Biomembranes
structure and function

B. Balen

✓All cells are surrounded by membranes

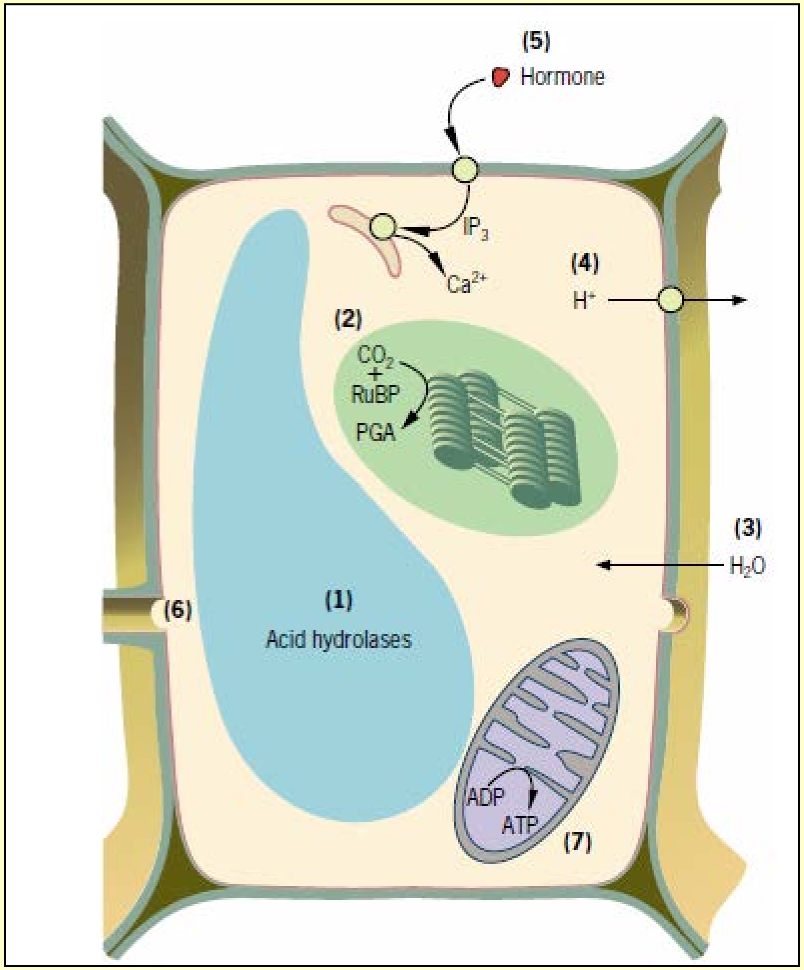


Figure 4.2. Karp, Cell Biology, 7th edition, 2013.

- Selective barrier

- **But also important for:**

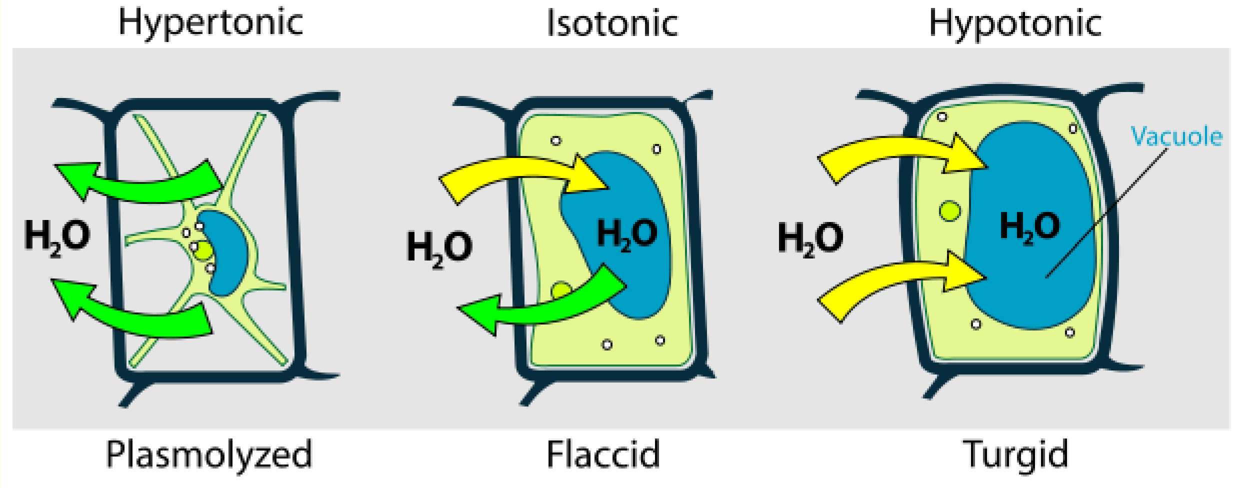
1. Compartmentalization
2. Biochemical activities
3. Transport of dissolved substances
4. Transport of ions
5. Signal transduction
6. Cell-cell interaction
7. Energy conversion

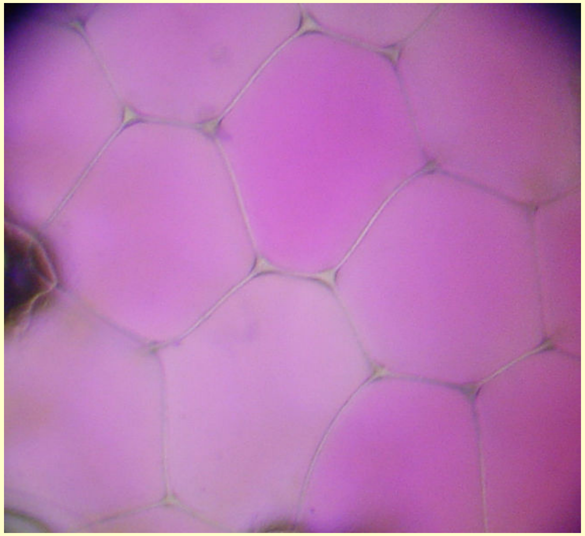
- **Dynamic structures:**

1. Constant movements
2. Continuous building and degradation of their components

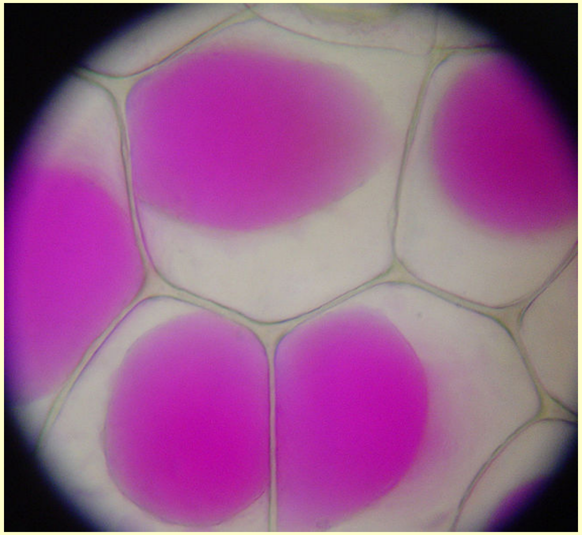
Indirect membrane observations:

➢**Nägeli** (1855.)





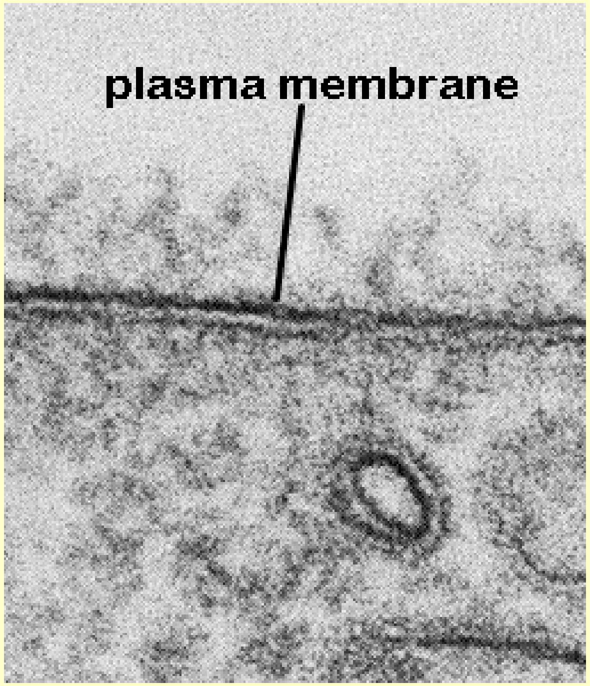
Isotonic solution



Hypertonic solution

✓ Biomembrane thickness: 5-10 nm
(not visible with light microscope)

✓ **J.D. Robertson** (1950s) first EM photos of membranes → membranes of bacteria, plant and animal cells have equal structural plan



❖ All biological membranes have common basic structure:

✓ very thin layer of lipid and protein molecules connected with non-covalent interactions

✓ dynamic and fluid structures

✓ biochemical composition: **lipids, proteins, sugars**

- membranes with similar functions (e.g. from the same organelles) are similar in different cells

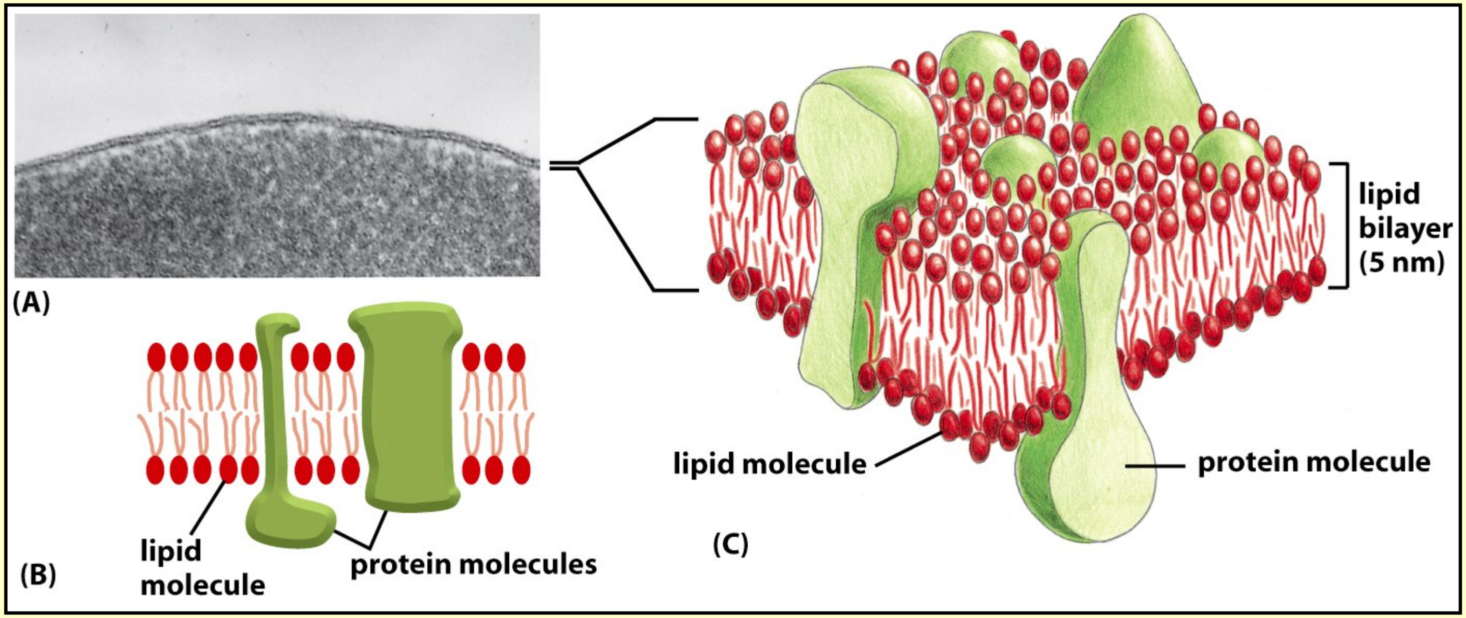
- membranes with different functions (e.g. different organelles) are very different within the same cell

✓ **Lipids**

- double bilayer (thickness 5-10 nm)
- basic fluid structure

✓ **Proteins**

- involved in membrane functions
- transport, catalyses, structure, receptors



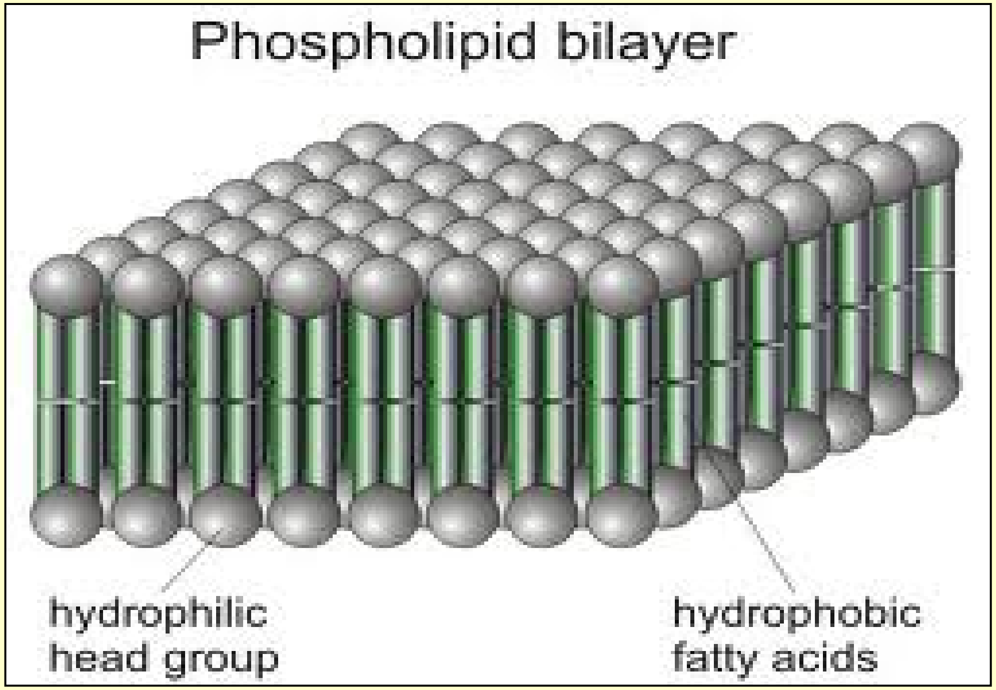
A – EM-photo erythrocyte membrane

B – 2D membrane

C – 3D membrane

Figure 10-1 *Molecular Biology of the Cell* (© Garland Science 2008)

Membrane lipids



- ✓ Amphipathic molecules
- ✓ Spontaneous formation of bilayer in aqueous solution

➢Lipid bilayer:

