BIOL 200 (Section 921)
Lecture # 6-7
June 26/27, 2006

UNIT 5: MEMBRANES

Reading:
ECB (2nd ed.) Chap 2, pp 70-74 (to review carbohydrate and lipid chemistry); **Chap 11**, pp 365 –386; **Chap 12** pp. 389-410 (essential) 411-421 (optional), and related questions [11-9a,b,c,d,e,f, 11-10 to 11-14, 11-17, 11-18; 12-9abce; 12-11; 12-12; 12.13; 12-15; 12-18]
or
ECB (1st ed.) Chap 2, pp 56-59 (to review carbohydrate and lipid chemistry); **Chap 11**, pp 347 –368; **Chap 12** pp. 371-394 (essential) 395-403 (optional), and related questions [11-9a,b,c,d,e,f, 11-10 to 11-13, 11-15, 11-18, 11-19; 12-9abce; 12-10; 12-11; 12-12; 12-14; 12-17]

I. MEMBRANES: LIPIDS, LIPID BILAYERS

Study Objectives:

1. Explain the condensation reactions that occur to assemble lipids and to form glycolipids
2. Explain the connection between the fluid mosaic model and the evidence supporting it.
3. Recognize that models of membranes have to be revised constantly to account for new experimental data.
4. Understand the properties and general synthesis of phospholipids, glycolipids, cholesterol, and various glycosides in membrane structure
5. Understand the properties of integral and peripheral proteins in membrane structure

Classes of Membrane Lipids:
1. Phospholipids: the most abundant type of membrane lipid. Made of hydrophobic long chain fatty acid tail and hydrophilic "head". Fig. 11-6.
2. Sterols-remember that these multiring structures are formed from "isoprene" subunits and have amphipathic properties due to the OH group (see Fig. 11-7)
3. Sphingolipids- (Fig. 11-7) important in PMs , especially in the nervous system.
- based on the molecule sphingosine, which is derived from serine instead of glycerol.
- More complex than phospholipids.
- sphingosine + 1 fatty acid=ceramide

Question: How are lipids and proteins organized within the membranes?
Answer: Available data support the **"Fluid Mosaic Model"** (ECB, **Fig. 11-4**), proposed by Singer and Nicolson in 1972. This model depicts a fluid lipid bilayer with proteins embedded in the bilayer like icebergs in an ocean.

Key Features of Fluid Mosaic Model:
Membrane lipids are
- arranged in a bilayer

- fluid (free to move in plane of bilayer) - Experimental evidence using FRAP (Fluorescence recovery after photobleaching) technique (see course website for details of this experiment)
- asymmetrically arranged (different lipid components on one face of the bilayer than the other)

Membrane proteins are

- globular units with hydrophobic domains embedded in the hydrophobic core of the membrane,
- "fluid", in the lipid bilayer, unless anchored by interactions with other proteins.

Membrane of each organelle has its own unique lipid composition. Example: Rat liver cells

Lipid	**ER**	**PM**
PC	40	24
PE	17	7
Cholesterol	6	17
Sphingomyelin	5	19
Glycolipids	Trace	7

II. MEMBRANE PROTEINS

Study Objectives:

- Explain the difference between peripheral and integral membrane proteins
- Explain the forces that anchor proteins of each of these classes to membranes.
- Explain how proteins can form 'aqueous pores' for transport of water, ions and other charged molecules.
- Explain how membranes differ from bimolecular phospholipid leaflets.
- Explain the evidence for fluid mobility of proteins within the plane of the membrane

Question: What are the cellular functions of membrane proteins?
Answer:

a. Proteins are required for selective permeability and transport of molecules across membranes.

b. Transporters (pumps and channels in membranes)- molecules (enzyme systems) that transport specific molecular types across membranes.

c. Linkers between things inside and outside of the membrane, or between the membrane and outside, e.g. integrins. They also provide for linkage between membranes and the

inside of the cell, for example the cell cortex (the part of the cytoskeleton interacting with the plasma membrane).

d. Receptors - Signal transduction - role of hormones etc. these agents cause different response in different cell types.

e. Enzymes - attached to membranes

f. Membranes form cellular compartments (compositionally distinct)

Membrane of each organelle has its own unique lipid and protein composition.

