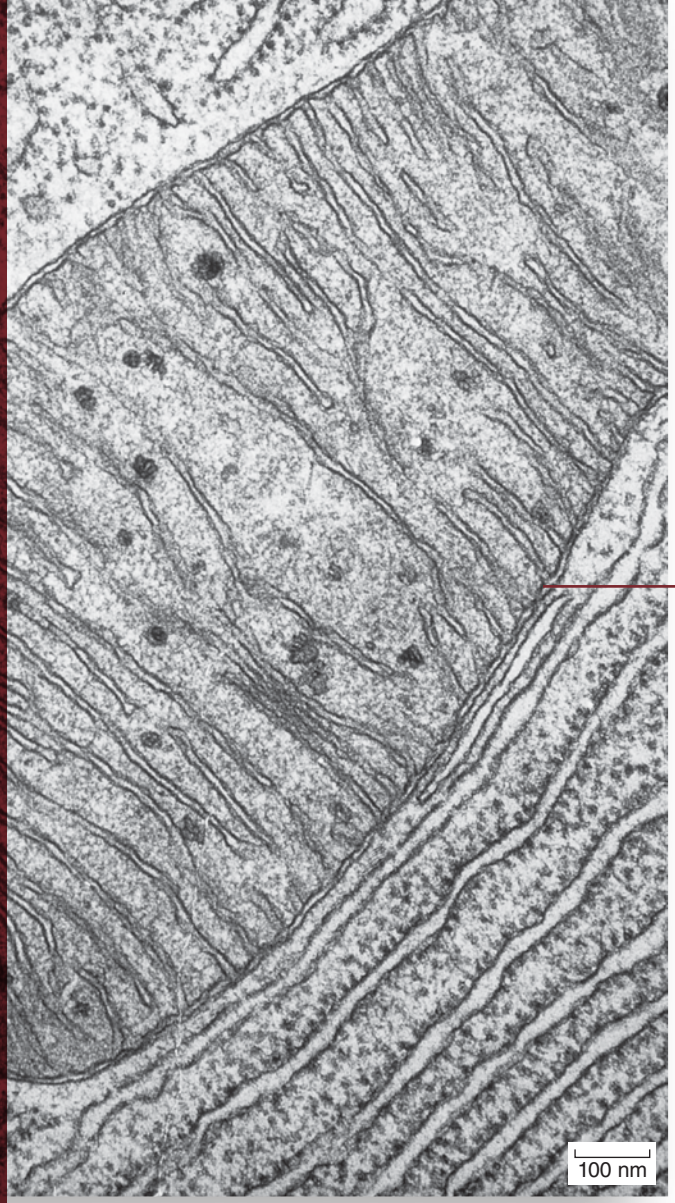
CHAPTER 5

AP BIG IDEAS



Chapter 5

Membranes

Chapter Contents

Introduction

Borders and highways . . . that's one way to think about membranes. Inside and outside cells, they provide protection, pathways, compartmentalization, and points of entry. One Big Idea 2 Enduring Understanding proclaims, "cells create and maintain internal environments that are different from their external environments." When membranes malfunction, as in cystic fibrosis and Duchene muscular dystrophy, the entire organism suffers in numerous ways. So much more than a wrapper around the organelle-strewn cytoplasm, the plasma membrane of a cell with its guarded gates and channels keeps what should be inside in, what should be outside out, and ensures that all is right in the cell.

5.1 The Structure of Membranes

Learning Outcomes

1. *Describe the components of biological membranes.*
2. *Explain the fluid mosaic model of membrane structure.*

The membranes that encase all living cells are two phospholipid sheets that are only 5–10 nm thick; more than 10,000 of these sheets piled on one another would just equal the thickness of this sheet of paper. Biologists established the components of membranes—not only lipids, but also proteins and other molecules—through biochemical assays, but the organization of the membrane components remained elusive.

We begin by considering the theories that have been advanced about membrane structure. We then look at the individual components of membranes more closely.

The fluid mosaic model shows proteins embedded in a fluid lipid bilayer

The lipid layer that forms the foundation of a cell's membranes is a bilayer formed of **phospholipids.** These phospholipids include primarily the glycerol phospholipids (figure 5.1), and the sphingolipids such as sphingomyelin (figure 5.2). Note that although these look superficially similar, they are built on a different carbon skeleton. For many years, biologists thought that the protein components of the cell membrane covered the inner and outer surfaces of the phospholipid bilayer like a coat of paint. An early model portrayed the membrane as a sandwich; a phospholipid bilayer between two layers of globular protein.

