Embryonic Development: Toward a Synthesis

Topobiology. An Introduction to Molecular Embryology. GERALD M. EDELMAN. Basic Books, New York, 1988. xvi, 240 pp., illus. $21.95.

As Edelman explains, topobiology (a term of his creation) is the study of the position-dependent regulation of cell behavior in an organism, particularly the regulation of those cellular activities that are involved in morphogenesis during embryonic development. The topobiological agenda (p. 4) contains two main items: the developmental genetic question of how the one-dimensional genetic code specifies the three-dimensional animal; and the evolutionary question of how genetic change can lead rapidly to large changes in the morphology of an animal.

Edelman's answers to these questions are found in his "morphoregulator hypothesis," here summarized: Morphogenesis, all would agree, results from cell proliferation, cell movement, cell repacking, changes of cell shape, and cell death. These "primary driving processes" of morphogenesis are under the control of the cell's surface, which, in association with the cytoskeleton, discriminates, integrates, and transduces a variety of molecular inputs from the cell's environment. The cell's subordination of its behavior, including its gene expression, to position-specific conditions of the local environment, allows epigenesis to emerge as an aspect of development.

A cell's environment is composed of the surfaces of neighboring cells, the extracellular matrix, and bordering lamina. According to Edelman, cell adhesion molecules (CAMs), those linking a cell's surface to neighboring cell surfaces, are the main "morphoregulators" of the primary morphogenetic processes. "CAMs regulate morphology and are regulated by it" (p. 100). Although there are only a few CAMs (two or three at early stages, a few more later), they can vary on the cell surface in combination, amount, and post-translational modification, to exert a wide variety of effects on primary processes. CAM-mediated effects are further enhanced, opposed, or otherwise modified at the cell surface by other surface and extracellular components, especially the SAMs (substrate adhesion molecules, including membrane-associated as well as matrix and lamina components). SAMs, furthermore, hold a special significance for development since their numerous extracellular non-diffusible components can occur in a myriad of combinations ("SAM modulation networks") exerting a myriad of influences on CAMs and therefore on morphogenesis. SAMs to a large extent, then, define the many position-specific environments of the organism's cells.

Continuing further with the hypothesis, we find that CAMs, SAMs, and their numerous modulators are encoded by "morphoregulatory genes," the expression of which is also subject to the conditions of the cell's environment: to the state of CAMs and SAMs, and to inductors released from neighboring tissues and presumably bound by receptors at the cell's surface. With each change of morphoregulatory gene expression, a cell modifies its surface and its environment (that is, its CAMs and SAMs), thus altering both the conditions that would select its behavior and the behaviors available for selection.

While CAMs and SAMs mediate morphogenesis and the differentiation of position-specific cell environments, they are not responsible for tissue-specific gene expression, the largely separate province of selector genes and historegulatory genes. The former, through their products, activate or inhibit specific historegulatory genes, whose products have three consequences: they create not only (i) tissue-specific differentiation, but also (ii) tissue-specific effects on the CAM-SAM modulations at the cell surface (diagram on p. 138), and therefore on morphogenesis, and (iii) also, in some cases, serve as inductors that diffuse to neighboring tissues and affect both selector genes and morphoregulatory genes in those cells. Inductors, it is seen, serve the significant roles of integrating the development of separate tissues and of connecting histogenesis to morphogenesis. This connection is further strengthened by the need for cells of a tissue to reach a particular CAM-SAM state before they are competent to respond to an inductor.

Finally, in light of the central importance of CAMs and SAMs for morphogenesis, it should be expected that small heritable changes in morphoregulatory genes would in the course of evolution produce large changes in the body plan of organisms, constrained however by the requirement that the new morphogenesis must still allow the proper trading of inductors between tissues. These, by my reading, are the main tenets of the morphoregulator hypothesis. The developmental genetic issue is settled by the environment-dependent control of gene expression and cell behavior, mediated by morphoregulatory CAMs and SAMs at the cell's surface, whereas the evolutionary question is settled by constrained variation of morphoregulatory genes.

Overall, I appreciate several major aspects of the book. Edelman gives epigenesis its rightful place in development and aims to bring reality to this elusive concept by exploring its molecular and cell biological basis. No reader can escape the lesson of the importance of a cell's environment for its behavior or the paradox arising from the fact that the cell must also create that environment. Furthermore, Edelman, rather than just parading a bewildering array of molecules, genes, and cell behaviors before the reader, attempts to unify them in a hypothesis answering his two main questions of topobiology. His sights are set very high and he strives to structure his subject.

The above-described morphoregulator hypothesis, which represents Edelman's unification, seems to me, though, to have failings in both its global and its specific forms. In its global form it strikes me less as a hypothesis than as an interim program for surveying a vast amount of material, to see where might lie the deficiencies of our knowledge. To this end, Edelman classifies molecules and cell activities according to their possible functions and then relates the classes according to their possible regulatory interactions. Functions and regulatory interactions, though, are far from known, and in the hypothesis an "interaction" means only that one class affects another qualitatively or quantitatively, positively or negatively. The outcome (the hypothesis) of this enterprise is summarized in a few systems diagrams (see pp. 138, 147, 152) in which 10 or 12 blocks (the classes) are connected by a slightly larger number of arrows (each class affecting one or more others). Ultimately, because of the weakness and ambiguity of the interactions, the global hypothesis achieves no economical completeness or generative power, but only loosely associates a set of not unreasonable yet not remarkable suggestions. The hypothesis concerns a slice of developmental time and contains no provisions that would make predictable the direction or end state of development of an organism. These are left to the inherent nature of the morphoregulatory and histo-regulatory genes, the circuit logic of which remains undisclosed. Also, while we learn that cells can make and respond to a great variety of environmental differences, the hypothesis contains no consideration of a possible systematic relatedness of all these differences within a developing organism; environments are just different and changing in unspecified ways. The global hypothesis, then, strikes me as a serviceable "way to review the material" rather than an effective grand synthesis.

