Thermodynamics of evolution

The ideas of nonequilibrium order and of the search for stability extend Darwin's concept back to the prebiotic stage by redefining the "fittest"

Ilya Prigogine, Gregoire Nicolis and Agnes Babloyantz

We have seen that the formation and maintenance of self-organizing systems are compatible with the laws of physical chemistry. We must now confront this idea with the major problem of biology: How did biological systems arise?

Present-day theory of evolution is a subtle combination of the results accumulated in molecular biology since 1952 and of Darwin's original ideas. Evolution is considered to be the result of random mutations arising from *errors* in the replication of the genetic material. The errors are inevitable, in view of the complexity of the various biochemical processes. Obviously, in the absence of further constraints, these errors propagate indefinitely and could not lead to any well defined result. Darwin's fundamental discovery was to realize that natural selection directs the mechanism by which an organism can survive and increase in number and complexity. This mechanism will operate as soon as the environment cannot support a population exceeding a critical size. It will select those species or genotypes that produce the highest number of descendants under the existing external conditions. In this way, natural selection prevents the accumulation of mistakes and at the same time allows improvements (through mutations) to take place.

This picture of selection through "survival of the fittest" already implies the existence of self-maintaining and self-reproducing systems. Strictly speaking therefore, it is not a theory of the origin of life. This crucial problem may be formulated in successive steps:

- It is generally believed that under primitive earth conditions (probably prevailing three or four billion years ago), small organic compounds such as acids, bases, sugars, and so on could be synthesized at an appreciable rate.
- These molecules must join into polymers having a new type of activity. The concentration of these molecules would have been very low under prebiotic conditions; some mechanism therefore must have operated to concentrate this dilute mixture in preferential places. These two points will be discussed in the next section.
- The next step is crucial: Is it possible to conceive of a type of selection pressure, compatible with the interactions between these active polymers, that would direct the system to increasing complexity and organization? There is little chance that the "survival of the fittest" dogma, in the sense of maximum offspring, would be of great help here. Well before this stage, it was necessary for the system to accumulate information from past experience, in some type of primitive genetic code. What are the rules that have prevailed in the formation of this code, whose existence is now a well established fact in biology? We will discuss this problem in some length further on.

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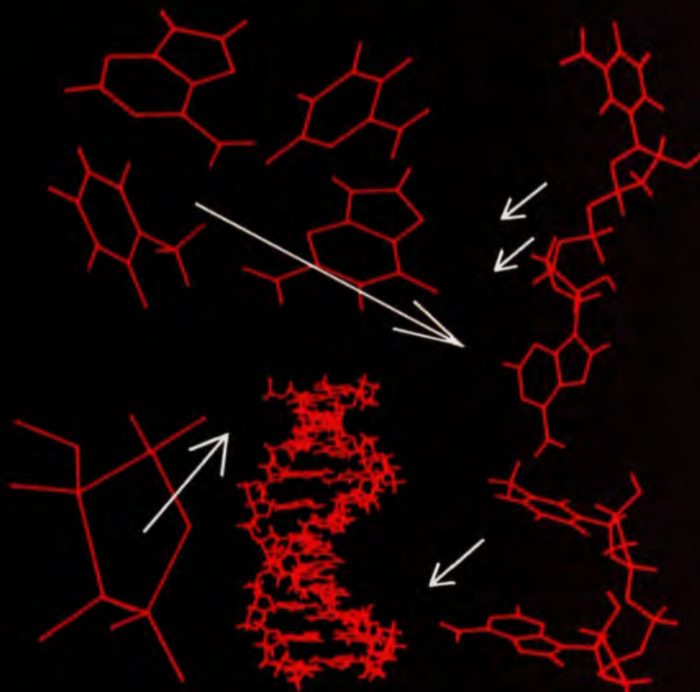
Prebiotic polymer formation

The most common mechanism of polymer formation is linear chain propagation. However, the binding free energy of the monomers that constitute the actual biopolymers is such that the yield of this process would be extremely small. Hence we assume 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 involved. In principle we can imagine three kinds of autocatalytic cycles: polypeptide–polypeptide; polynucleotide–polynucleotide; polynucleotide–polypeptide. The first case is considered to be quite improbable,[18] and we shall discuss briefly the second possibility.

Recall that a polynucleotide has a

This is the second part of a two-part article. In the first part, which appeared last month, we summarized the basic laws of nonequilibrium thermodynamics, with special reference to open systems. We showed that under far-from-equilibrium conditions, new types of structures may appear as a consequence of fluctuations, and we indicated some biological situations that illustrate the importance of such "dissipative" structures.



