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18

Information, Entropy, and the Origin of Life

Walter L. Bradley

1. INTRODUCTION

Darwin's theory of evolution and the development of the Second Law of Thermodynamics by Clausius, Maxwell, Boltzmann, and Gibbs are two of the three major scientific discoveries of the nineteenth century. Maxwell's field equations for electricity and magnetism are the third. The laws of thermodynamics have had a unifying effect in the physical sciences similar to that of the theory of evolution in the life sciences. What is intriguing is that the predictions of one seem to contradict the predictions of the other. The Second Law of Thermodynamics suggests a progression from order to disorder, from complexity to simplicity, in the physical universe. Yet biological evolution involves a hierarchical progression to increasingly complex forms of living systems, seemingly in contradiction to the Second Law of Thermodynamics.

In his great book *The Nature of the Physical World*, Arthur Eddington (1928, 74) says, "If your theory is found to be against the second law of thermodynamics, I can give you no hope; there is nothing for it but to collapse in deepest humiliation." But while nonliving systems dutifully obey the Second Law of Thermodynamics, living systems seem to live in defiance of it. In fact, this is one of the simplest ways of distinguishing living from nonliving systems. Molton (1978, 147) defines life as "regions of order that use energy to maintain their organization against the disruptive force of entropy."

But how is this possible? Lila Gatlin (1972, 1) says, "Life may be defined operationally as an information processing system – a structural hierarchy of functioning units – that has acquired through evolution the ability to store and process the information necessary for its own accurate reproduction." In his classic book *What Is Life?* (1944), Erwin Schroedinger insightfully noted that living systems are characterized by highly ordered, aperiodic structures that survive by continually drawing "negentropy" from their environment

and "feeding" on it. Schroedinger used the term "negentropy" to refer to energy that was suitable for utilization by living systems, such as radiant energy and energy-rich compounds. Schroedinger's "highly ordered, aperiodic structures" we recognize today as the informational biopolymers of life – DNA, RNA, and protein. A half-century later, Schroedinger's seminal insights have been confirmed.

If these scientists are right, the characteristic feature of life appears to be its capacity, through the use of information, to survive and exist in a nonequilibrium state, resisting the pull toward equilibrium that is described by the Second Law of Thermodynamics. For them, the origin of life is nothing more or less than the emergence of sufficient biological information to enable a system of biopolymers to (1) store information, (2) replicate with very occasional mistakes, and (3) "feed on negentropy." Unlike biological evolution, where it is fashionable to believe that there is sufficient creative power in mutation combined with natural selection to account for the diversity of life in the biosphere, it is generally recognized that the origin of life is one of the great unsolved mysteries in science (Radetsky1992; Wade 2000).

At the heart of this mystery is the generation of the critical information that is necessary to provide the three life functions just mentioned, in a world in which the Second Law of Thermodynamics seems to naturally move systems in the opposite direction, toward greater randomness. This chapter will begin with a brief introduction to information theory, beginning with the early work of Shannon (1948). This will allow us to quantify the information in biopolymers – especially DNA, RNA, and protein, the molecules that are essential for information storage, replication, and metabolism. Then we will explore the concept of entropy and its ubiquitous increase in nature, usually called the Second Law of Thermodynamics. This will allow us to understand how living systems are able to sustain themselves against the downward pull of the Second Law of Thermodynamics and how thermodynamics affects the origin of information-rich, living systems. Finally, we will explore various scenarios that have been proposed to account for the significant quantity of information that is essential for the emergence of life in a world that so naturally consumes rather than creates information.

2. QUANTIFYING THE INFORMATION IN BIOPOLYMERS

Information theory was developed in 1948 by Claude Shannon of the Bell Laboratories to address issues in communications. However, his approach has found much broader application in many other areas, including the life sciences. Shannon's initial interest was in quantifying the transmission of information, which he considered to be contained in a series of symbols, like letters in an alphabet. For reasons clearly explained in his book, Shannon

chose to quantify the information "i" per register (or position) in his message as

$$i = K \log W \tag{1a}$$

where W is the total number of symbols or letters being used to create the message. If each symbol or letter used in his message is equally probable, then the probability of any given symbol is given by $p_i = 1/W$ or $W = 1/p_i$, and

$$i = K \log (1/p_i) = -K \log p_i \tag{1b}$$

In order to express this information in bits, let $K = 1$ and use log to the base 2, or $\log_2$. Equation 1b becomes

$$i = -\log_2 p_i \tag{2}$$

If the probabilities of each symbol are not equal, then Equation 2 becomes

$$i = -\sum p_i \log_2 p_i \tag{3}$$

Shannon Information in DNA. Information in living systems is stored in the DNA molecule, which has four bases called nucleotides that effectively serve as an alphabet of four letters: A-adenine, T-thymine, C-cytosine, and G-guanine. In *E. coli* bacteria, these bases appear equally often, such that $p_i = 1/4$ for each one. Thus, using Equation 2, we may calculate the information per nucleotide to be

$$i = -\log_2 (1/4) = 2 \text{ bits} \tag{4}$$

Since there are 4×10^6 nucleotides in the DNA of *E. coli* bacteria (Gatlin 1972, 34), the total amount of Shannon information would be

$$I_s = N \bullet i = 4 \times 10^6 \times 2 = 8 \times 10^6 \text{ bits of information} \tag{5}$$

The total Shannon information "I_s" represents the number of binary decisions that must be made in order to get any sequence of base nucleotides in DNA. It is simple (at least in principle) to calculate the number of different messages (or sequences) that one might create in a polynucleotide with 4×10^6 bases such as the polynucleotide in *E. coli*. The total number of unique messages "M" that can be formed from 4×10^6 binary decisions is given by

$$M = 2^{Is} = 2^{8,000,000} = 10^{2,400,000} \tag{6}$$

For comparison, the typing on this page requires only 10^4 bits of information, so the *E. coli* DNA has information equivalent to $8 \times 10^6 / 10^4 = 800$ pages like this one. It must be emphasized that each of the $10^{2,400,000}$ alternative sequences or messages in Equation 6 contains the same amount of structural, or syntactic, information – namely, 8,000,000 bits. Yet only a few of

these sequences or messages carry biologically "meaningful" information – that is, information that can guarantee the functional order of the bacterial cell (Küppers 1990, 48).

