

6

Membranes

Concept Outline

6.1 Biological membranes are fluid layers of lipid.

The Phospholipid Bilayer. Cells are encased by membranes composed of a bilayer of phospholipid.

The Lipid Bilayer Is Fluid. Because individual phospholipid molecules do not bind to one another, the lipid bilayer of membranes is a fluid.

6.2 Proteins embedded within the plasma membrane determine its character.

The Fluid Mosaic Model. A varied collection of proteins float within the lipid bilayer.

Examining Cell Membranes. Visualizing a plasma membrane requires a powerful electron microscope.

Kinds of Membrane Proteins. The proteins in a membrane function in support, transport, recognition, and reactions.

Structure of Membrane Proteins. Membrane proteins are anchored into the lipid bilayer by their nonpolar regions.

6.3 Passive transport across membranes moves down the concentration gradient.

Diffusion. Random molecular motion results in a net movement of molecules to regions of lower concentration.

Facilitated Diffusion. Passive movement across a membrane is often through specific carrier proteins.

Osmosis. Polar solutes interact with water and can affect the movement of water across semipermeable membranes.

6.4 Bulk transport utilizes endocytosis.

Bulk Passage Into and Out of the Cell. To transport large particles, membranes form vesicles.

6.5 Active transport across membranes is powered by energy from ATP.

Active Transport. Cells transport molecules up a concentration gradient using ATP-powered carrier proteins.

Coupled Transport. Active transport of ions drives coupled uptake of other molecules up their concentration gradients.



FIGURE 6.1

Membranes within a human cell. Sheets of endoplasmic reticulum weave through the cell interior. The large oval is a mitochondrion, itself filled with extensive internal membranes.

Among a cell's most important activities are its interactions with the environment, a give and take that never ceases. Without it, life could not persist. While living cells and eukaryotic organelles (figure 6.1) are encased within a lipid membrane through which few water-soluble substances can pass, the membrane contains protein passageways that permit specific substances to move in and out of the cell and allow the cell to exchange information with its environment. We call this delicate skin of protein molecules embedded in a thin sheet of lipid a **plasma membrane**. This chapter will examine the structure and function of this remarkable membrane.

6.1 Biological membranes are fluid layers of lipid.

The Phospholipid Bilayer

The membranes that encase all living cells are sheets of lipid only two molecules thick; more than 10,000 of these sheets piled on one another would just equal the thickness of this sheet of paper. The lipid layer that forms the foundation of a cell membrane is composed of molecules called **phospholipids** (figure 6.2).

Phospholipids

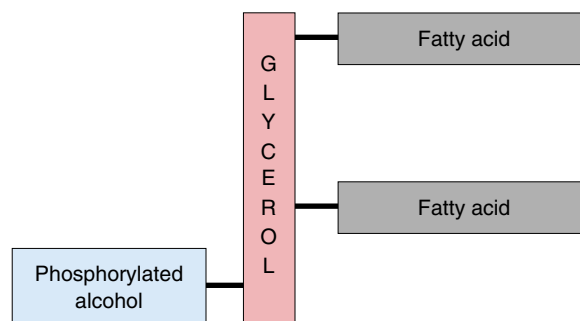
Like the fat molecules you studied in chapter 3, a phospholipid has a backbone derived from a three-carbon molecule called glycerol. Attached to this backbone are fatty acids, long chains of carbon atoms ending in a carboxyl (—COOH) group. A fat molecule has three such chains, one attached to each carbon in the backbone; because these chains are nonpolar, they do not form hydrogen bonds with water, and the fat molecule is not water-soluble. A phospholipid, by contrast, has only two fatty acid chains attached to its backbone. The third carbon on the backbone is attached instead to a highly polar organic alcohol that readily forms hydrogen bonds with water. Because this alcohol is attached by a phosphate group, the molecule is called a *phospholipid*.

One end of a phospholipid molecule is, therefore, strongly nonpolar (water-insoluble), while the other end is strongly polar (water-soluble). The two nonpolar fatty acids extend in one direction, roughly parallel to each other, and the polar alcohol group points in the other direction. Because of this structure, phospholipids are often diagrammed as a polar head with two dangling nonpolar tails (as in figure 6.2*b*).

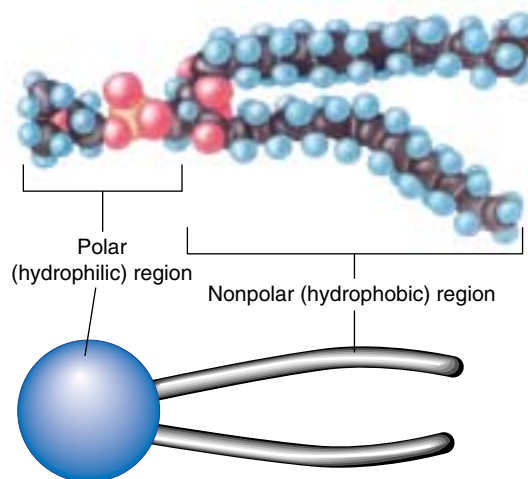
Phospholipids Form Bilayer Sheets

What happens when a collection of phospholipid molecules is placed in water? The polar water molecules repel the long nonpolar tails of the phospholipids as the water molecules seek partners for hydrogen bonding. Due to the polar nature of the water molecules, the nonpolar tails of the phospholipids end up packed closely together, sequestered as far as possible from water. Every phospholipid molecule orients to face its polar head toward water and its nonpolar tails away. When *two* layers form with the tails facing each other, no tails ever come in contact with water. The resulting structure is called a **lipid bilayer** (figure 6.3). Lipid bilayers form spontaneously, driven by the tendency of water molecules to form the maximum number of hydrogen bonds.

The nonpolar interior of a lipid bilayer impedes the passage of any water-soluble substances through the bilayer,



(a)



(b)

FIGURE 6.2

Phospholipid structure. (a) A phospholipid is a composite molecule similar to a triacylglycerol, except that only two fatty acids are bound to the glycerol backbone; a phosphorylated alcohol occupies the third position on the backbone. (b) Because the phosphorylated alcohol usually extends from one end of the molecule and the two fatty acid chains extend from the other, phospholipids are often diagrammed as a polar head with two nonpolar hydrophobic tails.

just as a layer of oil impedes the passage of a drop of water (“oil and water do not mix”). This barrier to the passage of water-soluble substances is the key biological property of the lipid bilayer. In addition to the phospholipid molecules that make up the lipid bilayer, the membranes of every cell also contain proteins that extend through the lipid bilayer, providing passageways across the membrane.

The basic foundation of biological membranes is a lipid bilayer, which forms spontaneously. In such a layer, the nonpolar hydrophobic tails of phospholipid molecules point inward, forming a nonpolar barrier to water-soluble molecules.

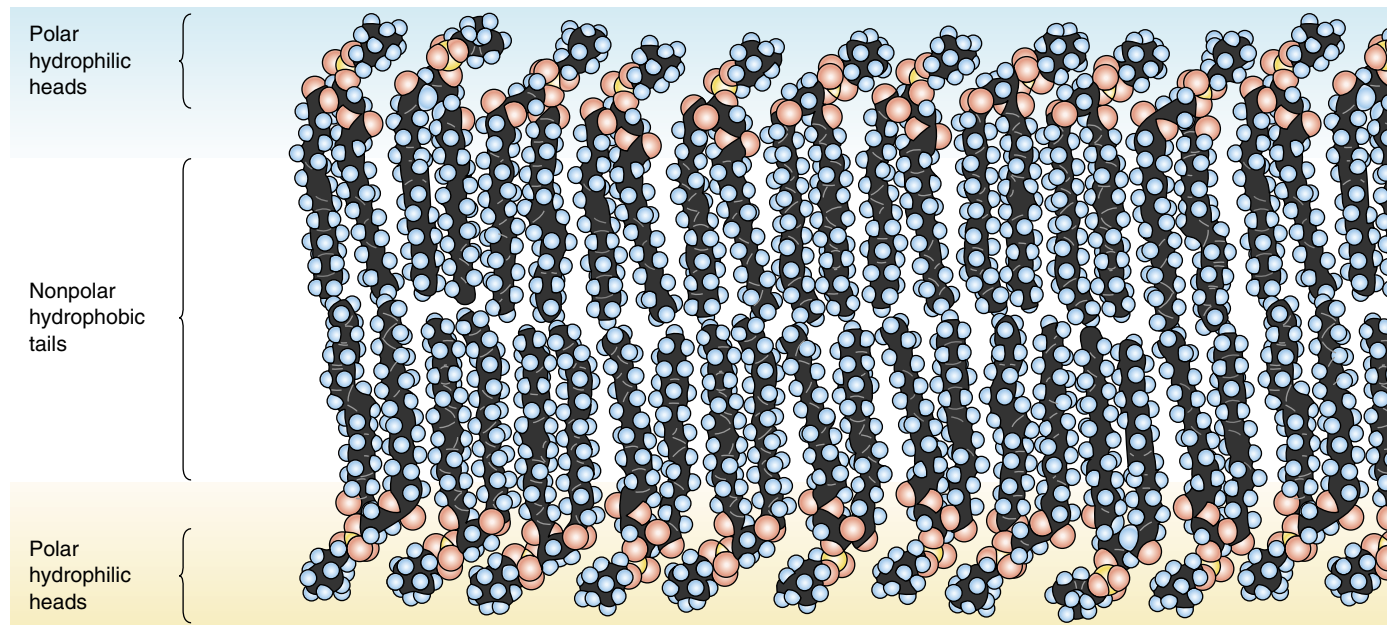


FIGURE 6.3

A phospholipid bilayer. The basic structure of every plasma membrane is a double layer of lipid, in which phospholipids aggregate to form a bilayer with a nonpolar interior. The phospholipid tails do not align perfectly and the membrane is “fluid.” Individual phospholipid molecules can move from one place to another in the membrane.

The Lipid Bilayer Is Fluid

A lipid bilayer is stable because water’s affinity for hydrogen bonding never stops. Just as surface tension holds a soap bubble together, even though it is made of a liquid, so the hydrogen bonding of water holds a membrane together. But while water continually drives phospholipid molecules into this configuration, it does not locate specific phospholipid molecules relative to their neighbors in the bilayer. As a result, individual phospholipids and unanchored proteins are free to move about within the membrane. This can be demonstrated vividly by fusing cells and watching their proteins reassemble (figure 6.4).

Phospholipid bilayers are fluid, with the viscosity of olive oil (and like oil, their viscosity increases as the temperature decreases). Some membranes are more fluid than others, however. The tails of individual phospholipid molecules are attracted to one another when they line up close together. This causes the membrane to become less fluid, because aligned molecules must pull apart from one another before they can move about in the membrane. The greater the degree of alignment, the less fluid the membrane. Some phospholipid tails do not align well because they contain one or more double bonds between carbon atoms, introducing kinks in the tail. Membranes containing such phospholipids are more fluid than membranes that lack them. Most membranes also contain steroid lipids like cholesterol, which can either increase or decrease membrane fluidity, depending on temperature.

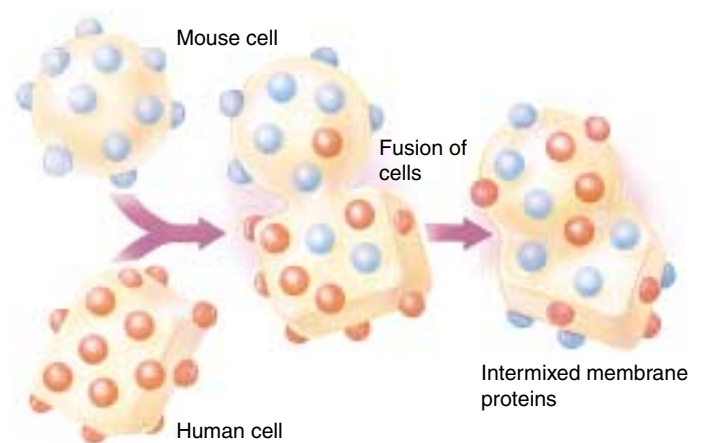


FIGURE 6.4

Proteins move about in membranes. Protein movement within membranes can be demonstrated easily by labeling the plasma membrane proteins of a mouse cell with fluorescent antibodies and then fusing that cell with a human cell. At first, all of the mouse proteins are located on the mouse side of the fused cell and all of the human proteins are located on the human side of the fused cell. However, within an hour, the labeled and unlabeled proteins are intermixed throughout the hybrid cell’s plasma membrane.

