

STRUCTURAL AND FUNCTIONAL CONSIDERATIONS IN THE MODELLING OF BIOLOGICAL ORGANIZATION

Robert Rosen

Center for Theoretical Biology
State University of New York at Buffalo

I. *Introduction*

Biology begins with the recognition of what we call living *organisms* as a separate class of entities, distinguished in structure and properties from the rest of the natural world. The intuitions on which this recognition is based are a mixture of introspections and experience, which despite great effort have never been completely formalized; that is, no one has ever been able to put forward a finite set of structural propositions which are satisfied by exactly those physical systems which our intuition tells us are organisms. Nevertheless, most of us take our intuitions on this matter seriously enough to believe that we can make a useful, scientifically significant distinction between living and non-living, organic and inorganic. The absence of formalization means, however, that we cannot sharply specify the boundaries which separate the living from the non-living. We encounter such boundaries when we ask, as some people do, whether viruses are alive, or whether it is possible to construct machines which can “live” in some sense, or whether there are other kinds of physico-chemical systems (e.g. on the planet Jupiter) which we would want to classify as “living systems”.

The absence of a formal characterization of a definite class of “living organisms” by means of a finite set of either-or propositions has long bothered biologists and philosophers of science. It seems to me that the difficulty arises simply from the fact that our biological intuitions are in fact not based primarily on the kinds of structural or metric considerations which, for example, dominate physics, but are rather of a *relational* or *functional* character. The same difficulty of definition in fact arises whenever we try to specify in purely structural terms a class whose elements are defined functionally. To give one example; Wittgenstein asks:

“How should we explain to someone what a game is? I imagine that we should describe *games* to him, and we might add, ‘This *and similar things* are called *games*.’”

Replace the word “game” by the word “organism” and we have exactly the biological situation.

We can see already that such relationally or functionally defined classes, and the intuitions to which they correspond, lean heavily on behavioral or dynamical analogies exhibited by the members of the class, or better, in the way in which we ourselves interact with the members of the class. And as we shall see, a study of such classes depends heavily on metaphors

and metaphorical arguments. In the following remarks we shall sketch one manner in which we can attempt to arrive at some understanding of the behavior of systems which our intuition tells us are “living organisms”; how such understandings are to be related to our understanding of other areas of knowledge; and how the methods used to achieve this understanding can be applied to the study of other kinds of systems.

II. *Generalities on the Modelling of Biological Systems*

The only consensus found among biologists about their subject is that biological systems are complicated, by any criterion of complexity that one may care to specify. Therefore, if we are to achieve any kind of insight into the behavior of organisms, we must find some way of circumventing their inherent complexity; we must simplify them or abstract from them in some way; we must make models. Here the term “model” is to be taken in the widest sense; a molecular biologist, preparing a precisely definable fraction of the contents of the cell, is performing an abstraction; his resultant fraction is a simplified or abstract cell; it is a model. However, sharp controversies have arisen regarding the nature of biological modelling, the kinds of modelling which are acceptable, and the meaning and interpretation of biological models in this sense. At one pole we find the extreme reductionists, whose position will be considered in detail below; at the other we find holists who claim that any attempt to reduce the inherent complexity of organism thereby automatically destroys their organic character, and that therefore any information pertaining to a model cannot pertain to the organism itself and must be erroneous.

A proper understanding of modelling in biology must, I feel, begin with an understanding of the inter-relationships of physics and biology, which are profound and many-faceted. On the one hand, biological organisms are composed of atoms and molecules, and hence they simply *are* physical systems. The physicist is concerned with understanding the behavior of all assemblages of physical particles, including those that comprise organisms. And it is the fundamental principle of reductionism in biology that we have no real understanding of biological activities unless and until this understanding is expressed directly in terms of the interactions between the physical particles of which the organism is composed, i.e. in terms acceptable and recognizable to the physicist. This view then implicitly denies that there is any useful distinction between the organic and inorganic; between biology and physics.