If we consider *Micrococcus lysodeikticus*, the probabilities for the various nucleotide bases are no longer equal: $p(C) = p(G) = 0.355$ and $p(T) = p(A) = 0.145$, with the sum of the four probabilities adding to 1.0, as they must. Using Equation 3, we may calculate the information "i" per nucleotide as follows:

$$i = -(0.355 \log_2 0.355 + 0.355 \log_2 0.355 + 0.145 \log_2 0.145 + 0.145 \log_2 0.145) = 1.87 \text{ bits} \quad (7)$$

Comparing the results from Equation 4 for equally probable symbols and from Equation 7 for unequally probable symbols illustrates a general point; namely, that the greatest information is carried when the symbols are equally probable. If the symbols are not equally probably, then the information per symbol is reduced accordingly.

Factors Influencing Shannon Information in Any Symbolic Language. The English language can be used to illustrate this point further. We may consider English to have twenty-seven symbols – twenty-six letters plus a "space" as a symbol. If all of the letters were to occur equally frequently in sentences, then the information per symbol (letter or space) may be calculated, using Equation 2, to be

$$i = -\log_2(1/27) = 4.76 \text{ bits/symbol} \quad (8)$$

If we use the actual probabilities for these symbols' occurring in sentences (e.g., space = 0.2; E = 0.105; A = 0.63; Z = 0.001), using data from Brillouin (1962, 5), in Equation 3, then

$$i = 4.03 \text{ bits/symbol} \quad (9)$$

Since the sequence of letters in English is not random, one can further refine these calculations by including the nearest-neighbor influences (or constraints) on sequencing. One finds that

$$i = 3.32 \text{ bits/symbol} \quad (10)$$

These three calculations illustrate a second interesting point – namely, that any factors that constrain a series of symbols (i.e., symbols not equally probable, nearest-neighbor influence, second-nearest-neighbor influence, etc.) will reduce the Shannon information per bit and the number of unique messages that can be formed in a series of these symbols.

Understanding the Subtleties of Shannon Information. Information can be thought of in at least two ways. First, we can think of syntactic information,

which has to do only with the structural relationship between characters. Shannon information is only syntactic. Two sequences of English letters can have identical Shannon information "N • i," with one being a beautiful poem by Donne and the other being gibberish. Shannon information is a measure of one's freedom of choice when one selects a message, measured as the $\log_2$ (number of choices). Shannon and Weaver (1964, 27) note,

> The concept of information developed in this theory at first seems disappointing and bizarre – disappointing because it has nothing to do with meaning (or function in biological systems) and bizarre because it deals not with a single message but with a statistical ensemble of messages, bizarre also because in these statistical terms, the two words information and uncertainty find themselves as partners.

Gatlin (1972, 25) adds that Shannon information may be thought of as a measure of information capacity in a given sequence of symbols. Brillouin (1956, 1) describes Shannon information as a measure of the effort to specify a particular message or sequence, with greater uncertainty requiring greater effort. MacKay (1983, 475) says that Shannon information quantifies the uncertainty in a sequence of symbols. If one is interested in messages with meaning – in our case, biological function – then the Shannon information does not capture the story of interest very well.

Complex Specified Information. Orgel (1973, 189) introduced the idea of *complex specified information* in the following way. In order to describe a crystal, one would need only to specify the substance to be used and the way in which the molecules were packed together (i.e., specify the unit cell). A couple of sentences would suffice, followed by the instructions "and keep on doing the same thing," since the packing sequence in a crystal is regular. The instructions required to make a polynucleotide with any random sequence would be similarly brief. Here one would need only to specify the proportions of the four nucleotides to be incorporated into the polymer and provide instructions to assemble them randomly. The crystal is specified but not very complex. The random polymer is complex but not specified. The set of instruction required for each is only a few sentences. It is this set of instructions that we identify as the *complex specified information* for a particular polymer.

By contrast, it would be impossible to produce a correspondingly simple set of instructions that would enable a chemist to synthesize the DNA of *E. coli* bacteria. In this case, the sequence matters! Only by specifying the sequence letter by letter (about 4,600,000 instructions) could we tell a chemist what to make. It would take 800 pages of instructions consisting of typing like that on this page (compared to a few sentences for a crystal or a random polynucleotide) to make such a specification, with no way to shorten it. The DNA of *E. coli* has a huge amount of *complex specified information.*

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Brillouin (1956, 3) generalizes Shannon's information to cover the case where the total number of possible messages is W_o and the number of functional messages is W_1. Assuming the complex specified information is effectively zero for the random case (i.e., W_o calculated with no specifications or constraints), Brillouin then calculates the *complex specified information*, I_{CSI}, to be:

$$I_{CSI} = \log_2 (W_o/W_1) \tag{11}$$

For information-rich biological polymers such as DNA and protein, one may assume with Brillouin (1956, 3) that the number of ways in which the polynucleotides or polypeptides can be sequenced is extremely large (W_o). The number of sequences that will provide biological function will, by comparison, be quite small (W_1). Thus, the number of specifications needed to get such a functional biopolymer will be extremely high. The greater the number of specifications, the greater the constraints on permissible sequences, ruling out most of the possibilities from the very large set of random sequences that give no function, and leaving W_1 necessarily small.

