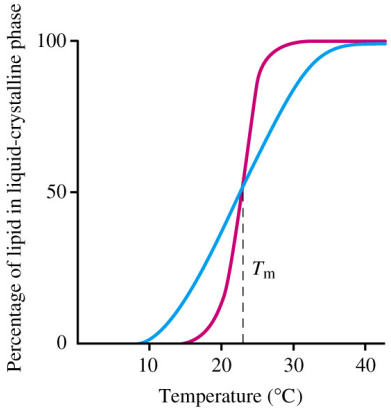
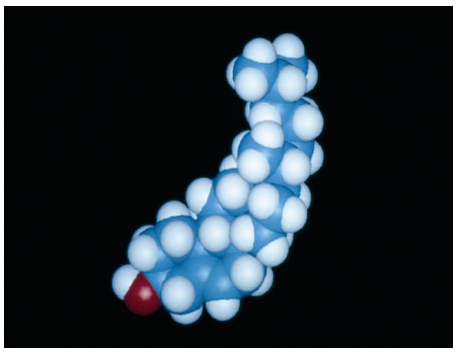
LIPIDS III

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





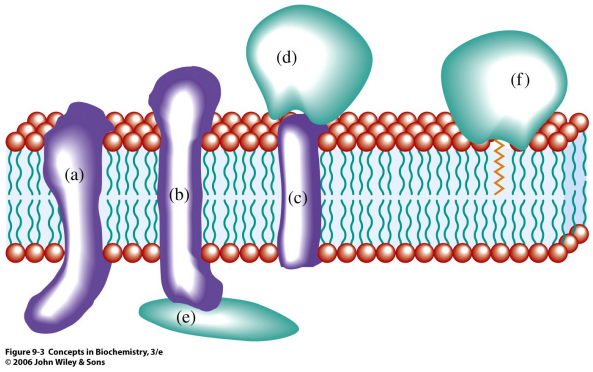
BIOLOGICAL MEMBRANES CONTAIN PROTEINS AS WELL AS LIPIDS:

Table 9.1

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

	Percentage by Weight	
Membrane Source	Lipid	Protein
Myelin	80	18
Mouse liver	52	45
Human erythrocyte (plasma)	43	49
Corn leaf	45	47
Mitochondria (outer)	48	52
Mitochondria (inner)	24	76
Escherichia coli	25	75

- 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**



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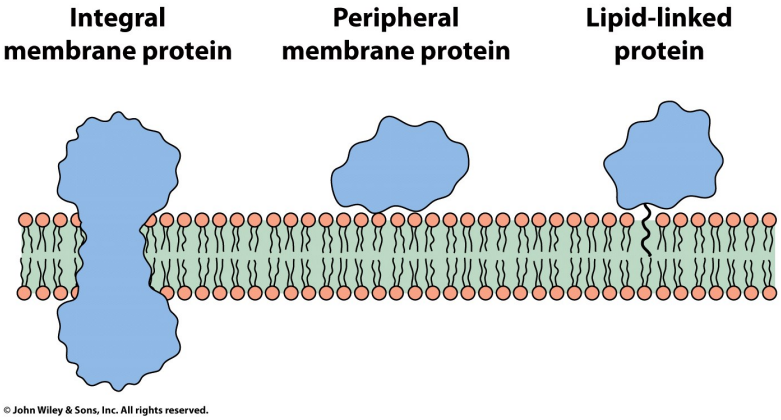

- **INTEGRAL MEMBRANE PROTEINS**
  - Located **WITHIN** the lipid bilayer
  - Usually span the bilayer one or more times – called transmembrane (TM) proteins
  - Hydrophobic amino acids interact with fatty acid chains in the hydrophobic core of the membrane
  - Can be removed from the membrane with detergents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

