
CHAPTER 8

MEMBRANE STRUCTURE AND FUNCTION

OUTLINE

- I. Membrane models have evolved to fit new data: *science as a process*
- II. A membrane is a fluid mosaic of lipids, proteins and carbohydrates
 - A. The Fluid Quality of Membranes
 - B. Membranes as Mosaics of Structure and Function
 - C. Membrane Carbohydrates and Cell-Cell Recognition
- III. A membrane's molecular organization results in selective permeability
 - A. Permeability of the Lipid Bilayer
 - B. Transport Proteins
- IV. Passive transport is diffusion across a membrane
- V. Osmosis is the passive transport of water
- VI. Cell survival depends on balancing water uptake and loss
 - A. Water Balance of Cells Without Walls
 - B. Water Balance of Cells With Walls
- VII. Specific proteins facilitate the passive transport of selected solutes
- VIII. Active transport is the pumping of solutes against their gradients
- IX. Some ion pumps generate voltage across membranes
- X. In cotransport, a membrane protein couples the transport of one solute to another
- XI. Exocytosis and endocytosis transport large molecules
- XII. Specialized membrane proteins transmit extracellular signals to the inside of the cell

OBJECTIVES

After reading this chapter and attending lecture, the student should be able to:

1. Describe the function of the plasma membrane.
2. Explain how scientists used early experimental evidence to make deductions about membrane structure and function.
3. Describe the Davson-Danielli membrane model and explain how it contributed to our current understanding of membrane structure.
4. Describe the contribution J.D. Robertson, S.J. Singer and G.L. Nicolson made to clarify membrane structure.
5. Describe the fluid properties of the cell membrane and explain how membrane fluidity is influenced by membrane composition.
6. Explain how hydrophobic interactions determine membrane structure and function.
7. Describe how proteins are spatially arranged in the cell membrane and how they contribute to membrane function.
8. Describe factors that affect selective permeability of membranes.
9. Define diffusion; explain what causes it and why it is a spontaneous process.
10. Explain what regulates the rate of passive transport.
11. Explain why a concentration gradient across a membrane represents potential energy.
12. Define osmosis and predict the direction of water movement based upon differences in solute concentration.
13. Explain how bound water affects the osmotic behavior of dilute biological fluids.
14. Describe how living cells with and without walls regulate water balance.
15. Explain how transport proteins are similar to enzymes.
16. Describe one model for facilitated diffusion.
17. Explain how active transport differs from diffusion.
18. Explain what mechanisms can generate a membrane potential or electrochemical gradient.
19. Explain how potential energy generated by transmembrane solute gradients can be harvested by the cell and used to transport substances across the membrane.
20. Explain how large molecules are transported across the cell membrane.
21. Give an example of receptor-mediated endocytosis.
22. Explain how membrane proteins interface with and respond to changes in the extracellular environment.
23. Describe a simple signal-transduction pathway across the membrane including the roles of first and second messengers.

KEY TERMS

phospholipid bilayer	carrier-mediated	water potential	proton pump
amphipathic	transport	osmotic potential	cotransport
fluid mosaic model	permease	solution	exocytosis
J.F. Danielli	diffusion	solvent	endocytosis
H. Davson	osmosis	solute	phagocytosis
J.D. Robertson	dialysis	hypertonic	pinocytosis
S.J. Singer	facilitated diffusion	hypotonic	receptor-mediated
G.L. Nicolson	active transport	isotonic	endocytosis
integral proteins	concentration	membrane potential	signal-transduction
peripheral proteins	gradient	electrogenic pump	pathway
selective permeability	bulk flow	sodium-potassium pump	second messenger

LECTURE NOTES

The *plasma membrane* is the boundary that separates the living cell from its nonliving surroundings. It makes life possible by its ability to discriminate in its chemical exchanges with the environment. This membrane:

- Is about 8 nm thick.
- Surrounds the cell and controls chemical traffic into and out of the cell.
- Is *selectively permeable*; it allows some substances to cross more easily than others.
- Has a unique structure which determines its function and solubility characteristics.

NOTE: This is an opportune place to illustrate how form fits function. It is remarkable how much early models contributed to the understanding of membrane structure, since biologists proposed these models without the benefit of "seeing" a membrane with an electron microscope.

I. Membrane models have evolved to fit new data: *science as a process*

Membrane function is determined by its structure. Early models of the plasma membrane were deduced from indirect evidence:

1. Evidence: Lipid and lipid soluble materials enter cells more rapidly than substances that are insoluble in lipids (C. Overton, 1895).

