Scientific Study of the Origins of Life: The Basics

Why is the study of the origins of life so difficult and perplexing? One reason is that it took place a long time ago—more than 3.5 billion years. Second, the planetary conditions on ancient Earth may have been dramatically different than now, making questionable any inferences we draw from the present. Third, we're only familiar with the history of life on one planet, so we don't even know whether life is an extremely rare or common phenomenon in the Universe.

Given these challenges, one might wonder why we trouble ourselves with such an immensely difficult question. The fact that we struggle with it says a lot about ourselves. Humans are not satisfied simply to be fed, clothed, and sheltered. Regardless of one's worldview, we all want to know something about where we come from, who we are, and where we are headed. Questions about the origins of life are not merely a matter of curiosity, but of human identity. Are we alone in the Universe? How did we get here? What can the past tell us about the present and future of life on Earth?

If we want to apply the tools of science to the origins of life, there are several different ways to approach it, each with advantages and disadvantages. One way would be to start with what we know about contemporary biology and work backwards to reconstruct the past. This approach employs the hypothesis that remnants from the origin of life can still be found in currently living creatures. To the degree that there is evolutionary continuity all the way back to a universal common ancestor, this can be a very insightful approach. But there may have been fundamentally different biochemical or environmental conditions on ancient Earth, and such a top-down approach would be largely blind to those.

If we think that the very earliest life was dramatically different from what we can infer from present organisms, then one could start from chemistry and work forwards through time. The upside of this approach is that it is not constrained by the conditions of the present Earth and the organisms that happen to be alive now. On the downside, how do you discern from the vast set of possibilities what ancient Earth conditions could have been? To be successful, this approach depends on an accurate understanding of primitive Earth and Solar System environments, drawing heavily from planetary science, geosciences, and chemistry. The holy grail would be to find a simple, self-replicating chemical system that could complexify over time.

Whether one takes a forward- or backward-looking approach requires dramatically different scientific skill sets, which makes origins of life research a sprawling, multi-disciplinary endeavor that no one person can completely master. Will thousands of specialists, each working in their own domain, ultimately be able to provide a unified picture of life's origins? No one knows at this point—that's part of what makes science so exciting (and unpredictable).

Here we address some basic questions about origins of life research, to give readers a general overview and pique their curiosity. For those wanting to dive deeply into specific areas, we recommend Professor H. James Cleaves' more extensive review, from which this summary draws.

Did life arise spontaneously from a primordial soup?

By the 19th century it became clear that organic compounds—the building blocks of life—could form naturally, and in the absence of living organisms. But the transition from these building blocks to a completely self-sustaining, self-replicating system is a huge step, and still shrouded in mystery.

One might wonder, why isn't life emerging spontaneously right now? There's certainly no shortage of chemical building blocks. One of the key differences between the present and the primordial Earth is the presence of oxygen (O_2) in our atmosphere. Chemistry teaches us that it's much easier to form complex molecules essential to life when there is a preponderance of hydrogen (or other reduced gases) rather than oxygen. Since plants are the primary producers of O_2, it's likely there was little or no oxygen in the atmosphere when life came into existence.

Louis Pasteur demonstrated convincingly that today's microbes do not spontaneously arise out of non-living material, but how could the first living cells have come into being? In the 1920s, the Russian biochemist Alexander Oparin and British biologist J.B.S. Haldane independently developed theories of chemical evolution. They proposed that in an atmosphere very different from our own, simple chemicals could react to become more complex, catalyzing even more complexity, eventually leading to stable, self-replicating molecules that could be shaped by competition and natural selection. It would take several decades to begin testing these theories empirically.

In the middle of the 20th century, Stanley Miller succeeded in creating a number of organic compounds from simple gases (hydrogen, ammonia, methane, and water vapor) thought to be present in early Earth's atmosphere. This simple experiment has been repeated in laboratories throughout the world and opened up a new field called "prebiotic chemistry." It seemed like scientists were on the right track to recreating life! Unfortunately, geochemists have pointed out that the early atmosphere was very unlikely to resemble Miller's mixture of gases, and while the experiment was elegant, it was not a good model for primordial Earth.