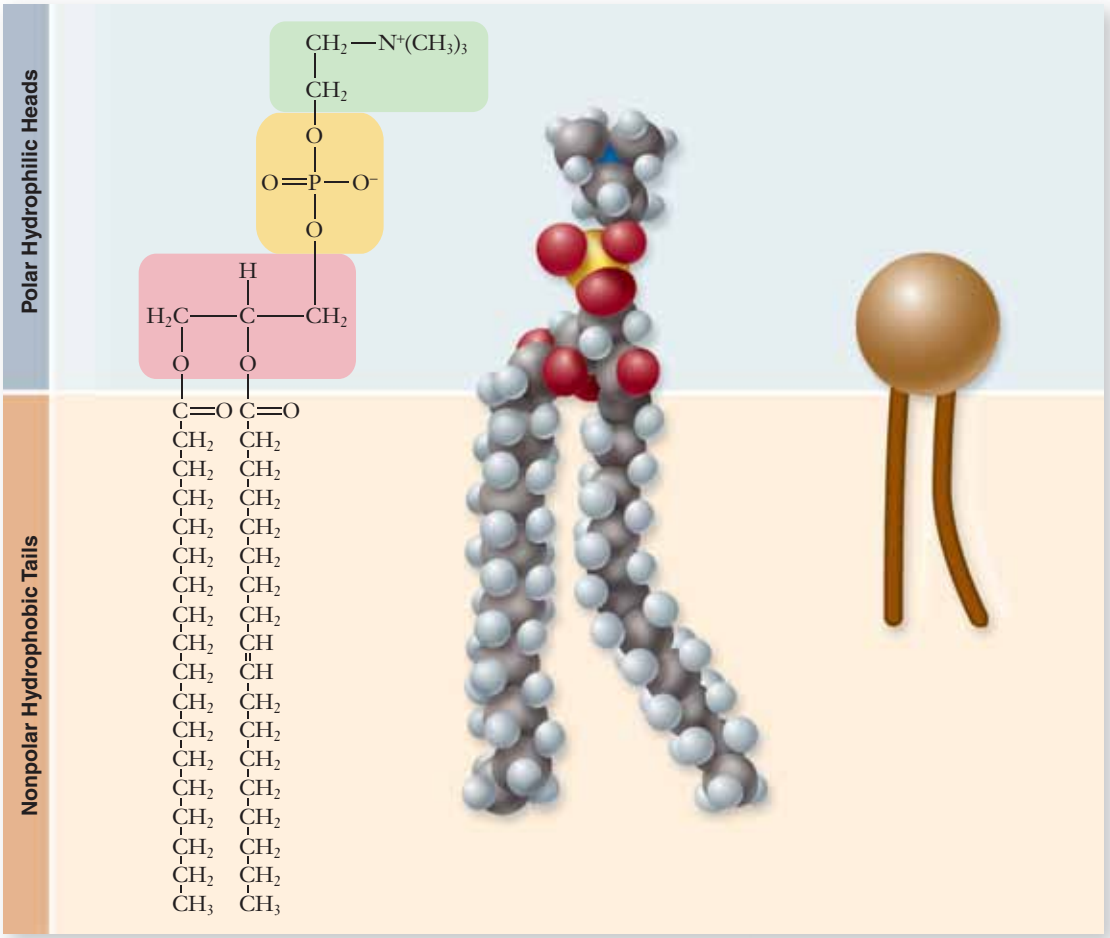
In 1972, S. Jonathan Singer and Garth J. Nicolson revised the model in a simple but profound way: They proposed that the globular proteins are *inserted* into the lipid bilayer, with their nonpolar segments in contact with the nonpolar interior of the bilayer and their polar portions protruding out from the membrane surface. In this model, called the *fluid mosaic model,* a mosaic of proteins floats in or on the fluid lipid bilayer like boats on a pond (figure 5.3).

We now recognize two categories of membrane proteins based on their association with the membrane. *Integral membrane proteins* are embedded in the membrane, and *peripheral proteins* are associated with the surface of the membrane.

Cellular membranes consist of four component groups

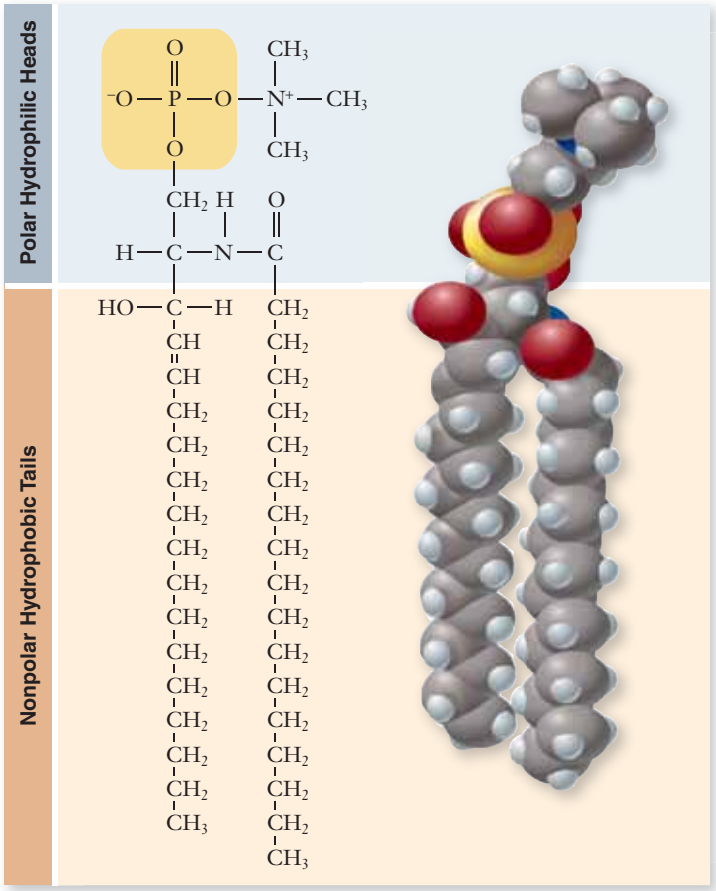
A eukaryotic cell contains many membranes. Although they are not all identical, they share the same fundamental architecture. Cell membranes are assembled from four components (table 5.1):