Order in biological molecules appears as polymers form. Computer art is from Lou Katz, director of the Computer Graphics Facility, Department of Biological Sciences, Columbia.

backbone of phosphate and sugar molecules. To each sugar molecule one of the four bases, adenine (A), guanine (G), cytosine (C) and either thymine (T) or uracil (U) is attached. Experiment shows that A or G monomers at moderate concentrations in aqueous solutions form stacks (loosely connected aggregates) of various sizes.[19] Furthermore, A binds to poly-U (polyuridylic acid) by a cooperative mechanism. Finally, the formation of small polymers of adenylic acid from monomers is facilitated[20] by the presence of poly-U; the stacks of A apparently condense on the poly-U surface to give the so-called "complementary" polynucleotide according to the by now classical Watson–Crick pairing rules, which imply that A binds preferentially to U or T, and G to C. In the usual terminology, we say that poly-U is the "template" in the synthesis of poly-A.

Starting from these experimental facts a mathematical model for the polynucleotide polymerization has been constructed.[21] The model comprises two competing polymerization pathways, one via linear chain propagation and the other by template action. The system is assumed open with respect to monomer flow from the outside. The kinetic equations for this model have been studied numerically, with plausible values for the rate constants. The results, in summary, are:

- In the neighborhood of thermodynamic equilibrium there is no interference between the two pathways. The system reaches a stable steady state of small polymer-to-monomer ratio.
- As the distance from equilibrium is increased by adding monomers, cooperative polymerization on templates takes over. A sharp increase of polymer concentration occurs, which, for certain values of the rate constants, is combined with instability of the low (polymer) concentration state that belongs to the thermodynamic branch. We shall discuss the model further in connection with evolution through error copies.

This example suggests the possible importance of dissipative instabilities and nonlinear kinetics in the efficient formation of polymers under prebiotic conditions. Particularly interesting is the possibility that polymer concentration is enhanced as a response to small changes in monomer entry. Assuming now that polymers can be formed at an appreciable rate, is there a mechanism able to localize these molecules, which in prebiotic conditions would certainly be very disperse? Aharon Katchalsky recently emphasized the important role that may be played by inorganic catalytic surfaces on which monomers (in his case amino acids) may condense to form fairly high polymers.[22] Also apparent from his analysis is that the enhancement of polymer concentration may be due to a complicated interplay between diffusion and (surface) reactions, giving rise to a dissipative structure. An alternative possibility is suggested by the results from equation 6 (page 25 last month): The possibility of creating, in a limited region of space, concentrations that may be much higher than in the homogeneous mixture provides a general mechanism for reaching and maintaining new configurations. The probability for certain important reactions is then enhanced and the system may begin to evolve further.

Eigen on biopolymer evolution

We are now concerned with the next stage of evolution, the behavior of interacting populations of biopolymers. Manfred Eigen has recently reported[23] the first really quantitative study of this question. The problem is formulated by first assuming that by some mechanism (for example, the one outlined in the previous section) it has been possible to produce appreciable amounts of polymers having certain properties:

- Under the maintenance of a finite energy and matter flow (related, for example, to the entry of monomers in the system) these substances can *metabolize* in the sense that one may have chemical transformations from energy-rich to energy-deficient material.
- The substances have certain autocatalytic properties arising from template action. In particular, the overall rate of production of constituent i is at least proportional to its concentration.
- The self-production (or replication) of i is subject to errors. This implies that there is a probability for producing from i a set of other substances $j(i \neq j = 1, \ldots n)$.

These assumptions imply that the

time variation of the concentrations X_i will obey the rate equations

$$dX_i/dt = (A_iQ_i - D_i)X_i + \sum_{i \neq j=1}^{n} \varphi_{ij}X_j \quad (15)$$

where i goes from 1 to n. The system is assumed to remain uniform in space. A_i and D_i represent respectively the rate of formation of substances as directed by the template i and the rate of decomposition of i. The factor Q_i measures the *quality* of this template action: its ability to replicate faithfully. Clearly $0 \leq Q_i \leq 1$. Finally φ_{ij} represents the rates of spontaneous production of i arising from errors in the replication of j's. Clearly Q_i and φ_{ij} must be related by the condition

$$\Sigma_i A_i(1 - Q_i)X_i = \Sigma_{j \neq i}\varphi_{ij}X_j \quad (16)$$

We must now specify the constraints acting on system 15. In addition to the nonequilibrium conditions related to the monomer flow into the system, one has to impose a constraint implying some sort of selection. One of the conditions proposed by Eigen for this purpose is the conservation condition

$$\Sigma_i X_i = \text{constant} \quad (17)$$

That this condition may lead to selection is obvious from the fact that any increase in the concentration of one of the i constituents will imply necessarily a decrease in the other substances.