Calculating the Complex Specified Information in the Cytochrome c Protein Molecule. If one assembles a random sequence of the twenty common amino acids in proteins into a polymer chain of 110 amino acids, each with $p_i = .05$, then the average information "I" per amino acid is given by Equation 2; it is $\log_2(20) = 4.32$. The total Shannon information is given by $I = N \cdot i = 110 \cdot 4.32 = 475$. The total number of unique sequences that are possible for this polypeptide is given by Equation 6 to be

$$M = 2^1 = 2^{475} \cong 10^{143} = W_o \tag{12}$$

It turns out that the amino acids in cytochrome c are not equiprobable ($p_i = 0.05$) as assumed earlier. If one takes the actual probabilities of occurrence of the amino acids in cytochrome c, one may calculate the average information per residue (or link in our 110-link polymer chain) to be 4.139, using Equation 3, with the total information being given by $I = N \cdot i = 4.139 \times 110 = 455$. The total number of unique sequences that are possible for this case is given by Equation 6 to be

$$M = 2^{455} = 1.85 \times 10^{137} = W_o \tag{13}$$

Comparison of Equation 12 to Equation 13 illustrates again the principle that the maximum number of sequences is possible when the probabilities of occurrence of the various amino acids in the protein are equal.

Next, let's calculate the number of sequences that actually give a functional cytochrome c protein molecule. One might be tempted to assume that only one sequence will give the requisite biological function. However, this is not so. Functional cytochrome c has been found to allow more than

one amino acid to occur at some residue sites (links in my 110-link polymer chain). Taking this flexibility (or interchangeability) into account, Yockey (1992, 242–58) has provided a rather more exacting calculation of the information required to make the protein cytochrome c. Yockey calculates the total Shannon information for these functional cytochrome c proteins to be 310 bits, from which he calculates the number of sequences of amino acids that give a functional cytochrome c molecule:

$$M = 2^{310} = 2.1 \times 10^{93} = W_1 \tag{14}$$

This result implies that, on average, there are approximately three amino acids out of twenty that can be used interchangeably at each of the 110 sites and still give a functional cytochrome c protein. The chance of finding a functional cytochrome c protein in a prebiotic soup of randomly sequenced polypeptides would be:

$$W_1/W_o = 2.1 \times 10^{93}/1.85 \times 10^{137} = 1.14 \times 10^{-44} \tag{15}$$

This calculation assumes that there is no intersymbol influence – that is, that sequencing is not the result of dipeptide bonding preferences. Experimental support for this assumption will be discussed in the next section (Kok, Taylor, and Bradley 1988; Yeas 1969). The calculation also ignores the problem of chirality, or the use of exclusively left-handed amino acids in functional protein. In order to correct this shortcoming, Yockey repeats his calculation assuming a prebiotic soup with thirty-nine amino acids, nineteen with a left-handed and nineteen with a right-handed structures, assumed to be of equal concentration, and glysine, which is symmetric. W_1 is calculated to be 4.26×10^{62} and $P = W_1/W_o = 4.26 \times 10^{62}/1.85 \times 10^{137} = 2.3 \times 10^{-75}$. It is clear that finding a functional cytochrome c molecule in the prebiotic soup is an exercise in futility.

Two recent experimental studies on other proteins have found the same incredibly low probabilities for accidental formation of a functional protein that Yockey found; namely, 1 in 10^{75} (Strait and Dewey 1996) and 1 in 10^{63} (Bowie et al. 1990). All three results argue against any significant nearest-neighbor influence in the sequencing of amino acids in proteins, since this would make the sequencing much less random and the probability of formation of a functional protein much higher. In the absence of such intrinsic sequencing, the probability of accidental formation of a functional protein is incredibly low. The situation for accidental formation of functional polynucleotides (RNA or DNA) is much worse than for proteins, since the total information content is much higher (e.g., $\sim 8 \times 10^6$ bits for *E. coli* DNA versus 455 bits for the protein cytochrome c).

Finally, we may calculate the complex specified information, I_{CSI}, necessary to produce a functional cytochrome c by utilizing the results of Equation

15 in Equation 11, as follows:

$$I_{CSI} = \log_2 (1.85 \times 10^{137}/2.1 \times 10^{93}) = 146 \text{ bits of information, or}$$
$$I_{CSI} = \log_2 (1.85 \times 10^{137}/4.26 \times 10^{62}) = 248 \text{ bits of information} \quad (16)$$

The second of these equations includes chirality in the calculation. It is this huge amount of complex specified information, I_{CSI}, that must be accounted for in many biopolymers in order to develop a credible origin-of-life scenario.

Summary. Shannon information, I_s, is a measure of the complexity of a biopolymer and quantifies the maximum capacity for complex specified information, I_{CSI}. Complex specified information measures the essential information that a biopolymer must have in order to store information, replicate, and metabolize. The complex specified information in a modest-sized protein such as cytochrome c is staggering, and one protein does not a first living system make. A much greater amount of information is encoded in DNA, which must instruct the production of all the proteins in the menagerie of molecules that constitute a simple living system. At the heart of the origin-of-life question is the source of this very, very significant amount of complex specified information in biopolymers. The role of the Second Law of Thermodynamics in either assisting or resisting the formation of such biopolymers that are rich in information will be considered next.