1. **Phospholipid bilayer.** Every cell membrane is composed of phospholipids in a bilayer. The other components of the membrane are embedded within the bilayer, which provides a flexible matrix and, at the same time, imposes a barrier to permeability. Animal cell membranes also contain cholesterol, a steroid with a polar hydroxyl group (—OH). Plant cells have other sterols, but little or no cholesterol.
2. **Transmembrane proteins.** A major component of every membrane is a collection of proteins that float in the lipid bilayer. These proteins have a variety of functions, including transport and communication across the membrane. Many integral membrane proteins are not fixed in position. They can move about, just as the phospholipid molecules do. Some membranes are crowded with proteins, but in others, the proteins are more sparsely distributed.
3. **Interior protein network.** 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 made



a. Formula ***b.*** Space-filling model ***c.*** Icon

Figure 5.1 Different views of phospholipid structure. Phospholipids are composed of glycerol *(pink)* linked to two fatty acids and a phosphate group. The phosphate group *(yellow)* can have additional molecules attached, such as the positively charged choline *(green)* shown. Phosphatidylcholine is a common component of membranes. It is shown in ***(a)*** with its chemical formula, ***(b)*** as a space-filling model, and ***(c)*** as the icon that is used in most of the figures in this chapter.



a. Formula *b.* Space-filling model

Figure 5.2 Sphingomyelin. Sphingomyelin is a sphingolipid found in animal cells. ***a.*** Formula. ***b.*** Space-filling model.

of a protein 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. **Cell-surface markers.** As you learned in the preceding chapter, membrane sections assemble in the endoplasmic reticulum, transfer to the Golgi apparatus, and then are transported to the plasma membrane. The ER adds chains of sugar molecules to membrane proteins and lipids, converting them into **glycoproteins** and **glycolipids.** Different cell types exhibit different varieties of these glycoproteins and glycolipids on their surfaces, which act as cell identity markers.

Cellular membranes have an organized substructure

Originally, it was believed that because of its fluidity, the plasma membrane was uniform, with lipids and proteins free to diffuse rapidly in the plane of the membrane. However, in the last decade evidence has accumulated suggesting the plasma membrane is not homogeneous and contains microdomains with distinct lipid and protein composition. This was first observed in epithelial cells in which the lipid composition of the apical and basal membranes was shown to be distinctly different. Theoretical work also showed that lipids can exist in either a disordered or an ordered phase within a bilayer.

This led to the idea of lipid microdomains called *lipid rafts* that are heavily enriched in cholesterol and sphingolipids. These lipids appear to interact with each other, and with raft-associated proteins—together forming an ordered structure. This is now technically defined as "dynamic nanometer-sized, sterol and sphingolipid-enriched protein assemblies." There is evidence that signaling molecules, such as the B- and T-cell receptors discussed in chapter 51, associate with lipid rafts and that this association affects their function.

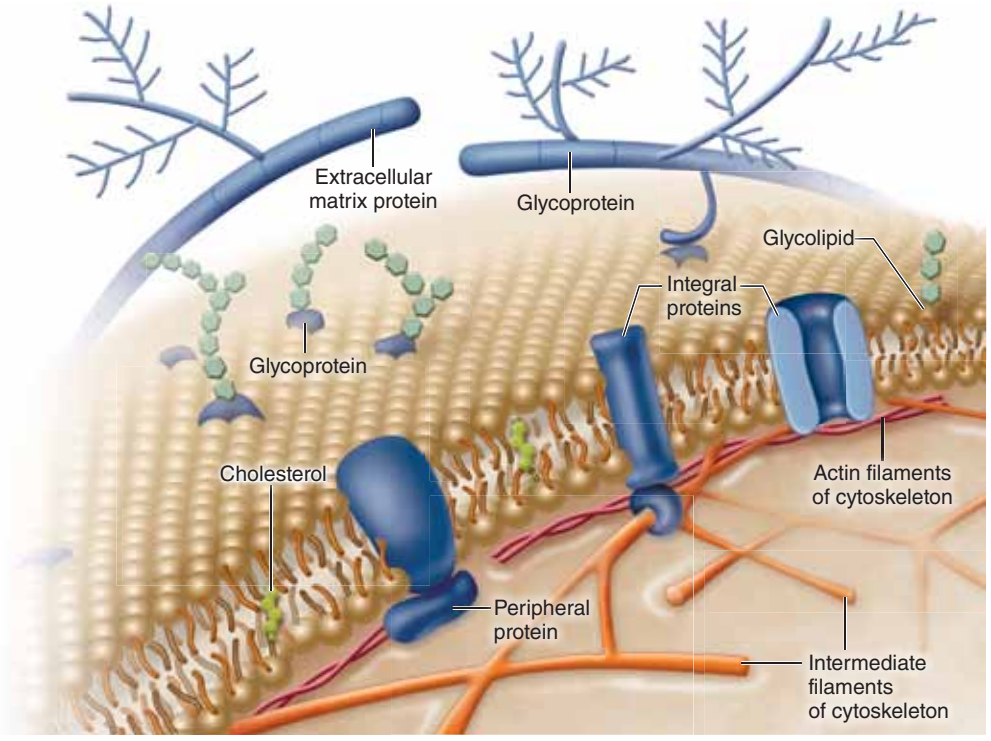


Figure 5.3 The fluid mosaic model of cell membranes. Integral proteins protrude through the plasma membrane, with nonpolar regions that tether them to the membrane's hydrophobic interior. Carbohydrate chains are often bound to the extracellular portion of these proteins, forming glycoproteins. Peripheral membrane proteins are associated with the surface of the membrane. Membrane phospholipids can be modified by the addition of carbohydrates to form glycolipids. Inside the cell, actin filaments and intermediate filaments interact with membrane proteins. Outside the cell, many animal cells have an elaborate extracellular matrix composed primarily of glycoproteins.