Relations 17 and 16 imply that A_i and D_i must satisfy the condition

$$\Sigma_i(A_i - D_i)X_i = 0 \quad (18)$$

We may now transform equation 15 into a form with conditions 16 to 18 built in. Defining excess productivity as

$$E_i \equiv A_i - D_i \quad (19a)$$

mean productivity as

$$\langle E \rangle \equiv \Sigma_k E_k X_k / \Sigma_k X_k \quad (19b)$$

and selective value as

$$W_i^0 \equiv A_iQ_i - D_i \quad (19c)$$

we find

$$dX_i/dt = (W_i^0 - \langle E \rangle)X_i + \Sigma_{j \neq i}\varphi_{ij}X_j \quad (20)$$

These equations are now applied to what is known of the interactions of biopolymers likely to be present in the prebiotic mixture, that is, protein and nucleic-acid chains. From a thorough examination of known data on reaction rate constants for some nucleotide-nucleotide, nucleotide-peptide and peptide-peptide combinations, Eigen arrives at the plausible conclusion that nucleic acids are a necessary prerequisite for self-organization because they possess the ability to act as templates. However, they require a catalytic factor that couples the different template mechanisms; this factor may be provided by the presence of protein chains. In this way, an error corresponding to a "favorable" mutation may be propagated very efficiently, owing to the intrinsic nonlinearity of the protein-template coupling.

Evolution through hypercycles

Eigen has constructed models for this type of system.[24] Figure 3 depicts such a "self-reproductive catalytic hypercycle," according to his terminology. The polynucleotides I_i may reproduce themselves, preferably with the catalytic action of the previous polypeptide chain E_{i-1} in the cycle. Moreover, they provide information for the synthesis of the polypeptide chain E_i. The whole hypercycle is assumed closed, that is, the final enzyme E_n feeds back on I_1; the systems then exhibit autocatalytic growth properties. Numerical analysis of the rate equations[24] shows that, depending on the number n of the members of the hypercycles, I_i and E_i may grow abruptly (for small n) or oscillate in time (for large n).

Imagine now that, as a result of errors, the hypercycle of figure 3 gives rise to side branches. As a consequence of the conservation condition (equation 17), these new hypercycles will compete with the original one. Under certain conditions this competition may lead to selection and, because of the nonlinearities, selection will be very sharp. Thus, among many competing systems only one will survive in an appreciable quantity. In the examples of reference 24 the survivor is characterized by the highest "value function" (see definition 19). This suggests the appealing conclusion that the code as well as the symmetry in the stereospecific configurations of the macromolecules must be universal.

So far, evolution and selection have been formulated as a problem of competition between preëxisting hypercycles. Eigen points out that, in fact, this competition has two aspects: On the one hand, the nature of the error term $\Sigma_{j \neq i}\varphi_{ij}X_j$ in equation 20 giving rise to the side branches is fundamentally stochastic. But once an error distribution (errors may be thought of as a new kind of fluctuation) is realized, evolution will become an inevitable event. The course of this event will be described by the deterministic equations 20. Qualitatively, this picture recalls our earlier remarks about evolution as a stochastic process (see page 25 last month).

Now a system will respond to an error and evolve further only if it is not sufficiently stable initially, and one is tempted to think that evolution will have to direct the system to a state of optimal stability toward its own errors (or fluctuations). This search for optimal stability should then replace the old "survival of the fittest" principle. The final state will be a system possessing a means for minimizing errors. This device could be thought of as the precursor of the genetic code.

In his original paper Eigen did not quantitatively formulate the stability problem with respect to fluctuations that correspond to error copies. (We shall soon analyze this question along the lines of the theory outlined in the first part of this article.) What Eigen shows however is that for certain classes of systems, evolution through competition of the hypercycles leads to an optimum of the mean productivity and hence to an increase of the quality factor or, equivalently, of the selective value W_i^0 (see definition 19). In spite of the appealing character of this result, we believe that there is little chance that evolution can be characterized rigorously by a variational principle. In a nonlinear differential system with many variables, the mean productivity $\langle E \rangle$ is a very complicated function of the state of the system. It is far from obvious that $\langle E \rangle$ should increase as evolution proceeds, especially given that the behavior of the X_i's may well not be monotonic in time.

Stability and evolution

The evolution problem can be formulated in terms of stability theory.[25] Of particular interest is the formulation of thermodynamic criteria for stability and evolution (see also the box on page 25 last month). We shall remain as general as possible, postponing for a while the discussion of particular models.