Can evolutionary biology tell us what form of life came first?

Instead of working forwards from chemistry, what if we worked backwards from biology, reconstructing the ancestors of today's complex forms of life? In contemporary organisms, hereditary information is stored in DNA molecules, which are copied into RNA molecules, which are translated into proteins, which carry out most of life's functions. Proteins are needed to create DNA, and DNA is necessary to create proteins, so which of these complex molecules came first? It is a classic "chicken or egg" paradox. Since RNA serves as an intermediary between DNA and proteins, many scientists have speculated that RNA was the critical precursor to the origin of life as we know it. Many of the world's leading researchers are developing this "RNA World" hypothesis.

Contemporary biology classifies all life on Earth into three fundamental groups—Archaea, Bacteria, and Eukarya. Multicellular organisms evolved from simpler single-celled organisms, and all three of these foundational groups ultimately derive from what is called the Last Universal Common Ancestor (LUCA). Biology can perhaps tell us some of the features of LUCA, but how much time elapsed between LUCA and the very first appearance of life on Earth? Some scientists surmise that as much as a billion years could have separated life's origin from an ancestor that gave rise to all subsequent forms of life on Earth. Such is the challenge of working backwards from contemporary biology.

What does the history of the Earth tell us about the origins of life?

If we are going to peer back into the time before biological processes were fully active, then we will need to rely on planetary and geological history. Nevertheless, it is really hard to learn about the primordial Earth, not only because it's billions of years old, but because a lot of potential evidence is inaccessible (particularly if it's in outer space). Additionally, because of the continuous plate tectonic activity on our planet, ancient rocks are constantly being re-melted and destroyed. On the bright side, recent discoveries of thousands of exoplanets in other star systems provide scientists with a basis of comparison for how our Solar System may have formed, and what conditions may have been present on Earth during its earliest days.

Planetary scientists estimate that our Moon formed approximately 4.5 billion years ago, shortly after the Earth itself formed. The most widely accepted model for the formation of the Earth-Moon system is that a Mars-sized body collided with the proto-Earth. That apocalyptic impact would have been violent enough to melt Earth's entire surface, ruling out a pre-Lunar origin of life.

There is evidence from zircon minerals (remarkably durable minerals that are among the oldest known on Earth) that liquid water was present on Earth as early as 4.4 billion years ago. This is significant because nearly all scientists believe that the first living things were based on organic compounds and lived in water.

Besides Earth-shattering planetary collisions and the presence of liquid water, there are other major constraints on the origin and continuity of life. The Earth's magnetic field deflects radiation from the Sun that would otherwise strip away the upper atmosphere and degrade the ozone layer. Our magnetic field is thought to have been continuous for the past 3.5 billion years. Before that time, conditions for life may have been extremely harsh.

What direct evidence do we have of life's early history? The first fossil discoveries are of animal and plant remains, which extend back as far as the beginning of the Cambrian period (~550 million years ago). During the 1960s, scientists who study microscopic organisms preserved in ancient rocks began to find evidence for Precambrian life, in the form of fossilized bacteria. Presently, the oldest commonly agreed upon fossil microorganisms are dated to approximately 3.5 billion years ago.

Earth's oldest known rocks offer some clues to what the early surface environment was like during the origin and early evolution of life. However, due to tectonic recycling, rocks older than approximately 3.5 billion years are rare on Earth's surface. The Moon's surface, on the other hand, has essentially been geologically "frozen" for billions of years and thus has an exquisitely well-preserved geological history.

Radiometric dating of rocks returned from the Apollo missions to the Moon suggests that meteorite bombardment of Earth would have been so intense from approximately 4 billion to 3.8 billion years ago that our oceans would have been repeatedly sterilized (raised to well above the boiling point of water for long periods of time). Would this turbulent period have extinguished all forms of life? Or could some tiny remnant have survived, perhaps buried in the Earth's crust? This is an open question debated by scientists.