TABLE 5.1 Components of the Cell Membrane

Component	Composition	Function	How It Works	Example
Phospholipid bilayer	Phospholipid molecules	Provides permeability barrier, matrix for proteins	Excludes water-soluble molecules from nonpolar interior of bilayer and cell	Bilayer of cell is impermeable to large water-soluble molecules, such as glucose
Transmembrane proteins	Carriers	Actively or passively transport molecules across membrane	Move specific molecules through the membrane in a series of conformational changes	Glycophorin carrier for sugar transport; sodium–potassium pump
	Channels	Passively transport molecules across membrane	Create a selective tunnel that acts as a passage through membrane	Sodium and potassium channels in nerve, heart, and muscle 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 plasma 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

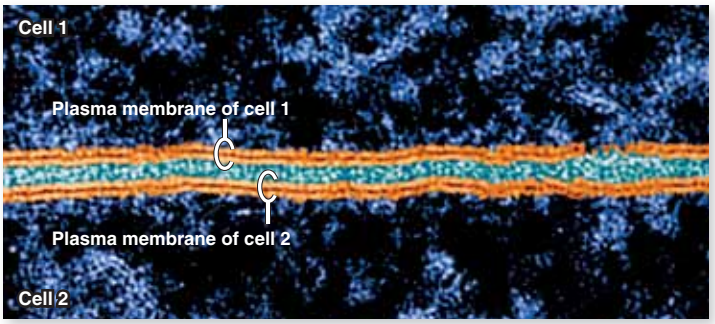
In addition to these horizontal structures there is also vertical structure to the plasma membrane. That is, the distribution of membrane lipids in the plasma membrane is asymmetrical, with the outer leaflet enriched in the glycerol phospholipid phosphatidylcholine and in sphingolipids. This is despite being symmetrically distributed in the ER where they are synthesized. Some of this sorting occurs in the Golgi and is also affected by enzymes that transport lipids across the bilayer from one face to the other.

Electron microscopy has provided structural evidence

Electron microscopy allows biologists to examine the delicate, filmy structure of a cell membrane. We discussed two types of electron microscopes in chapter 4: the transmission electron microscope (TEM) and the scanning electron microscope (SEM). Both provide illuminating views of membrane structure.

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 epoxy matrix. The epoxy block is then cut with a microtome, a machine with a very sharp blade that makes incredibly thin, transparent "epoxy shavings" less than 1 μm thick that 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. False color can be added to the micrograph to enhance detail.



Freeze-fracturing a specimen is another way to visualize the inside of the membrane (figure 5.4). 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 or the other side of the split membrane.

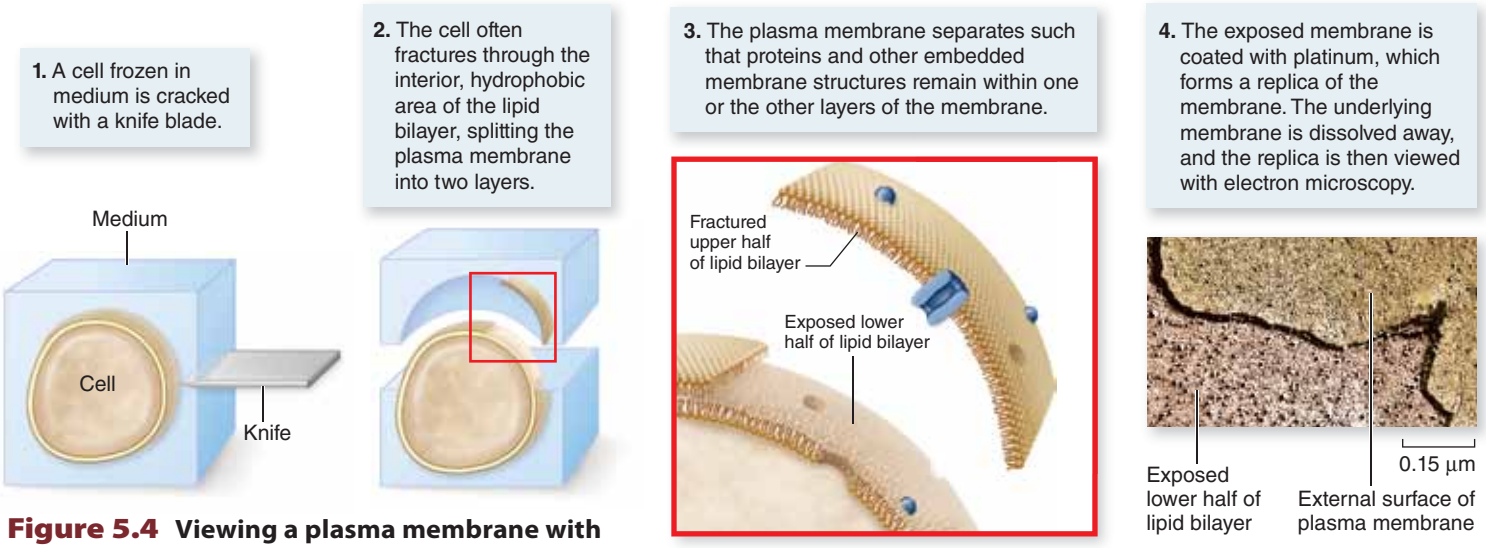


Figure 5.4 Viewing a plasma membrane with freeze-fracture microscopy.

Next, a very thin coating of platinum is evaporated onto the fractured surface, forming a replica or "cast" of the surface. After 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 textured and three-dimensional view of the membrane.

Learning Outcomes Review 5.1

Cellular membranes contain four components: (1) a phospholipid bilayer, (2) transmembrane proteins, (3) an internal protein network providing structural support, and (4) cell-surface markers composed of glycoproteins and glycolipids. The fluid mosaic model of membrane structure includes both the fluid nature of the membrane and the mosaic composition of proteins floating in the phospholipid bilayer. Transmission electron microscopy (TEM) and scanning electron microscopy (SEM) have provided evidence supporting the fluid mosaic model.

