A REALISTIC CHEMICAL BASIS FOR THE ORIGIN OF LIFE

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ABSTRACT: Polyphosphate complexes are proposed as template and polymerizing agent for the origin of polynucleotides and proteins. Inorganic polyphosphates are contemporary biopolymers, and there is evidence indicating their primordial occurrence. Complexes of polyphosphate with the cations of seawater have the necessary chemical properties to facilitate the selection and polymerization of organic monomers in an aqueous environment. In this respect, they satisfy the need for existence of a simpler, biologically relevant, chemical system that could serve as the forerunner of organic biopolymers. Based on the expected interactions of these complexes with the primordial environment, a dynamic system theory for the development of increasing complexity in nature has been derived. Application of this theory to biosystems places them in a common mechanistic framework with physical systems.

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INTRODUCTION

For several decades, the problem of the origin of life has received attention from physical scientists as well as biologists. The research of chemists within this topic has focused on the stepwise origin of biologically relevant organic monomers, polymers, and self-replicating systems. Despite this effort, the goal of a plausible scenario for the abiotic progression of these chemicals has not been realized. At this writing, fundamental issues regarding the mechanisms for prebiotic selection and polymerization remain unresolved. Also missing is some concept of functional objective, other than continual replication, that could have been served by the structural arrangement of these molecules.

The approach to the origin of life that is presented here is based on the excitability hypothesis [1-3]. In it, I proposed (25 years ago) that the response of mixed organic-inorganic polyphosphate complexes to external stimuli from their primordial brackish environment led to the stepwise formation of biopolymers [1]. The plausibility of this scenario can now be supported by sufficient geological, chemical, and biological evidence to warrant its renewed investigation [4-37]. Moreover, properties of these complexes are such that they would be expected to facilitate the selection of organic monomers from a dilute aqueous environment and then provide the template and energy for their polymerization. In this hypothesis, the functional objective of resulting molecular arrangements is resistance of the complex to further change when responding to repeated stimulation, i.e., survival of the complex at near-equilibrium with the environment.

From the excitability hypothesis, I have now derived a theory for the development of increasingly complex structures in nature. I have called it "natural complexification," and it is presented here in the format of a dynamic system theory that can be applied to both physical and biological systems. This theory describes the process by which some natural systems develop increasing complexity, while others appear static and still others degenerate. The argument for this theory constitutes the main section of this document. It has been organized to logically demonstrate that development of increasingly complex structures in nature is general and inevitable. In this latter aspect, I have contrasted it with origin-of-life theories based on thermodynamic modeling. As a dynamic system theory for both physical and biological transformations, natural complexification provides a consistent, general mechanism for the origin of life on this planet. Its usefulness for interpretation of biological phenomena is demonstrated by example in the argument and is discussed further within the context of evolution.

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The writing of the excitability hypothesis took place at the University of Illinois, Chicago, in the Psychiatry Department's Biological Research Laboratory. After its completion, I sent the manuscript to Academician A. I. Oparin at the Bach Institute of Biochemistry in Moscow. There, he graciously reviewed and accepted it for publication in Life Sciences, as one of the international editors of that journal [38]. Thus encouraged, I applied for and won a one-year fellowship at NASA Ames Research Center (1966-1967), and afterward continued research on the origin of life for 10 years. The ideas expressed in this present treatise have, therefore, been in a process of development since that first writing in 1965. They have, of course, been influenced by my current work in environmental chemistry, assessing risks to public health from the release, transport, and degradative persistence of hazardous substances. I have prepared the present document with the same care that I apply to these contemporary problems.

The primordial earth is generally looked upon as a poorly defined system in which to consider chemical transformations and transport. In doing so, I relied upon professional judgement and acquired expertise. As measurement of my ability to exercise this expertise, I cite the following:

  o   First to propose inorganic polyphosphates as template and condensing agent for prebiotic polymerization [1].

  o   First to investigate and demonstrate the reaction of dilute aqueous formaldehyde with clays as a possible prebiotic source of ribose and other monosaccharides [4].

  o   First to investigate and thoroughly document the occurrence of inorganic polyphosphates throughout the vertebrates and throughout all mammalian organs tested [5].

  o   First to point out that transition from a highly reducing primitive atmosphere to an oxidizing one during the early Precambrian cannot be chemically substantiated, as this transition would have generated a worldwide thermal disaster [3].

Presentation of the excitability hypothesis and its derivative theory, natural complexification, has been arranged in consecutive sections, beginning with conception of the initial ideas and proceeding to their application. Following the introduction, the second section (Source of the Concept) describes where the ideas originated, and the third section (Generalization of the Concept) relates the excitability and evolution of an open, natural system to natural information, natural complexity, and structural dynamics. This is followed by the fourth (and main) section, The Argument for Complexification. The fifth section gives a statement of natural complexification as an evolutionary principle, and in the sixth section, this approach to the origin of life is discussed from the perspective of five questions: (1) What does it do? (2) Where does it fit into origin-of-life theories? (3) Where does it fit into biological theory? (4) What does it predict? and (5) How can it be tested? Conclusions are then given in the seventh (and final) section.

SOURCE OF THE CONCEPT

The initial ideas had their beginning in a critical examination of phenomena associated with excitable tissues. In 1965, Abood and I [39] recognized that many of the properties of a viable neuronal membrane would also be exhibited by a macromolecular, polyphosphate complex (VIII) in which calcium and magnesium ions have a crosslinking function, and sodium and potassium serve as accessory counter ions [6]. (Roman numerals in parentheses refer to structures depicted in the accompanying figure.) Further development of this model led me [1] to an origin-of-life hypothesis in which I proposed that inorganic polyphosphates (III), released during the weathering of primordial rocks, would form complexes with the cations of brackish shoreline environments, where they could serve as template and condensing agent for the formation of prebiotic organic polymers and act as the forerunner of biological membranes.
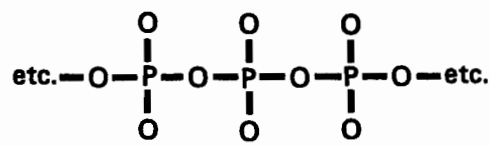
These complexes, whose molecular weights can range from 10^3 to 10^7 [6], would interact with primordial organic monomers [3] via their bonding with metal cations of the complex. Moreover, molecules susceptible to hydrolysis, such as peptides or oligonucleotides, may have been afforded some protection, if formed within a complex of this type, due to the concurrent
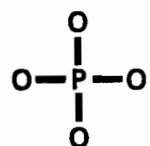
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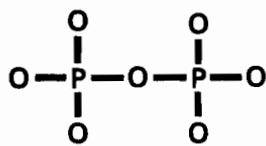
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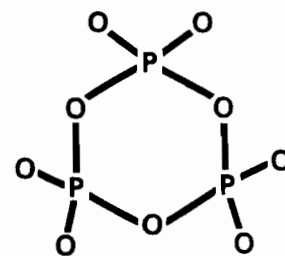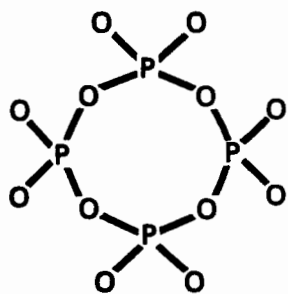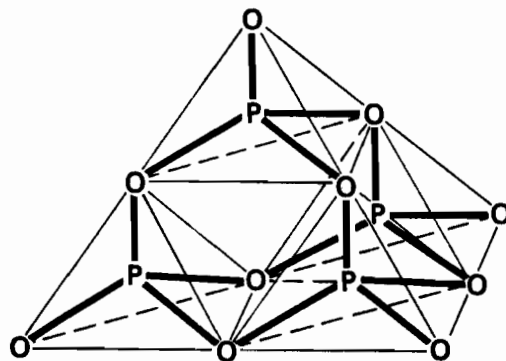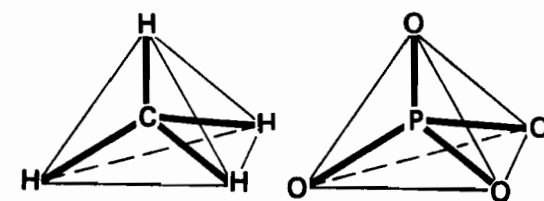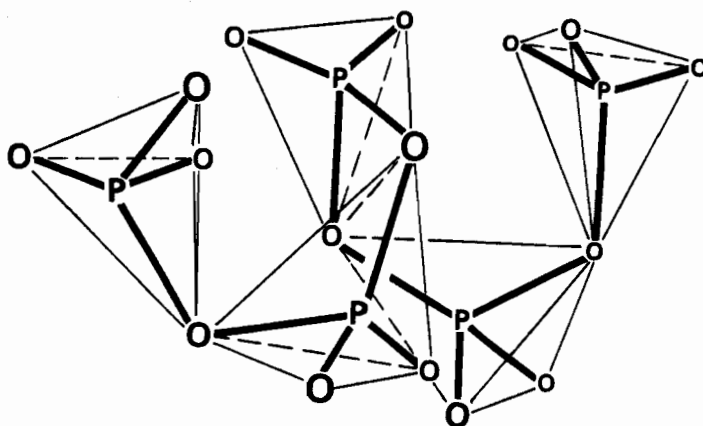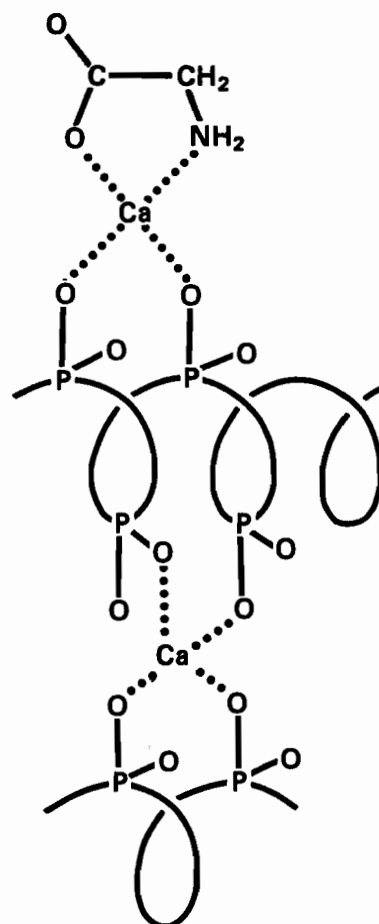
VII

VIII

PHOSPHATE STRUCTURES

Solid lines represent covalent bonds and dotted lines indicate electrostatic attraction. Bond multiplicity and electrostatic charges are not shown. Lightly drawn lines are included for stereochemical perspective.

incorporation of relatively more hydrophobic material such as carboxylic acids.   Additional inorganic polyphosphates, freshly transported from the lithosphere, could also interact and be incorporated intermittently. It is important to recognize in this conceptual model that inorganic polyphosphates have much less tendency to precipitate from seawater or brackish water than does ordinary orthophosphate [7-9].

