

I. Membrane Structure and Function

A. Lipid structures

1. Phospholipids
2. Sterols
3. Proteins

The physical concept of hydrophobicity was explored by example, including predictive models and experimental descriptions of protein structure in membranes.

B. Fluidity

The interplay between temperature and fluidity was explored from experimental examples.

The coverage of lipid and membrane protein biochemistry fulfills a Learning Objective of providing students with an in depth knowledge of the structural and functional properties of biological membranes: Chemical structure and function and physical properties. The objective is reinforced by assignments and test questions that probe the ability of students to design and analyze novel solutions to biological problems relevant to membrane structure and function.

II. Molecular Motion

A. Diffusion

1. Einstein's explanation of Brownian motion
2. Membrane partitioning

Einstein's explanation was the starting point of a mathematical description of the flux of neutral solutes, in solution (Fick's equations) and across membranes.

The derivation of Brownian motion from first principles fulfills a Learning Objective of giving students an opportunity to explore foundational concepts in transport. The objective is reinforced by assignments and test questions that probe student abilities to apply and integrate their understanding of the properties and limitations of diffusion in tissues, cells, and membranes.

III. Gramicidin Channel

A. Historical

1. Antibiotic
2. Bioenergetics

B. Channel properties

1. Current-voltage relations
2. Ionic motion
3. Ion properties, permeability and conductance

The gramicidin channel provided a template for the exploration of the underlying causes of the flux of charged ions, in solution, and across membranes (current-voltage relations, Goldman equation, etc.), including a physical explanation of Stoke's radius, all important to the understanding of ion flux through any ion channel.

The derivation of the Goldman (and other) equations from first principles fulfills a Learning Objective of providing students an opportunity to understand the physical bases behind the Nernst Potential and other simple descriptions of the contribution of ion distributions to the electrical potentials common to all biological cells. Successful attainment of the objective is achieved through assignments and test questions that probe student abilities to apply their understanding of the ion properties and ion transport to real problems in biological transport.

IV. Potassium Channel

A. Channel structure and the mechanism of selectivity

The concepts of ion selectivity rely heavily on an understanding of the remarkable energetics and steric nature of ionic hydration.

The exploration of the nature of ion selective transport fulfills a Learning Objective of demonstrating to students the complexity of the mechanisms affecting selectivity at the level of proteins and specific amino acid domains with transport proteins. The objective is reinforced by assignments and test questions that probe student abilities to apply their understanding of the integrated interplay of ion properties and selective transport to novel and real problems in ion transport.

V. Arsenate transport

- A. Historical and environmental overview of arsenicals
 - 1. Chemistry and redox properties
 - 2. Toxicology
- B. ATPase and channel mediated arsenic extrusion
 - 1. ars operon of *E. coli*
 - 2. other transport mechanisms

We explored the bioenergetics of oxidative phosphorylation, using the bacterial system as an experimental tool to assess the driving forces for arsenic extrusion via channel and pump mechanisms.

The evolution of active (energy-requiring) ion transport is exemplified by the arsenic pump(s). Here the Learning Objective is to place the energetics of transport in the context of real biological transport, and introduce a conceptual framework for the evolution of transport and the evolution of scientific discovery of transport mechanisms. The Learning Objective outcome is established by requiring the students to integrate and apply the conceptual framework of energetics to novel biological transport phenomena.

VI. Mechanosensitive Channels

- A. Methods of measurement (patch clamp)
- B. Biological examples of mechanosensation
 - 1. Osmotic shock
 - a. pressure-volume relations
 - 2. *Eschericia coli* mechanosensitive channels: cloning and phenotype
 - 3. Mechanosensitive channels in cellular growth
 - 4. Mecahnosensitive channels in the heart
- C. Spider Venom (GsMTx4)
 - 1. Mechanism of action: Membrane disruption

The discovery of the specific inhibitor of mechanosensitive channels, GsMTx4 from Tarantula spiders presages a new era of discovery, unraveling the divers roles of mechanosensitive channels.

The case study approach for mechanosensitive ion channels fulfills the Learning Objective of introducing students to an integrative framework of transport, in which physical properties of cells play a crucial role intertwined with the structure and function of the transporters themselves. Also, the students are introduced to experimental methods used to measure transport. Successful achievement of the Learning Objectives is demonstrated by assignments and test questions that challenge the students to apply and integrate their understanding to solve novel biological transport problems.

VII. Light-activated channels

- A. Introduction to algal vision
 - 1. Phototactic responses
 - 2. Ultrastructure and photobiological properties
 - 3. Identification of putative channels by heterologous expression and analysis in *Xenopus laevis*
- B. A working model of vision and signal transduction in a protist
The integration of ion transport to create a system of vision and response. Here as in the bacteriorhodopsin and halorhodopsin, the mechanism involves a retinol.
- C. Optogenetics
The application of basic biological discoveries is exemplified by the expression of light-gated ion channels in brain to directly control the central nervous system.

The integration of transduction and transport are exemplified in algal vision, and fulfill the Learning Objective of giving students an opportunity to integrate and apply their knowledge to understand and interpret systems approaches to biological transport.

VII. Archaeal Transport

- A. Membrane permeability and temperature
 - 1. First order kinetics
 - 2. Adaptations to elevated temperature
 - a. ether *versus* ester linkage
 - b. bilayer *versus* monolayer
 - c. phytanal and cyclopentane modifications
- B. Bacteriorhodopsin
 - 1. *Halobium salinarum*
 - 2. H⁺ Pump mechanism
- C. Halorhodopsin
 - 1. Cl⁻ Pump mechanisms
 - 2. Optogenetics

The extremophiles offer a glimpse into life at the edges of survivability. Modifications of lipids offer one example of the adaptive capabilities of life. The light-driven pumps offer an insight into a primordial mechanism of transport, one that is being harnessed in applied research.

Transport under extreme conditions fulfills the Learning Objective of giving students clear examples of the diversity of transport solutions to environmental stresses. Again, integration and application are crucial aspects tested to ensure the Learning Objective is fulfilled.

Assignments and Grading:

Three term assignments (short work problems): 30% (lowest, 5%; middle, 10%; highest, 15%)

Two term tests and final exam: 70% (lowest, 10%; middle, 20%; highest, 40%)

Textbooks

Berg, H.C., Random Walks in Biology. Princeton University Press.

Berg presents the physical basis of random walks: the movements of molecules. Random walks are the foundation of diffusive fluxes, and are the starting point for a rigorous exploration of molecular transport at membranes. The presentation is physics-oriented.

Byrne, J.H. and S.G. Schultz. Membrane Transport. An Introduction to Membrane Transport and Bioelectricity. (Course Kit)

Byrne and Schultz are writing for a medical student audience. So, the presentation is not very rigorous. It is a gentler introduction to all aspects of transport, including action potentials. It should be helpful to students as an overview.

Lecture Notes (provided on e-reserve)

- 01_Membrane_Structure.pdf
- 02_Movement_of_Molecules_Through_Membranes.pdf
- 03_Gramacidin_Channel.pdf
- 04_Potassium_Selectivity.pdf
- 05_Arsenic_Pumps.pdf
- 06_Mechanosensitive_Channels.pdf
- 07_Algal_Vision.pdf
- 08_Archael_Transport.pdf

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