A Natural Origin-of-Life: Every Hypothetical Step Appears Thwarted by Abiogenetic Randomization

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Abstract

The study of the origin-of-life (abiogenesis) presents a history of failed experiments. Abiogenesis is viewed as a series of steps of increasing complexity, such that an initial supply of chemicals naturally present on a planet or moon gradually turn into living cells. Yet, not a single step has been observed that turns starting chemicals into new ones which represent an advance towards life, such that the new ones can be used as produced as the starting point in the next step. Steps do not flow smoothly from one to another. Yet, an eventual appearance of living cells requires a natural, smooth flow between steps along the entire pathway, without external guidance or intervention by scientists. If scientists cannot accomplish this for any step using controlled processes and conditions, it is implausible that the entire path could be traversed in nature under uncontrolled conditions. Historically, the causes for failures have been viewed as isolated instances, with hope that in time solutions can be found. By contrast, this article represents new science in that it proposes a common root cause leading to most if not all of the various failures.

We propose the following hypothesis of Abiogenetic Randomization as this root cause: 1) prebiotic processes naturally form many different kinds of products; life requires a few very specific kinds. 2) The needs of abiogenesis spatially and temporally are not connected to and do not change the natural output of prebiotic processes. 3) Prebiotic processes naturally randomize feedstock—they turn starting chemicals into more random molecular combinations. A lengthy passage of time only results in more complete randomization of the feedstock, not eventual provision of chemicals suitable for life. The Murchison meteorite provides a clear example of this. 4) At each hypothetical step of abiogenesis, the ratio of randomized to required products proves fatal for that step. 5) The statistical law of large numbers applies, causing incidental appearances of potentially useful products eventually to be overwhelmed by the overall, normal product distribution. 6) The principle of emergence magnifies the problems: the components used in the later steps of abiogenesis become so intertwined that single-step first appearance of the entire set is required. Small molecules are not the answer. Dynamic self-organization requires from the beginning large proteins for replication, metabolism and active transport. Many steps across the entire spectrum of abiogenesis are examined, showing how the hypothesis appears to predict the observed problems qualitatively. There is broad experimental support for the hypothesis at each observed step with no currently known exceptions. If this hypothesis is valid, then abiogenesis is a closed field. There would be natural barriers against the appearance of life at every step along any proposed path. This appears confirmed by experiment. This has a number of philosophical implications, although these are outside the scope of the paper.

Keywords: abiogenetic disconnects; emergence; abiogenesis; natural selection; systems chemistry; discontinuity; Virchow; entropy; randomization; dynamic self-organization

1. Introduction

1.1 Overview

In 1953 Stanley Miller and Harold Urey reported an experiment that successfully converted certain simple, naturally occurring compounds—methane, ammonia, hydrogen, and water—into various amino acids [1]. Amino acids are the building blocks of life. It appeared that natural processes were sufficient in themselves to provide the chemicals needed for a natural, spontaneous origin of life. The ensuing excitement was so great that it set off a new field of scientific study, initially called chemical evolution and now more frequently called abiogenesis. Sara J. Walker *et al*, in the British Royal Society’s publication *Philosophical Transactions A*, commented on the reactions to the experiment, “There was some optimism that, had the experiment been left running, living creatures would soon be crawling out of the laboratory [2].” It has been over sixty years since Miller and Urey reported their results. However, the results have not come close to living up to these early expectations.

Steve Benner is the founder and president of the Westheimer Corporation, a private research organization, and a prior Harvard University professor. He is one of the world’s leading authorities on abiogenesis. This is his evaluation of what he has observed:

We are now 60 years into the modern era of prebiotic chemistry. That era has produced tens of thousands of papers attempting to define processes by which “molecules that look like biology” might arise from “molecules that do not look like biology” For the most part, these papers report “success” in the sense that those papers define the term.... And yet, the problem remains unsolved [3].

As we study the various stages of abiogenesis and hear about all of the optimism, it is well to keep Benner’s comments in mind. The origin of life still cannot be explained scientifically.

We suggest the following hypothesis explains the root cause of most if not all of the observed failures in abiogenesis over the entire 60 plus years of its modern research activity.

2. We hypothesize:

1. Product Possibilities. At each hypothetical step of abiogenesis prebiotic processes at work in that step will be capable of forming a significantly larger number of products than are suitable for an advance towards the appearance of living cells.

2. Abiogenetic Disconnects. There is no connection between the natural products of prebiotic processes at a given step and the principles of biology and biochemistry that determine which products need to be provided for use spatially and temporally.

3. Randomization. Prebiotic processes are inherent randomizers. They tend to provide a random assortment of possible products according to a natural statistical distribution. Products suitable for life may appear on an incidental basis, but not systematically at higher yield than the natural distribution. Lengthy, extended spans of time for abiogenesis result in greater randomization of initial feedstock, not biochemicals.

4. Fatal Ratios. Because of randomization the ratio of wrong products provided at each step to those that are required for an advance towards life will be large enough to prevent any given step from successfully providing usable feedstock to its successor. This is the ultimate cause of the consistently failed steps and experiments in abiogenesis.

5. Law of Large Numbers. The statistical *law of large numbers* applies to prebiotic processes. A single mole of a given compound contains 6×10^{23} instances of the compound. This is a large number. In abiogenesis there will be a natural distribution of possible products for the outcome of a given set of conditions and processes. Fluctuations within the distribution are normal, but the larger the total number of instances worked on, the closer the average distribution yielded

comes to the natural distribution. This effectively neutralizes the significance of incidental deviations.

6. Emergence. The principle of emergence can exponentially compound the difficulties of the above assertions, particularly in later hypothetical steps towards the appearance of living cells.

These assertions are not difficult to understand. Neither is their application. Yet, they lead to conclusions with far reaching implications. Their simplicity and their ease of application to a given scenario make the hypothesis a powerful tool.

Two generations of consistent failures without a single success should tell us that something is fundamentally wrong with current foundational premises. We suggest that the above hypothesis explains the problem. The assertions represent fundamental properties of nature and any and every hypothetical step appears to be affected by them. In the Analysis section to follow, we will look at a number of the major proposed steps to see if the hypothesis provides a qualitative prediction/explanation of the outcome of experiments associated with the steps. Over the past sixty years, there have been reputedly thousands of experiments performed representing various postulated steps. None have been able to provide product usable as feedstock for its successor, which is the standard defining success within this analysis. The vast number of already performed experiments provides a substantial base for evaluating the validity of the hypothesis.

3. Discussion on the hypothesis

3.1 Product possibilities

Carbon, nitrogen, oxygen, hydrogen, sulfur, and phosphorous are the primary elements used in living cells. There are virtually an unlimited number of compounds that can be made using all or some of the possible combinations of these elements. The Beilstein Database lists over seven million organic compounds by their names and characteristics. Isomers are treated as separate entries. Polymers are not included. Along the same lines the Murchison meteorite contains over a million different organic compounds when isomers are included in the count [4]. Isomers are properly treated as separate chemicals because they are not interchangeable among themselves within proteins and nucleic acids.

The Murchison meteorite provides a true-life instance of prebiotic processes at work on initial compounds without any kind of interference or guidance. An initial feedstock plausibly consisting of only a handful of simple compounds was converted into over a million variants. By contrast, most of cellular chemistry is based on proteins and nucleic acids, which are built from a feedstock of twenty-eight kinds of building block molecules—twenty canonical amino acids (coded for in DNA), four kinds of RNA nucleotides, and four kinds of DNA nucleotides. Abiogenesis requires large, pure quantities of these 28 molecules to the exclusion of most others. Natural processes appear to work towards provision of random arrangements of the million plus possibilities, not to focus provision on the handful of building blocks needed for life.

The pattern of a prebiotic processes providing more unusable product than useable appears to repeat itself at each of the remaining steps of abiogenesis.

3.2 Abiogenetic disconnects

There appears to be no dependency, relationship, or connection of any kind between the products naturally produced by prebiotic process and those needed for life. Chemicals useful to life do appear, but only on an incidental basis. Potential utility towards life does not override the randomness of the normal statistical distribution. We have coined the term *abiogenetic disconnects* to represent this lack of connection [5]. On the one hand, *abiogenetic disconnects* is merely stating

the obvious. On the other, it defines a standard of reference and perspective for the ensuing discussion.

Chemical engineers regularly design processes and equipment to form complex products with controlled precision. Nature frequently provides processes which under tightly controlled conditions are capable of restricting their yield to specific targets from a broad range of possible outputs. The work of the chemical engineer is to sequence and control these processes so that the target is provided with sufficient purity for use in a succeeding step or final product. Accomplishing this in an industrial chemical plant typically requires suitable feedstock, suitable processing equipment, suitable mechanisms for environmental modification, suitable sensory equipment to supply feedback information, and a suitable mechanism for operational control. Living cells also feature these mechanisms. However, they are not available to prebiotic process. For instance, there is no feedback mechanism available to regulate the effect of an electric discharge on a mixture of methane, ammonia, water, and hydrogen, the constituents of Miller's experiment. A reputed prebiotic process which is dependent on the pre-existence of specialized equipment or on human intervention to mimic it in order to accomplish these tasks is not prebiotic.

Environmental disconnects. There are also environmental disconnects between the factors which determine the physical environmental conditions at a site and conditions required for abiogenesis. For example, just because too much rain could wash out a pond with incipient abiogenesis underway will not result in the appearance of a protective shield, diverting an approaching severe thunderstorm. The needs of abiogenesis have no restraining impact on the normal physical and chemical behavior. For another example, entrained mud flowing into a lake during spring run-off may potentially adsorb all of the organic molecules involved in abiogenesis and bury them during sedimentation, either at the lake or at some distant site downstream. This could prove fatal to incipient abiogenesis at the site. This would be similar to what happens to pollutants in Lake Michigan [6]. Yet, this possibility does not result in any restraint on the potential mud flow into a lake. There is a disconnect between the principles which determine environmental conditions at a site and those which are needed for successful abiogenesis.

This is important because most environmental conditions tend to fluctuate randomly over large values over periods of time. By contrast, chemical engineers exert precise control over a number of factors relevant to the processes used. Precise control is required in order to restrict output to a selected target or range of targets from an otherwise broad range of possibilities. One serious disadvantage of abiogenesis is that feedback mechanisms are generally sufficiently complex that their implementation requires cellular capabilities of genome specification, translation, implementation, and replication. Our assumption is that once this level of sophistication has been reached, abiogenesis has met its goals and living cells are now subject to Darwinian evolution. Thus, these tools are not available for use in abiogenesis.

Cellular products are far more complicated than those of any chemical plant. This plausibly makes them more sensitive to environmental variation than industrial chemical processes. If relatively simple industrial processes fail without feedback control and the ability to sustain a specified environment, it is even less plausible for abiogenesis to succeed without it. Perhaps current emphasis in abiogenesis does not emphasize environmental constraints because potential processes are not defined well enough to define constraint boundaries. Yet, we suggest that this is an extremely critical, often overlooked factor.