→ TEM - the railroad track appearance of the plasma **membrane**

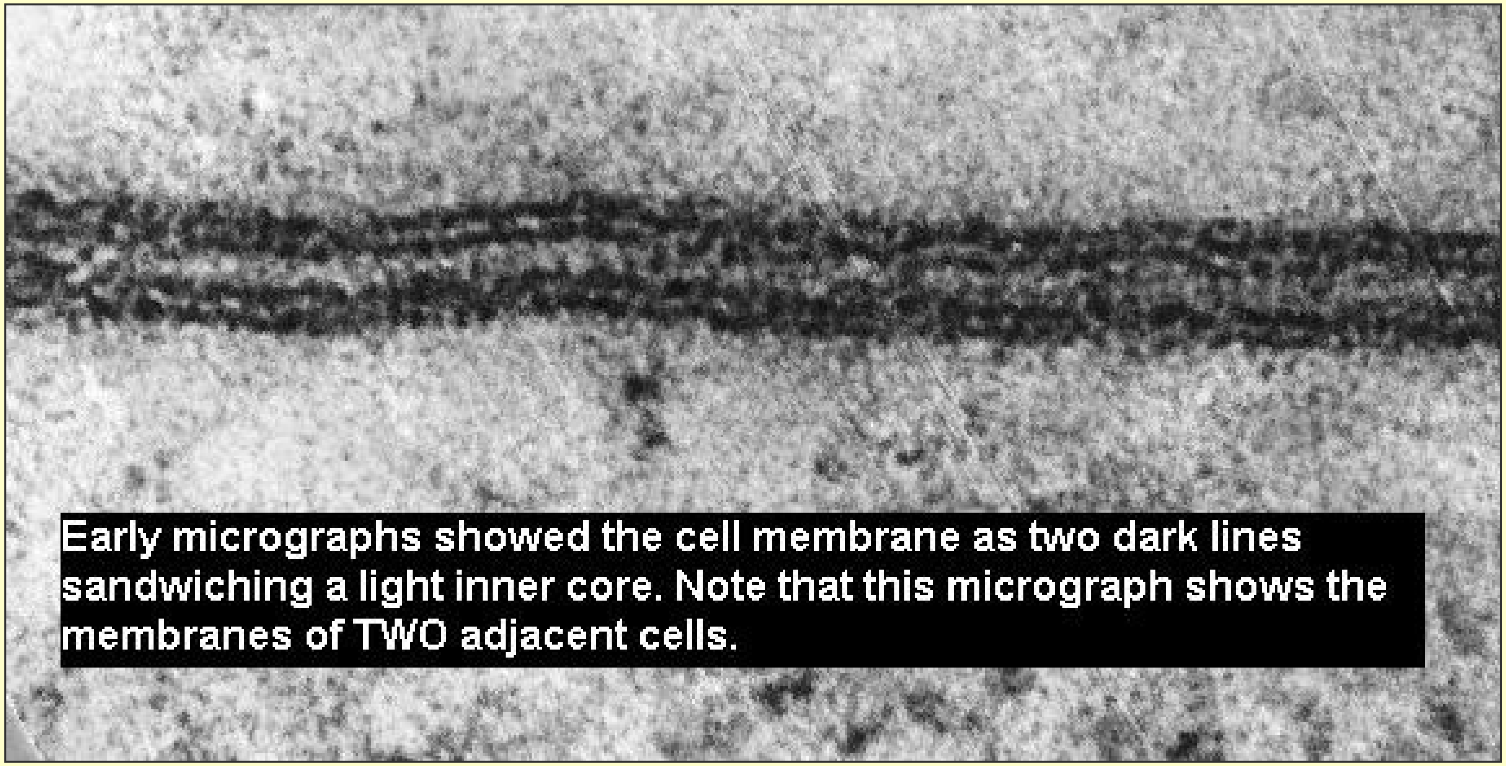


Figure 12-1. 2000. Cooper

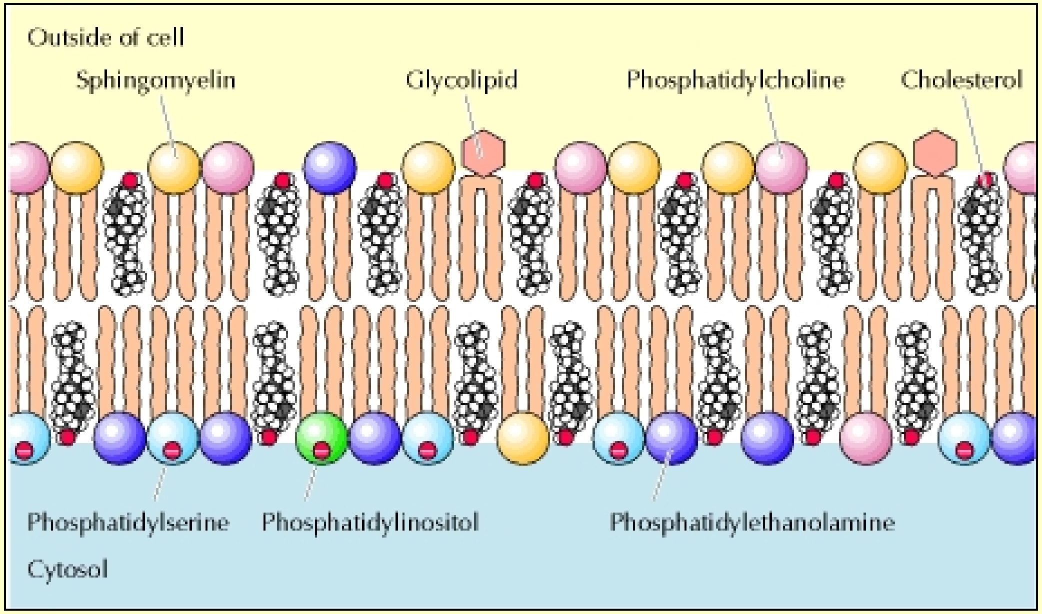
✓**Phospholipids**

- phosphatidylcholine
- sphingomyelin

} **outer (extracellular) leaflet**

- phosphatidylethanolamine
- phosphatidylserine
- phosphatidylinositol

} **inner (cytoplasmic) leaflet**

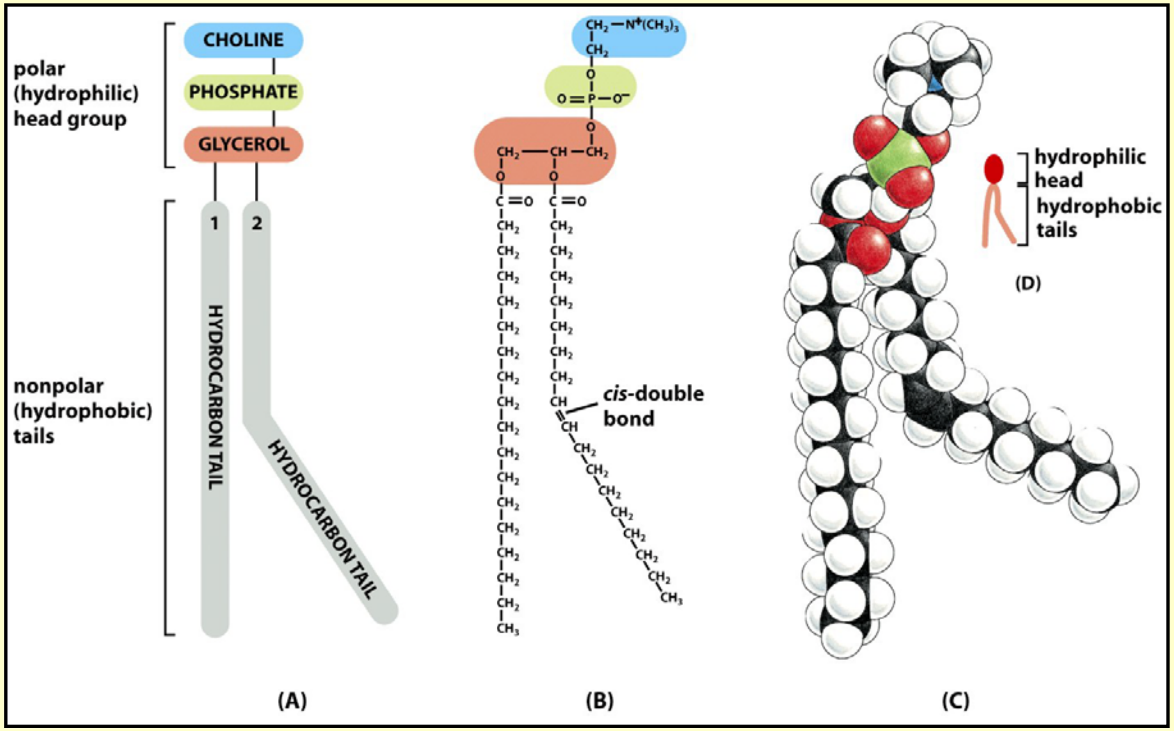


✓**Cholesterol**

✓**Glycolipids**

Figure 12-2. 2002. Cooper

Phospholipids



- **Phosphatidylcholin**

✓ polar head + two hydrophobic carbohydrate chains

✓ tails – fatty acids (14 – 24 C atoms)

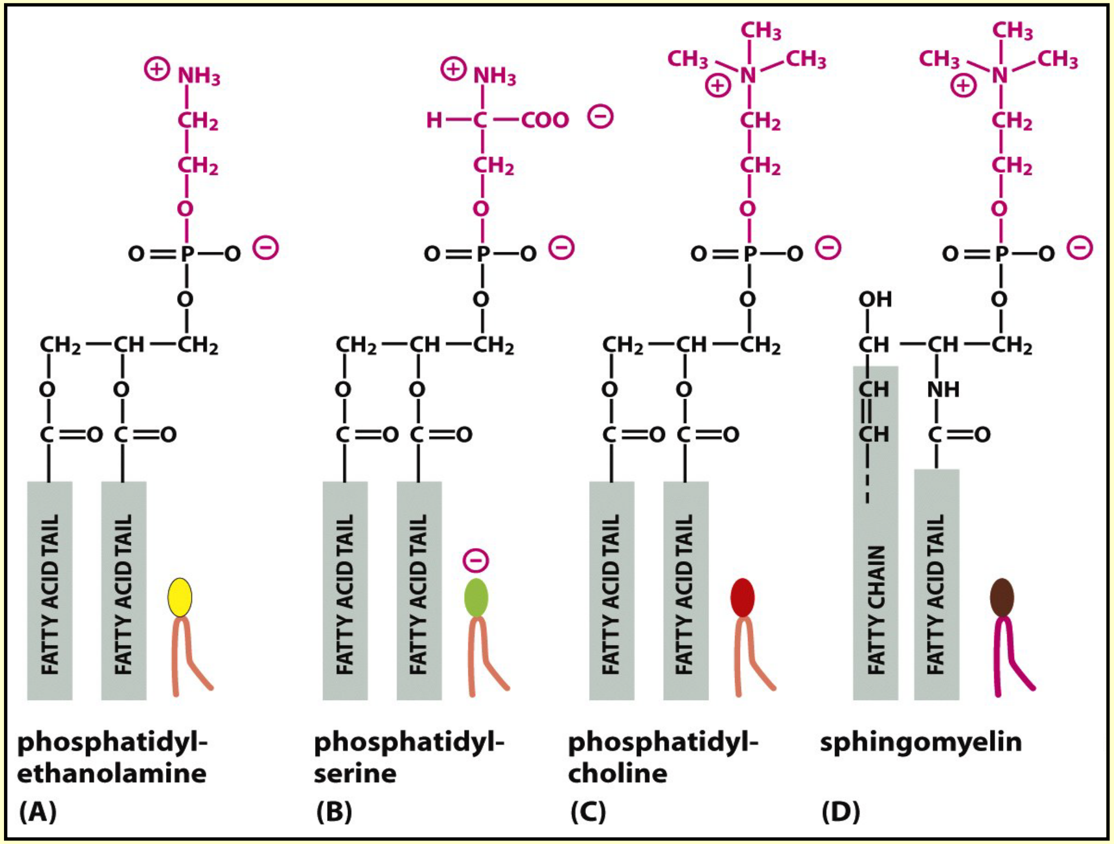
→ 1st tail – no double bonds (**saturated**)
→ 2nd tail – 1 or more cis-double bonds (**unsaturated**)

✓ differences in length and saturations → membrane fluidity

Figure 10-2 *Molecular Biology of the Cell* (© Garland Science 2008)

✓ **Bacteria** – mostly one phospholipid type; no cholesterol

✓ **Eucaryota** – mixture of different phospholipid types + cholesterol + glycolipids



derived from glycerol (phosphoglycerides)

derived from sphingosine (sphingolipid)

Figure 10-3 *Molecular Biology of the Cell* (© Garland Science 2008)

outer leaflet:

→ phosphatidylcholine

→ sphingomyelin

inner leaflet:

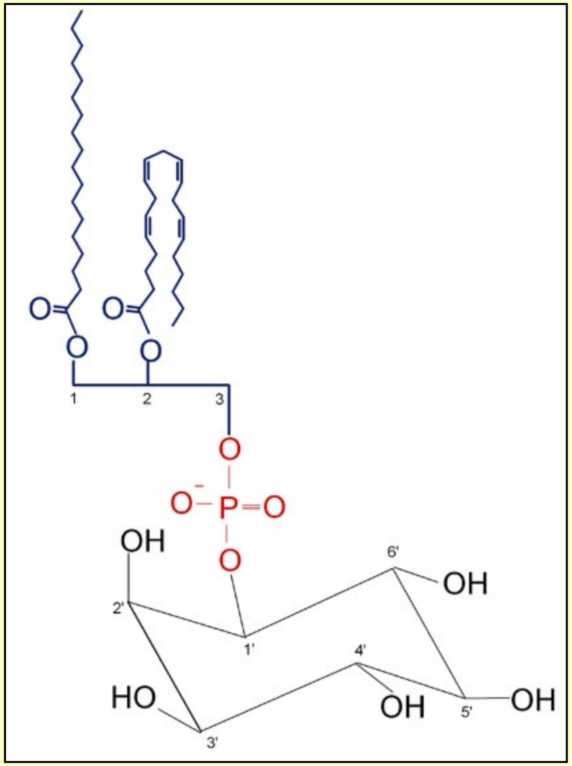
→ phosphatidylethanolamine

→ phosphatidylserine*

→ phosphatidylinositol

* translocation to the outer leaflet → apoptosis

❖ phosphatidylinositol

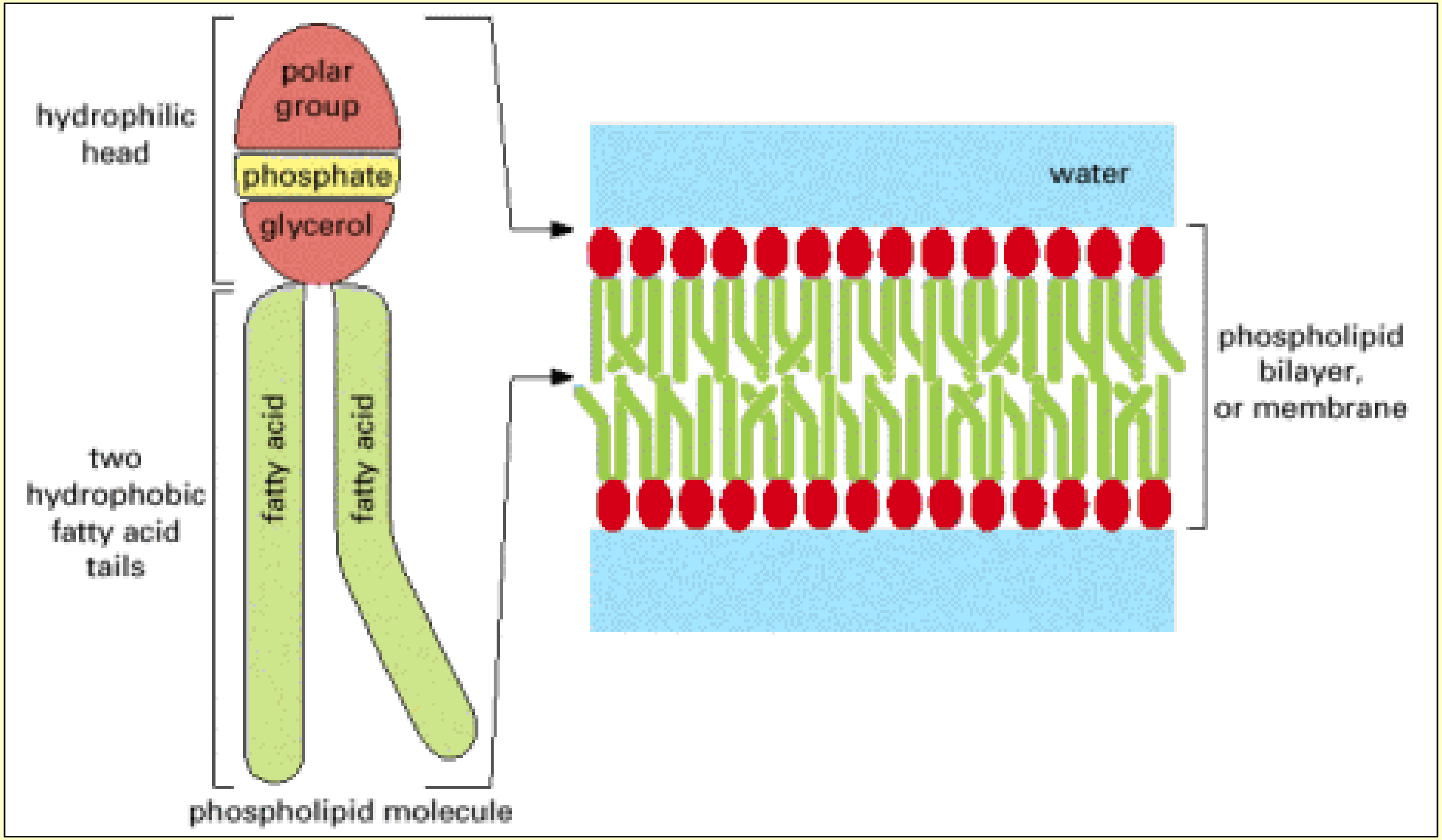


→ glycerole derivative

→ important for cell signalization

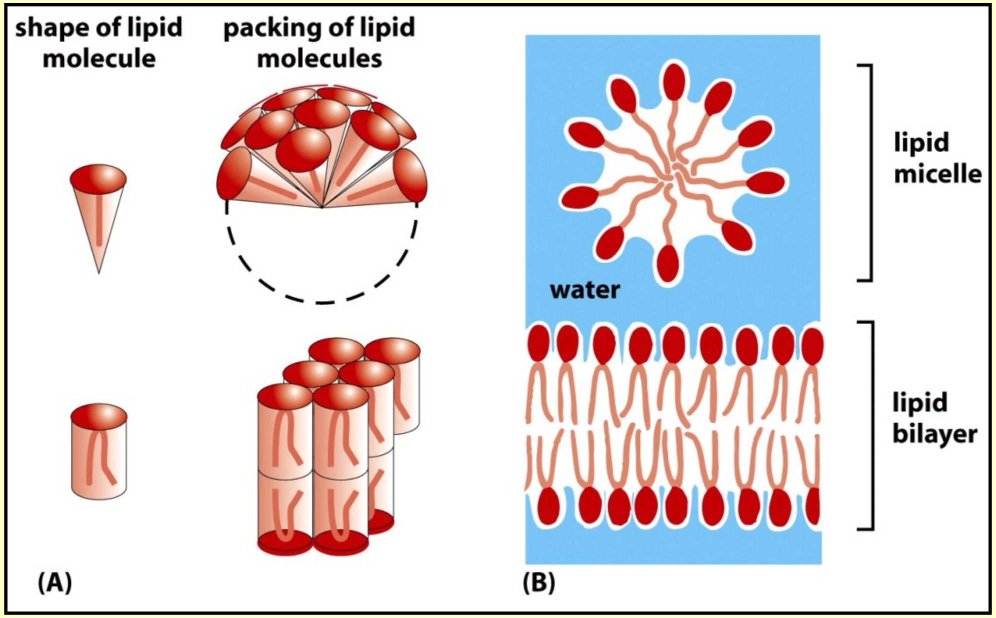
→ carries - charge – contributes to negative charge of the inner leaflet

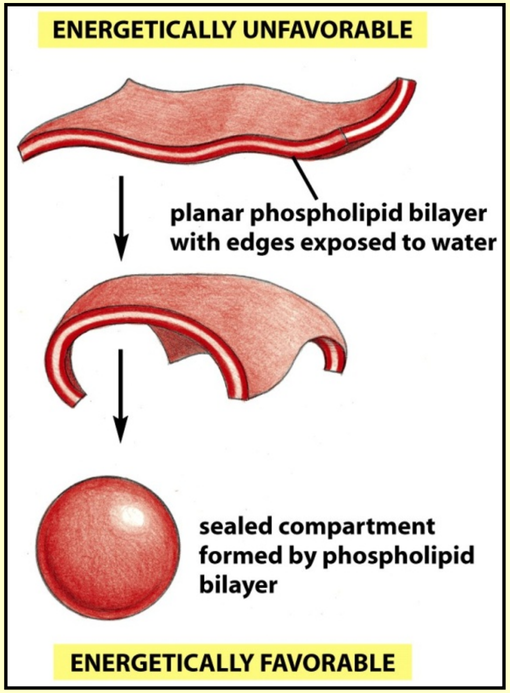
Orientation in membrane



2002 Bruce Alberts, et al.

Spontaneous formation of lipid bilayer





Spontaneous closure of lipid bilayer

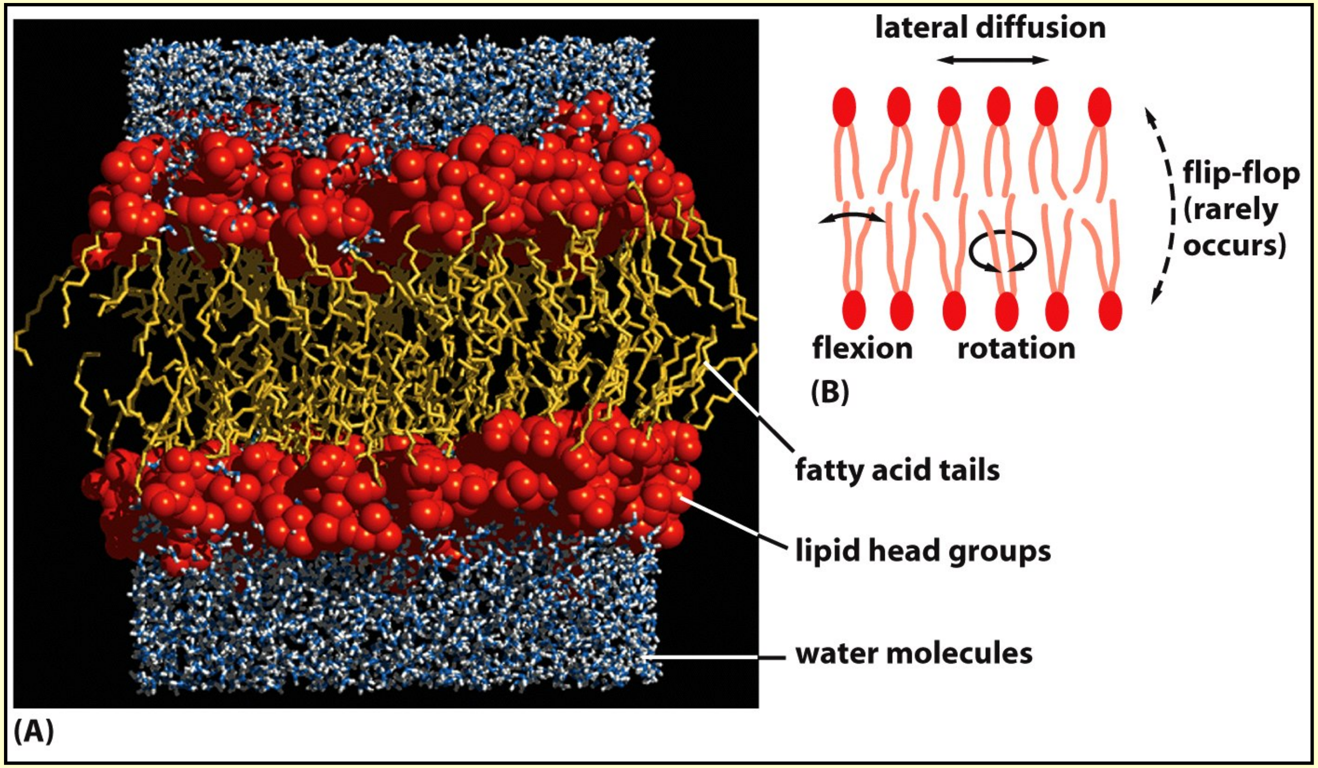
- one tail → **micelle**
- two tails → **bilayer**

