Water Transport Mechanisms

Water Movement Through Lipid Bilayers, Pores, and Plasma Membranes. Theory and Reality. ALAN FINKELSTEIN. Wiley-Interscience, New York, 1987. xii, 228 pp., illus. $39.95. Distinguished Lecture Series of the Society of General Physiologists, vol. 4.

Water transport, or "osmosis," is one of the most venerable problems in biology. Superficially, the phenomenon seems quite simple: water moves in response to gradients of hydrostatic and osmotic pressure. However, inquiry into the mechanistic details of this process often leaves one with the uneasy feeling that it may never be possible to understand why water moves in one direction or another. *Water Movement Through Lipid Bilayers, Pores, and Plasma Membranes: Theory and Reality*, by Alan Finkelstein, may not eliminate this chronic uneasiness, but it is sure to bring the underlying causes into sharp focus.

The book is divided into three parts. The first outlines the fundamental physical principles that pertain to water movement by diffusion and bulk flow. Part 2 reviews the water-transport properties exhibited by lipid bilayers in the presence and in the absence of the well-characterized, pore-forming antibiotics Nystatin and gramicidin A. The final section considers the results and implications of water-transport measurements on red blood cells and epithelial sheets. Each of these sections would have been a valuable contribution alone. Together they provide an enormous resource that enables the reader to examine the application of basic principles in model systems as well as in biological membranes.

Part 1, the theory section, is important for several reasons. First, it is the only source known to this reviewer that presents a systematic development of the physical laws governing water flow. More important, however, the author keeps the discussion firmly rooted in physical reality by exploring the fundamental physics of water flow in terms of two limiting cases: the "oil" membrane, through which water and solute must permeate by simple solubility and diffusion, each interacting only with the substance of the membrane, and the "porous" membrane, in which the dominant transport route consists of water-filled pores within which water-water and water-solute interactions are important. A central feature of this section is an analysis of the driving force for bulk water flow in a pore due to a transmembrane osmotic gradient. The author develops the concept that an applied osmotic gradient results in a pressure gradient within the pore despite the absence of a net difference in hydrostatic pressure across the membrane. Although this is not a new idea, its implications have never been so fully explored.

The development of the physics of water flow proceeds inexorably from the basic notion of solubility and diffusion in an "oil" membrane to the final conflict: the analysis of volume flow in a porous membrane that is also permeable to solute. A central character in this drama is the reflection coefficient, σ, a phenomenological parameter derived from a purely thermodynamic analysis of fluid flow which has been widely used to "correct" the driving force for osmotic volume flow in the case of a permeant solute. The goal is to penetrate beyond equations to the physical underpinnings of the process, and the author pits the physical-intuitive view of water flow in leaky membranes against that derived from the phenomenological theories of irreversible thermodynamics. The battleground is the well-known "uphill water flow" experiment of Meschia and Setnikar, in which water is induced to move in a direction *opposite* to the orientation of its chemical potential gradient by bathing the opposite sides of a porous membrane with solutions containing a permeant solute (urea) and an impermeant solute (dextran). Several related experimental situations are discussed for which the underlying physics appears transparent, whereas the "explanation" derived from a thermodynamic analysis seems hopelessly muddled. The author argues convincingly that the irreversible thermodynamic approach, because of its tendency to cast thermodynamic potentials in the role of mechanical driving forces, can suggest an interpretation of osmotic flow that "completely distorts reality." There will doubtless be those who are offended by Finkelstein's somewhat irreverent treatment of irreversible thermodynamics, but even devotees of the theories will be forced to admit that this book represents a long overdue attempt at a critical analysis of our collective thinking about the concepts of solute and water flow embodied in the reflection coefficient.

The material in the second section comes largely from the author's laboratory, in which the relatively simple planar bilayer, with or without added pore-forming molecules, has been used as a proving ground for the analytical approaches to water transport described in part 1. Part 2 highlights the invaluable role that such studies play in providing a sound conceptual basis for an attack on the more formidable problems posed by the complexities of biological membranes. A prime example is the concept of single-file water flow and the effect of this flow mechanism on the ratio of osmotic to diffusional water permeability.