All things considered, in attempting to construct a timeline for the origins of life on Earth, most scientists consider the upper and lower boundaries to be sometime between 4.4 billion years ago, when Earth's surface was cool enough to support liquid water, and 3.5 billion, when there is generally accepted fossil evidence for microorganisms on Earth. Depending on how one interprets other constraints—meteor bombardment, the composition of the Earth's early atmosphere, and changes in the Sun's brightness—it is as yet very hard to further narrow down the window of time in which life originated.

What ingredients do you need to produce life?

In addition to the quest to pinpoint *when* life originated, it is equally exciting to explore *how* life originated. Think of it this way—if you were going to build a simple, self-sustaining, self-replicating machine, what would your list of parts include? Nature started this process over 3 billion years ago, resulting in the vast diversity of life that we see today. But when you look more closely, you see that the same basic ingredients comprise every living thing:

Proteins—carry out the work inside the cell
Fats—form the cell membrane to protect it from the outer environment
Sugars—provide the primary fuel for cells
DNA and/or RNA—supply the instructions needed to develop, survive, and replicate.

These four ingredients, combined with a few other things like vitamins and minerals, are the foundation of life on Earth. Of course, this begs the question, how did these molecules come into existence in the absence of any organisms to manufacture them? This is a mystery that has flummoxed scientists for well over a century, and it has inspired the development of a field called prebiotic ("before life") chemistry.

Prebiotic chemistry attempts to not only produce the ingredients that could have been used to assemble the first living organisms, but also to explain the self-assembly of the first living organisms. For many researchers, the goal of prebiotic chemistry is the assembly of a simple living system with some of the common attributes of modern cells, such as a lipid membrane, RNA and/or DNA, and small protein-like peptides.

While the list of compounds that can be synthesized in the lab is impressive, not all ingredients essential for life have been created under plausible prebiotic conditions, nor have they been found in extraterrestrial sources, such as meteorites. One possible explanation is that some cellular components only arose after organisms had developed a considerable degree of complexity and could manufacture novel molecules.

Meteorites—basically chunks of rocks from outer space that have fallen to Earth—are a useful subject of study because they can show us what kinds of molecules can form in the absence of life. The Murchison meteorite, estimated to be 4.5 billion years old, crashed through the Earth's atmosphere and landed in Australia in 1969. A recent study of this meteorite revealed the presence of as many as 14 million distinct types of organic compounds. This can be contrasted with the approximately 1,500 common molecules found in contemporary cells. The list of potential candidates for inclusion in the first forms of life seems overwhelming.

Although we do not know which compounds were available or required for the origins of life, prebiotic chemists tend to focus on compounds that are present in modern organisms, ignoring this large fraction of compounds found in meteorites or produced in simulations that are not found in biology. It's a good example of starting from what we know and working outwards from the boundaries of our knowledge. So let's start with examining the four basic ingredients of life with which we are familiar: proteins, fats, sugars, and DNA/RNA. These, in turn, are composed of more basic materials.

Amino Acids

Proteins carry out many essential activities in cells—they facilitate chemical reactions (including the replication of DNA), provide cellular structure, and transport molecules where needed. There is a vast number of protein types, different ones for each task, but they are all composed of the same basic material—chains of amino acids. Some of these chains are short, and others are hundreds of units long. Twenty different amino acids, arranged in various combinations, are used to form proteins.

It is unlikely that all of the modern amino acids were present in the primitive environment, and it is unknown which, if any, would have been important for the origin of life. In any case, a variety of prebiotic processes can form amino acids; for example, Stanley Miller's electric discharge experiments in the 1960s produced several amino acids of biological importance. The main mechanism by which amino acids form in this type of experiment is the Strecker synthesis, named for Adolf Strecker, a 19^{th} century German chemist who was the first to artificially synthesize an amino acid.

It should be noted that as elegant as Miller's laboratory experiments were, it is likely that the Sun—not atmospheric electricity—was the major source of energy driving chemical reactions in the prebiotic environment.