✓ **energetically most favored distribution**

Animation http://www.youtube.com/watch?v=lm-dAvbl330

Figures 10-7;10-8 *Molecular Biology of the Cell* (© Garland Science 2008)

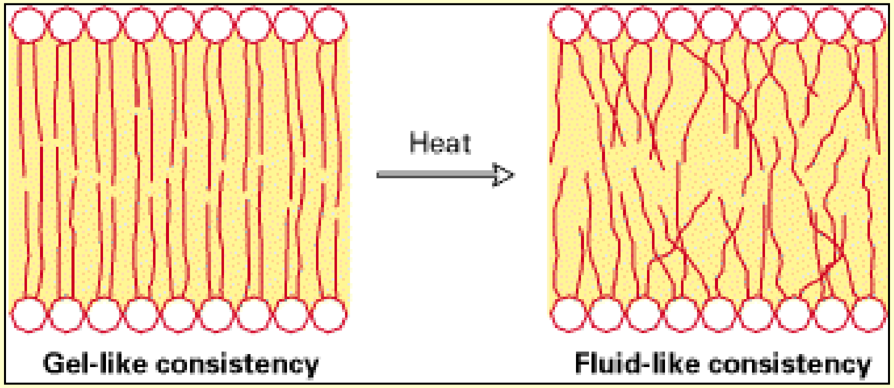
Phospholipid mobility in lipid bilayer



- **Flip-flop** – rare (< 1x per month)
- **Lateral diffusion** – frequent (~10^7 per sec)
- **Rotation**
- **Flexion**

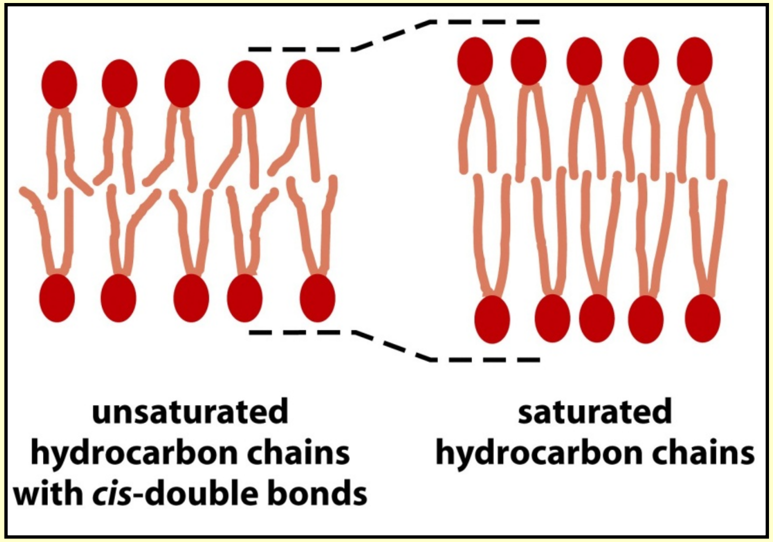
Figure 10-11 *Molecular Biology of the Cell* (© Garland Science 2008)

Phases and phase transitions



✓ **Membrane fluidity is dependent on:**

- composition
- temperature



✓ **Composition**

- the double bonds make it more difficult to pack the chains together → lipid bilayer more difficult to freeze

- because the fatty acid chains of unsaturated lipids are more spread apart → lipid bilayers are thinner than bilayers formed from saturated lipids

*bacteria, yeast – adjust their lipid composition according to the environmental temperature

Figure 10-12 *Molecular Biology of the Cell* (© Garland Science 2008)

Lipid unsaturation effect

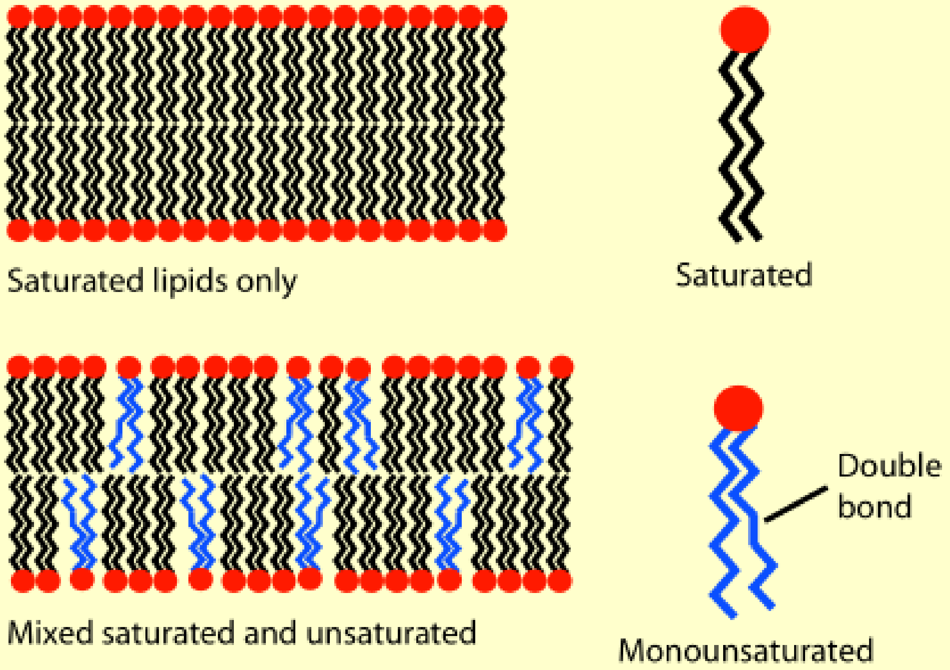


Diagram showing the effect of unsaturated lipids on a bilayer.

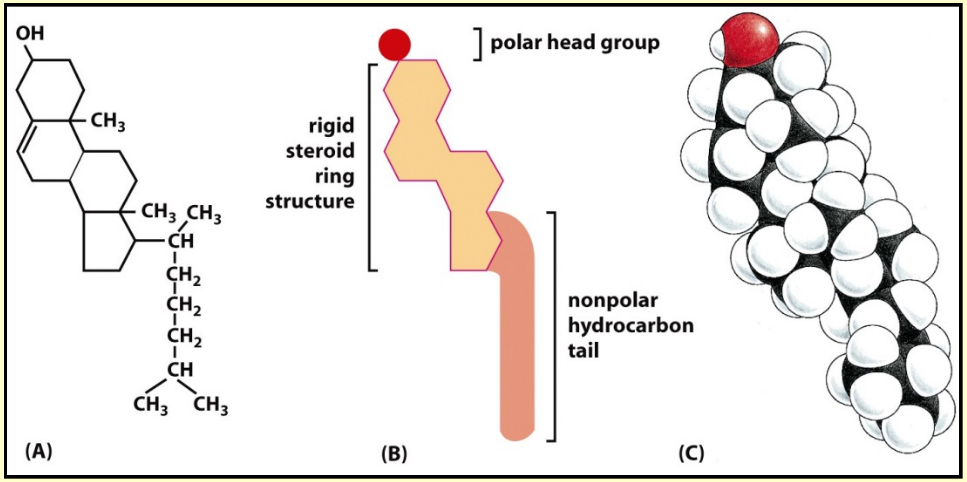
✓The lipids with an unsaturated tail (blue) disrupt the packing of those with only saturated tails (black)

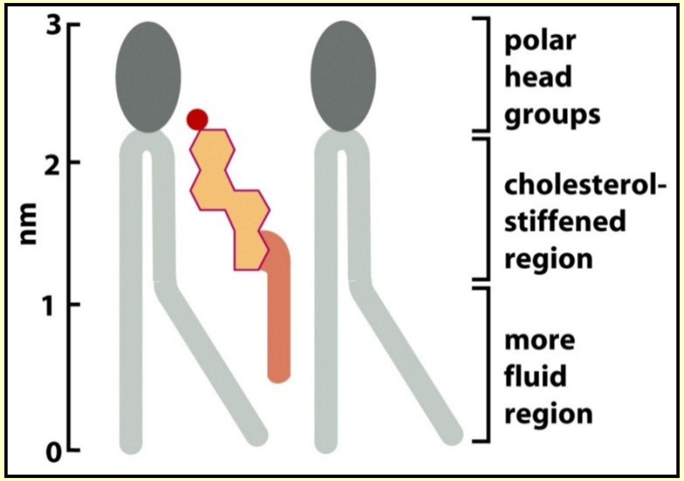
✓The resulting bilayer has more free space and is consequently more permeable to water and other small molecules

Cholesterol

✓ steroid - amphipathic molecule important for membrane fluidity regulation

✓ eucaryotic cells. – animal cells → cholesterol
– plant cells → cholesterol + similar compounds (sterols)





Figures 10-4; 10-5 *Molecular Biology of the Cell* (© Garland Science 2008)

✓ cholesterol inserts into the membrane with its polar hydroxyl group close to the polar head groups of the phospholipids

✓ high temp. – decreases permeability for small water-soluble molecules

✓ low temp. – separates tails and prevents phase transition

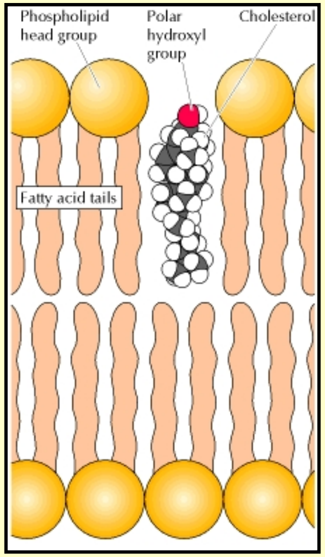


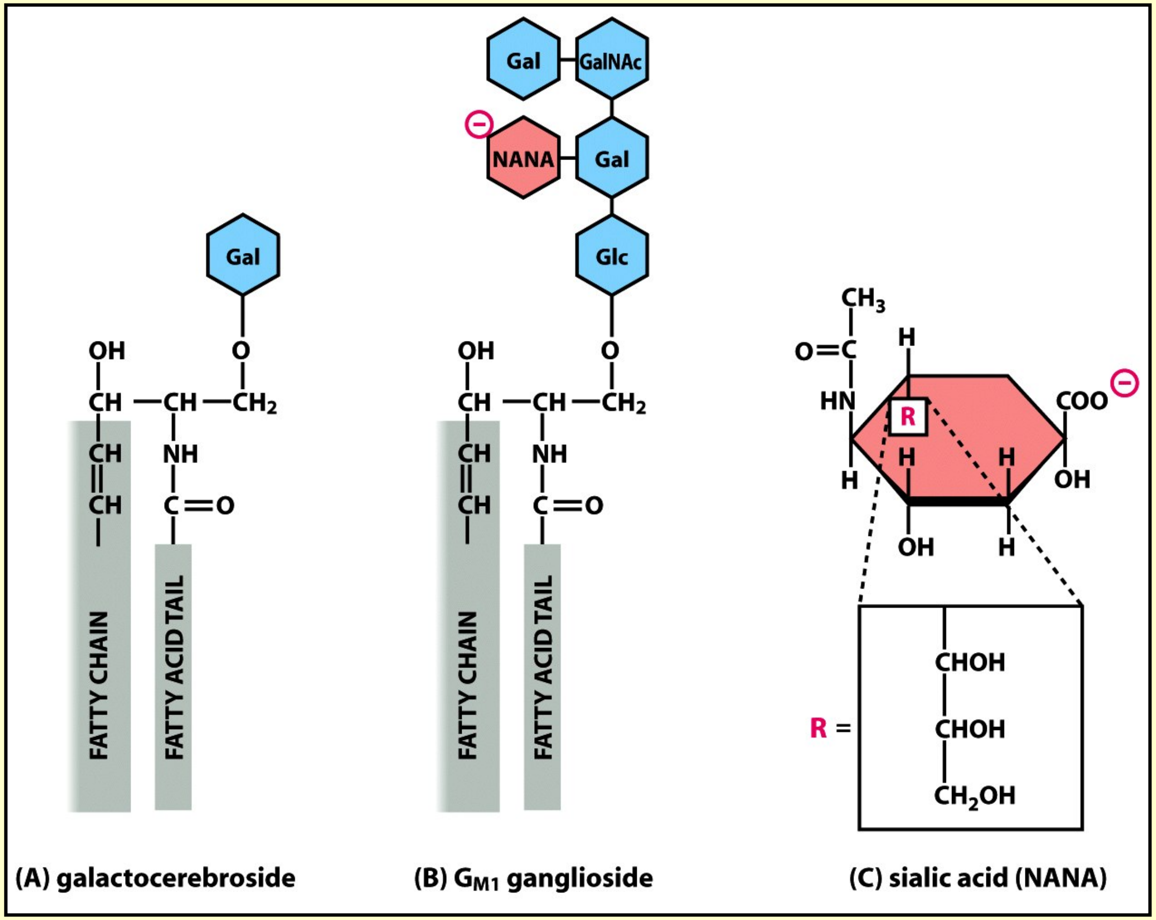
Figure 2.47 2000 Cooper

Glycolipids

✓ lipids with sugars

✓ lipid molecules with the highest asymmetry

✓ only in outer leaflet



• **Plants**
– glycerol derivatives

• **Animal cells**
– sphingosine derivatives

• **Bacteria**
– no glycolipids

Figure 10-18 *Molecular Biology of the Cell* (© Garland Science 2008)

Lipid composition of different cell membranes

Table 10–1 **Approximate Lipid Compositions of Different Cell Membranes**

LIPID	PERCENTAGE OF TOTAL LIPID BY WEIGHT					
	LIVER CELL PLASMA MEMBRANE	RED BLOOD CELL PLASMA MEMBRANE	MYELIN	MITOCHONDRION (INNER AND OUTER MEMBRANES)	ENDOPLASMIC RETICULUM	*E. COLI* BACTERIUM
Cholesterol	17	23	22	3	6	0
Phosphatidylethanolamine	7	18	15	28	17	70
Phosphatidylserine	4	7	9	2	5	trace
Phosphatidylcholine	24	17	10	44	40	0
Sphingomyelin	19	18	8	0	5	0
Glycolipids	7	3	28	trace	trace	0
Others	22	13	8	23	27	30

✓Others – phosphatidylinositol and some other minor lipids

Table 10-1 *Molecular Biology of the Cell* (© Garland Science 2008)

Asymmetrical distribution of phospholipids and glycolipids in lipid bilayer of human red blood cells

