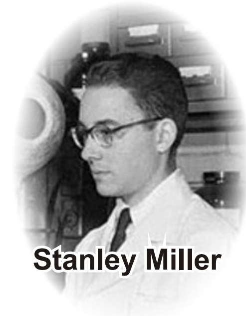
A Distinctly Human Quest

The Demise of Vitalism and the Search for Life's Origins



Stanley Miller

"Beilstein," said Harold Urey, describing his thoughts in 1953 on his graduate student Stanley Miller's ongoing experiment to synthesize amino acids from inorganic matter. He meant that the experiment would revolutionize chemistry and produce more work than Friedrich Beilstein's 100-volume *Handbuch der Organische Chemie*. But as quickly as chemists and biologists hailed Miller for determining a possible mechanism for the formation of life on Earth, they turned on his idea as incomplete. Miller's experiment demonstrated how amino acids and other organic compounds could be formed on a prehistoric Earth with an atmosphere featuring the right combination of chemicals. But it almost never happened. It was hampered by personality problems and lack of money. Most seriously, Miller's experiment contradicted centuries of scientific tradition and long-established thought. The Miller experiment demonstrates that significant scientific changes do not happen overnight, and in some cases, they may take well over a century to take place.

For centuries scientists had struggled with the question of life and how it differed from non-living matter. Vitalism, the view that at some level living organisms are fundamentally different from non-living matter, had existed since the Greeks. Most vitalist arguments reduce to two forms. One is that both living things and the organic matter that make them up contain some non-physical 'vital' force. The second is that the very organization of organic matter gives it unique characteristics. Hence, not all living processes can be explained by physics and chemistry.

Prior to 250 B.C., the Greek physician Erasistratus put forth the idea that 'vital pneuma' was carried by the arteries to the brain, where it was changed to the 'animal spirits' responsible for movement and sensation. How he came to this conclusion is interesting. He captured a bird in a pot and recorded its weight and the weight of its excrement, finding a continual weight loss despite feedings. He accounted for this by suggesting an invisible force was leaving the body. In the 2^{nd} century, the physician Galen put forth ideas regarding blood generation and flow and argued that pulmonary veins carried air to the heart where it was converted to vital spirits that was then sent to the rest of the body.

Approximately 1500 years later the physician William Harvey asked questions and conducted studies that overthrew Galen's ideas and resulted in the now accepted idea that blood circulates through the body. However, while he provided a mechanical view of blood circulation, he maintained that blood was a spiritual fluid. This is understandable given that he was unable to provide a mechanical explanation for body heat or energy. Vitalism persisted into the eighteenth and nineteenth centuries. Those accepting some sort of vitalistic position included most of the well known figures in the history of the life sciences. At this time vitalism, the view that living processes could not all be explained by chemistry and physics, made sense to most scientists.

The scientific conflict over vitalism came to the forefront in the early 1800s. Scientists thought that vital spirits acted much like Newton's forces and "many capable scientists treated forces as active powers superimposed on inert matter." An international group of three chemists – Jöns Jacob Berzelius, Justus von Liebig, and Friedrich Wöhler – would be largely responsible for providing evidence that raised questions about the scientific basis for vitalism. In 1828 Wöhler synthesized urea, a common organic chemical found in urine. But maintaining that this creation of an organic molecule in a lab was the 'deathblow' to vitalism is mistaken. Examination of Wöhler's story will demonstrate why.

Friedrich Wöhler was born in 1800 near Frankfurt, Germany. In 1821 he went to the University of Marburg to work with the famous chemist Leopold Gmelin. Upon arrival Gmelin told Wöhler not to attend any of his lectures. In an unusual college education, he had absolutely no classroom lectures or work. Instead, it consisted solely of research. Earning a doctorate in 1823, he moved to Stockholm, Sweden to work with Jöns Jacob Berzelius.

Berzelius was one of the most renowned chemists of the time, having discovered the elements thorium and selenium and having been responsible for the classification of elements by the first two letters of their Latin name. He was also the first to use the empirical formulas so common in modern chemistry. Wöhler was ecstatic to be working with a living legend in chemistry. However, Wöhler found the laboratory workshop rather sparse, describing that "adjoining the living-room, the laboratory consisted of two ordinary chambers with the simplest fittings; there was neither oven nor fume chamber, neither water nor gas supply." Still, he was a student of a great chemist.

Wöhler's workmanship needed some tempering. Berzelius was often known for telling him, "Doctor, that was quick but bad." He assigned Wöhler the menial task of mineral examination to practice using a balance. The elder Berzelius had a knack for details and scolding. Once when his maid was washing a flask and said it smelt of oxymuriatic acid, Berzelius chided her answer, saying, "Anna, thou must no longer speak of oxymuriatic acid, henceforward thou must say chlorine." It was this educated, prudent Berzelius that later assigned Wöhler to work on cyanates.


Friedrich Wöhler

In 1827, Justus von Liebig produced a substance now called 'fulminic acid.' Upon hearing his friend's discovery, Wöhler realized that cyanic acid had the same chemical composition as fulminic acid, although they had different properties. This discovery, which Berzelius called 'isomerism,' became a crucial set of knowledge for chemistry. These 'isomers' also played a significant role in Wöhler's synthesis of urea.