A second and rather more subtle relation between physics and biology, which impinges even on holistic and systemic attempts to model biological systems, is that *the very machinery of system description*, the only tool we possess for this purpose, was developed for the analysis of simple physical systems (originating in Newtonian mechanics) and that despite extensive generalizations and refinements we still have no other conceptual tools available to describe systems and their behavior than those which proved convenient for physics.

A third relation, which plays a decisive though implicit role in motivating the reductionist viewpoint, is a counterpart of the preceding; namely that the only *experimental* tools available for the study of biological systems are also of a physical character. We have already mentioned that it is the manner in which we interact with systems which defines their character for us; in experimental biology we are constrained to interact with biological systems by means of techniques and tools invented by the physicist for studying inorganic nature. This bias on the manner in which we can observe biological systems automatically constrains us to a highly

physical view of these systems, selectively emphasizing those aspects of biological systems which our observing procedures, drawn from physics, are geared to detect.

Thus, both the experimental tools with which we observe biological systems, and the conceptual constructs by means of which we attempt to describe them, are both drawn from a non-biological science, not concerned specifically with the complexity and the highly interactive character typical of biological organisms. Therefore, in order to orient ourselves properly with regard to understanding how the modelling of biological systems is to be effectively accomplished, we must understand more specifically the nature of the biases which our physical tools, both experimental and theoretical, impose on us. We therefore turn now to a discussion of these matters.

III. *Systems and Their Descriptions*

In both physics and biology, and indeed in all other sciences of systems, there are essentially two ways in which we can attempt to obtain meaningful information regarding system behavior and system activities. We can either passively watch the system in its autonomous condition and catalogue appropriate aspects of system activity, or else we can actively interfere with the system by perturbing it from its autonomous activity in various ways, and observe the response of the system to this interference.

In systems for which the passive, autonomous aspect is paramount, a kind of system description is appropriate which we shall call an *internal description*. Typically such a description begins with a characterization of what the system is like at an instant of time; such a characterization is said to define a *state* of the system. The totality of all the possible states of the system, meaning the totality of different aspects the system can assume for us at an instant of time, forms a set called the *state space* of the system. In physics these states are typically defined through the measurement of certain numerical-valued observables of the system; these are called *state variables* and typically have the property that if two states are at all different in any observable way, they already differ in the values assigned to them by one or more of the state variables; if two states are identical in the values assumed on them by the state variables, they are identical in all other observables as well. In Newtonian mechanics it is a consequence of Newton's laws that a system consisting of N particles may be described by a set of only $6N$ state variables; out of the infinity of system observables these are conventionally taken to consist of three variables of spatial displacement for each particle in each of the three spatial dimensions, and three variables of velocity or momentum for each particle in the direction of the corresponding displacements. Thus the state space (or phase space) for such a system can be identified with a subset of ordinary Euclidean $6N$ -dimensional space, and each state with a point of this space. But it must be carefully noted that there is nothing unique about a set of state variables.

The fundamental problem of system description is to determine how the internal states change with time under the influence of the *forces* acting on the system. In physics such dynamical problems are formulated in terms of differential equations, which specify the rate at which each of the state variables is changing with time. The solution of a dynamical problem thus involves the integration of a set of differential equations, with each solution specified uniquely when the initial state of the system, and the particular set of forces acting upon it, are

known. The temporal evolution of the system thus takes the form of a curve, or *trajectory* in the state space.

The other kind of system description is called an *external* description, sometimes graphically called a *black-box* description. In this situation we make no attempt to identify a set of state variables for the system. Rather we have at our disposal a family of perturbations which we can apply to the system, variously called system *forcings* or *inputs*, and one or more observables of the system which we use to index the effect of applying a particular forcing or input to the system. Such system observables are generally called system *outputs*, or *responses*. In general, in this approach, it is desired to determine what the system response will be to an arbitrary input.