In his book *A Skeptics Guide to Origins*, Roberts Shapiro discusses the possibility of streamflow supply of feedstock [7]. Sometimes a process may require provision of multiple chemicals having incompatible formation chemistries. Shapiro proposes a solution for this in having the different chemistries take place in different ponds, with local conditions providing the proper environment for

each of the required chemicals. Streams then transport the chemicals from the supply ponds into the main processing pond, wherein the different intermediate reactants are processed together. This is obviously a scenario capable of many more wrong possibilities than correct ones.

The most significant problem with environmental variables is that they vary widely from day to day, month to month, year to year, century to century, etc. They have no stability. We suggest that it is implausible for a natural setting to provide adequate stability for any proposed situation which depends on streamflow from different locations meeting at a common downstream location for additional processing. RNA decays in only a matter of days [8]. Therefore, interruption of nucleotide supply for more than this could be catastrophic, potentially destroying all progress towards life. When nucleotide supply is dependent on environmental conditions such as specific rates of streamflow from multiple supply ponds simultaneously feeding into a mixing pond, the risk of an interruption in nucleotide supply becomes great.

3.3 Prebiotic processes appear to yield random mixtures of the possible products

Prebiotic processes inherently function as random product generators, using an external energy source to rearrange the chemical elements of substrate into a random set of new product molecules. The species and probabilities of the new molecules will be formed in accordance with the laws of physics and chemistry on a molecule-by-molecule basis in accordance with local environmental conditions. The total results will be the sum of individual, independent interactions.

As a general observation, energy utilization will typically take place in one of two settings: controlled or uncontrolled. Controlled energy usage requires a precisely defined physical mechanism to convert a specific form of energy into a new form suitable to accomplish a specific function. For instance, gasoline is a rigidly specified form of energy. It can be taken from a tank, metered into a cylinder, mixed with a suitable proportion of air, compressed, ignited by a spark, and then produce a controlled displacement of a piston which can be converted into rotary motion to turn the wheels of a car. A specific physical mechanism matched to the energy source is provided to perform all of the tasks required in order to burn gasoline as a controlled source of motive energy. There must be a good match between the form of energy supplied and the machinery. By contrast, simply dumping a tank of gasoline onto a car and igniting it will typically result in an uncontrolled fire or explosion. There is an exceedingly great probability that this will not improve the car but damage it. The energy from a tank of gasoline poured onto a car and then ignited will most certainly not provide a means for the car to be driven through heavy stop-and-go traffic for hundreds of miles. Uncontrolled energy does not provide controlled results.

Prebiotic processes are similar in character to dumping a tank of gasoline on a car and igniting it. By contrast, living cells have machinery which converts energy appearing in a specified form into ATP, which is useful for biotic processes. The form of energy to be converted into ATP varies among cellular types, such as UV light, visible light, methane, metallic ion flow, or digestible nutrients. Without machinery matched to the form of energy, energy tends either to have no effect or to act like a tank of gas dumped on a car.

Long periods of time do not make life inevitable; they only make randomization more complete. The large number of molecules in just a few kilograms of material overrides any temporarily useful fluctuations that might appear.

Since prebiotic processes are natural randomizers and abiogenesis requires specific products, it does not appear that prebiotic processes have inherent capability to meet the requirements necessitated for successful abiogenesis. This plausibly characterizes every hypothetical step of abiogenesis and explains why none have succeeded.

3.4 Emergence

3.4.1 Definition of Emergence

Life is noted for its highly organized structure across many different levels. Products and processes in living systems are typically the result of interactions between multiple components: a number of components need to be in place and functioning before the desired phenomena can appear. *Emergence* is the term used to describe this behavior.

Harvard biologist Ernst Mayr described emergence like this:

Systems almost always have the peculiarity that the characteristics of the whole cannot (not even in theory) be deduced from the most complete knowledge of the components, taken separately or in other partial combinations. This appearance of new characteristics in wholes has been designated as *emergence*.... Actually, emergence is equally characteristic of inorganic systems. As far back as 1868, T. H. Huxley asserted that the peculiar properties of water, its ‘aquosity,’ could not be deduced from our understanding of the properties of hydrogen and oxygen [9].

Notice, Mayr mentioned that systems in general almost always exhibit emergence. It is not a rare phenomenon, but pervasive throughout nature.

Penzlin explained emergence in more detail, explaining how knowing details of component behavior does not allow one to predict their combined behavior. This starts with elementary particles combining into atoms and applies to each step as one works up from atoms to molecules to cells, and yet higher levels [10].

3.4.2 Virchow’s aphorism and emergence

During the 1850s a number of researchers were concluding that cells form exclusively through the division of existing cells. Rudolph Virchow is generally credited with the aphorism *omnis cellula e cellula* (all cells from cells) [11].

Petra Schulle, a synthetic biologist and a director and scientific member of the Max Planck Institute in Biochemistry in Germany, gave a recent summary of the significance of this aphorism: “We still do not have a strategy to escape the circular dictum of the 19th century—attributed to Rudolf Virchow—that every cell derives from a cell (‘*omnis cellula e cellula*’). Presumably there wasn’t one right after the big bang, so where did the first one really come from [12]?”

There is an obvious discontinuity in the aphorism. At one point in time, cells did not exist and the aphorism was not active. At a later time, cells did exist and the aphorism was effective. Continuing with the question, “What is life and how could it originate?” Schulle declares “we are ironically still far from giving a convincing answer to this question.... [12]”

This paper will arbitrarily use the standard that the objective of abiogenesis is to bridge the discontinuity between naturally occurring non-biological chemicals and operational status of Virchow’s aphorism. On one side of the discontinuity is abiogenesis. On the other is a fully-functioning cell subject to traditional Darwinian evolution. The goal of abiogenesis is to bridge the gap, at which point its role is finished. A major question facing abiogenesis is whether or not this gap is bridgeable by natural processes. This question needs to be answered on the basis of scientific observation, not dictated by metaphysical presuppositions of any sort. The question is, “Where does science lead?”

In the same paper cited earlier, Penzlin also explained why he believes Virchow’s aphorism still applies despite the work of Oparin, Haldane and Miller. His comments show the ramifications of emergence applied to biology: “The whole cell is the most elementary unit that can maintain life; it is the least complex thing that properly lives [10].”

Penzlin’s basic point, as summarized above and further developed in the paper, is that a cell functions as a complete unit. Life is an emergent feature which is more than the sum of its parts.

This was the root of Virchow's statement, "All cells from cells." Penzlin also adds issues of dynamic self-organization as an inherent component of cellular existence. All of a cell's essential components need to be present from the beginning, including many mutual interactions in dynamic self-organization far from equilibrium. In a static state at thermodynamic equilibrium, a cell rapidly degrades beyond recovery. His thesis is that prebiotic organic chemistry (i.e., the gradual steps of abiogenesis) does not have the capability to deal with the new complexities revealed.

Philosophers discuss the degree to which sufficient understanding of basic principles would allow emergent phenomena to be predicted [13]. We suggest that these discussions are irrelevant to abiogenesis. Natural processes work on what is actually present, not what could be. Philosophical discussions are irrelevant. Either everything is in place and an emergent phenomenon appears, or if any component is missing it does not appear. There is a discontinuity. No matter how close a system might be for all of the pieces to work together properly, there is no success until they actually do. Then, with all of the pieces in place, success suddenly appears. Discontinuity is the exact opposite of Darwin's continuity principle and where discontinuity exists by definition there is no continuity.

Emergence might not be a big issue if all of the components are statistically likely to appear on a frequent basis. Then it should only be a matter of time for random processes to bring them together. However, if their appearances are virtually impossible statistically, if random processes are all that are available, and if a number of these components need to appear together spatially, temporarily, and in a specified environment, the likelihood for success becomes exceedingly implausible. This appears to be the situation facing abiogenesis.

4. Miscellaneous Issues:

4.1 Entropy, random behavior, and free-energy machines

It is frequently understood that entropy results in random changes to an organized system making it less organized. Claude Shannon showed that randomization is the fundamental behavior and entropy is simply a mathematical expression of certain of its aspects [14]. Since randomness is intuitively simpler to understand than entropy, since it is more fundamental than entropy, and since it is adequate for purposes of this discussion, we will focus discussion on the effects of randomness. Entropy will only be mentioned in citations or discussion about them.

It is generally understood that perpetual motion machines and free energy are impossible because of entropy. Shannon's analysis of randomness was very broad in scope and applies to any probability distribution. When the rules of thermodynamic molecular behavior are applied to his analysis, the laws of statistical mechanics appear [14A]. A mathematical expression of entropy appears naturally in statistical mechanics.

Every experimentally tested step of abiogenesis appears to be plagued by randomness in the products yielded. Some of the later steps that are too complex to be tested are known to have many more wrong possible results than required ones. Randomness is plausibly going to be an issue for these as well. If randomization is an underlying root to the observed failed steps throughout abiogenesis then there is little basis to expect natural, prebiotic processes to be capable of overcoming its effects. Therefore, it appears that randomization is at the root of both free-energy machine failure and the failed steps of abiogenesis. With a common root cause for both application, there is little basis to expect abiogenesis to be any more successful than efforts to build a free-energy machine. Perhaps this explains the past sixty years of failure. If this is the case, then the problem will prevail no matter how many more years of effort are made. 6,000 more years will not solve anything.

This discussion appears to provide plausible basis to consider abiogenesis a closed field, even as are free-energy machines. A primary goal of abiogenesis should be to falsify this conclusion.

4.2 Prigogine, abiogenetic disconnects, and randomization

Ilya Prigogine won the Nobel Prize in Chemistry in 1977. He demonstrated that in a system far from equilibrium, self-organization can take place. A dramatic example of this would be the formation of an organized thunderstorm complete with tornado when a calm, stable mass of cold, dry air collides with and flows over a calm, stable mass of warm, moist air. Prigogine suggested (without evidence) that the phenomenon of self-organization could be extrapolated to account for the appearance of life [15]. Normally, random changes to organized systems destroy existing order. Since the emergence of life requires unorganized chemicals to become extremely organized, this would appear to be contrary to entropy. However, following Prigogine's lead abiogenists have postulated that an initially disorganized system in a far from equilibrium condition can self-organize using energy from an external source such as sunlight, with the resultant self-organization leading to life.

