

people in whose skeletons evidence of ancient diseases has been found, the disease process must be understood, not merely identified. Only in this way can such studies add to our knowledge of the daily lives, hereditary relationships, cultural practices, diets, and contacts of prehistoric peoples.

#### References and Notes

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## Antireductionism and Molecular Biology

Though the antireductionist thesis is unwarranted, research in classical biology may well be of value.

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The question of whether biological organisms are anything "more than" chemical systems has often been confused in the minds of many thinkers with the question of whether there are alternative ways of studying biological organisms. It seems to many that an unequivocal no to the first question implies that the chemical description and explanation of a biological organism is the only one. I think that both the history of genetics and simple prudence indicate that this implication is wrong.

Associated with this question of what point of view to take have been claims asserting that the chemical description is an essentially incomplete one for a living organism. Distinguished biologists and physicists have argued in the past, as well as quite recently, that it is impossible, not merely difficult or impossible at the present time, to explain the behavior of living organisms on the basis of their chemical consti-

tution. In this article I take into account both the question of the point of view and the question of the impossibility of chemical explanation of vital phenomena. Bentley Glass (1, p. 223), Walter Elsasser (2-4), and Barry Commoner (5) have had things to say on these topics in recent years, and I think that it is important to assess what is correct and incorrect in what they claim (6).

I begin with an argument which Bentley Glass has proposed to demonstrate that chemical explanation—of the type molecular biologists might attempt—is insufficient to account for existing biological laws, and then follow up this argument and deepen it by considering the thesis which Elsasser developed in several articles in the *Journal of Theoretical Biology* (2-4). The relevance to Barry Commoner's concerns of the position which I take will be obvious I think, so I do not need to recount what he says.

In his article entitled "The relation of the physical sciences to biology—indeterminacy and causality" (1, pp. 241-243), Bentley Glass states:

Statistical behavior . . . exists at all levels of organization, from elementary particles to galaxies. It clearly operates at all biological levels, from the molecule to the organism. . . . The Mendelian ratios depend upon the equal probability of an egg's fertilization by any one of two or more kinds of sperms when these kinds exist in equal numbers.

The randomness of the behavior of the units involved at one level does not necessarily depend on the randomness of units at lower levels of organization, [and the] . . . laws of science . . . arising directly from the nature of chance, and the mathematical expression of probabilities do not seem to be reducible to laws at a lower level of physical organization, because they describe the random behavior of entities at one particular level of organization.

[Accordingly] we may conclude that the statistical laws of one level of organization [for example the cellular] are not reducible to the statistical laws of another [for example, the chemical].

This is an intriguing argument but one which I believe contains a *non sequitur*. The fact that a macroscopic probabilistic generalization—say, that the average number of times the "head" side of a fair coin will turn up in 1000 throws will be near 500—can be asserted does not warrant the claim that this relative frequency could not have been explained in terms of microscopic variables. There easily could have been a randomization of the initial (microscopic) conditions. Of course one need not give a microscopic explanation, but Glass's claim is far

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stronger than that: he asserts that one *cannot* give a microscopic explanation.

To clarify the issue, and to indicate where Glass fails in his attempt to establish irreducibility, let me consider a very different matter—von Neumann's celebrated theorem concerning the impossibility of "hidden parameters" in quantum mechanical theory. My reasons for doing this will soon be apparent.

In his book *The Mathematical Foundation of Quantum Mechanics* (7), von Neumann questions whether the *prima facie* statistical theory of quantum mechanics can be transformed into a "causal theory" by identifying "hidden parameters," which, if specified in addition to the data provided by the function, would determine everything causally. "The statistics of the homogeneous ensemble [the statistically determined system] would then have resulted from the averaging over all the actual states of which it was composed, i.e., by averaging over that region of values of the 'hidden parameters' which is involved in those states."

Von Neumann then proves that, if his given characterization of quantum mechanics is assumed to be a true one—that is, if the theory is not assumed to be false—then undiscovered physical quantities that would fulfill the role of hidden parameters cannot exist: they would involve "dispersion-free" quantities, and von Neumann, assuming the current axioms of quantum theory, deductively proved that there can be no such quantities (8).

The relevance of von Neumann's theorem is that it indicates what Glass would have to do to eliminate the possibility of interlevel reduction—that is, reduction by a theory of one level (say biological) by a theory, or theories, on another level (say chemical). Glass would have to present an appropriate axiomatization of a true probabilistic theory in biology and demonstrate that the identification of biological entities with physicochemical entities and explanation of the biological entities' behavior on the basis of either causal or statistical laws involving physicochemical terms would entail a contradiction. This, I believe, he has not done.

