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BIOLOGICAL TRANSPORT—AN AREA FOR APPLICATION OF ENGINEERING METHODS?

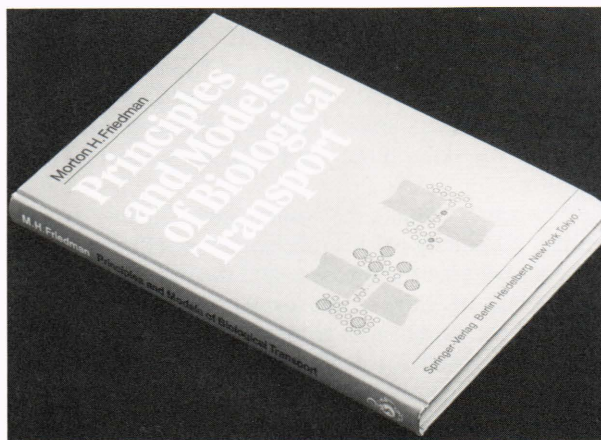
PRINCIPLES AND MODELS OF BIOLOGICAL TRANSPORT

Morton H. Friedman, *The Johns Hopkins University Applied Physics Laboratory and the School of Medicine*
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Biological transport has been a subject of interest and curiosity for engineers for some time. That interest has already resulted in several important textbooks, most notably *Transport Phenomena in the Cardiovascular System* by S. Middleman (1972), *Transport Phenomena and Living Systems* by E. N. Lightfoot (1974), *Transport Phenomena in Medicine and Biology* by M. M. Lih (1975), and *Biomedical Engineering Principles* by D. O. Cooney (1976). The books were written as traditional textbooks on chemical engineering transport phenomena; the fundamental principles and equations of mass, momentum, and energy balance were presented first and subsequently applied to physiological transport phenomena. The approach was phenomenological with relatively little emphasis on molecular mechanisms of transport phenomena. Indeed, browsing through these texts, one would find no mention of many concepts that dominate modern cell biology: receptors, the mosaic model of cell membrane, or microscopic models of ion-specific channels. Of course, many important results have been obtained in the last decade after the above texts appeared.

A new textbook by M. H. Friedman approaches the subject in a very different manner and is complementary to the previous texts. The approach is best defined by the author in the Preface:

What distinguishes biological transport from other mass transfer processes is the fact that biological transport is *biological*. Thus, we do not start with the engineering principles of mass transport (which are well presented elsewhere) and then seek biological applications of these principles; rather, we begin with the biological processes themselves, and then develop the tools that are needed to describe *them*. As a result, more physiology is presented in this text than is often found in books dealing with engineering applications in the life sciences.



This approach makes the book unique in the world literature; its content places it in the category of biophysical and physiological literature, yet it is quantitative and, where possible, uses methods of engineering analysis. Thus, it is a valuable addition to biomedical engineering literature.

There are nine chapters. The first five are devoted to fundamental principles of biological transport, the sixth analyzes general features of membrane transport, and the last three chapters consider particular examples of physiological transport systems. Although it is assumed that the reader has a limited familiarity with thermodynamics, the author attempts to make the material self-contained and introduces, at least briefly, all necessary concepts. Chapter 1 covers equilibrium thermodynamics; it contains the formulation of the First and Second Laws of Thermodynamics, including the chemical and electrochemical potentials, and such implications of the fundamental laws as the Gibbs-Duhem equation. An important situation commonly encountered in biology is ionic equilibrium across a membrane. Both the physical and the mathematical aspects of two most important forms—the Nernst and Donnan ionic equilibria—are discussed in detail. The material of this chapter paves the way to the theory of different forms of mass transport.

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Perhaps the most commonly known form of mass transport is free diffusion, which is the subject of Chapter 2. In the case of nonelectrolytes, the mechanism of diffusion is random Brownian motion. In this case, the mass flux is proportional to the concentration gradient, a relationship known as Fick's first law of diffusion. For electrolytes, random Brownian motion is mediated by the effect of the electrostatic potential gradient; the resulting relationship between the flux and the concentration and electrostatic potential gradients is expressed by the Nernst-Planck equation. Cases of both nonelectrolytes and electrolytes are considered in application to diffusion through membranes.