There is a fallacy with this hypothesis. Although self-organization can take place in far-from-equilibrium conditions with the result that complex molecules form out of simpler ones, yet abiogenetic disconnects and randomization still determine the nature of the products that are produced. The number of possible products that could be formed far exceeds the number suitable for life temporally and spatially. The Miller-Urey experiment illustrates how, because it presents a simple example of Prigoginian self-organization as applied to the origin of life at its initial step. First, start with simple, non-biological chemicals in an equilibrium state. Then add energy. The starting chemicals are randomly ionized, placing them in a far from equilibrium condition. The interactions of the ionic mix produce self-organization leading to new products, including many that are more complex than the original ones. Hence, the process represents self-organization. Importantly, though, these products still appear in accordance with a normal, random distribution of the possible outcomes. Biochemicals appear in their natural proportion to the whole; they are not superabundant as would be required for abiogenesis. The near total randomization of the Murchison meteorite compounds [4] is the plausible destiny of Prigoginian self-organization. Most of the products will be more organized than the starting compounds. However, their distribution among the possibilities will not be restricted to providing temporally and spatially those needed for abiogenesis.

Prigogine did not discuss how disequilibrium from sunlight could cause unorganized chemicals to invent a triplet code for protein translation, create the information to build an organism using the triplet code, and form the hardware to process the information. Emergence requires all of these to appear simultaneously. They represent essential capabilities necessary for transition into cellular life. Most if not all of the components to implement them are so complex that it is virtually impossible to form them using random processes. By contrast our thesis of interaction between abiogenetic disconnects and randomness leads to the expectation that any self-organization that takes place from the external energy source will produce a random set of molecules, ones that in general can have increased organizational complexity but without the specific organization required for an advance towards life.

We will see that instead of dynamic self-organization providing a simple solution for life as the required molecules spontaneously appear, it actually places new, significantly increased demands on origin-of-life processes. Prigogine plausibly did not understand that the dynamic self-organization observed in a living cell does not randomly appear, but is extremely controlled. It needs to be implemented by interactions explicitly defined in the genome of a cell and precisely implemented by cellular machinery. Being in an out-of-equilibrium state opens up the door to many possible forms of self-organization. The number of possible characteristics of a molecule's behaviour is significantly greater for a molecule used in a dynamic, self-organizing system than for a static system. Without a means of pre-existing control, random self-organization will not meet the specific requirements of abiogenesis. Dynamic self-organization does not simplify chemical evolution as is commonly presented. It significantly increases the difficulties. This will be discussed in more detail later.

.5. Methods

No original experiments were performed in this investigation. A broad study of the literature in abiogenesis, biochemistry, and cell theory was undertaken. The initial interest was on the relationship between Miller's experiment and the impact of entropy on the products it produced, particularly from the perspective of Prigoginian self-assembly/organization in systems far from equilibrium. The initial investigation was broadened substantially as the subject was pursued and newly discovered issues led to new topics for investigation. It appeared that randomness prevented the self-organization observed in Miller's experiment from organizing into the chemicals of life. The question then became whether or not the principles of randomness that governed the results of this experiment applied to abiogenesis as a whole. The answer to this question became the foundation for this paper.

6. Analysis of Steps from the Perspective of the Hypothesis

In this section we will examine a number of different steps/of abiogenesis from the perspective of our hypothesis presented earlier.

6.1 The initial step—conversion of raw, naturally appearing chemicals into biological building blocks.

6.1.1 Miller's Experiment and Variations

The initial step of abiogenesis transforms naturally appearing raw chemicals into building block chemicals, typically amino acids or nucleotides. These in turn would be used to form protein or nucleic acid polymers, which would be the next step.

The question is whether our hypothesis can explain qualitatively the results of experiments performed at this step. Do the products generally produced represent a random assortment of those possible or are products suitable for life preferentially provided? Is the randomness so extensive as to thwart progression into the next step, polymerization?

The Miller-Urey experiment of 1953 provides a clear example of this step. Miller started with an initially high concentration of four very simple compounds: methane, ammonia, hydrogen, and water. This represents a high degree of organization, occupying only four out of more than a million possible combinations of the initial elements. However, the initial compounds did not represent the organization required for life. Molecular rearrangement would be needed to provide for that. The initial compounds were subjugated to a high-voltage spark in batch mode until all of the carbon in the methane had been consumed and the process was stopped. Our hypothesis predicts increased randomness to the point that any useful molecules will be overwhelmed by those interfering with subsequent steps.

In Miller's initial report of 1953, he stated,

On this basis the amino acids glycine, α-alanine and β-alanine are identified. The identification of the aspartic acid and α-amino-n-butyric acid is less certain because the spots are quite weak. The spots marked A and B are unidentified as yet, but may be β and γ amino acids. These are the main amino acids present, and others are undoubtedly present but in smaller amounts [1].

In 1953 only amino acids were discussed as products of the experiment, nothing else was mentioned. It was specifically anticipated that there were yet other amino acids, although in smaller amounts.

This report gives the impression that prebiotic processes do not work towards total randomness in chemical complexity, but favor formation of amino acids, the building blocks of life. This would imply that natural processes favor the appearance of life, which in turn implies that there is some as yet unknown connection between the results of natural processes and the requirements of life. This suggests that abiogenetic disconnects, the second assertion of our proposed hypothesis, had been

falsified by the results of the experiment, at least for this step. Harold Urey, Miller's graduate advisor and a Nobel Prize winner, co-authored the paper. This gave it credibility. It is not surprising that this experiment set off serious research in origin-of-life studies. It established a perspective which still seems to continue to this day among many abiogenists, that prebiotic processes naturally lead to supply of chemicals needed for life spatially and temporally; if we can just get the proper process methodology, then the problems associated with randomness will disappear.

Two years later Miller updated his report. By this time he had run three versions of the experiment, with one of the three being a repeat of his first one. He also had had time to do a more complete product analysis. This time the amino acids represented only a small portion of the reported compounds. Miller listed the following as identified in the yield: "HCN, amines, aldehydes, alcohols, most of the volatile acids, acrylonitrile, polymers, nitriles" ... "amino acids, hydroxy acids, part of aliphatic acids, polyhydroxy compounds, part of polymers [16]."

The chemicals of life were not favored after all. The original chemicals started out representing only four very simple chemicals (methane, ammonia, hydrogen, and water) in high concentration. In the span of one week, this had increased to a broad range of product categories with multiple kinds of compounds in them. These are randomized compounds as predicted by and consistent with our hypothesis. In the course of a single week, the initial feedstock was significantly randomized.

Miller also reported in the 1955 paper that in one variation of the experiment, the condenser and electrodes were interchanged. In this case "a considerable quantity of hydrocarbons was formed and only a very small quantity of amino acids." This shows that not only are a wide range of products besides amino acids possible, but even getting amino acids is dependent upon having the correct process mechanism in place. Otherwise, randomization still takes place, but most of it in product space far away from amino acids.

A later report by Miller *et al* showed that the amino acid concentration was consistent with equilibrium reactions when one mixed methane and ammonia together in approximately equal amounts, as was done in the experiment [17]. Thus, Miller acknowledged that the observed amino acids appeared only in accordance with normal chemical reaction theory; they did not indicate any tendency to concentrate the chemicals of life. This acknowledgment is the exact opposite of the impression given by his initial 1953 report.

Upon close examination the experiment appears to confirm our hypothesis. A broad range of new products are formed which randomizes the initial chemicals provided. Chemicals suitable for life appear, but in what appears to be part of a natural distribution without any special emphasis on requirements for life. The products yielded by the experiment would not make suitable substrate for the next step, polymerization.

From a practical perspective, all initial step experiments appear to be mere variations of Miller's original. The starting chemicals can be varied, the energy source can be varied, and environmental features can be varied. However, in general all of the variants give the same kinds of qualitative results. An initial substrate is acted on by an external energy source with sufficient energy to reorganize the molecules. However, being prebiotic, there is no mechanism to harness the energy and apply it in a controlled manner, thereby restricting the yield to specific products—such as happens in a living cell or an industrial chemical plant. As a result, the products will represent a random assortment of those possible temporally and spatially. No special preferences are given to those needed for life. This observed behavior appears to be due to fundamental properties of nature which have no plausible workarounds.

There is no basis to believe that in a natural setting steps after the initial one will ever have the chemicals they need for satisfactory function. It is perhaps ironic that Miller's experiment set off all of the excitement to begin abiogenesis studies in earnest. However, it actually demonstrates clearly how abiogenetic disconnects and randomness combine to prevent the step from supplying new

chemicals in a form usable in subsequent steps. With Miller's experiment abiogenesis has reached a dead end before it gets started. There appear to be no workarounds for the problems it has revealed. Sixty years of intense study has not made a dent in resolving the problems revealed by this, the first experiment.

6.1.2 The Murchison Meteorite

In 1969 a large meteorite landed on earth near Murchison, Victoria, Australia. Over one hundred kilograms of its fragments were collected within a short time of landfall, while it was still essentially uncontaminated. It was of a class known as carbonaceous chondrite. Of these fragments two percent (2.0 kg) were of organic matter. Amino acids were among the organic compounds [18].

The Murchison meteorite and others similar to it provide unique examples of natural, prebiotic processes at work over an extended period of time apart from any form of human interference. S. Pizzarello gives an overview of the organic content of carbonaceous chondrite meteorites reporting, "Overall, their molecular composition appears to fulfill the expectations of abiotic syntheses governed by purely physicochemical processes and is quite dissimilar to the structural specificity characterizing biochemistry, a contrast that also vouches for meteorite organics' indigeneity [19]."

The above comment is significant. Pizzarello *et al* revealed that meteoritic prebiotic processes lead away from the chemicals of life, not towards them. Therefore, it was evident that the meteorite was not contaminated from earthly microbes. This is not what would be expected from claims that the appearance of life is essentially inevitable given suitable initial compounds, suitable energy sources, and a suitable environment. The meteorite appeared to meet all three of these requirements, but used them as an opportunity to produce a random assortment of chemicals far from those characteristic of life. Furthermore, Pizzarello acknowledged that this is what should be expected from "purely physicochemical processes." This is not orthodox abiogenetic theory.

Philippe Schmitt-Kopplin *et al* provided a detailed analysis of high-resolution mass spectroscopy of Murchison meteorite samples over the limited mass/charge range of 150-1,000. Over 14,000 unique molecular compositions were observed. Extrapolation over a fuller range and accounting for "a realistic minimum of several thousand isomers for each chemical composition" resulted in a projection of several million different compounds residing in the meteor. This suggested that "Constraints of temperature, radiation, accessibility, and selectivity of reaction pathways (e.g. aromatization) have likely guided the trajectory of organics evolution into a complex mixture, eventually approaching an entropy-driven near continuous distribution of molecular compositions and structures characteristic of abiotic syntheses [4]." The continuous distribution referred to represents near-complete randomization, where the observed species have been randomized until they occupy almost all of the multiple millions of possible molecular configurations.

If one starts with high concentrations of the naturally appearing non-biological chemicals located only a few "steps" away from those needed for life and if these quickly randomize into a broad range of products of near-complete randomization, then it is difficult to comprehend how one could start with the broad range and for them randomly to converge on the twenty-eight compounds needed for life.

