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New Glimpses of Life's Puzzling Origins

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Some 3.9 billion years ago, a shift in the orbit of the Sun's outer planets sent a surge of large comets and asteroids careening into the inner solar system. Their violent impacts gouged out the large craters still visible on the Moon's face, heated Earth's surface into molten rock and boiled off its oceans into an incandescent mist.

Yet rocks that formed on Earth 3.8 billion years ago, almost as soon as the bombardment had stopped, contain possible evidence of biological processes. If life can arise from inorganic matter so quickly and easily, why is it not abundant in the solar system and beyond? If biology is an inherent property of matter, why have chemists so far been unable to reconstruct life, or anything close to it, in the laboratory?

The origins of life on Earth bristle with puzzle and paradox. Which came first, the proteins of living cells or the genetic information that makes them? How could the metabolism of living things get started without an enclosing membrane to keep all the necessary chemicals together? But if life started inside a cell membrane, how did the necessary nutrients get in?

The questions may seem moot, since life did start somehow. But for the small group of researchers who insist on learning exactly how it started, frustration has abounded. Many once-promising leads have led only to years of wasted effort. Scientists as eminent as Francis Crick, the chief theorist of molecular biology, have quietly suggested that life may have formed elsewhere before seeding the planet, so hard does it seem to find a plausible explanation for its emergence on Earth.

In the last few years, however, four surprising advances have renewed confidence that a terrestrial explanation for life's origins will eventually emerge.

One is a series of discoveries about the cell-like structures that could have formed naturally from fatty chemicals likely to have been present on the primitive Earth. This lead emerged from a long argument between three colleagues as to whether a genetic system or a cell membrane came first in the development of life. They eventually agreed that genetics and membranes had to have evolved together.

The three researchers, Jack W. Szostak, David P. Bartel and P. Luigi Luisi, published a somewhat adventurous manifesto in Nature in 2001, declaring that the way to make a synthetic cell was to get a protocell and a genetic molecule to grow and divide in parallel, with the molecules being encapsulated in the cell. If the molecules gave the cell a survival advantage over other cells, the outcome would be "a sustainable, autonomously replicating system, capable of Darwinian evolution," they wrote.

"It would be truly alive," they added.

One of the authors, Dr. Szostak, of the Massachusetts General Hospital, has since managed to achieve a surprising amount of this program.

Simple fatty acids, of the sort likely to have been around on the primitive Earth, will spontaneously form double-layered spheres, much like the double-layered membrane of today's living cells. These protocells will incorporate new fatty acids fed into the water, and eventually divide.

Living cells are generally impermeable and have elaborate mechanisms for admitting only the nutrients they need. But Dr. Szostak and his colleagues have shown that small molecules can easily enter the protocells. If they combine into larger molecules, however, they cannot get out, just the arrangement a primitive cell would need. If a protocell is made to encapsulate a short piece of DNA and is then fed with nucleotides, the building blocks of DNA, the nucleotides will spontaneously enter the cell and link into another DNA molecule.

At a symposium on evolution at the Cold Spring Harbor Laboratory on Long Island last month, Dr. Szostak said he was "optimistic about getting a chemical replication system going" inside a protocell. He then hopes to integrate a replicating nucleic acid system with dividing protocells.

Dr. Szostak's experiments have come close to creating a spontaneously dividing cell from chemicals assumed to have existed on the primitive Earth. But some of his ingredients, like the nucleotide building blocks of nucleic acids, are quite complex. Prebiotic chemists, who study the prelife chemistry of the primitive Earth, have long been close to despair over how nucleotides could ever have arisen spontaneously.

Nucleotides consist of a sugar molecule, like ribose or deoxyribose, joined to a base at one end and a phosphate group at the other. Prebiotic chemists discovered with delight that bases like adenine will easily form from simple chemicals like hydrogen cyanide. But years of disappointment followed when the adenine proved incapable of linking naturally to the ribose.

Last month, John Sutherland, a chemist at the University of Manchester in England, reported in Nature his discovery of a quite unexpected route for synthesizing nucleotides from prebiotic chemicals. Instead of making the base and sugar separately from chemicals likely to have existed on the primitive Earth, Dr. Sutherland showed how under the right conditions the base and sugar could be built up as a single unit, and so did not need to be linked.

"I think the Sutherland paper has been the biggest advance in the last five years in terms of prebiotic chemistry," said Gerald F. Joyce, an expert on the origins of life at the Scripps Research Institute in La Jolla, Calif.