These interactions of a macromolecular complex with its exterior chemical environment can be regarded as excitation-relaxation phenomena. The initial response to an external stimulus is the perturbing excitation, and the resulting chemical and physical transport (or transformation) is the relaxation. Excitation-relaxation properties are inherent to the structural relationships of systems at all levels of hierarchy and can be described as a system's potential for response and return to a structurally stable state when the system is subject to external stimuli. These properties are central to the excitability hypothesis and the theory of natural complexification.

Physical Justification

Structure of Polyphosphate Complexes: It should be helpful at this point to briefly review some aspects of phosphate structure. The properties of the element phosphorus are such that it would have been present in the primordial environment at an oxidation state corresponding to phosphate [7]. Orthophosphate (I) is only one form in which this phosphate would have existed, because several condensed forms (i.e., dimers, trimers, and polymers) are also possible. The simplest condensed form is pyrophosphate (II). Inorganic polyphosphates of greater chain length (III) are condensed forms with serially arranged pyrophosphate bonds (i.e., POP linkages). Metaphosphates are cyclic compounds that have at least three pyrophosphate bonds (IVa). The ultraphosphates are condensed structures in which individual phosphate groups are linked to three other phosphate groups by pyrophosphate bonds. The one most relevant to the present discussion is the symmetrically shaped phosphorus pentoxide (V).

The arrangement of oxygen atoms attached to phosphorus in a phosphate group is tetrahedral, i.e., their positions are similar to those of hydrogen atoms in methane. As a consequence of this geometric arrangement (VI), inorganic polyphosphates can assume a helical shape (VII) in aqueous solution [10]. The metal cations in this solution are electrostatically attracted to polyphosphate chains and (with the exception of sodium and potassium) form crosslinking bonds with oxygen atoms of two or more chains. In this way, high-molecular-weight macromolecules are built up, involving several polyphosphate chains and many cations [6]. Other anions and any molecules (e.g., amino acids, sugars, carboxylate anions) capable of forming similar types of bonds with metal cations can also participate in these macromolecules (VIII).

Generation of Condensed Phosphates: Griffith et al. [7] have described some ways in which condensed phosphates could have been generated during the early Precambrian. For example, phosphorus pentoxide (V) vaporizes from all calcium orthophosphates above 1350°C. On the primordial earth, volcanic outgassing of phosphate-containing magma [11]--or lightning that struck outcroppings of igneous phosphate minerals [7,12]--would have produced phosphorus pentoxide vapor.   This symmetrical molecule is rapidly hydrolyzed in water to tetrametaphosphate (IVb), which then slowly produces tetrapoly-, tripoly-, and pyrophosphate. Yamanaka et al. [13] have recently reported the detection of tripolyphosphate and pyrophosphate in the aqueous condensate of volcanic gases, presumably generated via this mechanism. In the lithosphere, the contact of acidic sulfates or sulfur trioxide with phosphate-containing magmas could also have generated condensed phosphates. Another possibility is the reduction of metal phosphates by carbon monoxide (e.g., $2FePO_4 + CO \longrightarrow Fe_2P_2O_7 + CO_2$).   Further polymerization to polyphosphate chains would have depended primarily on removal of the metal as a volatile carbonyl or an insoluble sulfide.

Evidence for Primordial Occurrence: As supporting evidence for the localized occurrence of primordial condensed phosphates, Griffith et al. [7] cite two examples. First, several deposits of sodium dihydrogen phosphate, NaH_2PO_4, in the western United States [14] are very likely the hydrolytic degradation product of condensed phosphates. Any other explanation for the presence

of these deposits cannot be chemically substantiated. The other example is the occurrence of two minerals, metalomonosovite and lomonosovite, in granitic pegmatites from the Lovozero Massif, located on the Kola Peninsula where igneous rocks have been dated as solidifying 3.6 billion years ago [15]. These two minerals have composition formulas that indicate condensed phosphates [16,17]. Two other minerals, brushite and monitite, are cited as prime candidates to have been derived from condensed phosphates, if they had been associated with igneous deposits [7]. Finally, the reported detection of condensed phosphates in the aqueous condensate of contemporary volcanic gases [13] is indicative of their occurrence during primordial volcanic outgassing.

Rouse et al. [18] have reported the identification of a naturally occurring, condensed phosphate mineral, canaphite. This mineral had previously been misidentified as an orthophosphate until it was found to be identical with a synthetic pyrophosphate mineral, alpha-$CaNa_2P_2O_7 \cdot 4H_2O$. Although this sample of canaphite was not collected from an ancient igneous deposit, it is reported to have an apparently abiotic origin. Rouse et al. [18] state that the identification of this pyrophosphate mineral contradicts the widely held view (among geochemists) that "all naturally occurring phosphates are monophosphates because the POP bond of the condensed phosphates is readily hydrolyzed by water [19, p. 15A1]." This view, moreover, is not consistent with the observed slow rate of pyrophosphate hydrolysis in water [7,20] and, in any case, would not apply to igneous minerals formed under hypohydrous or anhydrous conditions.

Initially, canaphite had been reported to have the composition formula $CaNa_2H_2(PO_4)_2 \cdot 3H_2O$. Griffith [11] has noted that a similar mineral is found in the granitic pegmatites of Branchville, Connecticut [21]. Its composition formula is reported to be $Mn_5H_2(PO_4)_4 \cdot 4H_2O$. When inorganic phosphates of similar composition are heated, they yield condensed phosphates [22]. If the composition formula of this latter mineral is correct as reported, it is reasonable to assume that the source had contained condensed phosphates and that they may have degraded before solidification. Although this mineral too is not from the early Precambrian period, its occurrence indicates that minerals of this type can be present during the formation of granite.

Biological Relevance

There is also biochemical evidence supporting the validity of this origin-of-life scenario. Inorganic polyphosphates of widely varying chain length are present and metabolically active in contemporary organisms [5,23-26], and enzymatic activity for both short-chain and long-chain phosphate polymers has been detected throughout the biosphere [5,23-28]. Regarding their role as template and condensing agent for the formation of prebiotic organic polymers, the reaction of inorganic polyphosphates with an aqueous solution of amino acids has been demonstrated to yield peptides [3,13,29-31]. Furthermore, the ability of metal cations in a polyphosphate complex to scavenge organic molecules from water would have allowed the juxtapositioning of primordial monomers in the complex before polymerization took place [1,3]. (This scavenging, incidentally, is one of the properties that made polyphosphates useful in heavy-duty washing formulations).

Calcium has been observed to become bonded as an external cation to helical coils of inorganic polyphosphate chains in water [10]. Although calcium forms somewhat unstable complexes with amino acids [32,33], it can selectively complex with ribose from an aqueous mixture of pentoses [34-36], and preferentially complex with cytidine from an aqueous mixture of ribonucleosides [37]. In addition, polyphosphates can yield considerable energy for dehydration-type polymerizations of other molecules, but they are unique among poly(oxyanions) in their slow rate of uncatalyzed hydrolysis [7]. For example, pyrophosphate bonds have an aqueous half-life of about 2,000 years [7,20], a value intermediate between those of geochemical and biochemical transformations.

These biologically and geologically extant condensed phosphates have the appropriate chemical and physical properties to form complexes (with metal cations and organic monomers) that will respond to their chemical environment in a way that produces structures with increased

complexity of form. Functionally, these macromolecular complexes incorporate--and chemically transform--the organic and inorganic mass and energy of their environment. As their structural complexity increased, this functional capability could also have become more developed. Through such activitiy, some of these mixed organic-inorganic complexes would have increased the time during which they were able to interact with their environment without disruption.

There are, however, environmental factors (such as acidity, monomer concentration, and interfacial tension) that limit the size of organic-inorganic complexes in aqueous media. These factors have been studied for systems with many different types of components [40]. When size limitations are exceeded, disruptions of the complexes can occur with either subsequent formation of small fragments or complete dissolution of components into the medium. The small fragments can now, of course, restructuralize and include other materials from the aqueous medium. In fact, it is inherent within a population of these macromolecular complexes that some heterogeneity of components and spatial arrangement should accrue, and subpopulations with varying capability to respond to the environment by achieving near-equilibrium with it would be inevitable. The survival of a particular subpopulation would depend on how it responds to potentially disruptive external stimuli.

Matheja and Degens [41] have previously hypothesized that polyphosphates were not important to the origin of prebiotic organic polymers, because phosphoric anhydride bonds are described as lacking aqueous stability [19]. Nonetheless, it is this thermodynamic instability with respect to hydrolysis that would have provided the necessary energy for prebiotic polymerizations. Moreover, polyphosphates hydrolyze very slowly in the absence of a catalyst. Although they may react rapidly when subjected to the controlled action of an enyzme (or other catalyst), they are unique among poly(oxyanions) in their ability to resist rather drastic changes in the aqueous environment without sudden changes in form [7]. In other words, hydrolysis is impeded by a high activation energy that must be overcome before the thermodynamic free energy is released. These properties of the phosphoric anhydride bond--enabling it to store and transfer energy--are important to the biochemistry of contemporary living organisms, just as they would have been important to the origin of life.

GENERALIZATION OF THE CONCEPT

An argument for the hierarchical development of natural systems with structures of incrementally increasing complexity can be inferred from the interactions of polyphosphate complexes with the primordial aqueous environment. A generalization of this type is appropriate. For example, von Bertalanffy [42] proposes that, since systems in different disciplines of science have important features in common, general system theories should be constructed to address these features. In a dynamic, general system theory, such as the one presented here, the mechanisms that apply to one system of a hierarchy must also apply to systems in other positions of the hierarchy. Similarly, all transitions from one postion to another must also follow some common mechanism. In other words, the generalized steps and the language used to describe them must be the same. The purpose of presenting natural complexification as a system theory is two fold: first, to logically demonstrate that the development of complex structures throughout nature has a high probability; and, second, to relate the phenomena of physical systems to those of biosystems, because this is the only way we can trace a path from one to the other in discussing the origin of life.