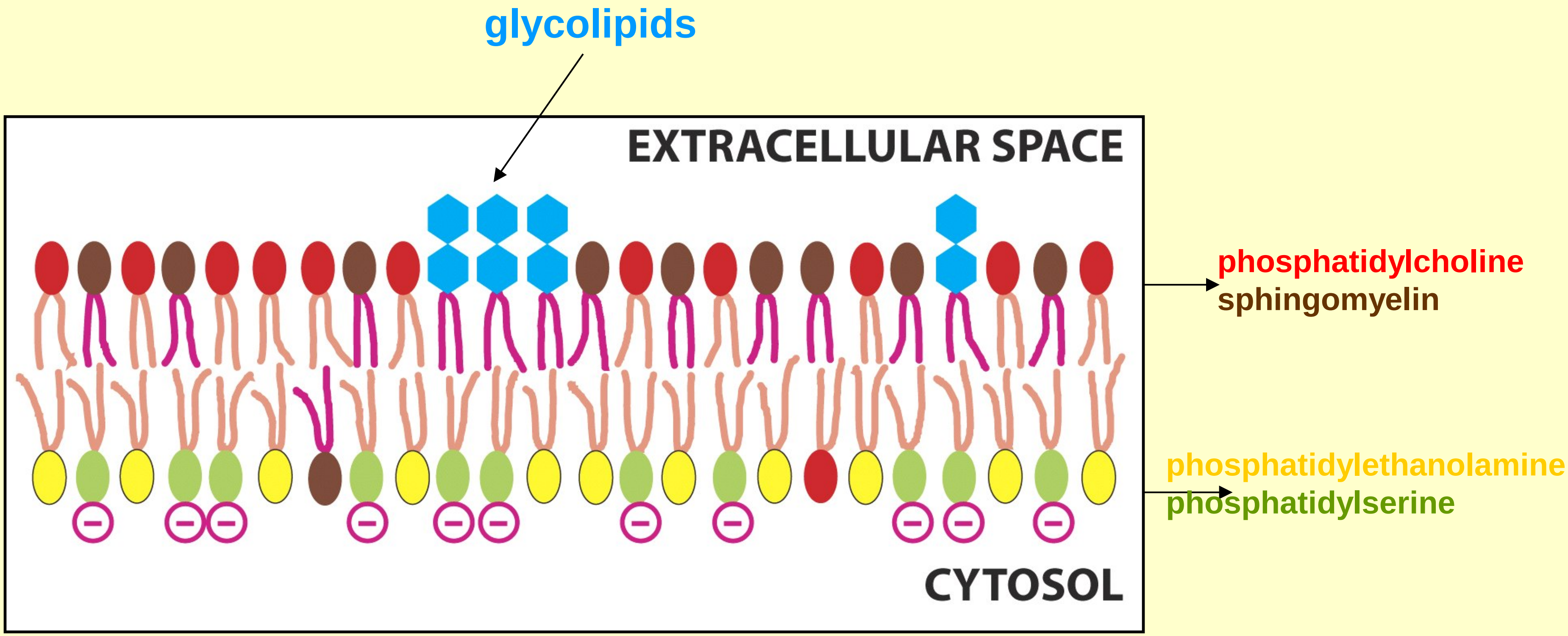
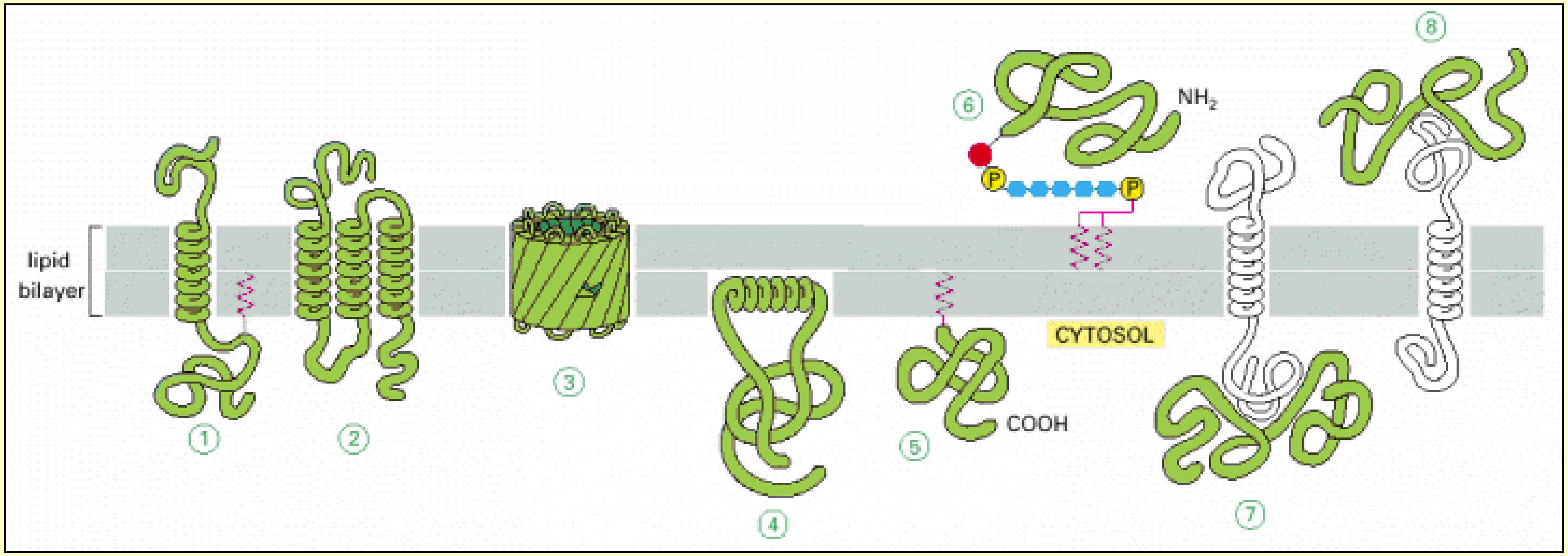


Figure 10-16 *Molecular Biology of the Cell* (© Garland Science 2008)

Membrane proteins

➢ **Membrane proteins can be associated with the lipid bilayer in various ways**



✓ **1, 2, 3** – transmembrane proteins (amphipathic)

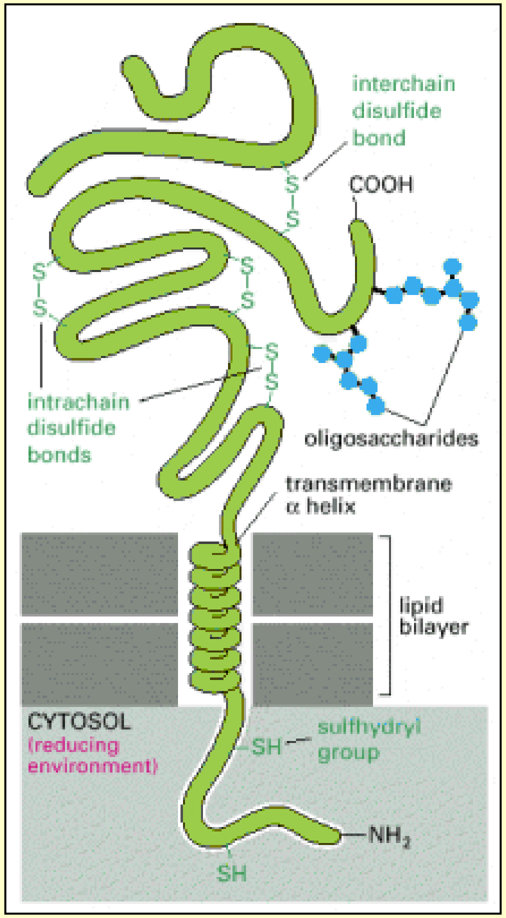
✓ **4, 5, 6** – anchored proteins (exposed at only one side)

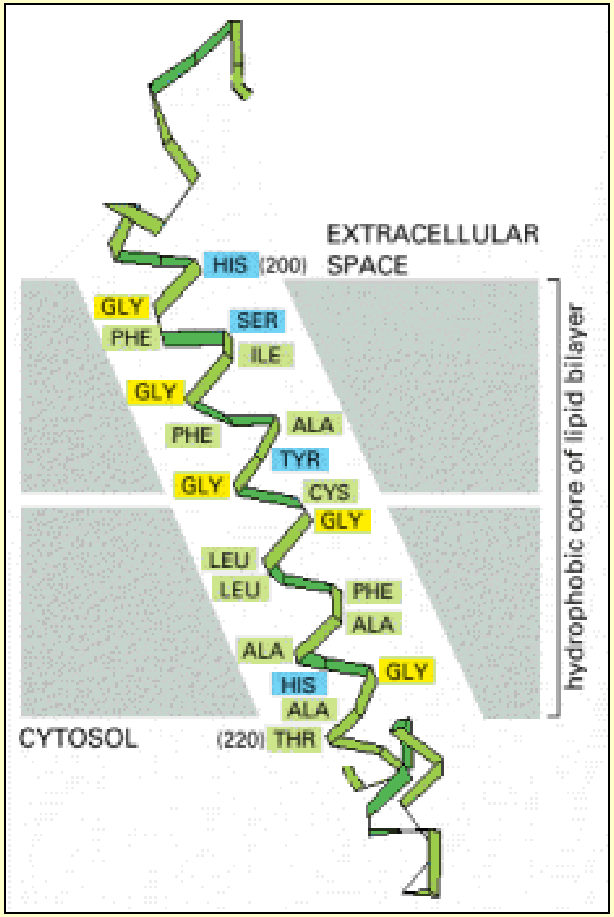
✓ **7, 8** – periphery proteins (noncovalent interactions with other proteins)

Figure 10-17. 2002 Bruce Alberts, et al.

Transmembrane protein

A) α-helix





❖α-helix is neutralizing polar character of peptide bonds

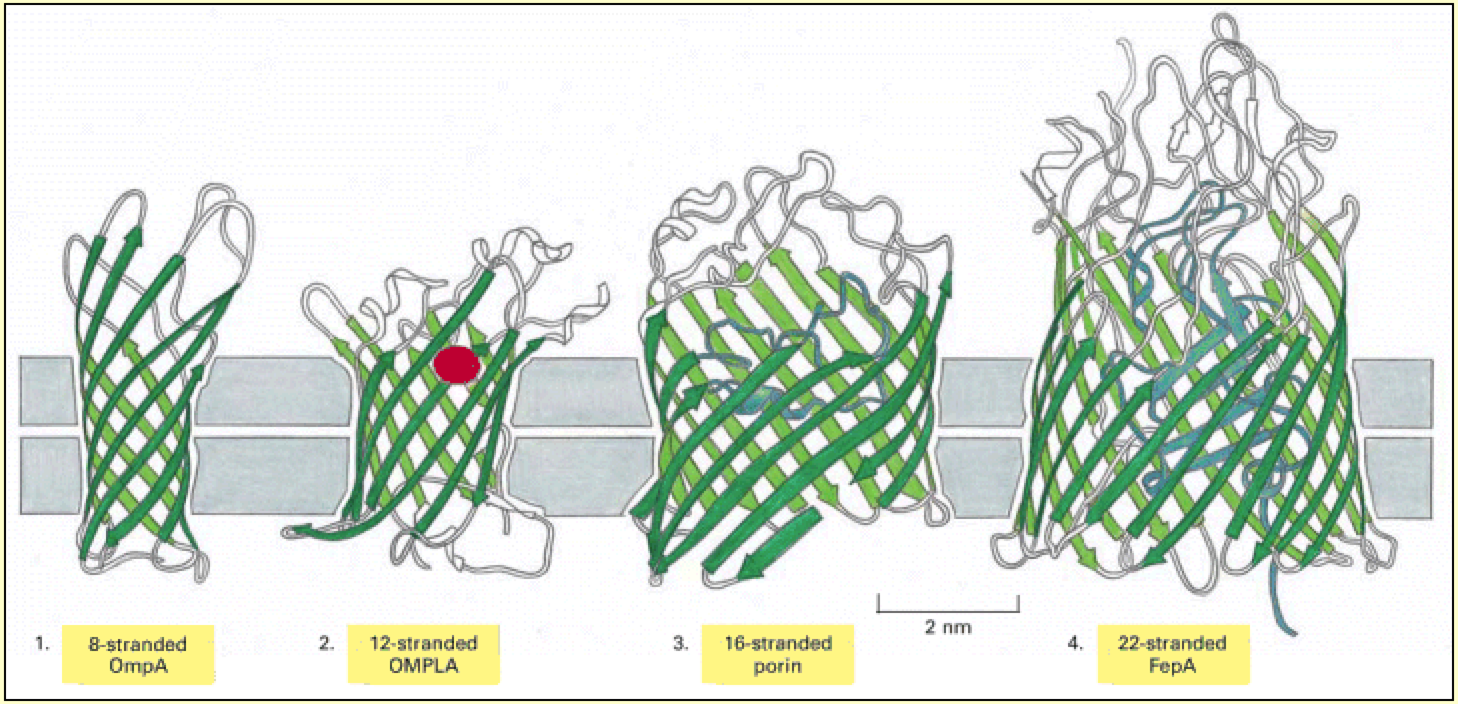
✓Gly and Phe – hydrophobic aminoacids

Figure 10-19; 10-22. 2002 Bruce Alberts

Transmembrane protein

b) β-barrel

→ folding of β-sheets (8 - 22) into a barrel conformation



❖ **β –barrel formation is neutralizing polar character of peptide bonds**

2002 Bruce Alberts, et al.

Anchored proteins

✓ examples of proteins anchored in the plasma membrane by lipids and prenyl group

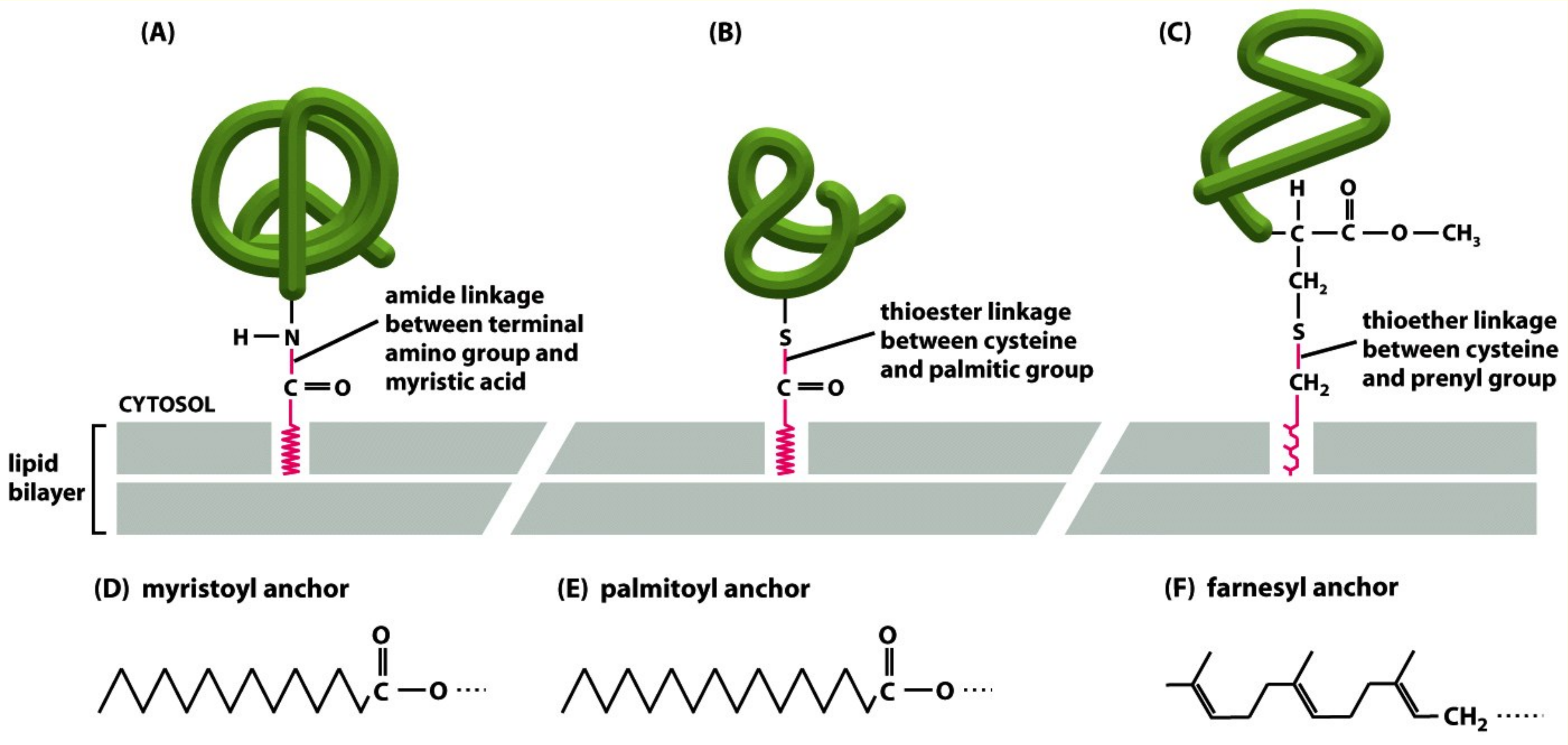
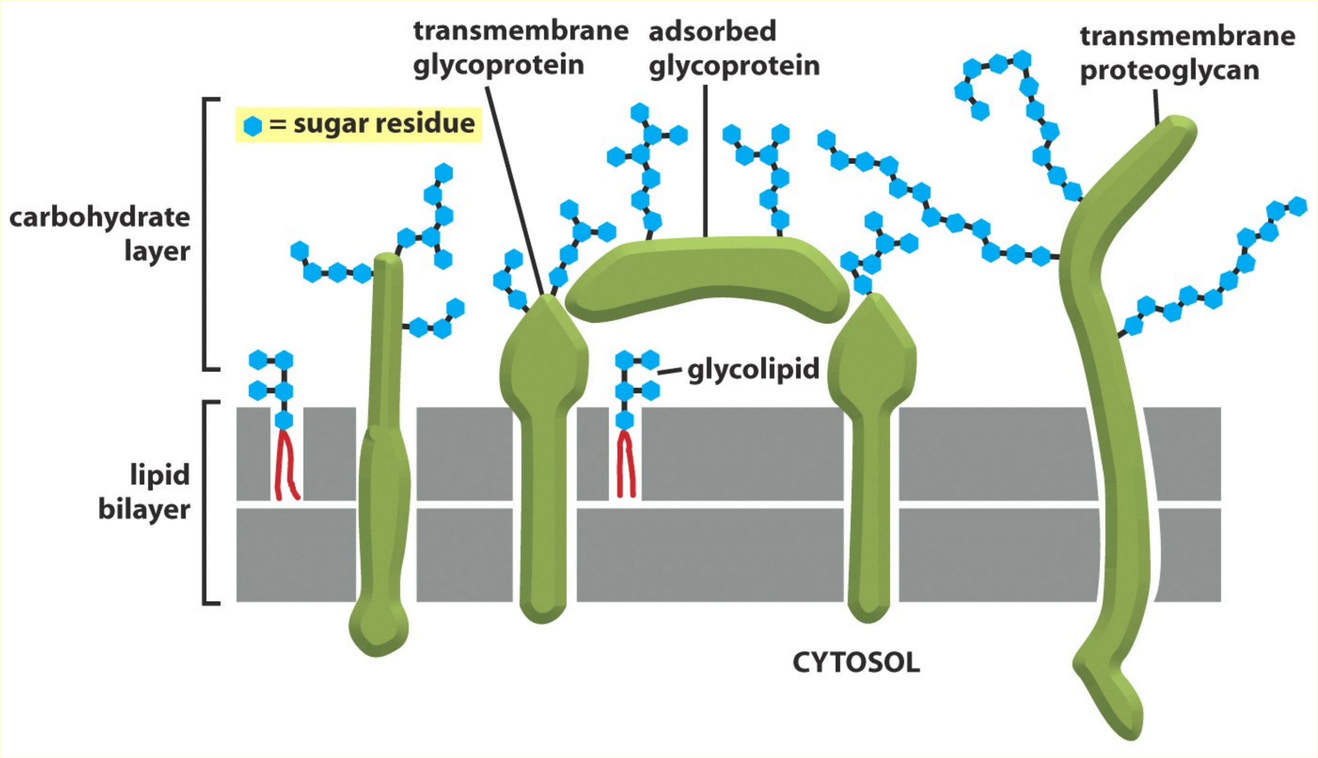


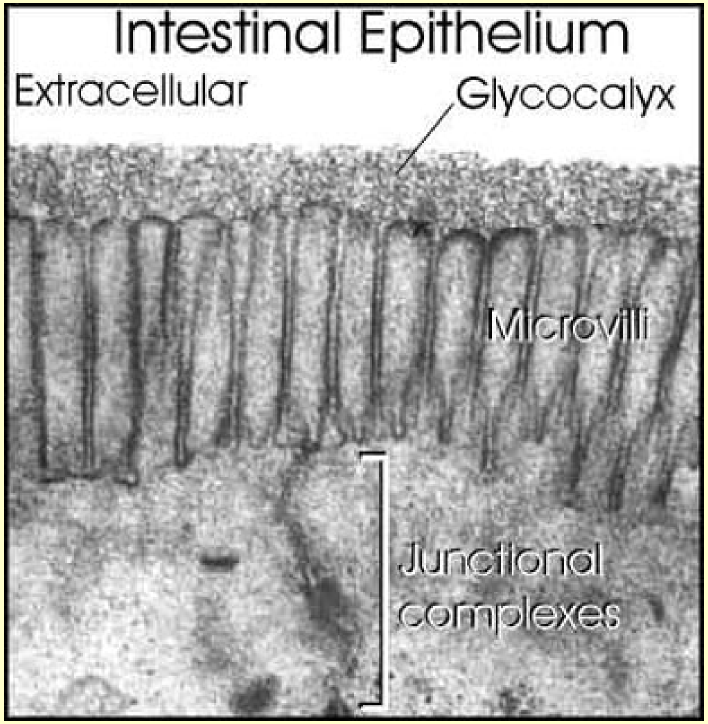
Figure 10-20 *Molecular Biology of the Cell* (© Garland Science 2008)