These two approaches are, of course, closely related conceptually. By the way in which internal state variables are defined, any system observable (and in particular the system outputs) must be already a function of the state variables themselves. Each forcing or input in our repertoire must correspond to a set of equations of motion of the system, and hence the system response to each particular forcing can be calculated by integrating the corresponding equations of motion. But in dealing with any particular problem, it is often most cumbersome to try to find an appropriate set of state variables, and we can proceed simply by an input-output analysis without talking about state variables at all. On the other hand, given a particular input-output analysis, it is theoretically possible to formally find a set of state variables for the box itself; what these formal state variables mean is usually not obvious.

It is one of the goals of science to be able to match up the two kinds of system description we have described. The external description is a functional description; it tells us what the system does, but not in general how it does it. The internal description, on the other hand, is a structural description; it tells us how the system does what it does, but in itself contains no functional content. We would like to be able to pass effectively back and forth between the two kinds of system description; i.e. we would like to be able to infer the system function (the external description) from a knowledge of system structure (the internal description), and conversely, knowing the system function we would like to be able to determine at least something about its structure.

In actual practice, theoretical physics is dominated by internal descriptions; the natural systems with which the physicist deals is generally of a simple type to which the concept of “function” is not appropriate. External descriptions begin to become important when we discuss artificial systems, especially the regulation and control of machines which we build for ourselves. Since in engineering we do things in the fashion simplest for us, our regulatory and control systems are related in a rather transparent way to corresponding internal descriptions.

In biology the situation is quite different, for a variety of reasons (some of which will be explored shortly). The crux of the matter is that a biological system is built on quite different (and largely unknown) principles from those systems which we build for ourselves, and our descriptions of organisms possess a curious mixture of internal and external characteristics. Many biological activities are in fact defined and observed only functionally, in terms of an input-output formalism. On the other hand, we can, as noted previously, employ many observational techniques (borrowed from physics) to obtain a wide variety of structural information. But there is no reason to expect that the structural information we find easy to measure should be related in a simple way to the external functional descriptions in terms of which so many biological phenomena are defined. Stated another way, the internal state variables which we find easily accessible bear no simple relation to the functional activities

carried out by a biological system; and conversely, the internal descriptions appropriate to the functional behavior of biological systems bears no simple relation to the structural observables which our physical techniques can measure. In the next few sections we shall explore some of the ramifications of this peculiar situation.

IV. *The Structural Characterization of Functional Properties*

The remark closing the preceding section has an important bearing on the reductionist hypothesis, which asserts that the basic problems of biological systems can all be effectively understood in terms of the internal descriptions of physics (using as state variables the states defined through the use of observing systems likewise drawn from physics). The question is then: how does a physicist approach a physico-chemical system too complex to be studied as a whole? As indicated previously, he must abstract from or simplify the system in some way; the customary way is to physically fractionate the system; break it up by physical means into a spectrum of simpler subsystems, if necessary iterating the process by fractionating the individual fractions, until we are left with a family of subsystems each of which is simple enough to be studied as a whole, he then will attempt to assemble the information he has obtained regarding each of the fractions into information about the original system with which we began. Implicit in this are two crucial hypotheses, of a system-theoretic character: namely, that any physico-chemical system, however complex, can be resolved into a spectrum of fractions such that (a) each of the fractions, in isolation, is capable of being completely understood, and, most important, that (b) *any* property of the original system can be reconstructed from the relevant properties of the fractional subsystems.

This last hypothesis is demonstrably false for many systems, including most of those of biological interest. A simple physical counterexample is a system of three gravitating masses in space (three-body problem). We can surely fractionate a three-body system into various two-body and one-body systems, each of which is simple enough to be completely understandable in isolation. But the crucial stability properties of a general three-body system can never be reconstructed from a knowledge of two- or one-body systems, however comprehensive. The basic reason for this is that the fractionation techniques employed are not compatible with (or do not *commute* with) the dynamical properties of the original system; we irreversibly destroy this dynamics, the very object of interest, by the process of fractionation itself.

