MATHEMATICAL BIOSCIENCES

The Relational Formalism in Multicomponent Biosystems: On the Interrelation between Statistico-Mechanical and Stochastic Theories (or Models*)

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ABSTRACT

A meaningfully operational methodology for relating theories along the micro-to macroscopic axis is presented, together with its application to certain highly multiple interacting biological systems, The connection between classical statistical mechanics and stochastic approaches, together with their subsumptive dependence within the relational formalism, is also sketched.

INTRODUCTION

Biology is characteristically concerned with the delineation of a very complex hierarchy of multiple interacting systems. In recent times various attempts have emerged to apply existing physical theories to biological systems at different levels of observability. Such approaches have often suffered by unnecessary complications due to their particular historical development and to a general lack of conceptual formalization even in the original domains in which they were first formulated. It is a principal merit of relational systems formalisms [1] to have explicated the conceptual mechanisms that allow the recognition of formal and experiential components in any theory and thus the formation of criteria for a meaningful application of any theory to new domains.

In previous work we have dealt with three levels of interaction in biosystems: molecular (chemical kinetics) [2], cellular (neural nets) [3], and organismic (population dynamics) [4]. Here we want to summarize this work and to sketch the relationship between these three levels. In particular, we will exhibit the explicit connections between two important approaches to multiple interacting systems: statistical mechanics and stochastic processes [5].

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THE MINIMAL STRUCTURE OF A PHYSICAL THEORY [1]

Any relational formalism essentially begins with the fundamental recognition of the philosophical and logical presuppositions implicit in specific formal systems. The most pervasive primitive concepts emerging universally from man's immediate experience are those of *system* (including subsystem and image system) and *relation* (in particular, decision relation). We are here especially interested in formal decision systems, which we will symbolize as

$$S \xleftrightarrow[D]{R} S' ,$$

in that any physical theory is an ordered sequence of formal decision systems subsumptively adjoined

$$\cdots \; \Big(\; S \xleftrightarrow[D]{R} S' \; \Big) \; S \xleftrightarrow[D]{R'} S'' \; \Big) \; \xleftrightarrow[D]{R''} S''' \; \Big) \; \cdots .$$

Subsumed by the basic presumptions are the notions of order and disorder. It is in terms of order-disorder relations that experience is in fact imaged by man in formal systems.

In previous work we have separated and outlined the minimal components of a physical theory. When only the system variables are presumed, together with the experiential-formal relations thereon, the minimal components can be arranged in the following hierarchical structure.

1. ORDER RELATIONS

   (a) Deterministic kinematics
   (b) Deterministic dynamics

2. INITIAL ORDER DECISION RELATIONS

   Choice of initial space-time relations

3. DISORDER RELATIONS

   (a) Probabilistic kinematics
      i. Subsystemic probabilities
      ii.Systemic probabilities
   (b) Probabilistic dynamics
      i. Subsystemic probabilities
      ii.Systemic probabilities

4. INITIAL DISORDER DECISION RELATIONS

   Choice of initial probabilities

5. ACTION

Relation to the "real"

It is necessary to realize that this structure is minimal and thus that additional decision processes may be present in specific theories. For instance, variational; principles (decision processes) can be added to generate both the deterministic and probabilistic dynamics.

The foregoing construction can of course be hierarchically repeated as many times as needed. At each step the system variables are thus generated by appropriate functions on the variables of the preceding step, where the term appropriate indicates the compatibility that must exist between successive steps.

It is clear then what must be meant when a theory of certain phenomena is "translated" to apply to different phenomena: appropriate experiential and formal presuppositions must be substituted for the previous ones *throughout* the hierarchy.

MOLECULES, NEURONS, POPULATIONS

Although it is often the case that the content of an article with the foregoing title is in fact a mere aggregation of unrelated theories, we want here to briefly outline three theories concerning these three types of systems and suggest a meaningful approach to the problem of their interrelation.

Classical Chemical Dynamics and Kinetics [1,2]

The system variables are here the position and momentum of each "molecule," plus time. For classical systems, the deterministic kinematics can be given by a Boolean algebra on a set of propositions over the space-time coordinates. Having thus specified the deterministic kinematics, the deterministic dynamics is obtained by the adjunction of the equations of motion (e.g., Newton's laws) or via an appropriate variational principle [5]]. Through the addition of specific initial or boundary conditions, or both, as well as the correspondence of the symbols to observation, thus obtain classical mechanics. Since we are dealing here with a very large number of molecules, the specification of the initial conditions becomes totally impractical, and disorder (ignorance) emerges and has to be taken into account, via a suitable introduction of probabilistic decision processes. Again, for classical systems ordinary probability theory applies (subsystemic probabilistic kinematics) and the Liouville equation describing the evolution in time of said probabilities is derivable [4,6] (subsystemic probabilistic dynamics). The system of all the molecules in question can be considered as as whole; hence, it is done [5], for example, through the introduction of the information function or entropy (systemic probabilistic kinematics) together with its evolutionary behavior (systemic probabilistic dynamics). The nest step is obvious, since to proceed we have to decide how to choose the initial values of the structure that has come to be known as *maximal (optimal) entropy inference* [5,7]. The decision rule is the following.

Choose those subsystemic probabilities that maximize the entropy subject to any given relational constraint.