- ***If the plasma membrane were just a phospholipid bilayer, how would this affect its function?***

5.2 Phospholipids: The Membrane's Foundation

Learning Outcomes

1. ***List the different components of phospholipids.***
2. ***Explain how membranes form spontaneously.***
3. ***Describe the factors involved in membrane fluidity.***

Like the fat molecules (triglycerides) described in chapter 3, glycerol phospholipids have a backbone derived from the three-carbon polyalcohol *glycerol.* Attached to this backbone are one to three fatty acids, long chains of carbon atoms ending in a carboxyl (—COOH) group. A triglyceride 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 triglycerides are not water-soluble.

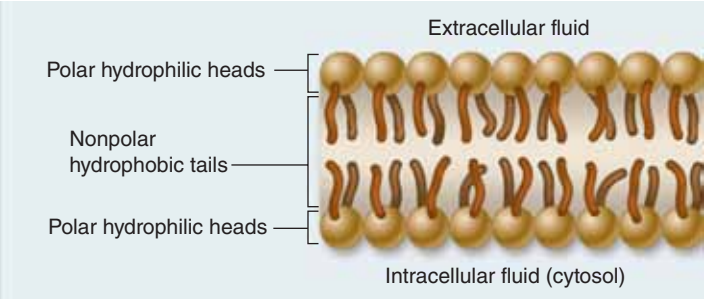
A phospholipid, by contrast, has only two fatty acid chains attached to its backbone. The third carbon of the glycerol carries a phosphate group, thus the name *phospho*lipid. An additional polar organic molecule is often added to the phosphate group as well. By varying the polar organic group, and the fatty acid chains, a large variety of lipids can be constructed on this simple molecular framework.

In addition to the glycerol phospholipids, eukaryotic cell membranes have sphingolipids, which usually have saturated fatty acid chains that may aid in organizing the membrane into lipid rafts and other microstructures.

Phospholipids spontaneously form bilayers

The phosphate groups are charged, and other molecules attached to them are polar or charged. This creates a huge change in the molecule's physical properties compared with a triglyceride. The strongly polar phosphate end is hydrophilic, or "water-loving," while the fatty acid end is strongly nonpolar and hydrophobic, or "water-fearing." The two nonpolar fatty acids extend in one direction, roughly parallel to each other, and the polar phosphate group points in the other direction. To represent this structure, phospholipids are often diagrammed as a polar head with two dangling nonpolar tails, as in figure 5.1*c.*

What happens when a collection of phospholipid molecules is placed in water? The polar water molecules repel the long, nonpolar tails of the phospholipids while seeking partners for hydrogen bonding. Because of 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 is oriented with 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 the phospholipid bilayer. Phospholipid 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, just as a layer of oil impedes the passage of a drop of water. This barrier to water-soluble substances is the key biological property of the lipid bilayer.

The phospholipid bilayer is fluid

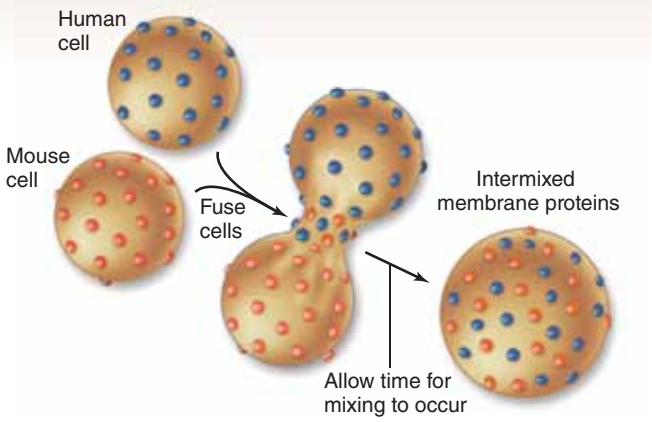
A lipid bilayer is stable because water's affinity for hydrogen bonding never stops. Just as surface tension holds a soap bubble together, even though it is made of a liquid, so the hydrogen bonding of water holds a membrane together. Although water drives phospholipids into a bilayer configuration, it does not have any effect on the mobility of phospholipids and their nonlipid neighbors in the bilayer. Because phospholipids interact relatively weakly with one another, individual phospholipids and unanchored proteins are comparatively free to move about within the membrane. This can be demonstrated vividly by fusing cells and watching their proteins intermix with time (figure 5.5).

SCIENTIFIC THINKING

Hypothesis: *The plasma membrane is fluid, not rigid.*

Prediction: *If the membrane is fluid, membrane proteins may diffuse laterally.*

Test: *Fuse mouse and human cells, then observe the distribution of membrane proteins over time by labeling specific mouse and human proteins.*



Result: *Over time, hybrid cells show increasingly intermixed proteins.*

Conclusion: *At least some membrane proteins can diffuse laterally in the membrane.*

Further Experiments: *Can you think of any other explanation for these observations? What if newly synthesized proteins were inserted into the membrane during the experiment? How could you use this basic experimental design to rule out this or other possible explanations?*

Figure 5.5 **Test of membrane fluidity.**

Membrane fluidity can change

The degree of membrane fluidity changes with the composition of the membrane itself. Much like triglycerides can be solid or liquid at room temperature, depending on their fatty acid composition, membrane fluidity can be altered by changing the membrane's fatty acid composition.

Saturated fats tend to make the membrane less fluid because they pack together well. Unsaturated fats make the membrane more fluid—the "kinks" introduced by the double bonds keep them from packing tightly. You saw this effect on fats and oils earlier in chapter 3.