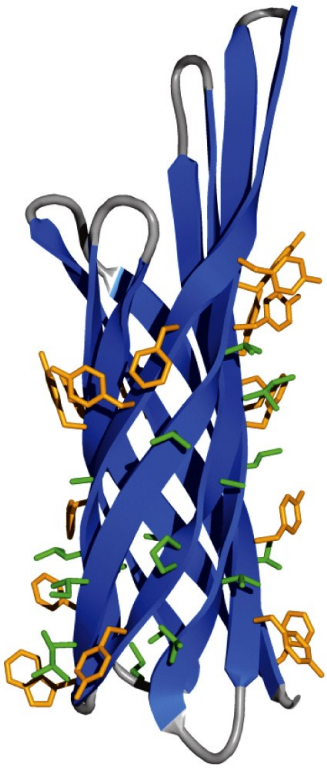

Figure 9-4 Concepts in Biochemistry, 3/e
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- **β Barrel Integral Membrane Proteins**
  - Barrel-shaped membrane protein that is made up of antiparallel β-strands with hydrophilic (interior) and hydrophobic (facing lipid tails).
  - So far found only 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

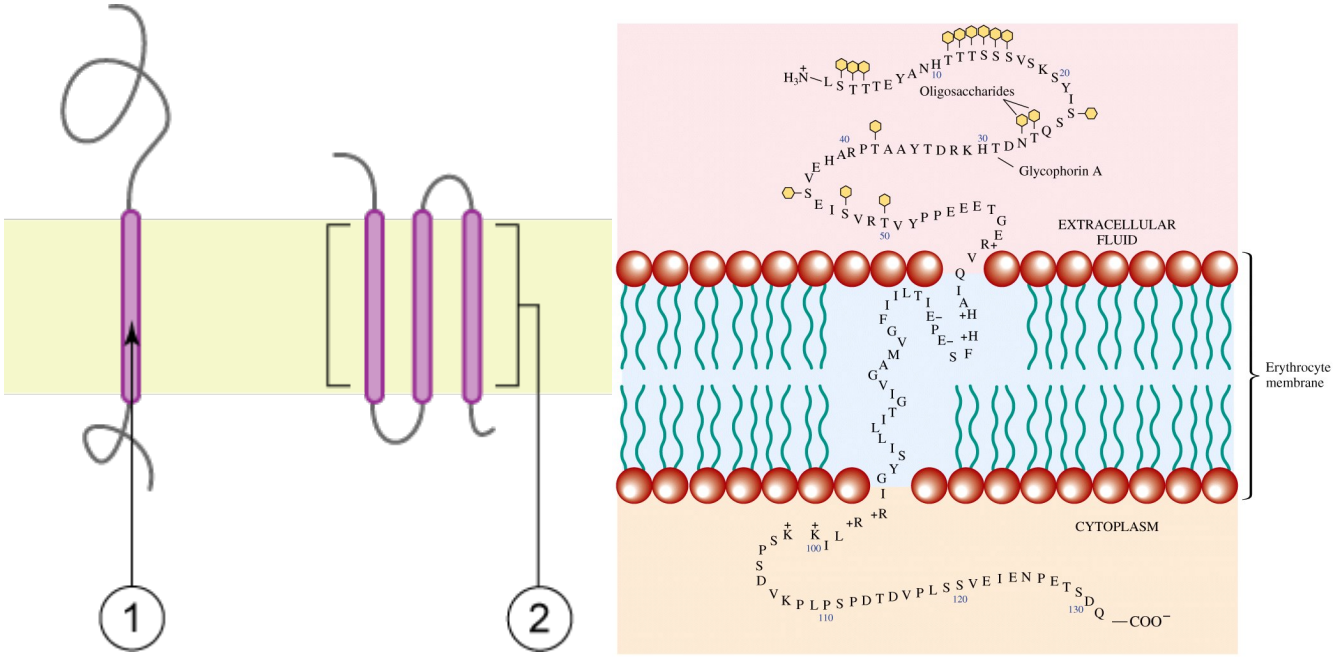

Figure 9-12 Concepts in Biochemistry, 3/e
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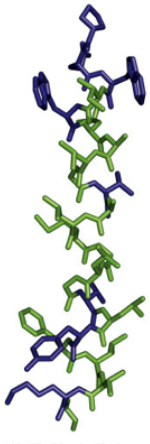
Membrane – Spanning α-helix

