Science Fact

Out of “Some Warm Little Pond,” Part I: “Rifters” and the RNA World

Kelly Lagor

> “It is often said that all conditions for the first production of a living organism are now present, which could have ever been present. But if (& oh what a big if) we could conceive in some warm little pond with all sorts of ammonia & phosphoric salts—light, heat, electricity, etc. present, that a protein compound was chemically formed, ready to undergo still more complex changes, at the present day [would] be instantly devoured, or absorbed, which would not have been the case before living creatures were formed.”
>
> -From Charles Darwin’s 1871 letter to Joseph Lee Hooker

> Scanlon winced. “. . . What are you looking for, anyway?”
>
> “Pyranosal RNA.”
>
> “I’m—I’m not sure I remember what that is.”
>
> “No reason you should. It’s been out of fashion for three and a half billion years.”
>
> “No shit.”
>
> “Don’t you wish.” The probe withdrew. “It was all the rage in primordial times . . .”
>
> —Excerpt from *Starfish* (1999)

While science fiction has long imagined myriad different forms of alien life—from the human-like alien races of the *Star Trek* universe, to incomprehensible, planet-sized intelligences, as in *Solaris* (1961)—no stories have delved as deeply into the probiotic origins of such life as the writer and marine biologist, Peter Watts, did in his Rifters series (1999-2004). One main reason is the relevant field of necessarily interdisciplinary study, astrobiology, didn't have much of a basis to build from prior to the 21st century, aside from a few imaginative chemistry experiments. Understanding how life got started on Earth (still the only life in the universe we know of) required a sophistication in the understanding and techniques of cellular and molecular biology that didn't emerge until the 1980s. The slow snowballing of knowledge that followed has only begun to paint a detailed picture of the time when life got started here, which Watts fully explored in his design of the βehemoth parasitic symbiote. Looking at what we knew in 2000, when the first book in the Rifters series, *Starfish*, came out, and what we know now makes for an interesting trip through modern biological history.

While life is a surprisingly thorny thing to define, NASA paints a fairly comprehensive picture with their definition: life is a self-sustaining chemical system capable of Darwinian evolution. While this definition is based entirely on an understanding of the nature of life on our planet, it is thought to be inclusive of all in the universe. Inherent in the definition are three requirements: life maintains an inner, homeostatic environment; it has a metabolism that collects energy from its environment which it uses to sustain itself; and it can transmit its traits in a somewhat imperfect way to the next generation. This means that all life should share these three features. All life must therefore have derived such features from the energy and chemicals that were on hand when life was getting started. On Earth, for example, all life has decided to go with permeable membranes to maintain an inner homeostasis; uses proteins and either light or organic forms of energy to fuel its metabolism; and uses DNA as its genetic material.

The current theorized timeline of when life emerged puts it soon after the formation of Earth and its oceans ~4.5 billion years ago (Gya—giga years ago). The environment during this earliest Hadean eon (4.6-4.03 Gya) was very hostile to life as we know it. Unfiltered UV light bathed the flowing magma surface of the planet, and the atmosphere was mostly comprised of hydrogen gas, water, methane, and ammonia, most of which was driven off by the Moon-forming event (~4.5 Gya). The impact of the protoplanet Theia added a lot of rock vapor to the atmosphere, which was mostly carbon dioxide, hydrogen gas, and water. The atmospheric pressure then caused the condensation of the oceans, which acted as a CO^2 sink. The atmosphere evolved over the first half billion years as the earth cooled, and the Late Heavy Bombardment (LHB, 4.1-3.8 Gya) added different organic and silicate compounds to the oceans. Volcanic eruptions, meanwhile, added even more carbon dioxide and water vapor to the atmosphere, as well as sulfur compounds. The primordial ocean was likely slightly acidic, rich in the stuff life today is made of: carbon dioxide, magnesium, iron, phosphorous, potassium, chloride, and calcium.