Membrane carbohydrates

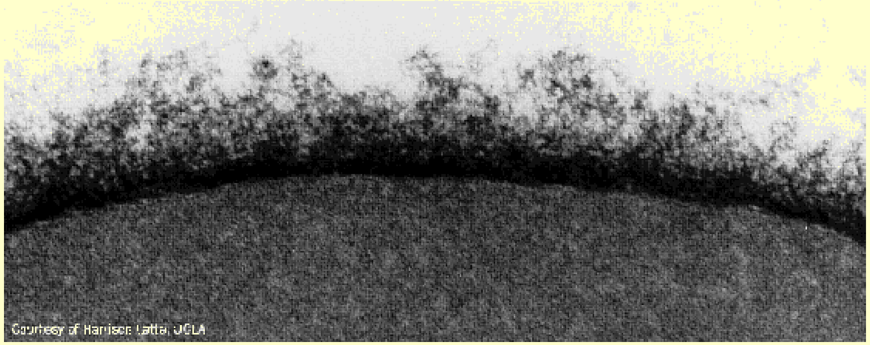
- ✓ Bind to **proteins** or **lipids**
- ✓ Only in outer leaflet



Glycocalix revealed by TEM



http://www.nfsdsystems.com/w3bio315/



The erythrocyte glycocalyx as revealed by electron microscopy using special staining techniques

Complex carbohydrates are present on the outer surface of erythrocytes; components of glycoproteins and glycolipids

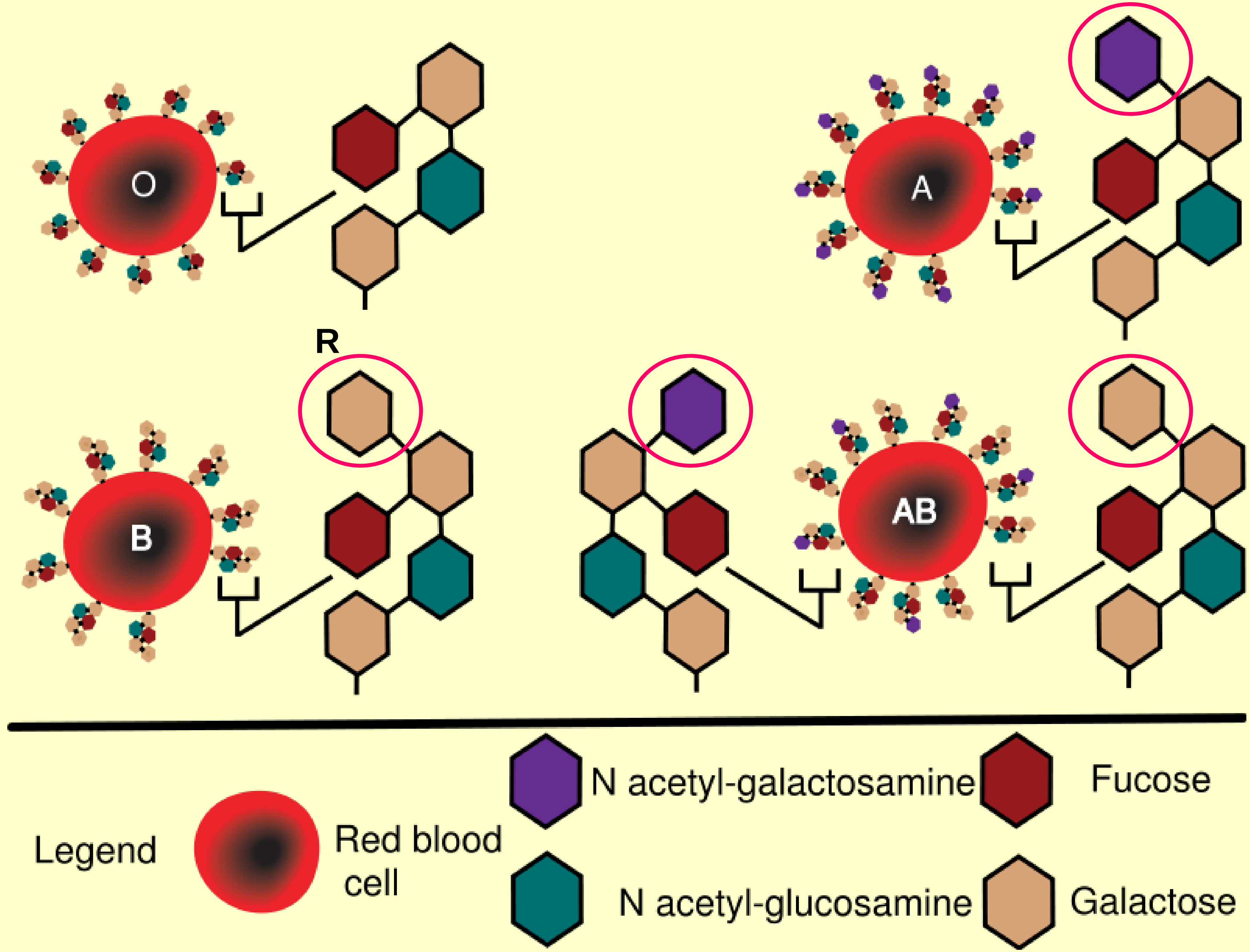
https://www3.nd.edu/~aseriann/CHAP12B.html/sld071.htm

Electron microscopy image of the endothelial glycocalyx in a coronary capillary

http://www.nature.com/nrneph/journal/v6/n6/fig_tab/nrneph.2010.59_ft.html

Glycocalix → composed of sugars from:

- ✓ glycolipids
- ✓ glycoproteins
- ✓ proteoglycans


O
A
R
B
AB
N acetyl-galactosamine
Fucose
Legend
Red blood cell
N acetyl-glucosamine
Galactose

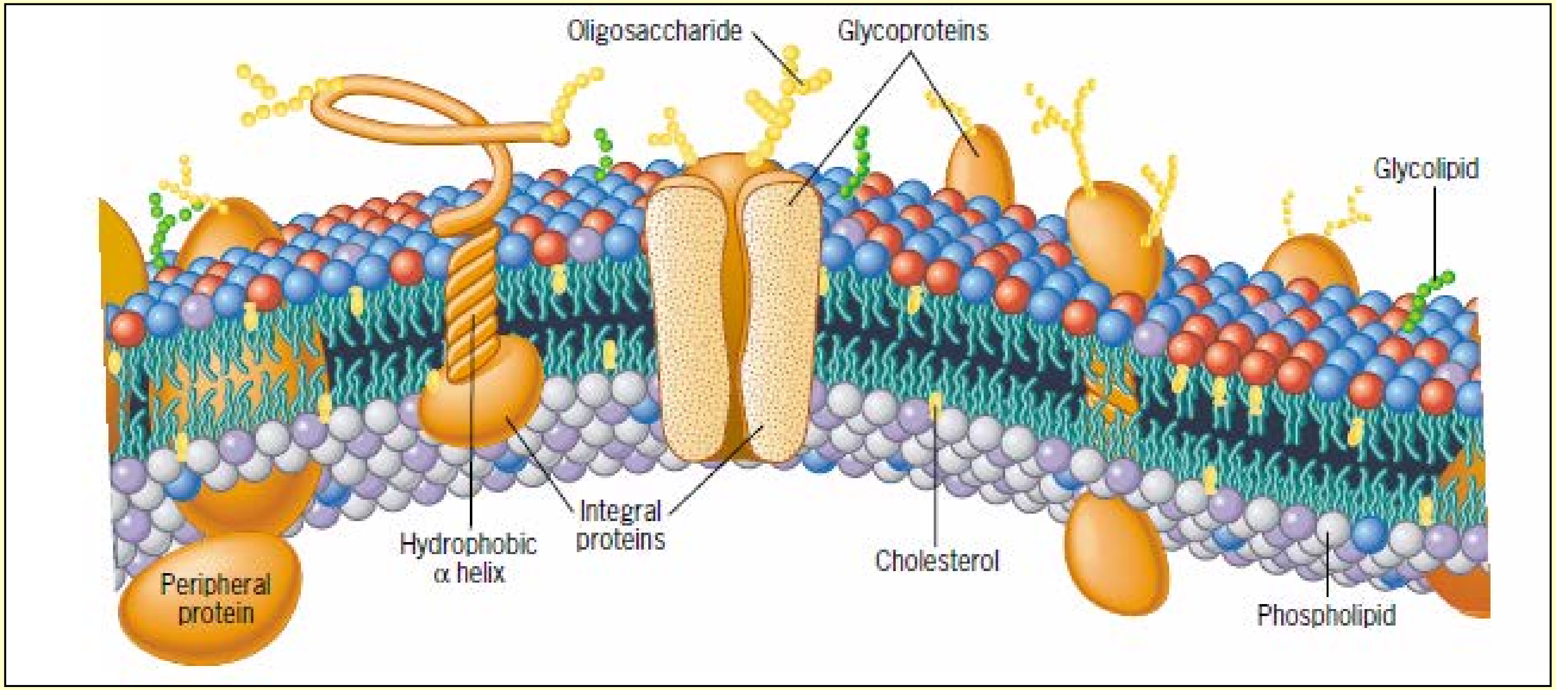


Figure 4.4. Karp, Cell Biology, 7th edition, 2013.

Membrane transport

The relative permeability of a synthetic lipid bilayer to different classes of molecules

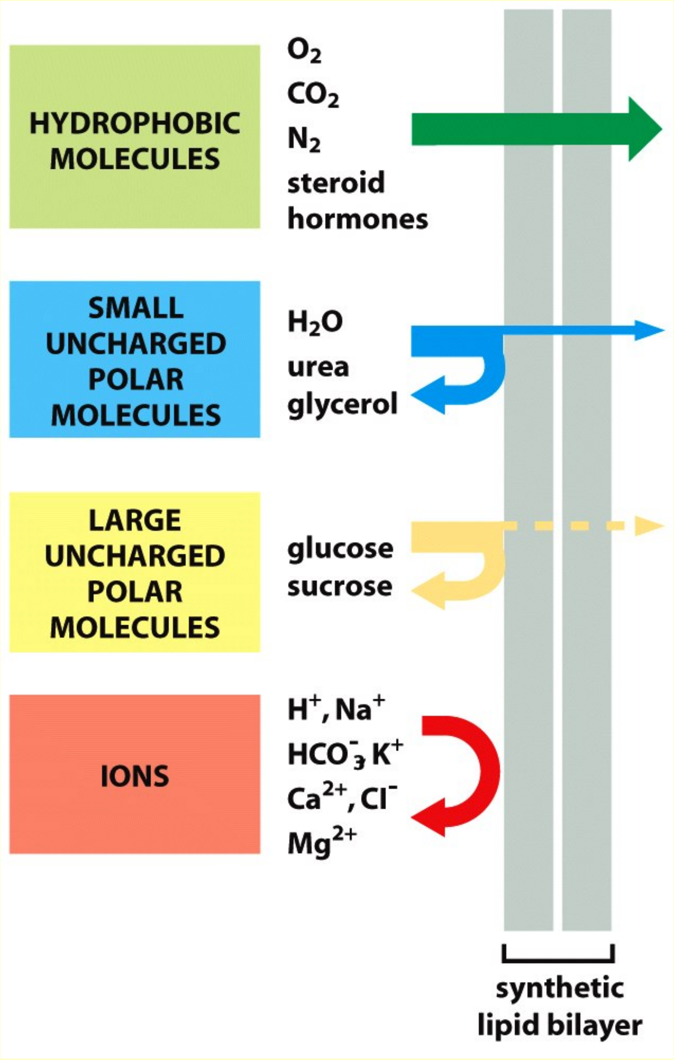


Figure 11 *Molecular Biology of the Cell* (© Garland Science 2008)

✓ small uncharged molecules can diffuse freely through a phospholipid bilayer

✓ bilayer is impermeable to:
- larger polar molecules (such as glucose and amino acids)
- ions

✓ the smaller the molecule and, more importantly, the less strongly it associates with water, the more rapidly the molecule diffuses across the bilayer

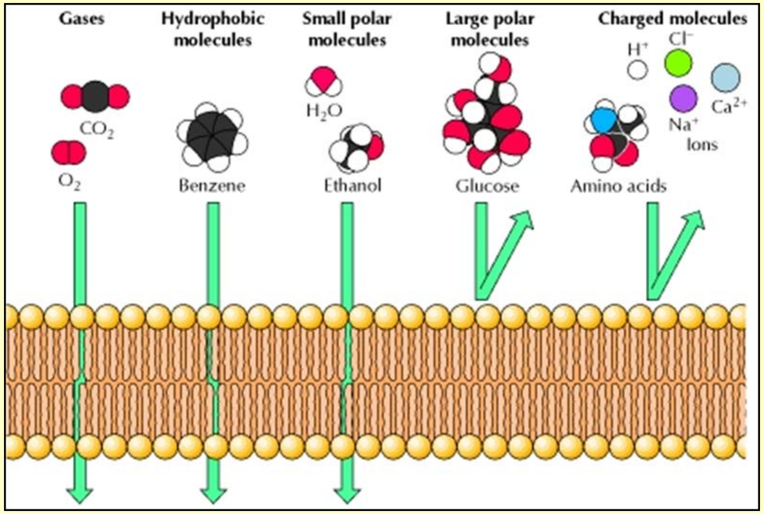


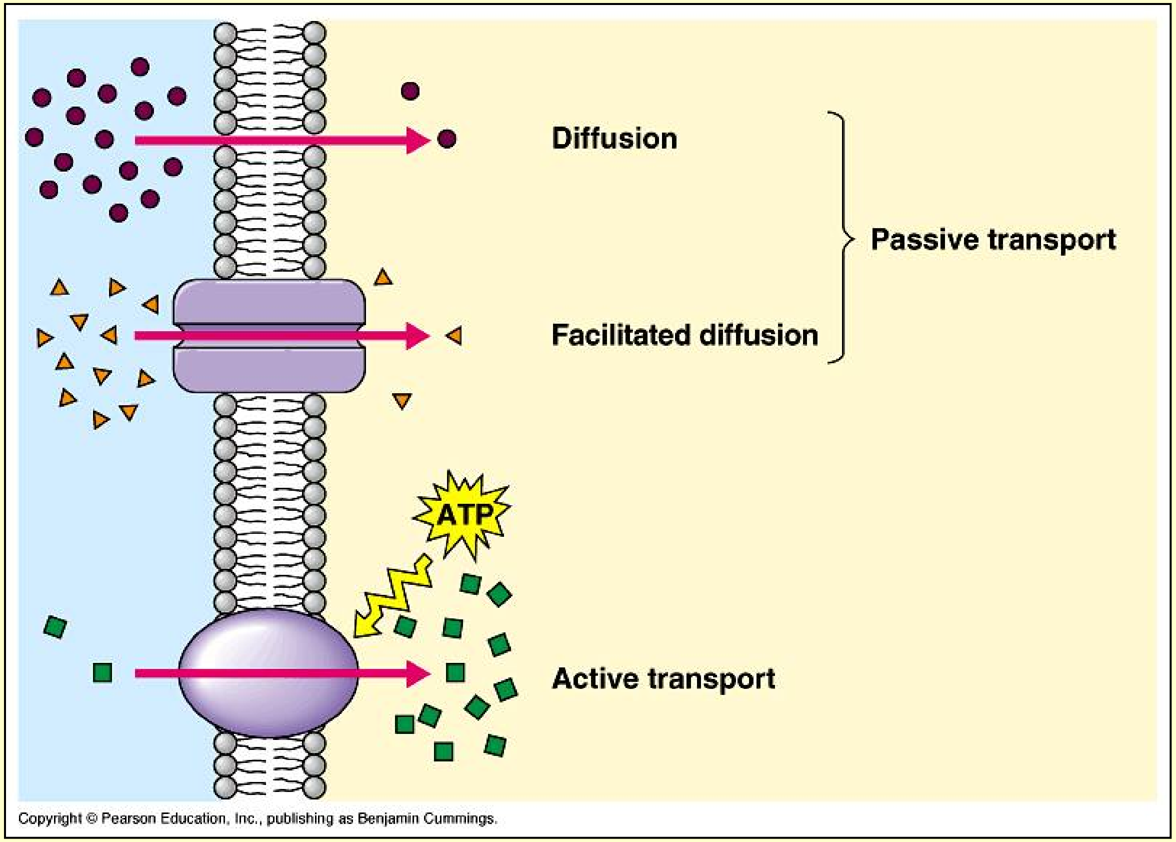
Figure 12.15 2000. Cooper

Three ways in which molecules can cross the membrane

- Passive diffusion
- Facilitated diffusion

Passive transport - down the concentration gradient!