3. THE SECOND LAW OF THERMODYNAMICS AND THE ORIGIN OF LIFE

Introduction. "The law that entropy always increases – the 2nd Law of Thermodynamics – holds I think the supreme position among the laws of nature." So said Sir Arthur Eddington (1928, 74). If entropy is a measure of the disorder or disorganization of a system, this would seem to imply that the Second Law hinders if not precludes the origin of life, much like gravity prevents most animals from flying. At a minimum, the origin of life must be shown somehow to be compatible with the Second Law. However, it has recently become fashionable to argue that the Second Law is actually the driving force for abiotic as well as biotic evolution. For example, Wicken (1987, 5) says, "The emergence and evolution of life are phenomena causally connected with the Second Law." Brooks and Wiley (1988, xiv) indicate, "The axiomatic behavior of living systems should be increasing complexity and self-organization as a result of, not at the expense of increasing entropy." But how can this be?

What Is Entropy Macroscopically? The First Law of Thermodynamics is easy to understand: energy is always conserved. It is a simple accounting exercise.

When I burn wood, I convert chemical energy into thermal energy, but the total energy remains unchanged. The Second Law is much more subtle in that it tells us something about the nature of the available energy (and matter). It tells us something about the flow of energy, about the availability of energy to do work. At a macroscopic level, entropy is defined as

$$\Delta S = Q/T \quad (17)$$

where S is the entropy of the system and Q is the heat or thermal energy that flows into or out of the system. In the wintertime, the Second Law of Thermodynamics dictates that heat flows from inside to outside your house. The resultant entropy change is

$$\Delta S = -Q/T_1 + Q/T_2 \quad (18)$$

where T_1 and T_2 are the temperatures inside and outside your house. Conservation of energy, the First Law of Thermodynamics, tell us that the heat lost from your house ($-Q$) must exactly equal the heat gained by the surroundings ($+Q$). In the wintertime, the temperature inside the house is greater than the temperature outside ($T_1 > T_2$), so that $\Delta S > 0$, or the entropy of the universe increases. In the summer, the temperature inside your house is lower than the temperature outside, and thus, the requirement that the entropy of the universe must increase means that heat must flow from the outside to the inside of your house. That is why people in Texas need a large amount of air conditioning to neutralize this heat flow and keep their houses cool despite the searing temperature outside. When people combust gasoline in their automobiles, chemical energy in the gasoline is converted into thermal energy as hot, high-pressure gas in the internal combustion engine, which does work and releases heat at a much lower temperature to the surroundings. The total energy is conserved, but the residual capacity of the energy that is released to do work on the surroundings is virtually nil.

Time's Arrow. In reversible processes, the entropy of the universe remains unchanged, while in irreversible processes, the entropy of the universe increases, moving from a less probable to a more probable state. This has been referred to as "time's arrow" and can be illustrated in everyday experience by our perceptions as we watch a movie. If you were to see a movie of a pendulum swinging, you could not tell the difference between the movie running forward and the movie running backward. Here potential energy is converted into kinetic energy in a completely reversible way (no increase in entropy), and no "arrow of time" is evident. But if you were to see a movie of a vase being dropped and shattered, you would readily recognize the difference between the movie running forward and running backward, since the shattering of the vase represents a conversion of kinetic energy into the surface energy of the many pieces into which the vase is broken, a quite irreversible and energy-dissipative process.

What Is Entropy Microscopically? Boltzmann, building on the work of Maxwell, was the first to recognize that entropy can also be expressed microscopically, as follows:

$$S = k \log_e \Omega \tag{19}$$

where k is Boltzmann's constant and Ω is the number of ways in which the system can be arranged. An orderly system can be arranged in only one or possibly a few ways, and thus would be said to have a small entropy. On the other hand, a disorderly system can be disorderly in many different ways and thus would have a high entropy. If "time's arrow" says that the total entropy of the universe is always increasing, then it is clear that the universe naturally goes from a more orderly to a less orderly state in the aggregate, as any housekeeper or gardener can confirm. The number of ways in which energy and/or matter can be arranged in a system can be calculated using statistics, as follows:

$$\Omega = N!/(a!b!c!.....) \tag{20}$$

where a+b+c+ . . . . . = N. As Brillouin (1956, 6) has demonstrated, starting with Equation 20 and using Stirling's approximation, it may be easily shown that

$$\log \Omega = -\sum p_i \log p_i \tag{21}$$

where $p_1 = a/N$, $p_2 = b/N$, ... A comparison of Equations 19 and 21 for Boltzmann's thermodynamic entropy to Equations 1 and 3 for Shannon's information indicate that they are essentially identical, with an appropriate assignment of the constant K. It is for this reason that Shannon information is often referred to as Shannon entropy. However, K in Equation 1 should not to be confused with the Boltzmann's constant k in Equation 19. K is arbitrary and determines the unit of information to be used, whereas k has a value that is physically based and scales thermal energy in much the same way that Planck's constant "h" scales electromagnetic energy. Boltzmann's entropy measures the amount of uncertainty or disorder in a physical system – or, more precisely, the lack of information about the actual structure of the physical system. Shannon information measures the uncertainty in a message. Are Boltzmann entropy and Shannon entropy causally connected in any way? It is apparent that they are not.