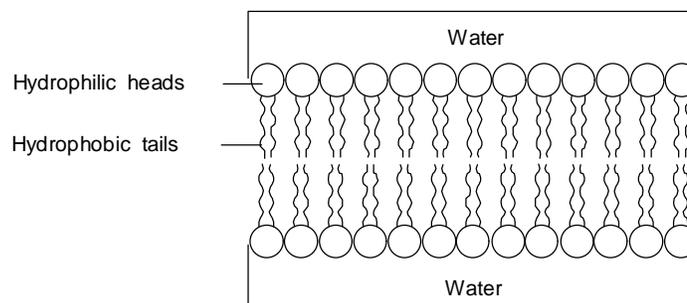
Deduction: Membranes are made of lipids.

Deduction: Fat-soluble substance move through the membrane by dissolving in it ("like dissolves like").

2. Evidence: *Amphipathic* phospholipids will form an artificial membrane on the surface of water with only the hydrophilic heads immersed in water (Langmuir, 1917).

Amphipathic = Condition where a molecule has both a hydrophilic region and a hydrophobic region.

Deduction: Because of their molecular structure, phospholipids can form membranes.



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argument not specified.

- Evidence: Phospholipid content of membranes isolated from red blood cells is just enough to cover the cells with two layers (Gorter and Grendel, 1925).

Deduction: Cell membranes are actually phospholipid bilayers, two molecules thick.

- Evidence: Membranes isolated from red blood cells contain proteins as well as lipids.

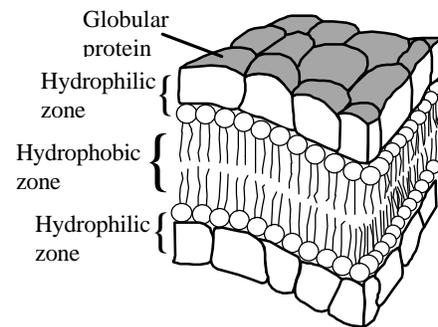
Deduction: There is protein in biological membranes.

- Evidence: Wettability of the surface of an actual biological membrane is greater than the surface of an artificial membrane consisting only of a phospholipid bilayer.

Deduction: Membranes are coated on both sides with proteins, which generally absorb water.

Incorporating results from these and other solubility studies, J.F. Danielli and H. Davson (1935) proposed a model of cell membrane structure:

- Cell membrane is made of a phospholipid bilayer sandwiched between two layers of globular protein.
- The polar (hydrophilic) heads of phospholipids are oriented towards the protein layers forming a hydrophilic zone.
- The nonpolar (hydrophobic) tails of phospholipids are oriented in between polar heads forming a hydrophobic zone.
- The membrane is approximately 8 nm thick.



In the 1950's, electron microscopy allowed biologists to visualize the plasma membrane for the first time and provided support for the Davson-Danielli model. Evidence from electron micrographs:

- Confirmed the plasma membrane was 7 to 8 nm thick (close to the predicted size if the Davson-Danielli model was modified by replacing globular proteins with protein layers in pleated-sheets).
- Showed the plasma membrane was trilaminar, made of two electron-dense bands separated by an unstained layer. It was assumed that the heavy metal atoms of the stain adhered to the hydrophilic proteins and heads of phospholipids and not to the hydrophobic core.
- Showed internal cellular membranes that looked similar to the plasma membrane. This led biologists (J.D. Robertson) to propose that all cellular membranes were symmetrical and virtually identical.

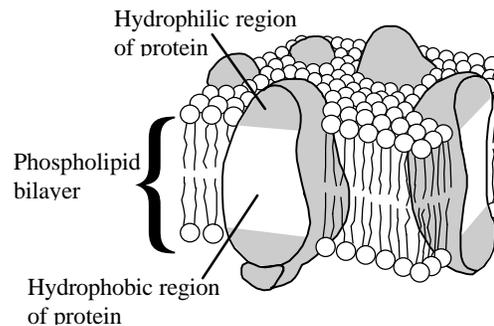
Though the phospholipid bilayer is probably accurate, there are problems with the Davson-Danielli model:

- Not all membranes are identical or symmetrical.
 - Membranes with different functions also differ in chemical composition and structure.
 - Membranes are bifacial with distinct inside and outside faces.

2. A membrane with an outside layer of proteins would be an unstable structure.
 - Membrane proteins are not soluble in water, and, like phospholipid, they are *amphipathic*.
 - Protein layer not likely because its hydrophobic regions would be in an aqueous environment, and it would also separate the hydrophilic phospholipid heads from water.