Glass has another argument (1, p. 247) for the inherent irreducibility of biology by theories drawn from the physical sciences. This is based on the argument that biological entities are *unique*, and that consequently there do not exist a sufficiently large number

of similar individuals to permit predictions of the type one encounters in the physical sciences:

The probability mathematics of small numbers and unique events is simply not the same as the probability mathematics of large samples and large populations. This is the reason why the "explanations" of biology can in some respects not be reduced to the laws of physical science.

This assertion is perhaps not sufficiently clear. To find elucidation, we can turn to a similar argument which has been put forth by W. M. Elsasser in slightly different formulations in some of his recent articles (2–4) appearing in the *Journal of Theoretical Biology*. Elsasser's claim is that organismic laws (laws applying to extremely complex living systems) are not deducible from the principles of quantum mechanics; chemistry *is* so deducible—at least in principle.

The basis of his claim is the individuality of organisms (2):

One basic assumption which characterizes the physical sciences is the assumption of homogeneity of classes [for example, all electrons are alike and constitute a homogeneous, potentially infinite class. This assumption, however,] . . . does not apply to biological classes . . . [since] organisms are structurally and dynamically so complex that one can always find individual differences, at least microscopic ones . . . between any two organisms of the same class no matter how one defines the class.

This inhomogeneity of biological classes is apparently supposed to restrict the possibility of formulating a physicochemical explanation of biological, or "organismic," phenomena. Elsasser claims (2) that the "methodology [of experimental physics and chemistry] will break down in the course of any attempt to relate . . . [organismic] regularities to pure physics and chemistry by the conventional procedures of precise experimentation as understood in physical science." His conclusion is (4) that "the main result of inhomogeneity of individuals and classes is to make predictions based on the laws of physics so ineffective that no contradiction between the two sets of laws [physicochemical and organismic] can ever be constructed." By restricting the classes to one member, then, Elsasser hopes to demonstrate that physicochemical explanation (and reduction) of the biological sciences is not possible.

It seems, however, that with respect to this type of argument both Glass and Elsasser have assumed in advance

what they hope to demonstrate. Genuine and unanalyzable uniqueness entails irreducibility, but in order to make the argument compelling one must assume that the uniqueness of the biological individual cannot be explained on the basis of the concatenation of amino acids and other chemical structures. The Empire State Building is unique, nevertheless one would not expect that the laws of stresses and strains would not apply because of this uniqueness, and that the structure of the building would not be explicable on the basis of the principles of mechanics (9).

Elsasser supplements his claim by introducing a generalized version of Bohr's principle of complementarity (10; see also 11). In Elsasser's words (2):

If we make elaborate measurements precise enough to determine the microscopic state of a system at a given instant, we can indeed find out what the state is but the disturbance engendered (for instance the breaking of chemical bonds) would be so radical that the system would behave thereafter in a quite different way from the way it did before; it can no longer be considered as the same dynamical system. . . . We have killed the organism by our too detailed measurements.

There is an analogy here with our inability to simultaneously determine the position and the momentum of an electron. From this extension of the uncertainty principle (11) Elsasser concludes that the phenomena of life complement chemical phenomena: "biological" phenomena and "chemical" phenomena cannot be simultaneously determined, and if we believe that all living individuals are absolutely unique, knowledge that is obtained from one killed specimen does not assist our efforts.

But this pessimistic claim seems not to be justified in the light of the developing techniques of contemporary molecular biology, even if Elsasser's dubious uniqueness principle is assumed to be true. Though quite often the organism is killed and its chemical content is analyzed, as a matter of fact the molecular biologist *is* able to fruitfully apply his knowledge to other, similar organisms. In addition, artificially synthesized chemicals whose structure is known in advance can be "fed" into living creatures and used to reveal a wealth of information about their functioning chemical processes. Molecular biology is still young, but

so far none of its features seem to support the thesis of Elsasser, Bohr, and Glass. Their claims are at best conjectures, and conjectures that seemingly could lead to exacerbation of the division in biology which Commoner deplores.

## A Unifiable Science

From a study of the historical papers in genetics and molecular biology, and from a perusal of the current journals, I think I can draw some substantive conclusions. First, I do think that there is still an enormous amount of work to be done at the macroscopic nonmolecular level. It is only because of the genuinely *biological* techniques that were developed in the areas of genetics and cytology that molecular biology has made such startling breakthroughs. As a contemporary text in molecular biology asserts (12), "it is the final convergence of the different approaches [genetics, cytology, chemistry, and physics] which has brought us to the point where we can tentatively identify [the gene with chemical constructs]." The antireductionist biologist, accordingly, seems to be restricted to asserting a type of "make-believe" autonomy. He may plan, execute, and interpret his experiments without worrying about reduction to a molecular level, but this is no reason for maintaining that a biological entity is anything *more than* something ultimately characterizable and explicable by molecular biology. (To be sure, contemporary molecular biology *may* not be adequate to effect reductions of all classical biology; Newtonian mechanics without statistical assumptions was not adequate for reducing thermodynamics. But, as far as I am aware, there is no good basis for assuming that that complex of chemistry and physics which constitutes molecular biology is inadequate.) This make-believe autonomy may well be heuristically valuable, though perhaps relative to a particular stage of development of the sciences. There seems to be no positive evidence, either logical or empirical, for any real autonomy (13).