The probability space for Boltzmann entropy, which is a measure of the number of ways in which mass and energy can be arranged in biopolymers, is quite different from the probability space for Shannon entropy, which focuses on the number of different messages that might be encoded on the biopolymer. According to Yockey (1992, 70), in order for Shannon and Boltzmann entropies to be causally connected, their two probability spaces would need to be either isomorphic or related by a code, which they are not. Wicken (1987, 21–33) makes a similar argument that these two entropies

are conceptually distinct and not causally connected. Thus the Second Law cannot be the proximate cause for any observed changes in the Shannon information (or entropy) that determines the complexity of the biopolymer (via the polymerized length of the polymer chain) or the complex specified information having to do with the sequencing of the biopolymer.

Thermal and Configurational Entropy. The total entropy of a system is a measure of the number of ways in which the mass and the energy in the system can be distributed or arranged. The entropy of any living or nonliving system can be calculated by considering the total number of ways in which the energy and the matter can be arranged in the system, or

$$S = k \ln (\Omega_{th}\Omega_{conf}) = k \ln \Omega_{th} + k \ln \Omega_{conf} = \Delta S_{th} + \Delta S_c \tag{22}$$

with ΔS_{th} and ΔS_c equal to the thermal and configurational entropies, respectively. The atoms in a perfect crystal can be arranged in only one way, and thus it has a very low configurational entropy. A crystal with imperfections can be arranged in a variety of ways (i.e., various locations of the imperfections), and thus it has a higher configurational entropy. The Second Law would lead us to expect that crystals in nature will always have some imperfections, and they do. The change in configurational entropy is a force driving chemical reactions forward, though a relatively weak one, as we shall see presently. Imagine a chemical system that is comprised of fifty amino acids of type A and fifty amino acids of type B. What happens to the configurational entropy if two of these molecules chemically react? The total number of molecules in the systems drops from 100 to 99, with 49 A molecules, 49 B molecules, and a single A-B bipeptide. The change in configurational entropy is given by

$$\begin{aligned} S_{cf} - S_{co} = \Delta S_c &= k \ln [99!/(49!49!1!)] - k \ln [100!/50!50!] \\ &= k \ln (25) \end{aligned} \tag{23}$$

The original configurational entropy S_{co} for this reaction can be calculated to be k ln 10^{29}, so the driving force due to changes in configuration entropy is seen to be quite small. Furthermore, it decreases rapidly as the reaction goes forward, with ΔS_c= k ln (12.1) and ΔS_c= k ln (7.84) for the formation of the second and third dipeptides in the reaction just described. The thermal entropy also decreases as such polymerization reactions take place owing to the significant reduction in the availability of translational and rotational modes of thermal energy storage, giving a net decrease in the total entropy (configuration plus thermal) of the system. Only at the limit, as the yield goes to zero in a large system, does the entropic driving force for configurational entropy overcome the resistance to polymerization provided by the concurrent decrease in thermal entropy.

into a crystalline array. Thus water goes from a random to an orderly state due to a change in the bonding energy between water and ice – a bonding potential-energy well, so to speak. The release of the heat of fusion to the surroundings gives a greater increase in the entropy of the surroundings than the entropy decrease associated with the ice formation. So the entropy of the universe does increase as demanded by the Second Law, even as ice freezes.

Energy-rich Biomass. Polymerization of biopolymers such as DNA and protein in living systems is driven by the consumption of energy-rich reactants (often in coupled chemical reactions). The resultant biopolymers themselves are less rich than the reactants, but still much more energy-rich than the equilibrium chemical mixture to which they can decompose – and will decompose, if cells or the whole system dies. Sustaining living systems in this nonequilibrium state is analogous to keeping a house warm on a cold winter's night. Living systems also require a continuous source of energy, either from radiation or from biomass, and metabolic "machinery" that functions in a way analogous to the heater in a house. Morowitz (1968) has estimated that *E. coli* bacteria have an average energy from chemical bonding of .27eV/atom greater (or richer) than the simple compounds from which the bacteria is formed. As with a hot house on a cold winter's night, the Second Law says that living systems are continuously being pulled toward equilibrium. Only the continuous flow of energy through the cell (functioning like the furnace in a house) can maintain cells at these higher energies.

Summary. Informational biopolymers direct photosynthesis in plants and the metabolism of energy-rich biomass in animals that make possible the cell's "levitation" above chemical equilibrium and physical death. Chemical reactions that form biomonomers and biopolymers require exothermic chemical reactions in order to go forward, sometimes assisted in a minor way by an increase in the configurational entropy (also known as the law of mass action) and resisted by much larger decreases in the thermal entropy. At best, the Second Law of Thermodynamics gives an extremely small yield of unsequenced polymers that have no biological function. Decent yields required exothermic chemical reactions, which are not available for some critical biopolymers. Finally, Shannon (informational) entropy and Boltzmann (thermodynamic) entropy are not causally connected, meaning in practice that the sequencing needed to get functional biopolymers is not facilitated by the Second Law, a point that Wicken (1987) and Yockey (1992) have both previously made.

The Second Law is to the emergence of life what gravity is to flight, a challenge to be overcome. Energy flow is necessary to sustain the levitation of life above thermodynamic equilibrium but is not a sufficient cause for the formation of living systems. I find myself in agreement with Yockey's (1977) characterization of thermodynamics as an "uninvited (and probably unwelcome) guest in emergence of life discussions." In the next section, we will critique the various proposals for the production of complex specified information in biopolymers that are essential to the origin of life.