In 1972, S.J. Singer and G.L. Nicolson proposed the *fluid mosaic model* which accounted for the amphipathic character of proteins. They proposed:

- Proteins are individually embedded in the phospholipid bilayer, rather than forming a solid coat spread upon the surface.
- Hydrophilic portions of both proteins and phospholipids are maximally exposed to water resulting in a stable membrane structure.
- Hydrophobic portions of proteins and phospholipids are in the nonaqueous environment inside the bilayer.
- Membrane is a mosaic of proteins bobbing in a fluid bilayer of phospholipids.
- Evidence from freeze fracture techniques have confirmed that proteins are embedded in the membrane. Using these techniques, biologists can delaminate membranes along the middle of the bilayer. When viewed with an electron microscope, proteins appear to penetrate into the hydrophobic interior of the membrane. (See Campbell, Methods Box)



II. A membrane is a fluid mosaic of lipids, proteins and carbohydrates

A. The Fluid Quality of Membranes

Membranes are held together by hydrophobic interactions, which are weak attractions. (See Campbell, Figure 8.3)

- Most membrane lipids and some proteins can drift laterally within the membrane.
- Molecules rarely flip transversely across the membrane, because hydrophilic parts would have to cross the membrane's hydrophobic core.
- Phospholipids move quickly along the membrane's plane, averaging 2 μm per second.
- Membrane proteins drift more slowly than lipids. The fact that proteins drift laterally was established experimentally by fusing a human and mouse cell (Frye and Edidin, 1970):

Membrane proteins of a human and mouse cell were labeled with different green and red fluorescent dyes.



Cells were fused to form a hybrid cell with a continuous membrane.



Hybrid cell membrane had initially distinct regions of green and red dye.



In less than an hour, the two colors were intermixed.

- Some membrane proteins are tethered to the cytoskeleton and cannot move far.

Membranes must be fluid to work properly. Solidification may result in permeability changes and enzyme deactivation.

- Unsaturated hydrocarbon tails enhance membrane fluidity, because kinks at the carbon-to-carbon double bonds hinder close packing of phospholipids.
- Membranes solidify if the temperature decreases to a critical point. Critical temperature is lower in membranes with a greater concentration of unsaturated phospholipids.
- Cholesterol, found in plasma membranes of eukaryotes, modulates membrane fluidity by making the membrane:
 - ⇒ Less fluid at warmer temperatures (e.g. 37°C body temperature) by restraining phospholipid movement.
 - ⇒ More fluid at lower temperatures by preventing close packing of phospholipids.
- Cells may alter membrane lipid concentration in response to changes in temperature. Many cold tolerant plants (e.g. winter wheat) increase the unsaturated phospholipid concentration in autumn, which prevents the plasma membranes from solidifying in winter.

B. Membranes as Mosaics of Structure and Function

A membrane is a *mosaic* of different proteins embedded and dispersed in the phospholipid bilayer. These proteins vary in both structure and function, and they occur in two spatial arrangements:

1. *Integral proteins*, which are inserted into the membrane so their hydrophobic regions are surrounded by hydrocarbon portions of phospholipids. They may be:
 - unilateral, reaching only partway across the membrane.
 - transmembrane, with hydrophobic midsections between hydrophilic ends exposed on both sides of the membrane.

2. *Peripheral proteins*, which are not embedded but attached to the membrane's surface.
 - May be attached to integral proteins or held by fibers of the ECM.
 - On cytoplasmic side, may be held by filaments of cytoskeleton.

Membranes are bifacial. The membrane's synthesis and modification by the ER and Golgi determines this asymmetric distribution of lipids, proteins and carbohydrates:

- Two lipid layers may differ in lipid composition.
- Membrane proteins have distinct directional orientation.
- When present, carbohydrates are restricted to the membrane's exterior.
- Side of the membrane facing the lumen of the ER, Golgi and vesicles is topologically the same as the plasma membrane's outside face. (See Campbell, Figure 8.7)
- Side of the membrane facing the cytoplasm has always faced the cytoplasm, from the time of its formation by the endomembrane system to its addition to the plasma membrane by the fusion of a vesicle.

C. Membrane Carbohydrates and Cell-Cell Recognition

Cell-cell recognition = The ability of a cell to determine if other cells it encounters are alike or different from itself.

Cell-cell recognition is crucial in the functioning of an organism. It is the basis for:

- Sorting of an animal embryo's cells into tissues and organs.
- Rejection of foreign cells by the immune system.

The way cells recognize other cells is probably by keying on cell markers found on the external surface of the plasma membrane. Because of their diversity and location, likely candidates for such cell markers are membrane carbohydrates:

- Usually branched *oligosaccharides* (<15 monomers).
- Some covalently bonded to lipids (*glycolipids*).
- Most covalently bonded to proteins (*glycoproteins*).
- Vary from species to species, between individuals of the same species and among cells in the same individual.

III. A membrane's molecular organization results in selective permeability

The *selectively permeable* plasma membrane regulates the type and rate of molecular traffic into and out of the cell.