It is difficult to imagine a clearer testimony against the possibility of natural processes supplying the chemicals of life than that offered by the composition of the Murchison meteorite.

6.1.3 RNA

6.1.3.1 Problems with traditional approaches to RNA fabrication. RNA nucleotides are composed of three moieties: a phosphate molecule, the sugar ribose, and one of four bases. For years scientists have tried without success to simulate a prebiotic process that could properly assemble

these with each other. Saidul Islam and Matthew Powner give a thorough analysis of the problems that underlie the failures. In a paper on systems chemistry they have a discussion under the heading “The Traditional Disconnection of RNA Leads to Impossibly Difficult Ribonucleotide Assembly.” The heading summarizes the issue. Natural processes make traditional approaches to a prebiotic fabrication of RNA nucleotides virtually impossible. They go into great analytical detail justifying this statement. They then offer as an alternative the systems chemistry approach pioneered by John Sutherland and cohorts at Cambridge University [20].

6.2.3.2 The systems chemistry approach to RNA fabrication. “The origin of life is now considered as that of co-evolution of different subsystems than a self-organization process in a system made of a single biopolymer [21].” Systems chemistry is the current hope of abiogenists to get past the problems of RNA nucleotide production that have plagued them for so long. A simple definition of systems chemistry is “a multi-component reaction giving many products [22].”

We will examine the issue of systems chemistry as represented by the work of John Sutherland in detail. Since this has become the current focus of emphasis in abiogenesis, it warrants careful, thorough analysis.

Sometimes Sutherland and cohorts had better results than expected. This resulted in claims that chemistry is predisposed to provide the chemicals of life [23]. If this were true on a broad scale and across a broad range of steps, it would falsify the abiogenetic disconnects phenomenon of our hypothesis, at least for this step. However, close examination reveals that the apparent predisposition is limited in scope and requires constraints too strict for natural, unguided implementation. In a prebiotic setting randomization should still prevail over predisposition.

We suggest that the predisposition being spoken of by Sutherland and others is in essence no different than other well-known processes providing specific chemicals, except it applies to simultaneous “multi-component reactions giving many products.” This would be analogous to claiming that amino acids are predisposed structures and therefore prebiotic processes favor the appearance of amino acids. The Strecker synthesis could be provided as evidence. However, Miller’s experiment plausibly makes use of the Strecker synthesis to form its amino acids. That does not prevent other syntheses from working simultaneously and in parallel, with an overall effect of significantly increased randomization. This has just been discussed. Likewise, it could be claimed that there is a predisposition to form sugars and then using the formose reaction or the Kiliani-Fischer synthesis as evidence. The reality is that nature does provide paths to form various specific products. This is the basis for chemical engineering as well as the underlying chemistry used in living organisms. The issue is that any specific paths/products are only a small portion of the total available and they require strict process control lest the target not be reached, being diverted into some other direction. A true predisposition would be so robust in favoring a particular route that it would be difficult not to take it. By contrast it takes very strictly applied conditions for the systems chemistry of Sutherland to be effective.

Initially, Sutherland’s goal was to synthesize a nucleotide in a single pot using a systems chemistry approach [24]. By 2017, the goal had expanded to forming all of the basic building blocks—lipids for compartments, amino acids for metabolism, and nucleotides for information—starting with cyanide as a common initial substrate. However, this ended up requiring six separate ponds with their own unique geochemical conditions and whose products then needed to be mixed together in a specific sequence. Even this degree of complexity did not supply required product, but only precursors [25]. The requirement of so many unique ponds and associated chemistries in such close proximity to each other begins to stretch plausibility. Their latest paper [27] discusses further refinement of one of these paths. It requires drying and wetting cycles, with a suggestion that a wetting cycle would take place when rain had resumed after a drying cycle. This has the potential to represent a long period of time, particularly during drought conditions. It is implausible for a process

554 based on this mechanism to serve as a nucleotide source for RNA, which degrades in a matter of
555 days and needs to be replicated before it degrades. Between rains it is plausible that any incipient
556 progress towards overcoming Virchow's discontinuity would be undone, resetting progress back to
557 the beginning. Sutherland just introduced a step which plausibly could preclude his approach from
558 meeting its target objective.

559 One of the authors, TS, has four decades of industrial design engineering experience. Standard
560 engineering procedure for a big design project is to break the overall task into a series of subtasks.
561 The subtasks would be assigned to specific engineers or engineering teams as appropriate. The goal
562 was for a subtask to represent a design effort which could meet a specified schedule by those
563 assigned to it. The subtasks would then need to be integrated into a final, total solution. Generally, in
564 a large design effort far more time is spent in debug of unanticipated problems than in the initial
565 design. Even gifted, well-trained, well-experienced engineers working on complex projects spend
566 most of the project time debugging unanticipated problems. Good designs of complicated processes
567 do not just happen. There are far, far too many wrong ways to do something and even the most
568 brilliant and well-trained engineers are frequently "blind-sided" by various unexpected "wrong
569 ways."

570 Sutherland's approach provides a good example of a design engineer at work. Whether this was
571 deliberate or unintended is irrelevant. The important thing is that his approach represents an
572 elaborate engineering design. This approach can be readily observed by reading the papers reviewed
573 here [21-27] as well his many others. He characteristically starts off with a general objective as well
574 as an assumed set of variables which include feedstock, environmental conditions, and energy
575 source. He experimentally tests what happens to the feedstock when energy is applied. He modifies
576 the variables to observe what gives the best results towards meeting his goal. When intermediate
577 reactants start to veer away from the target, he then analyzes what happens, proposes possible
578 solutions, and tests them to see what works best. He pieces together a flowchart as he constructs a
579 model of how abiogenesis could work. Whenever the model "goes off in the wrong direction", he
580 "tinkers" with it until he discovers some kind of process constraint which resolves the issue. He adds
581 this to his flowchart and then proceeds to the next deviation away from a path to his target
582 chemicals. As a result of repeating this process a number of times with a gifted, trained team for
583 many years, he can as of now provide precursors for a number of products. But, he still does not
584 yield suitable products for use as substrate in a subsequent stage of abiogenesis, the standard we
585 have set as a successful experiment. Furthermore, he in effect assumes replication. He latches onto
586 what "works" when his intellect tells him it is closer to his target and then attempts to progress to the
587 target from the known, successful setting. In a natural setting, because of emergence, the target is an
588 unknown possibility. Even if a potentially useful process step appears, it would plausibly be only
589 temporary. There would be no way to start from it for future steps.

590 What Sutherland has discovered—and this represents a significant advance in chemistry—was
591 that nature not only provides paths for single-molecule synthesis, but also provides for systems
592 synthesis allowing multiple substrates to form multiple products simultaneously. Nonetheless, his
593 proposed synthesis still needs strict control over all of its variables. This includes substrate
594 composition and timed introduction along with controlled environmental conditions—wetting and
595 drying, temperature, pH, specific concentrations of dissolved metals, etc. Failure to meet the
596 conditions required for effective systems chemistry at any process step quickly leads to provision of
597 the wrong products.

598 A general predisposition to biological products would result in many paths leading to them
599 starting from widely scattered initial locations. There would be a general tendency to head towards
600 specific biochemicals regardless of where one started. This does not happen, either with
601 Sunderland's approach or any other approach.

A chemical engineer can specify feedback sensors and control mechanisms to modify substrate flow and environmental conditions to keep a process under control, allowing it to make necessary corrections to produce the desired product. Living cells have similar mechanisms. Prebiotic processes do not have this. There is no means to sense what a lower mixing pond needs and then use this information to control what a higher-level pond produces or to regulate streamflow as it carries intermediate reactants into a lower mixing pond. There is no means for the needs of the mixing pond to be reflected in determining the kind and concentration of minerals to be dissolved into stream waters during the flow. There is no means to adjust the spectrum, intensity, or timing of ultra-violet light falling on a pond. An industrial chemical plant has control over all relevant factors. It fails to produce target product when any aspect of process control breaks down. An abiogenetic process does not have control over any of the factors affecting its success. Yet, the flowcharts being developed by Sutherland and cohorts are plausibly much more complicated than the process flowcharts used for many industrial chemical processes. Sutherland is designing what is needed in order to use natural process capabilities to produce lipids, amino acids, and nucleotides, but nature ostensibly does not provide the process control means to implement the design effectively.

We suggest that the single biggest obstacle to the success of Sutherland's approach is its dependence on precise environmental conditions, with rainfall variation presenting one of the more serious difficulties. Extreme variations in rainfall will plausibly occur at any given site throughout the Earth when observed over an extended period of time, particularly when one contrasts typical variations in instantaneous streamflow values between drought conditions and flood conditions. Furthermore, a frozen stream in winter acts like a drought, stopping flow. The problem is that even if a site could be found which could naturally implement Sutherland's flowchart without any outside intervention some of the time, this should plausibly be only a temporary phenomenon. Normal fluctuations of rainfall and other environmental variables could periodically lead away from suitable environmental conditions with resultant cessation of nucleotide production. Although this may be only temporary from a long-term perspective, it only needs to be long enough for degradation of all incipient progress to make the approach unviable. The only protection against this is for progression of an incipient cell into a living, autonomous cell, one capable of independent, standalone existence, such as we observe in bacteria today. The progression to autonomy needs to be completed before drought or flood conditions reset progress.

Sutherland hints at our hypothesis

In the closing comments of his 2018 paper cited above, Sutherland discusses the plausibility of his postulated processes, stating:

However, it is not the authors wish or intent to persuade the reader that all roads must have led to Rome. In fact, we caution the opposite. While there are many small, and large, variances of sequence that could have still permitted a route to life, there are far, far more that would not... It follows that the sequence of events that led to life must have been highly contingent and the origin of life as we know it could have been a low probability event [27].

It has taken years of effort for Sutherland *et al* to reach their current stage of development. When they say that even though there are many variances in the path along the route to life, that there are far, far more that do not lead there, they speak from long experience and hard work in studying and experimentally testing this issue. No one living today understands more than them the problems they have faced and the effort it took to keep the reactions from heading off into randomness. Significantly, their observations have led them to conclude what amounts to the essence of our hypothesis.

We suggest that the evidence supports the understanding that systems chemistry falls within the scope of behaviors impacted by our hypothesis. Many abiogenists today view systems chemistry as their hope of breaking out of the pattern of failures that have plagued the field since its inception.

Just as Sutherland eventually recognized that there are far, far more wrong ways than correct paths that lead to life, problems he still faced even with systems chemistry, we predict that others who are hoping for systems chemistry to give them breakthrough success will ultimately face a similar scenario as Sutherland. There are far, far more wrong paths than correct ones. Randomization rules.