The final section reviews two biological situations for which most of the data on water transport have been obtained, the red cell and ADH-sensitive epithelia, with emphasis on the identification of the major pathways for water transport.

Finkelstein's clarity of exposition and his dedication to revealing the physical basis of biological transport phenomena make this a monograph that can be read with profit by a wide audience, including beginning students as well as experienced practitioners. It is such a genuinely satisfying book that I have considered not only giving it to my friends but simply leaving it where it can be discovered by others who might benefit from it.

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Control of Development

Developmental Genetics of Higher Organisms. A Primer in Developmental Biology. GEORGE M. MALACINSKI, Ed. Macmillan, New York, 1988. xxxvi, 503 pp., illus. $74.95. Primers in Developmental Biology, vol. 3.

The ultimate goals of developmental genetics are to elucidate the logic of the "genetic program" specifying development and to reduce the complexities of development to problems in cell and molecular biology. Current research is aimed either at identifying by classical genetic analysis those genes that control development or at understanding the role played during development by genes that have been identified by other means (for example, oncogenes or tissue-specific cDNAs). The essence of modern developmental genetics can be extracted from this volume, but not without some work by the reader. As the editor admits in his introduction, some of the main issues in developmental genetics are addressed only indirectly. Moreover, the order of the 20 chapters does not directly reflect the four main themes of the book.

One theme is that the intense application of classical genetic analysis to the fruitfly and the nematode, organisms with simple genetics, has identified a large number of developmental control genes. The methods and logic of the genetic analysis of *Caenorhabditis elegans*, for example the determination of null phenotypes and the construction of genetic pathways from tests of epistasis, are clearly described by Kimble and Schedl for genes controlling sex determination. The genetic analysis of early embryogenesis, focusing primarily on lethal mutations that define the maternal contribution to embryonic development, are concisely described for *Caenorhabditis* by Kemphues and for *Drosophila* by Perrimon and Mahowald.

Four chapters convey the state of the art of genetic analysis in assorted vertebrates: fish, chickens, amphibians, and mice. The reader is presented not only with the problems inherent in carrying out the genetic analysis in these organisms but also with compelling reasons why one should try. In a delightfully clear chapter, McCormick and Alton discuss in simple and critical terms the significance of the mouse T/t complex. They conclude that this complex probably does not comprise a set of genes with related functions such as the *Antennapedia* and *Bithorax* complexes in *Drosophila* (described from anterior to posterior in the chapter by Mahaffey and Kaufman) but that it nonetheless offers excellent opportunities to study developmentally important genes in a mammal.

A third theme is how new molecular methods extend the power of genetics in any organism, as described in the four chapters on transgenesis in fruitflies, nematodes, plants, and mice. In addition, ways in which gene function can be studied without involving the isolation of mutants are also described. Jäckle *et al.* review studies in which antisense RNA is used to inactivate gene activity and hence to mimic mutant phenotypes. Flytzanis *et al.* discuss gene transfer experiments with sea urchin eggs that facilitate studies of the regulation of gene expression during development of this hitherto genetically unstudied organism.

Four chapters cover the theme of DNA rearrangements and transposable elements well, but the reasons for their inclusion are often left unclear. For example, Federoff provides a lucid account of transposable elements in maize, but it may not be obvious to the uninitiated that this chapter is included because mobile elements have played an important role in the development of molecular genetics and somatic mosaicism caused by transposition is an important method of establishing cell lineage relationships.

Overall, this volume leaves the reader with an appreciation for the wealth of developmental phenomena still to be understood, a feel for the current excitement in developmental genetics, and an optimistic view of the future based on new technologies. In addition, one glimpses the thought processes of some of the researchers in the field. The candid questions posed by the editor to the contributors provoke dialogue such as one hears spoken among developmental geneticists during reflective moments. Although this volume makes interesting reading for the professional, it is neither comprehensive nor balanced and thus will not be useful as an introductory textbook. However, because it contains many excellent articles that provide lucid reviews of a variety of topics, it would serve well as a companion book for upper-division and graduate-level courses.

