, is simply impossible without anatomy: no one can hope to learn how a watch or printing press works without knowing where the gears or springs are.

In their development, both neuroanatomy and neurophysiology have had to wait until the physical sciences could provide them with several necessary techniques. The nerve cell, or neurone, which is the unit or building block out of which the brain is constructed, is too small to see with the unaided eye, except as a mere speck, and far too small for its signals to be recorded with ordinary wires. Hence to advance beyond the most rudimentary stages anatomy required the microscope, first the light and then the electron microscope, and physiology required the microelectrode. The crowning achievements of the neuroanatomists of the past century have been the recognition that the nerve cell is the basic unit of nervous tissue, and the discovery that nerve cells are interconnected with a high degree of order and specificity. The physiologist, using the microelectrode, has made a strong beginning by learning, in electrical and chemical terms, how the neurone transmits its messages. These two sets of accomplishments by no means tell us how the brain works, but they provide an absolutely essential groundwork.

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