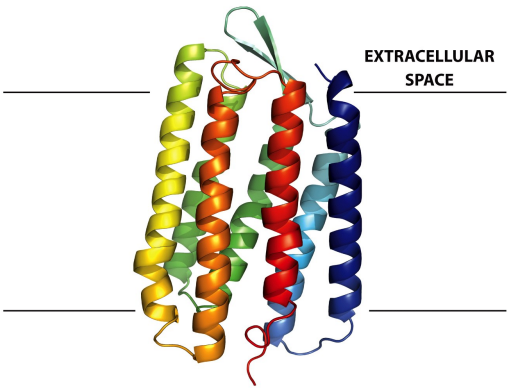
Pro–Glu–Trp–Ile–Trp–Leu–Ala–Leu–Gly–Thr–Ala–Leu–Met–Gly–Leu–Gly–Thr–Leu–Tyr–Phe–Leu–Val–Lys–Gly



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 distrupt **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)

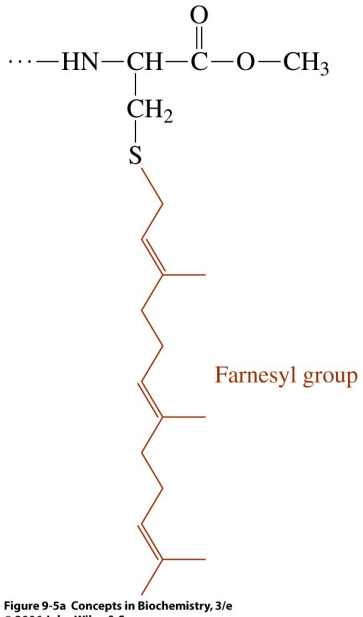


Figure 9-5a Concepts in Biochemistry, 3/e
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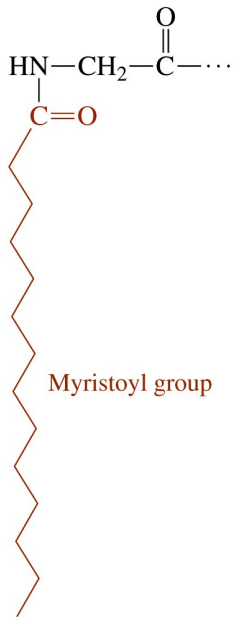

Figure 9-5b Concepts in Biochemistry, 3/e
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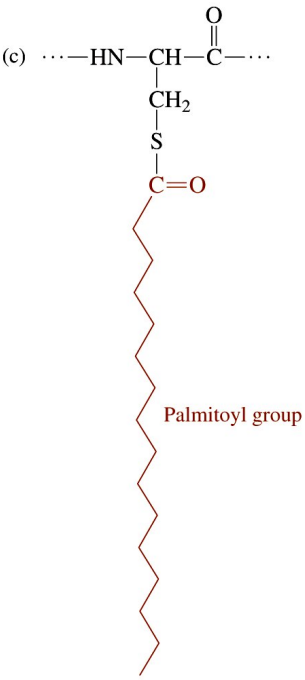

Figure 9-5c Concepts in Biochemistry, 3/e
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- **FLUID MOSAIC MODEL OF MEMBRANE STRUCTURE**
  - A ***mosaic*** of lipid and proteins
    - Lipids and proteins exist side by side
  - The membrane is ***fluid*** in its functional state
    - Lipids and 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