We won't ever be able to directly observe how life emerged from that prebiotic soup. The oldest direct evidence we have of microbial life is from 3.5 Gya-old fossils, and the earliest evidence we have that life existed at all is based on the ratios of different carbon isotopes found in a grain of 4.1 Gya-old zircon. This means life got started around the same time the LHB did, but what that earliest life and its precursors looked like we've only been able to imagine, thanks to clever experimental designs and a truly multidisciplinary approach.

Darwin wasn't the only one to wonder if replicating the environmental conditions present on the prebiotic earth could help us understand how life emerged. Half a century after Darwin's musings, other influential figures in biology, including British polymath J.B.S. Haldane and Soviet biochemist Alexander Oparin, independently proposed similar experimental designs at a time when biochemistry and cell biology were in their infancy. They supposed life got started thanks to equilibrium imbalances in the environment, and that such conditions could induce the chemical reactions needed to convert atmospheric nitrogen, carbon dioxide, and hydrogen into the complex molecules found in cells, like sugars and amino acids.

The first success in such a venture was the 1952 Miller-Urey experiment. At the time, it was commonly believed life started on Earth's surface, not in the ocean, as so much water being present would have immediately diluted any compounds that were made. Therefore, the atmospheric conditions of early Earth were thought to be the key catalyst. Harold Urey, a chemist at the University of Chicago, whose work on isotopes won him the 1934 Nobel Prize, was an expert on ancient atmospheres and the early days of the solar system. During a 1951 chemistry seminar, his future student, Stanley Miller, heard Urey opine, "It is possible to create an experiment to recreate the conditions of early Earth and see what lightning, in the form of electrical discharges, might produce." Miller approached Urey about conducting the experiment and Urey agreed. Miller put the supposed stuff of the ancient environment—water, methane, ammonia, and hydrogen gasses—into a sealed glass apparatus, which was then heated and had an electrical current applied. In two days, Miller found amino acids and bitumen (a mix of simple hydrocarbon moieties)—all fundamental components of cellular metabolism. Their paper, proof that the building blocks of life could be created abiotically, was published in 1953, just a few weeks after James Watson and Francis Crick's landmark paper on the structure of DNA. The experiment became one of the foundational works of the field of astrobiology.

While the Miller-Urey experiment demonstrated one possible way amino acids could have arisen on earth, only three were confidently identified—glycine, alpha- and beta-alanine. Later iterations of the experiment took into consideration updated understandings of the components of Earth's early atmosphere (that it was mostly carbon dioxide, nitrogen, and sulfurous compounds, rather than methane and ammonia), and used either the original Miller-Urey apparatus, or made modifications to its design to simulate the influence of things like volcanic activity. Results have since shown a much wider array of amino acids can be made, including many, though not all, that are part of the core twenty-two amino acids of life.

Another potential source of the organic compounds prebiotic life arose from was space. A meteorite found in Australia in 1969 was discovered to contain various amino acids, alkane compounds, and nucleobase compounds (both purines, like alanine and guanine; and pyrimidines, like cytosine and thymine). These compounds are thought to have formed on the meteorite's surface as the result of reactions between the simple organic compounds present in the circumstellar disk our solar system arose from, like carbon monoxide, hydrogen, ammonia, and the meteorite's own water and carbon, with ambient cosmic radiation and UV light. Experiments by NASA in the 2010s, which include landing a probe on the surface of a comet in 2015, have also confirmed the presence of amino acids, fatty acids, and nucleotides on such bodies, implying these building blocks of proteins, cellular membranes, and genetic material, respectively, need not have an exclusive origin on earth. Such meteorites regularly pummeled the Earth's surface during the LHB, and likely contributed such compounds to life's early toolbox.