This system theory also conforms to the geological principle of uniformitarianism, inasmuch as the origin of life and its evolution are certainly part of the natural history of the earth. Through application of this principle, valid extrapolations of evolutionary trends can be accomplished. Before proceeding to the argument for complexification of natural systems, a brief discussion of uniformitarianism, natural information, natural complexity, and structural dynamics is desirable. The latter three are unique to this theory and have not been presented elsewhere. Of these latter three, the first is comparable to theoretic information [43], but includes a definition for "value;" the second is a modification of ecological complexity [44] that takes account of excitation-relaxation; and the third describes the dynamics involved in a

natural system's approach to near-equilibrium with its surroundings. This discussion is then followed by the argument for stepwise complexification.

Uniformitarianism

Geological thought is presently based on the principle of uniformitarianism, i.e., that processes now operative on and in the earth should be utilized to explain the events of geologic history [45]. Uniformitarianism replaced the earlier principle of catastrophism, which was the accepted concept at the beginning of the nineteenth century. Catastrophism postulated catastrophies (not surprisingly) of great magnitude occurring at specific times in geologic history, each purportedly leading to sudden geological transformations, faunal crises, mass extinctions, etc. These catastrophies were presumed, moreover, to be due to causes not presently operative in the contemporary environment. Uniformitarianism does not deny that sudden catastrophies have occurred—and still occur—but the principle does maintain that their effects are never of comparable magnitude to processes that are taking place at slower rates over longer time spans.

Uniformitarianism further requires that a sufficiently general theory for the origin of life and its evolution must encompass both physical and biological transformations. Separate explanations for the complexity of physical and biological systems are not compatible with this principle, since the basic natural relationships that apply to geological systems must also apply to the origin and evolution of life. In addition, events of very low probability (e.g., the spontaneous formation of esters in a dilute aqueous solution of acids and alcohols) are not considered to have an overbearing consequence on major trends of evolutionary progression.

Natural Information

Natural systems are geologically open and, therefore, cannot be totally isolated from their surroundings. They are, however, differentiated from their external environment by the boundaries that essentially define them. When properties are shared between two entities or between an open system and its environment, there is obviously a potential for interaction, and such interactions of shared properties provide the means by which natural information is transmitted. Interactions between a system and entities in its external environment relate external information to the system, while interactions within the system relate internal information between its parts. The more unexpected or deviant the external interactions (from the perspective of the open system), the more potential there is in them to bring about some alteration of the system.

Assuming that the system survives the interaction, the result will: (1) render the system less capable of sustaining a repetition of the interaction, (2) render the system more capable of survival with a repetition of the interaction, or (3) leave the system's response unchanged. In Case 1, the system's internal information regarding the environment has effectively decreased; while in Case 2, the internal information has, effectively, increased. In Case 3, the information has either been transported or deflected without altering the system. Putting it another way, the more expected any external interaction becomes, the more information there is already existing within the system's internal structure. This relationship of external and internal information is similar to the transmission of information described by Shannon [46], insofar as the quantity of information in a communications signal depends on changes in the state of the waveform, i.e., the greater (more unexpected or more improbable) the change, the more information there is contained within that change.

Natural information requires an extension of Shannon's theory [43,46], however, since it introduces conditions under which the information has value to the system receiving it. (In fact, "value" is not defined in information theory, because it was considered too subjective [47].) To the systems here considered, the value of external, natural information depends on whether it alters its receptor system [2]. If the internal information of a system is increased (through incorporation or alteration brought about by information from the environment), succeeding

experiences with the same stimuli (external information) become less and less disruptive. Changes of state in an interaction (i.e., the signal) determine the amount of information present in the process, but the resultant effect of the interaction on the receptor must ultimately determine its value.

Information's value can be measured by the direction and magnitude to which the information alters the ratio of the system's excitation-relaxation response to succeeding stimuli. Thus, the more that an external stimulus induces a system's alteration to a one-to-one balance of its excitation-relaxation properties, the greater is the value of the information in the resulting interaction. In this sense, the value of the information that is used to maintain a system can be measured by how much further the excitation-relaxation ratio deviates from a system not containing this information (i.e, not having been subject to the same stimuli). The relevancy of this definition will become apparent in the discussion of structural dynamics and the argument for complexification.

Natural Complexity

The term "complexity" has generally been used to describe the assemblage of structural relationships between parts in a system; this is the way May [44] defines complexity for ecosystems. Natural complexity, however, requires that the definition also takes account of balance in the system's excitation-relaxation properties. Specifically, the more structural relationships there are that promote maintenance of a one-to-one balance in excitation-relaxation during transport (or deflection) of information, the greater the natural complexity of the system. In this context, the more different the types of internal relationships that facilitate transport or deflection, the less order there is in the system. (Order restricts the type of internal relationships and potential interactions in a system and thereby the type of information that can be transported.) Natural systems, nonetheless, are never totally "complexified" or totally ordered. Whatever the system's predominant state, there is also some degree of the other state in it.

Chaitin [48] and Wicken [49] have previously discussed the meanings of complexity, order, and organization within the context of structure. According to Chaitin [48], if internal structural relationships are expressed as a mathematical sequence, the measure of a system's complexity is the minimum algorithm required for its unambiguous specification. The order of the system, then, is its degree of internal patternedness (or repetitiveness) as measured by algorithmic compressibility. The internal relationships of complex structures (as opposed to highly ordered structures) tend to have a low degree of patternedness, and their algorithms, therefore, would be relatively incompressible. Wicken [49] looks upon the word "organization" as a term expressing function rather than structure, i.e., organizations are always for something. In this sense, both the complexified and ordered states for natural systems are organized, whereas the random state is disorganized. Rather than measuring organization in a biological system, Saunders and Ho [50] have suggested that the important parameter to be measured with regard to evolution is the complexity of this organization.

Natural complexity does not designate specific structures for a system, i.e., many possible structural arrangements can have the same complexity. In heterogeneous systems with natural boundaries, the structural parts are dissimilar with respect to their properties, and their relationships will thus be differently distributed, irrespective of the scale of the distribution. The extent of these internal relationships (i.e., the degree of the complexity) in an open system depends on its boundaries and on the amount of the external environment with which it has achieved dynamic near-equilibrium. The stepwise process by which this dynamic near-equilibrium is achieved will be described in the argument for natural complexification.

Structural Dynamics

Thermodynamics vs. Mechanics: Following the publication of Eddington's influential treatise in 1929 [51], it has generally been believed that the laws of thermodynamics predict the

universal dissipation of structural elements. This belief is based on the supposition that the concentration of energy is equivalent to "organisation of the energy [51, p. 70]," and that any extension differing from this concentration is dissipative and increases the "disorganisation or random element [51, p. 71]." This concept was inferred from the behavior of an ideal gas in a closed system; therefore, it seemed reasonable to assume an analogy between the fluid-like transport of the energy and the motion of the molecules. Accordingly, if the thermal energy (or motion of the molecules) could not be converted into useful work, the energy and the molecules themselves were considered to be disorganized or random.

There is a fundamental incongruence regarding mechanical and thermodynamic concepts of equilibrium that is relevant to the question of whether the universe is proceeding toward ultimate dissipation of its structural elements. Classical mechanics defines a system to be at equilibrium (i.e., dynamic equilibrium) when the vector sum of forces operating on its structural elements is equal to zero. Forces have direction and magnitude, and thus, when acting in concert upon the masses of structural elements in a natural system, alter the elements' positions in distinct directions and amounts. As mechanical equilibrium is approached, the alteration of relative movement decreases, and the structure of the system becomes increasingly apparent. (This does not mean, of course, that the structure is rigid or highly ordered.)

In contrast, thermodynamics defines a system to be at equilibrium when its energy has macroscopically ceased being transported and is thereby considered to be homogeneously contained. Inferentially, Eddington [51] interpreted progression toward thermodynamic equililbrium as an increasing introduction of structural randomness. However, because this randomness (or uncertainty of structure) is obviously related in an inverse manner to the positioning (i.e., complexity and order) of structural elements, the elements' relative positions would become completely uncertain at thermodynamic equilibrium. Thus, the use of a thermodynamic model as the starting point or reference in a discussion of structure is inconvenient and requires the origin of structure to be sought in far-from-equilibrium states. It should also be emphasized that thermodynamic equilibrium properly pertains to the energetics of systems which must ultimately be closed rather than to the structure of systems which are ultimately open.

Near-equilibrium of Natural Systems: Equilibrium, as it is used throughout this discourse, refers to a balanced, dynamic equilibrium rather than homogeneity. This means that if the forces of a system are balanced (i.e., the vector sum of forces acting on structural elements equals zero), and if the transport of mass and energy is balanced (i.e., the sum of their influx and efflux equals zero), the system is considered to be at equilibrium. From the perspective of mechanical theory, whenever a system is isolated, its structural elements proceed to accommodate each other through a balancing of forces within the system. By way of accomplishing this balance, individual elements interact in accordance with the forces associated with them, eventually producing equilibrium relationships that appear as the structure of a system. The number and type of these equilibrium relationships in a system depend, of course, on the number of structural elements and the inhomogeneity of their properties. As equilibrium is approached, these relationships, and hence the complexity in this system, increase as a result of this progressive balancing process.

If this isolated system were now opened, and it became stable as an open system for any length of time, the internal forces would have had to become balanced not only with each other, but also with whatever external forces to which the system was subjected. It would, therefore, be at equilibrium with its environment during this length of time. (The effect of the resulting equilibrium relationships, i.e., the structure, would be a storing by the now open system of its potential interactions with entities of the external environment.) For a natural system, however, neither time of openness nor forces to which it may be subjected (in that time) can be predetermined, so the system can at best achieve only near-equilibrium with its environment. Regardless of the extent to which the system interacts with the environment, information that is unexpected may still be approaching from beyond the system's interactive horizon.