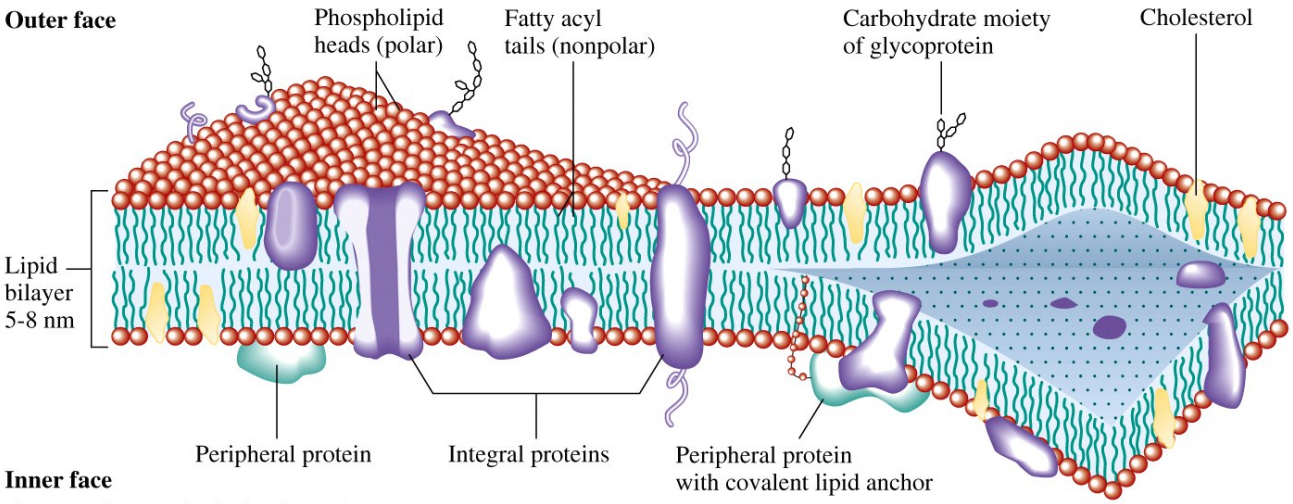


Figure 9-6 Concepts in Biochemistry, 3/e

Plasma membrane animations

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

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

MEMBRANE FUNCTION

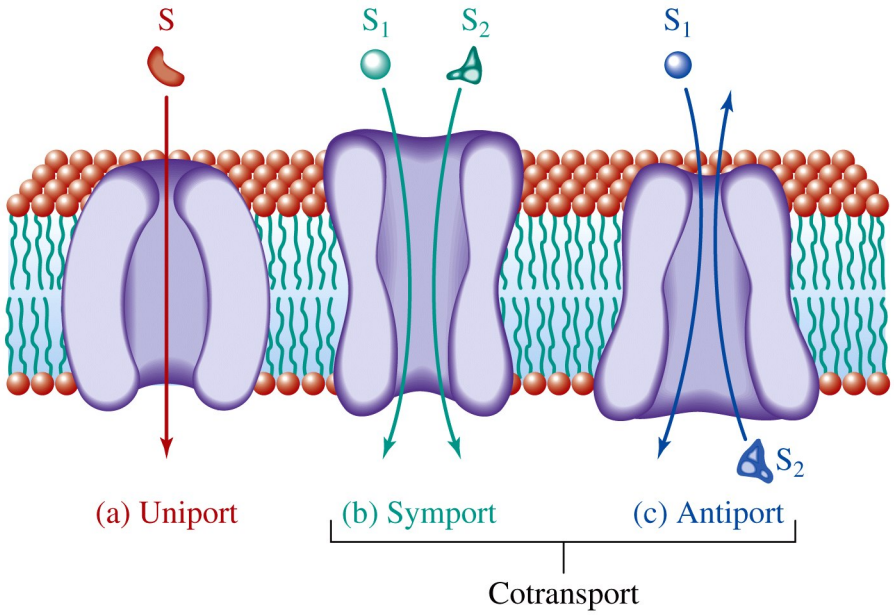
- **Separate cytoplasm from environment**
  - Provide selective barrier to uptake
- **Provide system for uptake and export of compounds**
  - Nutrient transporters
- **Mediate interactions with environment**
  - Receptors
- **Provide environment for catalysis**
  - Electron transport chains

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



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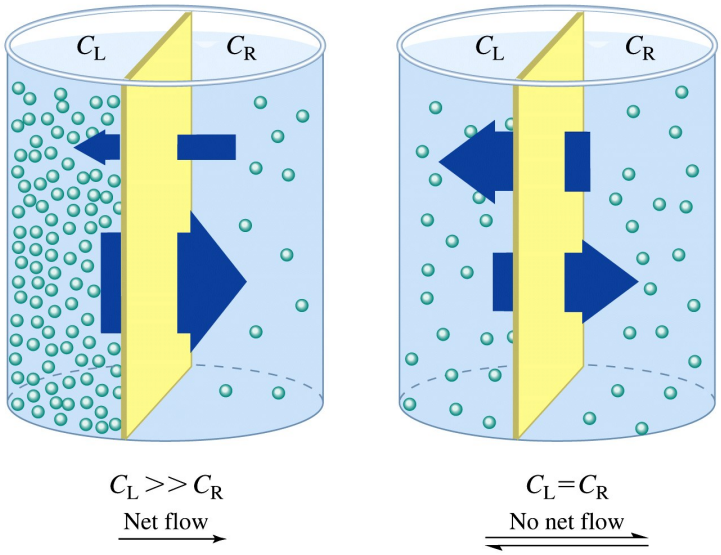
- **PASSIVE TRANSPORT**
  - Small molecules pass through the membrane on their own
  - Move from **HIGHER** concentration to **LOWER** concentration region
  - **NO** need for energy input for this transport
  - **TWO TYPES:**
  - **Simple Diffusion** – Molecule passes through membrane pore or opening **WITHOUT** interacting with other molecules