As it was supposed that the LHB may have repeatedly sterilized the surface of the earth, some researchers began to favor a hypothesis that life may have started near underwater hydrothermal vents, or near vents on the surface where water would go through cycles of accumulation and evaporation. A popular theory from 1988, known as the "iron-sulfur world" theory, proposed life began at such an interface between the organic and the inorganic. Such vents generate large amounts of thermal energy that could have fueled prebiotic metabolism. The vents themselves are made of high concentrations of metals, like iron and nickel, whose charge could theoretically trap any complex molecules that formed, thus preventing them from being diluted away. Additionally, all the atomic requirements of life are abundantly present in such locations in the form of carbon monoxide, hydrogen sulfide, and cyanide. Various experiments, like those by geologist Robert Hazen in the 1990s and 2000s, demonstrated that, indeed, such an environment at high pressure could produce amino acids and sugars and other organic molecules. Early metabolic pathways could have arisen in such an environment as well. For example, chemical reactions catalyzed today by enzymes in the citric acid cycle in aerobes have been shown to also be capable of being catalyzed in the presence of just iron and sulfur.

But such reactions as recreated in the above conditions aren't like those found within cells

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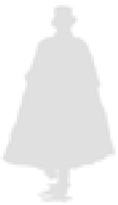

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today, and in 1993 it was hypothesized that perhaps instead of life arising near hydrothermal vents, life arose on cooler, long-lived deep ocean alkaline vents. The problem was, such vents were only hypothesized to exist, and weren't discovered until 2000 in the Atlantic Ocean. The formation was dubbed the "Lost City," due to the height and abundance of tower-like structures formed by the deposition of calcium carbonate precipitated out of the water due to the water's relatively cool temperature and alkalinity. Such vents use available carbon dioxide and water to produce hydrogen and methane, and can catalyze the formation of more complex hydrocarbons. These then become trapped in the rock's pores via the process of serpentinization, a geological synthetic pathway that the earliest hypothesized methanogenic bacteria are thought to have moved inside their cell membranes.

Starfish was released one year prior to the discovery of the Lost City alkaline vents. At the time Watts was writing it, therefore, the origin of much of the basis of all life on earth was still an open question. He therefore combined evidence of the abiogenic generation of prebiotic compounds on deep sea hydrothermal vents with the knowledge that the kind of reactions typical of most life on earth looked different than hydrothermal vent chemistry—and thus had the rest of life on Earth arise thanks to a "Martian panspermia" event.

Starfish is primarily set in the deep-sea, among the black smokers of the Juan de Fuca Ridge in the Pacific Ocean's "Ring of Fire" chain of volcanoes. Hundreds of species live in these environments, like tube worms and various crustaceans and mollusks, including many that are only found there. In Watts' book, the normal fauna around the Juan de Fuca vents is abnormally large and strangely brittle. Employees of the multinational corporation in charge of the geothermal station built along the ridge, known as rifters, have had numerous physical modifications and adaptations so they can do the maintenance work required to keep the power station running. The rifters soon discover that the gigantism in the sea life around them is due to the work of a semi-symbiotic parasite, later dubbed βehemoth.

βehemoth's ancestors were thought to have arisen 300 million years before the Martian panspermic event. It is a sometimes free-living, sometimes symbiotic single-celled organism whose biochemistry evolved in a high-sulfur, high-temperature, high-pressure environment. Its cell wall lacks the expected lipids and is instead made of primarily sulfur-phosphate compounds. Its greater metabolic need for sulfur leeches the element from its hosts, thus causing a brittleness in skeletons and teeth. In return, it makes a huge amount of ATP, which causes the accelerated growth observed. In humans, it leads at first to increased strength and endurance, but eventually it causes organ failure and death.

The thematic interaction of the biochemistry of βehemoth with the psychology of the misfit rifters makes *Starfish* both a compelling and, at times, repellent read. It's no mistake the two first characters we encounter are named for the optimistic, hard science fiction writer Arthur C. Clarke and lyrical, yet atavistic writer J.G. Ballard.

While we now know quite a bit about how and where required prebiotic components arose, how did they begin to organize themselves into life? A 2023 review article in the journal *RNA* by Jacob L. Fine and Ronald E. Pearlman, "On the Origin of life: an RNA-focused synthesis and narrative" gives a wonderful contemporary outline of the current theories and experimental evidence to support the dominant "RNA World" hypothesis for how life emerged from such a rich, hot soup.