The lipid bilayer is liquid like a soap bubble, rather than solid like a rubber balloon.

6.2 Proteins embedded within the plasma membrane determine its character.

The Fluid Mosaic Model

A plasma membrane is composed of both lipids and globular proteins. For many years, biologists thought the protein covered the inner and outer surfaces of the phospholipid bilayer like a coat of paint. The widely accepted Davson-Danielli model, proposed in 1935, portrayed the membrane as a sandwich: a phospholipid bilayer between two layers of globular protein. This model, however, was not consistent with what researchers were learning in the 1960s about the structure of membrane proteins. Unlike most proteins found within cells, membrane proteins are not very soluble in water—they possess long stretches of nonpolar hydrophobic amino acids. If such proteins indeed coated the surface of the lipid bilayer, as the Davson-Danielli model suggests, then their nonpolar portions would separate the polar portions of the phospholipids from water, causing the bilayer to dissolve! Because this doesn't happen, there is clearly something wrong with the model.

In 1972, S. Singer and G. Nicolson revised the model in a simple but profound way: they proposed that the globular proteins are *inserted* into the lipid bilayer, with their nonpolar segments in contact with the nonpolar interior of the bilayer and their polar portions protruding out from the membrane surface. In this model, called the **fluid mosaic model**, a mosaic of proteins float in the fluid lipid bilayer like boats on a pond (figure 6.5).

Components of the Cell Membrane

A eukaryotic cell contains many membranes. While they are not all identical, they share the same fundamental architecture. Cell membranes are assembled from four components (table 6.1):

- 1. Lipid bilayer.** Every cell membrane is composed of a phospholipid bilayer. The other components of the membrane are enmeshed within the bilayer, which provides a flexible matrix and, at the same time, imposes a barrier to permeability.

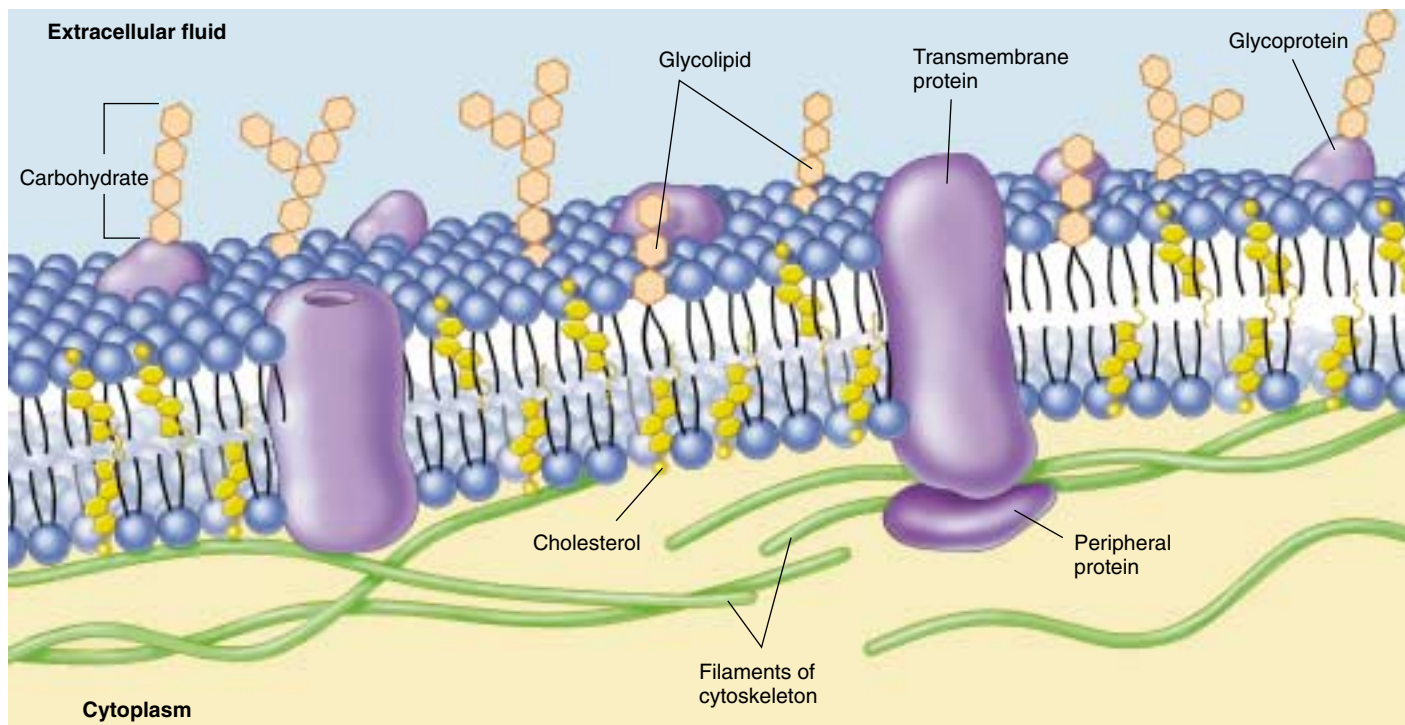


FIGURE 6.5

The fluid mosaic model of the plasma membrane. A variety of proteins protrude through the plasma membrane of animal cells, and nonpolar regions of the proteins tether them to the membrane's nonpolar interior. The three principal classes of membrane proteins are transport proteins, receptors, and cell surface markers. Carbohydrate chains are often bound to the extracellular portion of these proteins, as well as to the membrane phospholipids. These chains serve as distinctive identification tags, unique to particular cells.

Table 6.1 Components of the Cell Membrane

Component	Composition	Function	How It Works	Example
Phospholipid molecules	Phospholipid bilayer	Provides permeability barrier, matrix for proteins	Excludes water-soluble molecules from nonpolar interior of bilayer	Bilayer of cell is impermeable to water-soluble molecules, like glucose
Transmembrane proteins	Carriers	Transport molecules across membrane against gradient	“Escort” molecules through the membrane in a series of conformational changes	Glycophorin carrier for sugar transport
	Channels	Passively transport molecules across membrane	Create a tunnel that acts as a passage through membrane	Sodium and potassium channels in nerve cells
	Receptors	Transmit information into cell	Signal molecules bind to cell-surface portion of the receptor protein; this alters the portion of the receptor protein within the cell, inducing activity	Specific receptors bind peptide hormones and neurotransmitters
Interior protein network	Spectrins	Determine shape of cell	Form supporting scaffold beneath membrane, anchored to both membrane and cytoskeleton	Red blood cell
	Clathrins	Anchor certain proteins to specific sites, especially on the exterior cell membrane in receptor-mediated endocytosis	Proteins line coated pits and facilitate binding to specific molecules	Localization of low-density lipoprotein receptor within coated pits
Cell surface markers	Glycoproteins	“Self”-recognition	Create a protein/carbohydrate chain shape characteristic of individual	Major histocompatibility complex protein recognized by immune system
	Glycolipid	Tissue recognition	Create a lipid/carbohydrate chain shape characteristic of tissue	A, B, O blood group markers

2. Transmembrane proteins. A major component of every membrane is a collection of proteins that float on or in the lipid bilayer. These proteins provide passageways that allow substances and information to cross the membrane. Many membrane proteins are not fixed in position; they can move about, as the phospholipid molecules do. Some membranes are crowded with proteins, while in others, the proteins are more sparsely distributed.

3. Network of supporting fibers. Membranes are structurally supported by intracellular proteins that reinforce the membrane’s shape. For example, a red blood cell has a characteristic biconcave shape because a scaffold of proteins called spectrin links proteins in the plasma membrane with actin filaments in the cell’s cytoskeleton. Membranes use networks of other proteins to control the lateral movements of some key membrane proteins, anchoring them to specific sites.

4. Exterior proteins and glycolipids. Membrane sections assemble in the endoplasmic reticulum, transfer to the Golgi complex, and then are transported to the plasma membrane. The endoplasmic reticulum adds chains of sugar molecules to membrane proteins and lipids, creating a “sugar coating” called the glycocalyx that extends from the membrane on the outside of the cell only. Different cell types exhibit different varieties of these glycoproteins and glycolipids on their surfaces, which act as cell identity markers.

The fluid mosaic model proposes that membrane proteins are embedded within the lipid bilayer. Membranes are composed of a lipid bilayer within which proteins are anchored. Plasma membranes are supported by a network of fibers and coated on the exterior with cell identity markers.

Examining Cell Membranes

Biologists examine the delicate, filmy structure of a cell membrane using electron microscopes that provide clear magnification to several thousand times. We discussed two types of electron microscopes in chapter 5: the transmission electron microscope (TEM) and the scanning electron microscope (SEM). When examining cell membranes with electron microscopy, specimens must be prepared for viewing.

In one method of preparing a specimen, the tissue of choice is embedded in a hard matrix, usually some sort of epoxy (figure 6.6). The epoxy block is then cut with a microtome, a machine with a very sharp blade that makes incredibly thin slices. The knife moves up and down as the specimen advances toward it, causing transparent “epoxy shavings” less than 1 micrometer thick to peel away from the block of tissue. These shavings are placed on a grid and a beam of electrons is directed through the grid with the TEM. At the high magnification an electron microscope provides, resolution is good enough to reveal the double layers of a membrane.

Freeze-fracturing a specimen is another way to visualize the inside of the membrane. The tissue is embedded in a medium and quick-frozen with liquid nitrogen. The frozen tissue is then “tapped” with a knife, causing a crack between the phospholipid layers of membranes. Proteins, carbohydrates, pits, pores, channels, or any other structure affiliated with the membrane will pull apart (whole, usually) and stick with one side of the split membrane. A very thin coating of platinum is then evaporated onto the fractured surface forming a replica of “cast” of the surface. Once the topography of the membrane has been preserved in the “cast,” the actual tissue is dissolved away, and the “cast” is examined with electron microscopy, creating a strikingly different view of the membrane (see figure 5.10*b*).

Visualizing a plasma membrane requires a very powerful electron microscope. Electrons can either be passed through a sample or bounced off it.