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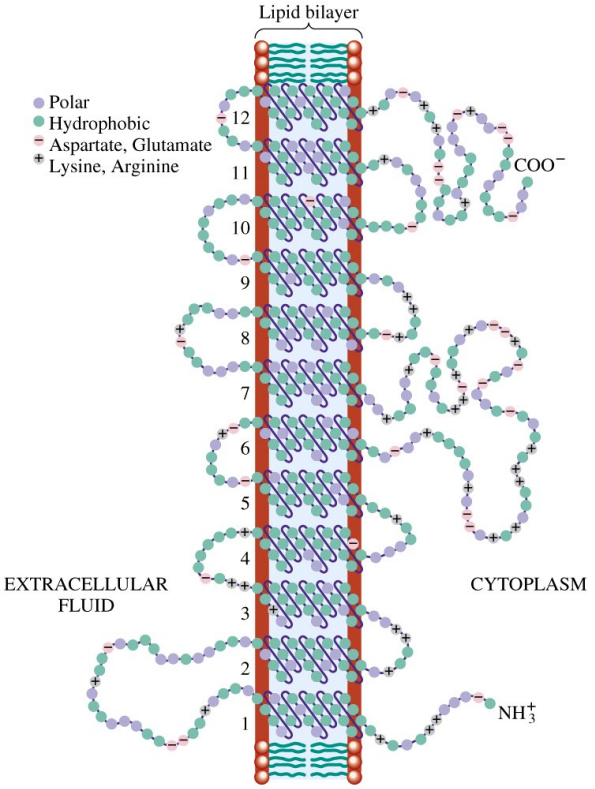
  - **Facilitated Diffusion** – Transport assisted by specific membrane protein
    - Still no need for energy input
    - Example: **Glucose Permease** in red blood cells: Bind glucose on one side of the membrane, pass through channel, release on other side of the membrane



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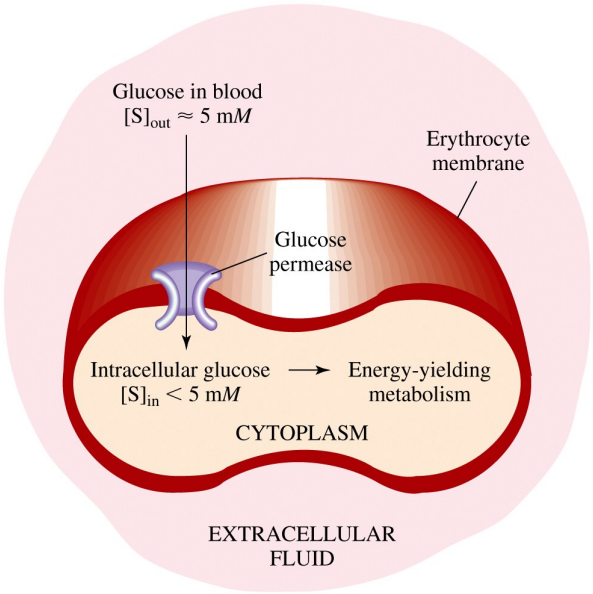