Selective permeability = Property of biological membranes which allows some substances to cross more easily than others. The selective permeability of a membrane depends upon:

- membrane solubility characteristics of the phospholipid bilayer
- presence of specific integral transport proteins.

A. Permeability of the Lipid Bilayer

The ability of substances to cross the hydrophobic core of the plasma membrane can be measured as the rate of transport through an artificial phospholipid bilayer:

1. Nonpolar (Hydrophobic) Molecules

- Dissolve in the membrane and cross it with ease (e.g. hydrocarbons and O₂).
- If two molecules are equally lipid soluble, the smaller of the two will cross the membrane faster.

2. Polar (Hydrophilic) Molecules

- Small, polar uncharged molecules (e.g. H₂O, CO₂) that are small enough to pass between membrane lipids, will easily pass through synthetic membranes.
- Larger, polar uncharged molecules (e.g. glucose) will *not* easily pass through synthetic membranes.
- All ions, even small ones (e.g. Na⁺, H⁺) have difficulty penetrating the hydrophobic layer.

B. Transport Proteins

Water, CO₂ and nonpolar molecules rapidly pass through the plasma membrane as they do an artificial membrane.

Unlike artificial membranes, however, biological membranes *are* permeable to specific ions and certain polar molecules of moderate size. These hydrophilic substances avoid the hydrophobic core of the bilayer by passing through *transport proteins*.

Transport proteins = Integral membrane proteins that transport specific molecules or ions across biological membranes. (See Campbell, Figure 8.6)

- May provide a hydrophilic tunnel through the membrane.
- May bind to a substance and physically move it across the membrane.
- Are specific for the substance they translocate.

IV. Passive transport is diffusion across a membrane

NOTE: Students have particular trouble with the concepts of *gradient* and *net* movement, yet their understanding of diffusion depends upon having a working knowledge of these terms.

Concentration gradient = Regular, graded concentration change over a distance in a particular direction.

Net directional movement = Overall movement away from the center of concentration, which results from random molecular movement in all directions.

Diffusion = The *net* movement of a substance down a *concentration gradient*.

- Results from the intrinsic kinetic energy of molecules (also called thermal motion, or heat).
- Results from random molecular motion, even though the *net* movement may be directional.
- Diffusion continues until a dynamic equilibrium is reached — the molecules continue to move, but there is no net directional movement.

In the absence of other forces, a substance will diffuse from where it is more concentrated to where it is less concentrated.

- A substance diffuses down its *concentration gradient*.
- Because it decreases free energy, diffusion is a spontaneous process ($-\Delta G$). It increases entropy of a system by producing a more random mixture of molecules.
- A substance diffuses down its *own* concentration gradient and is not affected by the gradients of other substances.

Much of the traffic across cell membranes occurs by diffusion and is thus a form of *passive transport*.

Passive transport = Diffusion of a substance across a biological membrane.

- Spontaneous process which is a function of a concentration gradient when a substance is more concentrated on one side of the membrane.
- Passive process which does not require the cell to expend energy. It is the potential energy stored in a concentration gradient that drives diffusion.
- Rate of diffusion is regulated by the permeability of the membrane, so some molecules diffuse more freely than others.
- Water diffuses freely across most cell membranes.

V. **Osmosis is the passive transport of water**

Hypertonic solution = A solution with a greater solute concentration than that inside a cell.

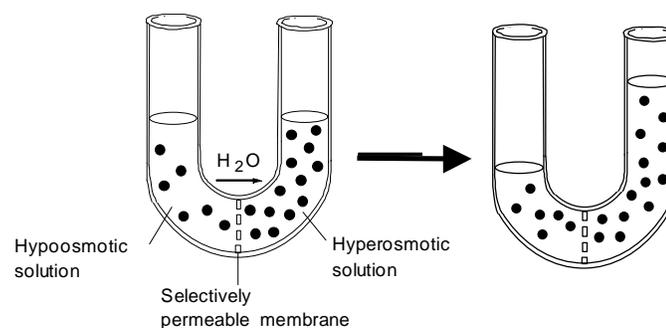
Hypotonic solution = A solution with a lower solute concentration compared to that inside a cell.

Isotonic solution = A solution with an equal solute concentration compared to that inside a cell.

NOTE: These terms are clearly a source of confusion for students. It helps to point out that these are only relative terms used to compare the osmotic concentration of a solution to the osmotic concentration of a cell.

Osmosis = Diffusion of water across a selectively permeable membrane.

- Water diffuses down its concentration gradient.
- For example, if two solutions of different concentrations are separated by a selectively permeable membrane that is permeable to water but not the solute, water will diffuse from the hypoosmotic solution (solution with the lower osmotic concentration) to the hyperosmotic solution (solution with the higher osmotic concentration).