6.2 The appearance of protein and nucleic acid polymers

The goal of the next step is to convert the amino acids and/or nucleotides supplied by an initial process, as represented by Miller's experiment, the Murchison meteorite, or Sutherland's systems chemistry into polymers of sufficient length and purity for use in replication or metabolism. Plausibly the most serious issue here is that random assembly of building block molecules, such as amino acids and nucleotides, produce aggregate instead of forming biopolymers of amino acids or nucleic acids [4]. Aggregated compounds are called by many names in the literature, including inert organic matter, tar, asphalt, tholin, chaotic polymers, intractably complex mixtures of organic compounds, and gunk. *Tar* is the term of choice used here.

According to our hypotheses, the uncontrolled energy of prebiotic processes results in uncontrolled self-assembly of molecules. We saw in the first step that small, initial compounds can increase into larger, more complex ones. But, there is no reason for the process to stop there. Larger molecules can also join together randomly. Apparently, this is what happens. For instance, living cells need polymers of amino acids linked into proteins using peptide bonds, a specific kind of bond formed when the amino moiety of one molecule links to the acid moiety of a second and a water molecule is formed at the junction and then removed. Life requires this specific bond to form. However, there is nothing in prebiotic processes to constrain this reaction instead of alternatives.

R. Shapiro observed that considerations of entropy [i.e., randomization] would lead one to expect that prebiotic mixtures should "combine haphazardly, producing chaotic polymers [28]." In other words, the effect of randomization on prebiotic mixtures should result in the production of tar.

A.W. Schwartz commented, "Attempts to model the spontaneous chemistry which presumably preceded the origin of life on Earth commonly result in the production of intractably complex mixtures of organic compounds. It is, therefore, difficult to understand how any kind of evolutionary process might have begun [29]." Thus, prebiotic processes preferentially form inert organic matter. After discussing the issue at length, he offers several hypothetical solutions. He then concludes with the following statement:

Without such selectivity [some kind of protective structure capable of selectivity] and its consequences, or some equivalent mechanism of selection, nothing but intractable mixtures (*i.e.*, gunk) would have been deposited on the shores and in the sediments of ancient seas and streams. Identifying such organizing phenomena may be the path to the future, leading to a resolution of the mixture problem sketched above. On the other hand, the solution to the problem is very likely something we have not thought of yet [29].

Steve Benner commented about the problem, "An enormous amount of empirical data have established, as a rule, that organic systems, given energy and left to themselves, devolve to give uselessly complex mixtures, 'asphalts' [3]."

In summary the *asphalt* problem, also known as the tar problem, is the typical, expected outcome of prebiotic processes. Randomly joined assemblies of random molecules of either covalent or hydrogen bonds should plausibly form random, chaotic mixtures not linear polymers. This has been repeatedly, consistently observed experimentally.

6.1.2.1. Miller and peptide polymers.

Did Miller form any peptide polymers? E. T. Parker *et al* first addressed the general case with the statement, "... the transition from simple molecules, such as amino acids, to more complex ones, such as peptides, has proven challenging under plausible primordial conditions [30]." However, they had recently found an archived solution of an experiment Miller performed in 1958 in which cyanamide was intermittently added to the solution. The amino acids formed were approximately equivalent to his original 1953 experiment. However, ten different dipeptides were detected and two tripeptides were tentatively detected. Parker *et al* continued, "The ratio of amino acids to dipeptides in the cyanamide samples was calculated to be approximately 1000:1 – 100:10, which agrees well with experimental data that indicates that the amino acid to dipeptide ratio is approximately 1000:1 under equilibrium conditions." In another experiment R. B. Martin observed that in general there is a seeding effect, such that the equilibrium ratio between the concentrations of the first two amino acids in a chain and the chain is about 400:1, but adding subsequent amino acids to an existing chain reduces the concentration by a factor of about 50:1 for each additional amino acid [31]. These ratios are in approximate agreement with Miller's samples as measured by Parker.

This observation is significant. Monomers in aqueous solution do not spontaneously form peptide chains of several hundred amino acids such as characterize typical proteins. This explains why plausibly prebiotic polymerization experiments, even using pure substrate constituents and controlled environmental conditions, have only limited success. Concentrations drop off exponentially as the incipient polymer lengthens. For instance, an experiment by Imai *et al* reported a maximum detectable chain length of 6 amino acids [32]. An experiment by Huber and Wächtershäuser reported a maximum detectable chain length of 4 amino acids [33]. When a short chain is so dilute as to be barely detectable and when it has a relatively short lifetime, it is useless as a component of a prebiotic soup leading to a formation of life [5]. It is perhaps also significant that the above experiments started with pure solutions of reactant monomers, not the contaminated, chaotic mixtures characteristic of natural, initial-step processes such as Miller's experiment. Contamination was not an issue with their feedstock. Yet, long peptide chains still did not appear. They do not report on whether tar formation was an issue or not.

In summary Miller's experiment readily and preferentially forms tar, but not peptide polymers. There is a disconnect between the products of natural processes and those required for the appearance of life.

Sohan Jheeta reported results of polymerizing RNA nucleotides on an ion-primed Montmorillonite clay surface. However, the concentration decayed exponentially with each additional nucleotide and was only a trace at 10 nucleotides [34]. This does not appear to be a plausible approach for provision of the approximately two hundred nucleotides estimated to be needed for a self-replicating molecule.

6.1.2.2. The Murchison meteorite and tar

Two classes of organic matter have been observed in the Murchison meteorite, soluble and insoluble. The soluble matter constitutes about 30% of the total and the insoluble the remainder. The insoluble is mostly kerogen-like but difficult to analyze [4]. It is found in a chaotic mixture of compounds with chaotic bonding between them. However, one kind of bond is almost completely missing: peptide bonds between the extant amino acids. Yet, these are the ones needed for chemical evolution. Shimoyama and Ogasawara report that in their spectral analysis of the organic matter of the Murchison meteor, they detected peptide dimers of glycine - glycine, but at a concentration four orders of magnitude less than that of the glycine monomers. Thirty-one other, specific dimeric combinations of amino acids were analyzed; all were below detection limits. No mention was made of tripeptides or greater [35]. From a practical standpoint this represents effectively no peptide polymerization. Apparently, the unguided prebiotic processes at work in the Murchison meteorite

preferentially provided chaotic mixtures of product (tar and kerogen) instead of chains of amino acids joined by peptide bonds. Life requires the opposite.

The Murchison meteorite provides an example of natural processes at work without human interference. There was plenty of energy available to randomize molecular components towards nearly complete randomization. Inert organic matter was formed in abundance. Yet, peptide bonds, which are the kind needed for life, were virtually non-existent. There is a disconnect between products produced naturally and products needed for life. As a result of the disconnect, randomization controls the output.

Earlier we looked at Shapiro's comment that because of entropy, "The components of a mixture should combine haphazardly, producing chaotic polymers." The original paper continued,

The formation of an information-bearing homopolymer through undirected chemical synthesis appears very improbable. The difficulties involved in such a synthesis are illustrated by considering the prospects for the assembly of a polypeptide of L-amino acids, based on the contents of the Murchison meteorite as an example of a mixture of abiotic origin. In that mixture, potential replicator components would be accompanied by a host of interfering substances, which include chain terminators (simple carboxylic acids and amines), branch-formers, D-amino acids, and many classes of substances for which incorporation would disrupt the necessary structural regularity of the replicator. Laboratory experiments dealing with the nonenzymatic synthesis of biopolymers have not addressed the specificity problem [28].

If one speculates that the Murchison meteor plausibly started off with simple natural materials, such as methane, ammonia, cyanide, cyanamide, or similar simple molecules of carbon and nitrogen, then the above statement is revealing. It describes a mixture which has become chaotic through extensive randomization of initial products. Randomization was the primary action of uncontrolled energy sources acting on a substrate through prebiotic processes.

6.3 Appearance of Specific Polymers.

According to our hypothesis, there should be many more wrong ways than correct ones to sequence a protein or nucleotide suitable for use in a living cell. Yet, extant cells do have proteins and nucleic acids with usable sequences. How does the hypothesis apply to this step?

6.3.1 Protein Analysis: Provision of enzymes for use in cellular metabolism

Proteins are long strings of amino acids joined by peptide bonds. How hard is it to get a sequence that can provide a specifically needed function? The average protein length in extant archaea, which constitute the simplest ones observable, is approximately 270 amino acid residues [36]. There are 20 alternative amino acids coded for in DNA for use in protein fabrication. The number of possible combinations of a 270-amino acid sequence is 20^{270} , which converts to approximately 10^{351} . This certainly counts as a large number of possible arrangements of a polymerization process.

There is some redundancy in protein sequencing. It is known that a number of specific substitutions can be made to a protein without destroying its functionality. This is not always the case; hemophilia and sickle cell anemia are two well-known diseases, both of which result from a single improper amino acid substitution in the hemoglobin molecule.

Anthony Keefe (a Harvard professor) and Jack Szostak (a Harvard professor and Nobel Laureate) established experimentally and confirmed with computer database analysis that only about 1 in 10^{11} randomly-sequenced proteins are functional [37]. That ratio is in itself sufficient to thwart life. In an assortment of randomly sequenced proteins, functional ones represent a concentration of only 10 parts per trillion. This concentration is certainly too low to form any kind of metabolic pathway useful for life.

The next question concerns how many different kinds of proteins are possible among the functional proteins. The Protein Data Base lists about 150,000 unique proteins [38] in late 2018, with the number increasing daily. Assume for discussion purposes that these 150,000 proteins represent the total number of possible uniquely functioning proteins, although the actual number is expected to be far, far greater than this. In this case, the odds for random processes to provide a specifically needed protein are 1 in 10^{11} times 1 in 150,000. This calculates to 1 in 1.5×10^{16} , which is about 70 parts per pentillion. In a solution of randomly formed proteins, this concentration would be too dilute to be useful.

The issue of redundancy can be looked at from a different perspective. It is known that there is a certain number of substitutions permitted in sequence and still have a functional protein. This number is not actually known, but we can make some estimates which provide a useful perspective. For purposes of discussion, we will assume on the average, each amino acid site in a protein can be satisfied by a choice between two amino acids. It appears that three alternatives would be too high, in that if there were three alternatives for every position, it would be plausibly very difficult to align sequence maps between homologous proteins. However, it is not generally that difficult. So, only one choice means no redundancy, which we know is not true. Three choices plausibly give too much. So, two is a reasonable estimate and adequate for our purposes.

P	=	odds against getting a usable protein sequence.	[1]
C	=	average number of amino acid alternatives per position	[2]
N	=	number of proteins	[3]
20	=	number of amino acid species	[4]
P	=	$(20/C)^N$	[5]
P	=	10^{270} for an average archaea protein.	[6]

This calculation is extremely easy to work with for a protein of any length. The odds against getting a suitable protein with an average of two choices per position is simply 10 raised to the power which equals the number of amino acids comprising the protein. Thus, the odds against getting a useful protein sequence for a 500-residue protein is 1 in 10^{500} .