All life on Earth obeys what Crick dubbed the "Central Dogma" in 1957: that information can flow from a nucleic acid into another nucleic acid, or a nucleic acid into a protein, but it cannot transfer between proteins, or from a protein into a nucleic acid. In its simplified, but not entirely accurate form today, this theory states that DNA is transcribed into RNA, which then is translated into the protein. Crick later regretted the use of the term "dogma," as it implies a rigidity that belies how complex these interactions are. All life (barring the borderline case of viruses, of which some have only RNA genomes) uses DNA as its information storage system and uses RNA as an intermediary template from which proteins are made. Where it gets sticky is with RNA, some varieties of which have cellular functions well beyond acting as simple templates for translation.

Proteins do the bulk of the cellular work on earth today, but they are not thought to have been the first complex molecules to catalyze the initial steps toward life. While amino acids were certainly abundant on the primitive earth, Crick was right. Once information passes from a coded template into a protein, that information can't come back out again. The vast majority of proteins can't replicate themselves, save for certain types of simple structural proteins and protein aggregates. While such small, catalytically active peptide chains could have formed by luck in the conditions present in the Hadean Era, in a general sense, randomly made proteins can't copy themselves. If such a process was a key step in the development of life on this planet, we would expect to see "fossilized" remains of that process in life today, and we simply do not.

This leaves two varieties of nucleic acids as our remaining candidates: DNA and RNA. Ribonucleotides and deoxyribonucleotides are both capable of being made prebiotically. In all cells today, DNA is used as the archival material, packed away in the nucleus in its stable, double-stranded form, coiled up and folded in on itself in precise ways that impact how its genes are expressed. Its backbone is a repetitive sequence of fairly rigid sugar phosphates that interact primarily with structural proteins. The only way the side of the molecule with the base pair information can interact with anything other than its complementary strand is if the hydrogen bonds that bind the two strands together are interrupted, which is typically only achieved by large changes in pH, high temperatures, or through the action of "unzipping" enzymes like helicases, which are found in all life. Furthermore, while DNA can be made to act like an enzyme under certain conditions in labs, such DNAzymes are not naturally occurring.

RNA, on the other hand, mostly exists in its single-stranded form, and it has a much more flexible sugar phosphate backbone. Thanks to that flexibility and its un-paired, and thus reactive, nucleotides, it can fold into a variety of shapes, hydrogen bond with other nucleic acids, and catalyze reactions. It can even interact with cofactor elements, like magnesium, which help in cellular processes by stabilizing molecular structures, facilitating interactions with other molecules, imparting energy to catalytic reactions, or changing a molecule's reactive capabilities. RNA also has a hand in more than just one cellular process. It plays critical roles in processes necessary for cellular functioning and survival, like gene regulation, epigenetic silencing, translation, and pathogen defense, to name a few.

RNA's ability to act as an enzyme was first discovered in 1982, when the first ribozyme was discovered (a self-splicing intron from a pre-RNA was described in a single-celled eukaryote). Since then, RNA has also been shown to display other hallmarks of enzymatic behavior. Riboswitches are found in all kingdoms of life, and they bind small ionic or molecular compounds that can turn their function on or off. They play roles in such fundamental processes as RNA processing, transcription, and translation. RNA is also capable of polymerizing off itself to add additional nucleotides to its length, to ligate amino acids together, and to add chemical modifications, like activity-altering phosphate groups, to itself and other proteins.