- Some solute molecules can reduce the proportion of water molecules that can freely diffuse. Water molecules form a *hydration shell* around hydrophilic solute molecules, and this bound water cannot freely diffuse across a membrane.
- In dilute solutions including most biological fluids, it is the difference in the proportion of unbound water that causes osmosis, rather than the actual difference in water concentration.
- Direction of osmosis is determined by the difference in *total* solute concentration, regardless of the type or diversity of solutes in the solutions.
- If two *isosmotic* solutions are separated by a selectively permeable membrane, water molecules diffuse across the membrane in both directions at an equal rate. There is no *net* movement of water.

NOTE: Clarification of this point is often necessary. Students may need to be reminded that even though there is no *net* movement of water across the membrane (or osmosis), the water molecules do not stop moving. At equilibrium, the water molecules move in both directions at the same rate.

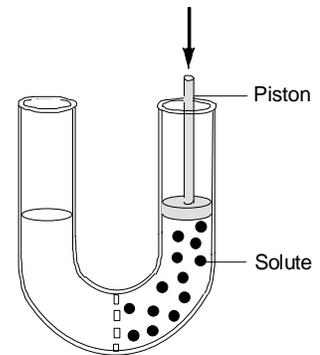
Osmotic concentration = Total solute concentration of a solution.

Osmotic pressure = Measure of the tendency for a solution to take up water when separated from pure water by a selectively permeable membrane.

- Osmotic pressure of pure water is zero.
- Osmotic pressure of a solution is proportional to its osmotic concentration. (The greater the solute concentration, the greater the osmotic pressure.)

Osmotic pressure can be measured by an *osmometer*:

- In one type of osmometer, pure water is separated from a solution by a selectively permeable membrane that is permeable to water but not solute.
- The tendency for water to move into the solution by osmosis is counteracted by applying enough pressure with a piston so the solution's volume will stay the same.
- The amount of pressure required to prevent net movement of water into the solution is the *osmotic pressure*.



VI. Cell survival depends on balancing water uptake and loss

A. Water Balance of Cells Without Walls

Since animal cells lack cell walls, they are not tolerant of excessive osmotic uptake or loss of water.

- In an isotonic environment, the volume of an animal cell will remain stable with no net movement of water across the plasma membrane.
- In a hypertonic environment, an animal cell will lose water by osmosis and *crenate* (shrink).

- In a hypotonic environment, an animal cell will gain water by osmosis, swell and perhaps *lyse* (cell destruction).

Organisms without cell walls prevent excessive loss or uptake of water by:

- Living in an isotonic environment (e.g. many marine invertebrates are isosmotic with sea water).
- Osmoregulating in a hypo- or hypertonic environment. Organisms can regulate water balance (osmoregulation) by removing water in a hypotonic environment (e.g. *Paramecium* with contractile vacuoles in fresh water) or conserving water and pumping out salts in a hypertonic environment (e.g. bony fish in seawater).

B. Water Balance of Cells With Walls

Cells of prokaryotes, some protists, fungi and plants have cell walls outside the plasma membrane.

- In a hypertonic environment, walled cells will lose water by osmosis and will *plasmolyze*, which is usually lethal.

Plasmolysis = Phenomenon where a walled cell shrivels and the plasma membrane pulls away from the cell wall as the cell loses water to a hypertonic environment.

- In a hypotonic environment, water moves by osmosis into the plant cell, causing it to swell until internal pressure against the cell wall equals the osmotic pressure of the cytoplasm. A dynamic equilibrium is established (water enters and leaves the cell at the same rate and the cell becomes *turgid*).

Turgid = Firmness or tension such as found in walled cells that are in a hypoosmotic environment where water enters the cell by osmosis.

⇒ Ideal state for most plant cells.

⇒ Turgid cells provide mechanical support for plants.

⇒ Requires cells to be hyperosmotic to their environment.

- In an isotonic environment, there is no net movement of water into or out of the cell.

⇒ Plant cells become *flaccid* or limp.

⇒ Loss of structural support from turgor pressure causes plants to wilt.

VII. Specific proteins facilitate the passive transport of selected solutes

Facilitated diffusion = Diffusion of solutes across a membrane, with the help of transport proteins.

- Is passive transport because solute is transported down its concentration gradient.
- Helps the diffusion of many polar molecules and ions that are impeded by the membrane's phospholipid bilayer.