Entropy and Natural Complexity: Information theory defines entropy as the measure of uncertainty in the outcome of an experiment [43,52]. However, unlike natural systems, most experiments are, by design of the observer, closed systems, and, unlike natural information, theoretic information does not have a defined "value." Therefore, what is meant by "the outcome of an experiment" for an open, natural system requires clarification before an entropy can be related to its complexity. In the case of an open, natural system, the "outcome of an experiment" is equivalent to the change in the excitation-relaxation ratio resulting from an external stimulus. This means that as uncertainty decreases with regard to the magnitude of this change, the informational entropy decreases. The direction of this change or outcome, however, can be either positive or negative (with respect to a system's survivability) and is irrelevant to the magnitude of change in informational entropy. For example, if an external stimulus, subsequent to the one considered, is more certain to destroy the system structure, then the informational entropy has decreased. Similarly, if a different stimulus, subsequent to the first, is more certain not to destroy the system structure, the informational entropy has likewise decreased.

As previously discussed under natural information, the resultant effect of an interaction on a receptor ultimately determines its value. This value can be measured by the direction and magnitude to which the information in an external interaction alters the system's excitation-relaxation ratio, thereby affecting its capability to survive subsequent stimuli. A positive value renders the system more capable of surviving repetitions of external stimuli and means that previous interaction effectively increased information content, structural relationships, and complexity. As information content increases, survival of the system becomes less uncertain. Therefore, if a natural entropy were defined as the measure of uncertainty in survival of an open system, then this natural entropy would decrease as the natural complexity increases.

Increases in thermodynamic entropy, on the other hand, have been interpreted as a decrease in organization of energy in systems proceeding toward equilibrium [51]. Several attempts to formulate a relationship between informational and thermodynamic entropies have been unsuccessful [47]. Again, as pointed out by Wicken [49], the term "organization" expresses function, i.e., there is a functional objective inherent within the organization. Of course, the thermodynamic objective inherent within the organization of energy is the conversion of energy to useful work (but whether anything is useful is obviously a matter of perspective). For energy to be converted to useful work from the perspective of an observer, it should be concentrated with respect to the work being done on specified objects. As the concentration decreases, the useful organization of the energy decreases and is expressed as an increase in thermodynamic entropy.

In contrast, the organization of structural relationships within a natural system has as its function the survival of the system, and thus, this organization is not necessarily related to relative concentrations of energy. As an analogy, if elements of a military unit are deployed in a tactical arrangement, energy associated with the unit would become less concentrated (assuming no augmentation). The tactical arrangement, however, could be either more or less disorganized with respect to the concentration of elements in a fortress, depending upon available information regarding potential opponents. It is the available information that determines the tactical arrangement, but the usefulness of the arrangement depends on the completeness of this information. Stated another way, the more information that exists in the unit on potential interaction with entities of its environment, the more probable is the unit's success.

THE ARGUMENT FOR COMPLEXIFICATION

The external information that impinges on natural systems has the form of interactions of mass, energy, and associated properties. As described in the discussion on natural information, a system that survives such interaction may have undergone an alteration of its structure. Thus, the result of the interaction: (1) renders the system less capable of sustaining a repetition of the interaction, (2) renders the system more capable of sustaining it, or (3) leaves the system response unchanged. In Case 1, the system's complexity and internal information (regarding

potential interaction with its environment) have decreased; while in Case 2, the complexity and internal information have increased. In Case 3, external information has been transported or deflected without a resultant alteration in system structure. In all three cases, nonetheless, the system survives, i.e., its identity remains intact. In essence, the alterations considered in these three cases did not affect the primary structure or identity of the system.

Natural systems have several levels of structure, which can be designated as primary, secondary, and higher level. When applied to polymer chemistry, this designation is used to differentiate the bonding (i.e., structural relationship) responsible for the repetitive "backbone" from the bonding responsible for macromolecular shape and surface reactivity. In such molecules, secondary structure is dependent on the prior existence of primary structure, tertiary structure on prior secondary, etc. Similar hierarchical levels of structure in other natural systems also depend on prior existence of the preceding lower levels of structure. Furthermore, disruption, restructuring, or incorporation of external entities, which occur only at secondary or higher levels, do not directly affect primary structure and hence do not affect the identity of the system.

Alterations of primary structure, which change the identity of the system, are brought about through either breakdown of the primary structure or its further structural buildup. After the primary structure has been altered, the initial system should be considered extinct, and the resulting new systems are either degenerate (following breakdown) or more complex (following structural buildup). Both primary breakdown and structural buildup occur as the result of system responses to an interactive environment, and they are similar to the results of higher level system responses heretofore described as Cases 1 and 2. They differ only insofar as their effect is evident in the primary structure (or identity) of the system.

Classification of System Response

Cases 1, 2, and 3 can be expanded to serve as a classification for essentially all system responses and ensuing events, if survival of identity is not assumed. Under this broadened classification, survival of system identity is made a subordinate condition for the now-expanded Cases 1 and 2, which are categorized further with respect to the level of structure that is affected by a response. In an expanded Case 3, distinction is made between transport and deflection. The usefulness of this formal classification lies in its provision of a general system framework in which certain responses (Case 1) lead to degenerate systems, while others (Case 2) lead to more complex ones. Relative stability with the environment is achieved when the response of the system results in either transport or deflection of the external information which initiated stimulus (Case 3).

Case 1. Primary Structure: This response initiates a structurally disintegrative event, affecting the primary structure of a system and resulting in the formation of two or more different systems, each with diminished structural complexity. The resultant new systems are separate entities, no longer bounded by the initial system's identity and degenerate with respect to its complexity. The initial system, in this sense, is extinct.

Example: Some of the chemical and physical changes in the primordial environment would have been disruptive to the primary structure of polyphosphate complexes, even with their incorporated organic oligomers. Specifically, hydrolysis of phosphoric anhydride bonds--as well as disruption in the bonding of polyphosphates with divalent cations--can be initiated by environmental acid/base changes [8,53]. In addition, some molecules with chelating capabilities are capable of removing the crosslinking cations from a complex, if they are present in sufficient concentration.
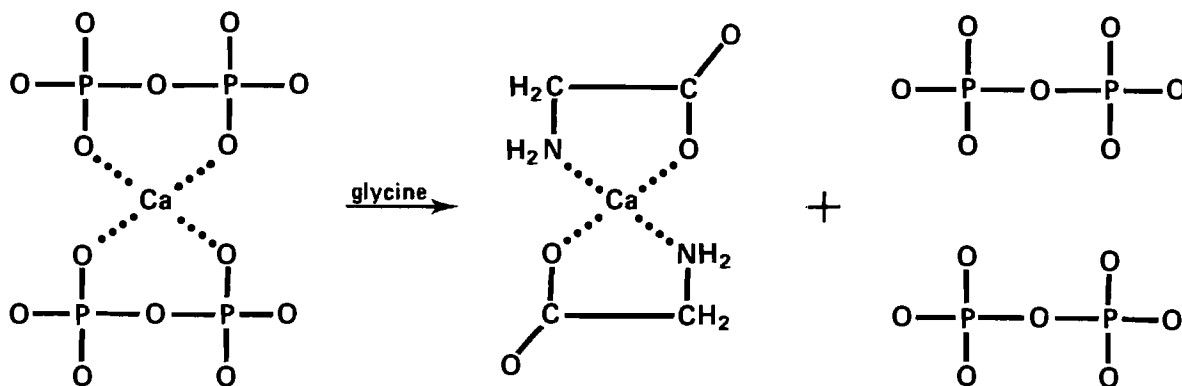
Example: It has been observed paleontologically [54] that biological speciation seems to occur at the periphery of a cross-fertilizing population's habitat. Presumably, the population is more subject to environmental stress (external stimulus) at its periphery, and newly developing biological species would have to adapt to this somewhat different subhabitat [54]. Within the context of natural complexification, the peripheral subpopulation would be not quite as balanced with its subhabitat as the main part of the population is with the majority of the habitat. Therefore, this peripheral subpopulation is much more subject to disintegrative events, which could result in its extinction. Replacement of the subpopulation by either a degenerate or more complex biosystem depends on succeeding events.

Case 1. Secondary and Higher Level Structure: This response initiates a structurally disruptive event, affecting the secondary or higher level structure but allowing survival of the initial system with diminished complexity. During this response, parts of the secondary or higher level structure may become separated from the system as individual entities. This event facilitates subsequent Case-1 or -2 responses, because it induces the system to deviate further from a balance of its excitation-relaxation properties.

Example: Breakdown of biopolymers, e.g., proteins, polysaccharides, and polynucleotides, in a living organism's digestive tract is usually initiated by disruptions in the secondary (i.e., shape) or tertiary (i.e., surface) structure, thereby allowing easier access of hydrolytic enzymes to amide and ester bonds of the primary structure. Before its ultimate hydrolysis, however, the biopolymer is still identifiable as a member of its class of chemical compounds.

Double-
Stranded
Helix

Single-
Stranded
Polymer
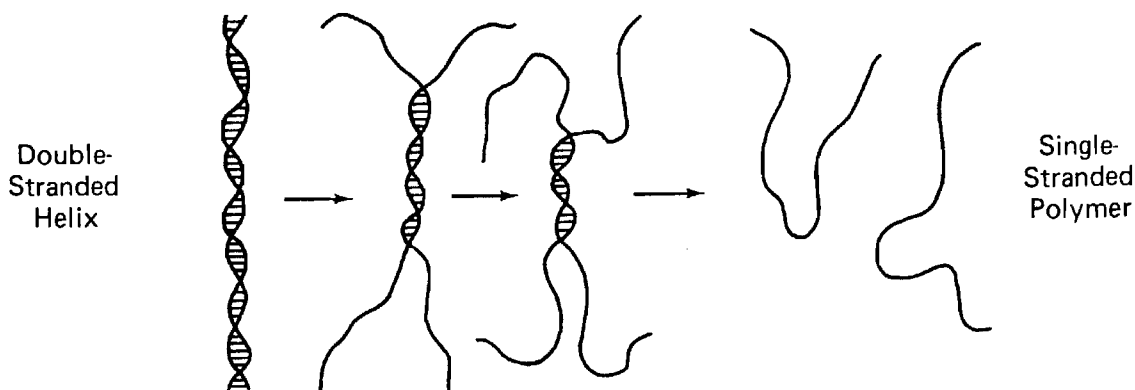
Example: Eutrophication and cultural stresses have diminished--and in some places eliminated--the spawning grounds of many fish that were present in Lake Erie 150 years ago [55]. The primary lake ecosystem has not been destroyed, but it is definitely endangered by the loss of ecological complexity and balance it previously exhibited. The streams and marshes that were serving as spawning grounds are no longer suitable for that purpose, though some have continued to develop as degenerate subsystems of the lake.