The relation between the antireductionist approach, sometimes called the organismic approach, and the standpoint of the molecular biologist might be clarified by mention of a notion that Ashby has developed. In his book *An Introduction to Cybernetics* (14, p.

103), Ashby borrows the notion of a "homomorphism" from mathematics in an attempt to elucidate the relation between a biological description and the physicochemical principles which underlie it. A homomorphism is best defined as follows:

If two . . . [systems] are so related that a many-one transformation can be found that applied to one of the . . . [systems] gives a . . . [system] that is isomorphic with the other (the simpler of the two), then the other is a homomorphism of the first.

The notion of a transformation is that of a set of operations which operate on a set of terms in a specified way, turning them into other terms. The notion of operation used here is this: an operation or operator  $\phi$  is one that, when applied to a letter of the alphabet, gives the next letter—for example  $\phi [c] = d$ . The idea of a "transformation" can be generalized so that (in principle) some chemical systems can be transformed into biological ones, and vice versa.

It seems plausible to claim that the classical biologist is working with a homomorphism of the system of the molecular biologist. The two systems are accordingly equivalent with respect to physical referents, but they differ with respect to detail (14, p. 106). Ashby indicates that the engineer who in building bridges confines his attention to blocks and girders as rigid bodies is working with a homomorphism of an "atomic" system. "As it happens" Ashby says, "the nature of girders permits this simplification and the engineer's work becomes a practical possibility" (14, p. 107). The same type of reasoning can be applied to the system of the organismic biologist.

An interesting consequence of this approach is the fact that there is no necessity to limit the number of simplifications to one. There may be several, each system a homomorphism of the one below it. This indeed seemed to be the case with respect to investigations in genetics by my associates and myself (15), the most complete system being chemical, the next "level" being the cellular system with its chromosomes construed as sets of genes, and the simplest system being Mendel's, concerned with unlinked genes that segregate in the traditional way. The existence of various approaches, then, does not imply an antireductionist thesis.

I tend to favor the position taken

by Morton Beckner, who suggests (16) that the "organismic biologist is proposing that we describe the parts of organic wholes in their activities *qua* parts by employing concepts that are defined by reference to the higher-level phenomena exhibited by the whole . . . [and that this is a proposal which] can only be justified by its success in yielding generalizations."

Accordingly, the organismic point of view may well prove heuristically valuable at certain stages of biological inquiry (17). Nevertheless, no evidence has been unearthed in our inquiries into genetics and molecular biology that would argue positively and persuasively for the inherent autonomy of biology. Moreover, since genetics occupies a central position with respect to the problem of growth and differentiation of an organism, there is evidence that these processes will eventually admit of a complete chemical explanation.

## Organization and Emergence

In their arguments, antireductionist biologists often place a good deal of emphasis on the *organization* present in living organisms. For example, L. von Bertalanffy has asserted (18):

Mechanism . . . [read "molecular biology"] provides us with no grasp of the specific characteristics of organisms, of the organization of organic processes among one another, of organic "wholeness". . . . It is a self-contradictory conceptual system, because it can deal with the undeniable "wholeness" of life only by means of notions which contradict its own fundamental principles.

I am not proposing to eliminate the need for an emphasis on organization, but I do not believe that the complex interdependencies and structures so characteristic of living organisms constitute an argument for the autonomy of biology. The reason why organization is so important, and why mechanists might well be criticized for understressing it, can, I believe, be stated more or less as follows.

For a given complex of chemical elements, the possible number of arrangements of molecules which are consistent with the current theories of chemistry is very large. Molecules can be composed of elements in many different ways, and the molecules in turn can be strung into macromolecular configurations which allow of many permutations and which consequently can

exhibit many different modes of behavior. In order to account for the perceived behavior of an organized system, one must note the arrangement of the system's parts, and this arrangement must appear as "initial conditions" in the explanans—the sentences that will yield an explanation of the system's behavior.

The fact that these initial conditions are not easily (or even possibly) derivable from the physicochemical theory is not an argument against reduction. The history of the system—or of its parent system and other related systems—is undoubtedly a record which is explicable in terms of the physicochemical theory (or of other theories in the physicochemical domain) when they are supplemented by statements describing the actions of wind, water, radiation, heat, air pressure, and so on, throughout time. To explain the system in these terms would be pragmatically impossible; consequently we take the organization of the chemical elements of the biological system as given in most cases, the chemistry of biological evolution being a significant exception.