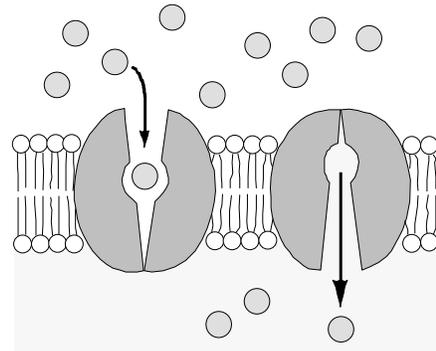
Transport proteins share some properties of enzymes:

- Transport proteins are *specific* for the solutes they transport. There is probably a specific binding site analogous to an enzyme's active site.
- Transport proteins can be *saturated* with solute, so the maximum transport rate occurs when all binding sites are occupied with solute.
- Transport proteins can be inhibited by molecules that resemble the solute normally carried by the protein (similar to competitive inhibition in enzymes).

Transport proteins differ from enzymes in they do not usually catalyze chemical reactions.

One Model for Facilitated Diffusion:

- Transport protein most likely remains in place in the membrane and translocates solute by alternating between two conformations.
- In one conformation, transport protein binds solute; as it changes to another conformation, transport protein deposits solute on the other side of the membrane.
- The solute's binding and release may trigger the transport protein's conformational change.



Other transport proteins are selective channels across the membrane.

- The membrane is thus permeable to specific solutes that can pass through these channels.
- Some selective channels (gated channels) only open in response to electrical or chemical stimuli. For example, binding of neurotransmitter to nerve cells opens gated channels, so that sodium ions can diffuse into the cell.

In some inherited disorders, transport proteins are missing or are defective (e.g. cystinuria, a kidney disease caused by missing carriers for cystine and other amino acids which are normally reabsorbed from the urine).

VIII. Active transport is the pumping of solutes against their gradients

Active transport = Energy-requiring process during which a transport protein pumps a molecule across a membrane, *against* its concentration gradient.

- Is energetically uphill ($+\Delta G$) and requires the cell to expend energy.
- Helps cells maintain steep ionic gradients across the cell membrane (e.g. Na^+ , K^+ , Mg^{++} , Ca^{++} and Cl^-).
- Transport proteins involved in active transport harness energy from ATP to pump molecules against their concentration gradients.

An example of an active transport system that translocates ions against steep concentration gradients is the *sodium-potassium pump*. Major features of the pump are:

1. The transport protein oscillates between two conformations:
 - a. High affinity for Na^+ with binding sites oriented towards the cytoplasm.
 - b. High affinity for K^+ with binding sites oriented towards the cell's exterior.
2. ATP phosphorylates the transport protein and powers the conformational change from Na^+ receptive to K^+ receptive.
3. As the transport protein changes conformation, it translocates bound solutes across the membrane.
4. Na^+K^+ -pump translocates three Na^+ ions out of the cell for every two K^+ ions pumped into the cell. (Refer to Campbell, Figure 8.13 for the specific sequence of events.)

IX. Some ion pumps generate voltage across membranes

Because anions and cations are unequally distributed across the plasma membrane, all cells have voltages across their plasma membranes.

Membrane potential = Voltage across membranes.

- Ranges from -50 to -200 mv. As indicated by the negative sign, the cell's inside is negatively charged with respect to the outside.
- Affects traffic of charged substances across the membrane.
- Favors diffusion of cations into cell and anions out of the cell (because of electrostatic attractions).

Two forces drive passive transport of ions across membranes:

1. Concentration gradient of the ion.
2. Effect of membrane potential on the ion.

Electrochemical gradient = Diffusion gradient resulting from the combined effects of membrane potential and concentration gradient.

- Ions may not always diffuse down their concentration gradients, but they *always* diffuse down their electrochemical gradients.
- At equilibrium, the distribution of ions on either side of the membrane may be different from the expected distribution when charge is not a factor.
- Uncharged solutes diffuse down concentration gradients because they are unaffected by membrane potential.

Factors which contribute to a cell's membrane potential (net negative charge on the inside):

1. Negatively charged proteins in the cell's interior.
2. Plasma membrane's selective permeability to various ions. For example, there is a net loss of positive charges as K^+ leaks out of the cell faster than Na^+ diffuses in.
3. The sodium-potassium pump. This *electrogenic pump* translocates 3 Na^+ out for every 2 K^+ in - a net loss of one positive charge per cycle.

Electrogenic pump = A transport protein that generates voltage across a membrane.

- Na^+/K^+ ATPase is the major electrogenic pump in animal cells.
- A *proton pump* is the major electrogenic pump in plants, bacteria and fungi. Also, mitochondria and chloroplasts use a proton pump to drive ATP synthesis.
- Voltages created by electrogenic pumps are sources of potential energy available to do cellular work.

NOTE: This is a good place to emphasize that electrochemical gradients represent potential energy. Spending lecture time on cotransport and the proton pump will help prepare your students for the upcoming topic of chemiosmosis.