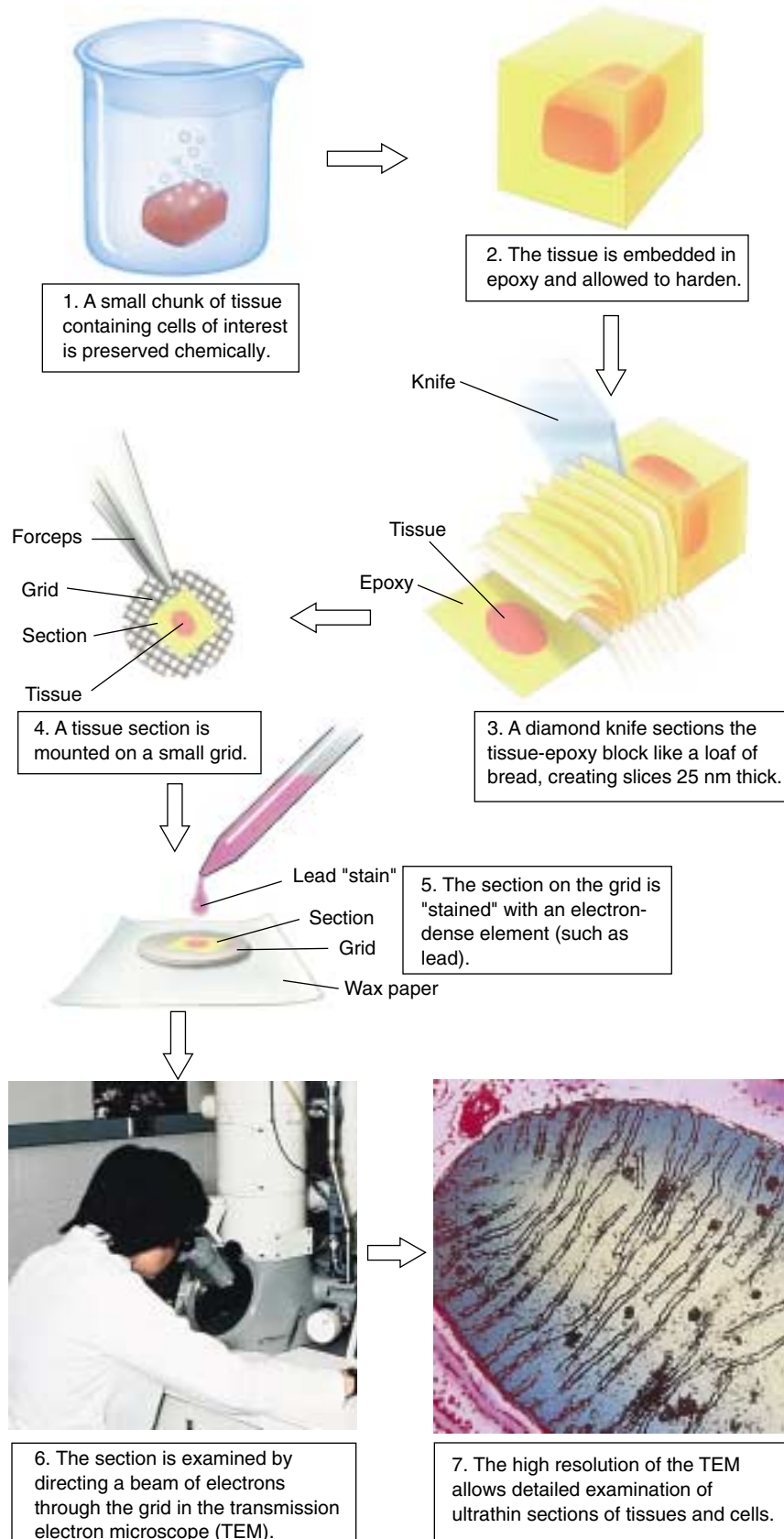


FIGURE 6.6
Thin section preparation for viewing membranes with electron microscopy.

Kinds of Membrane Proteins

As we've seen, the plasma membrane is a complex assembly of proteins enmeshed in a fluid array of phospholipid molecules. This enormously flexible design permits a broad range of interactions with the environment, some directly involving membrane proteins (figure 6.7). Though cells interact with their environment through their plasma membranes in many ways, we will focus on six key classes of membrane protein in this and the following chapter (chapter 7).

- 1. Transporters.** Membranes are very selective, allowing only certain substances to enter or leave the cell, either through channels or carriers. In some instances, they take up molecules already present in the cell in high concentration.
- 2. Enzymes.** Cells carry out many chemical reactions on the interior surface of the plasma membrane, using enzymes attached to the membrane.

- 3. Cell surface receptors.** Membranes are exquisitely sensitive to chemical messages, detecting them with receptor proteins on their surfaces that act as antennae.
- 4. Cell surface identity markers.** Membranes carry cell surface markers that identify them to other cells. Most cell types carry their own ID tags, specific combinations of cell surface proteins characteristic of that cell type.
- 5. Cell adhesion proteins.** Cells use specific proteins to glue themselves to one another. Some act like Velcro, while others form a more permanent bond.
- 6. Attachments to the cytoskeleton.** Surface proteins that interact with other cells are often anchored to the cytoskeleton by linking proteins.

The many proteins embedded within a membrane carry out a host of functions, many of which are associated with transport of materials or information across the membrane.

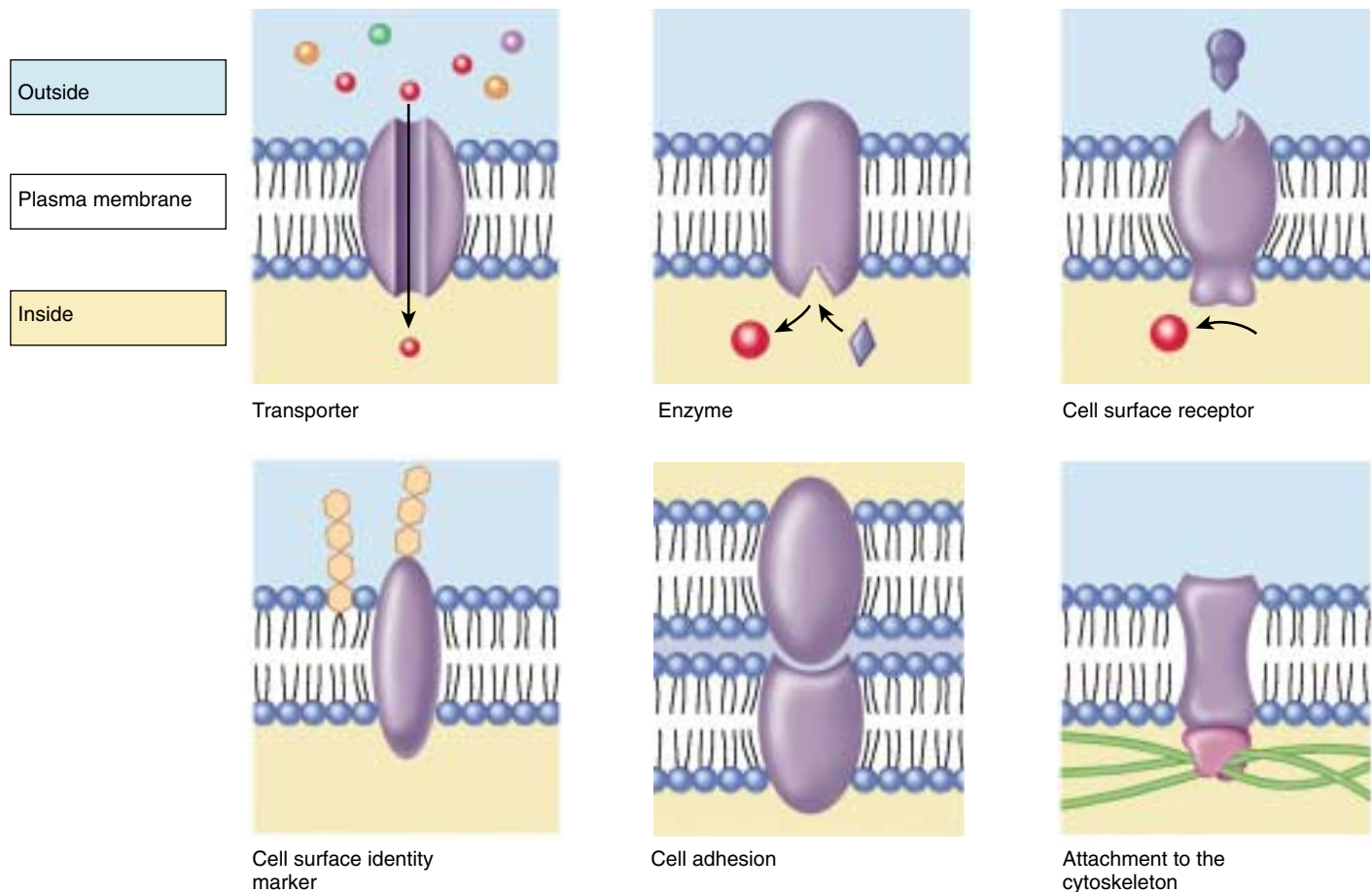


Figure 6.7

Functions of plasma membrane proteins. Membrane proteins act as transporters, enzymes, cell surface receptors, and cell surface markers, as well as aiding in cell-to-cell adhesion and securing the cytoskeleton.

Structure of Membrane Proteins

If proteins float on lipid bilayers like ships on the sea, how do they manage to extend through the membrane to create channels, and how can certain proteins be anchored into particular positions on the cell membrane?

Anchoring Proteins in the Bilayer

Many membrane proteins are attached to the surface of the membrane by special molecules that associate with phospholipids and thereby anchor the protein to the membrane. Like a ship tied up to a floating dock, these proteins are free to move about on the surface of the membrane tethered to a phospholipid.

In contrast, other proteins actually traverse the lipid bilayer. The part of the protein that extends through the lipid bilayer, in contact with the nonpolar interior, consists of one or more nonpolar helices or several β -pleated sheets of nonpolar amino acids (figure 6.8). Because water avoids nonpolar amino acids much as it does nonpolar lipid chains, the nonpolar portions of the protein are held within the interior of the lipid bilayer. Although the polar ends of the protein protrude from both sides of the membrane, the protein itself is locked into the membrane by its nonpolar segments. Any movement of the protein out of the membrane, in either direction, brings the nonpolar regions of the protein into contact with water, which “shoves” the protein back into the interior.

Extending Proteins across the Bilayer

Cells contain a variety of different **transmembrane proteins**, which differ in the way they traverse the bilayer, depending on their functions.

Anchors. A single nonpolar segment is adequate to anchor a protein in the membrane. Anchoring proteins of this sort attach the spectrin network of the cytoskeleton to the interior of the plasma membrane (figure 6.9). Many proteins that function as receptors for extracellular signals are also “single-pass” anchors that pass through the membrane only once. The portion of the receptor that extends out from the cell surface binds to specific hormones or other molecules when the cell encounters them; the binding induces changes at the other end of the protein, in the cell’s interior. In this way, information outside the cell is translated into action within the cell. The mechanisms of cell signaling will be addressed in detail in chapter 7.

Channels. Other proteins have several helical segments that thread their way back and forth through the membrane, forming a channel like the hole in a doughnut. For example, bacteriorhodopsin is one of the key transmembrane proteins that carries out photosynthesis in bacteria. It contains seven nonpolar helical segments that traverse the

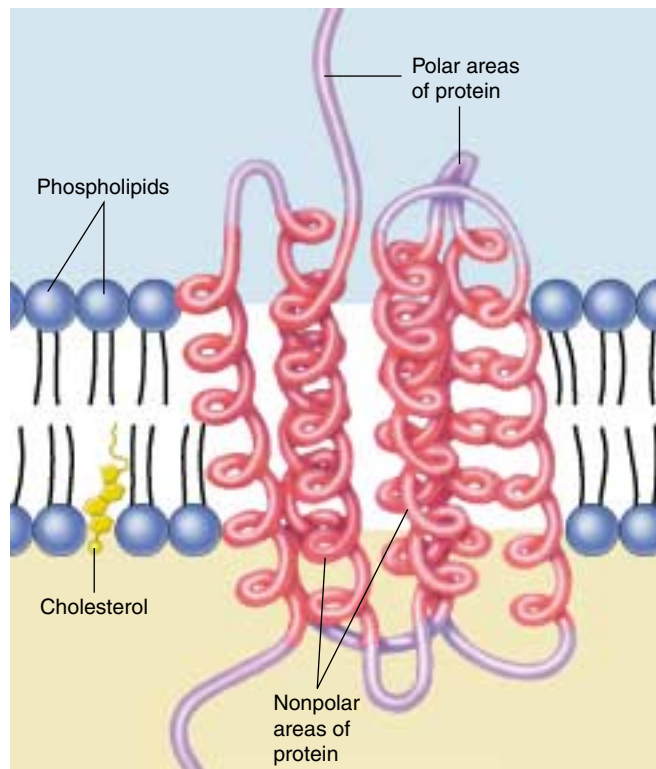


FIGURE 6.8

How nonpolar regions lock proteins into membranes. A spiral helix of nonpolar amino acids (red) extends across the nonpolar lipid interior, while polar (purple) portions of the protein protrude out from the bilayer. The protein cannot move in or out because such a movement would drag nonpolar segments of the protein into contact with water.

membrane, forming a circular pore through which protons pass during the light-driven pumping of protons (figure 6.10). Other transmembrane proteins do not create channels but rather act as carriers to transport molecules across the membrane. All water-soluble molecules or ions that enter or leave the cell are either transported by carriers or pass through channels.

