What Is Life? What Was Life? What Will Life Be?

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Our laboratory is exploring self-assembly processes and polymerization reactions of organic compounds in natural geothermal environments and related laboratory simulations. Although the physical environment that fostered primitive cellular life is still largely unconstrained, we can be reasonably confident that liquid water was required, together with a source of organic compounds and energy to drive polymerization reactions. There must also have been a process by which the compounds were sufficiently concentrated to undergo physical and chemical interactions. In earlier work we observed that macromolecules such as nucleic acids and proteins are readily encapsulated in membranous boundaries during wet-dry cycles such as those that would occur at the edges of geothermal springs or tide pools. The resulting structures are referred to as protocells, in that they exhibit certain properties of living cells and are models of the kinds of encapsulated macromolecular systems that would have led toward the first forms of cellular life. However, the assembly of protocells is markedly inhibited by conditions associated with extreme environments: High temperature, high salt concentrations, and low pH ranges. From a biophysical perspective, it follows that the most plausible planetary environment for the origin of cellular life would be an aqueous phase at moderate temperature ranges and low ionic strength, having a pH value near neutrality and divalent cations at submillimolar concentrations. This suggestion is in marked contrast to the view that life most likely began in a geothermal or marine environment, perhaps even the extreme environment of a hydrothermal vent. A more plausible site for the origin of cellular life would be fresh water pools maintained by rain falling on volcanic land masses resembling present-day Hawaii and Iceland. After the first cellular life was able to establish itself in a relatively benign environment, it would rapidly begin to adapt through Darwinian selection to more rigorous environments, including the extreme temperatures, salt concentrations and pH ranges that we now associate with the limits of life on the Earth.

§1. Introduction

Could there be a connection between stars and life? Astrologers have always thought so, or course, but astronomers know better. Or at least they thought they did, until the birth of a new scientific discipline in 1996. The startling claim from Johnson Space Center scientists in Houston, Texas, was that they had discovered fossil microorganisms in a meteorite that was indisputably a chunk of the surface of Mars, sent sailing into space at escape velocity by the impact of a small asteroid. The excitement generated by this claim was not lost on Dan Goldin, the director of NASA. Goldin soon announced a significant new source of research funding, to be distributed under the auspices of a scientific program called Astrobiology. And that is how a seemingly impossible connection was made between astronomy and biology, by taking pieces of those two words, combining them into a new word, and most importantly, providing the research dollars in a competition that was certain to attract the finest scientific talent.

One of the goals of astrobiology is to discover how life originated on our planet and whether it exists beyond the Earth. To get some idea of the scope of the question of life's origins, let us consider for a moment what a planetary surface in our solar system was like four billion years ago. Before life began, the surfaces of the Earth and Mars were hot, mostly covered by salty oceans containing a dilute solution of thousands of organic compounds. Volcanic land masses were emerging from boiling seas, and tidal wet-dry cycles occurred daily where seas met land. Water continuously evaporated from the interface between sea and atmosphere, condensed as rain and fell on the volcanic islands where it formed small pools containing organic solutes, then evaporated again. From this unpromising chaos of land, sea and atmosphere, the first life somehow emerged, certainly on the Earth, perhaps on Mars.

Because life today is so much a phenomenon of chemistry, it has been mostly chemists who are attracted to the question of how life began. Chemists see this question through their perception that the origin of life is best understood as a chemical process. And of course, this is true, at least in part. When the first organisms began to grow and reproduce on the early Earth, chemical reactions associated with growth, metabolism and replication were central to much of what we call the living state. But how could the chemistry begin?

I believe that the answer will be found in the realm of physics, and more specifically biophysics, defined as the physical processes that we now associate with the living state. The chemistry of life only becomes possible after physical processes permit specific chemical reactions to begin in compartmented systems of molecular assemblages that emerge when the laws of physics and chemistry intersect. On the early Earth, over a period of time measured in tens to hundreds of millions of years, vast numbers of microscopic compartments were produced at interfaces of minerals, water and atmosphere. One or a few of these molecular systems happened to be capable of capturing energy and nutrients to begin the polymerization process that we call growth. At some point in time, one set of compartmented polymers not only grew in size, but also interacted in such a way that the polymers could reproduce and evolve. The chance assembly of a compartmented set of polymers capable of energy-dependent growth, reproduction and evolution marked the beginning of life as we know it today.

One of the reasons why this scenario seems plausible is that it is so easy to make encapsulated systems of macromolecules. The figure below on the left shows a preparation in which short strands of DNA were captured in vesicles composed of a fatty acid, and on the right are vesicles produced by lipid-like compounds extracted from a meteorite. In both cases, lipid bilayer membranes spontaneously self-assemble from dried lipid molecules when water is added, a simulation of the wet-dry cycles that must have been ubiquitous in the early Earth environment. If anything else is present in the mixture, such as DNA or proteins, it is encapsulated in the vesicles and results in the emergence of protocells, cell-like structures that are not alive, but exhibit certain properties of life.