4. CRITIQUE OF VARIOUS ORIGIN-OF-LIFE SCENARIOS

In this final section, we will critique major scenarios of how life began, using the insights from information theory and thermodynamics that have been developed in the preceding portion of this chapter. Any origin-of-life scenario must somehow explain the origin of molecules encoded with the necessary minimal functions of life. More specifically, the scenario must explain two major observations: (1) how very complex molecules such as polypeptides and polynucleotides that have large capacities for information came to be, and (2) how these molecules are encoded with complex specified information. All schemes in the technical literature use some combination of chance and necessity, or natural law. But they differ widely in the magnitude of chance that is invoked and in which natural law is emphasized as guiding or even driving the process part of this story. Each would seek to minimize the degree of chance that is involved. The use of the term "emergence of life," which is gradually replacing "origin of life," reflects this trend toward making the chance step(s) as small as possible, with natural processes doing most of the "heavy lifting."

Chance Models and Jacques Monod (1972). In his classic book *Chance and Necessity* (1972), Nobel laureate Jacques Monod argues that life began essentially by random fluctuations in the prebiotic soup that were subsequently acted upon by selection to generate information. He readily admits that life is such a remarkable accident that it is almost certainly occurred only once in the universe. For Monod, life is just a quirk of fate, the result of a blind lottery, much more the result of chance than of necessity. But in view of the overwhelming improbability of encoding DNA and protein to give functional biopolymers, Monod's reliance on chance is simply believing in a miracle by another name and cannot in any sense be construed as a rational explanation for the origin of life.

Replicator-first Models and Eigen and Winkler-Oswatitsch (1992). In his book *Steps toward Life*, Manfred Eigen seeks to demonstrate that the laws of nature can be shown to reduce significantly the improbability of the emergence of life, giving life a "believable" chance. Eigen and Winkler-Oswatitsch (1992, 11) argue that

> [t]he genes found today cannot have arisen randomly, as it were by the throw of a dice. There must exist a process of optimization that works towards functional

Wicken (1987) argues that configurational entropy is the driving force responsible for increasing the complexity, and therefore the information capacity, of biological polymers by driving polymerization forward and thus making longer polymer chains. It is in this sense that he argues that the Second Law is a driving force for abiotic as well as biotic evolution. But as noted earlier, this is only true for very, very trivial yields. The Second Law is at best a trivial driving force for complexity!

Thermodynamics of Isolated Systems. An isolated system is one that does not exchange either matter or energy with its surroundings. An idealized thermos jug (i.e., one that loses no heat to its surroundings), filled with a liquid and sealed, would be an example. In such a system, the entropy of the system must either stay constant or increase due to irreversible energy-dissipative processes taking place inside the thermos. Consider a thermos containing ice and water. The Second Law requires that, over time, the ice melts, which gives a more random arrangement of the mass and thermal energy, which is reflected in an increase in the thermal and configurational entropies.

The gradual spreading of the aroma of perfume in a room is an example of the increase in configurational entropy in a system. Your nose processes the gas molecules responsible for the perfume aroma as they spread spontaneously throughout the room, becoming randomly distributed. Note that the reverse does not happen. The Second Law requires that processes that are driven by an increase in entropy are not reversible.

It is clear that life cannot exist as an isolated system that monotonically increases its entropy, losing its complexity and returning to the simple components from which it was initially constructed. An isolated system is a dead system.

Thermodynamics of Open Systems. Open systems allow the free flow of mass and energy through them. Plants use radiant energy to convert carbon dioxide and water into sugars that are rich in chemical energy. The system of chemical reactions that gives photosynthesis is more complex, but effectively gives

$$6CO_2 + 6H_2O + \text{radiant energy} \rightarrow 6C_6H_{12}O_6 + 6O_2 \qquad (24)$$

Animals consume plant biomass and use this energy-rich material to maintain themselves against the downward pull of the Second Law. The total entropy change that takes place in an open system such as a living cell must be consistent with the Second Law of Thermodynamics and can be described as follows:

$$\Delta S_{cell} + \Delta S_{surroundings} > 0 \qquad (25)$$

The change in the entropy of the surroundings of the cell may be calculated as Q/T, where Q is positive if energy is released to the surroundings by exothermic reactions in the cell and Q is negative if heat is required from the surroundings due to endothermic reactions in the cell. Equation 25, which is a statement of the Second Law, may now be rewritten using Equation 22 to be

$$\Delta S_{th} + \Delta S_{conf} + Q/T > 0 \qquad (26)$$

Consider the simple chemical reaction of hydrogen and nitrogen to produce ammonia. Equation 26, which is a statement of the Second Law, has the following values, expressed in entropy units, for the three terms:

$$-14.95 - 0.79 + 23.13 > 0 \qquad (27)$$

Note that the thermal entropy term and the energy exchange term Q/T are quite large compared to the configurational entropy term, which in this case is even negative because the reaction is assumed to have a high yield. It is the large exothermic chemical reaction that drives this reaction forward, despite the resistance provided by the Second Law. This is why making amino acids in Miller-Urey-type experiments is as easy as getting water to run downhill, if and only if one uses energy-rich chemicals such as ammonia, methane, and hydrogen that combine in chemical reactions that are very exothermic (50–250 kcal/mole). On the other hand, attempts to make amino acids from water, nitrogen, and carbon dioxide give at best minuscule yields because the necessary chemical reactions collectively are endothermic, requiring an increase in energy of more than 50 kcal/mole, akin to getting water to run uphill. Electrical discharge and other sources of energy used in such experiments help to overcome the kinetic barriers to the chemical reaction but do not change the thermodynamic direction dictated by the Second Law.