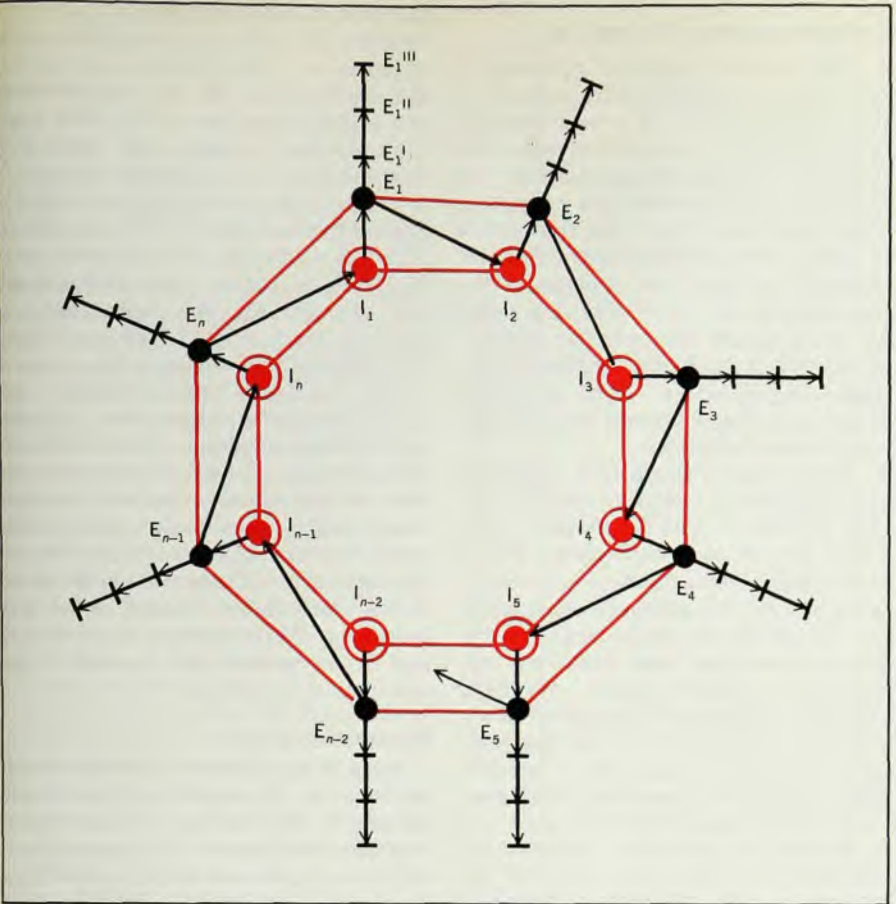
Consider a set of n interacting chemical substances X_i ($i = 1, \ldots, n$) and assume that all X's may exist in relatively abundant quantities. The time evolution of the set $\{X_i\}$ is described by the chemical rate equations

$$dX_i/dt = F_i^e(X_1, \ldots, X_n) + \langle F_i \rangle(X_1, \ldots, X_n) \quad (21)$$

where we take X_i as a measure of the concentration of constituent X_i. The term F_i^e describes the flow of matter (for example, in the form of monomers) from the surroundings and $\langle F_i \rangle$ the reactions inside the system. It will be assumed that F_i^e is constant throughout the system, which will be maintained uniform in space.

We assume that equation 21 has at least one asymptotically stable steady solution; this implies that all n roots of the characteristic equation of system 21 have negative real parts.[26]

Suppose now that we take into consideration the formation, by random fluctuations, of "error copies" of X_i which we call Y_j ($j = 1, \ldots, m$). The order of the differential system describing the joint evolution of X and Y will increase by m. For simplicity take m



An *n*-membered self-reproductive catalytic hypercycle of the type developed by Manfred Eigen.[23] The polynucleotides I are "information carriers," which are able to reproduce themselves. In addition, the polypeptides E serve as catalysts for the production of the polynucleotides (E_{i-1} catalyzes the production of I_i), and, moreover, I_i provides information for the synthesis of E_i. The hypercycle is closed; that is, E_n catalyzes the production of I_1. Such autocatalytic systems may have advantages during evolution. **Figure 3**

= 1. Then the characteristic equation of the enlarged system will contain a correction term of order ϵ ($\epsilon > 0$) multiplying either the $(n + 1)$th power of the characteristic root or the term of the characteristic equation that is independent of the characteristic root. Thus, the characteristic equation of system 21 will be recovered in the limit $\epsilon \to 0$ and the effect of the new substance in the evolution of X will disappear. For ϵ not equal to zero but small, the equation will have $(n + 1)$ roots and n of these must have values close to those of the original characteristic equation and, in particular, have the same sign for the real parts. The stability of the steady state of the enlarged system can only be affected by the new root, ω_{n+1}. For ϵ sufficiently small this root will depend on ϵ in one of two ways:

$$\omega_{n+1} \propto 1/\epsilon \qquad (22a)$$

if the correction term multiplies the $(n + 1)$th power of the characteristic root, or