- Active transport

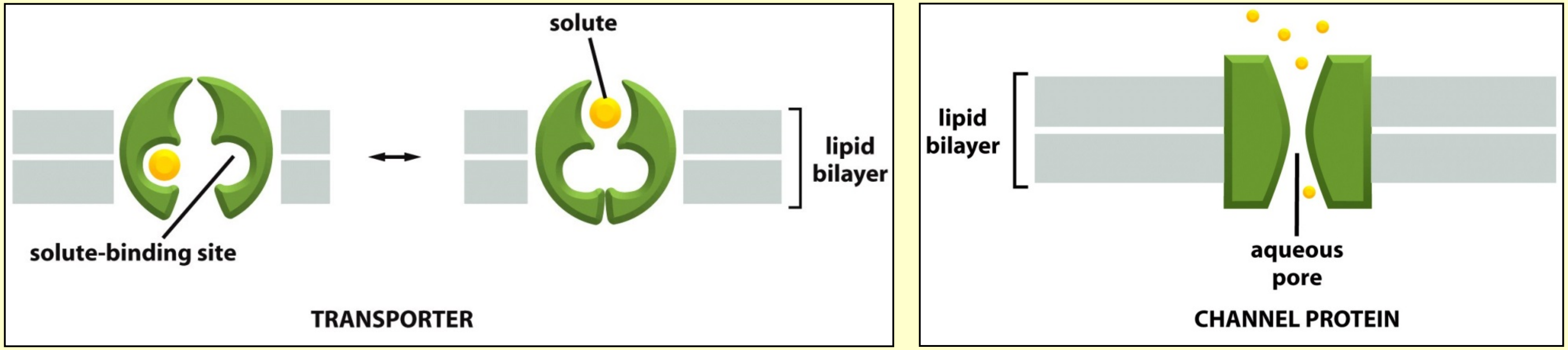


http://science.nayland.school.nz/graemeb/yr12%20biology/Cells/Cells.html

Two main classes of membrane transport proteins

✓ **Carriers** → bind the specific solute to be transported and undergo a series of conformational changes to transfer the bound solute across the membrane

✓ **Channels** → interact with the solute to be transported much more weakly



A - carrier protein alternates between two conformations,
→ solute-binding site is sequentially accessible on one side of the bilayer and then on the other

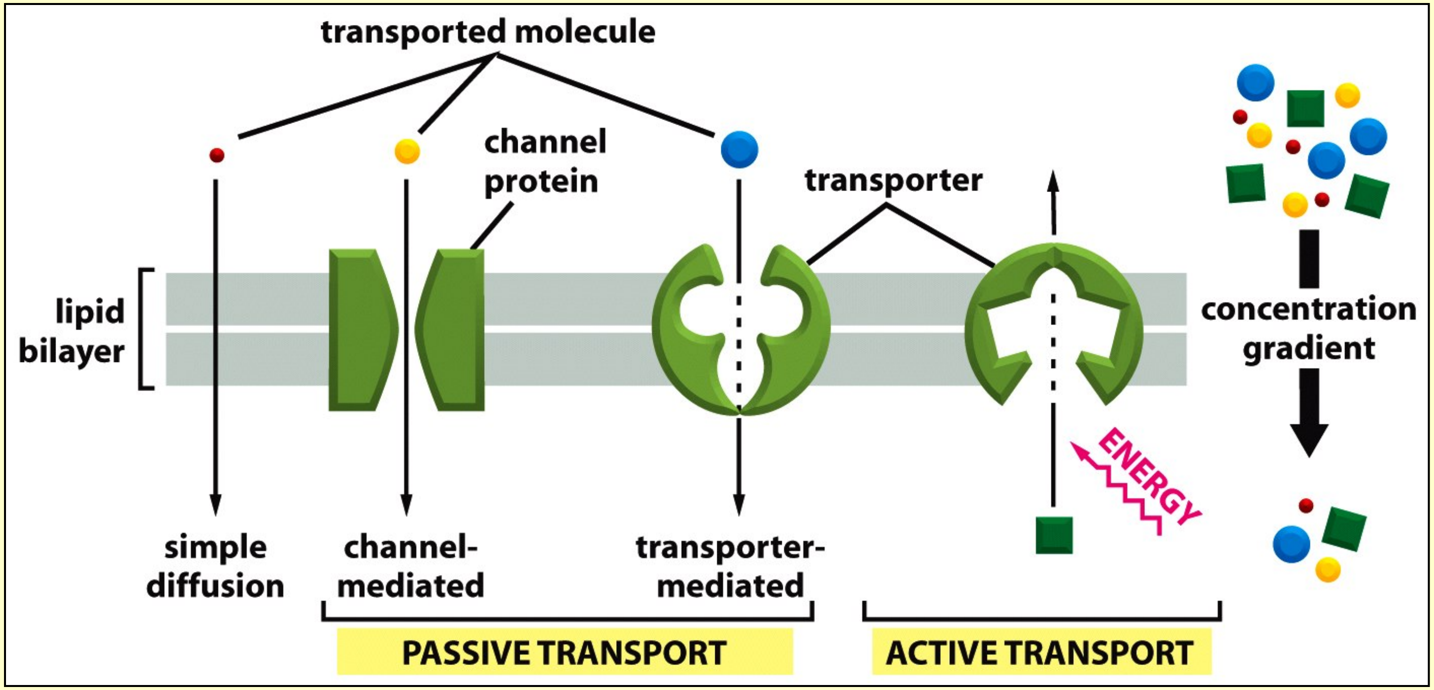
B - channel protein forms a water-filled pore across the bilayer through which specific solutes can diffuse

Figure 11-3. 2002 Bruce Alberts, et al.

Passive and active transport

✓ **Passive transport** – all channel proteins and many carriers

✓ **Active transport** – only carriers; requires energy



✓ **Passive transport** down an electrochemical gradient occurs spontaneously
→ simple diffusion through the lipid bilayer
→ facilitated diffusion through channels and passive carriers

✓ **Active transport**
→ requires an input of metabolic energy
→ mediated by carriers that harvest metabolic energy to pump the solute against its electrochem. gradient

Figure 11-4. 2002 Bruce Alberts, et al.

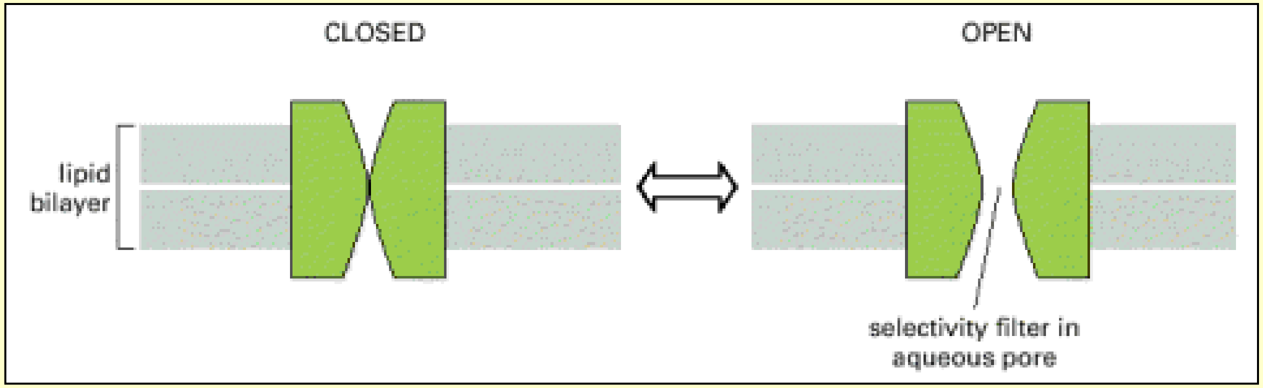
Channels

✓ simply form open pores in the membrane, allowing small molecules of the appropriate size and charge to pass freely through the lipid bilayer

✓ **porins** → permit the free passage of ions and small polar molecules through the outer membranes of bacteria

✓ **aquaporins** → water channel proteins → water molecules cross membrane much more rapidly than they can diffuse

✓ **ion channels** → mediate the passage of ions across plasma membranes



2002 Bruce Alberts, et al.

Porins

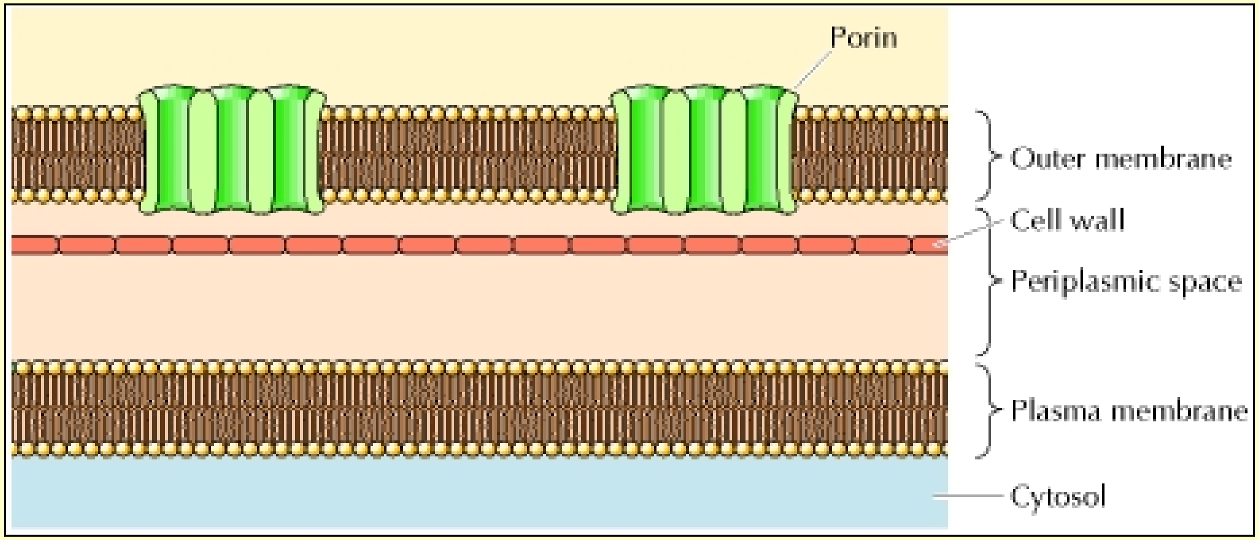


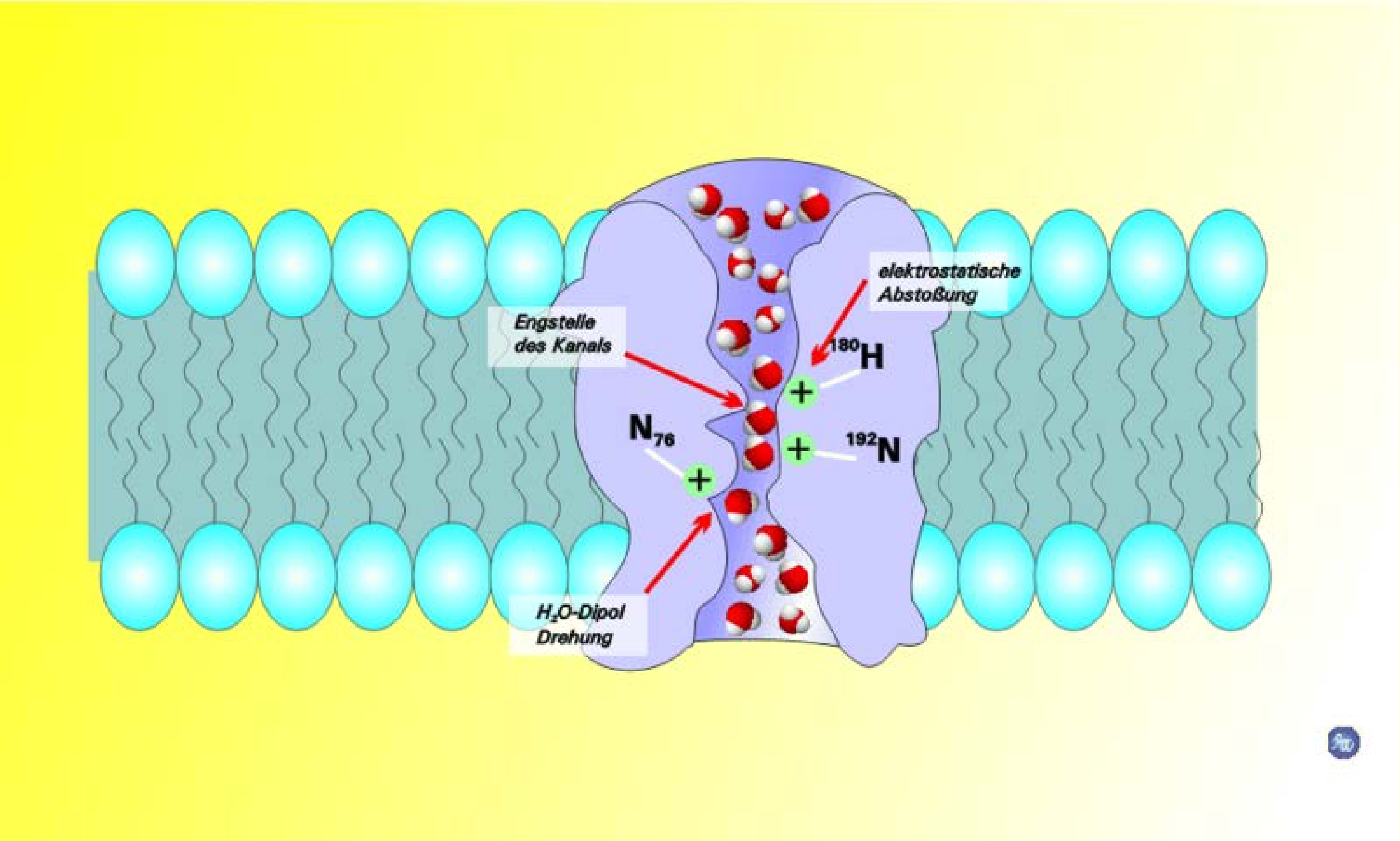
Figure 12.8 Bacterial outer membranes

✓The plasma membrane of some bacteria is surrounded by a cell wall and a distinct outer membrane

✓The outer membrane contains **porins** → form open aqueous channels allowing the free passage of ions and small molecules

Cooper 2000.

Aquaporins



Schematic depiction of water movement through the narrow selectivity filter of the aquaporin channel

Ion channels

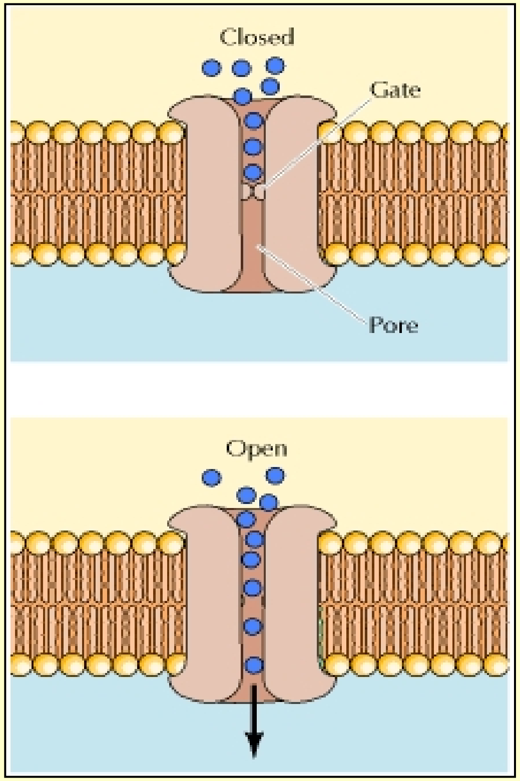


Figure 12.18. Model of an ion channel

✓ in the closed conformation, the flow of ions is blocked by a gate

✓ opening of the gate allows ions to flow rapidly through the channel

✓ channel contains a narrow pore that restricts passage to ions of the appropriate size and charge

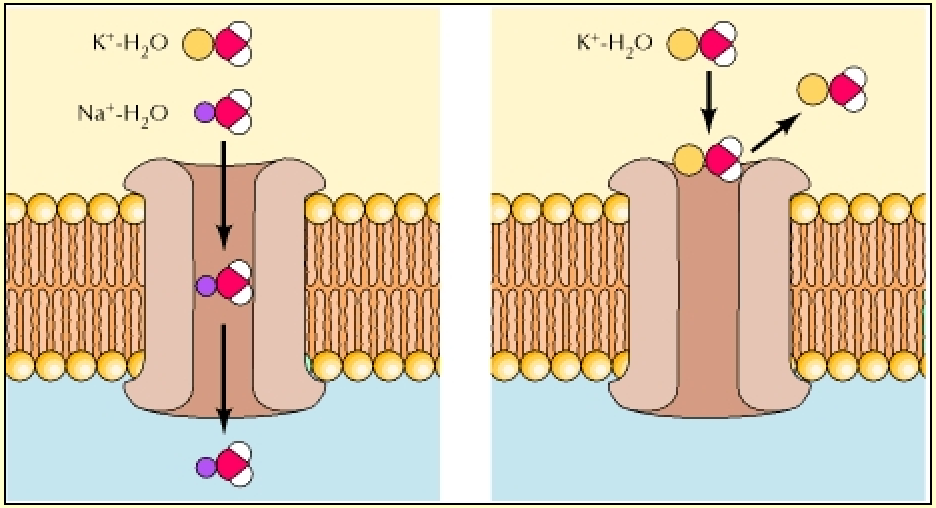


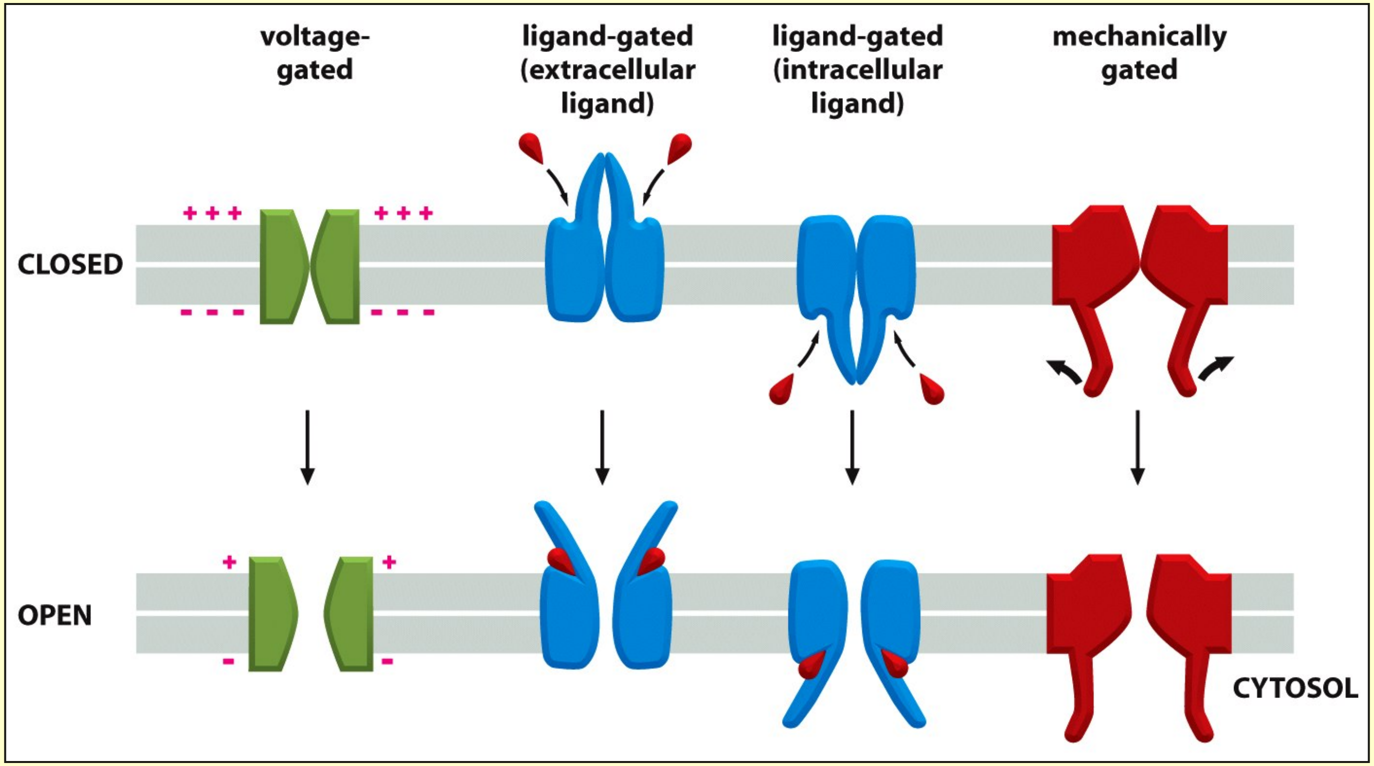
Figure 12.24. Ion selectivity of Na^{+}channels

✓ narrow pore permits the passage of Na^{+} bound to a single water molecule

✓ but interferes with the passage of K^{+} or larger ions

Cooper 2000.