Energy-Rich Chemical Reactants and Complexity. Imagine a pool table with a small dip or cup at the center of the table. In the absence of such a dip, one might expect the pool balls to be randomly positioned on the table after one has agitated the table for a short time. However, the dip will cause the pool balls to assume a distinctively nonrandom arrangement – all of them will be found in the dip at the center of the table. When we use the term "energy-rich" to describe molecules, we generally mean double covalent bonds that can be broken to give two single covalent bonds, with a more negative energy of interaction or a larger absolute value for the bonding energy. Energy-rich chemicals function like the dip in the pool table, causing a quite nonrandom outcome to the chemistry as reaction products are attracted into this chemical bonding energy "well," so to speak.

The formation of ice from water is a good example of this principle, with $Q/T = 80\text{cal/gm}$ and $\Delta S_{th} + \Delta S_{conf} = 0.29$ cal/K for the transition from water to ice. The randomizing influence of thermal energy drops sufficiently low at 273K to allow the bonding forces in water to draw the water molecules

efficiency. Even if there were several routes to optimal efficiency, mere trial and error cannot be one of them. . . . It is reasonable to ask how a gene, the sequence of which is one out of 10^{600} possible alternatives of the same length, copies itself spontaneously and reproducibly.

It is even more interesting to wonder how such a molecule emerged in the first place. Eigen's answer is that the emergence of life began with a self-replicating RNA molecule that, through mutation/natural selection over time, became increasingly optimized in its biochemical function. Thus, the information content of the first RNA is assumed to have been quite low, making this "low-tech start" much less chancy. The reasonableness of Eigen's approach depends entirely on how "low-tech" one can go and still have the necessary biological functions of information storage, replication with occasional (but not too frequent) replicating mistakes, and some meaningful basis for selection to guide the development of more molecular information over time.

Robert Shapiro, a Harvard-trained DNA chemist, has recently critiqued all RNA-first replicator models for the emergence of life (2000). He says,

A profound difficulty exists, however, with the idea of RNA, or any other replicator, at the start of life. Existing replicators can serve as templates for the synthesis of additional copies of themselves, but this device cannot be used for the preparation of the very first such molecule, which must arise spontaneously from an unorganized mixture. The formation of an information-bearing homopolymer through undirected chemical synthesis appears very improbable.

Shapiro then addresses various assembly problems and the problem of even getting all the building blocks, which he addresses elsewhere (1999).

Potentially an even more challenging problem than making a polynucleotide that is the precursor to a functional RNA is encoding it with enough information to direct the required functions. What kind of selection could possibly guide the encoding of the initial information required to "get started"? In the absence of some believable explanation, we are back to Monod's unbelievable chance beginning. Bernstein and Dillion (1997) have recently addressed this problem as follows.

Eigen has argued that natural selection itself represents an inherent form of self-organization and must necessarily yield increasing information content in living things. While this is a very appealing theoretical conclusion, it suffers, as do most reductionist theories, from the basic flaw that Eigen is unable to identify the source of the natural selection during the origin of life. By starting with the answer (an RNA world), he bypasses the nature of the question that had to precede it.

Many models other than Eigen's begin with replication first, but few address the origins of metabolism (see Dyson 1999), and all suffer from the same shortcomings as Eigen's hypercycle, assuming too complicated a starting point, too much chance, and not enough necessity. The fundamental question remains unresolved – namely, is genetic replication a necessary prerequisite for the emergence of life or just a consequence of it?

Metabolism-first Models of Wicken (1987), Fox (1984), and Dyson (1999). Sidney Fox has made a career of making and studying proteinoid microspheres. By heating dry amino acids to temperatures that drive off the water that is released as a byproduct of polymerization, he is able to polymerize amino acids into polypeptides, or polymer chains of amino acids. Proteinoid molecules differ from actual proteins in at least three significant (and probably critical) ways: (1) a significant percentage of the bonds are not the peptide bonds found in modern proteins; (2) proteinoids are comprised of a mixture of L and D amino acids, rather than of all L amino acids (like actual proteins); and (3) their amino acid sequencing gives little or no catalytic activity. It is somewhat difficult to imagine how such a group of "protein wannabes" that have attracted other "garbage" from solution and formed a quasi-membrane can have sufficient encoded information to provide any biological function, much less sufficient biological function to benefit from any imaginable kind of selection. Again, we are back to Monod's extreme dependence on chance.

Fox and Wicken have proposed a way out of this dilemma. Fox (1984, 16) contends that "[a] guiding principle of non-randomness has proved to be essential to understanding origins. . . . As a result of the new protobiological theory the neo-Darwinian formulation of evolution as the natural selection of random variations should be modified to the natural selection of non-random variants resulting from the synthesis of proteins and assemblies thereof." Wicken (1987) appeals repeatedly to inherent nonrandomness in polypeptides as the key to the emergence of life. Wicken recognizes that there is little likelihood of sufficient intrinsic nonrandomness in the sequencing of bases in RNA or DNA to provide any basis for biological function. Thus his hope is based on the possibility that variations in steric interference in amino acids might give rise to differences in the dipeptide bonding tendencies in various amino acid pairs. This could potentially give some nonrandomness in amino acid sequencing. But it is not just nonrandomness but complex specificity that is needed for function.