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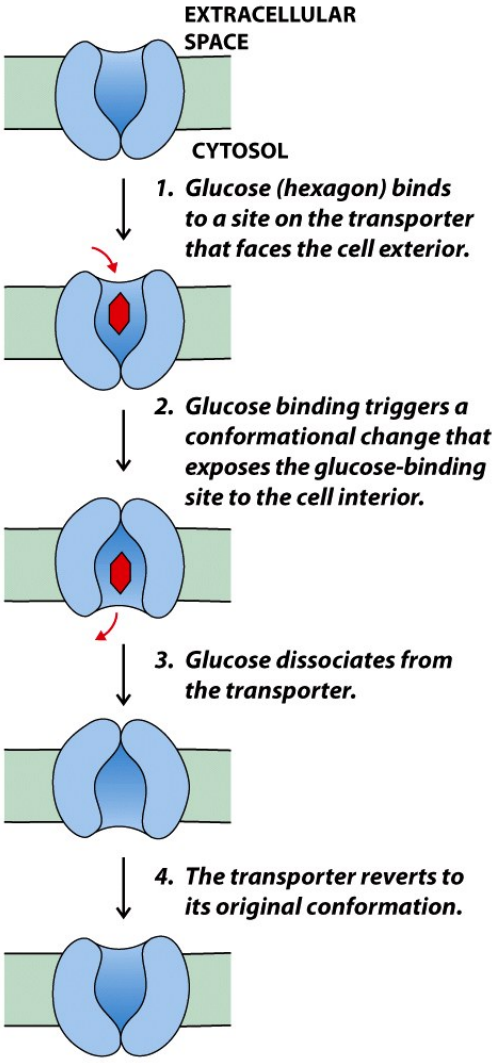

- Glucose transporter from red blood cells undergoes a **CONFORMATIONAL CHANGE** in order to move glucose from one side of the membrane to the other.

- 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

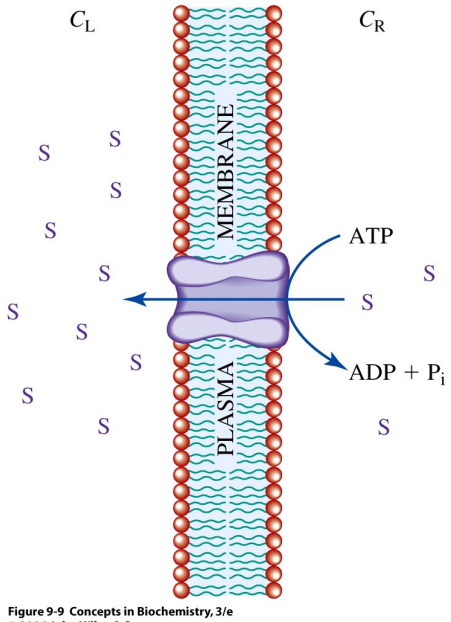

Figure 9-9 Concepts in Biochemistry, 3/e
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- **Examples:**
- **Glucose Transport into Intestinal Cells**
  - The glucose concentration in intestinal cells is higher than that in either the intestine or the blood. That means a source of energy is required 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.**

