The Emergence of Order in Developing Systems

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The biologist poses questions to developing systems at various levels of organization, and each answer he obtains is appropriate to a particular level. It does not necessarily have meaning nor depend for its validity on phenomena occurring at other levels, although one would expect that the cross-level meaning would ultimately become clear and that it would be of no trivial significance. This Symposium reflects the multiple levels at which we presently direct our inquiries. Thus, Zwilling's questions about the limb-forming potency of lateral plate mesoderm in the chick embryo are answered through the morphologic patterns formed by tissue isolates and grafts. The answers do not require information about specific synthetic patterns and they do not reveal anything directly about them. Conversely, data about the synthesis of collagen and of chondroitin sulfate by early embryonic chick cells do not enable us to decide whether these cells have as their definitive morphogenetic assignment the formation of cartilage or, if so, whether the cartilage will be that of forelimb, hindlimb, vertebral column, or rib.

This Symposium also reflects some degree of confidence that the order that one observes at successively higher organizational levels emerges automatically from pre-existing order at a lower level. Anfinsen shows here with dramatic clarity that the three-dimensional structure of the protein molecule issues essentially from the sequence in which its component amino acids are assembled; the entire molecule automatically and necessarily selects and fixes its three-dimensional structure in the most favorable free energy conformation. Structural units, such as protein molecules, may polymerize to form patterns of higher order, as Harrington describes here for myosin, and as J. Gross demonstrated for collagen at the Symposium in 1963. Formation of the microtubules of axonemes, of the mitotic spindle (Tilney), and the origin of microtubules associated with the patterning of plant cell walls (Heslop-Harrison) likewise may occur by self-assembly from pre-existing subunits.

Robbins noted that the principle of self-assembly assists in understanding and predicting the structures of such organelles as flagella and bacteriophage tails, but he questioned, as did H. Stern in the introduction to the 1965 Symposium, to what extent this principle finds application in the formation of more complex structures. We should probably distinguish automatic "self assembly" from the no less automatic assembly of subunits requiring the presence of prototype structures and the appropriate catalysts.

The essence of the challenge to this Symposium to interpret the emergence of order during development was recognized and issued, facetiously to be sure but very provocatively, by Anfinsen who, in informal introductory remarks to his paper, offered the proposition that if a rat were disassembled into its native macromolecular components, given the right conditions these could automatically assemble themselves into a rat once more! Laughter at this sally served to cover more than a little discomfiture. Surely this statement is naive, but with what does one counter it that is not equally naive? Does it suffice to say that construction of an organism requires more than just the appropriate amounts of materials and energy; that their input must be at the proper place, in the right sequence, and with the correct timing? Have we really confronted the question whether normal ontogeny is the only way to put an organism together?

Normal development is progressive and most frequently leads to an increase in complexity of organization. Even so, the underlying events that occur at any one cross-section of developmental time are those that occur automatically and inevitably—the principles of self-assembly and of catalytic assembly on pre-existing templates do apply. But our concern at Anfinsen's playful challenge may reflect our inability to come to grips with the problems posed by the sequence and timing of these underlying events—it may reflect our ignorance of developmental alternatives and our inability to choose correct ones from among the multiplicity of possible relationships that have been recognized, especially at lower organizational levels. It may issue from the poverty of our knowledge about mechanisms whereby higher levels emerge from preceding lower levels.

Perhaps as DeHaan suggested, we must now seek to describe at all levels the properties of the systems whose development we seek to analyze. We must know the properties of their component cells, their behavior, synthetic abilities, and step-by-step developmental alternatives. But, is our principal problem just one of clarifying details?

Do we have already the conceptual framework within which to relate, for example, the relationship between morphogenesis of the nervous system and the origin of behavior (Kollros, Hamburger)? Do we have the insights that will make it possible to interpret the plasticity of cortical maturation (Sperry) in view of the high degree of specificity with which synaptic connections are made in the brain of the embryo? Do our insights lead to an understanding of the development of consciousness or of social responsibility?

In effect this Symposium is a challenge to us to assess the merits of our present insights into the emergence of order at all levels of developing systems. It is an appropriate challenge to issue in a volume honoring Professor Viktor Hamburger who has, himself, contributed so much to that conceptual fabric of developmental biology that is ours today and from which will emerge the conceptual framework that will serve a future generation of developmental biologists.