Thus when we apply a pre-specified set of fractionation techniques to an unknown system, there is no reason why the fractions so obtained should be simply related to properties of the original system. Yet this is exactly what happens when a molecular biologist fractionates a cell and attempts to reconstruct its functional properties from the properties of his fractions.

This is not at all to say that fractionation *per se* will give no information about the properties of a complex system (although holists will go that far). What we must do to accomplish this is seek fractionations compatible with the system dynamics, in a definite, well-defined sense. We have argued that the fractionation techniques imported into biology from physics will not in general be compatible with the dynamics of biological systems. This does not imply that such fractionations do not exist; they may well exist, but they will generally be of a different character from those which have heretofore been important in analytical biology. They will be, in some sense, “function-preserving”, as in the following simple example. We all know that a bird’s wing is a combination propeller and airfoil with both functions inextricably

intertwined. This is different from the case of an artificial system like an airplane; we can physically fractionate an airplane into physically distinct parts which preserve such functions, but such procedures fail in the case of the bird's wing. This example illustrates on one hand the different principles of construction on which biological structures and engineering structures are built, and at the same time illustrates that the fractionation procedures appropriate to biological organization must be of a different character than those appropriate to simpler physico-chemical systems. Basically, this is because in biological systems the same physical structure typically is simultaneously involved in a wide variety of functional activities.

The situation with regard to physico-chemical fractionations of arbitrary systems is actually much worse than this, as will appear in the next section. But we have already shown enough to demonstrate that a simple reductionist hypothesis cannot be true for at least many of the functionally defined properties of the greatest biological interest.

V. System Analogies

As we say in the preceding section, a set of structurally meaningful state variables for a biological system is most difficult to identify, particularly if we restrict ourselves, as we usually do, to those quantities defined by purely physical observation techniques. We may always have recourse to an external description, i.e. to an input-output analysis; this is always appropriate to a system defined primarily in functional terms to begin with. But such black-box descriptions, though they are very useful (and allow us to make predictions about our system) carry with them only a limited understanding. Only an internal description, or something very much like it, can allow us to say that we fully understand the behavior of our system.

There is a sort of halfway-house between internal and external descriptions which allows us to go a bit further than we can with external descriptions alone; this depends on the concept of system, and what I have called elsewhere the construction of dynamical metaphors for biological activity. Let us begin with the notion of analog, which has long been employed by experimental biologists in the study of complex systems, under the generic term of *model systems*. Thus we find enzymologists attempting to learn about enzymes by studying systems ("enzyme models") which are not enzymes; we find physiologists attempting to learn about the properties of biological membranes by studying collodion films, thin glass, artificial lipid bilayers and other types of "model membranes"; we find neurophysiologists attempting to learn about the nervous system by studying a variety of artificial switching mechanisms or other forms of "neuromimes", and all kinds of scientists attempting to understand the dynamics of their system of interest, whatever its character, by modelling on an analog computer; i.e. an electrical system so constructed as to mimic the original dynamics.

The reason that the use of model systems is possible at all is that the same dynamical or functional properties can be exhibited by large classes of systems, of the utmost physical or chemical diversity. Two systems which are physically different but dynamically equivalent will be called *analog*s of one another (the terminology obviously drawn from analog computation, which embodies this concept in a particularly transparent way). If our interest is in the system dynamics, then this dynamics can be studied equally well (and often better) in any convenient system analogous to our original system.

Modelling by system analogy has obviously a completely different basis than the kind of fractionation we discussed in the preceding section. System analogy shows us that dynamical or

functional properties can be studied essentially independently of specifics of physico-chemical structure, while fractionation, or other reductionist techniques, are bound up with these specifics in an essential way.