In animal cells cholesterol may make up as much as 50% of membrane lipids in the outer leaflet. The cholesterol can fill gaps left by unsaturated fatty acids. This has the effect of decreasing membrane fluidity, but it increases the strength of the membrane. Overall this leads to a membrane with intermediate fluidity that is more durable and also less permeable.

Changes in the environment can have drastic effects on the membranes of single-celled organisms such as bacteria. Increasing temperature makes a membrane more fluid, and decreasing temperature makes it less fluid. Bacteria have evolved mechanisms to maintain a constant membrane fluidity despite fluctuating temperatures. Some bacteria contain enzymes called *fatty acid desaturases* that can introduce double bonds into fatty acids in membranes. Genetic studies, involving either the inactivation of these enzymes or the introduction of them into cells that normally lack them, indicate that the action of these enzymes confers cold tolerance. At colder temperatures, the double bonds introduced by fatty acid desaturase make the membrane more fluid, counteracting the environmental effect of reduced temperature.

Learning Outcomes Review 5.2

Biological membranes consist of a phospholipid bilayer. Each phospholipid has a hydrophilic (phosphate) head and a hydrophobic (lipid) tail. In water, phospholipid molecules spontaneously form a bilayer, with phosphate groups facing out toward the water and lipid tails facing in, where they are sequestered from water. Membrane fluidity varies with composition and conditions: unsaturated fats disturb packing of the lipid tails and make the membrane more fluid, as do higher temperatures.

- ***Would a phospholipid bilayer form in a nonpolar solvent?***

5.3 Proteins: Multifunctional Components

Learning Outcomes

1. ***Illustrate the functions of membrane proteins.***
2. ***Illustrate how proteins can associate with the membrane.***
3. ***Identify a transmembrane domain.***

Cell membranes contain a complex assembly of proteins enmeshed in the fluid soup of phospholipid molecules. This very flexible organization permits a broad range of interactions with the environment, some directly involving membrane proteins.

Proteins and protein complexes perform key functions

Although cells interact with their environment through their plasma membranes in many ways, we will focus on six key classes of membrane protein in this chapter and in chapter 9 (figure 5.6).

1. **Transporters.** Membranes are very selective, allowing only certain solutes to enter or leave the cell, either through channels or carriers composed of proteins.
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, which are detected by receptor proteins on their surfaces.
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 and protein complexes such as glycoproteins that are characteristic of that cell type.
5. **Cell-to-cell adhesion proteins.** Cells use specific proteins to glue themselves to one another. Some act by forming temporary interactions, and others form a more permanent bond. (See chapter 4.)
6. **Attachments to the cytoskeleton.** Surface proteins that interact with other cells are often anchored to the cytoskeleton by linking proteins.

Structural features of membrane proteins relate to function

As we've just detailed, membrane proteins can serve a variety of functions. These diverse functions arise from the diverse structures of these proteins, yet they also have common structural features related to their role as membrane proteins.

The anchoring of proteins in the bilayer

Some membrane proteins are attached to the surface of the membrane by special molecules that associate strongly with phospholipids. Like a ship tied to a floating dock, these anchored proteins are free to move about on the surface of the membrane tethered to a phospholipid. The anchoring molecules are modified lipids that have (1) nonpolar regions that insert into the internal portion of the lipid bilayer and (2) chemical bonding domains that link directly to proteins.

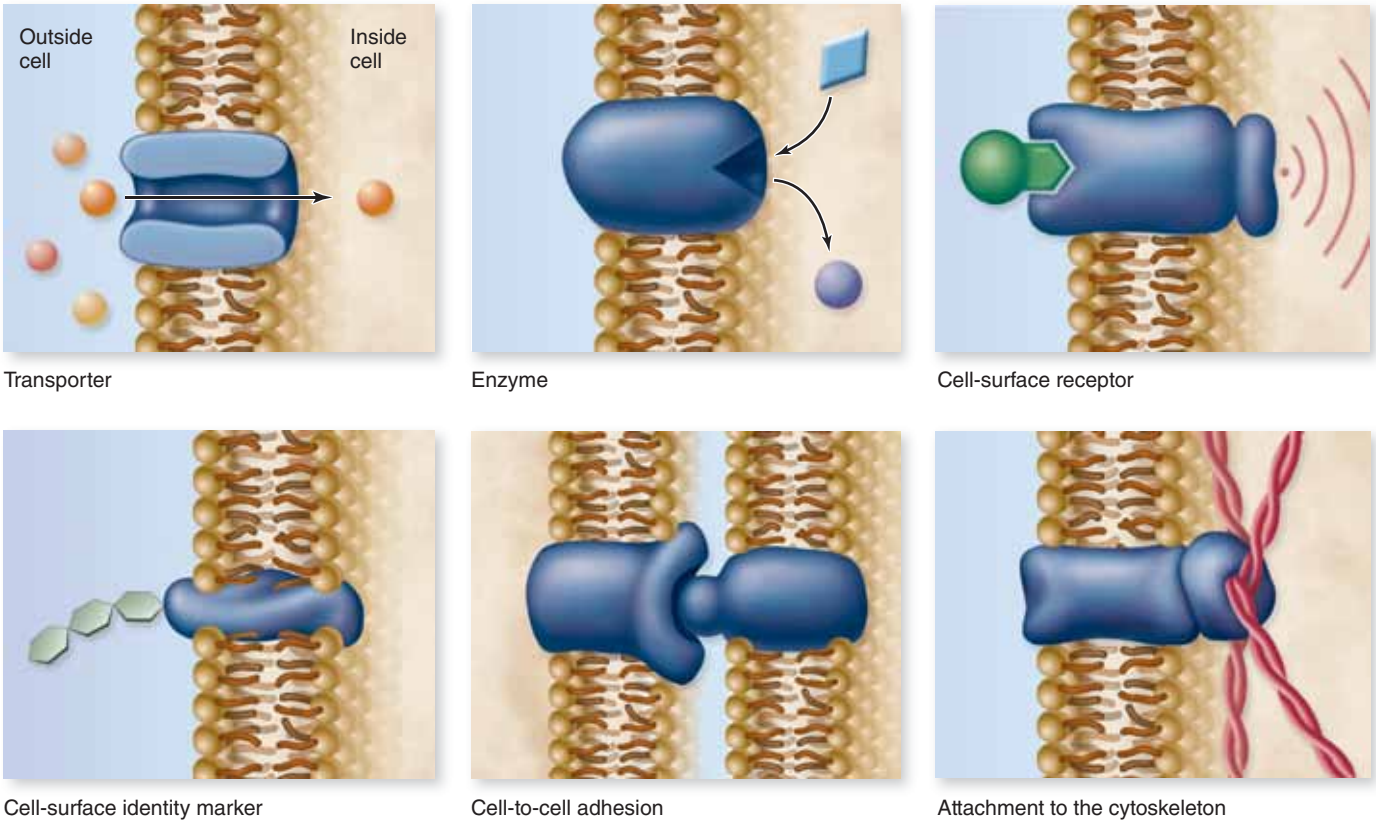
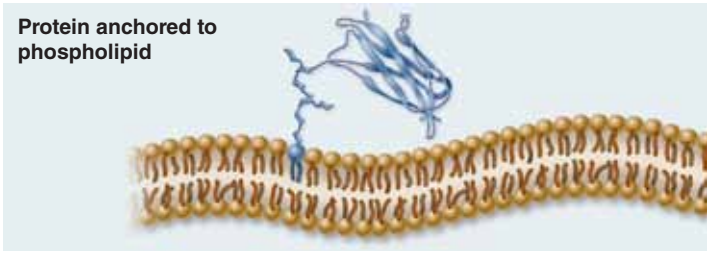