Pores. Some transmembrane proteins have extensive nonpolar regions with secondary configurations of β -pleated sheets instead of α helices. The β sheets form a characteristic motif, folding back and forth in a circle so the sheets come to be arranged like the staves of a barrel. This so-called β barrel, open on both ends, is a common feature of the porin class of proteins that are found within the outer membrane of some bacteria (figure 6.11).

Transmembrane proteins are anchored into the bilayer by their nonpolar segments. While anchor proteins may pass through the bilayer only once, many channels and pores are created by proteins that pass back and forth through the bilayer repeatedly, creating a circular hole in the bilayer.

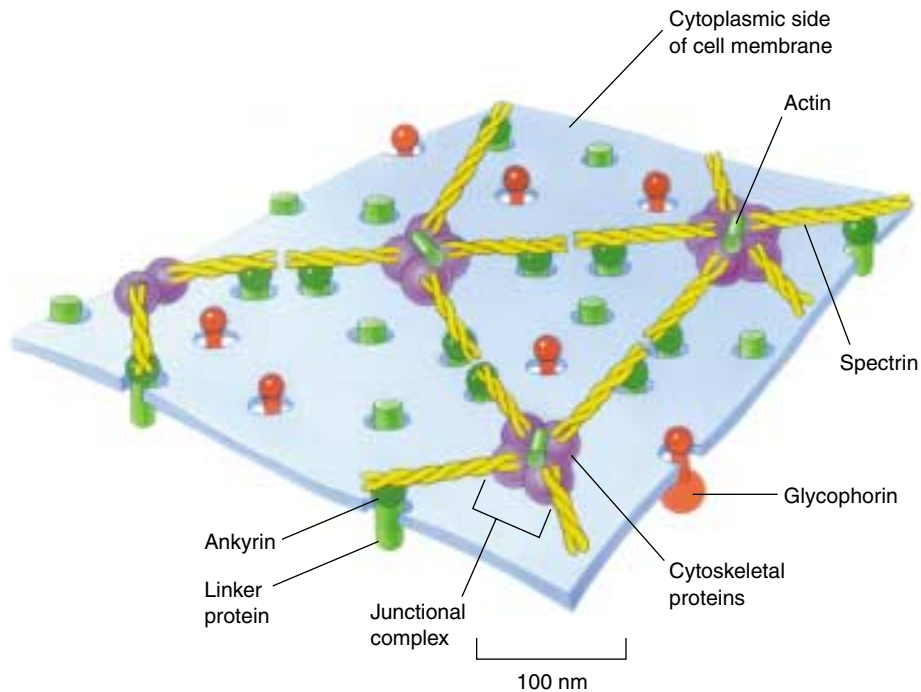


FIGURE 6.9

Anchoring proteins. Spectrin extends as a mesh anchored to the cytoplasmic side of a red blood cell plasma membrane. The spectrin protein is represented as a twisted dimer, attached to the membrane by special proteins such as junctional complexes and ankyrin; glycophorins can also be involved in attachments. This cytoskeletal protein network confers resiliency to cells like the red blood cell.

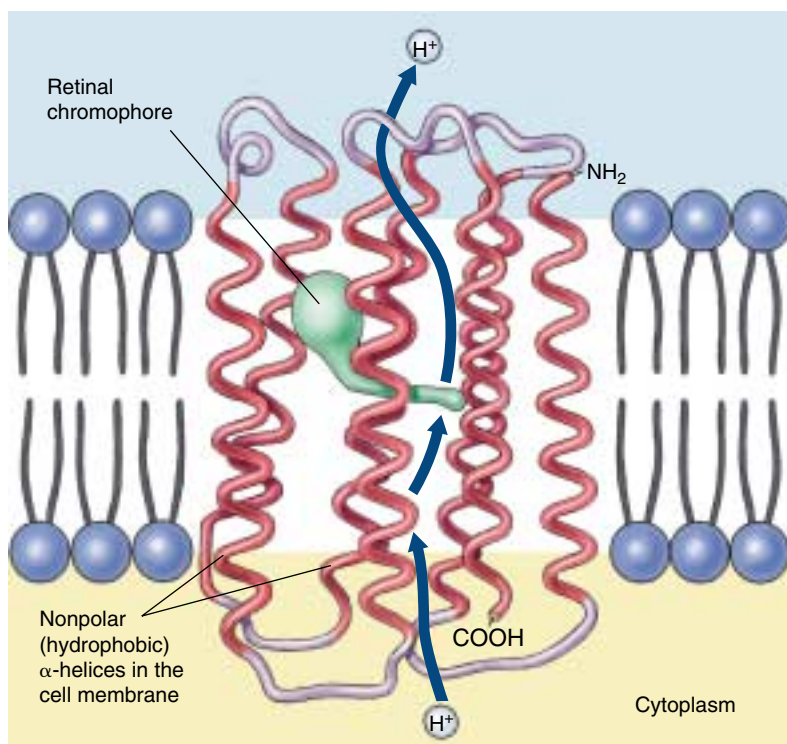


FIGURE 6.10

A channel protein. This transmembrane protein mediates photosynthesis in the bacterium *Halobacterium halobium*. The protein traverses the membrane seven times with hydrophobic helical strands that are within the hydrophobic center of the lipid bilayer. The helical regions form a channel across the bilayer through which protons are pumped by the retinal chromophore (green).

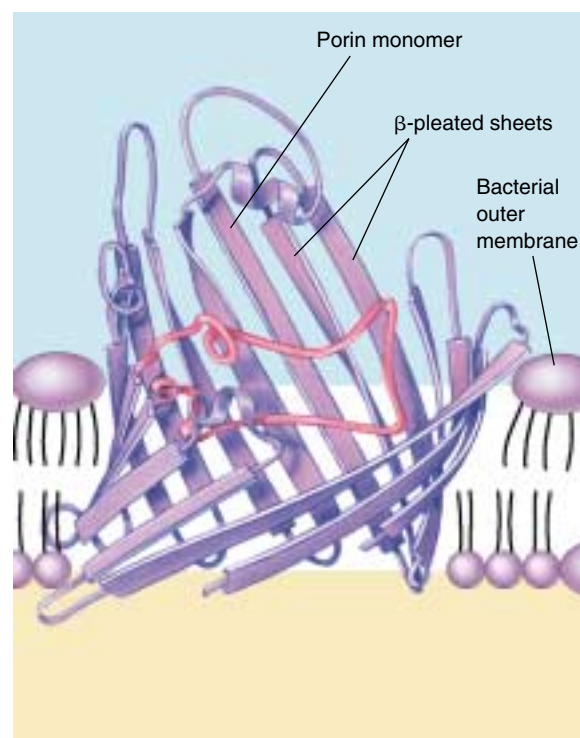


FIGURE 6.11

A pore protein. The bacterial transmembrane protein porin creates large open tunnels called pores in the outer membrane of a bacterium. Sixteen strands of β -pleated sheets run antiparallel to each other, creating a β barrel in the bacterial outer cell membrane. The tunnel allows water and other materials to pass through the membrane.

6.3 Passive transport across membranes moves down the concentration gradient.

Diffusion

Molecules and ions dissolved in water are in constant motion, moving about randomly. This random motion causes a net movement of these substances from regions where their concentration is high to regions where their concentration is lower, a process called **diffusion** (figure 6.12). Net movement driven by diffusion will continue until the concentrations in all regions are the same. You can demonstrate diffusion by filling a jar to the brim with ink, capping it, placing it at the bottom of a bucket of water, and then carefully removing the cap. The ink molecules will slowly diffuse out from the jar until there is a uniform concentration in the bucket and the jar. This uniformity in the concentration of molecules is a type of equilibrium.

Facilitated Transport

Many molecules that cells require, including glucose and other energy sources, are polar and cannot pass through the nonpolar interior of the phospholipid bilayer. These molecules enter the cell through specific channels in the plasma membrane. The inside of the channel is polar and thus “friendly” to the polar molecules, facilitating their transport across the membrane. Each type of biomolecule that is transported across the plasma membrane has its own type of transporter (that is, it has its own channel which fits it like a glove and cannot be used by other molecules). Each channel is said to be selective for that type of molecule, and thus to be **selectively permeable**, as only molecules admitted by the channels it possesses can enter it. The plasma membrane of a cell has many types of channels, each selective for a different type of molecule.

Diffusion of Ions through Channels

One of the simplest ways for a substance to diffuse across a cell membrane is through a channel, as ions do. Ions are solutes (substances dissolved in water) with an unequal number of protons and electrons. Those with an excess of protons are positively charged and called *cations*. Ions with more electrons are negatively charged and called *anions*. Because they are charged, ions interact well with polar molecules like water but are repelled by the nonpolar interior of a phospholipid bilayer. Therefore, ions cannot move between the cytoplasm of a cell and the extracellular fluid without the assistance of membrane transport proteins. **Ion channels** possess a hydrated interior that spans the membrane. Ions can diffuse through the channel in either direction without coming into contact with the hydrophobic tails of the phospholipids in the membrane, and the transported ions do not bind to or otherwise interact with the channel proteins. Two conditions determine the direction of net movement of the ions: their relative concentrations on either side of the membrane, and the voltage across the membrane (a topic we’ll explore in chapter 54). Each type of channel is specific for a particular ion, such as calcium (Ca^{++}) or chloride (Cl^-), or in some cases for a few kinds of ions. Ion channels play an essential role in signaling by the nervous system.

Diffusion is the net movement of substances to regions of lower concentration as a result of random spontaneous motion. It tends to distribute substances uniformly. Membrane transport proteins allow only certain molecules and ions to diffuse through the plasma membrane.

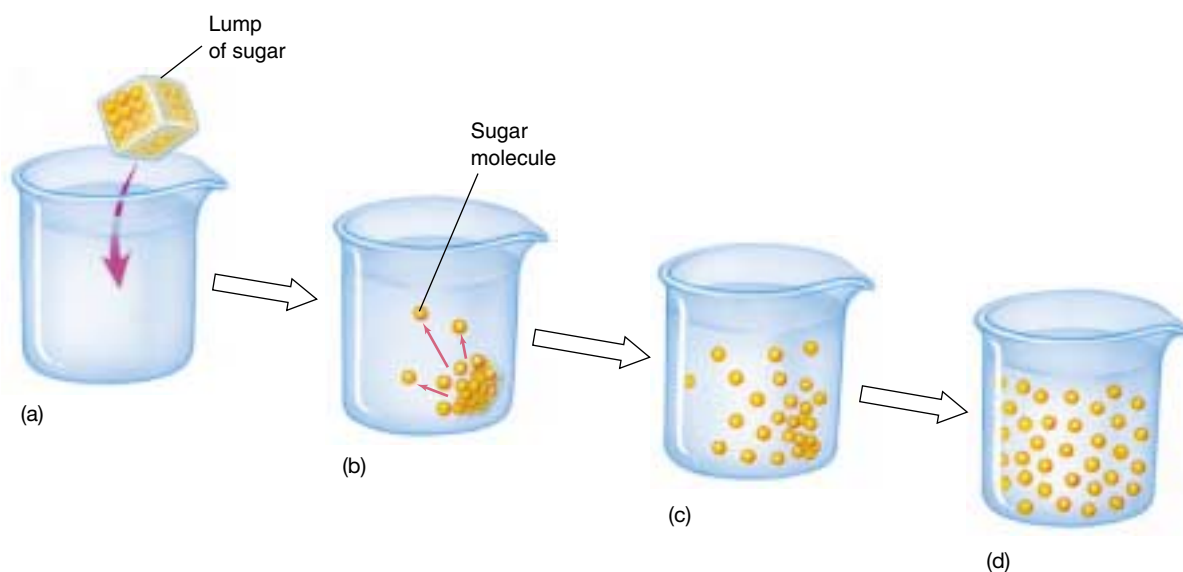


FIGURE 6.12

Diffusion. If a lump of sugar is dropped into a beaker of water (a), its molecules dissolve (b) and diffuse (c). Eventually, diffusion results in an even distribution of sugar molecules throughout the water (d).