The gating of ion channels



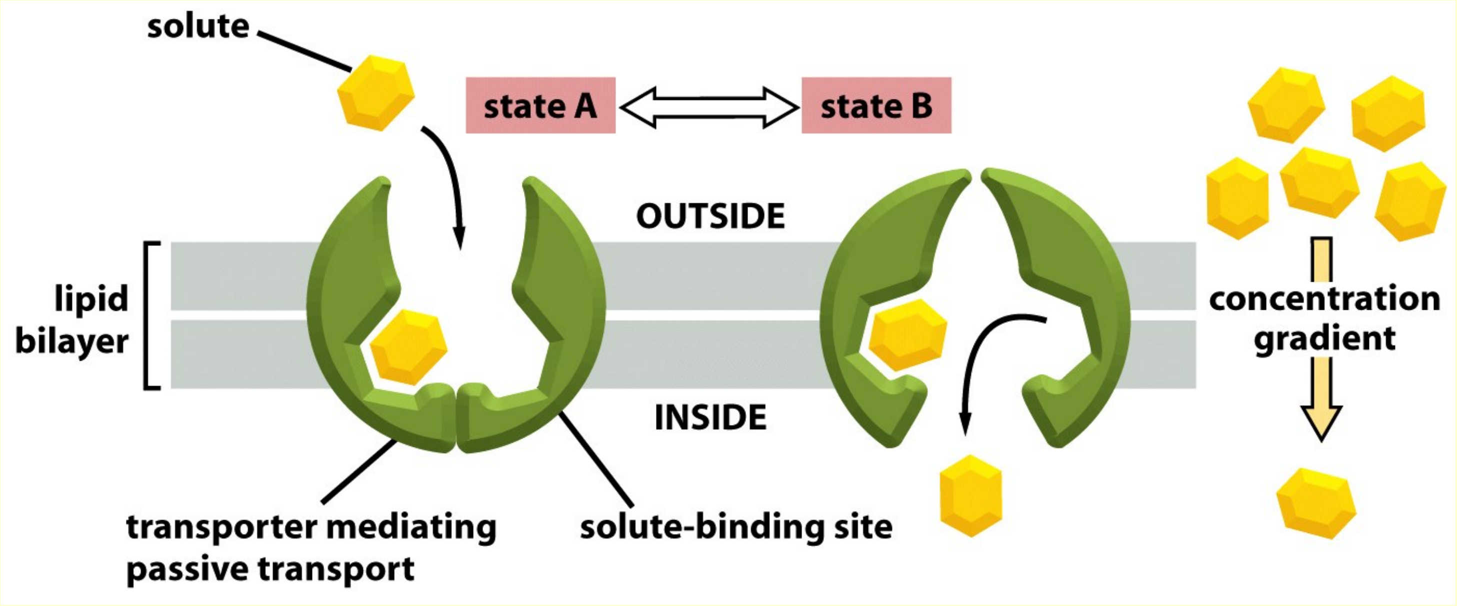
Animations - http://www.youtube.com/watch?v=Du-BwT0Ul2M

-http://www.youtube.com/watch?v=mKalkv9c2iU

Figure 11-21 *Molecular Biology of the Cell* (2008)

Carriers

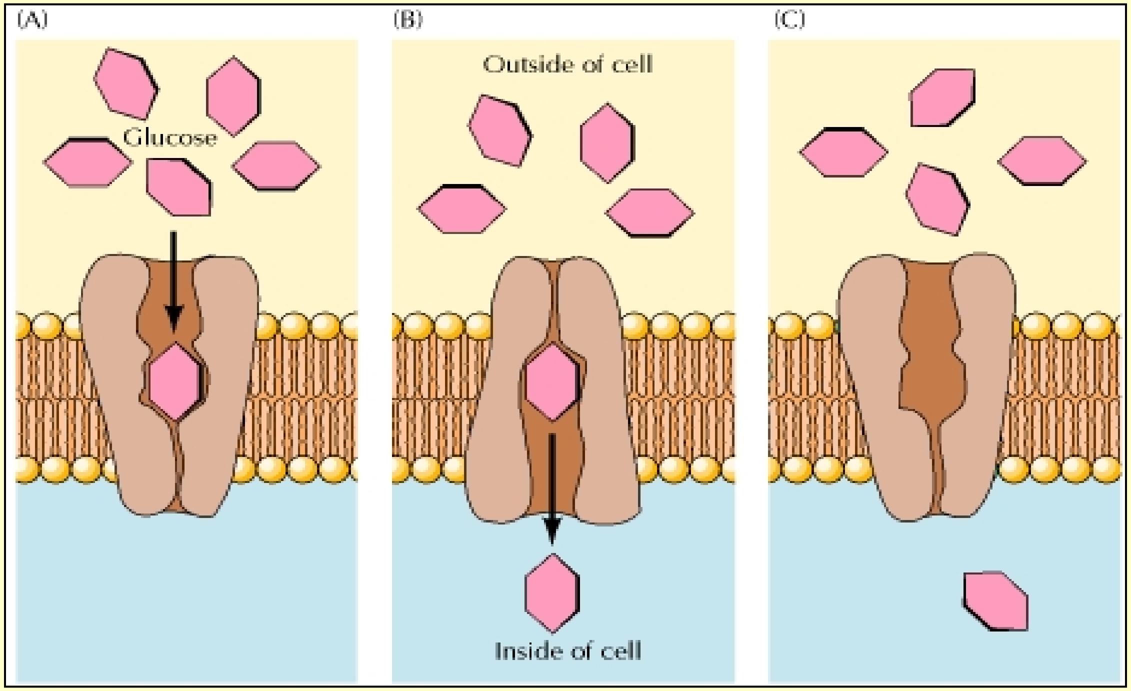
- ✓ **bind the specific solute to be transported**
- ✓ **involved in passive and active transport**



Passive transport – down the conc. gradient

Figure 11-5 *Molecular Biology of the Cell* (© Garland Science 2008)

Model for the facilitated diffusion of glucose



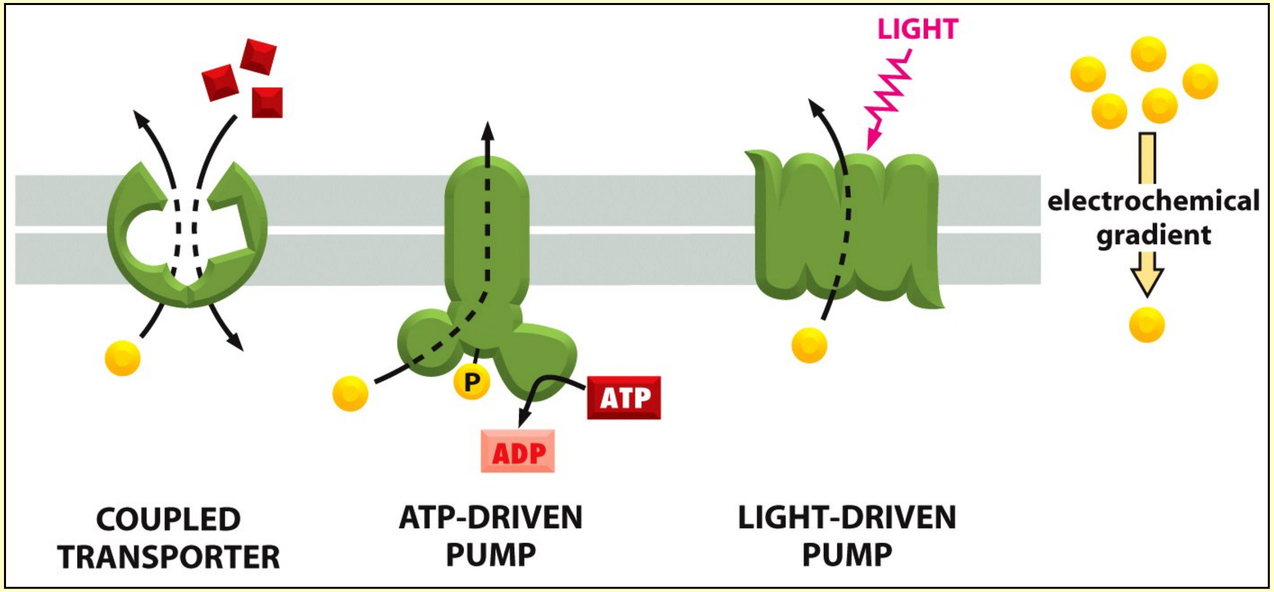
- glucose transporter alternates between two conformations
- glucose-binding site is alternately exposed on the outside and the inside of the cell
- glucose binds to a site exposed on the outside of the plasma membrane
- transporter then undergoes a conformational change
- glucose-binding site faces the inside of the cell and glucose is released into the cytosol
- transporter then returns to its original conformation

Figure 12.17. 2000. Cooper

Active transport

✓ requires energy

✓ there are three ways of driving active transport



➢Actively transported molecule

➢Energy source

A B C

A – coupled carriers → couple the uphill transport of one solute to the downhill transport of another

B – ATP-driven pumps → ATP hydrolysis

C – light-driven pumps → mainly in bacterial cells

Figure 11-8. 2002 Bruce Alberts, et al.

Three ways of carrier-mediated transport

✓ **uniport**

✓ **coupled carriers** – transport of one molecule is dependent on the transport of the another

- in the same direction – **symport**
- in the opposite direction – **antiport**

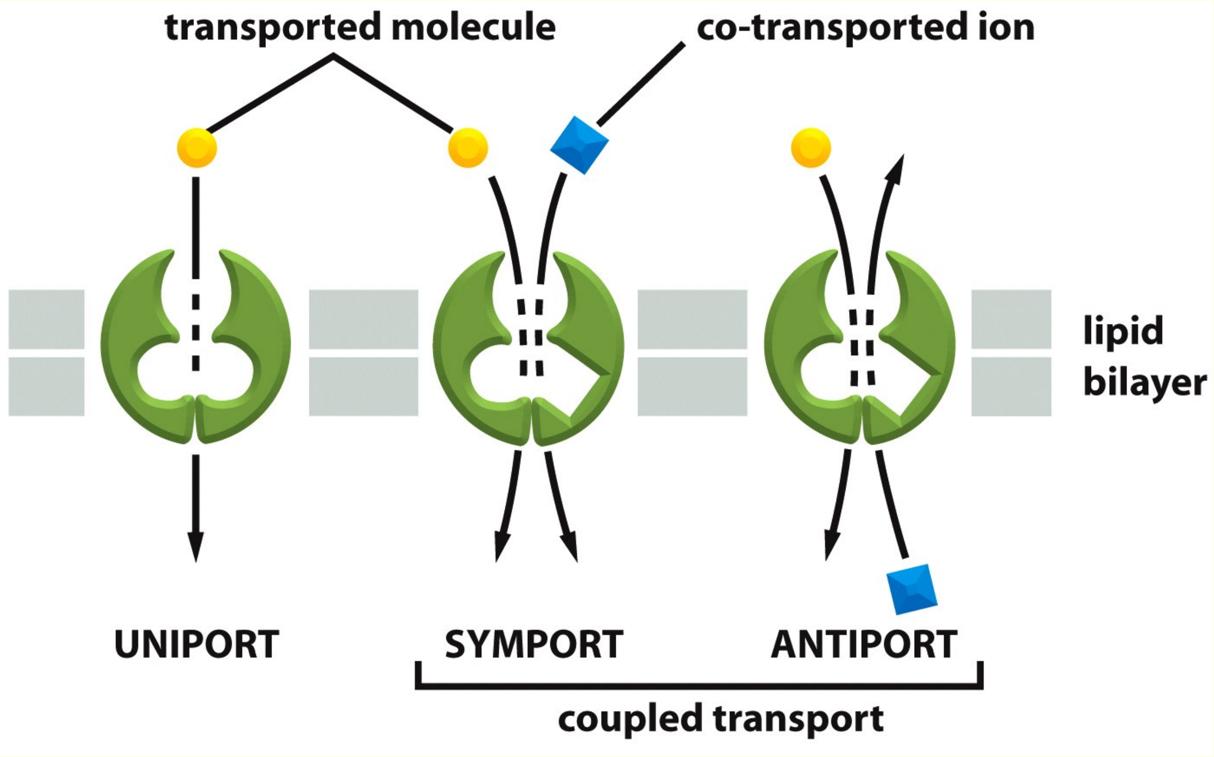
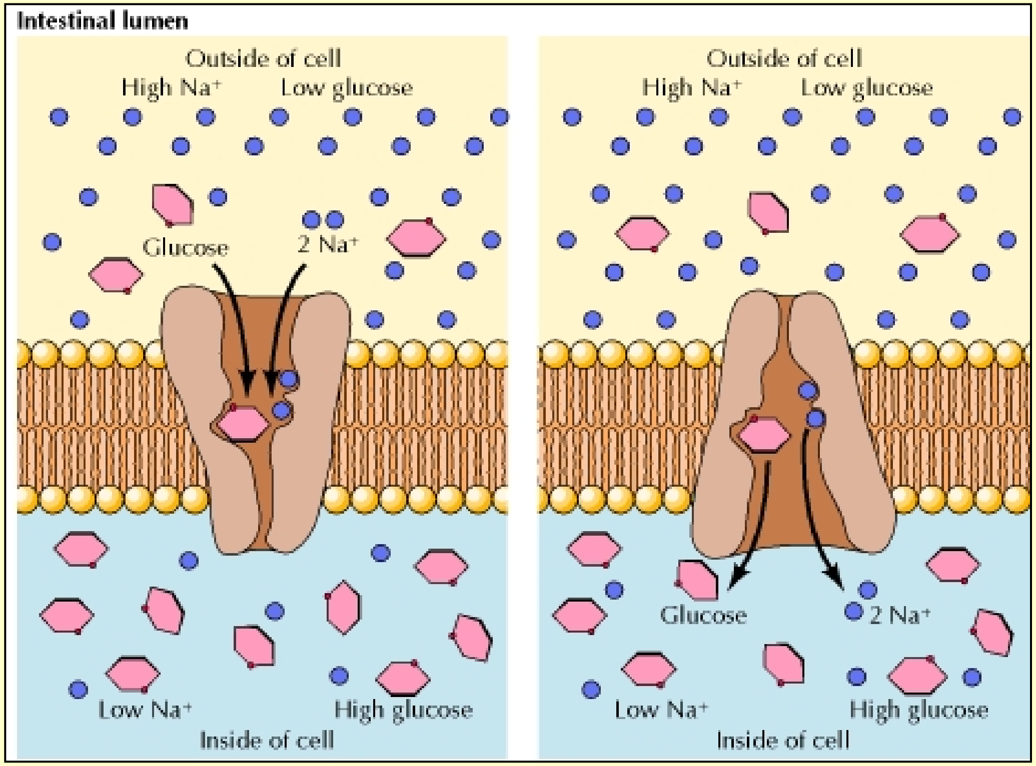


Figure 11-8 *Molecular Biology of the Cell* (© Garland Science 2008)

Active transport of glucose → symport



✓ active transport driven by the Na^+ gradient is responsible for the uptake of glucose from the intestinal lumen

✓ transporter coordinately binds and transports 1 glucose and 2 Na^+ into the cell

✓ transport of Na^+ in the energetically favorable direction drives the uptake of glucose against its concentration gradient

Figure 12-31. 2000. Cooper

Na^+/K^+ pump → antiport

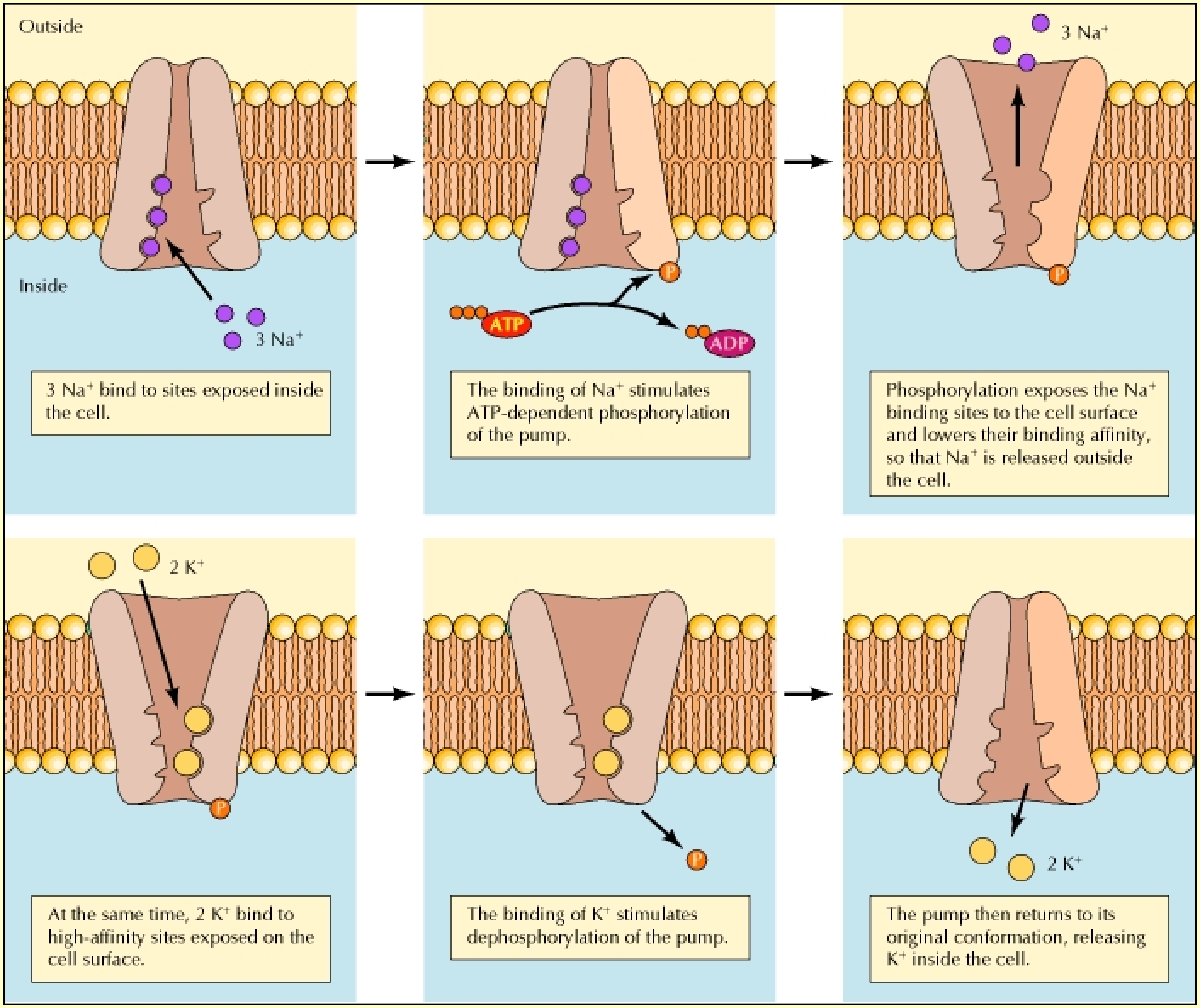


Figure 12.28. 2000 Cooper

http://highered.mcgraw-hill.com/sites/0072495855/student_view0/chapter2/animation__how_the_sodium_potassium_pump_works.html