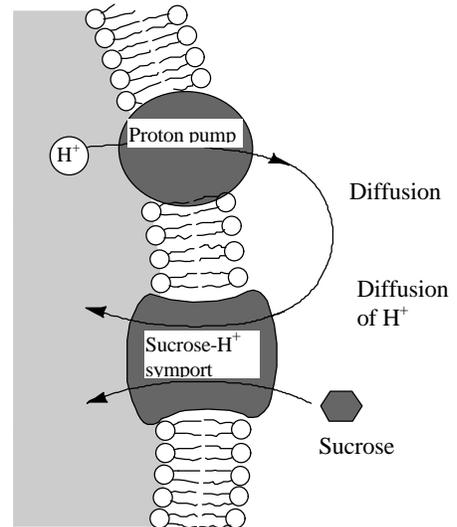
X. In cotransport, a membrane protein couples the transport of one solute to another

Cotransport = Process where a single ATP-powered pump actively transports one solute and indirectly drives the transport of other solutes against their concentration gradients.

One mechanism of cotransport involves two transport proteins:

1. ATP-powered pump actively transports one solute and creates potential energy in the gradient it creates.
2. Another transport protein couples the solute's downhill diffusion as it leaks back across the membrane with a second solute's uphill transport against its concentration gradient.

For example, plants use a proton pump coupled with sucrose- H^+ symport to load sucrose into specialized cells of vascular tissue. Both solutes, H^+ and sucrose, must bind to the transport protein for cotransport to take place.



XI. Exocytosis and endocytosis transport large molecules

Water and small molecules cross membranes by:

1. Passing through the phospholipid bilayer.
2. Being translocated by a transport protein.

Large molecules (e.g. proteins and polysaccharides) cross membranes by the processes of *exocytosis* and *endocytosis*.

Exocytosis	Endocytosis
<p>Process of exporting macromolecules from a cell by fusion of vesicles with the plasma membrane.</p> <p>Vesicle usually budded from the ER or Golgi and migrates to plasma membrane.</p> <p>Used by secretory cells to export products (e.g. insulin in pancreas, or neurotransmitter from neuron).</p>	<p>Process of importing macromolecules into a cell by forming vesicles derived from the plasma membrane.</p> <p>Vesicle forms from a localized region of plasma membrane that sinks inward; pinches off into the cytoplasm.</p> <p>Used by cells to incorporate extracellular substances.</p>

There are three types of endocytosis: (1) *phagocytosis*, (2) *pinocytosis* and (3) *receptor-mediated endocytosis*.

Phagocytosis = (cell eating) Endocytosis of solid particles.

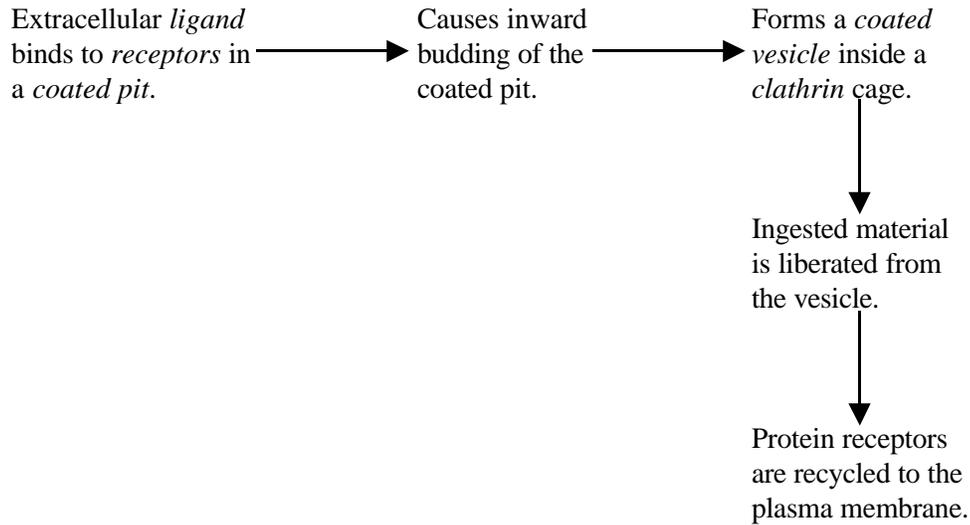
- Cell engulfs particle with *pseudopodia* and pinches off a food vacuole.
- Vacuole fuses with a lysosome containing hydrolytic enzymes that will digest the particle.

Pinocytosis = (cell drinking) Endocytosis of fluid droplets.

- Droplets of extracellular fluid are taken into small vesicles.
- The process is not discriminating. The cell takes in all solutes dissolved in the droplet.

Receptor-mediated endocytosis = The process of importing specific macromolecules into the cell by the inward budding of vesicles formed from *coated pits*; occurs in response to the binding of specific *ligands* to receptors on the cell's surface.