III. MEMBRANE STRUCTURE - PLASMA MEMBRANE

Study Objectives

- Recognize a glycolipid; distinguish a glycolipid from a glycoprotein
- Explain the role of membrane carbohydrates in protection, cell-cell recognition, and adhesion
- Explain how the cell cortex reinforces the membrane.
- Explain the connection between the fluid mosaic model and the evidence supporting it.
- Recognize that models of membranes have to be revised constantly to account for new experimental data
- Explain that the fluid mosaic model of membrane structure is not a 'picture' but a theory of membrane structure based on experimental observations.

IV. MEMBRANE FUNCTION -TRANSPORTES, CHANNELS AND MEMBRANE POTENTIAL

Learning Objectives:

- Each membrane has specific functions which are reflected in the functioning systems located in it.
- To understand fundamental transport processes across membranes and the role of membrane proteins.
- To understand the linkages between electrical forces, ATP hydrolysis and specific ion transport pumps.
- To understand ion selectivity, gated channels and membrane potential. Nernst equation
- To understand how a membrane potential is generated and propagated.
- To understand the link between ion channels and nerve impulses.
- Understand the control of directed secretion and its relation to nerve impulse transmission

Facilitated diffusion vs. Active Transport

Facilitated diffusion requires membrane proteins that are either

- transport enzymes (permeases) or
- channels

Active Transport

- Active transport occurs via enzyme-like transporter proteins.
- Energy to drive transport of a molecule or ion against its concentration gradient may come from
  ATP, Energy stored in an electrochemical gradient, or Light
- Transport proteins carry out active transport through a series of protein conformation changes that are driven by binding of substrates or by phosphorylation of the protein. These changes take place in a fixed sequence in which the binding of a molecule in one step produces a conformation al change that enables the next step in the cyclical process.

Carriers - pick up solute molecule and moves it, usually requiring input of energy.
Channels - allow a solute to pass through (passively) without requiring energy input.
Ion channels are membrane transport systems in which protein molecules form a passageway through a membrane that is permeable to a particular ion only under certain conditions. The major types of ion channels in membranes are:

- l**igand gated channels**, in which the binding of another molecule, the ligand determines whether the channel is open or closed,
- **ion gated channels** that open or close in response to the intracellular concentration of some ion. and
- **voltage gated channels**, which are open or closed in response to trans membrane potential.
- **stress activated channels**, in which mechanical deformation of the protein results in opening of the channel.

Membrane Potential is result of the sum total of differences in ion concentrations across the membrane. Membrane potential is maintained by ATP driven ion pumps.

Action Potentials are a stereotyped pattern of changes in membrane potential that are the result of opening and closing of gated channels. The have several phases:

- initiation - when Na+ channels are brought to their firing threshold potential and open
- depolarization - as the Na+ channels open and let Na+ ions into the cell
- repolarization - as Na+ channels close and K+ channels open restoring normal polarity

Propagation of action potentials occurs because

- depolarization of the membrane brings adjacent channels to their firing threshold and
- inactivation of channels after they have opened ensures that the action potential can spread in one direction only - outward from its point of initiation.

Transmission of action potentials from one nerve cell to another across a synapse occurs through

- regulated secretion of vesicles containing a neurotransmitter that is triggered by an action potential reaching the nerve ending;
- neurotransmitter then diffuses across the synaptic cleft and binds to ligand gated receptors in the post-synaptic cell and leads to the opening of a channel that causes a small receptor potential;
- the receptor potential causes initiation of a new action potential that moves across the post-synaptic cell.