In the sentence above I used the term emergence, and this concept is affecting the way we think about scientific knowledge related to the origin of life. In common usage, emergence is an unexpected happening, as an emergency. But the word emergence is acquiring a new meaning beyond common usage. It is also in the sense

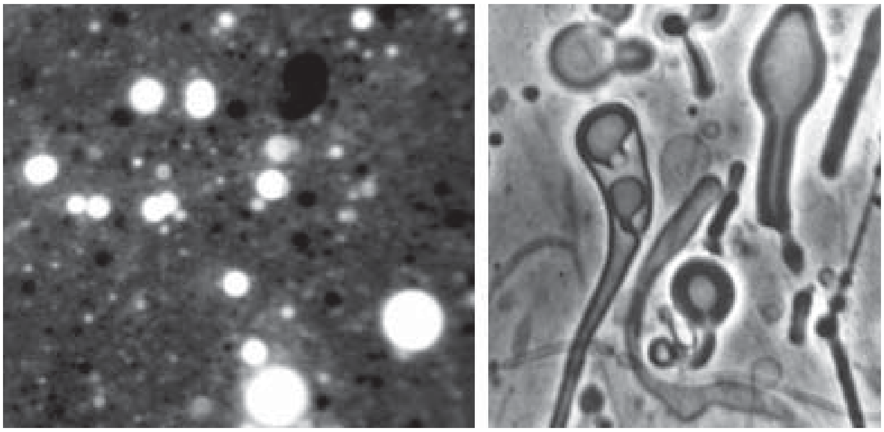

Fig. 1. Self-assembled celluar structures related to the origin of life. The image on the left shows DNA captured in fatty acid vesicles, and the DNA has been stained with a fluorescent dye called acridine orange. The image on the right shows vesicles produced by lipid-like molecules extracted from a carbonaceous meteorite. This result demonstrates that cellular compartments can form from non-biological organic compounds likely to have been available on the prebiotic Earth.

of an unexpected phenomenon that the word is used by the scientific community, yet it is more nuanced than that. Emergence in science is now being used to connote the process by which increased complexity emerges from a less complex system under the influence of an energy flux through the system. There is a certain mysterious quality to its use in this regard, in that the emergent property is typically unexpected and cannot be predicted in advance of the observation. For this reason, some scientists with a philosophically reductionistic mindset dislike the word. Its use is the opposite of reductionism, in which everything is believed to be explainable by understanding ever simpler components of a system.

But reductionism is unable to account for the observation that under certain conditions systems become increasingly and unpredictably complex. The reality of emergent phenomena was first demonstrated by the initial attempts to use mathematical models to predict the weather, which is fundamentally a process in which a source of energy (sunlight) interacts with vast masses of gas (the atmosphere). Equations were formulated that worked for a while, but were discovered to be disturbed by extremely small variations in the numerical inputs so that the outcomes became unpredictable. This is why, as Mark Twain put it, "Everyone talks about the weather, but nobody does anything about it". Out of this discrepancy between mathematics and the real world grew an astonishing concept called chaos theory, which held that certain aspects of physical reality are governed by processes that cannot be precisely modeled by a set of equations. When energy interacts with matter under certain conditions, we can confidently predict that *something* will happen, but we can never predict where, when or how it will happen. That *something* is what we will refer to as emergence.

Because living systems emerged through the action of physical laws that in turn permitted certain chemical reactions to occur, the difference between physics and chemistry should be made clear at this point. In general, chemistry can be considered to be a subset of physics, and certainly physicists would agree with this claim. Why am I taking the trouble to make this distinction? The reason, as noted earlier, is that the field of origins of life research has been dominated by chemists who have tended to overlook the physical foundations. So here I will refer to chemical reactions as those processes by which changes occur in the electronic structure of atoms and molecules in such a way that compounds with new properties emerge. Chemical reactions are also characterized by changes in the energy content of the system of molecules, and the reactions always have an end point called equilibrium, when no further net changes occur. A common example of a chemical reaction is to light a match. The compounds in the match head contain a certain amount of chemical energy which is released as heat when they react, with water and carbon dioxide as products of the reaction. The biological analogy is the oxidative metabolism of animals, which was referred to as the "fire of life" by physiologist Max Kleiber in his groundbreaking book having the same title. In contrast, when a physical process occurs, it typically changes the energy content of the system but does not alter the electronic structure of components of the system. A common example of a physical process is to add energy to a soap solution by blowing air through a straw into the solution. The energy is used to arrange soap molecules into transient structures called soap bubbles, but no permanent changes occur in the properties of the soap molecules.