- **<u>Na^+-K^+ Ion Pump</u>**

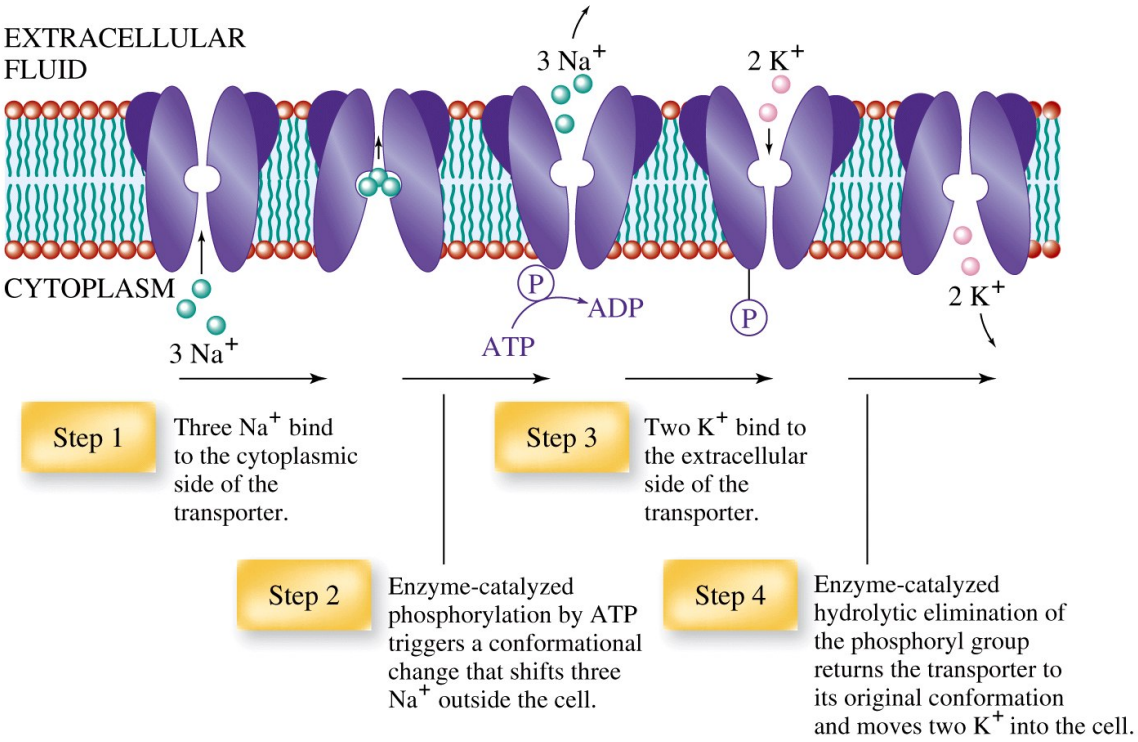
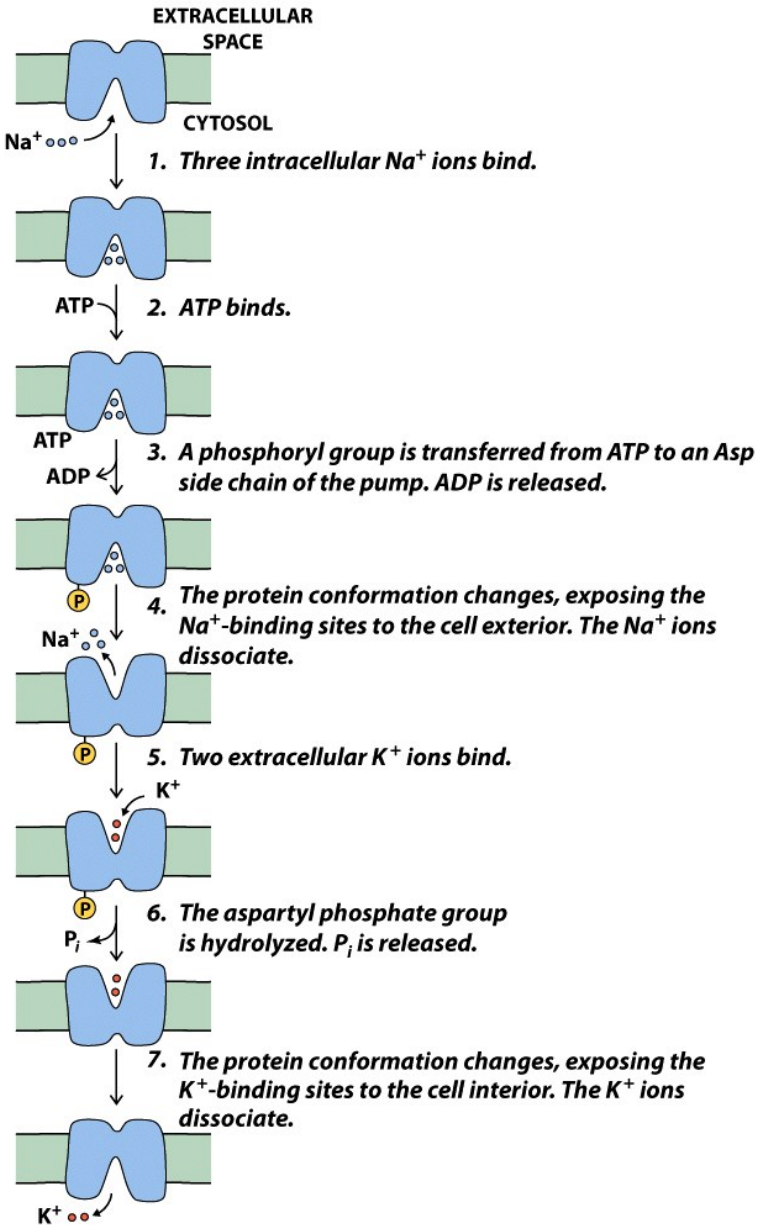