Case 2. Primary Structure: This response initiates a constructive event, combining the primary structure of one system with the structure of a second system and thereby producing a new structurally stable system that is more complex than its now extinct precursor. It is assumed, of course, that this constructive event is not accompanied by a loss of integrity in some other part of the system. Specifically, some structural increases (e.g., in mass or volume), while ostensibly increasing the primary structure of a system, may concertedly disrupt sufficient structural relationships to bring about a net decrease in complexity. As an illustration of this apparent (but not actual) exception, suspended micelles may disintegrate as their volume is increased due to an accompanying decrease in interfacial tension [40].

Example: Organic monomers were formed in the primordial environment from simpler molecules that were introduced into the earth's atmosphere and surface by volcanic outgassing. Mixtures of these molecules, i.e., water, nitrogen, carbon monoxide, carbon dioxide, sulfur dioxide, hydrogen sulfide, and hydrogen, were converted to multi-carbon compounds when exposed to primordial energy sources [3]. Within the context of natural complexification, the primordial gases collided to form larger molecular aggregates.

$$2CO + 2H_2O \longrightarrow 2HCOOH \xrightarrow{\text{energy}} H_2CO + CO_2 + H_2O$$
$$\text{formic acid} \qquad\qquad \text{formaldehyde}$$

$$\text{formaldehyde} \xrightarrow[\text{colloidal clay}]{\text{energy}} \text{monosaccharides}$$
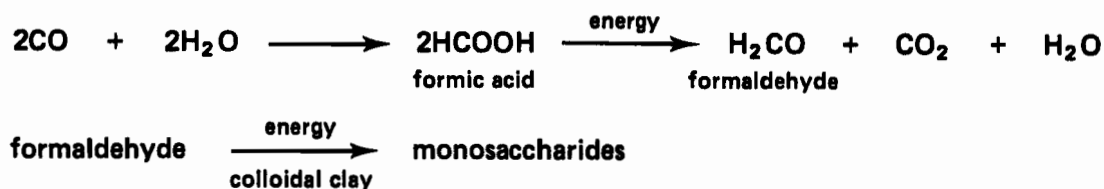
(Reference 4)

Case 2. Secondary and Higher Level Structure: This response initiates an incorporative event, occurring with changes in secondary or higher level structures of a system, but without changes in primary structure. The basic identity of the system remains unchanged, as complexity and internal information increase. This event facilitates subsequent Case-3 responses, because it induces the system to approach closer to a one-to-one balance of excitation-relaxation.

Alteration of secondary or higher level structure by incorporation of environmental information may not immediately affect the system's capability for Case-3 transport and deflection. Inevitably, however, if the information has significantly increased the number or type of structural relationships, an increase in that capability will eventually be evident. During some natural events, the incorporation of environmental information into a system may be only apparent but not actual. To illustrate, when a parasite invades a host, it may appear to be incorporated as an addition of environmental information. But unless (or until) that information is incorporated into the host as a defensive structural relationship (e.g., immunity), the invasion remains a Case-1 disruptive event.

Example: In a primordial environment, the macromolecular polyphosphate/metal-cation complexes would have incorporated organic monomers and other chemicals primarily through electrostatic attraction. Within the hypohydrous interior of the complex, peptides and other oligomers could have formed through the previously mentioned reaction of monomers with polyphosphate bonds. These peptides may have increased the capability of the complex for deflection (by adding to structural cohesiveness) or transport (by adding to catalytic activity).

glycine   +   trimetaphosphate ⟶ diglycine   +   phosphates

(Reference 29)

diglycine   +   trimetaphosphate ⟶

tetraglycine   +   hexaglycine   +   phosphates

(Reference 13)

Example: New characteristics are introduced into a biological species when the genetic material of a mutant or hybrid interacts repeatedly through reproductive back-crossing with the corresponding genetic material of its parent species. This process is used by breeders of plants and animals to improve the commercially useful characteristics of existing species. When this process occurs as a natural phenomenon, it can be looked upon as an example of phyletic gradualism, if the new characteristics are introduced homogeneously throughout the parent population over a long period of time [54]. The system, in this case, is the genetic material of the parent population, which—in a reproductive milieu—incorporates the deviant genetic material of the mutant.

Case 3. Transport: System responses associated with transport or deflection result in an unaltered structure; therefore, it is not as useful to distinguish between primary and higher level structures as it was in Cases 1 and 2. In transport, the system response initiates a sorption-emission event that (after completion) leaves system composition and structural relationships unaltered. Some structural relationships may be interrupted during the course of transport (as internal excitations occur), but structural integrity is restored through relaxation and ultimate emission of the absorbed entity (or its equivalent transformation product). Transport that involves primary structure should be regarded as a concerted buildup and breakdown (Case-2 primary plus Case-1 primary) in which system identity is ultimately restored.

The efficiency of transport depends on the system's structure. Those structures that allow the system to transport a greater amount and variety of impinging external information promote greater stability and survival. The extent to which some material systems transport external information is sometimes quantified as the system's elasticity. If a continuous impingement of information is being transported by an open system, the condition is usually described as a steady-state.

Example: In the brackish water of a primordial shoreline, a chemical change occurring at some specific site on the aqueous exterior of the polyphosphate complexes could have been transformed and transported to another site within the complex where a further chemical change would restore its near-equilibrium with the environment. Specifically, attraction of an anionic chemical species (e.g., orthophosphate anion) from the brackish

medium to a cation at the periphery of the complex could initiate successive bond-breaking and bond-making within the complex until another anion is ejected [1]. This ejection, of course, could occur at a site other than the original site of anionic-cationic interaction. Reorganization of polyphosphate chains and orthophosphate-exchange reactions have been observed in solution and in the molten state [56].
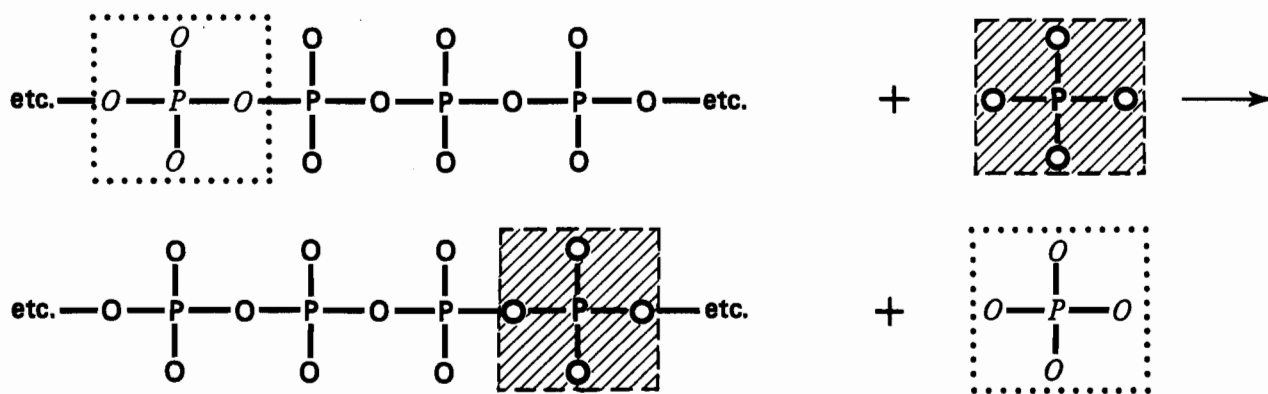
Example: Solar energy is transformed, transported, and ejected by chaparral ecosystems in the mountains of east-central California. During the growth season, solar energy accumulates in the chaparral as plant life transforms carbon dioxide and water into biomass. When seasonal climatic changes produce the hot, dry season, plant debris is ignited by the continuing solar radiation, thus releasing the accumulated energy. The burning also brings about dissemination of seeds and fertilization of the soil, which leads to new growth and renewal of the ecosystem.

Case 3.   Deflection.   This response initiates a collision-like event occurring without apparent alteration of a system's structural relationships. Deflection results essentially from the transport of external information via interaction with the system's boundary properties or its peripheral elements. A boundary property, in this sense, prevents or impedes the interaction of other parts of the system with the exterior environment, even if these properties (or the elements responsible for them) are not at the system's spatial perimeter. In both of the following examples, interactions involving boundary properties are occurring. The deflected information that is present in the interaction is actually being transported at the periphery of the system.

Example: In the water of primordial, brackish shorelines, the previously described polyphosphate complexes would have deflected external information that was being transmitted via interactions such as electrostatic repulsion or differences of hydrophobicity. As an illustration, hydrophobic groups (e.g, the aliphatic end of carboxylate anions) bonded to metal cations at the peripheral surface of the complex could impede the penetration of water molecules, thus helping to maintain a hypohydrous interior and reducing the hydrolysis of internal, structural polymers.
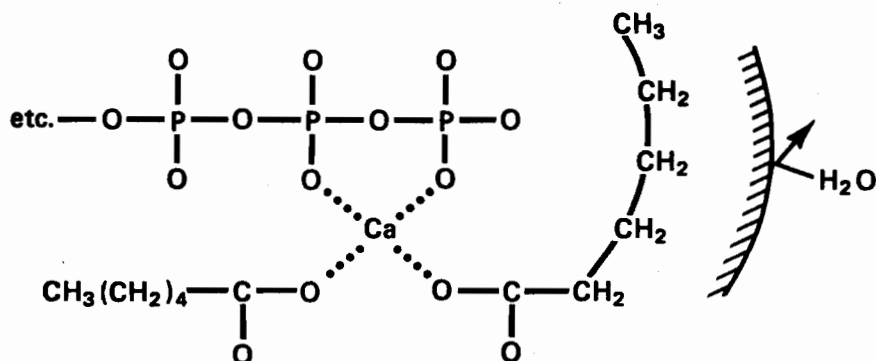
Example: Some biological populations avoid predators by displaying deceptive coloration or secreting noxious chemicals. The predator's perception of this coloration or secretion is received as a recognition of danger, and ultimately results in avoidance of contact between predator and prey.