Facilitated Diffusion

Carriers, another class of membrane proteins, transport ions as well as other solutes like sugars and amino acids across the membrane. Like channels, carriers are specific for a certain type of solute and can transport substances in either direction across the membrane. Unlike channels, however, they facilitate the movement of solutes across the membrane by physically binding to them on one side of the membrane and releasing them on the other. Again, the direction of the solute's net movement simply depends on its *concentration gradient* across the membrane. If the concentration is greater in the cytoplasm, the solute is more likely to bind to the carrier on the cytoplasmic side of the membrane and be released on the extracellular side. This will cause a net movement from inside to outside. If the concentration is greater in the extracellular fluid, the net movement will be from outside to inside. Thus, the net movement always occurs from areas of high concentration to low, just as it does in simple diffusion, but carriers facilitate the process. For this reason, this mechanism of transport is sometimes called **facilitated diffusion** (figure 6.13).

Facilitated Diffusion in Red Blood Cells

Several examples of facilitated diffusion by carrier proteins can be found in the membranes of vertebrate red blood cells (RBCs). One RBC carrier protein, for example, transports a different molecule in each direction: Cl^- in one direction and bicarbonate ion (HCO_3^-) in the opposite direction. As you will learn in chapter 52, this carrier is important in transporting carbon dioxide in the blood.

A second important facilitated diffusion carrier in RBCs is the glucose transporter. Red blood cells keep their internal concentration of glucose low through a chemical trick: they immediately add a phosphate group to any entering glucose molecule, converting it to a highly charged glucose phosphate that cannot pass back across the membrane. This maintains a steep concentration gradient for glucose, favoring its entry into the cell. The glucose transporter that carries glucose into the cell does not appear to form a channel in the membrane for the glucose to pass through. Instead, the transmembrane protein appears to bind the glucose and then flip its shape, dragging the glucose through the bilayer and releasing it on the inside of the plasma membrane. Once it releases the glucose, the glucose transporter reverts to its original shape. It is then available to bind the next glucose molecule that approaches the outside of the cell.

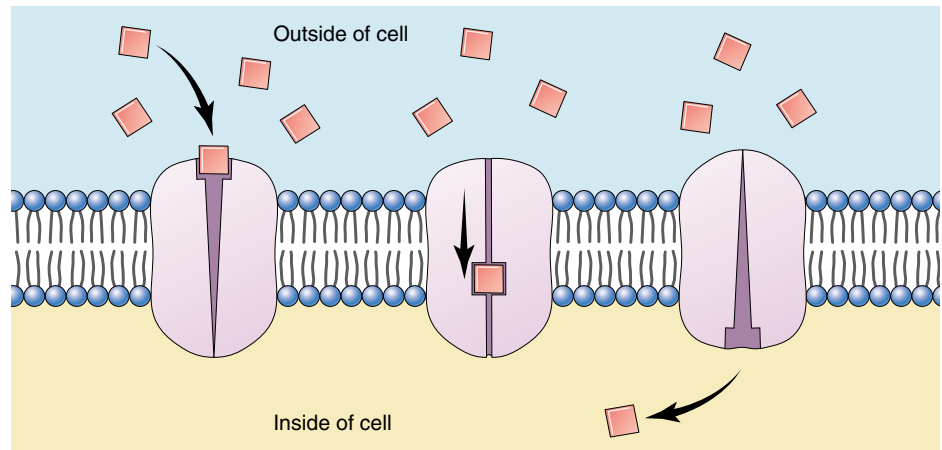


FIGURE 6.13 Facilitated diffusion is a carrier-mediated transport process. Molecules bind to a receptor on the extracellular side of the cell and are conducted through the plasma membrane by a membrane protein.

Transport through Selective Channels Saturates

A characteristic feature of transport through selective channels is that its rate is saturable. In other words, if the concentration gradient of a substance is progressively increased, its rate of transport will also increase to a certain point and then level off. Further increases in the gradient will produce no additional increase in rate. The explanation for this observation is that there are a limited number of carriers in the membrane. When the concentration of the transported substance rises high enough, all of the carriers will be in use and the capacity of the transport system will be saturated. In contrast, substances that move across the membrane by simple diffusion (diffusion through channels in the bilayer without the assistance of carriers) do not show saturation.

Facilitated diffusion provides the cell with a ready way to prevent the buildup of unwanted molecules within the cell or to take up needed molecules, such as sugars, that may be present outside the cell in high concentrations. Facilitated diffusion has three essential characteristics:

- 1. It is specific.** Any given carrier transports only certain molecules or ions.
- 2. It is passive.** The direction of net movement is determined by the relative concentrations of the transported substance inside and outside the cell.
- 3. It saturates.** If all relevant protein carriers are in use, increases in the concentration gradient do not increase the transport rate.

Facilitated diffusion is the transport of molecules and ions across a membrane by specific carriers in the direction of lower concentration of those molecules or ions.

Osmosis

The cytoplasm of a cell contains ions and molecules, such as sugars and amino acids, dissolved in water. The mixture of these substances and water is called an **aqueous solution**. Water, the most common of the molecules in the mixture, is the **solvent**, and the substances dissolved in the water are **solutes**. The ability of water and solutes to diffuse across membranes has important consequences.

Molecules Diffuse down a Concentration Gradient

Both water and solutes diffuse from regions of high concentration to regions of low concentration; that is, they diffuse down their concentration gradients. When two regions are separated by a membrane, what happens depends on whether or not the solutes can pass freely through that membrane. Most solutes, including ions and sugars, are not lipid-soluble and, therefore, are unable to cross the lipid bilayer of the membrane.

Even water molecules, which are very polar, cannot cross a lipid bilayer. Water flows through **aquaporins**, which are specialized channels for water. A simple experiment demonstrates this. If you place an amphibian egg in hypotonic spring water, it does not swell. If you then inject aquaporin mRNA into the egg, the channel proteins are expressed and the egg then swells.

Dissolved solutes interact with water molecules, which form hydration shells about the charged solute. When there is a concentration gradient of solutes, the solutes will move from a high to a low concentration, dragging with them their hydration shells of water molecules. When a membrane separates two solutions, hydration shell water molecules move with the diffusing ions, creating a net movement of water towards the low solute. This net water movement across a membrane by diffusion is called **osmosis** (figure 6.14).

The concentration of *all* solutes in a solution determines the **osmotic concentration** of the solution. If two solutions have unequal osmotic concentrations, the solution with the higher concentration is **hyperosmotic** (Greek *hyper*, “more than”), and the solution with the lower concentration is **hypoosmotic** (Greek *hypo*, “less than”). If the osmotic concentrations of two solutions are equal, the solutions are **isosmotic** (Greek *iso*, “the same”).

In cells, a plasma membrane separates two aqueous solutions, one inside the cell (the cytoplasm) and one outside

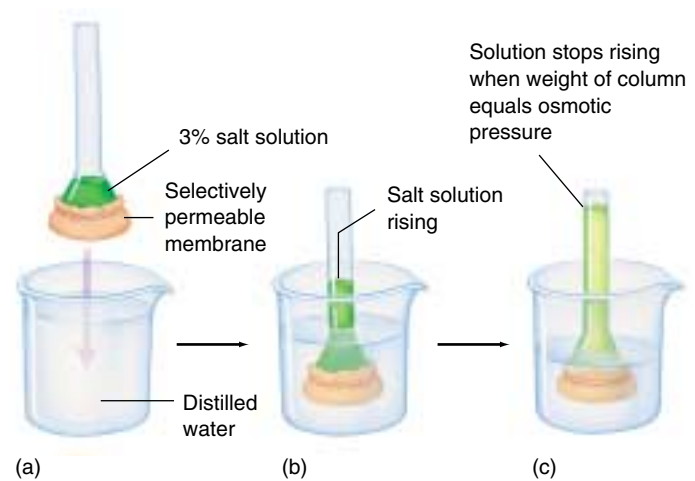


FIGURE 6.14

An experiment demonstrating osmosis. (a) The end of a tube containing a salt solution is closed by stretching a selectively permeable membrane across its face; the membrane allows the passage of water molecules but not salt ions. (b) When this tube is immersed in a beaker of distilled water, the salt cannot cross the membrane, but water can. The water entering the tube causes the salt solution to rise in the tube. (c) Water will continue to enter the tube from the beaker until the weight of the column of water in the tube exerts a downward force equal to the force drawing water molecules upward into the tube. This force is referred to as osmotic pressure.

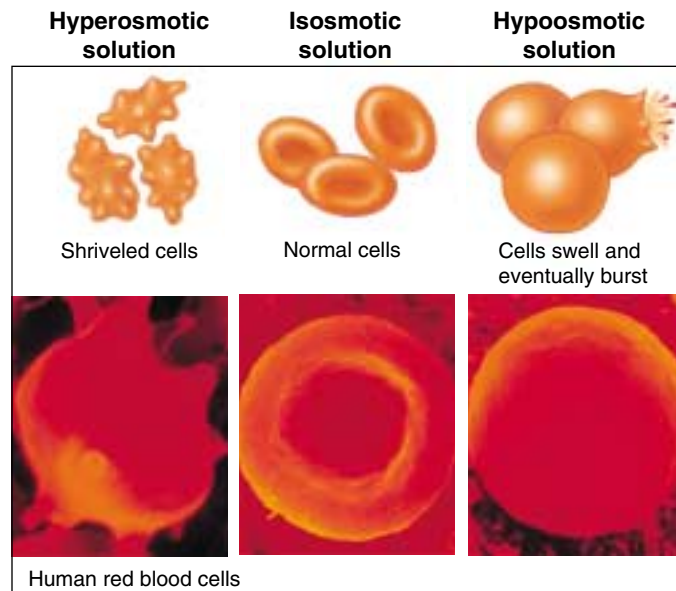


FIGURE 6.15

Osmosis. In a hyperosmotic solution water moves out of the cell toward the higher concentration of solutes, causing the cell to shrivel. In an isosmotic solution, the concentration of solutes on either side of the membrane is the same. Osmosis still occurs, but water diffuses into and out of the cell at the same rate, and the cell doesn't change size. In a hypoosmotic solution the concentration of solutes is higher within the cell than without, so the net movement of water is into the cell.

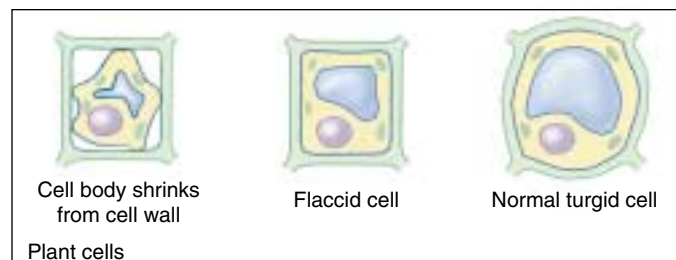
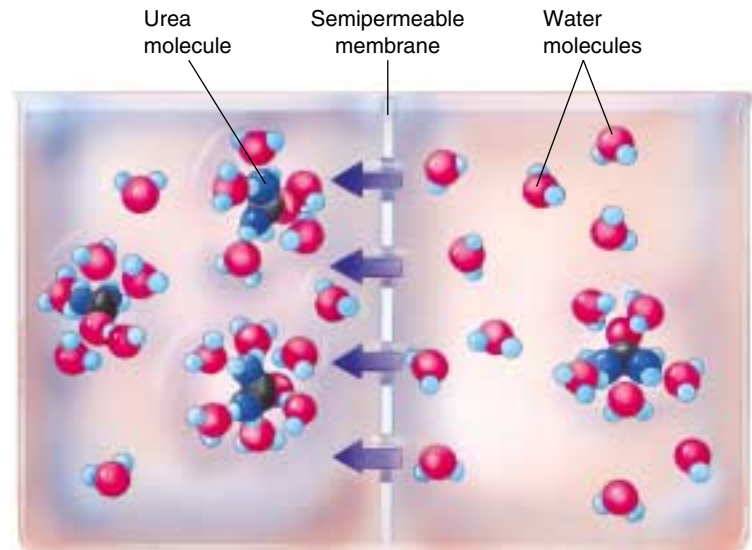


FIGURE 6.16

How solutes create osmotic pressure.