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Neural Differentiation

From Message to Mind. Directions in Developmental Neurobiology. STEPHEN S. EASTER, JR., KATE F. BARALD, and BRUCE M. CARLSON, Eds. Sinauer, Sunderland, MA, 1987. x, 368 pp., illus. $55; paper, $35. Based on a symposium, Ann Arbor, MI, June 1986.

To furnish even an outline of how molecular messages control the cellular differentiation that results in the thinking brain may be too much to ask from any single book. This one offers instead a series of careful reviews by people engaged in investigating various aspects of this general question. Each contributor is a specialist in a system that is adding useful information about neural development at a particular level. There are six chapters at the molecular and molecular genetic level, ten that deal with cellular differentiation and cellular interactions, and four at the level of emerging mental properties. Together, they constitute a fragmentary tale made up of isolated pieces of one of the most challenging puzzles facing scientists today. Of the several collections of papers in developmental neurobiology published during the last ten or so years, this one—because of the broad focus and the generally high quality of the reviews—may be the best.

Most of the reviews have general appeal, but some seem too focused on the contributors' own work to be of interest to nonspecialists. The introductions at the beginning of each section of the book help to put these reviews into broader context. In his chapter on the sexual differentiation of the brain, Roger Gorski describes how steroid hormones, notably estrogen, influence the development of a sexually dimorphic nucleus (SDN) in the hypothalamus. Estrogen, as a metabolite of testosterone, masculinizes the SDN. Gorski points out that the whole mammalian brain is "inherently female." He takes us through experiments that show how estrogen enlarges the SDN in males, possibly by promoting the survival of its developing neurons. Could it then be that the inherently female SDN is sculpted out of a set of neurons ready, given the signal, to become the male nucleus? A single injection of testosterone given shortly after birth can permanently modify the brain structure of a genetic female and her adult sexual behavior. Gorski makes it clear that for other dimorphic nuclei the hormones involved and their modes of action may be quite different.

Lynn Landmesser, in her excellent chapter on the formation of motor connections in the chick embryo, does not ask how the different pools of motor neurons acquire their individuality, but she shows that presumable differences in their membrane proteins lead the growing axons of these neurons to react selectively to the extracellular terrain through which they navigate the route to their target muscles. The review by Harrelson *et al.* offers a glimpse of a class of membrane-associated glycoproteins which in insects appear to be involved in pathfinding and in vertebrates may be central to target finding by axons, though it is not yet known if homologous proteins even exist in vertebrates.

To become individualized and express the membrane proteins that will ultimately regulate connections, a neuron must turn on a specific set of genes. Two chapters, one by McKinnon *et al.* and one by Chikaraishi, expertly discuss approaches to neural differentiation by studying populations of brain-specific messenger RNAs. At this level of analysis, the results are extremely sketchy and mechanistically disappointing but nevertheless intriguing. Are there special "identifier sequences" that tag genes to be turned on in neural tissues? Are there RNA messengers without polyadenylate in the brain, and if so what are their roles? Time will judge the ultimate significance of these unexpected molecular findings.

I have worked backward from sexual behavior to RNA molecules. The book goes forward and points to future research into the link between message and mind.

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Books Received

Anaerobic Bacteria. K. T. Holland, J. S. Knapp, and J. G. Shoesmith. Blackie, Glasgow, and Chapman and Hall (Methuen), New York, 1987. x, 206 pp., illus. $49.95; paper, $24. Tertiary Level Biology.

Body Posture. Experimental-Physiological Investigations of the Reflexes Involved in Body Posture, Their Cooperation and Disturbances. R. Magnus. National Institutes of Health, Bethesda, MD, 1987 (available from National Technical Information Service, Springfield, VA). xxiv, 801 pp., illus. $40. Translated from the German edition (Berlin, 1924).

The Butterflies of Indiana. Ernest M. Shull. Indiana Academy of Science, Indianapolis, 1987 (distributor, Indiana University Press, Bloomington). viii, 262 pp.,