Stepwise Complexification

In the discussion on structural dynamics, it was pointed out that despite the extent to which the system interacts with its environment, information that is unexpected may still be approaching from beyond the system's interactive horizon. The response of the system to information from beyond this interactive horizon cannot be predicted; but within the interactive horizon, the response depends on internal information regarding potential external interactions. This stored information constitutes the system's structure.

In Case 3, the system has achieved near-equilibrium with external information corresponding to its internal structural relationships. The system will continue without change until it interacts with something in its external environment that stimulates a Case-1 or Case-2 response. If the events ensuing from this response affect only secondary or higher level structure, the system will survive.

In a Case-1 secondary disruption, the system is adversely affected, but it can be rebuilt via Case-2 incorporation. The incorporation, however, may introduce different relationships into the secondary or higher level structure. External information, of course, can also be incorporated into some systems without adverse disruption. In fact, a system with the capability to incorporate large amounts of external information (without disruption of its identity) will achieve near-equilibrium with a correspondingly large amount of the external environment. Biosystems with this capability should be regarded as very successful and highly adaptable. Moreover, biosystems with the capability to increase their interactive horizon—and thus increase the potential for incorporation—should be considered even more successful.

Case-1 or Case-2 extinction of a system results from interactions of the primary structure with external information that has newly entered the interactive horizon. In Case 1, the resultant systems are degenerate with respect to the initial system's complexity and information content. Subsequent new stimuli could bring about further primary disintegration, but other system responses may occur as well. In Case 2, the resultant system is more complex. This latter system has surpassed its predecessors in primary complexity and information content, and thereafter should be capable of achieving near-equilibrium with more of the exterior environment via Case-2 incorporation.

There is, obviously, a high probability for succeeding steps of Case-2, primary structural buildup to produce new systems of incrementally increasing complexity (despite interspersal with

other system responses). Also obvious is the high probability for succeeding steps of Case-1 primary disintegration to produce new systems of incrementally decreasing complexity. The result of these stepwise events is: (1) the development and survival of increasingly complex systems, and (2) the degeneration and extinction of systems that have experienced a decreasing complexity.

From another perspective, systems with a structural complexity tending to facilitate a one-to-one balance of excitation-relaxation, will tend to transport or deflect external information. Conversely, lack of balance in excitation-relaxation with respect to impinging information will result in either incorporation of information or disruption of the system. If the primary structure becomes disintegrated, its parts may converge to form a new structure that could also encompass additional parts from the environment. These multiple events result in: (1) the development and survival of structures tending to facilitate balance in their system's excitation-relaxation and (2) the degeneration and extinction of structures tending to destabilize their system's excitation-relaxation.

COMPLEXIFICATION AS AN EVOLUTIONARY PRINCIPLE

The process that has been described is a general one, applicable to all considered systems. Simply stated as a principle: the structural complexity of successive, evolving natural systems ultimately increases in response to (a large amount of) impinging external information until additional information is transported or deflected, at which time the excitation-relaxation properties are near balance at a ratio approaching one. Conversely, the structural complexity of successive, degenerating systems decreases in response to impinging external information until their boundary conditions become irrelevant. As a corollary, systems that transport or deflect essentially all information within their interactive horizon can exhibit great stability in the evolutionary process until something unexpected appears from beyond that horizon.

The application of this principle to natural systems requires correspondence between systems and environment, e.g., an event affecting molecular systems requires stimulus on a molecular level (or lower) for interaction to occur. As can be expected, events affecting individual entities in a population group occur on a broader scale, corresponding to the systems (and subsystems) of which the individual entities are composed. The population itself would be affected, in addition, by events of still larger scale, corresponding to its habitat. Those natural systems that do not seem to be interacting with their environment are, in fact, deflecting it, i.e., they are operating with a Case-3 response. This latter statement is intended, of course, to describe environmental interactions of the germlines of multicellular organisms.

DISCUSSION

What Does It Do?

The foregoing theory places the interaction of a natural system with its environment into the simple framework of Cases 1, 2, and 3, i.e., a negative, positive, or neutral response involving specific levels of the system's structure. As a consequence of these interactions, some systems become more complex, while others appear static and still others degenerate. This is a general and inevitable development, which contradicts predictions of random structural dissipation improperly inferred from thermodynamics. Since natural complexification is derived from the excitability hypothesis, the two are obviously consistent with each other and, insofar as the theory can generally be applied to open, natural systems, the argument in which it is presented provides a mechanism that relates evolution in the biosphere to developmental changes in other natural systems.

Natural complexification relates the evolution of natural systems to their progress in acquiring information (stored as structure) on potential interactions with the environment, but it does not predict specific form or structure. Both the alteration and stability of systems undergoing natural complexification can be discussed in terms of the system's approach to a dynamic near-equilibrium; far-from-equilibrium states would be considered only when discussing

transitional populations. The theory, furthermore, regards life as an inevitable development in the history of the earth.

Where Does It Fit Into Origin-of-Life Theories?

Explanations for the origin of life have been grouped by Keosian [57] into five categories which were designated: special creation, vitalism, panspermia, mechanism, and materialism. The first one denies any natural origin for life, and the next two actually avoid explanation for this origin. "Mechanist" theories contend that, although the activities and properties of life are derived from natural laws, "the first living thing was a macromolecule...formed by chance coming together of the elements that composed it in the proper proportions and arrangements [57, p. 2]." (Within the present discussion, however, a "chance coming together" is not regarded as a mechanism for system interaction.) Materialism also affirms natural laws but attributes the origin and evolution of life to successive steps of increasing complexity, inevitably leading to contemporary forms.   The essential difference between the "mechanist" and materialist viewpoints is whether the origin of life was an event of low probability or high probability. Most current explanations for the origin of life are based on the latter two viewpoints.

Oparin-Haldane Hypothesis: According to Oparin [58] and Haldane [59], solar radiation, as well as other primordial sources of energy, induced the synthesis of organic compounds from the simpler molecules of an early atmosphere that contained little or no molecular oxygen [3]. The organic compounds then served as the material from which life arose through successive steps, involving the formation of polymers that were the precursors of proteins and nucleic acids. This hypothesis is the cornerstone of modern theories on the origin of life, but it recently has fallen on hard times.   Shapiro [60] points out that the weakly reducing or redox-neutral gaseous mixtures, now thought to mimic the primordial atmosphere, fail to yield under experimentation a sufficient amount of organic material to ensure formation of macromolecules in a primitive sea. In other words, the "primordial soup-of-the-day" is a very thin broth of inorganic salts without much organic content.

In the scenario from which natural complexification was derived, large amounts of organic monomers need not be present to induce the formation of protobiotic polymers.   Inorganic polyphosphates naturally complex with calcium cations of seawater or brackish environments [10], and these cations will complex further with amino acids [32, 33] and other monomers such as ribose [36] and ribonucleosides [37]. This scavenging of the primordial aqueous environment could easily have occurred before the initiation of polymerization within this macromolecular complex [1,3]. A very dilute "primordial soup" would have been sufficient for this scenario, and thus, there may not be any need to discard the Oparin-Haldane hypothesis.

Self-Organization: This is a "mechanist" hypothesis, attributable to Eigen and his coworkers [61,62] and to Nicolis and Prigogine [63]. It was conceived within the consensus of opinion, held until recently, that an abundant amount of organic material had existed on the prebiotic earth.   As a "mechanist" hypothesis (based on thermodynamic modeling), it was assumed that the formation of the first protobiotic macromolecule was a spontaneous event, the low probability of which was mitigated by the abundance of organic monomers thought to be available in the primitive seas. Since the amount formed of this macromolecule would have been exceedingly small, it was proposed that "a biopolymer having a direct evolutionary significance must be a part of an autocatalytic cycle that enhances the rate of synthesis of the polymers invovled [63, p. 430]." When introducing this origin-of-life hypothesis, Eigen [61, p. 465] states: "Such a system may be compared to a closed loop. Although it is evident that the line from which the loop is formed must have originated somewhere, the starting point will have lost all its importance as soon as the circle is closed."

Notwithstanding diminution of cause-and-effect, this is a proposal for the exceedingly improbable, direct formation and persistence in an aqueous medium of a polyamide or polyester, i.e., a polypeptide or polynucleotide, that generates more of itself by catalyzing the polymerization of so-called "active monomers [63, p. 430]." As stated, this polymerization requires (at minimum) an unexplained source of chemical energy to produce these "active monomers." Laboratory experiments, conducted to study self-organization, have always been

carried out with added "active monomers," e.g., nucleoside triphosphates [62], or added xenobiotic polymerization agents, e.g., carbodiimides [64], presumably supplied from that now-defunct abundance of organic material in the primitive seas. Self-organization theory has never addressed the primary questions of biochemical origins. Specifically, how and with what did it all start? What was the source of chemical energy for polymerization, and how did the protobiotic polymers achieve any amount of stability in a hydrolyzing medium?

In contrast, the scenario from which natural complexification was derived offers a reasonable alternative to the very low-probability, spontaneous formation of organic polymers purported to occur by self-organization. Within this scenario, the energy for formation of the amide or ester bonds is provided by the phosphoric anhydride bonds of the inorganic polyphosphates that have been transported from the lithosphere. The cations of the brackish water that are bound to the inorganic polyphosphates slowly select organic monomers from a dilute, brackish solution. The interactions involved would have been similar to those that occur in ion exchange columns. (Thilo [65] has observed that polyphosphates in aqueous solution exhibit the same type of complexing behavior as do ion-exchange resins.) Polymerization of the organic monomers could have been initiated by any external interaction capable of inducing ionic bond-breaking of a phosphoric anhydride. Stability of the resulting polyamides or polyesters would have been enhanced by the hypohydrous environment generated within the interior of this macromolecular complex. Possible formation of an autocatalytic system in the primordial (or later) environment is not prohibited by the polyphosphate scenario, but its exceedingly improbable, spontaneous appearance is not required.