Figure 5.6 Functions of plasma membrane proteins. Membrane proteins act as transporters, enzymes, cell-surface receptors, and cell-surface identity markers, as well as aiding in cell-to-cell adhesion and securing the cytoskeleton.

Inquiry question According to the fluid mosaic model, membranes are held together by hydrophobic interactions. Considering the forces that some cells may experience, why do membranes not break apart every time an animal moves?



In contrast, other proteins actually span the lipid bilayer (transmembrane proteins). The part of the protein that extends through the lipid bilayer and that is in contact with the nonpolar interior are α helices or β-pleated sheets (see chapter 3) that consist of nonpolar amino acids. Because water avoids nonpolar amino acids, these portions of the protein are held within the interior of the lipid bilayer. The polar ends protrude from both sides of the membrane. 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. These forces prevent the transmembrane proteins from simply popping out of the membrane and floating away.

Transmembrane domains

Cell membranes contain a variety of different transmembrane proteins, which differ in the way they traverse the lipid bilayer. The primary difference lies in the number of times that the protein crosses the membrane. Each membrane-spanning region is called a **transmembrane domain.** These domains are composed of hydrophobic amino acids usually arranged into α helices (figure 5.7).

Proteins need only a single transmembrane domain to be anchored in the membrane, but they often have more than one such domain. An example of a protein with a single transmembrane domain is the linking protein that attaches the spectrin network of the cytoskeleton to the interior of the plasma membrane.

Biologists classify some types of receptors based on the number of transmembrane domains they have, such as G protein–coupled receptors with seven membrane-spanning domains (chapter 9). These receptors respond to external molecules, such as epinephrine, and initiate a cascade of events inside the cell.

Another example is bacteriorhodopsin, one of the key transmembrane proteins that carries out photosynthesis in halophilic (salt-loving) archaea. It contains seven nonpolar helical segments that traverse the membrane, forming a structure within the membrane through which protons pass during the light-driven pumping of protons.

Pores

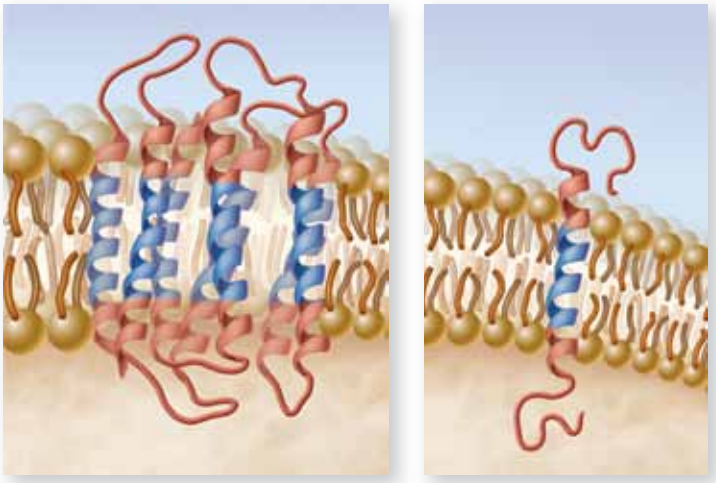
Some transmembrane proteins have extensive nonpolar regions with secondary configurations of β-pleated sheets instead of α helices (chapter 3). The β sheets form a characteristic motif, folding back and forth in a cylinder so the sheets arrange themselves like a pipe through the membrane. This forms a polar environment in the interior of the β sheets spanning the membrane. 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. The openings allow molecules to pass through the membrane (figure 5.8).