$$\omega_{n+1} \propto \epsilon \qquad (22b)$$

if the presence of the new substance adds a constant term in the characteristic equation. Depending on the values of the parameters and on the kinetics, the coefficient in front of the right-hand side of either equation 22a or 22b may have a positive real part. Thus we reach the important conclusion that by taking into account a small and at first sight "spurious" parameter corresponding to the addition of a new variable, the stability properties may change even if the original system 21 were stable with respect to random perturbations of the $\{X\}$ variables. In different terms, one deals here with a problem of the structural stability of the reduced system 21 with respect to perturbations that introduce a side reaction that increases the order of the differential system. Note that in case 22a the departure from the unstable regime will be very fast, whereas for 22b the unstable mode will evolve very slowly.

Appearance of new substances

Next we must find the equations of evolution of the $\{X\}$ and Y variables that correspond to cases 22a or 22b. Clearly, relation 22a implies an evolution of Y according to

$$\epsilon(dY/dt) = G(\{X\}, Y, \epsilon) \qquad (23a)$$

where G is some function of the old and new substances and may also depend on ϵ. ($G(\{X\},Y,0)$ is different from zero.) This will affect the evolution of $\{X\}$, which now will be given by the system

$$dX_i/dt = F_i^e + F_i(\{X\}, Y, \epsilon) \quad (24a)$$

Of course F_i will have to be such that for $\epsilon = 0$, that is, for

$$G(\{X\}, \langle Y \rangle, 0) = 0 \qquad (25)$$

we get

$$\langle F_i \rangle(\{X\}, \langle Y \rangle(\{X\}), 0) \equiv \langle F_i \rangle(\{X\}) \quad (26)$$

Note that in equation 23a no flow-of-mass term is included. This is natural, because Y is produced solely by $\{X\}$ and is therefore essentially (except for diffusion terms, which can be taken as small as we please) a closed system.

On the other hand, equation 22b implies

$$dY/dt = G_1(\{X\}) + \epsilon G_2(\{X\}, Y, \epsilon) \quad (23b)$$

and correspondingly

$$dX_i/dt =$$
$$F_i^e + \langle F_{1i} \rangle(\{X\}) + \epsilon F_{2i}(\{X\}, Y, \epsilon) \quad (24b)$$

Equations 23 and 24 have been constructed in such a way that the appearance of the new substance Y may give rise to an instability of the original system. Mathematically, this would imply that the solution of equations 23 and 24 does not remain for all times in a neighborhood of order (ϵ) of the solution of equation 21. Thus we will have evolution through unstable transitions of the original system upon addition of new substances. This evolution may lead, for example, to a new state of high Y concentration, which will be dominated by the new substances. Let us now comment on the class of problems covered by this formulation. Consider first the situation described by relations 23a and 24a.

The most natural realization of these equations in the context of prebiotic evolution is, probably, the case where a new function appears in the system. For instance, one of the error copies of X may serve as template for the synthesis of a substance, which in turn catalyzes further the production of this error copy. One may expect this catalytic step to be more efficient than the previously existing mechanisms of synthesis. This efficiency will be translated by the appearance, in the right-hand side of the equation for Y, of terms containing some large kinetic constant k. Dividing by k and setting $\epsilon = k^{-1} \ll 1$ we obtain an equation of the form of equation 23a.

An alternative interpretation is suggested by rewriting equations 23a and 24a in the equivalent form

$$dY/d\tau = G(\{X\}, Y, \epsilon) \qquad (27a)$$

and

$$dX_i/dt = F_i^e + F_i(\{X\}, Y, \epsilon) \quad (27b)$$

We have introduced a new time variable $\tau = t/\epsilon \gg t$. Thus equations 23a and 24a describe systems that evolve according to two different time scales: One has a rapid motion describing the mechanism of production of the new substances—during this motion one could set, approximately, $\{X\} = \{\langle X\rangle\} =$ constant—and a slower evolution in the space-$\{X\}$ variables, after Y has already attained a value given by equation 25. Note that this picture of widely separated scales is in agreement with the microscopic, all-or-none character of a mutation and should be built into any stochastic theory of evolution through mutation and selection. It is only because we are limited here to a macroscopic description that we must introduce reaction mechanisms with artificially imposed time-scale differences, giving rise to kinetic equations of the type described in equations 27. One expects these equations to predict a very sharp selection during the evolution, in agreement with the numerical results of some model reaction mechanisms analyzed by Eigen.

Finally, let us turn to the class of problems described by relations 23b and 24b. In the case of instability, these equations predict a slow evolution of the mutant substance to the new regime. Comparing them with Eigen's equations 20 we see that ϵ may be interpreted here directly as an average mutation rate, so that the instability here is attributed directly to the copying errors. In contrast, in the previous case of equations 23a and 24a the role of mutations was primarily to couple the old and the new variables. The evolution through instabilities was attributed to another element, such as a new enzyme appearing in the system. In principle, both types of situation are conceivable in a prebiotic medium.