Analogies of this kind are common even in theoretical physics. The mechano-optical analogy of Hamilton and Jacobi, or more generally the organization of whole branches of physics around analogous variational principles, is well known. Indeed, the judicious exploitation of such variational principles is one of the most impressive unifying agencies which exists in physics, potentially binding all of physics together in terms of functional or dynamical analogies, instead of attempting a unification on the basis of the structural fact that every physical object is built out of the same set of elementary particles. We shall see that the concept of system analogy plays an equally striking unifying role in biology. Such a unification is the sole attractive aspect of naive biological reductionism; we shall suggest that we can hope to achieve unification on functional terms while avoiding reductionist pitfalls.

The concept of system analogy is a most interesting one mathematically, and even opens up new vistas in classical physics. System analogy is most conveniently defined in terms of internal descriptions; two systems are analogous if, roughly, there is a 1-1 mapping between their state spaces which commutes with the system dynamics. But in physical systems, we have not only the state variables, but the full set of system observables (i.e. real-valued functions on the state space) available to us. Once a set of state variables, and the equations of motion, of a system are specified, every observable of this system inherits a particular dynamics. It is generally possible to find sets of such observables which define dynamical systems in their own right, such systems are in effect subsystems of our original system. It turns out in fact that there exist physical systems which are *universal* in the sense that we can build a dynamical system out of appropriate observables of the universal system which is analogous to any arbitrary dynamical system. This kind of result has many profound implications. For one thing, We have already mentioned that we apprehend a system in terms of those system observables which are in some sense easy for us to measure. The same system would present itself to us quite differently if we interacted with it differently; i.e. if other observables of the system were made easy for us to measure. Indeed, a universal system could be made to appear as any arbitrary dynamical system, simply by interacting with it in an appropriate way. This may open novel possibilities for us. And, returning to the notion of fractionation: we can fractionate such a universal system in such a way that the isolated fractions have *arbitrary* dynamical properties. This shows in a particularly graphic a way the difficulties inherent in attempting to infer system dynamics from a study of fractional subsystems separated by conventional physico-chemical means.

Let us return to the statement made previously, that any functional or dynamical property of a given system can be studied equally well as any one of the system analogs, or even entirely in the abstract. Such an abstract functional property, exhibited by each of the system analogs which *realize* the abstract system, is what we call a dynamical metaphor. For example, there are a number of important biological properties which follow simply from the fact that biological systems are open systems in the dynamical sense. To understand such properties we do not need to know *which* open system, in complete structural terms, is in fact before us, but merely that it is open. This is a situation familiar even in mathematics; if a particular property of a group, say, follows simply from the group axioms, then it is redundant, and indeed, incorrect, to prove the result by invoking the specific properties of the group elements comprising the specific group before us. In this way we can begin to carry out what we may call “functional fractionations”,

which allow us to see what follows already from the simplest dynamical properties of a metaphor, and what properties require the invoking of more specific dynamical or structural assumptions.

Such dynamical metaphors are playing an increasingly important role in our understanding of biological processes, different as they are from conventional structural modelling. The use of model systems has already been mentioned, as has the employment of open systems as metaphors for switching systems, threshold elements, equifinality in development and regeneration, etc. Another popular dynamical metaphor is the employment of a single metastable steady state as a metaphor for the establishment of polarities or gradients in differentiating systems.

There is one difficulty in the study of dynamical metaphors which must be mentioned. A dynamical metaphor, by its very nature, refers to a *class* of analogous systems, which may be of the utmost physical diversity. A typical biologist, on the other hand, is interested in the specific system before him, and asks for specific structural implications of any theoretical scheme that he may test on his system, obviously the dynamical metaphors are not, by themselves, geared to provide us with specific structural information about individual systems in the class. Thus it is difficult to make explicit contact with the structural information available about individual biological systems, which after all comprises the vast bulk of our biological knowledge. We have suggested elsewhere that dynamical metaphors, appropriately supplemented with further conditions (in particular, with constraints arising from considerations of optimal design) allow us to pick individual systems out of a large class of analogous systems (namely those which satisfy the additional constraint of optimality) and about these individual systems we can make a great many more specific structural inferences.

