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Chance or Necessity- Modeling the Origins of Life

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SUMMARY

The fundamental nature of processes that led to the emergence of life has been a subject of long-standing debate. One view holds that the origin of life is an event governed by chance, and the result is unpredictable. This view was eloquently expressed by Jacques Monod in his book "Chance and Necessity." The alternative position is that, while the details need not be deterministic in every respect, the overall origin of life was a predictable event. A corollary to this position is that the emergence of life is determined primarily by universal chemistry and biochemistry rather than by subtle details of environmental conditions. Within this position, the dominant model holds that the origin of life was guided by information stored in nucleic acids (the "RNA World" hypothesis). An alternative hypothesis states that the formation of protocellular metabolism was driven by non-genomic processes. In this lecture the speakers explored these different paradigms for the emergence of life and discussed their implications for the predictability and universality of life-forming processes.

"Life is a self-reproducing chemical system capable of undergoing Darwinian evolution." With this definition, Dr. Andrew Pohorille, a researcher in the Exobiology Program of the NASA-Ames Research Center, began the lecture on "Chance or Necessity-Modeling the Origins of Life" that was part of the Public Lecture series sponsored by the AAAS Dialogue on Science, Ethics, and Religion (DoSER). He noted several things about this definition. First, this is "a" definition of life not "the" definition. It is essentially the same definition a NASA committee developed in the 1990s to orient its astrobiology program. Second, the definition has two parts, 1) life is a *chemical system* and 2) life is self-reproducing and involved in Darwinian evolution. It is possible to get stuck on the definition of life, but this is not where the problem lies in modeling the origin of life.

He showed three illustrations. The first was of vesicles, naturally forming envelopes that are cell-like except that they contain only water. Vesicles are like envelopes without letters. They are not very interesting and there appears to be a big gap between them and even a simple cell. The second was a micrograph of simple cells showing the complex structures within the cells. Origin of life research assumes that there is something, some structure (or a range of structures), between the vesicle and the cell, a protocell preceding the first truly cellular life. However, there is no fossil record of such structures, so they have to be conceived hypothetically though logically.

Pohorille's third illustration was a conceptual drawing of a hypothetical protocell. He noted five characteristics that such a protocell would need to exhibit: catalyzation of chemical reactions, forms of transport to move nutrients and wastes between the cell and the environment, means to transport ions across the cell boundary, methods of capturing energy from the environment and using it for work, and some means of transferring information into the next generation.

He identified three basic approaches to the question of the origin of life. 1) Skip the protocell issue altogether – this he suggested was the traditional special creationist approach. There is no need for protocells because God simply created each kind of life. 2) Chance – typified by such scientists as Jacque Monad. This approach views life as the product of nature's roulette, the consequence of a series of low probability events that were not predictable. 3) Necessity – illustrated by the work of Harold Morowitz. This approach views life as a deterministic event (though not in every respect). Pohorille indicated that the position that he would present sought to bridge the second and third approaches. Though the events that led to the origin of life were highly stochastic, the outcome was still fairly deterministic.

Life is based on two large molecule types: nucleic acids or information molecules like DNA and RNA, and proteins. Pohorille pointed out there is a "chicken and egg" puzzle. Nucleic acids code for proteins but proteins catalyze chemical reactions including those that lead to the formation of nucleic acids. In the mid 1980s, it was discovered that RNA could not only transfer information, but also could catalyze chemical reactions, thus functioning as an enzyme.

Pohorille indicated, however, that there was also the problem of a potential “combinatorial explosion.” When the length of a macromolecule increases or the number of potential constituent parts increases then the number of possible outcomes increases at a very fast rate. This is a problem if you are trying to find a natural pathway from prebiotic chemistry to organic chemistry to living organisms as complex chemical systems. The level of complexity of the outcome (for example, a living cell) makes the number of possible outcomes huge in principle so, unless there are natural constraints on the actual number of possible combinations, the apparent probability of any particular outcome is very small

Pohorille recounted how Manfred Eigen, in the 1970’s, addressed this problem by proposing a mechanism of autocatalysis. For example, the products of nucleic acid A might be catalysts for the products of nucleic acid B. The products of B might be catalysts for the products of A. If such feedback were the case, then after a time the products of A and B (particular proteins) would be more abundant than other nucleic acid products. Eigen proposed the “Eigen cycle” or “hypercycle” in which there is a circular chain of reactions that in the overall process catalyze themselves.