We emphasize that the picture of evolution as a succession of instabilities is meaningful *only if the original system* (equation 21) becomes unstable for arbitrarily small ϵ (formally, in the limit $\epsilon \to 0$). In the context of prebiotic evolution, this can only be an idealization of the real situation. If ϵ is interpreted as a mutation rate, one could easily imagine values of the order of 0.1 or more (see the numerical examples discussed by Eigen, reference 23). And if ϵ is interpreted as the inverse of a rate constant in an enzyme-catalyzed reaction, one would again expect a finite value owing to the rather poor catalytic ability of the primitive enzymes. Thus, the results derived from equations 23 and 24 can only indicate the general trend rather than the actual kinetics of prebiotic evolution.

We shall now describe briefly the main conclusions drawn from the analysis of equations 23 and 24. In this analysis we shall limit ourselves to the appearance of one single new substance.

Evolution based on 23a and 24a

a The original system of equation 21 may become unstable with respect to the addition of Y if G is an increasing function of Y in the neighborhood of the subspace described by equation 25. At the transition threshold the excess entropy production due to the fluctuation — that is, the additional dissipation introduced by the new substance—becomes negative. To derive this result we must regard entropy and entropy production as stochastic functions of the fluctuating variables. Thus, all results of thermodynamic interest will be averages of these functions.

b Every time a single new substance appears, one can construct a state function related to the dissipation introduced by the new substance. For a stable system, this function has a minimum around the subspace of equation 25. Evolution will take place once this function acquires more than one extremum or a saddle point. We have therefore a variational principle characterizing evolution. Note that this principle is local in the sense that it refers to particular stages of evolution dominated each time by a single new substance.

c Beyond the transition threshold for evolution the entropy production increases because the system switches, during some time, to a fast pathway for the synthesis of the new substance Y. This general result is also confirmed by model calculations[27] showing the possibility of a sharp increase of dissipation by several orders of magnitude (see also the box on page 24, last month).

Evolution based on 23b and 24b

a We assume $G_1 = 0$, that is, the new substance cannot be produced in the absence of mutations. Then one finds that the original system 21 may become unstable provided G_2 is an increasing function of Y in the neighborhood of $(\{X_{0i}\}, Y = 0)$, where $\{X_{0i}\}$ are solutions of the original system. At the transition threshold the additional dissipation introduced by the new substance and by the corresponding modification of the X_i's becomes negative. Moreover, the dissipation introduced by the new substance alone is also negative.

b A local variational principle can be constructed in the same way as before.

c No conclusive statement can be made about the entropy production beyond the transition threshold.

The most striking of these conclusions is result **c** of the first case, namely that *as evolution proceeds to a new stable regime, the system tends to increase its dissipation.* At first, this result appears to prohibit the realization of the minimum-dissipation regime (see relations 8 and 9) predicted by one of the classical results of nonequilibrium thermodynamics. In fact, (see the box on page 25 last month), both results represent two extreme but perfectly compatible kinds of behavior: The minimum dissipation theorem prevails in the neighborhood of a steady state (not very far from equilibrium) that is stable with respect to fluctuations; the increasing dissipation is on the other hand a transient behavior related to the evolution of the system to a regime where the new substance arising from mutation plays a dominant role. Once in this new regime, the system will again adjust to the constraints and will tend to *decrease* its dissipation.

The apparent incompatibility between increasing dissipation and the laws of thermodynamics has been noted by various authors working on the problem of individual organism development, which bears some resemblances to the problem of evolution.[28] We see that both types of behavior are described by the same theory applied in the first case near thermodynamic equilibrium and in the second case beyond a nonequilibrium instability.

Evolution models

Some of the ideas we have discussed can now be illustrated on a particular scheme.[25] In choosing a model representative of at least some aspects of prebiotic evolution, one is confronted from the very beginning with a crucial choice: Were there only nucleic acids present, or only proteins or both when natural selection started? Eigen's analysis suggests that the most promising of these possibilities is the third. Still, one must realize that any *ansatz* made on prebiotic evolution has, by the very nature of the problem, a speculative character. Thus, we shall try to present here models that retain some generality and some degree of insensitivity with respect to the protein-or-nucleic-acid controversy.