Lipids

From the largest organisms to the tiniest bacteria, all modern life is cellular. The membrane that forms the outer barrier of each cell is comprised of fatty acids called lipids, which come in many varieties. Under appropriate conditions, long-chain fatty acids and their derivatives spontaneously arrange themselves into cell-like spherical shells, and these can briefly trap organic material inside. One could imagine that the earliest forms of life were a happy conjunction of spherical lipid compartments engulfing some self-replicating molecules.

Does such an idea withstand critical scrutiny? Most prebiotic simulations don't generate large amounts of fatty acids. And although the Murchison meteorite contains small amounts of fatty acids, some of these may be due to laboratory contamination. Scientists are still on the hunt for natural processes that could produce substantial quantities of lipids needed for the formation of life.

Sugars

Plants produce sugars through photosynthesis, and animals eat them to sustain their cellular activities. But how did sugars, key building blocks for life, come into existence in the first place? The 19th-century Russian chemist Aleksander Butlerov discovered the formose reaction, in which sugars naturally form from the simple organic compound formaldehyde. Could something similar have happened at the dawn of life?

A problem is that the conditions for the natural synthesis of sugars are also conducive to their degradation. Sugars undergo various reactions on short time scales that are seemingly prohibitive to their accumulation in the environment. Nevertheless, both sugar derivatives and nucleic acid bases have been found in the Murchison meteorite, which means that there must be non-biological mechanisms for producing and preserving sugars.

Nucleic Acids

DNA is a fascinating substance because it contains all the information necessary for constructing and maintaining organisms. It is capable of producing copies of itself, mutating, and evolving through time. However, it is far too complex to arise spontaneously, leading many scientists to posit that another nucleic acid, RNA, was its precursor. Similar in many ways, RNA is slightly simpler in that it is single-stranded and shorter. Many researchers posit that RNA formed naturally in a prebiotic environment and may have been the key ingredient in the transition to life.

Although some scientists now doubt this hypothesis, numerous laboratory experiments have shown natural pathways for the formation of RNA's constituent parts: purines, pyrimidines, and sugars. The RNA World hypothesis is an active and exciting line of scientific inquiry.

Where did the first organisms arise?

Now that we've looked at *when* and *how* of the origins of life, we turn to the question of *where* it first popped up before spreading across the entire planet.

Charles Darwin never publicized his thoughts on the ultimate origins of life, but in a private letter to his friend Joseph Hooker in 1871 he wrote,

> *"But if (and oh what a big if) we could conceive in some warm little pond with all sorts of ammonia and phosphoric salts, light, heat, electricity etcetera present, that a protein compound was chemically formed, ready to undergo still more complex changes [...] "*

Science has advanced a lot in the past 150 years, but the basic principles of Darwin's musings still apply. Warm ponds are good candidates for two reasons: first, heat is necessary for driving many of the chemical reactions that life depends on. Second, water is such a vital ingredient that it would be a natural place for life to form.

An interesting variation of this hypothesis was first suggested by R.B. Harvey in 1924, who argued that the first life forms originated in hot springs such as those found in Yellowstone National Park. One advantage of high temperatures is that the chemical reactions could go faster and primitive enzymes could have been less efficient. However, high temperatures are also destructive to organic compounds.

Subsequent research has proposed that hydrothermal vents on the ocean floor could also be good candidates for life to originate. This area has attractive characteristics, including a source of energy, an aqueous solution, and dynamic chemistry. But for the same reason as hot springs, extreme temperatures can just as easily degrade complex chemicals as create them. In terms of pinpointing the location of the earliest life forms, we may not have progressed much further than Darwin's hunch.

Could there be forms of life completely different from what we find on Earth?

There is only one known example of a functioning biology, our own, and it is governed by the reactions of carbon-based compounds in water. Might there be other types of chemistry that could support a functioning biology?