The catalytic capacities of RNA and the existence of hypercycles seem to provide important foundation blocks for a consistent model of the origin of life. In this model, RNA acted both as an enzyme and an information molecule, evolution occurred through standard mechanisms of mutation and natural selection, and a combinatorial explosion was prevented through autocatalysis.

But a significant problem still remains. Where did the monomers (smaller organic molecules) for making RNA (a large polymer) come from? Monomers (in this case the nucleotides that comprise RNA) are hard to synthesize under the natural conditions that can be reasonably hypothesized for the early prebiotic Earth without the chemical power of contemporary enzymes. Pohorille concluded that there must have been another world prior to the monomer world. In this world, there would not have been any genetic transfer of information (RNA and DNA did not exist) but there could have been some forms of metabolism, or sets of organized chemical reactions. This possibility has led to the development of a “Metabolism First” hypothesis for the origin of life.

Pohorille characterized the argument for this hypothesis as a “Chekhovian Argument” referring to the Russian playwright, Anton Chekhov. Chekhov wrote: “If you say in the first chapter that there is a rifle hanging on the wall, in the second or third chapter it absolutely must go off. If it's not going to be fired, it shouldn't be hanging there.” In this light the “Metabolism First” argument is as follows: Making amino acids and proteins is much simpler than making monomers (nucleotides) and nucleic acids like RNA. Proteins are excellent catalysts for chemical reactions. So, it would seem reasonable that amino acids and proteins, present in the early prebiotic Earth, played roles in the origin of life. Proteins are like the rifle hanging on the wall. Why would they only hang there until an RNA world appeared?

Those advocating the “Metabolism First” hypothesis are heterogeneous regarding particular developmental models. They include Stuart Kauffman, Freeman Dyson, Doron Lancet, and Harold Morowitz. Pohorille, however, proposed yet another view, one that he called “non-genomic evolution.” The basic element of this view is that proteins do not replicate as such but can “reproduce” and evolve *in a population* even if they are synthesized by random processes. The only thing that evolution requires is function. The reproduction of function alone was sufficient for early prebiotic evolution. The precise transfer of information between generations was not necessary.

Pohorille noted that “if a protein has a structure, it is less likely to be cut than if in an unstructured form.” This meant that relatively unstructured, and so useless, proteins were more likely to be cut into pieces. The destruction of useless material was another way in which the combinatorial explosion could be averted. He suggested that a balance between construction and destruction is a fundamental feature of life. Things are constantly being made and things are being destroyed. At one time it was thought that there was a huge inventory of possible chemical reactions and that over time all of them would happen. He identified this as the “random chemistry assumption” and stated that it is assumed in many of the metabolism models for the origin of life. But it turns out not to be the case.

In the absence of powerful enzymes to catalyze the chemical reactions, thermodynamic and kinetic constraints, what Pohorille called “fundamental constraints of physics and chemistry,” greatly limit the number of chemical reactions that may happen (at least, he qualified, in the context of carbon based chemistry).

Although it is difficult to do laboratory experiments to test these ideas, it is possible to develop computer simulations. When simulations of the random synthesis of proteins in a chemical environment are run, the outcomes tend to be organized into sets of metabolic pathways with movement toward higher levels of complexity. These pathways can be classified into several “families.” Within the families, there is structural similarity; between the families there is structural difference. These families can be called different chemical “species,” Pohorille suggested. Once a steady state has been reached, the number of families and the number of members of each family tends to remain more or less constant. So, even without a genome, and with random processes at work, the “species” remain in about the same concentrations. If the parameters of the chemical environment are changed, then some “species die off,” some reappear and some develop better. There is a functional form of fitness at work.