VI. *Hierarchical Systems in Biology*

We have stated several times previously that biological systems are constructed along different principles than the simple physical systems and engineering artifacts with which we are most familiar. One of the most obvious of these differences is the pronounced hierarchical character of biological systems: the separation of biological activities into distinct levels of organization. I shall call a system *hierarchically organized* if it satisfies the following two conditions: (a) the system is engaged simultaneously in a variety of separate distinguishable activities, and (b) different system descriptions are necessary to describe these several activities. It is this second condition which characterizes biological systems, with their stratification into many levels of organization.

We must say a word about what is meant by “different system descriptions”. We pointed out above that the same system always admits at least an external description and an internal description, and that these are “different”. However, this is not the kind of difference which is meaningful for hierarchical organization. What is meant is that the system requires several essentially different internal descriptions (each of which carries with it a correct external description), to account for the various activities of the system. A simple physical example should make this clear. We can regard a gas in two quite different ways: on the one hand it can be regarded as a structureless fluid, describable in terms of the thermodynamic state variables (pressure, volume, temperature, etc.). On the other hand, a gas can be regarded as a very large number of small Newtonian particles, admitting an internal description in terms of the state variables appropriate to the dynamics of Newtonian systems: displacements and their

corresponding velocities or momenta. These two state descriptions are essentially different; they refer to different structural levels of organization of the gas, and are made apprehensible to us in quite different ways.

Biological systems are very highly stratified in this sense, into levels ranging from the submolecular to the ecological. A great deal of theoretical biology in the past was devoted to an attempt to find an “anchor” level in the hierarchy; a level which was biologically meaningful, understandable in its own terms, and most important, would allow us to infer the properties of all the levels above it and below it in the hierarchy. For many years it was thought that the cellular level was such a level; this was the deeper significance of the cell theory of Schleiden & Schwann. With the advent of biochemistry and molecular biology, many biologists regarded the biochemical level as the most appropriate “anchor” in the hierarchy. Indeed, the essential content of the reductionist hypothesis was that it asserted that it was possible to infer the properties of any level in the hierarchy from the biochemical level.

In the preceding sections we have seen some of the acute problems of the reductionist hypothesis; here we consider the question of whether it is, in fact, possible to pass *effectively* from the biochemical level to higher levels of biological organization. This is a question which has received ample attention in recent years, from such authors as Elsasser, Wigner, Polanyi, Pattee and others. This is not the place to go into specifics of these arguments; it needs only be stated that it is at best exceedingly problematic whether one can indeed effectively traverse organizational levels when one starts at the bottom. Even in physics, the tool used for passing between the dynamic and thermodynamic descriptions of a gas is statistical mechanics, a tool of the greatest difficulty and subtlety, which has hardly been fully mastered and is at best of limited applicability. And although it seems on the surface that statistical mechanical ideas can be readily imported into biology, the several attempts to do so have run into the gravest technical and conceptual difficulties.

There is, however, one aspect of the hierarchical organization of biological systems which bears mentioning at this point. Namely, it appears that the dynamical properties which emerge at successively higher levels of biological organization are *analogous*, in the strict sense employed in the preceding section, to those at the lower levels. One particularly striking instance of such analogies occurs between the biochemical and genetic control networks found by Jacob & Monod, and the neural networks in the central nervous system. The exploitation of this analogy may ultimately prove as fruitful for biology as the mechano-optical analogy has been for physics.

VI. *Implications for “Structural” Studies of Complex Systems*

The main points which have been made in the above discussion are:

- a. That the only way in which we know how to approach complex systems is to simplify or abstract from them in some way;
- b. That such simplification amounts to splitting our system into subsystems, which are simple enough to be characterized in isolation, and such that our knowledge of the isolated subsystems can be effectively employed to give us information about the original system;
- c. That in biology, the abstractions offered by physical reductionism do not in general satisfy the proposition (b), in that they are not generally compatible with the dynamics of the original system.