RNA World: This hypothesis was first discussed by Crick [66], Orgel [67], and Woese [68]. In it, they proposed that RNA was the initial biopolymer, responsible for further biological development. The catalytic functioning of this primordial RNA was envisioned as increasing with the incorporation of bits of protein (or peptides) until that activity was assumed by enzymes. Primordial DNA would have arisen later as a molecule specializing in the preservation of identity. Acceptance of this hypothesis has been strongly supported by the discovery that RNA can indeed function as a catalyst [69,70]. The weakest point in the RNA-world hypothesis has been lack of a plausible scenario for origin of the RNA itself. Now, however, this lack can be satisfied to an appreciable extent by the polyphosphate scenario.

Sodium, calcium, magnesium, and potassium are the principal cations of seawater [71]. Of these four, calcium becomes bound as an external cation to helical coils of polyphosphate in solution [10]. Calcium, in turn, is very selective toward organic compounds, forming complexes with ribose that are uniquely more stable than those with most other monomers [34-37]. (Of the sugars, only talose forms complexes with calcium of comparable stability.) These observations on the stability of calcium complexes with monosaccharides were initially reported in 1961 by Mills [34]. In some experiments I conducted at NASA Ames Research Center (1975-1976), I observed that calcium also forms stronger complexes with cytosine and cytidine than it does with other RNA bases and nucleosides [37]. Considering these preferential affinities, it is reasonable to propose that a polyphosphate complex, incorporating ribose and cytosine (or perhaps cytidine), led to the formation of oligonucleotides via condensation reactions resembling those that produce peptides from amino acids [13,29-31].

Several objections to the RNA-world hypothesis can be countered by this polyphosphate scenario. Specifically, these are the objections that have raised questions regarding: (1) source of energy for polymerization, (2) nature of a likely template, (3) selection of monomers from a primitive sea, (4) mechanism for maintaining stereoselectivity during chain elongation, (5) protection of oligonucleotides from subsequent hydrolysis, and (6) development of further complexity involving other RNA bases. Plausible answers corresponding to these questions are: (1) reaction with the phosphoric anhydride bond, (2) complex formation on the polyphosphate helix, (3) selection of ribose, cytosine or cytidine via bonding with calcium cations, (4) stereoselection in the complexing of these monomers by metal cations of the complex, (5) generation of a hypohydrous environment within the macromolecular polyphosphate complex, and (6) incorporation of other monomers according to their concentration in the environment and their relative affinities for metal cations of the complex.

Of these, the stereoselective complexing of monomers by metal cations deserves further explanation. Individual metal cations are observed to form complexes in solution with molecules preferentially of the same chirality [72]. For example, a partial resolution of racemic mixtures of organic acids can be obtained by selective chiral binding [73]. This behavior of metal cations with chiral organic molecules is a general characteristic, including the formation of mixed complexes with more than one type of organic molecule and more than a single cation as a complexing center. Basolo [72] states that "the presence of two or three optically active chelate groups...tends to fix a definite configuration upon the complex as a whole, and limits the number of stereoisomers which can be isolated to a small fraction of those theoretically possible [72, p. 315]." Ribose and its nucleosides are, of course, chiral molecules, and polyphosphate helices are obviously so. Although complexes of calcium with polyphosphates and sugars may not be sufficiently stable for physical isolation, nuclear-magnetic-resonance studies of alkaline-earth complexes in water indicate binding in distinct positions on the cation [35,74], which should thereby promote perpetuation of a particular chirality as further complexing proceeds. This selection of a particular chirality would be passed on to the resulting oligonucleotide.

Xenobiotic Theories: There are several current theories on the origin of life that are based on substances foreign to living things, i.e., there is no evidence that these substances are normally present in living organisms. If a specific substance were to have taken part in the formation of the first living organisms, it should be expected that it would still be present in the contemporary biosphere, even if its functional role had changed through evolution and its presence were only vestigially evident. This proposition is consistent with both biological theory and geological uniformitarianism. Yet, these xenobiotic theories continue to be investigated. Two of them are discussed here; more have been skeptically reviewed by Shapiro [60].

The most familiar xenobiotic theory is the proteinoid microsphere theory of Fox [75,76]. Note that this substance is not a protein [77] and is for this reason called "proteinoid." The polyamide chains in proteinoids are crosslinked due to the bonding contribution of their trifunctional amino acids (such as lysine), which are used for their laboratory preparation [60,78]. Cyclic structures are also present in these thermally generated polymers [77]. In a review of a recent book by Fox [79], Brack [80] complains that "when heating a mixture of selected L-amino acids, one gets a polycondensate which is about 50 percent peptidic, the peptide fraction is racemized, the peptide linkages are ambiguous since they include alpha, beta, and gamma functions, and the sequences are multiple although not completely random [80, p.78]."

The formation of proteinoids in the primordial environment would have required concentrated mixtures of amino acids located near sources of heat. Not surprisingly, an exhaustive search of the literature on transport of organic compounds in soils [81] revealed no abiotic mechanisms which would permit sufficient concentration of amino acids to produce these polymers. On the contrary, amino acids are mobile in the environment [82,83] and would resist the prebiotic accumulation necessary for the formation of proteinoids. Shapiro [60] has criticized reports that attribute "life-like" properties to proteinoid microspheres, because these stated properties can also be observed with microscopic particles of many other substances.

A similar objection can be raised against the primeval clay organisms of Cairns-Smith [84]. Shapiro [85] maintains that "if clay-based organisms ever existed, they should be present today. They are not competing with modern organisms for the same materials, so their extinction should not be expected. Further, the processes they use should be demonstrable in the lab [85, p. 41]." It has been postulated by Cairns-Smith [84] that primeval clay organisms incorporated organic molecules into the clay structure, and the resultant organic aluminosilicates eventually mutated to organic-based organisms. If this evolutionary progression were valid, some vestigial clay structure or biochemical activity related to organic aluminosilicates should still be discernible in contemporary living things. However, no structural supporting system in contemporary organisms is based on aluminosilicates nor does any biochemical activity appear to be associated with them. For many years, evidence for the biodegradation of poly(dimethylsiloxanes) has been sought by industrial scientists [86]. These compounds, which can be considered a reasonable facsimile for organic aluminosilicates, have proven to be inert to degradation by all organisms tested.

Excitability Hypothesis: The most striking evolutionary trend in multiorgan systems, invertebrates as well as vertebrates, is the tendency toward cephalization. This tendency toward increasing development of a central nervous system indicates some impetus toward increasing biological excitability as evolution proceeds. Within the context of uniformitarianism, a general evolutionary trend of this type should be amenable to extrapolation, i.e., if this trend toward increasing excitation-relaxation activity is significant in biological evolution, then it should have been significant in the origin of life and in the interactions of chemical systems preceding that origin.   As discussed under the argument for natural complexification, this incrementally increasing excitation-relaxation activity allows systems to approach closer to dynamic near-equilibrium with increasing amounts of their environment.

It was this evolutionary trend toward increasing excitation-relaxation activity--plus the similarity in chemical properties of a macromolecular polyphosphate complex to a viable neuronal membrane [39]--that led me to the ideas of the excitability hypothesis. I proposed in 1965 [1] that the excitation-relaxation activity of macromolecular polyphosphate complexes in a primordial brackish environment was responsible for the polymerization of organic monomers that had become part of the complex through bonding with its cations.   The increasing complexity of structure (brought about by polymerization of these monomers) allowed the complexes to transport (or transform) a larger amount and variety of interactions with their external environment, thereby facilitating a closer approach to dynamic near-equilibrium with it. Chemical and physical constraints [40] on the size of these complexes (as well as disruptive external interactions) would have resulted, however, in successive disruption and restructuring. Those complexes exhibiting greater transport or deflection in their interactions with the brackish environment would have had greater stability and duration in it.   The excitation-relaxation phenomena of these complexes were discussed in terms of chemical similarity to the excitability of biological membranes [1].

This is the materialist hypothesis from which I have now derived the theory of natural complexification.   In this hypothesis, the formation of prebiotic polymers and macromolecular structures therefrom proceeds in an inevitable stepwise fashion.   The commencement of this process is designated to be the transport of inorganic polyphosphates from the lithosphere to the brackish shorelines of large bodies of water.   It is assumed, through the Oparin-Haldane hypothesis, that low concentrations of organic monomers were present.   This process can be described as stepwise interactions of open, natural systems with their exterior environment.

Inorganic polyphosphates are naturally occurring biochemical substances. They have been isolated and identified in microorganisms [23-26], plants [87-89], and higher animals [5,25,27,90]. They were probably present in the primordial environment, as evidenced by the identification of early Precambrian, igneous minerals with composition formulas indicating condensed phosphates [7]. They have also been identified in the aqueous condensate of volcanic gases [13]. They are the only contemporary biopolymers for which there is any evidence of occurrence on earth before the origin of life. Polyphosphates are still present in the marine environment [91], but it may be difficult to distinguish between transport from the lithosphere, biological decay, and industrial production as their source. Although their biochemistry and physiological function are not as well-established as they are for other biopolymers [92], inorganic polyphosphates have been demonstrated to be important for active transport of glucose across yeast cell membranes [23,24].   Moreover, their neurochemistry has been investigated [5,27] as well as their possible involvement in RNA metabolism [93,94]. The Russian biochemist Kulaev has written a book on microbial inorganic polyphosphates [25], as most research in that area has appeared in the Russian literature.

Where Does It Fit Into Biological Theory?

The argument for natural complexification can be used to interpret certain biological observations germane to evolution.   This interpretation is desirable, because it provides a mechanism for these observations that is related to the behavior of natural physical systems. Until now, evolution has not been successfully related to the theories of physical science and, in

the absence of a mechanistic relationship, it is possible to argue that life on earth is an anomaly in the physical universe. With related mechanisms, however, the events of evolution become integrable parts of the progressive changes observed to occur on this planet. This is where a new theory, such as natural complexification, can be helpful, because it is, after all, derived from physical science.

Within the argument for this theory, natural selection would be interpreted as the adjustment of cross-fertilizing populations to near-equilibrium with their environment via the extinction of subpopulations most distant from that near-equilibrium. It follows that adjustments which allow a system, i.e., cross-fertilizing population, to become more capable of surviving repeated external interactions would promote stability. The familiar term "fittest," in this sense, becomes synonymous with "most stable" or "closest to near-equilibrium."

