LIPIDS III

EFFECT OF CHOLESTEROL ON MEMBRANES:
- Bulky rigid molecule
- Moderates fluidity of membranes – both increases and decreases
  - Cholesterol in membranes DECREASES fluidity because it is rigid
  - Prevents crystallization (making solid) of fatty acyl side chains by fitting between them. Disrupts close packing of fatty acyl chains. Therefore, INCREASED fluidity

![Graph showing the effect of cholesterol on lipid crystallization](image)

BIOLOGICAL MEMBRANES CONTAIN PROTEINS AS WELL AS LIPIDS:

<table>
<thead>
<tr>
<th>Membrane Source</th>
<th>Lipid</th>
<th>Protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myelin</td>
<td>80</td>
<td>18</td>
</tr>
<tr>
<td>Mouse liver</td>
<td>52</td>
<td>45</td>
</tr>
<tr>
<td>Human erythrocyte (plasma)</td>
<td>43</td>
<td>49</td>
</tr>
<tr>
<td>Corn leaf</td>
<td>45</td>
<td>47</td>
</tr>
<tr>
<td>Mitochondria (outer)</td>
<td>48</td>
<td>52</td>
</tr>
<tr>
<td>Mitochondria (inner)</td>
<td>24</td>
<td>76</td>
</tr>
<tr>
<td><em>Escherichia coli</em></td>
<td>25</td>
<td>75</td>
</tr>
</tbody>
</table>

Table 9.1
The lipid and protein compositions of several membranes. If the total is under 100%, the balance is made up by carbohydrate.

- Proteins are 20-80% of cell membrane
- Rest is lipid or carbohydrate; supramolecular assembly of lipid, protein and carbohydrate
- Proteins are also distributed asymmetrically

TWO classes of Membrane Proteins:
- Integral Membrane Proteins
- Peripheral Membrane Proteins
- **INTEGRAL MEMBRANE PROTEINS**
  - Located **WITHIN** the lipid bilayer
  - Usually span the bilayer one or more times – called transmembrane (TM) proteins
  - Hydrophobic amino acids interact with fatty acid chains in the hydrophobic core of the membrane
  - Can be removed from the membrane with detergents like SDS – need to disrupt the hydrophobic interactions
    - Membrane Disruption Animation:
    - [http://www.youtube.com/watch?v=AHT37pvcjc0](http://www.youtube.com/watch?v=AHT37pvcjc0)
  - Function:
    - Transporters – moving molecules into or out of cells or cell membranes
    - Receptors – transmitting signals from outside of the cell to the inside

- **β Barrel Integral Membrane Proteins**
  - Barrel-shaped membrane protein that is made up of antiparallel β-strands with hydrophilic (interior) and hydrophobic (facing lipid tails).
  - So far found only in outer membranes of Gram-negative bacteria, cell wall of Gram-positive bacteria, and outer membranes of mitochondria and chloroplasts.
- **α-Helical Membrane Proteins**
  - Can cross the membrane once or many times and have multiple transmembrane segments.
  - Major category of transmembrane proteins.
  - In humans, 27% of all proteins have been estimated to be alpha-helical membrane proteins.

**Membrane – Spanning α-helix**

- 20 – 30 aa long
- Span 30Å bilayer
- Polar = purple
- Non-polar = green

**Bacteriorhodopsin**

7 membrane-spanning α-helix bundle
- **PERIPHERAL MEMBRANE PROTEINS**
  - Interact weakly with the membrane lipid head groups or integral membrane proteins (usually α-helical containing integral membrane proteins)
  - Found associated with the inner or outer leaflet or integral membrane proteins protruding from the inner or outer leaflet
  - Interactions are mainly **hydrogen bonds** or **electrostatic interactions**
  - Removed from the membrane with MILD agents to disrupt **electrostatic interactions**
    - Salt – raise the salt concentration
    - pH – raise the pH
  - Functions: enzymes, signal transduction proteins, cytoskeletal proteins
  - Addition of lipids to proteins after they are made can guide otherwise soluble proteins to a cellular membrane. Lipid anchors protein in the membrane.
    - **Farnesyl** (15 carbon isoprene; modifies cysteine via thioether linkage). Carboxyl group often in the methyl ester form.
    - **Myristoyl** (14 carbon saturated chain at N-terminal glycine via amide linkage)
    - **Palmitoyl** (16 carbon saturated chain; modifies cysteine via thioester linkage)

![Farnesyl group](Figure 9-5a Concepts in Biochemistry, 3/e © 2006 John Wiley & Sons)
![Myristoyl group](Figure 9-5b Concepts in Biochemistry, 3/e © 2006 John Wiley & Sons)
![Palmitoyl group](Figure 9-5c Concepts in Biochemistry, 3/e © 2006 John Wiley & Sons)
• **FLUID MOSAIC MODEL OF MEMBRANE STRUCTURE**
  