Charged or polar substances are soluble in water because they form hydrogen bonds with water molecules clustered around them. When a polar solute (illustrated here with urea) is added to the solution on one side of a membrane, the water molecules that gather around each urea molecule are no longer free to diffuse across the membrane; in effect, the polar solute has reduced the number of free water molecules on that side of the membrane increasing the osmotic pressure. Because the hypoosmotic side of the membrane (on the right, with less solute) has more unbound water molecules than the hyperosmotic side (on the left, with more solute), water moves by diffusion from the right to the left.



(the extracellular fluid). The direction of the net diffusion of water across this membrane is determined by the osmotic concentrations of the solutions on either side (figure 6.15). For example, if the cytoplasm of a cell were *hypoosmotic* to the extracellular fluid, water would diffuse out of the cell, toward the solution with the higher concentration of solutes (and, therefore, the lower concentration of unbound water molecules). This loss of water from the cytoplasm would cause the cell to shrink until the osmotic concentrations of the cytoplasm and the extracellular fluid become equal.

Osmotic Pressure

What would happen if the cell's cytoplasm were *hyperosmotic* to the extracellular fluid? In this situation, water would diffuse into the cell from the extracellular fluid, causing the cell to swell. The pressure of the cytoplasm pushing out against the cell membrane, or **hydrostatic pressure**, would increase. On the other hand, the **osmotic pressure** (figure 6.16), defined as the pressure that must be applied to stop the osmotic movement of water across a membrane, would also be at work. If the membrane were strong enough, the cell would reach an equilibrium, at which the osmotic pressure, which tends to drive water into the cell, is exactly counterbalanced by the hydrostatic pressure, which tends to drive water back out of the cell. However, a plasma membrane by itself cannot withstand large internal pressures, and an isolated cell under such conditions would burst like an overinflated balloon. Accordingly, it is important for animal cells to maintain isosmotic conditions. The cells of bacteria, fungi, plants, and many protists, in contrast, are surrounded by strong cell walls. The cells of these organisms can withstand high internal pressures without bursting.

Maintaining Osmotic Balance

Organisms have developed many solutions to the osmotic dilemma posed by being hyperosmotic to their environment.

Extrusion. Some single-celled eukaryotes like the protist *Paramecium* use organelles called contractile vacuoles to remove water. Each vacuole collects water from various parts of the cytoplasm and transports it to the central part of the vacuole, near the cell surface. The vacuole possesses a small pore that opens to the outside of the cell. By contracting rhythmically, the vacuole pumps the water out of the cell through the pore.

Isosmotic Solutions. Some organisms that live in the ocean adjust their internal concentration of solutes to match that of the surrounding seawater. Isosmotic with respect to their environment, there is no net flow of water into or out of these cells. Many terrestrial animals solve the problem in a similar way, by circulating a fluid through their bodies that bathes cells in an isosmotic solution. The blood in your body, for example, contains a high concentration of the protein albumin, which elevates the solute concentration of the blood to match your cells.

Turgor. Most plant cells are hyperosmotic to their immediate environment, containing a high concentration of solutes in their central vacuoles. The resulting internal hydrostatic pressure, known as **turgor pressure**, presses the plasma membrane firmly against the interior of the cell wall, making the cell rigid. The newer, softer portions of trees and shrubs depend on turgor pressure to maintain their shape, and wilt when they lack sufficient water.

Osmosis is the diffusion of water, but not solutes, across a membrane.

6.4 Bulk transport utilizes endocytosis.

Bulk Passage Into and Out of the Cell

Endocytosis

The lipid nature of their biological membranes raises a second problem for cells. The substances cells use as fuel are for the most part large, polar molecules that cannot cross the hydrophobic barrier a lipid bilayer creates. How do organisms get these substances into their cells? One process many single-celled eukaryotes employ is **endocytosis** (figure 6.17). In this process the plasma membrane extends outward and envelops food particles. Cells use three major types of endocytosis: phagocytosis, pinocytosis, and receptor-mediated endocytosis.

Phagocytosis and Pinocytosis. If the material the cell takes in is particulate (made up of discrete particles), such as an organism or some other fragment of organic matter (figure 6.17a), the process is called phagocytosis (Greek *phagein*, “to eat” + *cytos*, “cell”). If the material the cell takes in is liquid (figure 6.17b), it is called pinocytosis (Greek *pinein*, “to drink”). Pinocytosis is common among animal cells. Mammalian egg cells, for example, “nurse” from surrounding cells; the nearby cells secrete nutrients that the maturing egg cell takes up by pinocytosis. Virtually all eukaryotic cells constantly carry out these kinds of endocytosis, trapping particles and extracellular fluid in vesicles and ingesting them. Endocytosis rates vary from one cell type to another. They can be surprisingly high: some types of white blood cells ingest 25% of their cell volume each hour!

Receptor-Mediated Endocytosis. Specific molecules are often transported into eukaryotic cells through receptor-mediated endocytosis. Molecules to be transported first bind to specific receptors on the plasma membrane. The transport process is specific because only that molecule has a shape that fits snugly into the receptor. The plasma membrane of a particular kind of cell contains a characteristic battery of receptor types, each for a different kind of molecule.

The interior portion of the receptor molecule resembles a hook that is trapped in an indented pit coated with the protein clathrin. The pits act like molecular mousetraps, closing over to form an internal vesicle when the right molecule enters the pit (figure 6.18). The trigger that releases the trap is a receptor protein embedded in the membrane of the pit, which detects the presence of a particular target molecule and reacts by initiating endocytosis. The process is highly specific and very fast.

One type of molecule that is taken up by receptor-mediated endocytosis is called a low density lipoprotein (LDL). The LDL molecules bring cholesterol into the cell

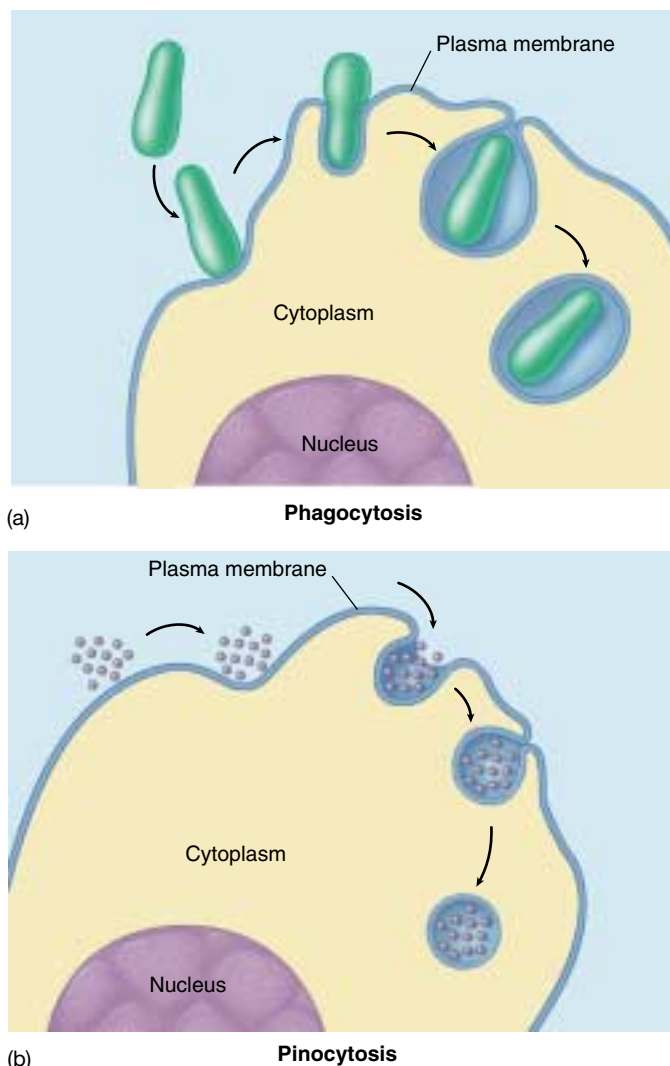


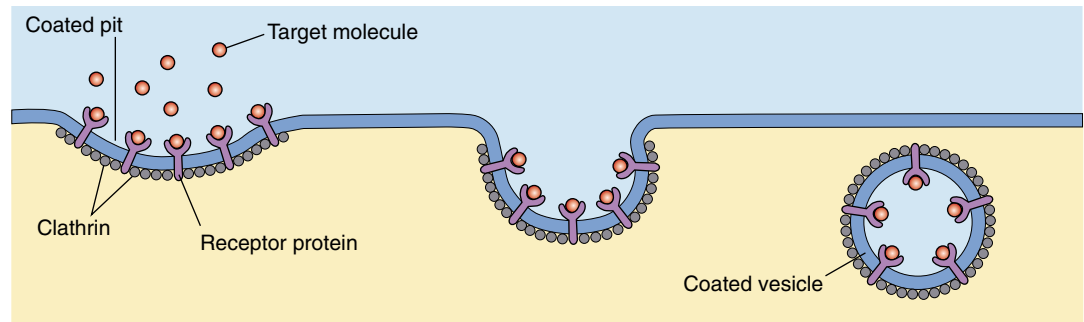
FIGURE 6.17
Endocytosis. Both phagocytosis (a) and pinocytosis (b) are forms of endocytosis.

where it can be incorporated into membranes. Cholesterol plays a key role in determining the stiffness of the body's membranes. In the human genetic disease called hypercholesterolemia, the receptors lack tails and so are never caught in the clathrin-coated pits and, thus, are never taken up by the cells. The cholesterol stays in the bloodstream of affected individuals, coating their arteries and leading to heart attacks.

Fluid-phase endocytosis is the receptor-mediated pinocytosis of fluids. It is important to understand that endocytosis in itself does not bring substances directly into the cytoplasm of a cell. The material taken in is still separated from the cytoplasm by the membrane of the vesicle.

FIGURE 6.18

Receptor-mediated endocytosis. (a) Cells that undergo receptor-mediated endocytosis have pits coated with the protein clathrin that initiate endocytosis when target molecules bind to receptor proteins in the plasma membrane. (b) A coated pit appears in the plasma membrane of a developing egg cell, covered with a layer of proteins (80,000 \times). When an appropriate collection of molecules gathers in the coated pit, the pit deepens (c) and seals off (d) to form a coated vesicle, which carries the molecules into the cell.