Once a self-replicating system develops from chemicals, this is the beginning of genetic history, since each molecule carries the imprint of its ancestor. Dr. Crick, who was interested in the chemistry that preceded replication, once observed, "After this point, the rest is just history."

Dr. Joyce has been studying the possible beginning of history by developing RNA molecules with the capacity for replication. RNA, a close cousin of DNA, almost certainly preceded it as the genetic molecule of living cells. Besides carrying information, RNA can also act as an enzyme to promote chemical reactions. Dr. Joyce reported in Science earlier this year that he had developed two RNA molecules that can promote each other's synthesis from the four kinds of RNA nucleotides.

"We finally have a molecule that's immortal," he said, meaning one whose information can be passed on indefinitely. The system is not alive, he says, but performs central functions of life like replication and adapting to new conditions.

"Gerry Joyce is getting ever closer to showing you can have self-replication of RNA species," Dr. Sutherland said. "So only a pessimist wouldn't allow him success in a few years."

Another striking advance has come from new studies of the handedness of molecules. Some chemicals, like the amino acids of which proteins are made, exist in two mirror-image forms, much like the left and right hand. In most naturally occurring conditions they are found in roughly equal mixtures of the two forms. But in a living cell all amino acids are left-handed, and all sugars and nucleotides are right-handed.

Prebiotic chemists have long been at a loss to explain how the first living systems could have extracted just one kind of the handed chemicals from the mixtures on the early Earth. Left-handed nucleotides are a poison because they prevent right-handed nucleotides linking up in a chain to form nucleic acids like RNA or DNA. Dr. Joyce refers to the problem as "original syn," referring to the chemist's terms syn and anti for the structures in the handed forms.

The chemists have now been granted an unexpected absolution from their original syn problem. Researchers like Donna Blackmond of Imperial College London have discovered that a mixture of left-handed and right-handed molecules can be converted to just one form by cycles of freezing and melting.

With these four recent advances — Dr. Szostak's protocells, self-replicating RNA, the natural synthesis of nucleotides, and an explanation for handedness — those who study the origin of life have much to be pleased about, despite the distance yet to go. "At some point some of these threads will start joining together," Dr. Sutherland said. "I think all of us are far more optimistic now than we were five or 10 years ago."

One measure of the difficulties ahead, however, is that so far there is little agreement on the kind of environment in which life originated. Some chemists, like Günther Wächtershäuser, argue that life began in volcanic conditions, like those of the deep sea vents. These have the gases and metallic catalysts in which, he argues, the first metabolic processes were likely to have arisen.

But many biologists believe that in the oceans, the necessary constituents of life would always be too diluted. They favor a warm freshwater pond for the origin of life, as did Darwin, where cycles of wetting and evaporation around the edges could produce useful concentrations and chemical processes.

No one knows for sure when life began. The oldest generally accepted evidence for living cells are fossil bacteria 1.9 billion years old from the Gunflint Formation of Ontario. But rocks from two sites in Greenland, containing an unusual mix of carbon isotopes that could be evidence of biological processes, are 3.830 billion years old.

How could life have gotten off to such a quick start, given that the surface of the Earth was probably sterilized by the Late Heavy Bombardment, the rain of gigantic comets and asteroids that pelted the Earth and Moon around 3.9 billion years ago? Stephen Mojzsis, a geologist at the University of Colorado who analyzed one of the Greenland sites, argued in Nature last month that the Late Heavy Bombardment would not have killed everything, as is generally believed. In his view, life could have started much earlier and survived the bombardment in deep sea environments.

Recent evidence from very ancient rocks known as zircons suggests that stable oceans and continental crust had emerged as long as 4.404 billion years ago, a mere 150 million years after the Earth's formation. So life might have had half a billion years to get started before the cataclysmic bombardment.

But geologists dispute whether the Greenland rocks really offer signs of biological processes, and geochemists have often revised their estimates of the composition of the primitive atmosphere. Leslie Orgel, a pioneer of prebiotic chemistry, used to say, "Just wait a few years, and conditions on the primitive

Earth will change again,” said Dr. Joyce, a former student of his.

Chemists and biologists are thus pretty much on their own in figuring out how life started. For lack of fossil evidence, they have no guide as to when, where or how the first forms of life emerged. So they will figure life out only by reinventing it in the laboratory.