Figure 9-16 Concepts in Biochemistry, 3/e

- Moves 2 K^+ into cell and 3 Na^+ out of cell; all mammalian cells have this pump.
- Uses ATP; each ion moved from lower concentration to higher
- $3\ Na^+_{in} + 2\ K^+_{out} + ATP + H_2O \rightarrow 3\ Na^+_{out} + 2\ K^+_{in} + ADP + Pi$
- 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



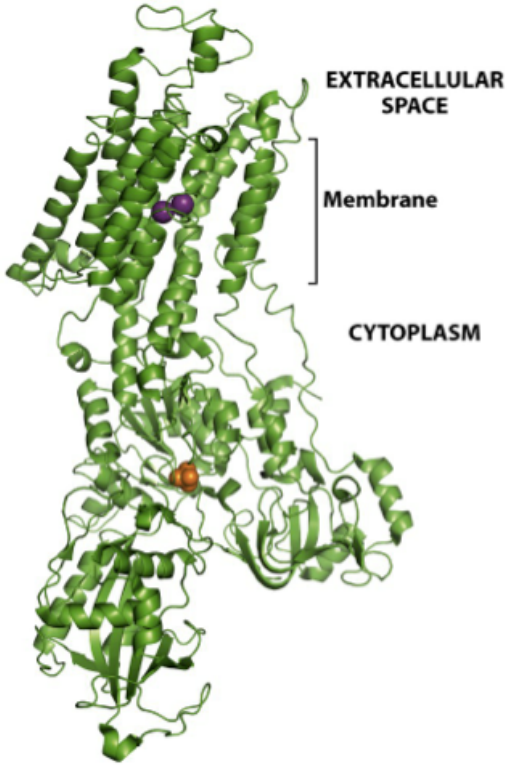
Na,K-ATPase

α-subunit with 10 transmembrane (TM) helices. Small β and γ subunits not shown – each contain one TM helix.

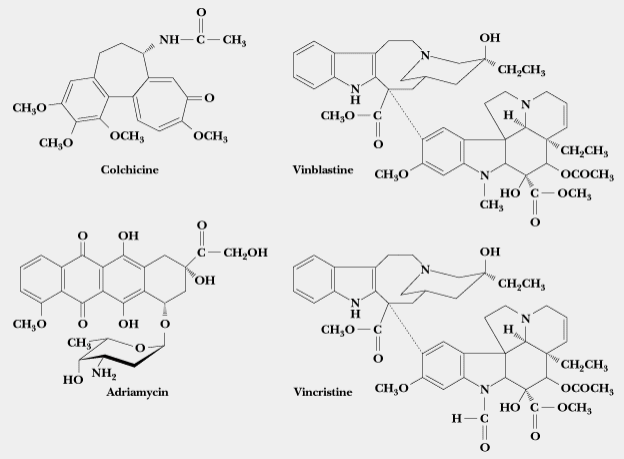
Shown in outward facing form.

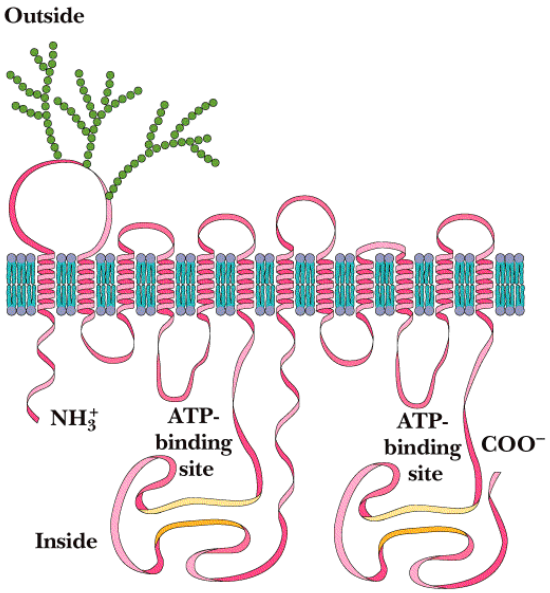
ATP binding and Asp residue are in the cytoplasmic domain.

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/genbiol1.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=j5Qway4LAkk&feature=related