Due to the abundance of oxygen and hydrogen in the early Solar System, most other atomic nuclei ended up combining with those two elements. Water, which is two-parts hydrogen and one-part oxygen (H_2O), is one of the most abundant compounds in the Universe. Depending on the temperature and pressure, water is found in one of three states: solid, liquid, or gas. Life in the solid state would be difficult, as the movement of molecules would occur only very slowly. It is likewise improbable that life in the gas phase would be able to carry out replication, as large molecules generally do not exist in a gaseous state. Liquid water is therefore essential. It has a large temperature stability range, and its ability to absorb and retain heat is uniquely important in many geochemical processes.

Let's turn our attention from water to the other key ingredient for life—carbon—the fourth most abundant element in the universe after hydrogen, helium, and oxygen. There are no other elements besides carbon that appear to be able to furnish the immense variety of chemical compounds that allow for a diverse biochemistry. While silicon, just below carbon on the periodic table, has also been hypothesized as an alternative building block for life, its large molecules are generally unstable or insoluble, especially in water, making it an inferior candidate.

All of this goes to say, if we were to find another form of life that is not based on carbon and water, we would be completely shocked—and totally fascinated.

Is there life beyond Earth?

Of the eight accepted planets in our Solar System and their moons, several appear compatible with the synthesis of organic compounds, and several are known to contain them. Fewer appear to be compatible with the existence of liquid water or the more complicated evolution of these compounds. For example, the extreme temperatures of Venus or Mercury's sunlit side are likely too hostile for the synthesis of complex organics. The immediate sub-surface of Mars appears to harbor both liquid and solid water, and it is widely believed that liquid water once flowed on Mars' surface.

A number of the outer planets' moons have intriguing environments that appear to foster prebiotic chemistry and could conceivably be capable of sustaining life. Saturn's moon Titan is now known to harbor a rich organic chemistry, and more recently organics have also been detected in geyser plumes emitted from Saturn's icy moon Enceladus. Jupiter's moon Europa is covered with a thick ice layer that likely harbors a water ocean several kilometers thick. Its organic content remains unknown.

Given the billions of Sun-like stars in any galaxy, there may be many rocky Earth-like planets in stellar habitable zones in the Universe, some of which may have undergone similar development compatible with the origin and evolution of life. The detection of such planets and possible signatures of alien biochemistry may not be far off, assuming that life is not limited to our planet. The detection of even one life-sustaining planet would signal a new era in human history—we are not alone in this vast Universe.

Concluding thoughts

Given adequate expertise and experimental conditions, it is possible to synthesize almost any organic molecule in the laboratory under simulated prebiotic conditions. The wide range of experimental conditions under which organic compounds can be formed also demonstrates that organic compounds are prebiotically "robust," making it more likely that life could arise, both on Earth and elsewhere. However, the fact that molecular components of contemporary cells can be formed in the laboratory does not tell us which ones were essential for the origin of life, or that they existed in the prebiotic era.

Although our ideas on the prebiotic synthesis of organic compounds are based largely on experiments in model systems, this type of chemistry is supported by the occurrence of diverse organic compounds in meteorites and comets, as well as elsewhere in the Solar System. It is therefore plausible, but not proven, that similar events took place on the primitive Earth. For all the uncertainties surrounding the emergence of life, it appears that the formation of a "prebiotic soup" is one of the most firmly established aspects of the primitive Earth, though its recipe remains difficult to decipher.

A comprehensive understanding of how prebiotic chemicals assembled into stable, self-replicating cells on primitive Earth remains elusive for now, despite considerable progress in chemistry, molecular biology, Earth sciences, planetary sciences, astronomy, and the search for extraterrestrial life. But with the frontiers of science expanding rapidly in each of these areas, we are in store for many exciting and surprising discoveries.

It seems plausible, and perhaps even likely, that in the near future, chemists will assemble living organisms entirely from scratch. The magnitude of such an achievement cannot be overestimated—these would be the first forms of life on Earth that did not have a lineage dating back more than 3 billion years. Should humans eventually endow them with the ability to adapt to their surroundings and self-replicate, there's no telling what their evolution would bring. Looking back on the history of life from single-celled bacteria to self-conscious organisms capable of exploring our own origins, one thing is certain—from simple beginnings, unimaginably complex life trajectories can follow.