We believe that the first two of these propositions are universally applicable to a study of complex systems of whatever type; social, economic, political, linguistic, etc. What we seek in the study of such systems is a spectrum of “atomic” subsystems which can be understood in isolation, and whose essential properties are preserved when a set of such “atomic” subsystems are recombined. What (c) above tells us is that we must avoid preconceptions as to nature of such “atomic” subsystems; that those subsystems which seem *a priori* to be the most natural candidates for this purpose may in fact not be so; and that we must let the overall system dynamics decide this for us.

Actually, the identification of such “atomic” subsystems implies far more than this. For by their very nature, such subsystems can be juxtaposed or recombined to produce new kinds of systems, different from those with which we originally started. That is, we may use these subsystems as elements from which new kinds of systemic organization can be synthesized by a set of canonical rules for the juxtaposition of our “atomic” subsystems. In such a situation, the systems with which we started are displayed as special cases of a generally much larger class of systems, all constructible from a family of “atomic” subsystems by means of a definite set of formal rules of combination or juxtaposition. This kind of analysis followed by resynthesis is typical of many fields within pure mathematics and the applied sciences; it is for example the basis of the numerous “canonical form” theorems for algebraic or topological structures.

It often happens, however, that we wish ultimately to restrict our attention to those synthetic reconstructions of our “atomic” subsystems which correspond to “natural” objects. We thus desire a set of rules which can characterize, out of the class of all such synthetically reconstructed systems, the subclass of those which are “natural”. This is in general a much harder problem even than isolating our “atomic” subsystems in the first place. It amounts to exhibiting a set of rules (a “grammar”, if you like) whereby the natural systems can be effectively exhibited, or at least effectively recognized. We pointed out the difficulties in carrying out such a program for biology at the outset of these remarks, when we noted that the class of “natural” biological organisms has never been successfully characterized within the class of all physical systems (implicitly taking for our “atomic systems” the set of real physical atoms). But this does not mean that we can never carry out this specification with *any* choice of atomic subsystems. We know already, indeed, that for biology the choice of such subsystems will be quite different from those the reductionist hypothesis gives us.

The entire process we have just sketched, beginning with the isolation of atomic subsystems, their recombination to generate a large class of systems, and the rules for selecting a subclass of systems of interest out of these, are implicit in the notion of “structuralism” or structural analysis for the study of complex systems. We have amply seen that the word “structural” has to be interpreted in a very wide sense; indeed in biology the relevant “structures” are always defined in *functional* terms.

It may be helpful to itemize the procedures involved in such a “structural analysis” of biological systems. This itemization is rather complicated, but once the essential aspects are systematically set down it will be recognized that exactly the same procedure is implicit in the structural study of all other kinds of organized complex systems.

We begin by supposing that we have already identified a class of “atomic subsystems” satisfying the hypothesis (b). We may as well suppose that these are completely abstract systems, because by hypothesis any real biological system can be decomposed into real subsystems which realize such atomic subsystems; but in general different biological systems will give us different

(but analogous) atomic subsystems realizing the same abstract systems. Let us designate this set of abstract atomic subsystems by the symbol A .

We now suppose that these abstract atomic subsystems can be combined or juxtaposed by a definite set of canonical operations or rules of composition, to form a large set of abstract systems, which we may suggestively designate as *abstract words*, and denote as $A^\#$. $A^\#$ is thus the set of abstract systems *generated* from A by the employment of the canonical composition rules.

Finally, we wish to identify or select out of $A^\#$ a subset, B , corresponding to the “abstract biological systems”. The words of $A^\#$ not in B are the “abstract non-biological systems”. The set of rules we use to make such a selection or identification of the elements of B we may suggestively call a “grammar”.