Wicken bases his hypothesis on early results published by Steinman and Cole (1967) and Steinman (1971), who claimed to show that dipeptide bond frequencies measured experimentally were nonrandom (some amino acids reacted preferentially with other amino acids) and that these nonrandom chemical bonding affinities are reflected in the dipeptide bonding frequencies in actual proteins, based on a study of the amino acid sequencing in ten protein molecules. Steinman subsequently coauthored a book with Kenyon (1969) titled *Biochemical Predestination* that argued that the necessary information for functional proteins was encoded in the relative chemical reactivities of the various amino acid "building blocks" themselves, which

directed them to self-assemble into functional proteins. However, a much more comprehensive study by Kok, Taylor, and Bradley (1988), using the same approach but studying 250 proteins and employing a more rigorous statistical analysis, concluded that there was absolutely no correlation between the dipeptide bond frequencies measured by Steinman and Cole and the dipeptide bond frequencies found in actual proteins.

The studies by Yockey (1992), Strait and Dewey (1996), Sauer and Reidhaar-Olson (1990), and Kok, Taylor, and Bradley (1988) argue strongly from empirical evidence that one cannot explain the origin of metabolic behavior by bonding preferences. Their work argues convincingly that the sequencing that gives biological function to proteins cannot be explained by bipeptide bonding preferences. Thus the metabolism-first approach would appear to be back to the "chance" explanation of Monod (1972). It is also interesting to note that Kenyon has now repudiated his belief in biochemical predestination (Thaxton, Bradley, and Olsen 1992).

Self-organization in Systems Far from Equilibrium – Prigogine. Prigogine has received a Nobel Prize for his work on the behavior of chemical systems far from equilibrium. Using mathematical modeling and thoughtful experiments, he has demonstrated that systems of chemical reactions that have autocatalytic behavior resulting in nonlinear kinetics can have surprising self-organization (Nicolis and Prigogine 1977; Prigogine 1980; Prigogine and Stengers 1984). There is also a tendency for such systems to bifurcate when the imposed gradients reach critical values. However, the ordering produced in Prigogine's mathematical models and experiments seems to be of the same order of magnitude as the information implicit in the boundary conditions, proving once again that it is hard to get something for nothing. Second, the ordering observed in these systems has no resemblance to the specified complexity characteristic of living systems. Put another way, the complex specified information in such systems is quite modest compared to that of living systems. Thus Prigogine's approach also seems to fall short of providing any "necessity" for the emergence of life, leaving us again with Monod's chance explanation.

Complexity and the Work of Kauffman and the Sante Fe Institute. Kauffman defines "life" as a closed network of catalyzed chemical reactions that reproduce each molecule in the network – a self-maintaining and self-reproducing metabolism that does not require self-replicating molecules. Kauffman's ideas are based on computer simulations alone, without any experimental support. He claims that when a system of simple chemicals reaches a critical level of diversity and connectedness, it undergoes a dramatic transition, combining to create larger molecules of increasing complexity and catalytic capability – Kauffman's definition of life.

Such computer models ignore important aspects of physical reality that, if included in the models, would make the models not only more complicated but also incapable of the self-organizing behavior that is desired by the modelers. For example, Kauffman's origin-of-life model requires a critical diversity of molecules so that there is a high probability that the production of each molecule is catalyzed by another molecule. For example, he posits 1/1,000,000 as the probability that a given molecule catalyzes the production of another molecule (which is too optimistic a probability, based on catalyst chemistry). If one has a system of 1,000,000 molecules, then in theory it becomes highly probable that most molecules are catalyzed in their production, at which point this catalytic closure causes the system to "catch fire" – in effect to come to life (Kauffman 1995, 64).

Einstein said that we want our models to be as simple as possible, but not too simple (i.e., ignoring important aspects of physical reality). Kauffman's model for the origin of life ignores critical thermodynamic and kinetic issues that, if included in his model, would kill his "living system." For example, there are huge kinetic transport issues in taking Kauffman's system with 1,000,000 different types of molecules, each of which can be catalyzed in its production by approximately one type of molecule, and organizing it in such a way that the catalyst that produces a given molecule will be in the right proximity to the necessary reactants to allow it to be effective. Kauffman's simple computer model ignores this enormous organizational problem that must precede the "spontaneous self-organization" of the system. Here he is assuming away (not solving) a system-level configurational entropy problem that is completely analogous to the molecular-level configurational entropy problem discussed in Thaxton, Bradley, and Olsen (1984). The models themselves seem to represent reality poorly, and the lack of experimental support makes Kauffman's approach even more speculative than the previous four, none of which seemed to be particularly promising.

5. SUMMARY

Biological life requires a system of biopolymers of sufficient specified complexity to store information, replicate with very occasional mistakes, and utilize energy flow to maintain the levitation of life above thermodynamic equilibrium and physical death. And there can be no possibility of information generation by the Maxwellian demon of natural selection until this significant quantity of complex specified information has been provided a priori. A quotation from Nicholas Wade, writing in the *New York Times* (June 13, 2000), nicely summarizes the dilemma of the origin of life:

> The chemistry of the first life is a nightmare to explain. No one has yet developed a plausible explanation to show how the earliest chemicals of life – thought to be RNA – might have constructed themselves from the inorganic chemicals likely to have been

around on early earth. The spontaneous assembly of a small RNA molecule on the primitive earth "would have been a near miracle," two experts in the subject helpfully declared last year.

The origin of life seems to be the ultimate example of irreducible complexity. I believe that cosmology and the origin of life provide the most compelling examples of Intelligent Design in nature. I am compelled to agree with the eloquent affirmation of design by Harold Morowitz (1987): "I find it hard not to see design in a universe that works so well. Each new scientific discovery seems to reinforce that vision of design. As I like to say to my friends, the universe works much better than we have any right to expect."

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