- More discriminating process than pinocytosis.
- Membrane-embedded proteins with specific receptor sites exposed to the cell's exterior, cluster in regions called *coated pits*.
- A layer of *clathrin*, a fibrous protein, lines and reinforces the *coated pit* on the cytoplasmic side and probably helps deepen the pit to form a vesicle.
- A molecule that binds to a specific receptor site of another molecule is called a *ligand*.

Progressive Stages of Receptor-Mediated Endocytosis:

Receptor-mediated endocytosis enables cells to acquire bulk quantities of specific substances, even if they are in low concentration in extracellular fluid. For example, cholesterol enters cells by receptor-mediated endocytosis.

- In the blood, cholesterol is bound to lipid and protein complexes called *low-density lipoproteins* (LDLs).
- These LDLs bind to LDL receptors on cell membranes, initiating endocytosis.
- An inherited disease called familial hypercholesterolemia is characterized by high cholesterol levels in the blood. The LDL receptors are defective, so cholesterol cannot enter the cells by endocytosis and thus accumulates in the blood, contributing to the development of atherosclerosis.

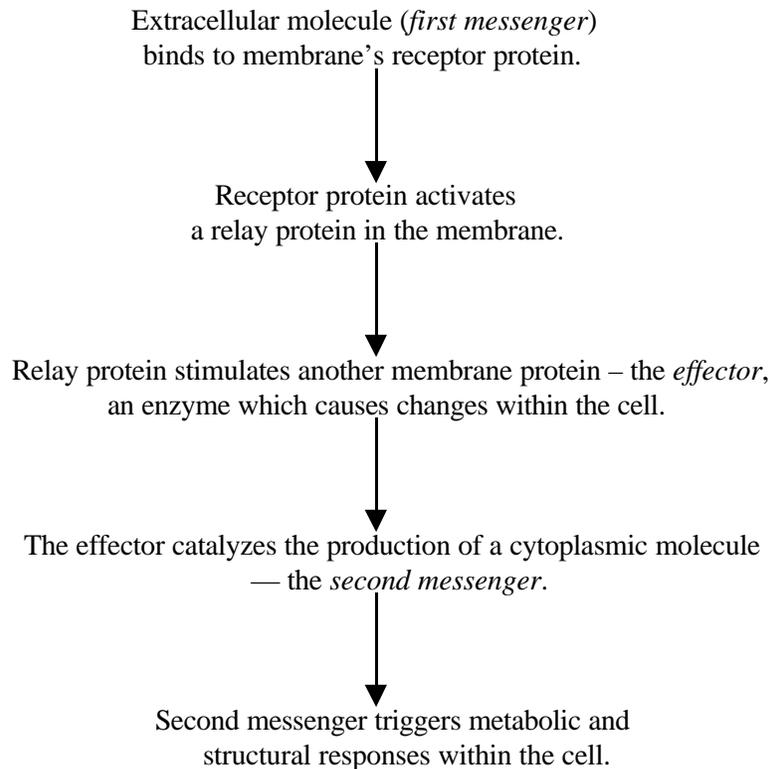
In a nongrowing cell, the amount of plasma membrane remains relatively constant.

- Vesicle fusion with the plasma membrane offsets membrane loss through endocytosis.
- Vesicles provide a mechanism to rejuvenate or remodel the plasma membrane.

XII. Specialized membrane proteins transmit extracellular signals to the inside of the cell.

In addition to their role in transport, membrane proteins interface with and respond to changes in the intracellular environment. For example,

- Specific integral proteins (*integrins*) transmit physical stimuli from the extracellular matrix to the cytoskeleton inside, influencing cell shape and movement.
- Some membrane proteins transduce chemical signals from the outside, beginning a cascade of responses inside the cell. Such *signal-transduction pathways* are often complex and begin with the binding of an extracellular molecule, such as a hormone, to a receptor. A simplified pathway might be:



REFERENCES

- Alberts, B., D. Bray, J. Lewis, M. Raff, K. Roberts and J.D. Watson. *Molecular Biology of the Cell*. 2nd ed. New York: Garland, 1989.
- Becker, W.M. and D.W. Deamer. *The World of the Cell*. 3rd ed. Redwood City, California: Benjamin/Cummings, 1996.
- Campbell, N. *Biology*. 4th ed. Menlo Park, California: Benjamin/Cummings, 1996.
- deDuve, C. *A Guided Tour of the Living Cell*. Volumes I and II. New York: Scientific American Books, 1984. Literally a guided tour of the cell with the reader as "cytonaut." This is an excellent resource for lecture material and enjoyable reading.
- Kleinsmith, L.J. and V.M. Kish. *Principles of Cell Biology*. New York: Harper and Row, Publ., 1988.