I think that something like this occurred on the early Earth. But instead of macroscopic bubbles, physical processes occurring at the microscopic level produced vast numbers of cell-sized compartments containing a near infinite variety of components. Within this multitude, a rare few happened to have a mix that could somehow capture energy and smaller molecules from the surrounding environment and use the energy to link them into larger molecules, a primitive version of growth by polymerization. At some point, again by happenstance, two chemical properties of life emerged within the compartmented growing polymers. The first property is catalysis, in which one polymeric molecule interacts with other polymers is such a way the growth reactions proceed more rapidly. The second is replication, in which a polymer is able to be copied by a catalyzed growth process. Life begins at this point, when catalyzed growth of a polymer somehow leads to its reproduction at the expense of energy and nutrients from the environment.

§2. How life begins: A hypothesis

There are numerous proposals about how life began. These are often very general and lack details, such as Oparin's original proposal in 1924 that life began as jelly-like blobs he called coacervates, or Bernal's later suggestion that clay mineral surfaces were somehow involved. At the other end of the spectrum are highly specific ideas, for instance, that life began as a self-replicating RNA molecule, or as a thin film of two-dimensional metabolism on the surface of iron sulfide (pyrite mineral, or fool's gold).

What I will propose here is not just an idea, but instead an integrated set of concepts that arise from plausibility arguments. Each concept represents a piece of the puzzle, and I will attempt to integrate the pieces into a descriptive scenario, essentially a hypothesis with testable predictions.

- The most plausible site for the origin of life was not the open ocean, or ice fields, or dry land. Instead, there is reason to think that a fresh water environment would be most conducive to life's beginnings, in the form of an interface between mineral surfaces as volcanic lava, a body of liquid water and the early atmosphere.
- The local environment of the site was not a warm little pond, as Darwin suggested in a letter to his friend Joseph Hooker in 1871. Instead it would more likely resemble the kinds of hot acidic pools that we see today in volcanic regions, in which the water is constantly being disturbed and going through cycles of wetting and drying.
- The pools contained complex mixtures of dilute organic compounds from a variety of sources, including extraterrestrial material delivered during late accretion, and other compounds produced by chemical reactions associated with volcanoes and atmospheric reactions.
- The compounds are of two varieties. One variety includes the familiar water soluble species that are monomers with the capacity to be chemically linked into polymers. Examples include amino acids, nucleobases such as adenine and uracil, simple sugars such as glyceraldehydes and ribose, and phosphate. The second variety includes amphiphilic compounds like fatty acids and fatty alcohols that self-assemble into membranous compartments.
- During the drying cycle, the dilute mixtures would be highly concentrated into very thin films on mineral surfaces, a process that is necessary for chemical reactions to proceed. Not only would the compounds react with one another under these conditions, but the products of the reactions become encapsulated in the microscopic compartments produced by the amphiphilic compounds.
- The result of this process was that vast numbers of what we call protocells appeared all over the early Earth, wherever water solutions were undergoing wet-dry cycles in volcanic environments similar to today's Hawaii or Iceland. Protocells are defined as compartmented systems of molecules, each different in composition from the next, and each representing a kind of natural experiment.
- Most of the protocells remained inert, but a few happened to contain a mixture that could be driven toward greater complexity by capturing energy and smaller molecules from outside the encapsulated volume. As the smaller molecules were transported into the internal compartment, energy was used to link them up into long chains. The nature of the reactions underlying this process represents a major gap in our knowledge of the origin of life.
- Up to this point, most of the processes leading to the production of protocells fall into the realm of physics, so in a very real sense physics came first in the pathway to life. But now, through the laws of physics, microscopic reaction vessels were produced in which chemical reactions could occur. It was these reactions that began the evolution toward the growing, dividing cells that were precursors to what we now call bacteria.

- As noted earlier, the smaller molecules are monomers, and the long chains are polymers. The monomers called amino acids form polymers called proteins, and nucleotides form nucleic acids (DNA and RNA). The biopolymers have emergent properties that are far beyond what the monomers can do by themselves. Most important is that both kinds of biopolymers today can act as catalysts, and one of the polymers -nucleic acids- can carry and transmit genetic information in specific sequences of the monomers that compose it.
- Life began when a tiny fraction of the immense numbers of protocells found a way not only to grow, but also to incorporate a cycle involving biopolymers with properties related to catalytic function and genetic information. Cells, not molecules, were the first forms of life. Again, the step from chemical protocells to simple cells with the minimal properties of life is the second major gap in our understanding of life's origin.

The bullets above are presented as an integrated hypothesis, and a hypothesis must be testable. Each of the bullets has an independent foundation of experimental and observational results in the literature, but no one yet has been bold enough (or foolish enough!) to try to put them all together in a working model. For me, this will be next major advance in origins of life research, when workers in the field accept that life has a certain minimal complexity, and that the only way to learn more is to work with increasingly complex model systems that incorporate both physical and chemical principles. And, referring to the title of the essay, this is what life will be, because a laboratory version of life is unlikely to be a simple copy of life as we know it. Instead, it will represent a second origin of life, a version of intelligent design, but with the intelligence supplied by the scientist who finally makes the breakthrough.

Rather than citing specific research papers, the references below are intended as a guide to further reading.

Books

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