In its specific form, the hypothesis does achieve unity and economy simply by making CAMs the central and most important elements of the complex web of components. While the central role of CAMs in regulating morphogenesis is far from proven, it is possible that Edelman, who has been studying these molecules with his colleagues for the past 12 years, has indeed apprehended their deep developmental significance. I am certainly more interested in CAMs as a result of reading the book, and found the parts about CAMs the most satisfying. However, the deeper the book led me into the global hypothesis, the less there seemed a need to look upon one kind of component as central (SAMs seem equally important, as do inductors and historegulatory genes). In the end, the emphasis on CAMs as the single most important component seemed to cross purposes with the attempt to integrate all aspects of development into an organic diagram.

At the level of mere reading, the book required intense scrutiny on my part well beyond the period intended by the author (one weekend for professional biologists, two weekends for non-professionals). To gain orientation, I turned to Edelman's short reviews of his hypothesis (for example, *Proc. Nat. Acad. Sci. U.S.A.* **81**, 1460 [1984]; *Ann. Rev. Cell Biol.* **2**, 81 [1986]) and then to Lewis Wolpert's essay on positional information ("A cell's competence provides the choices; position is the chooser," *Curr. Top. Dev. Biol.* **6**, 183 [1971]). Ultimately, I gained the clearest sense of what was being said and not said in this book by studying the system diagrams on pp. 138, 147, and 152 and the definitions of terms in the glossary. Non-biologists relying on this book alone may find themselves confronted by too much yet too little detail and confused by the citation of evidence that is consistent with the morphoregulator hypothesis yet seems to eliminate no counter-hypothesis, since none is raised.

Despite these shortcomings, I recommend Edelman's book to advanced students of embryology and cell biology for its attempt to originate an approach to the deep problems and scattered facts of these fields and to reach for a full synthesis. For others, it offers a compelling introduction to the molecular aspects of the cell surface and extracellular matrix and to the role of epigenesis in development.

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Nearshore Biomechanics

Biology and the Mechanics of the Wave-Swept Environment. MARK W. DENNY. Princeton University Press, Princeton, NJ, 1988. xiv, 329 pp., illus. $60; paper, $25.

Studies of organisms living in wave-swept environments such as the rocky intertidal and coral reefs have held a central position in the development of modern ecological theory. Ideas as diverse as the intermediate disturbance hypothesis, keystone predators, size-limited predation, and food web connectance were forged from careful studies of interacting populations of invertebrates and algae. The startling fact is that few seashore biologists have a clear view of the physical environment in which these organisms live. Imagine a human foraging for food and searching for a mate in a hurricane and you will have only an inkling of the physical constraints imposed on wave-swept life. Denny's goal is to explore "the mechanics of wave-induced water motion and how they affect the lives of organisms along the shore." The book is "intended more to teach the reader how to think about the subject than to present a compendium of what is known."

This book fills an important gap. The literature on wave mechanics is voluminous, often arcane, and sometimes wholly irrelevant to the questions biologists pose. Denny has done a yeoman's service by wading through this literature. His presentation of linear wave theory is refreshingly straightforward and error-free, unlike many books on this subject written for ocean engineers. Breaking and broken waves, tidal mechanics, the utility of spectral analysis in describing the random sea, and benthic boundary layers are expounded in exceptionally clear prose. Biomaterials, beam theory, hydrodynamic drag, and adhesion have been addressed in other books on biomechanics, but Denny succeeds in integrating them into his analysis of form and function. Given his talent for clear, clever explanation I was occasionally disappointed with certain omissions of derivation, for example, wave group velocity, cnoidal wave theory, fast Fourier transform techniques, and shear dispersion. However, throughout the text the reader is referred to more detailed sources.

The book is loaded with tables of useful mathematical expressions and well-executed graphs that enable the reader to make ball-park calculations of wave-induced water motion, boundary layer mechanics, hydrodynamic drag, and mechanical deformations of sessile creatures. Simple calculus and algebra are used in a semirigorous, even friendly manner that should reduce the math anxiety often felt by life scientists when tackling these subjects.

A more appropriate ordering of words in the title might be "Mechanics and Biology," since the emphasis is definitely on the mechanics. References to the ecological literature are relatively scarce in sections concerned with wave mechanics, since few biologists have known how to pose the important questions and make the appropriate measurements. Denny provides many interesting speculations, usually grounded in quantitative predictions, that should provide stimuli for future doctoral dissertations. The chapters on turbulent diffusion and its probable importance in external fertilization and larval recruitment, mechanical constraints on size and shape of intertidal organisms, and the potential effects of wave exposure on "mechanical survivorship" are the most explicit in relating physical theory to biology. A better integration of the extant literature on larval recruitment and the life history strategies and physiological adaptations of modular organisms would probably have made the book more appealing to biologists as yet uncommitted to a biomechanical approach.

The utility of the book as a reference is increased by a thorough index and a list of mathematical symbols. An excellent chapter on measurement techniques, many developed by Denny, concludes the book, although surprisingly there is no discussion of analog-digital techniques and dataloggers, valuable tools given the quantity and nature of the data sets often collected in these studies.

This book should be stimulating reading for all students of nearshore life. It equips marine scientists with the background necessary to tackle pressing and knotty problems in ocean science, such as the effects on larval recruitment of coupling between offshore and inshore oceanographic phenomena and the role of physical disturbance in the evolution of certain life history strategies, biomaterials, and structures.

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