The next year, Wöhler was working with cyanic acid and ammonia. When he combined the two, the resulting products were always oxalic acid and a strange white substance he could not identify. Expecting to produce ammonium cyanate, he decided this white substance needed further investigation. He noted the white substance always came "in colorless, clear crystals often more than an inch long in the form of slender, four-sided, dull-pointed prisms." In his words:

> *I found that after neutralization with bases it gave salts of nitric acid, from which the crystallizable substance could be extracted again with alcohol, with all the characteristics it had before the addition of nitric acid. This similarity to urea in behavior induced me to carry out comparative experiments with completely pure urea isolated from urine, from which it was plainly apparent that urea and this crystalline substance, or cyanate of ammonia, if one can so call it, are completely identical compounds.*

The significance of Wöhler's chemical synthesis of urea, a chemical excreted in human urine, is often thought of as the end of vitalism. As Wöhler wrote to Berzelius, "I can no longer, as it were, hold back my chemical urine; and I have to let out that I can make urea without needing a kidney, whether man or dog."

But really, nobody immediately saw any connection to vitalism. There was no mention of vitalism in the exchanged letters of Wöhler and Berzelius. Liebig, a devoted vitalist, pointed out that urea was not necessary in the life process; instead, it was a *byproduct* of the life process. He maintained a vitalist stance, colorfully described in this metaphor he provided in his book *Chemical Letters*:

> *If any one assured us that the palace of the king, with its entire internal arrangement of statues and pictures, started into existence by an accidental effort of a natural force, which caused the elements to group themselves into the form of a house–because the mortar of the building is a chemical compound of carbonic acid and lime, which any novice in chemistry can prepare–we should meet such an assertion with a smile of contempt.*

At most, scientists were interested that Wöhler discovered ammonium cyanate to be an isomer of urea, and not much more.

> **Note how scientists, rather than questioning vitalism, easily interpreted Wöhler's work within the prevailing vitalist framework of thinking.**

In 1835, noted vitalist Johannes Müller wrote, "The way that elements combine in organic bodies is peculiar and conditioned by chemical forces. Though chemistry can dissolve organic compounds it cannot create them." A millennium-old belief such as vitalism could not be overturned by one experiment. Even Wöhler had his doubts:

> *This artificial formation of urea, can one regard it as an example of the formation of an organic substance from inorganic crystals? It is conspicuous that one must have for the production of cyanic acid (and also of ammonia) always initially after all, an organic substance, and a Naturphilosoph [scientist] would say that the vital aspect has not yet disappeared from either the animal carbon or the cyanic compounds derived therefrom and an organic body, therefore, may always be produced from it.*

What Wöhler means here is that to make cyanic acid, he needed organic materials. He understood the vitalist's perspective that maintained these materials would retain their life-giving properties during the experiment and therefore could potentially produce organic materials. Wöhler would ultimately decide that urea was in-between organic and inorganic compounds.

While one experiment couldn't end vitalism, it certainly raised questions that eventually hastened its decline. Other scientists continued the search to make the first true organic compound from inorganic materials, the first successful effort being acetic acid by Adolph Kolbe in

1845. Organic chemistry became a scientific discipline. Scientists soon doubted vitalism as a scientific theory. Vitalism explained everything without evidence and moreover it denied the acceptance of new evidence. Essentially, it wasn't science.

1. One experiment rarely overthrows prevailing ideas in science. Why do you suppose this is the case?

The eventual decline of vitalism came from its failure to provide a scientific explanation and guide future research. It had an ultimate, yet vague, answer for everything. As eminent biologist Ernst Mayr describes, vitalism came to an end because 1) "it virtually leaves the realm of science by falling back on an unknown and presumably unknowable factor," and 2) "because it became eventually possible to explain in physico-chemical terms all the phenomena which according to the vitalists 'demanded' a vitalistic explanation."

2. Science's approach to explaining events in the universe without invoking supernatural action is called "methodological naturalism." Individual scientists often have a deep personal faith in a supernatural being, but when doing science, researchers must provide natural rather than supernatural explanations for phenomena. This approach has undeniably been successful and has provided useful scientific explanations for phenomena that in the past were attributed solely to supernatural intervention. How does reference to an unknowable factor (in this case, a vital force) make it not science?

With the growing success at creating organic molecules from inorganic chemicals, some scientists began to speculate on a scientific answer to the origin of life. Russian scientist Alexander Oparin and British scientist J.B.S. Haldane had speculated that the early Earth atmosphere was favorable to the formation of organic chemicals. Oparin published *The Origin of Life* in 1924, but it wasn't translated into English until 1938 and was largely ignored for this reason. Haldane wrote his own *The Origin of Life* in 1928, but it was considered wildly speculative and similar to science fiction. However, the importance of Haldane's speculations about the Earth's early atmosphere is in his prediction: "The above conclusions are speculative. They will remain so until living creatures have been synthesized in the biochemical laboratory. We are a long way from that goal." Harold Urey at the University of Chicago took both of their ideas and in 1950 proposed the Earth's atmosphere needed four essential chemicals–methane (CH_4), ammonia (NH_3), hydrogen (H_2), and water (H_2O)–to produce organic molecules. All three scientists said somebody in the future should test these ideas.