## Conclusion

My general conclusion, then, is that, given the current state of biological science, there may be good heuristic reasons for not attempting in all possible areas to develop physicochemical explanations of biological phenomena,

and good reasons for attempting to formulate specifically biological theories. This, however, is an argument which supports an irreducibility thesis for *methodological* reasons. Any attempt to twist this into a claim of *real* irreducibility for all time is, in the light of recent work in molecular biology, logically untenable, empirically unwarranted, and heuristically useless.

## References and Notes

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2. W. M. Elsasser, *J. Theoret. Biol.* 1, 27 (1961).
3. ———, *ibid.* 2, 164 (1962).
4. ———, *ibid.* 3, 166 (1963).
5. B. Commoner, *Science* 133, 1745 (1961).
6. Needless to say, many authors have written on these and closely related problems, and it is possible here to touch on only a few. For a good survey of the field (primarily from the antireductionist side), see *Interrelations: The Biological and Physical Sciences*, R. T. Blackburn, Ed. (Scott, Foresman, Chicago, 1966).
7. J. von Neumann, *The Mathematical Foundations of Quantum Mechanics*, R. T. Beyer, Trans. (Princeton Univ. Press, Princeton, N.J., 1955), p. 324.
8. Advances in "hidden variable" formulations since von Neumann (for example, D. Bohm's work) are easily seen to be largely irrelevant to the function which von Neumann's proof plays in my argument.
9. In neither the mechanical nor the biological case are we now concerned with the way in which the structure was formed; we only want to know why it is functioning as it does (the Empire State building stands, the organism lives).
10. Bohr himself proposed, in the 1930's, an extension of complementarity to biology, but the distinguished physicist's suggestions were greeted with critical skepticism by biologists. In part this was because Bohr was arguing by analogy with (and not deductively from) quantum mechanics when he suggested that "in every experiment on living organisms, there must remain an uncertainty . . . and the idea suggests itself that the minimal freedom we must allow the organism in this respect is just large enough to permit it, so to say, to hide its ultimate secrets from us." [N. Bohr, in *Interrelations: The Biological and Physical Sciences*, R. T. Blackburn, Ed. (Scott, Foresman, Chicago, 1966)]. Bohr is not really presenting persuasive arguments here, but only suggesting that there may be limitations. W. Heisenberg believes that "the experience available at present is certainly not sufficient to decide [the issue]." [See his *Physics and Philosophy* (Harper & Row, New York, 1958), p. 105.]
11. I must confess that I do not completely understand Elsasser's claim in this regard. The principle of complementarity—the inability to make a verifiable choice between a "wave" interpretation and a "particle" interpretation of electrons—follows from the uncertainty principle of quantum mechanics. It is debatable whether the Heisenberg explanation of the uncertainty principle, upon which Elsasser patterns the above argument, is legitimate, and whether the analogy can be extended to support a complementarity view of biological and chemical interpretations. See E. Nagel, *The Structure of Science* (Harcourt, Brace & World, New York, 1961), p. 297 ff., for an illuminating discussion of the Heisenberg interpretation.
12. The quotation is from G. H. Haggis, *Introduction to Molecular Biology* (Longman's Green, London, 1964), p. 137.
13. Two further points might be made in this connection. Delbruck in an interesting article (included in Blackburn) has suggested that an analysis of a living cell "should be done on . . . [its] own terms, and the theories should be formulated without fear of contradicting molecular physics." I would recommend a change of the "should" to a "may perhaps usefully." Elsewhere and earlier, E. Schrodinger [in his *What Is Life?* (Cambridge Univ. Press, New York, 1944)] warned that we must be prepared to find new laws in living things. If the warning is to be taken in the sense suggested by the mechanics-thermodynamics example cited in the text, I and other reductionists would agree that it is warranted. Schrodinger's warning has thus far not had to be taken seriously.
14. W. R. Ashby, *An Introduction to Cybernetics* (Wiley, New York, 1956).
15. K. F. Schaffner, thesis, Columbia University, in preparation.
16. M. Beckner, *The Biological Way of Thought* (Columbia Univ. Press, New York, 1959), p. 187.
17. Nagel has made a similar point in *The Structure of Science* (Harcourt, Brace & World, New York, 1961), pp. 363, 445.
18. L. von Bertalanffy, *Modern Theories of Development*, J. H. Woodger, Trans. (Dover, New York, 1963), p. 46. Also see Nagel's informative discussion on organismic biology in *The Structure of Science* (Harcourt, Brace & World, New York, 1961), pp. 428–46.