This probability number is useful in discussing complexity issues. If an assumption is made that a certain number of random sequences could plausibly be formed in one year, then adding 100 zeroes to that length multiplies the time average time per appearance, one year, by 10^{100} , a googol. Adding a second 100 amino acids to the protein multiplies the average time between appearances by another googol. Suppose a scenario existed such that 10^{70} random sequences of amino acids could be supplied in a year. Then, incrementing the number of amino acids in a chain to 71 would take ten times as long—10 years average time to supply a single instance of the protein. The time to supply a single instance of an average size archaea protein through random processes would then be 10^{200} years—a google times a google of years. The 15-billion years total projected age of the universe is rather small in comparison. It doesn't register until the 190th decimal place. For all practical purposes, this will never happen.

One might suggest that prebiotic proteins do not need to be as large as modern ones. Therefore, smaller ones might be viable for early stages of abiogenesis. However, if dynamic self-organization is required of cellular components from the beginning, then smaller proteins might not be adequate even from the beginning. Plausible reasons for this will also be discussed later. In this case we are stuck with the staggering odds just examined.

Obviously, with these kinds of odds independent, random assembly for each instance of a protein is not a viable source of supply useful to abiogenesis. Multiple googols of years between appearances of a single molecule represent too dilute a solution to be of value. Continuity of action or function would be impossible. Hence, translation and the information controlling it need to be available and active at the time Virchow's discontinuity is challenged. Actually, the problem does

not truly go away with translation. It would plausibly be more difficult to get the proper information to appear in a genome for use by translation to make a given protein than for random processes to make a single instance of it, because the task is more involved. So, although translation helps in the production of multiple copies, it poses more of a problem for the first copy—and the problem is severe. This will be elaborated on later in our discussion.

6.3.2. The appearance of self-replicators and their usefulness towards RNA-world cells.

By definition there can be no chemical evolution without replication. The above discussion of protein sequencing underscores this. The random appearance of a protein specifically needed to help bridge Virchow's discontinuity is too rare to be useful.

There are two possibilities of simple replication. The first is a single-molecule ribozyme capable of copying a random template as large as itself. It needs to have an average life-time long enough to do this many times before it degrades. Plausibly a ribozyme needs to be larger than 200 nucleotides to do this. The second is a molecular network composed of a number of smaller nucleotides which can self-assemble to form a replicator. Both of these have serious problems. Neither has been able to be demonstrated experimentally.

6.3.2.1 Single-molecule replicators. In 2011 Woehner *et al* fabricated a ribozyme RNA polymerase, an incipient self-replicating ribozyme, *tC19z*. It comprised a little under 200 nucleotides and was capable of replicating a 95-nucleotide ribozyme in vitro, about half of its length. It had greatly improved transcription fidelity over its precursors, although it was still inadequate for self-replication [39]. The following year Jack Szostak listed eight problems facing efforts to produce a molecule capable of replicating itself. Among these problems were 1) separating a template from its complement once the template exceeded about 60 nucleotides in length, 2) the copying fidelity was too low for sustained operation, and 3) template and ribozyme degradation occurred in about the same time it took the ribozyme to copy the template, typically “over a course of days.” These and the other problems would need to be resolved before an active self-replicating system could be demonstrated [8]. Gerald Joyce *et al* reported an improved version of the *tC19z* ribozyme they called *24-3* [40]. Despite the improvements, it still did not resolve any of the problems listed by Szostak. Nonetheless, based on continually improving reported results, it is plausibly only a matter of time until a ribozyme sequence capable of serving as a fully-functioning self-replicating ribozyme under controlled conditions for a brief period of time will be discovered. However, it is also plausible that eventually accumulated degradation products would act as parasites, dominating the template function and potentially leading to complete degradation of active replicators.

The self-replication experiments described above required the use of expensive equipment with extremely complicated processing directed by human guidance. After extensive randomization, purification, and testing they were still unable to discover an effective self-replicator. This conclusively demonstrates that there are many more wrong ways to sequence a replicator than correct ones. It also confirms that there is no connection between what is required for abiogenesis and what natural processes produce. Random sequences are the normal result. At this point we only understand reasons that prevent any lengthy RNA polymers from forming, not how to demonstrate plausible formation. Our hypothesis appears to explain why.

6.3.2.2 Replicating networks of small, cooperating RNA molecules. Robert Shapiro observed, “Several scientists have put forth theories that do not require an ordered polymeric replicator at the start of life. They propose, instead, that life began with a mutually sustaining set of catalytic reactions involving smaller molecules....Insufficient experimental attention has been given to such ideas, but if the hypothesis presented here is accepted, perhaps they will move to the forefront of origin-of-life research [28].”

Shapiro wrote this in 2000. In the eighteen years since then, there have been a number of studies on small, cooperative replicators. It appears this is another side trail which will need a major breakthrough for it to have true value. For example, J. Atwater and P. Holliger commented that these studies still require supply of preassembled polymers--they do not assemble monomers into the individual replicators [41].

A primary purpose of small, cooperative replicators is to provide the first step of replication. However, these experiments require feedstock of specific, preformed polymers. This skips the step that is most critically needed, assembly of free nucleotides into specific polymers. N. Vaidya *et al* reported on an experiment "among cooperative RNA replicators." They described a self-assembly process of a group of four interacting nucleotide strings. Significantly, these strings were not trivial in size, such as formed by a few monomers spontaneously assembling, but instead ranged from 43 to 65 nucleotides each. When mixed together in the experiment, they cooperatively assembled into a larger ribozyme.

Assume there is a natural setting with a suitable supply of nucleotides and an environment conducive to polymerization. A large number of polymers are formed having random lengths and sequences. The odds of forming a specific polymer of 43 nucleotides, the size of the smallest in the group, are one in 4^{43} , which equates to 1 in 8×10^{25} . Therefore, the odds against finding a polymer of 43 nt with the given sequence among the 43-nt products are a little over two orders of magnitude larger than Avogadro's number. The other three polymers were even larger and would face even greater odds against their appearance. Even with a certain amount of redundancy allowed due to permitted substitutions, this still represents extremely low relative concentration. Furthermore, provision of a solution of a large concentration of molecules comprising only lengths of the four polymers is implausible in a natural distribution of polymer lengths. A natural distribution should comprise a mixture of a wide range of lengths. The statistical law of large numbers should insure this takes place. Incidental beneficial fluctuations are quickly overridden. When one considers a natural distribution of polymer length as well as nucleotide sequence among the components plausibly present in a system, the expected ratio of wrong components to those needed is staggering. Also, RNA typically degrades in a matter of days and there is no known mechanism to remove the products of degradation from the setting. Eventually, accumulated degradation products should present yet another layer of contamination. Experiments on small replicating networks do not test for operation in a setting with this much contamination, although this would be more realistic than the current approach of restricting feedstock to pure solutions of purchased chemicals having a precise specification.

Our hypothesis appears well confirmed when applied to the observed results of replication experiments. Natural processes tend to make many more wrong products than usable ones and the ratio is plausibly large enough to prove fatal to abiogenesis.

7.1 The big barrier: overcoming the discontinuity hindering the initiation of Virchow's aphorism

As was discussed earlier, Virchow's aphorism still governs cell theory today. Cells only come from existing cells. From our perspective the study of abiogenesis has met its purpose when it can give a plausible explanation based on experimental evidence of how Virchow's aphorism can be initiated. A system of self-replicators, whether they are large individual molecules or a network of smaller ones are not living cells and fall short of this. The issue concerns whether Virchow's discontinuity can be crossed in tiny increments governed by natural selection or whether there are natural barriers preventing this and thus requiring it to be bridged in a single step.

In Penzlin's earlier citation, he tied Virchow's aphorism to the principle of emergence. Cells cannot be divided because qualities exist in a system of interacting components that do not exist in

the components individually [10]. This impacts abiogenesis, because even if simple replicators are extant, natural selection cannot favour emergent properties that do not yet exist. Incipient progress towards the appearance of a cell does not alter the probabilities for a needed target to appear. Only when everything is in place does it suddenly appear.

This leads to the question of what the likelihood might be for required components to appear suddenly through random processes. If small polymers can bootstrap themselves into more complex ones, perhaps Virchow's discontinuity would not be a true discontinuity; it would just be a bottleneck requiring passage by slow, gradual step-by-step random process. By contrast if the functions require a number of interacting components and if a large fraction of these components would plausibly be unlikely to appear once in a googol years, then the discontinuity represents a formidable barrier, unlikely to be overcome. We suggest that dynamic self-organization (DSO) is required in fully functioning form from the time of the first cell's initial appearance. Furthermore, the complexity of components required to implement DSO precludes small molecules from use. This provides a basis for plausible validity of the scenario presented earlier requiring an average of over a googol years between appearances of an average-size archaea molecule.

In a modern factory an assembly line features a series of workstations, each having specialized equipment to perform an operation on a product being fabricated. Gradually, as the product moves from station to station, the fabrication becomes more and more complete until it is finished. However, there are no assembly lines and workstations available to put build a cell. The observed solution is for the cell to build itself in DSO.

DSO described. Johnson and Lam summarize the essence of DSO. They include discussion on how 1) Self-organization requires specific cellular conditions to initiate self-organizing processes. 2) Molecular crowding of interacting components is characteristically required. 3) The components must be able to interact with each other in a manner capable of proving a specific self-organizing function. 4) Self-organizing processes are sensitive to the environmental conditions; therefore, the ability to control these conditions is essential. 5) An isolated group of interacting components does not have the capability of controlling environmental conditions, whereas extant cells do. 6) Self-organizing activity typically occurs in its entirety or not at all [42].

Johnson and Lam acknowledged that the gradual, small, incremental steps of evolutionary processes are incompatible with the requirements to form a usable metastable system. Their analysis continued with the observation that "...self-organizing mechanisms do not seem to be the products of slow, incremental change" and "...the evolution of the self-organizing process is dependent on an initial qualitative jump in phenotype." This description fits emergence as the root of the observations. Also, there are many, many more wrong ways than right ways to program DSO. This is consistent with predictions from our hypothesis.

In dynamic self-organization, energy is required to assemble components. They are metastable—stable for a brief time and then dissipate. However, a structure can be maintained over a long period of time as long as new, energized components can replace those that are decaying. Penzlin discussed that a fundamental purpose of cellular metabolism is to maintain the existence of various dynamic structures in a cell. Self-organizing structures in a living cell require minimum energy expenditure just to maintain existence.

A. Makarieva *et al* report that, "Despite the enormous biochemical, physiological, and ecological differences between the surveyed species that vary over 10^{20} -fold in body mass, mean metabolic rates of major taxonomic groups displayed at physiological rest converge on a narrow range from 0.3 to 9 W kg⁻¹. This 30-fold variation among life's disparate forms represents a remarkably small range..." "Endogenous metabolic rate [is] the rate of nongrowing, unicellular organisms in nutrient-free suspension [43]." Thus, without this minimally required energy expenditure, essential metastable structures dissipate and the cell dies. Endogenous metabolism of

prokaryotes and basal metabolism of eukaryotes represents the energy required to maintain minimally required metastable structures.