We thus have a sequence of operations going from the set A of abstract atomic systems to the set $A^\#$, the set of abstract words, to the set B (the set of abstract biological systems), which may be represented by the following diagram:

$$A \xrightarrow[\text{rules}]{\text{juxtaposition}} A^\# \xrightarrow[\text{"grammar"}]{\text{selection rules}} B.$$

Now the set A of abstract atomic systems can in principle be *realized* in physical terms in many different ways. Suppose that such sets of specific realizations are designated as

$$R_1(A), R_2(A), \dots, R_i(A), \dots$$

For each i , the real systems in $R_i(A)$ realize the abstract systems in A ; hence there is a natural mapping of A into $R_i(A)$ associating to each abstract atomic subsystem its realization, and a natural mapping of each $R_i(A)$ into each $R_j(A)$, associating to each system in $R_i(A)$ its analog in $R_j(A)$.

The rules of juxtaposition of abstract atomic subsystems, by which $A^\#$ is generated from A , may now be realized in terms of specific physical operations or processes in each $R_i(A)$, *perhaps in many different ways*; i.e. using different physical processes to combine the systems in $R_i(A)$. Thus in general each $R_i(A)$ can give rise to many sets of juxtaposed systems or words, which we may designate as

$$R_{i1}^\#(A), R_{i2}^\#(A), \dots, R_{ik}^\#(A), \dots$$

Each element of $R_{ik}^\#(A)$, for all i, k , is a realization of some word of $A^\#$; hence there is again a natural mapping of each of the sets $R_{ik}^\#(A)$ into each of the others which associates analogous words (two words being analogous if they realize the same word in $A^\#$).

Further, we may identify in each $R_{ik}^\#(A)$ a number of sets $B_{ik1}, B_{ik2}, \dots, B_{ikj}, \dots$, these being selected according to different physical “grammars” on the set of words $R_{ik}^\#(A)$.

We thus have many different candidates for “real” biological systems, specified by the diagram

$$R_i(A) \longrightarrow R_{ik}^{\#}(A) \longrightarrow B_{ikj}.$$

All such diagrams are connected by mappings into every other such diagram, which identify analogous but physically different systems. Presumably the study of “real” organisms is just one of these; whether the other diagrams are equally real (i.e. whether we can realize biological organization with novel physico-chemical structures, or whether other such diagrams are excluded on some kind of physical grounds, is an open question.

This formalism applies equally well to other kinds of organization, even non-dynamical ones like linguistics. Here we can assume that there is only one set $R_0(A)$ of realizations of the set A , comprising the linguistic “atoms” (morphemes or phonemes) and only one rule of juxtaposition leading to the set $R_{00}^{\#}(A)$ of linear sequences of linguistic atoms. But there are in general many “grammars” leading to different but analogous sets B_{00j} ($j=1,2,\dots$) of “natural languages”.

VII. *Evolutionary Problems*

Before concluding this brief note, it is necessary to add a further word regarding the evolution of biological structures in time. We have, in the preceding analysis, been concerned entirely with “physiological processes”, those which take place during the lifetime of single organisms. We have neglected developmental problems; and most particularly, we have neglected evolutionary problems, which are concerned with the way in which the class of organisms changes over long periods. Since a “structural” analysis pertains only to the class of biological systems at single instants of time (i.e. is a static description of the biological world, considered in evolutionary terms), there is an essential dynamical element missing from our discussion; in the terms used above, we have specified the instantaneous states of the biological world, but not the forces acting on them to produce changes of state, nor the equations of motion to which these forces give rise.

The way in which such equations of motion, corresponding to evolutionary processes, can be constructed and investigated is a vast and difficult problem, somewhat simplified in biology by the curious analogies which exist between evolutionary and developmental processes. In purely descriptive terms, evolutionary processes can be regarded as a temporal dependence of the “grammatical” rules whereby a set B is selected from the set $A^{\#}$. But such temporal dependence requires its own kind of “structural analysis”, and how to go about making such an analysis in any kind of evolutionary situation is, to my knowledge, a completely open question.