So, Pohorille explained, early evolution could progress without genetic polymers. The underlying processes were stochastic (or random), but the outcome was constrained. Familiar concepts of Darwinian evolution like species, heredity, fitness, and mutation were functionally present not in individuals but in populations. The apparently potential “combinatorial explosion” could be tamed by virtue of the constraints of physics and chemistry and the balance of constructive and destructive processes.

There is a common thread that runs through this structural chemistry, Pohorille observed. In none of the reactions that make the structures or create the biological functions is there the formation of any kind of chemical bond; rather the interactions are non-covalent. These are the most important interactions in biology especially with respect to processes of self-organization. In order to have self-organization non-covalent interactions cannot be too weak or else thermal fluctuations would cause havoc or uncontrolled changes in the chemical environment that would constantly change the state of the chemical system. But non-covalent interactions cannot be too strong or else slow and energetically costly regulation would emerge. The energy of interactions should be similar to that of high-energy chemical bonds.

To summarize, Pohorille stated that it has been shown that even very simple proteins, like those that could have been present in the early Earth environment, can form functional structures without the high sequence specificity found in the genome. Second, evolution has been able to achieve great diversity and complexity using this simple constructive motif. Finally, the underlying molecular principles are universal. He showed a slide with an artist's conceptual drawing of an extraterrestrial and the Murchison meteorite (a meteorite recovered in 1969 in which 18 amino acids were found, 12 of which were not found in life on Earth). He noted that if we looked at the meteorite, we would tend to only see a rock. If, on the other hand, we encountered the artist's character, we would immediately know two things: it was alive and it was not of the Earth. He asked rhetorically, "Is this all we need to know about the origin of life?"

In conclusion, Pohorille mentioned a 1981 article in *Scientific American* in which Manfred Eigen wrote: "The principles guiding the evolution and organization leading to the emergence of life have been formulated and experimentally verified. Now what remains to be discovered is just what the favorable molecular structures were." In contrast, biologist Ken Nealson stated in 2002, "Nobody understands the origin of life. If they say they do, they are probably trying to fool you." Pohorille declared that he thought Nealson was right and ended by saying, "The quest is still on."

The discussant for the lecture, Walter Shropshire, Jr., PhD, professor of science and religion at Wesley Theological Seminary, had a distinguished career as a physicist with the Smithsonian Institution before retiring, acquiring a seminary degree and being ordained as a minister in the United Methodist Church.

He began his comments with a brief biographical account of his interest in the origin of life question. He noted that while in high school he had learned about Lazzaro Spallanzani's work in the 18th century and Louis Pasteur's work in the 19th century which demonstrated that life did not spontaneously generate from non-living matter. Life, he declared, always comes from life.

Later in college he learned of the 20th century work of Aleksandr Ivanovich Oparin, the Russian biochemist, who outlined a way in which basic organic chemicals could form into microscopic precursors of cells. During this time Shropshire also read physicist Erwin Shrödinger's book entitled *What Is Life?* Intrigued by the origin of life question Shropshire consulted with senior scientists about whether he should choose an aspect of this topic for his doctoral work. But he was advised that the problem was too difficult. Later with the discovery of the double helix structure of DNA by James Watson and Francis Crick in the early 1950's, Shropshire again considered this field of research but was advised by colleagues that it was much too complicated and difficult. Nevertheless, when in 1957 he learned of a symposium in Moscow on the origin of life, he sent a postcard requesting the papers from the conference. Sometime later he received by airmail the volume of proceedings from the conference.

Having described his life-long interest in "origin of life" questions, Shropshire then noted that current public discussion of the issue occurs more often in the context of the abortion debate than astrobiology. But there, he argued, the question is misplaced. In the human reproductive process, life does not originate or begin. Rather, the gift of life is passed on from one generation to the next by means of two living cells: the ovum and the sperm.