Furthermore, while DNA only comes in one primary form, RNA comes in many that are structurally and functionally diverse: messenger RNA carries genetic information from the nucleus into the cytoplasm; ribosomal RNA acts as a ribozyme and works with transfer RNAs to recruit the proper amino acid to the RNA template to make proteins; to say nothing of the variety of small regulatory RNAs, like micro- or non-coding RNAs that are responsible for many different aspects of gene regulation and pathogen defense. As RNA is a somewhat labile molecule that's prone to degradation, RNA is currently thought to have evolved from earlier RNA-like polymers. Molecules like pyranose RNA or threos nucleic acid (TNA) (with six- or four-carbon sugar rings, respectively, instead of the five-carbon ring found in RNA), or even something like a peptide nucleic acid (PNA). All are capable of being made under prebiotic conditions, and have been synthesized in labs, and all three have structures that are more stable than RNA at higher temperatures and pressures.

All the above make RNA a prime candidate to have been the molecular basis of all life, and the reason why the RNA World hypothesis is the leading hypothesis for how life evolved on earth.

The second and third Rifters novels, *Maelstrom* (2001), and the diptych *βehemoth: β-Max* (2004) and *βehemoth: βehemoth Seppuku* (2004), make use of much of the above RNA World research to build out the conflict, as well as the resolution of the series. βehemoth's genome is an archaic throwback to this RNA World. It's entirely RNA-based, but it doesn't use the kind of RNA found in all life on earth. It instead uses one of the hypothetical, more structurally sound analogs: pyranose RNA. Not only is the pRNA used as the genetic material, but it uses it for its enzymatic activity as well.

Such a living fossil, were it to be found today, would promise an unprecedented look at what the earliest life on Earth looked like. Very likely there was quite a diversity in this earliest life, but once life arose that looks like everything on Earth today, it was able to outcompete any other life that may have been trying to get its own tenuous foothold. Watts' novels imagine an environment so harsh that dominant life never fully usurped what came before, and the conflict in the remaining books of the series explores what happens when that life, given a hand by humanity, can escape that very limited niche.

The final book(s) in the series describes yet another organism, named Seppuku, which has been artificially created and uses a TNA backbone and simplified enzyme designs, as a solution to the growing spread of βehemoth infections in North America. Watts draws from yet another hot field of research from the aughts, which was the quest to define the minimum parameters of life and related attempts to create the first completely artificial organisms—a fascinating subfield where astrobiology meets biotech industry, but which has fallen a bit off the radar in the decade plus since.

As for how it's thought life emerged from an RNA World: spontaneously formed RNA polymers could have had random enzymatic activity. Once an RNA developed a way to copy itself, using a still hypothetical ribozymal polymerase (all polymerases today, which are used for copying DNA and RNA, are thought to have evolved from an ancestral RNA polymerase), it was possible for RNA to start evolving.

Coded DNA and proteins then became more prevalent. RNA probably started working with small bits of randomly polymerized DNA and peptide chains, which could have acted like cofactors to help build more structures until translation arose out of the chaos. Evidence for this is found in the high degree of sequence similarity that exists in the genes that encode the different elements of the translation apparatus, like rRNA, and how such genes dominate the less than 100 genes that make up the Universal Gene Set of Life—strong evidence this was the first life process to evolve. Once translation emerged, coded proteins became available for cellular metabolism to emerge from. And only once ribozymes or enzymes emerged that could make DNA copies of existing RNA templates did DNA become the hereditary material.

This ancient RNA world never disappeared. It played an essential role in life's 4-billion-year evolution and is still critical to the functioning of all life. With how much more is known today, perhaps more science fiction writers will be inspired to imagine other, stranger beginnings for life. Until we find life on another planet, our scientific and science fictional imaginations can fill our oceans, our Solar System, and our Universe in the meantime. ■

Further Reading

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Anton, Ted. (2017). *Planet of the Microbes*. University of Chicago Press.

Fine JL, Pearlman RE. "On the origin of life: an RNA-focused synthesis and narrative." *RNA*. 2023 Aug;29(8):1085-1098

Kelly Lagor is a scientist by day and speculative fiction writer by night. Her fiction and nonfiction have appeared in places like Analog, Asimov's, Tor.com, *and* Uncanny. *You can keep up with her and her work on her website: kellylagor.com, or on various social media places as @klagor.*