We take a system open to the flow of two monomer species a and b (which may correspond to two kinds of nucleotides). Species a and b are converted within the system to two polymers (for example, nucleic acids A_1 and B). The formation of A_1 (which may be a poly-A or a poly-G) necessitates two preliminary forms V and V* corresponding to assembled monomers and to stacks of the same monomers. This part of the mechanism may be described as

$$\left.\begin{array}{ll} (na) \rightleftharpoons V & (I.1) \\ V \rightleftharpoons V^* & (I.2) \\ V \rightleftharpoons A_1 & (I.3) \\ (mb) \rightleftharpoons B & (I.4) \end{array}\right\} \quad \text{Part I}$$

As soon as A_1, V* and B are formed, an autocatalytic cycle is switched on wherein A_1 acts as a template for the synthesis of B from b, and B acts as template for the condensation of stacks V*, which yield A_1. Finally, A_1 and B diffuse outside the system or are deactivated (for example, by forming Watson–Crick pairs). We may represent these processes as

$$\left.\begin{array}{lcll} A_1 + (mb) & \rightleftharpoons & A_1 + B & (\mathrm{II}.1) \\ B + V^* & \overset{k}{\rightleftharpoons} & A_1 + B & (\mathrm{II}.2) \\ A_1 + B & \rightleftharpoons & AB & (\mathrm{II}.3) \\ A_1 & \xrightarrow{\text{diffusion}} & & (\mathrm{II}.4) \\ B & \xrightarrow{\text{diffusion}} & & (\mathrm{II}.5) \end{array}\right\}$$

Part II

The coefficients n, m denote the number of monomers involved in the polymer. Parts I and II can now be analyzed numerically, given exactly the polymerization model we have previously developed[21] from experimental observations[19,20] of polynucleotide formation. The result is that for certain values of the rate constants one can achieve multiple steady polymerization states corresponding to a small or to a large amount of polymer in the system. Curve a of figure 4 describes the variation of A_1 as a function of the entry of a-monomers. The variation of V^* is given by a similar curve.

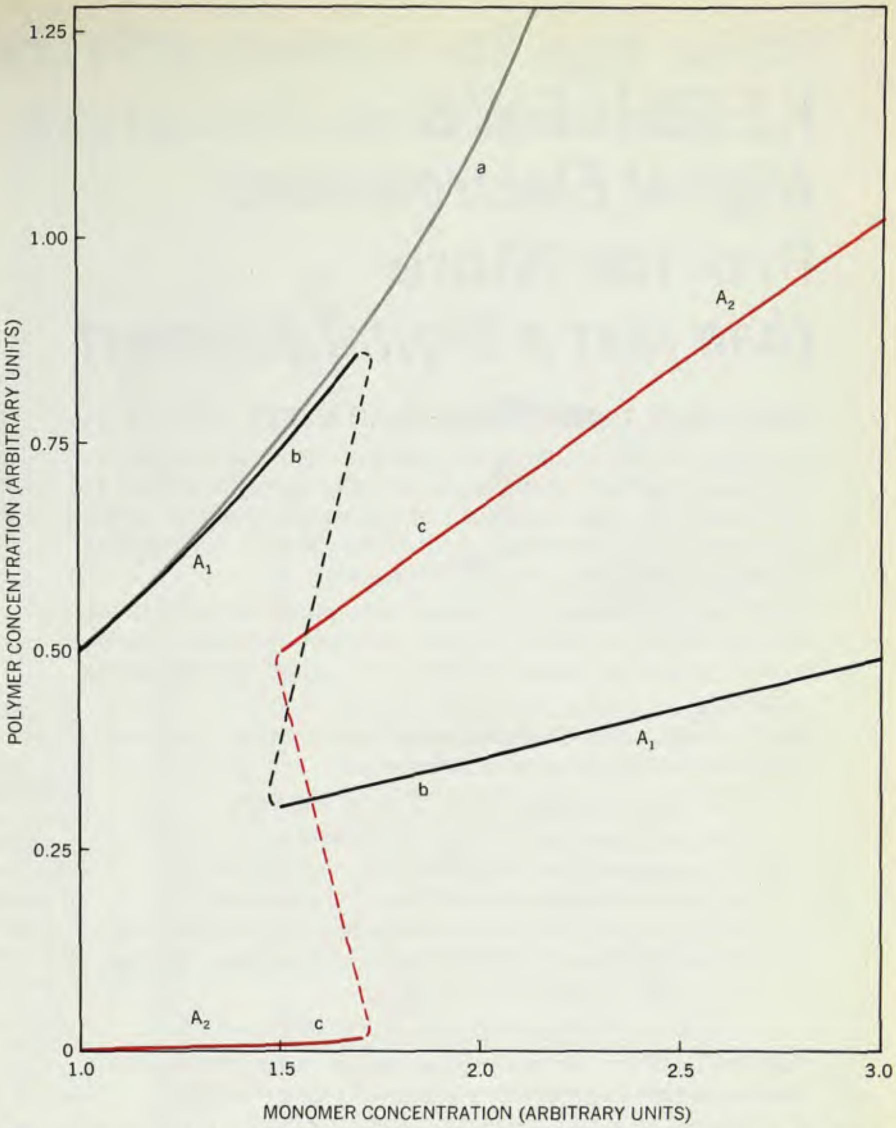
We now assume that in this (stable) polymerization, steady-state random fluctuations continuously cause errors in the formation of A_1 by B. As a consequence, a new species A_2 is produced. A_2 may now direct the synthesis of a new substance E (for example, a primitive enzyme) from r monomers of the kind c. Once produced, E further catalyzes the production of A_2 as well as its own production. Finally, E and A_2 diffuse out of the reaction volume. We may represent these processes by the scheme