It was a curious graduate student at the University of Chicago who would do this. Stanley Miller thought he could devise an experiment which would synthesize amino acids in a reproduction of the early Earth atmosphere. In 1953, he went to his advisor, Urey, and asked if he could make an experiment that might produce amino acids. Urey wasn't enthused. He felt graduate students should do straightforward experiments and suggested Miller work on determining the amount of the element thallium in meteorites.

Miller persisted and constructed an apparatus that contained all of these elements. While the experiment is often remembered as the 'Miller-Urey experiment,' Urey had little to do with it. Urey hated experiments. He found them dirty and time consuming. When Miller persisted in testing his advisor's theories, Urey found funds for the project. They diverted money from Urey's other grants and the total equipment cost was under one thousand dollars. The four chemicals were all placed in a loop of sterile glass flasks and tubes (Figure 1).

The system was sealed to ensure no outside contamination. The water was heated so that it would evaporate. Sparks were sent from one electrode to another to simulate lightning through the atmosphere containing the chemicals. The gaseous mixture was then cooled so that the water would condense and flow back to the first flask in a continuous cycle.

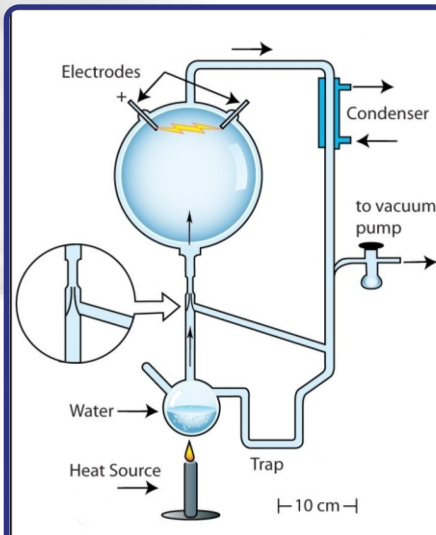


Figure 1. *Miller experiment set up.*
Photo courtesy of Ned Shaw, Indiana University

3. Note how different scientists enjoy different aspects of science. Miller enjoys laboratory work while Urey enjoys theoretical work. How are both important for doing science?

After the first day, the resulting pool of water was pink. After a week it was deep red. Miller and Urey determined that at the end of the first week of continuous operation as much 10-15% of the carbon in the system was in the form of organic compounds. Upon further analysis, they determined that amino acids, sugars, fats – precursors to nucleic acids – were formed. Miller wrote up their report and Urey declined to put his name on it – he refused to take any the credit. He would, however, use his clout to get the paper into the journal *Science*, which would otherwise be impossible for a grad student. They submitted and waited.

They waited a long time. *Science* wasn't publishing the article. An editor didn't believe the results. Meanwhile, *The New York Times* published a paper by W.M. MacNevin which was precariously close to producing similar results. Furious, Urey withdrew his paper. *Science* realized its error and published Miller's article immediately, and the scientific world was interested. Many other scientists were now inspired to perform similar experiments. However, many disagreements broke out regarding conditions on the early Earth and how that would promote or prevent the formation of prebiotic molecules. Moreover, while producing organic molecules from inorganic matter was an interesting and important development, it is still far from creating life.

Critics of Miller's work argued the primeval Earth didn't have the atmosphere he had assumed. In his original paper, Miller stated they were not looking for the optimal atmosphere, just one that would work. In the subsequent efforts by other scientists, it was fairly easy to reproduce amino acids–too easy, in fact. Any experiment including some of the elements always produced amino acids. In the fall of 1969 a meteorite fell in Australia. Analysis of the meteorite determined that it contained many amino acids, several which are found in living things on Earth. Miller was intrigued by the possibility of the origins of life on planets, and has since become a noted astrobiologist.

1953 was a significant year for the origins of life. Stanley Miller had demonstrated the production of amino acids from inorganic substances, and the structure of DNA had been determined. These two achievements enthralled the public. In Miller's experiment, people were reminded of the movie version of *Frankenstein*, in which life was produced with electricity. It seemed the origins of life could be explained through purely mechanistic principles. But as in Wöhler's case, one experiment could not refute centuries of thinking.

The origin of life on Earth continues to be a mystery. Much research into this mystery continues, and many controversies exist. Research regarding the origins of life cuts across most every scientific discipline. Vitalism and the origin of life illustrate that no single experiment can overthrow an entire way of thinking. It can, however, raise new interpretations and questions that push investigations into new areas never before conceived. The examples in this story remind us of that and illustrate how much of a human enterprise science is.

4. Science is done by people. List at least four ways how this story illustrates that science is a human enterprise.

A Distinctly Human Quest: The Demise of Vitalism and the Search for Life's Origin
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THE STORY BEHIND THE SCIENCE

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