  - A *mosaic* of lipid and proteins
    - Lipids and proteins exist side by side
  
  - The membrane is *fluid* in its functional state
    - Lipids and proteins free to move laterally within the bilayer
    - Degree of fluidity determined by types and length of fatty acids and presence of cholesterol
  
  - Membrane has *asymmetric* organization
    - Movement of lipids and proteins from one leaflet to the other is restricted
    - Particular lipid is in one leaflet of the membrane or the other (can sometimes flip-flop)
    - Particular protein is always located on one face of the membrane or oriented in one direction

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**Plasma membrane animations**

-http://www.youtube.com/watch?v=ULR79TiUj80

-http://www.youtube.com/watch?v=moPJkCbKjBs&feature=related
MEMBRANE FUNCTION

- Separate cytoplasm from environment
  - Provide selective barrier to uptake
- Provide system for uptake and export of compounds
  - Nutrient transporters
- Mediate interactions with environment
  - Receptors
- Provide environment for catalysis
  - Electron transport chains

**Membrane Transport**

- Why transport?
  - Cells need materials from surroundings for energy and biosynthesis
  - Cells need to get rid of wastes and toxins
  - Most transport occurs through proteins (pumps and channels) at the membrane
  - Three steps: Binding, Change in shape of protein, Release

**Classes of Active and Passive Transporters**

- Transport can be **passive** or **active**
  - **Symporters** – Moves a small molecule INSIDE a cell during transport of target molecule inside a cell
  - **Antiporters** – Moves a small molecule OUTSIDE the cell during transport of a target molecule inside a cell
  - **Uniporters** – Binds and transports target molecule only
PASSIVE TRANSPORT

- Small molecules pass through the membrane on their own
- Move from **HIGHER** concentration to **LOWER** concentration region
- **NO** need for energy input for this transport
- **TWO TYPES:**
  - **Simple Diffusion** – Molecule passes through membrane pore or opening **WITHOUT** interacting with other molecules
  - **Facilitated Diffusion** – Transport assisted by specific membrane protein
    - Still no need for energy input
    - Example: **Glucose Permease** in red blood cells: Bind glucose on one side of the membrane, pass through channel, release on other side of the membrane
• Glucose transporter from red blood cells undergoes a CONFORMATIONAL CHANGE in order to move glucose from one side of the membrane to the other.

• Glucose binding site alternately faces the inside and outside of the red blood cell.

• Can transport either direction – depends on concentration of glucose on each side of the membrane.

• Passive transporter – transports down a concentration gradient. (High → Low)

○ ACTIVE TRANSPORT
  • Molecule moves from low concentration area to high concentration area
  • Cell MUST use energy to transport
  • Often ATP (adenosine triphosphate) is used
    ▪ ATP is cellular energy currency
    ▪ Source of energy is from the cleavage of ATP → ADP + Pi
  • Release of the energy in that bond transports molecule
Examples:

- Glucose Transport into Intestinal Cells
  - The glucose concentration in intestinal cells is higher than that in either the intestine or the blood. That means a source of energy is required to pump the glucose from the intestine into the intestinal cell.
  
  - Unlike in red blood cells, transport goes against a concentration gradient – requires energy input – **ACTIVE TRANSPORT**.

- **Na\(^+\)-K\(^+\) Ion Pump**

  - Uses ATP; each ion moved from lower concentration to higher
  - \(3 \text{Na}^+ \text{in} + 2 \text{K}^+ \text{out} + \text{ATP} + \text{H}_2\text{O} \rightarrow 3 \text{Na}^+ \text{out} + 2 \text{K}^+ \text{in} + \text{ADP} + \text{Pi}\)
  - Net electrical potential difference across the membrane (neg inside, positive outside). In nerve cells important for nerve impulse generation.

  - ATP hydrolysis drives the unfavorable ion transport
  - Phosphorylated protein intermediate (Asp) – ensures that the transporter works in only one direction. Prevents Na\(^+\) and K\(^+\) diffusion back down the concentration gradient. Gets dephosphorylated during transport cycle
Na,K-ATPase

$\alpha$-subunit with 10 transmembrane (TM) helices. Small $\beta$ and $\gamma$ subunits not shown – each contain one TM helix.

Shown in outward facing form.

ATP binding and Asp residue are in the cytoplasmic domain.

Requires long distance communication through conformational changes.
MULTIDRUG TRANSPORTER – P-glycoprotein – ABC Transporter

Animation of P-glycoprotein Pump:
http://www.cancerquest.org/index.cfm?page=601#

ANIMATIONS:
http://www.uh.edu/sibs/tutorial/genbio1l.htm#biochem

Cell membrane and Transport

• Passive and Active Transport from Northland Community

(www.northland.cc.mn.us/biology/Biology1111/animations/transport1.html)

Nice transport video:
http://www.youtube.com/watch?v=j5Qway4LAlk&feature=related