On the question of the origin of life on Earth, Shropshire noted that Biblical literalists and theological fundamentalists argue that one need only consult the scriptures to discover the origin of life. From their perspective it took a supernatural act of God to bring all of the elements together to form living organisms. He suggested that such interpretations of the Bible emphasize the Hebrew word "ruach" which means "breath" and is used to describe how God "breathes" life into inanimate matter ("the dust of the ground").

Shropshire then noted that he was a United Methodist and that that religious community identifies four sources of truth, called the "Wesleyan Quadralatteral." The four sources are:

scripture, tradition, experience, and reason. Among the four sources, none is better than any other. At the same time truth claims amongst them need to be compatible.

John Wesley, the founder of the Methodist tradition, was very interested in scientific developments. When Benjamin Franklin brought an electrostatic generator to England, Wesley brought his congregation to view demonstrations. He even helped establish a clinic using shocks from such a generator to treat various ailments. It was perhaps the first introduction of electro-shock therapy.

Shropshire called attention to the three avenues of research that are contributing to discovering the origin of life on Earth: research on protocells, minimal cell research, and artificial cell research. All of these are seeking to understand "universal laws" about the physical and chemical requirements for life. He agreed that these "laws" would be universal such that the emergence of life would be inevitable if the conditions were right. This would be the case even if the history of the universe was filled with random, chance events. Some scientists, he noted, argue that the physical constants of the universe are "fine tuned" in such a way that if they varied even by a miniscule percentage, life as we know it would not have occurred. This is the so-called "Anthropic Principle." It is not known if a supernatural creator established these particular constants. Such a conclusion is a matter of faith, Shropshire stated. But it is of scientific interest to know the precise physical and chemical laws and constants that are required for life.

On the matter of randomness, Shropshire commented that most of his theological colleagues are not disturbed by random, stochastic, probabilistic mechanisms for the creation or the origin of life. For most theologians, he proposed, a creator of all the cosmos would have structured things so that the established universal laws would make the origin of life inevitable. If the whole cosmos is considered to be an evolving system, then from the Big Bang through the first stars which produced the atoms necessary for life and scattered them across the cosmos by supernova, one can think of the creator as being involved in all these processes.

Shropshire added that there are two particular features of life that need to be considered as part of the set of universal requirements when seeking to understand life's origin: life is active and it is tough. We know that life exists in very extreme environments and that as a consequence it is pervasive on the Earth. Life is everywhere. On the palm of one's hand there is an enormously large number of organisms. One consequence of this for origin of life research is the effort that needs to be made to avoid experimental or observational contamination. Shropshire offered the following anecdote to illustrate his point. In the very early days of commercial air travel, the wing tanks of aircraft were fueled on the tarmac where there was also a lot of water. To the horror of the airlines it was discovered that there were micro-organisms that thrived in the interface between the water and the fuel and that as a part of their metabolic cycle they were using metal from the struts that provided rigidity to the airplane wings. The organisms were slowly "eating" the wing-struts. A poison was discovered that halted the bacterial growth and also would not clog the jet engines, so travel today is safe. But this story is testimony to both the toughness and the pervasiveness of life on Earth. Life is "clever, ubiquitous, and tough. From a religious perspective God must be interested in having life everywhere," Shropshire declared.

Dr. Shropshire ended on a practical theological note. He reported that as part of a course he teaches to seminarians on science and religion, he has them fill out a survey. They are asked, among other things, whether they agree with the statement: "Scientists will never create life in the laboratory." He indicated that he was regularly amazed that the majority of students agreed that life would be created in the lab and that such an accomplishment would not disturb their faith. Their reasoning has seemed to be that researchers are themselves creatures made by God and so their efforts to create life in the lab are simply a part of the creative process. While the students are open to the possibility of this happening, in fact it has not happened and it is not clear that there has been much progress toward accomplishing this result.

Shropshire ended his comments with a question for Dr. Pohorille. "What is the probability that life will be created in the lab and when might we expect it to occur?" Pohorille's response was that there is still much that is not known about life, though much has been learned in the last decades. He expressed the view that life would be synthesized in the lab and that it would occur in the life-time of people in the audience.