The same 30-fold, absolute range of minimal metabolic rates applies to major taxonomic groups, from bacteria to elephants and in between. This is consistent with the understanding of a common level of dynamic self-organization that has existed in all cells from their beginning. It is not enough that the initiation of Virchow's aphorism would need to feature all required cellular components from a static perspective, they also plausibly need to make their initial appearances in fully-developed far-from-equilibrium conditions along with all of the required controls over the cellular environment and feedback. The initial genome needs the complexity to define component structure and cellular conditions to provide dynamic self-organization. There appears to be no plausible way to avoid this conclusion.

A. Kurakin makes a thorough analysis of the dynamic qualities of cellular self-organization. Some highlights of his observations:

"...Any given protein usually partitions into macromolecular organizations only when it is functionally competent. Inactive proteins tend to remain in a freely diffusing, 'unemployed' pool and/or to have significantly shorter residence times within the molecular organizations employing them....", "...A protein may be recruited to a given macromolecular organization only temporarily, when its particular activity/competence is needed, and it is discharged into the freely mobile pool when its services are no longer required...." "...it appears that many, perhaps all, macromolecular complexes and sub-cellular structures are assembled and maintained as steady-state molecular organizations only when they perform their functions. They are dissolved or restructured when their functions are no longer needed or altered within the cell." "...metabolic compartments are often assembled on demand to satisfy changing or local needs of cellular economy that emerge in response to transitory environmental challenges and opportunities." "It can even be generalized that any environmental change normally triggers the formation and stabilization of metabolic compartments or complexes that self-organize either to alleviate the problems or to take advantage of the opportunities created by environmental change within the economy of the cell [44]."

This description summarizes DSO. Modern cells clearly use it. However, it adds to an extreme degree the complexity of the proteins (or ribozymes) used. Modern cells primarily use protein. It is plausible that the complexity required for DSO goes beyond what a ribozyme can provide. The discussion below refers to protein with the recognition that in instances where a ribozyme can provide required functionality, its inclusion in the discussion is to be understood. Discussion of external or internal (DSO) fabrication

1) DSO characteristically joins molecules in a transitory capacity in a condition far from equilibrium. Static bonds interfere with the disassembly process, so temporary bonds such as hydrogen bonds or Van Der Waals interactions are used. With proteins, this requires a precise shape for alignment between the two molecules as well as a complimentary choice of amino acids which will form the correct bonds at the alignment site. We suggest this is part of the factors determining minimal protein size.

2) It is plausible that in order to avoid spurious bonding, each element in the set of all possible alignment sequences between the kinds of components in a system need to be filled by a single pair of components. This would permit only intended bonding to take place. In a large cell with many different kinds of proteins, the number of potential bonding surfaces will increase, increasing the size of the alignment set. This plausibly adds significant complexity to each of the proteins contained together; avoidance of spurious bonding requires each component to "know" not only how to make its appropriate bond, but also how to avoid spurious bonds. This capability needs to be present from the beginning. We suggest this is part of the factors determining minimal protein size.

3) DSO can be extremely sensitive to environmental cues. This sensitivity is built into the structure and choice of amino acids to fabricate a given protein. Environmental cues can be physical, such as pH or intensity of light. We suggest this is part of the factors determining minimal protein size.

We suggest the requirement for a cell to use DSO requires as a minimum all of the above elements to be in place and functioning from the time Virchow's aphorism is active, yet cannot be provided before the discontinuity has been bridged.

Prokaryotes (bacteria and archaea) typically gain selection advantage through speed of replication. Replication accuracy, translation accuracy, and redundancy are not as much of an advantage as are speed of replication and efficient use of nutrients. This would suggest that proteins in bacteria have high selection pressure to be as small as possible while meeting all functional requirements. Proteins are smaller in prokaryotes [36], an observation consistent with this hypothesis. This in turn suggests that protein size in prokaryotes is very close to the minimum required for a protein to provide DSO capability.

In line with the above train of thought, it appears implausible that proteins significantly smaller than extant proteins would be adequate for cellular self-fabrication using DSO. The choice appears to be external cellular fabrication using external machinery such as an assembly line in a factory or internal cellular fabrication using DSO. Despite the increased complexity posed by including DSO in the list of features that need to be present in order to bridge Virchow's Discontinuity, this appears to be a better solution than external workstations. It is difficult even to imagine how external workstations could be implemented.

Our hypothesis starts with the statement that there are many more wrong ways than correct ways to make a chemical suitable for life. The discussion on DSO underscores this.

DSO and our hypothesis

It was once assumed that self-organization would solve the problems of the complexity of a cell, with life spontaneously emerging in an extremely out of equilibrium environment. All that was needed was a source of raw material and an external energy source [28]. Self-organization would then produce preferentially the chemicals of life as needed spatially and temporarily. Since then we have come to recognize that self-organization has the exact opposite effect. Cellular self-organization requires path, sequence and end result built into the structure of a large number of interacting proteins and the stored information to provide them. It also requires simultaneous control over a number of critical cellular environmental conditions which control organization and disorganization. Self-organization in the cell is not some vague, mysterious mechanism which allows one to gloss over problems. It is a precisely defined process which needs to have all manner of interacting, predefined features come together in a single-step appearance. It increases the requirements of genome specificity by an incomprehensible degree. It is an application of abiogenetic disconnects, randomization, and emergence working together. There are many more wrong ways to attempt self-organization than proper ones. There is nothing to restrain the proper ones to appear as needed spatially and temporally in greater abundance than what is normally provided by a random distribution of possibilities. As a result, wrong ones would be consistently produced in overwhelming relative quantities by random processes.

The scope of difficulties is underscored when one remembers that the goal of abiogenesis is to provide an autonomous cell featuring minimal replication capability. Until replication appears, there is no means to reproduce a subsystem that might appear simultaneously in usable form. Ultimately, degradation and dilution will tend to render ineffective the spontaneous appearance of subsystems until a complete system capable of sustained replication has appeared temporally and spatially under favourable environmental conditions.

Single step, simultaneous first appearance of everything

In a living cell, DNA information is used to define structures and control their operation. This is perhaps the epitome of emergence. Cellular structures cannot be supplied in required frequency or spatiality by random processes, but must be manufactured according to a set of instructions. The information has independent existence from the structures.

The information, the code, and hardware to process the information and to use it to accomplish a specific task all need to appear simultaneously. None have value without the others in place. This requires single step first appearance of all of them. Required tasks for simultaneous first appearance include replication, information storage and processing, metabolism, organic compartments with active transport, and various additional miscellaneous functions, including DSO. All of these are so intimately connected together that none can function without the others in place. Together, they form the basics of a minimal cell. They provide a clear example of emergence. A living, autonomous cell can suddenly survive and replicate when everything is in place. Otherwise, whatever degree of life it might have had quickly dies and the organization degrades. Either the entire system including information and hardware to use and replicate it exists or none can appear in a controlled manner. Emergence precludes the ability to break the task into many small, simple steps of lesser difficulty and then synthesize them into a new whole, such as is done in chemical engineering. There is no means to perform the various individual tasks without the others in place. Nature does not provide prebiotic processes with the required tools to implement engineering designs as discussed earlier.

Information

Werner Gitt was a director and professor at the Federal Institute of Physics and Chemistry and the Head of the Department of Information Technology in Braunschweig, Germany. We have synthesized a number of his statements and observations about information scattered in his book *In the beginning was information* to give a working description of information suitable for abiogenesis: Information is an immaterial entity—it has no physical characteristics such as weight, mass, or energy, phenomena which characterize physical objects. It is an abstract representation of meaning, such that a code maps between the two. It is abstract in the sense that it is not the meaning, only a representation of the meaning. The code is completely arbitrary; there are an almost limited number of equivalent codes capable of being formed. Because of this there are no laws or principles of nature which can be used to define a code. There are various forms of information; the kind used in biological systems uses a set of symbols arranged in a particular pattern defined by the code. Although the information and the code mapping to it are immaterial, the information is stored in a physical medium. The choice of medium is arbitrary and information can readily be transferred or copied from one to another without any loss. For instance, genetic information can be stored in a sequence of nucleotides, computer bits, symbols printed on a page, or magnetic fluctuations on a disk without any loss. Information has no value unless there is means to read it and use it. Therefore, an arrangement of nucleotides can represent an amino acid sequence in a protein, but this is valueless unless there is a physical medium capable of reading the symbols, extracting the meaning from them through a decoding process, and then doing something with it. Since information is an abstract entity, as is also the code mapping it to a medium, there are no physical laws capable of creating it [45]. Gitt also discusses his personal perspective on the origin of information, but that is outside the scope of this paper.

Information represents a powerful tool for cellular control, as we can readily observe with the tools that technology has made available to us today. However, since its abstract nature is outside the bounds of physical processes, there has never been an adequate explanation of where it came from. Thirty years ago, K. Dose alluded to this problem with the comment, "...We do not actually know where the genetic information of all living cells originates [46]...." As of today, we still don't. We

are aware of and can explain many specific obstacles against its appearance. We cannot explain its appearance.

Our perspective is that Virchow's discontinuity cannot be bridged piece meal, but must do so in a single step. On the abiogenesis side of the discontinuity, scientists are struggling with the construction sequence of a self-replicating molecule of approximately 200 nt length. The biggest problem is that it degrades faster than it copies at this size. On the cellular-life side of the discontinuity is a fully functioning minimal cell. Hutchinson *et al* have experimentally observed basis to project that a minimal cell requires a genome of approximately 541,000 nt. Regardless of whether the actual minimum is 100,000 nt or 500,000 nt, this is all beyond a nucleic acid technology struggling with falling apart at 200 nt. Current understanding of information can give many explanations of the difficulties of creating it. It cannot explain where it comes from.

As a simple measure of the difficulty of creating information, consider the example of the average archaea protein of 270 nucleotides. Even under realistically favorable assumptions, it should take a googol of googol years to generate a single instance of this molecule. It would take three times this many, i.e., 780 nucleotides, to code for it. Prebiotic appearance of nucleotides and long polymers is more difficult than appearance of amino acids and proteins. Hence, it should take longer than a googol of googol years to for the appearance of a 780 nt gene able to code for a specifically required protein. Yet, a 200 nt ribonucleic acid degrades in a matter of days. It is implausible that a googol of googol years would be enough time. On a practical basis this discussion is nonsense. These numbers are so extreme that the human mind cannot comprehend their significance. Extending the time for the appearance of a genome of over 100,000 nt is meaningless. The information polymer degrades long before it can be built. Beyond this is the issue that abiogenesis is actually stuck at the starting blocks, unable even to provide a set of amino acids suitable for protein formation.

