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. Olfaction
- A. Overview of environmental sensing
- B. Insects as a model system
- C. CO_2-sensing

Receptor-transduction-outcome pathways were explored using insect sensilla as an example, with emphasis on the experimental techniques –electrophysiology, oocyte expression, and patch clamp– used to characterize the complete system.

The integration of ion transport into sensory/response networks is a major role of membrane transport in the cell. Here the Learning Objective is to present a systems approach in the context of experimental methodologies so that students are provided with an understanding of common techniques and their use in developing an evidence-based systems network. The Learning Objective outcome is established by requiring the students to integrate and apply the conceptual framework of systems analysis to novel biological transport phenomena.

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.

VIII. Acid-Sensing Ion Channels
- A. Acid gating in neurons
- B. Cloning the channel gene

C. Physiological function
   1. Acid gating in synaptic gaps
      a. pH buffering
      b. learning
      c. mouse knockout models
D. Channel structure
      a. x-ray crystallography
E. Snake Venoms
   1. Coral snake toxin: Pain inducer
   2. Mamba snake toxin: Pain inhibitor

The discovery of an acid-gated ion channel in neurons raised many questions with respect to its potential role, although it was quickly apparent that it played a role in the sensation of pain in mammals. With the discovery of specific peptides in snake venom that are either agonists or antagonists, many of the fundamental questions about physiological roles may be answered. The discovery of a pain inhibitor, as efficacious as opiates opens possible doors to pain management in humans.

The case study approach for acid-sensing 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.

Assignments and Grading:

Three term assignments (short work problems):	30% (10% each)
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_Olfaction.pdf
07_Algal_Vision.pdf
08_Acid_Sensing_Channels.pdf

Course Director: Roger R. Lew
1 December 2012