$$\left.\begin{array}{lcll} B + V^* & \overset{\epsilon k}{\rightleftharpoons} & A_2 + B & (\mathrm{III}.1) \\ (rc) + A_2 & \rightleftharpoons & E + A_2 & (\mathrm{III}.2) \\ B + V^* + E & \rightleftharpoons & B + A_2 + E & (\mathrm{III}.3) \\ (rc) + A_2 + E & \rightleftharpoons & 2E + A_2 & (\mathrm{III}.4) \\ E & \xrightarrow{\text{diffusion}} & & (\mathrm{III}.5) \\ A_2 & \xrightarrow{\text{diffusion}} & & (\mathrm{III}.6) \end{array}\right\}$$

Part III

We now want to see if the steady-state system (I and II) may evolve, as a result of the addition of the new substances, to a regime dominated by A_2 and E.

Before we report the results of the numerical analysis of system I–II–III we draw attention to the mechanism of fluctuation amplification built into the model. For a fixed V^*, III describes a nonlinear coupling between A_2 and E that is stronger the larger the V^*. Now (see figure 4) A_1 and V^* depend on the steady state reached in the polymerization process. In particular, on the upper branch, A_1 and V^* will be large in the absence of part III. Thus, the polymerization steady state acts as a selection pressure in the sense that it favors A_2 and E once the mutation (whose rate is measured by ϵk in step III.1) takes place and couples A_2 and E with the old variables.



Fluctuations affect polymer production. At low monomer concentration, polymer A_1 (black curves, b) dominates. This steady state could continue (gray curve, a), but fluctuations caused by errors produce a new polymer A_2 (colored curves, c) and a catalyst that enhances the production of A_2. Beyond a critical value of monomer concentration the fluctuations are amplified abruptly and the system switches to a new steady state. Figure 4

The results of the numerical analysis of the complete system I–II–III are shown by curves b and c in figure 4. We see that beyond some critical monomer concentration value, the fluctuation leading to A_2 is amplified in an abrupt fashion and the system switches to a new steady state dominated by A_2. Closer inspection shows that the transition is due both to the mutation and to the appearance of the catalytic function of E. The former appears to trigger the instability, whereas the latter contributes to the sharpness of the transition. From this point of view the model is a synthesis of the cases corresponding to equations 23a–24a and equations 23b–24b.

Arriving at new criteria

We have seen that a genuine nonequilibrium order can appear in systems beyond a critical distance from equilibrium, provided the kinetic laws have some specific types of nonlinearities. A number of representative phenomena related to the functioning of present-day living organisms appear to belong to this framework and to provide examples of the concept of dissipative structures. Conversely, then, we may use this idea to analyze these phenomena from a new point of view. The nonequilibrium order principle is also likely to be important in the understanding of prebiotic evolution and of the origin of life. In particular, the formulation of evolution in terms of stability theory permits us to arrive at new criteria, extending, in the prebiological stage, Darwin's "the survival of the fittest" idea. Thus the search for stability may lead, depending on the particular situation, to an increase in the quality factor, an increase in dissipation or even a local variational principle. In particular, the increase in dissipation may give rise to an evolutionary feedback that "prepares the way" for a new instability enabling the system to evolve further. In this sense, the basic Darwinian picture of evolution through selection is kept, but the notion of the "fittest" is defined, in the prebiological stage, by a more subtle criterion that is no longer equivalent to that of the maximum number of offspring.

The approach to evolution outlined here was purely deterministic. A stochastic treatment is necessary for several reasons: In the first place, the very event of mutation is a random process. Next, the evolution in the unstable region contains an irreducible statistical element because the fluctuations determine the behavior of the average values. A stochastic analysis will permit specification of the critical size and nature of the fluctuations that can nucleate[9] and reach a macroscopic level. Moreover, stochastic theory is needed to determine whether a fluctuation arising and nucleating locally will spread out or whether it will become extinct. Work presently in progress in several laboratories is aimed at improving the theoretical framework and constructing more complete models for prebiotic evolution.

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