Because of emergence a chicken and egg scenario in cellular function can be discovered at will. The essential components of a minimal cell cooperate with each other, such that when all work together life appears and missing any one of them prevents its appearance. If one tries to explain the appearance of any component through the gradual step by step process of natural selection, he will quickly find himself facing a chicken and egg scenario, a catch-22 situation, a paradox, a conundrum. Ignoring the fact that natural selection doesn't work for large genome systems before replication appears, there is another basic issue. How could natural selection define a proper genetic structure to produce a protein so that the protein could provide a step in the production of an essential product before all of the other proteins for the others steps have appeared? There is a long list of products essential to the appearance of the first cell. Pick any one of them and try to explain how this product could appear apart from single-step, sudden first appearance. You will find that emergence leads you straight to the chicken and egg scenario. This is the impact of emergence on abiogenesis.

The Appearance of Translation

The translation system of a cell consists of the cellular components used to extract information from DNA, feed it to a ribosome, and assemble amino acids into proteins. Wolf and Koonin (2007) made a concerted effort to figure out how this might have happened through the gradual, step-by-step evolutionary processes of the continuity principle. In the light of their following comments on irreducible complexity, it is worth pointing out that Koonin is one of the most respected of modern scientists. With an h-factor of 182 (182 papers written in established journals with at least 182 citations each) he is the 56th most cited scientist in history (Sigmund Freud is first) [47]. He and Wolf came to the following conclusion concerning the difficulty of the origin of translation:

The origin of the translation system is, arguably, the central and the hardest problem in all evolutionary biology. The problem has a clear catch-22 aspect: high translation fidelity hardly can be

achieved without a complex, highly evolved set of RNAs and proteins but elaborate protein machinery could not evolve without an accurate translation system.... The fundamental problem we wish to address here: the origin of the translation system and the genetic code. Indeed, the translation system might appear to be the epitome of irreducible complexity because, although some elaborations of this machinery could be readily explainable by incremental evolution, the emergence of the basic principle of translation is not. Indeed, we are unaware of translation being possible without the involvement of ribosomes, the complete sets of tRNA and aminoacyl-tRNA synthetases (aaRS), and (at least for translation to occur at a reasonable rate and frequency) several translation factors. In other words, staggering complexity is inherent even in the minimally functional translation system....Even this does not do the full justice to the difficulty of the problem. The origin of translation appears to be truly unique among all innovations in the history of life in that it involves the invention of a basic and highly non-trivial molecular-biological principle, the encoding of amino acid sequences in the sequences of nucleic acid bases via the triplet code... This principle, although simple and elegant once implemented, is not immediately dictated by any known physics or chemistry (unlike, say, the Watson-Crick complementarity) and seems to be the utmost innovation of biological evolution [48].”

They later bring up the issue of irreducible complexity a second time, “It might not be much of an exaggeration to note that, at least, at first glance, the origin of the translation system evokes the scary specter of irreducible complexity [48].”

The entire discussion above is consistent from the perspective that Wolf and Koonin were trying to explain the appearance of emergent system properties from the individual component focus of chemical evolution. They were amazed by the effectiveness of the behavior they observed, but could not account for it. More than once they alluded to “irreducible complexity.” It appears they were actually speaking of emergent phenomena. Perhaps it might have been appropriate to substitute *emergence* for *irreducible complexity* in describing the above problems. This would allow the issues to be discussed without the emotional connotations of irreducible complexity, which appeared to concern even them. Also, emergence is a recognized, well-established phenomenon throughout all of nature including chemistry related to origin-of-life issues. As Ashkenasy mentioned earlier, “The chemical sciences are entering the new territory of systems chemistry. This young field aims to develop complex molecular systems showing emergent properties: *i.e.*, properties that go beyond the sum of the characteristics of the individual constituents of the system [49]....”

The problems confounding Wolf and Koonin were plausibly more extreme than discussed. They assumed a fully functioning, replicating cell in an RNA-world with extant evolutionary capability. The only difficulties they addressed were those associated with the appearance of protein translation in an already functioning RNA world. However, if RNA genomes degrade upon attempts to provide complexity much beyond that of a 200-nt self-replicating ribozyme, then the RNA world is plausibly not capable of providing replication of the complex genomes which Wolf and Koonin assumed to be available as a starting point. Without an RNA world intermediary and because of emergence, the task becomes to go from a self-replicating molecular system past Virchow’s discontinuity and into a full-blown functioning cell in a single step. Observational science teaches why this must be done. It does not show how natural processes can do it.

If 1) there are no laws of physics or chemistry to define the triplet code, if 2) some of the components used in translation are extremely complex with many plausibly requiring googols of years between naturally occurring random appearances under ideal conditions, if 3) at least several dozen of these components need to make a simultaneous spatial-temporal first appearance in already working form, and if 4) this scenario is predictable from applying the principles of randomization, abiogenetic disconnects, and emergence, then it appears safe to conclude that at this point in time there is no experimental basis to illustrate how chemical evolution has removed Virchow’s

discontinuity and initiated the aphorism. Thus, in the light of what we understand from scientific investigation; the aphorism still stands, unchallenged by chemical evolution [5].

Metabolic Pathways.

A metabolic pathway is a general term used to describe any series of cellular reactions using enzymes to transform one chemical into another [50]. Metabolic Pathways appear to represent emergent processes. An initial substrate is acted upon by a sequence of operations to convert it into a final product, which does not appear until all of the operations required to make it have taken place. There is a discontinuity—until it appears, there is no indication of pending appearance. Even if replication had already appeared, the discontinuity would prevent natural selection from gradually providing the set of enzymes required which, when all are present and fully functional, could transform a substrate into a specifically-needed final product. When the topic is initial appearance of metabolic pathways, it is a non sequitur to ascribe the appearance of a new pathway as a serendipitous modification of an existing one—there are no pre-existing ones to modify. Therefore, in the pre-replication scenario of the appearance of the first cell, all of the pathways required to implement replication will need to make a simultaneous first appearance in functioning form [5].

In illustration a sample metabolic flowchart is published online by IMBUB [51]. Suppose an incipient cell needs to burn glucose for ATP production. The chart shows that glucose goes through ten enzyme-controlled reactions to be transformed into acetyl-CoA, which then can enter another pathway, the Krebs cycle, for the production of NADH. This in turn is fed into the electron transport pathway to supply the energy to convert ADP into ATP, where ATP acts as the energy source for most cellular activity. The enzymes controlling the reactions for all of the steps of all three pathways (or their alternatives) need to be present and available before ATP appears in a controlled manner. The pathways are emergent phenomena. The appearance of each enzyme presents a chicken and egg scenario with the others—none result in the required product until the others are available.

The pathways shown on the IMBUB chart would not be the only ways to make the required products, alternatives are feasible. Regardless of how many optional paths and optional enzyme structures to implement the paths may be available, emergence requires that any given path actually provided needs to be complete and functioning adequately at the time of its first appearance. According to our hypothesis, there will be many more ways to provide pathways which do not provide required product than there are ones that do. Randomization will result in a preponderance of the wrong ones.

All of the enzymes used in a pathway, regardless of which pathway may be provided to accomplish the transformation, need to be provided through a copying process such as replication (RNA world) or translation (protein-DNA world), because the enzymes need to appear in large, controlled quantities. By contrast random appearance is not a suitable means of provision because of the googols of years between each the appearance of each instance. Therefore, provision of a metabolic pathway requires specification in a genome first, along with all of the hardware apparatus required to process the genomic information. Then the required pathways can be provided in a controlled manner as needed. The perplexing question is where the information came from to build a protein that would take multiple googols time googols of years to appear through random assembly [5]. Dose didn't know thirty years ago. We still don't, either.

When Stanley Miller performed his origin-of-life experiments, he had no comprehension of the scope of the task facing him.

7.8 Cell Membranes with Transport, Passive and Active

Compartmentalization is generally accepted among abiogenists as a basic requirement for life. Cellular processes require interacting chemicals to be proximate for interaction. The cell membrane accomplishes this. A semi-permeable enclosure allows small, non-polar molecules to diffuse in and

out, while retaining larger molecules such as polymers. A simple phospholipid membrane may be adequate for a self-replicating ribozyme system. However, a genome-based system operating under DSO needs active transport proteins in order to provide required molecular crowding [52]. Nutrients need a means to pass through the membrane into the cell and waste products and secretions need to pass through it out of the cell [5]. The minimum genome bacterium of Hutchison III *et al* devoted 31 of its 473 genes (~6%) to membrane transport [53]. That shows how essential transport proteins are.

I. T. Paulsen *et al* compared the transport capabilities of eighteen prokaryotes whose complete genomes had been sequenced. The gene sequence of transport proteins tends to be conserved across species. They attempted to identify all transporter genes in each of the species analyzed. They show 76 families of transporters. All of these are not necessarily required for survival, based on the above analysis of Hutchinson, but many would be. Even in prokaryotes approximately 80% of the transporters had genes coding for 400 or more residues [54]. As a whole, these are large proteins. They need to be in order to provide a passageway for sometimes large molecules. The ability to select for specific molecules and to control their rate of passage under specific conditions is a DSO characteristic that needs to be built into the protein structure. The capability of a transporter to penetrate a cell membrane at a proper location and properly embed itself within it is a DSO function. Emergence and DSO working together require a significant minimum number of transporters to be functionally available at the first appearance of a cell. Yet, at 400 residues using overly generous standards, random processes would still average googols of googols of years between each isolated appearance. This is a rather dilute solution. We still do not know how to get the information to do this into a genome.

8. Conclusion

Prebiotic processes inherently provide random products. An already living cell has internal hardware for process control and is therefore able to restrain chemical activity to provide predetermined results. However, the conditions to do this successfully are very specific and allow little deviation. Natural variation in environmental variables, particularly stream flow variation, works against natural processes providing a required steady flow of products. Randomness appears to prevent formation of usable building block amino acids and nucleotides. It prevents formation of usable polymers of protein or nucleic acid. An autonomous, living cell needs all of its components to function properly, it cannot be divided beyond certain basic systems. Virchow's aphorism and emergence work together to require the first cell to appear fully assembled from the beginning.

This is not a paper on metaphysics. No solution is offered to these problems posed by the conclusion presented; they are beyond the scope of the paper. However, it appears that nature itself provides conclusive evidence that natural processes are incapable of assembling a living cell. Wherever one looks there are problems.

Most of these problems are due to randomization of feedstock chemicals by prebiotic processes. Just as there are no betting schemes that allow a person to overcome randomness in a casino, there appear to be no schemes able to overcome randomness using prebiotic processes. We suggest that an unwillingness to acknowledge this has led to the sixty plus years of failure in the field. There is a large body of evidence—essentially all experiments in abiogenesis performed since its inception sixty plus years ago—that appear to be consistent with the hypothesis presented in this paper. Randomization prevails.

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