(a)



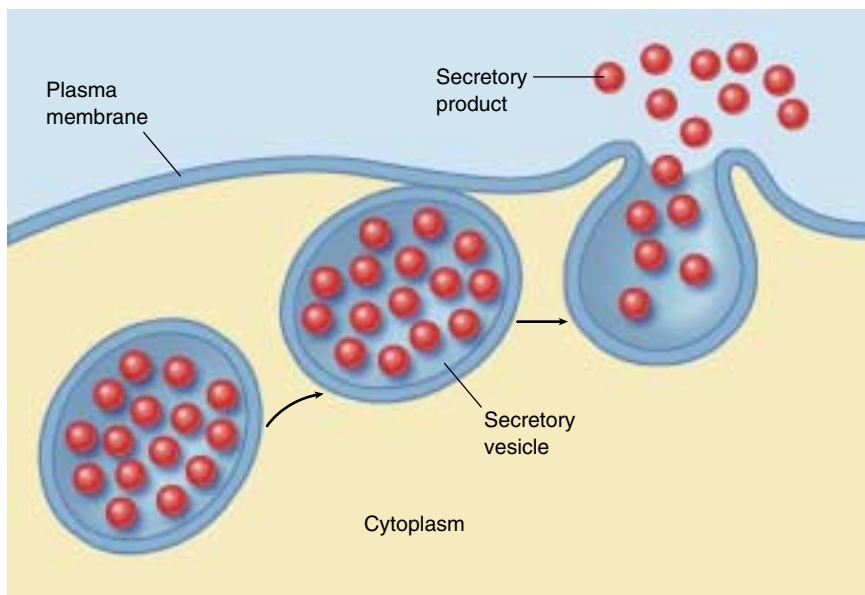
(b)



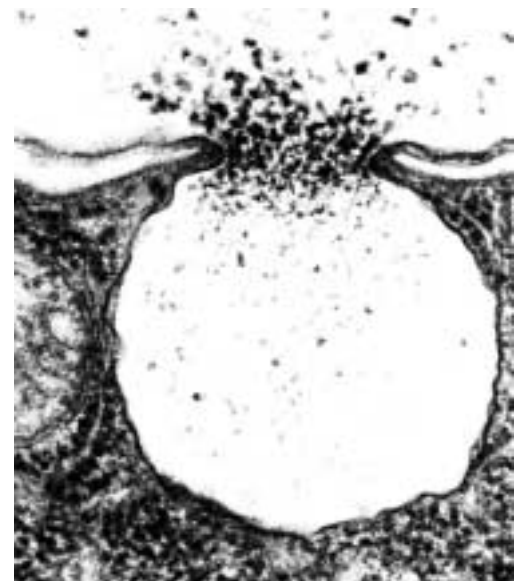
(c)



(d)



(a)



(b)

FIGURE 6.19

Exocytosis. (a) Proteins and other molecules are secreted from cells in small packets called vesicles, whose membranes fuse with the plasma membrane, releasing their contents to the cell surface. (b) A transmission electron micrograph showing exocytosis.

Exocytosis

The reverse of endocytosis is **exocytosis**, the discharge of material from vesicles at the cell surface (figure 6.19). In plant cells, exocytosis is an important means of exporting the materials needed to construct the cell wall through the plasma membrane. Among protists, contractile vacuole discharge is a form of exocytosis. In animal cells, exocytosis

provides a mechanism for secreting many hormones, neurotransmitters, digestive enzymes, and other substances.

Cells import bulk materials by engulfing them with their plasma membranes in a process called endocytosis; similarly, they extrude or secrete material through exocytosis.

6.5 Active transport across membranes is powered by energy from ATP.

Active Transport

While diffusion, facilitated diffusion, and osmosis are passive transport processes that move materials down their concentration gradients, cells can also move substances across the membrane *up* their concentration gradients. This process requires the expenditure of energy, typically ATP, and is therefore called **active transport**. Like facilitated diffusion, active transport involves highly selective protein carriers within the membrane. These carriers bind to the transported substance, which could be an ion or a simple molecule like a sugar (figure 6.20), an amino acid, or a nucleotide to be used in the synthesis of DNA.

Active transport is one of the most important functions of any cell. It enables a cell to take up additional molecules of a substance that is already present in its cytoplasm in concentrations higher than in the extracellular fluid. Without active transport, for example, liver cells would be unable to accumulate glucose molecules from the blood plasma, as the glucose concentration is often higher inside the liver cells than it is in the plasma. Active transport also enables a cell to move substances from its cytoplasm to the extracellular fluid despite higher external concentrations.

The Sodium-Potassium Pump

The use of ATP in active transport may be direct or indirect. Let's first consider how ATP is used directly to move ions against their concentration gradient. More than one-third of all of the energy expended by an animal cell that is not actively dividing is used in the active transport of sodium (Na^+) and potassium (K^+) ions. Most animal cells have a low internal concentration of Na^+ , relative to their surroundings, and a high internal concentration of K^+ . They maintain these concentration differences by actively pumping Na^+ out of the cell and K^+ in. The remarkable protein that transports these two ions across the cell membrane is known as the **sodium-potassium pump** (figure 6.21). The cell obtains the energy it needs to operate the pump from adenosine triphosphate (ATP), a molecule we'll learn more about in chapter 8.

The important characteristic of the sodium-potassium pump is that it is an *active* transport process, transporting Na^+ and K^+ from areas of low concentration to areas of high concentration. This transport up their concentration gradients is the opposite of the passive transport in diffusion; it is achieved only by the constant expenditure of metabolic energy. The sodium-potassium pump works through a series of conformational changes in the transmembrane protein:

Step 1. Three sodium ions bind to the cytoplasmic side of the protein, causing the protein to change its conformation.

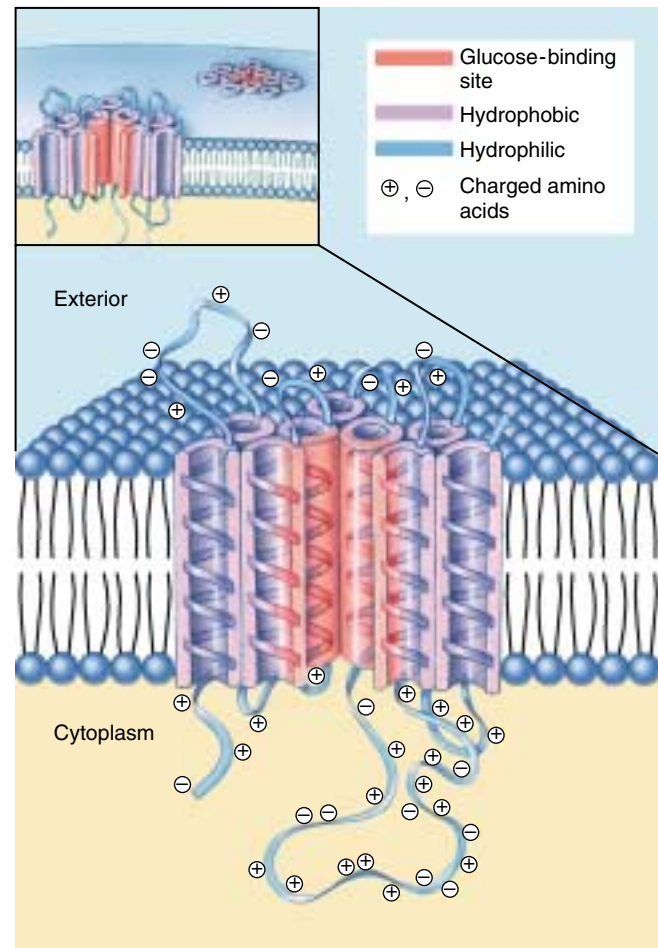


FIGURE 6.20

A glucose transport channel. The molecular structure of this particular glucose transport channel is known in considerable detail. The protein's 492 amino acids form a folded chain that traverses the lipid membrane 12 times. Amino acids with charged groups are less stable in the hydrophobic region of the lipid bilayer and are thus exposed to the cytoplasm or the extracellular fluid. Researchers think the center of the protein consists of five helical segments with glucose-binding sites (in red) facing inward. A conformational change in the protein transports glucose across the membrane by shifting the position of the glucose-binding sites.

Step 2. In its new conformation, the protein binds a molecule of ATP and cleaves it into adenosine diphosphate and phosphate ($\text{ADP} + \text{P}_i$). ADP is released, but the phosphate group remains bound to the protein. The protein is now phosphorylated.

Step 3. The phosphorylation of the protein induces a second conformational change in the protein. This change translocates the three Na^+ across the membrane,

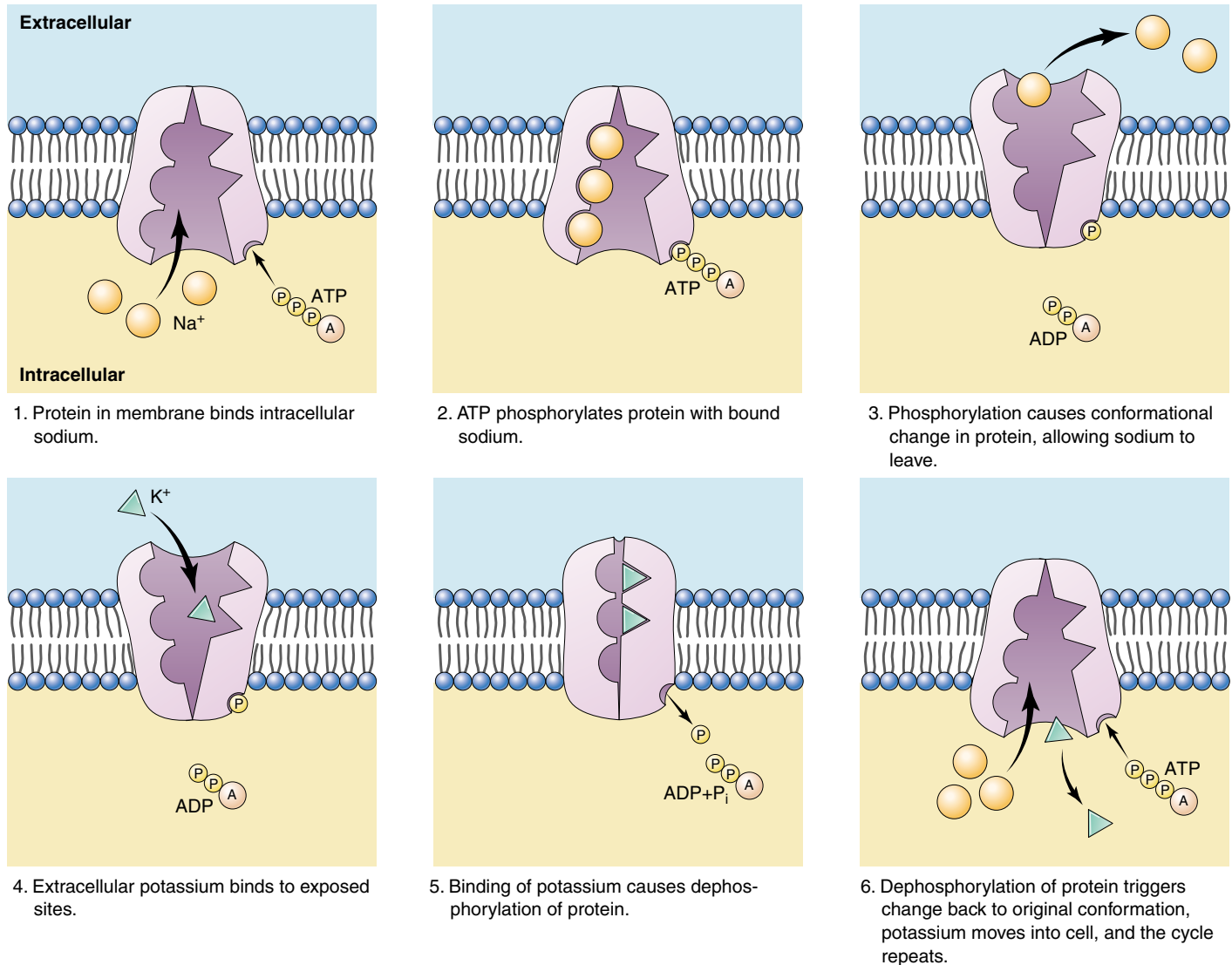


FIGURE 6.21

The sodium-potassium pump. The protein channel known as the sodium-potassium pump transports sodium (Na^+) and potassium (K^+) ions across the cell membrane. For every three Na^+ that are transported out of the cell, two K^+ are transported into the cell. The sodium-potassium pump is fueled by ATP.

so they now face the exterior. In this new conformation, the protein has a low affinity for Na^+ , and the three bound Na^+ dissociate from the protein and diffuse into the extracellular fluid.

Step 4. The new conformation has a high affinity for K^+ , two of which bind to the extracellular side of the protein as soon as it is free of the Na^+ .

Step 5. The binding of the K^+ causes another conformational change in the protein, this time resulting in the dissociation of the bound phosphate group.

Step 6. Freed of the phosphate group, the protein reverts to its original conformation, exposing the two K^+ to the cytoplasm. This conformation has a low affinity for K^+ , so the two bound K^+ dissociate from the protein

and diffuse into the interior of the cell. The original conformation has a high affinity for Na^+ ; when these ions bind, they initiate another cycle.