Some of these constraints are formal .g., the normalization of probabilities), while others are experiential (e.g., expected values of certain functions of the system variables). It is here that the last step, the relation to the real, intervenes. And it is also here that the connection to the subsequent interactive level is established. In the case of chemical kinetics, we want to choose those functions of molecular variables that are the variables upon which phenomenological theories of chemical reactions are based, for example, concentrations. Obviously we could proceed to other phenomenologies, like thermodynamics, in which case other functions of the molecular coordinates would be chosen.

We have thus completed the specified five levels of classical chemical dynamics. Within this structure we define concentrations in terms of the probabilistic relations. These concentrations then become the system variables in the next hierarchical level, which, if the dynamical laws are the phenomenological chemical kinetic equations, becomes a complete theory of classical chemical kinetics.

Neural Nets [3]

Proceeding to the cellular (neuronal) level, we have very likely to consider numerous other intermediate levels, such as the macromolecular and intercellular. However, the hierarchical, "nonreductionist" nature of such theories should be clear. Hence we discuss next an intercellular level in the hierarchy.

The neuronal level can be approached in the following way. Tentatively we assume that the deterministic kinematics is essentially a Boolean algebra, that ordinary probability theory represents the subsystemic probabilistic structure, and that entropy is the appropriate systemic probability. It has to be noted , however, that there is evidence from behavioral studies suggesting a conservative estimation of subjective probabilities relative to formal Bayesian estimation [3]. It cannot be excluded at present that such phenomenon is not of neural origin. If this be the case, then the experiential and formal presuppositions concerning the kinematical structure of the theory of neural nets should be changed accordingly.

The dynamical behavior of neural nets can be described in a variety of ways, depending on the experiential data that we want to take into account. In our previous work we have adopted Cowan's equations in the neuronal sensitivities (mean fraction of time during which the neurons are excitable). We want again to stress that the choice of the system variables is also contingent upon the possibilities, like certain EEG features.

Optimal entropy inference (with the usual definition of the information function) can again be used to generate the prior probability distribution that evolves in time according to an evolutionary equation that is easily determined by the deterministic dynamics, since the latter (apart from a simple coordinate transformation) is essentially Hamiltonian.

Population Dynamics [4]

From the cellular to the population levels it goes without saying that several intermediate stages must be inserted, but again, in principle there is no conceptual difficulty that cannot be met with repeated adjunctions of well-formed intermediate theories, along the relational lines discussed earlier.

Population mechanics in classical form again subsumes a Boolean algebra and ordinary probability theory as a kinematic levels. The deterministic dynamics we have taken to be the Volterra-Lotka equations with the numbers of individuals of each species as the system variables. This dynamic is then imposed upon the probabilistic kinematics, thus generating the time evolutionary equations for the continuous joint distribution function of the vectorial stochastic variable whose components are the population numbers, the latter being themselves random variables. By means of several explicit experiential and formal assumptions, the (subsystemic) probabilistic dynamics can also be cast into a form exhibiting a Liouville equation in the joint distribution function. The entropy is then defined as before, and the prior distribution is obtained by maximizing the entropy subject to consistency with, for example, the expected populations of certain of the species composing the ecosystem.

In conclusion, these three theories, while they exhibit several similar features, are not in fact simple "applications" of some classical statistical theory. The similarity reveals itself only after their construction, not before. This point also provides the basis for a meaningful discussion of reductionism in biology.

THE RELATION BETWEEN STATISTICO-MECHANICAL AND STOCHASTIC THEORIES [1-7]

It is well known that the formal treatment of highly multiple interacting systems can be approached in at least two ways. We here discuss their interrelation.

First is an application of Gibbs classical mechanics. It is also well known that in in order for this formalism to be applicable, four requirements have to be satisfied:

1. existence of a conserved quantity;
2. uniform prior probability distribution;
3. measure-conserve phase flow (Liouville equation);
4. ergodicity.

It is essential to realize, however, that "statistical mechanics" is still operable even in the absence of all four of these properties. The gist of the argument is that once we have subsystemic probabilistic dynamics we can always formally solve it in an operator form: as probability at times t = transition operator acting on probability at time t_o. By conditionally maximizing the systemic probability, the prior probability can in principle be obtained. This is essentially statistical mechanics, and in this sense we say that optimal entropy inference subsumes statistical mechanics, without the requirements 1-4 ever being considered. Moreover, this decision process does not depend, for its applicability, on equilibrium situations. Apart from computational problems, we thus have a way of extending naturally statistical mechanics as far from equilibrium as needed. Obviously, if the system is Hamiltonian, a Liouville equation does exist.

The second approach consists in viewing the system as a purely stochastic one. The relation between the two methods becomes immediately clear. The evolutionary equations for the subsystemic probabilities, when in fact requirements 1-3 are satisfied, reduce (at most up to a variables transformation) to a Liouville form.

As a final remark, let us observe that in case only the probabilistic kinematics is given, but not the probabilistic dynamics, an additional application of optimal systemic probability inference can yield the desired dynamics [5,7]. For example, appropriate use of the path probability method introduced by Kikuchi [9] (and equivalent to the foregoing decision process) may be made.

SUMMARY

We have abstracted and elucidated the general conceptual structure of our relational formalism as applied to certain many-component biosystems. We have outlined a meaningfully operational methodology for relating theories along the micro- to macroscopic axis, and have sketched the explicit connection between classical statistical mechanics and the stochastic approach, together with their subsumptive dependence within the more general relational formalism.

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