The advantage of interpreting natural selection in this manner is that it then becomes related to the behavior of physical systems. This generalized behavior is much more difficult for opponents of evolution to dispute, and it also provides continuity of transformation from physical to biological systems. Natural complexification is proposed not as an alternative to natural selection but as a means for its mechanistic description within a common framework of natural phenomena.

Species Stability: It has been observed by Eldridge and Gould [95], Stanley [96], and Vrba [97] that species stability appears to be a general condition within biological evolution. Natural complexification explains this stability by considering a species to be a natural system that has achieved dynamic near-equilibrium with its environment. It will remain stable for as along a time as it can transport or deflect impinging natural information. A species that is increasing its range, or increasing its biomass, could be looked upon as incorporating natural information (Case 2, secondary or higher level structure), if the system's boundaries include ecological considerations as well as taxonomic ones. Incorporation could cease at some point and be replaced by steady-state transport or deflection (Case 3), speciation in a subpopulation to produce a new system (Case 2, primary structure), or system disruption (Case 1).

In their theory of punctuated equilibria, Eldridge and Gould [54,95] postulate three possible responses of a species or ecosystem to environmental change: (1) adaptive accommodation, (2) extinction, or (3) simply moving on. In the terminology of natural complexification, adaptive accommodation is identified with Case-1 and -2 events involving secondary or higher level structure; extinction is identified with Case-1 and -2 events involving primary structure; and "simply moving on" is identified with Case-3 deflection. A stable, unchanging ecological situation is, of course, identified with Case-3 transport. Speciation itself would occur as the result of a cross-fertilizing population (or subpopulation) undergoing Case-1 disintegration, Case-2 structuralization, or both events concertedly. Rare examples of gradual lineage transformation, which generally involve size increase or simple phenotypic variation [95,96], can be identified with Case-2 (secondary or higher level) incorporation.

Species Mutability: The susceptibility of single-cell organisms and plants to environmental mutagens is well-known and noncontroversial. However, the germlines of the remaining biosphere are generally considered inviolable with respect to external influence on mutation. If this situation should prevail, it places the germlines of multicellular organisms in a unique position among natural systems of this planet. The germlines would constitute a class of systems that interact with their environment only via complete deflection of external information (Case 3) or total destruction of the system (Case 1, primary). Within the germline, mutations could perhaps be regarded as adjustments of molecular systems approaching near-equilibrium with each other. Their initial condition in the germline would be an effect of some prior condition that would have had its own beginning in still more distant conditions, undoubtedly attributable to the origin of that particular species. From the perspective of natural complexification, most interactions of a species germline with its environment should be expected to result in the deflection of impinging information. Clearly, the germline must exhibit some near-equilibrium stability (externally as well as internally) for the species to survive.

Biological Complexity: May [44] has noted that, in nature, the stability of a species population is typically greater in structurally complex communities than in simple ones. This observation is consistent with the present argument and with the discussion of natural complexity given earlier. Specifically, as an ecosystem becomes more complex in its internal structure, it becomes more capable of transporting (or deflecting) a greater variety of external information. Of course, this type of response provides the ecosystem with greater stability. It follows that an individual species population, well integrated into the ecosystem, also benefits.

Saunders and Ho [50,98]—as well as others [41,99,100]—have attempted to develop the concept of biological complexity directly from Shannon's information theory. In doing so, the "value" of biological information is only implied (though ambiguously), because—in Shannon's theory—"value" is explicitly left undefined [43,47]. For example, Matheja and Degens [41] refer to the input of "favorable information" when discussing survival of primitive organisms. However, if there really were no definable "value" in the information of biosystems, then having more or less of it should not affect evolutionary status or the outcome of interactions between system and environment. Yet, in these biological applications of Shannon's theory, acquiring more information is always regarded as a measure of evolutionary progression, both in status and prospect for survival. A more fruitful approach to biological complexity should be provided by regarding it as an example of natural complexity, since "value" would no longer be implied but could be measured by the effect of natural information on a biosystem's excitation-relaxation properties.

What Does It Predict?

As a dynamic system theory, applicable to both geochemical and biological systems, natural complexification predicts or is consistent with the following:
1) Complex biosystems will inevitably evolve on earth-like planets, assuming that the geochemical systems are similar in composition and duration to those on the earth's surface.
2) The geochemical systems responsible for the polymerization of primordial organic monomers are the macromolecular polyphosphate complexes formed in brackish water.
3) Both geochemical and biological systems are affected by the process of natural complexification, though not all will evolve to systems of greater complexity. Some will appear static; some will degenerate; and others will become extinct.
4) Geochemical systems and biological species that are very close to being at dynamic near-equilibrium with their environment can exhibit stability and have a long-term duration in it.
5) Individuals and populations with the capacity to incorporate further amounts of external information (without affecting their primary structural identity) will seek to increase their interactive horizon through exploration, research, or expansion of habitat.

How Can It Be Tested?

As temporal events in the earth's history, the origin of life and its evolution cannot be duplicated with certainty; but many parts of the excitability hypothesis are, nonetheless, amenable to investigation. Some proposals for testing, ranging from geochemical to biochemical approaches, are presented here.

Geochemical: In the excitability hypothesis, condensed phosphates are critical as template and polymerizing agent for organic monomers. Surveying the composition formulas of reported minerals may uncover some condensed phosphates, such as canaphite [18], that have been misidentified or not identified beyond composition. The minerals cited by Griffith [11] are examples. The two collected from early Precambrian deposits are especially interesting. The identification by Yamanaka et al. [13] of condensed phosphates in aqueous condensate from

volcanoes should be corroborated and investigated for generality. In this context, rapidly cooled, solid material from recently erupted volcanoes could also contain condensed phosphates (perhaps even ultraphosphates). Several chemical reactions cited by Griffith [11] may have been responsible for the generation of condensed phosphates in primordial environments. These reactions and their significance have not been studied sufficiently.

Organic Chemical: Thus far, glycine is the only organic monomer that has been tested and converted to oligomers by polyphosphates in water [13,29-31]. However, there are also indications that cytidine may be converted to a dimer or higher combination in a similar manner [37]. Experimentation with these and other monomers under a plausible simulation of primordial conditions would test the limits of this chemical reaction. The complexes of polyphosphates and nucleosides in simulated brackish water have received only preliminary investigation [37]. Further study should be given to the structure of polyphosphate complexes and their selective affinity for organic monomers. The origin of the monomers themselves also requires renewed attention, because the chemically reducing conditions previously simulated are no longer regarded as valid.

Biochemical: The function of polyphosphates and their structural relationships with other biopolymers in contemporary living organisms may be indicative of their evolutionary role. Several microorganisms synthesize inorganic polyphosphate granules that can be isolated for structural study [26]. Since polyphosphate chains have the geometry to form helices, the material in these granules may have a unique chirality. Determination of this chirality (via optical rotatory dispersion [101]) could provide insight into the origin of the unique chirality of biomolecules. In higher animals, the metabolism and function of polyphosphates also deserves further study. Existing evidence indicates their involvement in the rapid phosphate-exchange reactions that occur during neural excitation [5,27,92].

CONCLUSIONS

The excitability hypothesis—with its polyphosphate scenario—offers potential resolution of several prominent issues in the origin-of-life problem. Within this scenario, the source of energy and template for primordial polymerizations becomes apparent. Several objections raised against the RNA-world hypothesis are countered by the polyphosphate scenario. Some of these objections have also been raised against "protein-first" hypotheses and can be similarly turned aside.

Conclusions regarding the origin-of-life theories that were discussed can be summarized as follows: (1) The Oparin-Haldane hypothesis is still the most plausible explanation for the origin of organic monomers. (2) The proposal of self-organization theory for spontaneous appearance of an autocatalytic system in the primitive sea is unnecessary and exceedingly improbable. (3) Prebiotic formation of RNA may have occurred within a polyphosphate complex. (4) Xenobiotic theories are not well-founded within either the biological or physical sciences. And (5) the excitability hypothesis is backed up by geological, chemical, and biological evidence and also fits in well with the RNA world.

Several concepts and phenomena are brought together and related in the theory of natural complexification. Natural information is introduced as a concept comparable to theoretic information but having (as an extension) a definition for "value." This "value" is related to the stability of the system and is measured by the direction and magnitude to which external information alters the balance of excitation-relaxation. Structural relationships tending to maintain an excitation-relaxation balance with respect to a system's external interactions are a measure of its natural complexity. The acquisition and storage of natural information (as structure) increases the natural complexity of the system and hence its evolutionary status. In this dynamic system theory, the development of complex structures in nature is a general, stepwise, cause-and-effect process.

The writing of this document was undertaken as a counterproposal to self-organization theory and the "mechanist" perspective on the origin of life. It seemed unreasonable to me that the origin of complex structures in nature should be rare (or even accidental) occurrences,

depending upon systems in far-from-equilibrium states. I also did not think that structural elements coming together in a seemingly random manner (even over a time span of millions of years) is a satisfactory answer for the origin of life. Moreover, I can only think about the origin of life as part of the progressive changes we observe on this planet, in spite of proposals for spontaneous appearances, xenobiotic involvement, or certainly panspermia.

Past efforts to explain the origin of life have often neglected the functional objective of molecular arrangements with respect to their surroundings. Aside from continual replication (without further complexity), this functional objective has not been given adequate consideration. Obviously, the primary function of any arrangement is to ensure the system's survival. This is what excitation-relaxation properties accomplish in a system's response to its environment. They allow the system to maintain (via response and return) a structurally stable, dynamic state as the system is subjected to external stimuli. In fact, both replication and biological excitability are examples of such system responses to promote survival—replication at the level of a population and biological excitability at the level of an individual. Extrapolating the functional objective of these two biological responses back to a primordial environment is what yielded both the RNA-world and the excitability hypotheses.

In preceding sections, several approaches for investigating the RNA-world and the excitability hypotheses have been suggested. Pursuing these suggestions will project evolutionary theory into the prebiotic environment. Because inorganic polyphosphates are more stable with regard to geochemical changes than are the organic components of RNA, the excitability hypothesis can be projected back much farther than can the RNA-world. Polyphosphates in the primordial environment provide a good place to start thinking about the initiation of biochemical reactions on earth. They are, in this sense, a good place to start doing further research.

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