Three Na^+ leave the cell and two K^+ enter in every cycle. The changes in protein conformation that occur during the cycle are rapid, enabling each carrier to transport as many as 300 Na^+ per second. The sodium-potassium pump appears to be ubiquitous in animal cells, although cells vary widely in the number of pump proteins they contain.

Active transport moves a solute across a membrane up its concentration gradient, using protein carriers driven by the expenditure of chemical energy.

Coupled Transport

Many molecules are transported into cells up a concentration gradient through a process that uses ATP indirectly. The molecules move hand-in-hand with sodium ions or protons that are moving *down* their concentration gradients. This type of active transport, called **cotransport**, has two components:

1. **Establishing the down gradient.** ATP is used to establish the sodium ion or proton *down* gradient, which is greater than the *up* gradient of the molecule to be transported.
2. **Traversing the up gradient.** Cotransport proteins (also called coupled transport proteins) carry the molecule and either a sodium ion or a proton together across the membrane.

Because the *down* gradient of the sodium ion or proton is greater than the *up* gradient of the molecule to be transported, the net movement across the membrane is in the direction of the down gradient, typically into the cell.

Establishing the *Down* Gradient

Either the sodium-potassium pump or the proton pump establishes the down gradient that powers most active transport processes of the cell.

The Sodium-Potassium Pump. The sodium-potassium pump actively pumps sodium ions out of the cell, powered by energy from ATP. This establishes a sodium ion concentration gradient that is lower inside the cell.

The Proton Pump. The **proton pump** pumps protons (H^+ ions) across a membrane using energy derived from energy-rich molecules or from photosynthesis. This creates a proton gradient, in which the concentration of protons is higher on one side of the membrane than the other. Membranes are impermeable to protons, so the only way protons can diffuse back down their concentration gradient is through a second cotransport protein.

Traversing the *Up* Gradient

Animal cells accumulate many amino acids and sugars against a concentration gradient: the molecules are transported into the cell from the extracellular fluid, even though their concentrations are higher inside the cell. These molecules couple with sodium ions to enter the cell down the Na^+ concentration gradient established by the sodium-potassium pump. In this **cotransport process**, Na^+ and a specific sugar or amino acid simultaneously bind to the same transmembrane protein on the outside of the cell, called a **symport** (figure 6.22). Both are then translocated to the inside of the cell, but in the process Na^+ moves *down* its concentration gradient while the sugar or amino acid moves *up* its concentration gradient. In effect, the cell uses some of the energy stored in the Na^+ concentration gradient to accumulate sugars and amino acids.

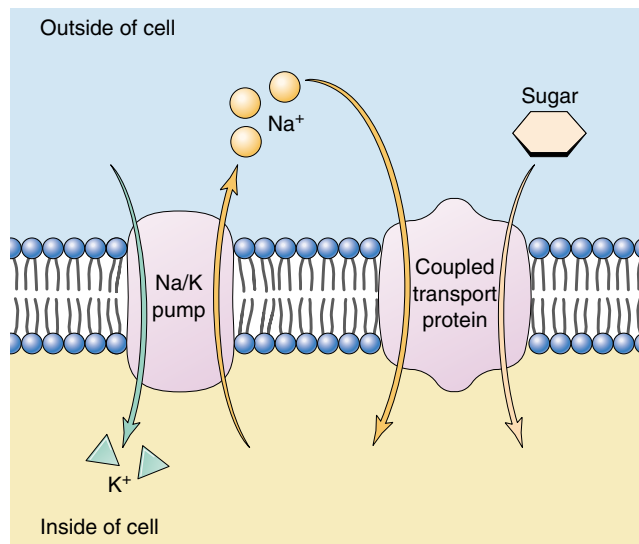


FIGURE 6.22

Cotransport through a coupled transport protein. A membrane protein transports sodium ions into the cell, down their concentration gradient, at the same time it transports a sugar molecule into the cell. The gradient driving the Na^+ entry is so great that sugar molecules can be brought in *against* their concentration gradient.

In a related process, called **countertransport**, the inward movement of Na^+ is coupled with the outward movement of another substance, such as Ca^{++} or H^+ . As in cotransport, both Na^+ and the other substance bind to the same transport protein, in this case called an **antiport**, but in this case they bind on opposite sides of the membrane and are moved in opposite directions. In countertransport, the cell uses the energy released as Na^+ moves down its concentration gradient into the cell to extrude a substance up its concentration gradient.

The cell uses the proton *down* gradient established by the proton pump (figure 6.23) in ATP production. The movement of protons through their cotransport protein is coupled to the production of ATP, the energy-storing molecule we mentioned earlier. Thus, the cell expends energy to produce ATP, which provides it with a convenient energy storage form that it can employ in its many activities. The coupling of the proton pump to ATP synthesis, called **chemiosmosis**, is responsible for almost all of the ATP produced from food (see chapter 9) and all of the ATP produced by photosynthesis (see chapter 10). We know that proton pump proteins are ancient because they are present in bacteria as well as in eukaryotes. The mechanisms for transport across plasma membranes are summarized in table 6.2.

Many molecules are cotransported into cells up their concentration gradients by coupling their movement to that of sodium ions or protons moving down their concentration gradients.

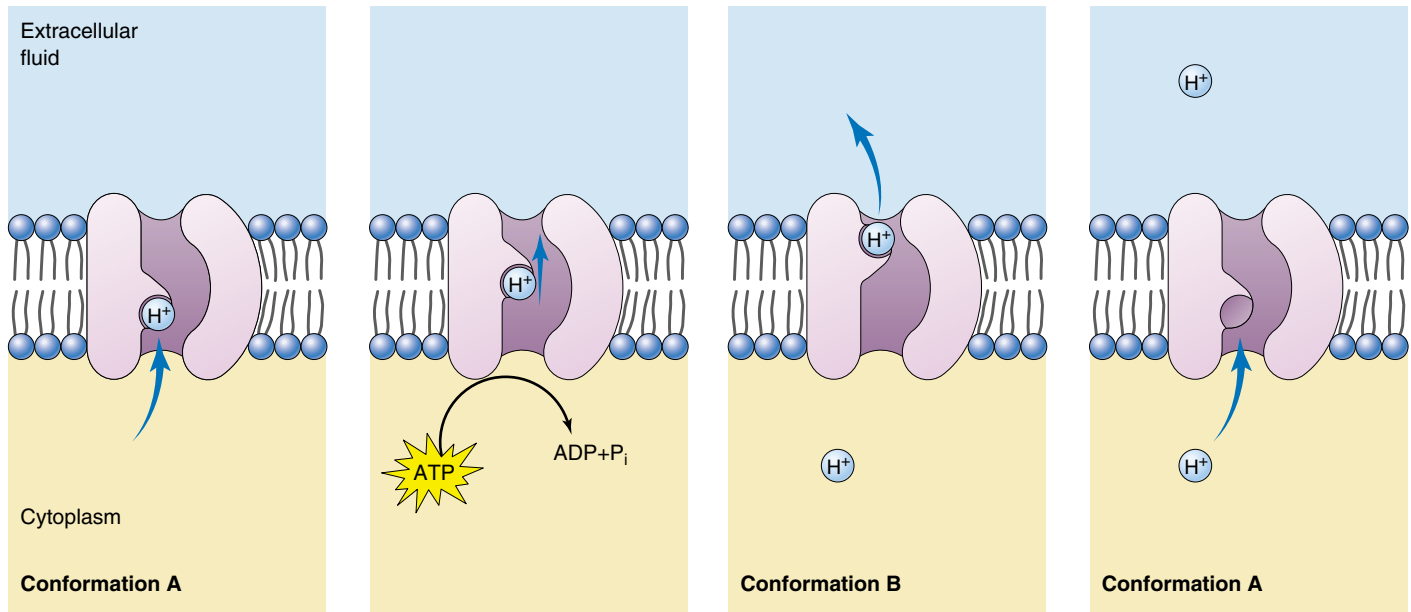


FIGURE 6.23

The proton pump. In this general model of energy-driven proton pumping, the transmembrane protein that acts as a proton pump is driven through a cycle of two conformations: A and B. The cycle A→B→A goes only one way, causing protons to be pumped from the inside to the outside of the membrane. ATP powers the pump.

Table 6.2 Mechanisms for Transport across Cell Membranes

Process	Passage through Membrane	How It Works	Example
PASSIVE PROCESSES			
Diffusion	Direct	Random molecular motion produces net migration of molecules toward region of lower concentration	Movement of oxygen into cells
Facilitated diffusion	Protein carrier	Molecule binds to carrier protein in membrane and is transported across; net movement is toward region of lower concentration	Movement of glucose into cells
Osmosis	Direct	Diffusion of water across differentially permeable membrane	Movement of water into cells placed in a hypotonic solution
ACTIVE PROCESSES			
Endocytosis			
Phagocytosis	Membrane vesicle	Particle is engulfed by membrane, which folds around it and forms a vesicle	Ingestion of bacteria by white blood cells
Pinocytosis	Membrane vesicle	Fluid droplets are engulfed by membrane, which forms vesicles around them	“Nursing” of human egg cells
Carrier-mediated endocytosis	Membrane vesicle	Endocytosis triggered by a specific receptor	Cholesterol uptake
Exocytosis			
	Membrane vesicle	Vesicles fuse with plasma membrane and eject contents	Secretion of mucus
Active transport			
Na ⁺ /K ⁺ pump	Protein carrier	Carrier expends energy to export Na ⁺ against a concentration gradient	Coupled uptake of glucose into cells against its concentration gradient
Proton pump	Protein carrier	Carrier expends energy to export protons against a concentration gradient	Chemiosmotic generation of ATP



Summary

Questions

Media Resources

6.1 Biological membranes are fluid layers of lipid.

- Every cell is encased within a fluid bilayer sheet of phospholipid molecules called the plasma membrane.

1. How would increasing the number of phospholipids with double bonds between carbon atoms in their tails affect the fluidity of a membrane?



- Membrane Structure

6.2 Proteins embedded within the plasma membrane determine its character.

- Proteins that are embedded within the plasma membrane have their hydrophobic regions exposed to the hydrophobic interior of the bilayer, and their hydrophilic regions exposed to the cytoplasm or the extracellular fluid.
- Membrane proteins can transport materials into or out of the cell, they can mark the identity of the cell, or they can receive extracellular information.

2. Describe the two basic types of structures that are characteristic of proteins that span membranes.



- Art Activity: Fluid Mosaic Model
- Art Activity: Membrane Protein Diversity

6.3 Passive transport across membranes moves down the concentration gradient.

- Diffusion is the kinetic movement of molecules or ions from an area of high concentration to an area of low concentration.
- Osmosis is the diffusion of water. Because all organisms are composed of mostly water, maintaining osmotic balance is essential to life.

3. If a cell's cytoplasm were hyperosmotic to the extracellular fluid, how would the concentration of solutes in the cytoplasm compare with that in the extracellular fluid?



- Diffusion
- Osmosis



- Diffusion
- Diffusion
- Osmosis



- Student Research: Understanding Membrane Transport

6.4 Bulk transport utilizes endocytosis.

- Materials or volumes of fluid that are too large to pass directly through the cell membrane can move into or out of cells through endocytosis or exocytosis, respectively.
- In these processes, the cell expends energy to change the shape of its plasma membrane, allowing the cell to engulf materials into a temporary vesicle (endocytosis), or eject materials by fusing a filled vesicle with the plasma membrane (exocytosis).

4. How do phagocytosis and pinocytosis differ?
5. Describe the mechanism of receptor-mediated endocytosis.



- Exocytosis/endocytosis



- Exocytosis/endocytosis

6.5 Active transport across membranes is powered by energy from ATP.

- Cells use active transport to move substances across the plasma membrane against their concentration gradients, either accumulating them within the cell or extruding them from the cell. Active transport requires energy from ATP, either directly or indirectly.

6. In what two ways does facilitated diffusion differ from simple diffusion across a membrane?

7. How does active transport differ from facilitated diffusion? How is it similar to facilitated diffusion?



- Exploration: Active Transport



- Active Transport



- Active Transport