Materials transported across living tissue encounter barriers, most often cell membranes. On the one hand, the barriers should be sufficiently impermeable to preserve the cellular *milieu interieur*, and, on the other hand, they should allow adequate delivery of nutrients and removal of wastes through them. How do living tissues reconcile these seemingly incompatible requirements? The tissues use a process of facilitated or mediated diffusion, which is a cornerstone of *biological* transport. Chapter 3 contains a detailed account of two forms of mediators: carriers and channels. Here, as in the rest of the book, the author gives preference to simple physical models, often at the level of molecular interactions, very well illustrated by figures throughout the book, and to simple mathematical relationships rather than complicated mathematical models. For this reason, the mathematical level required from the reader does not exceed basic calculus and, occasionally, ordinary differential equations. However, despite the simplicity of the mathematics, the author goes into considerable detail in analyzing different forms of mediated diffusion, including energy-barrier models of channel transport and inhibition of carrier transport.

Facilitated transport, however important it is in biological systems, is a passive form of transport in the sense that the process acts to equalize the chemical potentials, in particular, the concentrations. The hallmark of biological systems is the presence of active transport by which materials are being transported *against* the gradients of chemical potential. Clearly, this form of transport requires expenditures of energy, which in animal cells is carried primarily by adenosine triphosphate and is released in dephosphorylation reaction. The phenomena of active transport are the subject of Chapter 4. Three primary active transport systems that have been identified in animal cell membranes are analyzed here: the sodium-potassium exchange pump, calcium pump, and hydrogen-potassium exchange pump.

The relationships between mass fluxes and chemical potentials for passive and active transport discussed in Chapters 2 and 3 can be put into a unifying formalism known as nonequilibrium or irreversible thermodynamics (Chapter 5). Simply speaking, nonequilibrium thermodynamics imposes certain constraints on

possible relationships between fluxes (e.g., mass flux, heat flux, and electric current) and its conjugate driving forces (e.g., gradients of chemical potential, temperature, and electric potential). Equations formulated in accordance with these constraints are called phenomenological equations; they contain phenomenological coefficients that could be determined either experimentally or theoretically from a kinetic theory (e.g., Einstein's equation for the diffusion coefficient of spherical solute particles or molecules). The strategy in using the formalism is to formulate phenomenological equations in the most general form (although linear relationships between thermodynamic fluxes and forces are usually adequate) and then to assess the relative importance of different terms, representing different physical mechanisms. This approach reveals, for example, that there could be mass transport associated with temperature gradient (thermodiffusion). Of particular interest for biology is the description of passive transport through semipermeable membranes in terms of nonequilibrium thermodynamics. The analysis of solute and solvent transport leads to the concepts of osmotic pressure and streaming. Chapter 5 also contains a discussion of nonlinear effects in thermodynamic relationships based on the author's own studies.

Chapter 6 deals with specific models of transport across cell membranes. In recent years, the mosaic model of cell membrane has become the most commonly accepted. The model considers a lipid bilayer with different proteins penetrating the membrane. Some molecules can dissolve in the lipid and penetrate the membrane by free diffusion (e.g., oxygen) or by facilitated diffusion (e.g., sugars). The transport of other molecules or ions cannot be explained by direct penetration of the lipid bilayer; consequently, pore transport models have been formulated to account for this form of transport.

The concepts introduced are applied to three very important types of single cells: red blood cells, nerve cells, and muscle cells (Chapter 7). Transport through layers of epithelial cells is discussed separately in Chapter 8 because there are certain important differences between single cells and layers of cells. As areas of application of epithelial transport, the small intestine and the kidney are considered. Finally, Chapter 9 deals with gas transport, primarily oxygen. The pathway of oxygen is followed from the lung, where the oxygenation of red blood cell hemoglobin takes place, to the capillaries where the hemoglobin is deoxygenated, to the tissue cells where oxygen is utilized. The classical Krogh's model of oxygen transport and its subsequent modifications are discussed.

Until now, in teaching biological transport to undergraduate and graduate engineering students one has immediately encountered a problem: no textbook existed that clearly explained transport mechanisms at the molecular level and that was, on the one hand, quantitative, and, on the other hand, not based on deep knowledge of biochemistry and cell biology,

which engineering students are normally lacking. The book reviewed here fills this gap. It is an excellent introduction to biological transport phenomena that should give the conscientious reader enough background to comprehend the results of current research in the field. In teaching engineering students, it would probably be best to combine the material in the book with a more conventional mathematical approach to

transport phenomena developed in previous texts.

In recent years, applications of engineering methods in biology have been extended to include analyses of cellular and subcellular systems and processes, studies that are sometimes referred to as “cellular engineering.” If that term is defined as the area of cell biology studied by engineering methods, then we can certainly regard the book as an excellent text in this new area.