❖ **Na^+/K^+ important for:**

✓ osmotic balance

✓ stabilization of cell volume

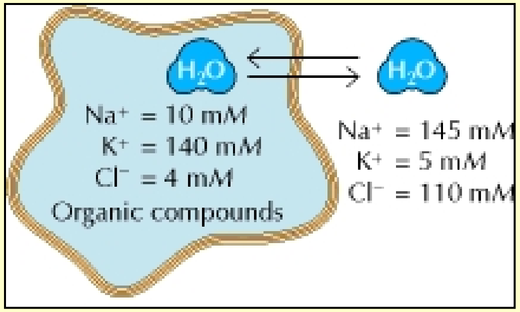


Figure 12.29. 2000. Cooper

✓ concentrations of Na^+ and Cl^- are higher outside than inside the cell
✓ concentration of K^+ is higher inside than out
✓ low concentrations of Na^+ and Cl^- balance the high intracellular concentration of organic compounds
→ equalizing the osmotic pressure and preventing the net influx of water

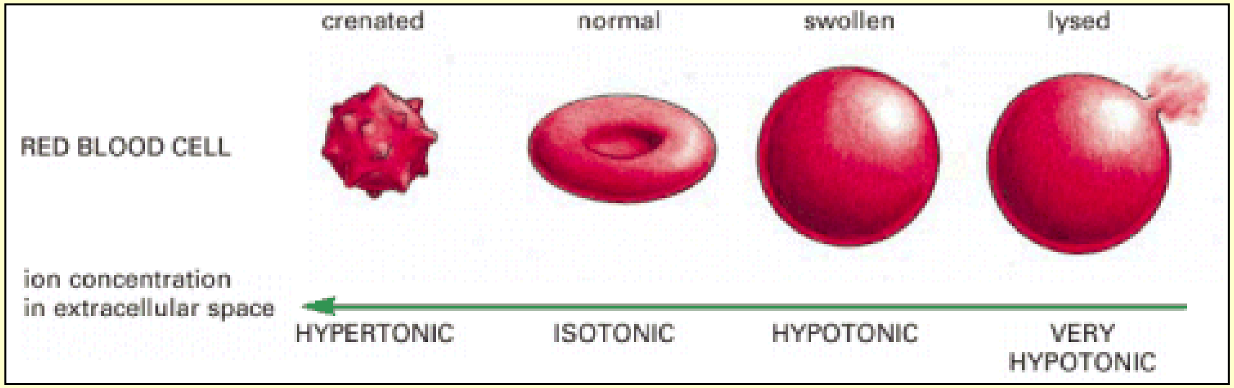


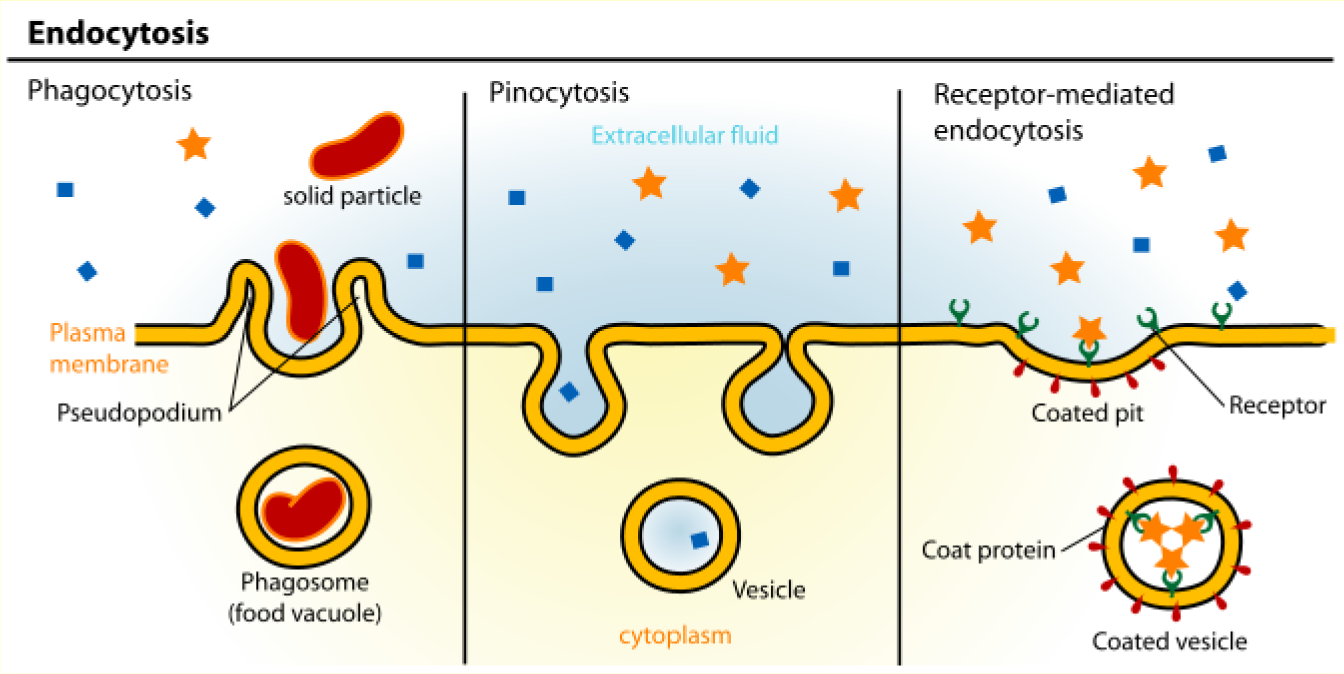
Figure 11-6. 2002 Alberts, et al.

Endocytosis

✓ an energy-using process by which cells absorb macromolecules and microorganisms by engulfing them

✓ it is used by all cells of the body because most substances important to them are large polar molecules that cannot pass through the hydrophobic plasma membrane

✓the opposite process is exocytosis

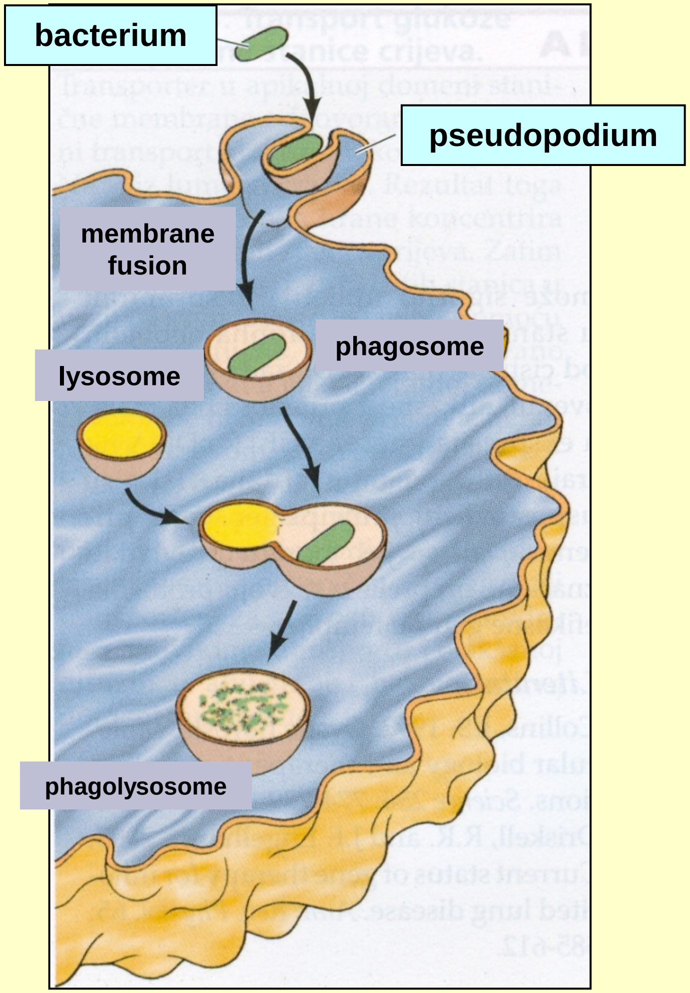


❖ Phagocytosis

✓process by which cells bind and internalize particulate matter larger than around 0.75 µm in diameter (small-sized dust particles, cell debris, microorganisms, apoptotic cells)

✓only occurs in specialized cells

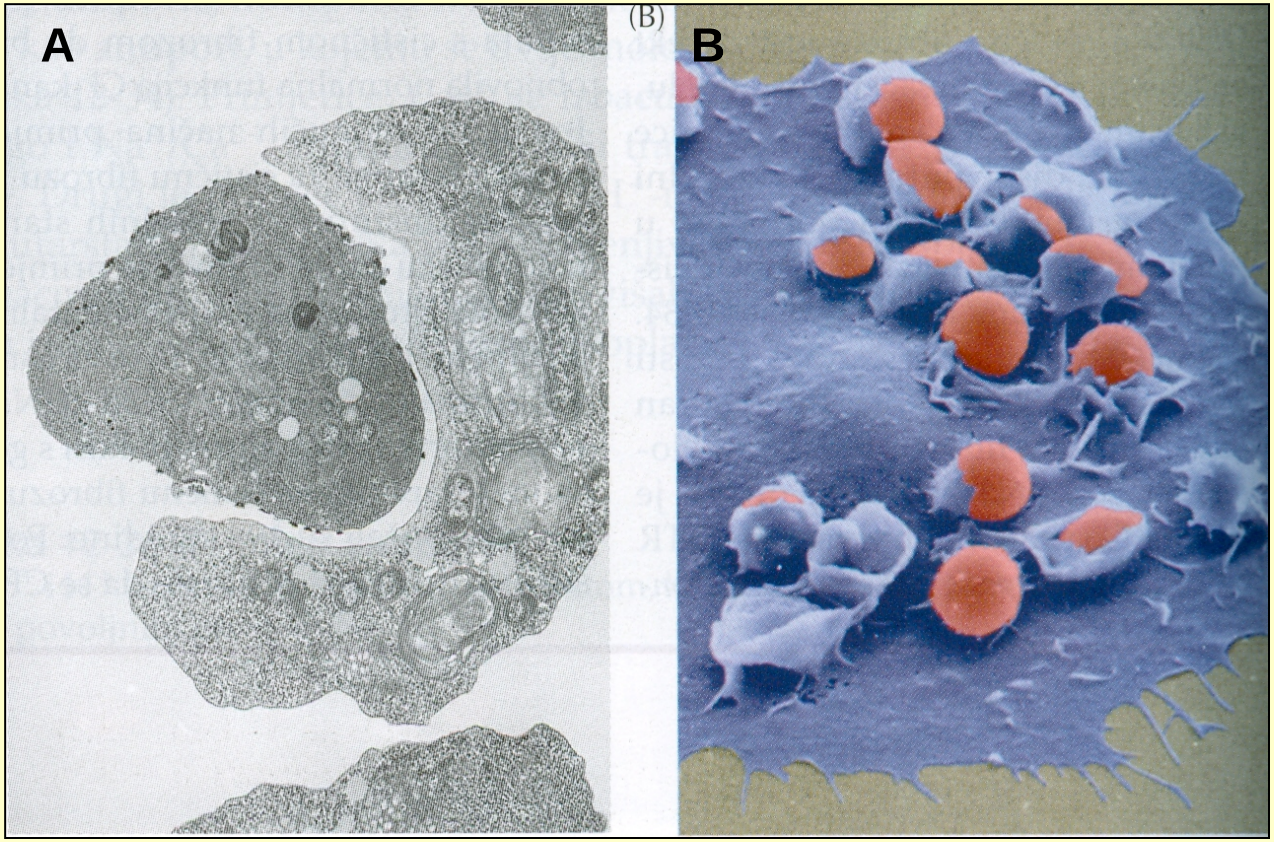
✓involve the uptake of larger membrane areas than clathrin-mediated endocytosis and caveolae pathway



2002 Cooper i Hausman

Animation

http://www.youtube.com/watch?v=4gLtk8Yc1Zc&feature=related



A – amoeba eating another protiste

B – makrohages eating red blood cells

Animation - Amoeba eats two paramecia (Amoeba's lunch)

http://www.youtube.com/watch?v=pvOz4V699gk

2002 Cooper and Hausman

❖ Receptor-mediated endocytosis

✓ Mechanism for selective uptake of specific molecules

- **receptors**
- formation of **clathrin-coated vesicles**
- fusion with **endosome** → material sorting
- fusion with **lysosome**

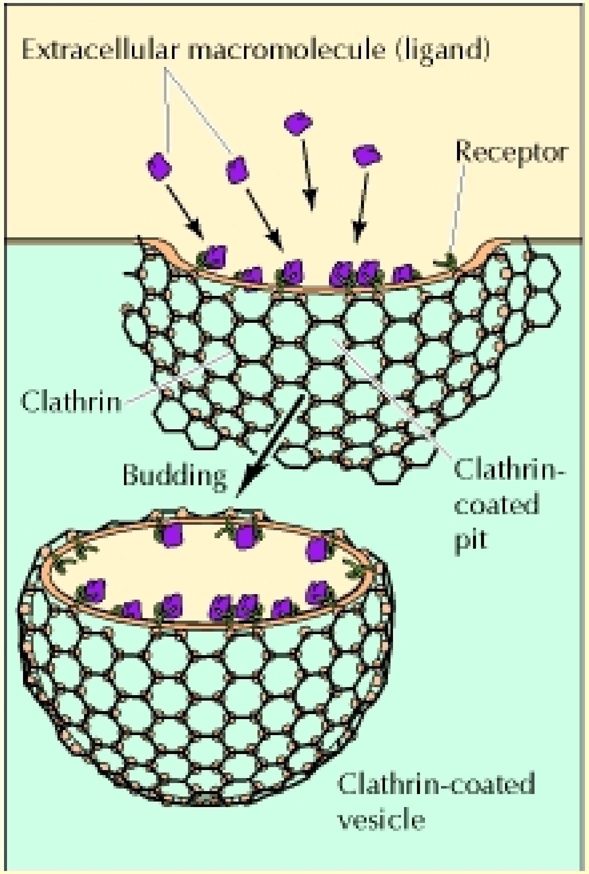
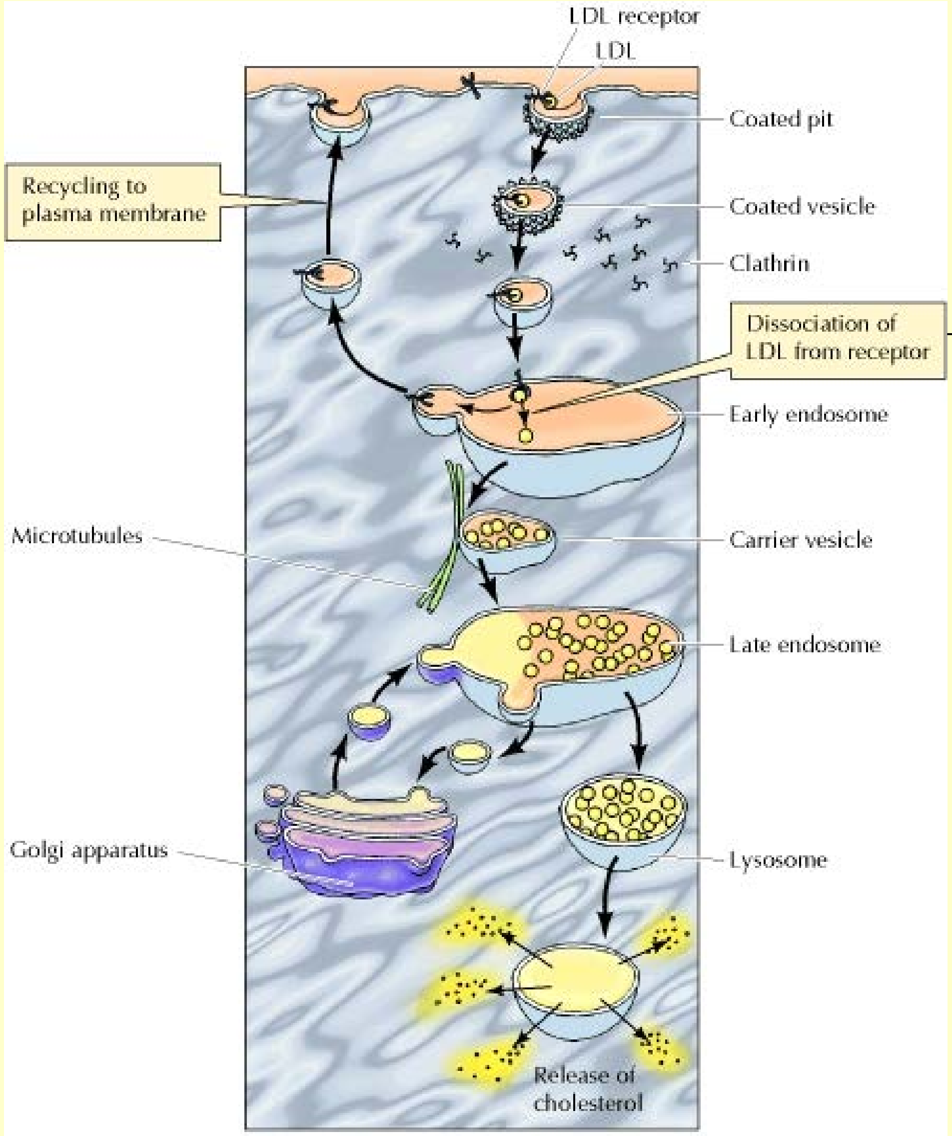


Figure 12.36, 2002 Cooper and Hausman

Cholesterol uptake by endocytosis



• LDL- *low density lipoprotein*

→ **Low pH!**

Figure 12.41, 2004 Cooper and Hausman