Learning Outcomes Review 5.3

Proteins in the membrane confer the main differences between membranes of different cells. Their functions include transport, enzymatic action, reception of extracellular signals, cell-to-cell interactions, and cell identity markers. Peripheral proteins can be anchored in the membrane by modified lipids. Integral membrane proteins span the membrane and have one or more hydrophobic regions, called transmembrane domains, that anchor them.

- ***Why are transmembrane domains hydrophobic?***

Inquiry question Based only on amino acid sequence, how would you recognize an integral membrane protein?



a. *b.*

Figure 5.7 Transmembrane domains. Integral membrane proteins have at least one hydrophobic transmembrane domain (shown in blue) to anchor them in the membrane. ***a.*** Receptor protein with seven transmembrane domains. ***b.*** Protein with single transmembrane domain.

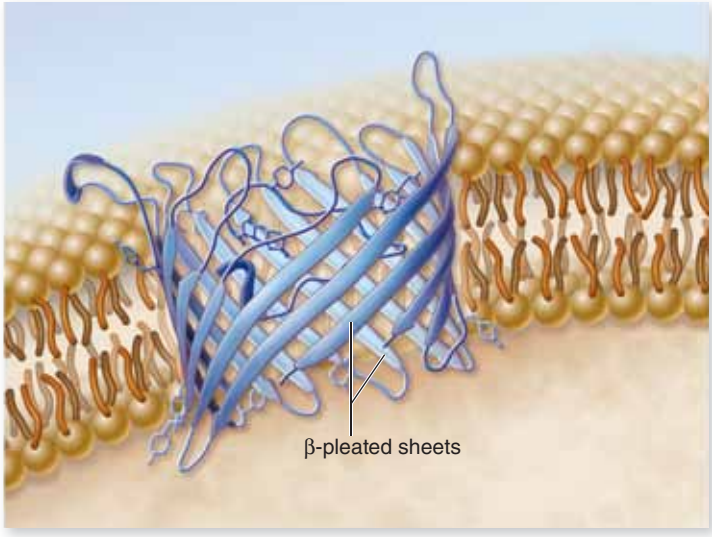


Figure 5.8 A pore protein. The bacterial transmembrane protein porin creates large open tunnels called pores in the outer membrane of a bacterium. Sixteen strands of β-pleated sheets run antiparallel to one another, creating a so-called β barrel in the bacterial outer cell membrane. The tunnel allows water and other materials to pass through the membrane.

5.4 Passive Transport Across Membranes

Learning Outcomes

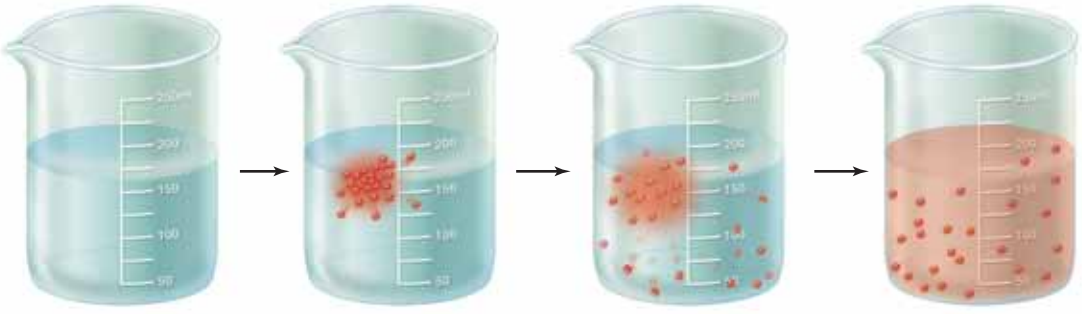
1. *Compare simple diffusion and facilitated diffusion.*
2. *Differentiate between channel proteins and carrier proteins.*
3. *Predict the direction of water movement by osmosis.*

Many substances can move in and out of the cell without the cell's having to expend energy. This type of movement is termed **passive transport.** Some ions and molecules can pass through the membrane fairly easily and do so because of a *concentration gradient*—a difference between the concentration on the inside of the membrane and that on the outside. Some substances also move in response to a gradient, but do so through specific channels formed by proteins in the membrane.

Transport can occur by simple diffusion

Molecules and ions dissolved in water are in constant random motion. This random motion causes a net movement of these substances from regions of high concentration to regions of lower concentration, a process called **diffusion** (figure 5.9).

Net movement driven by diffusion will continue until the concentration is the same in all regions. Consider what happens when you add a drop of colored ink to a bowl of water. Over time the ink becomes dispersed throughout the solution. This is due to diffusion of the ink molecules. In the context of cells, we are usually concerned with differences in concentration of molecules across the plasma membrane. We need to consider the relative concentrations both inside and outside the cell, as well as how readily a molecule can cross the membrane.



a. *b.* *c.* *d.*

Figure 5.9 Diffusion. If a drop of colored ink is dropped into a beaker of water ***(a)*** its molecules dissolve ***(b)*** and diffuse ***(c)***. Eventually, diffusion results in an even distribution of ink molecules throughout the water ***(d)***.

The major barrier to crossing a biological membrane is the hydrophobic interior that repels polar molecules but not nonpolar molecules. If a concentration difference exists for a nonpolar molecule, it will move across the membrane until the concentration is equal on both sides. At this point, movement in both directions still occurs, but there is no net change in either direction. This includes molecules like O_2 and nonpolar organic molecules such as steroid hormones.

The plasma membrane has limited permeability to small polar molecules and very limited permeability to larger polar molecules and ions. The movement of water, one of the most important polar molecules, is discussed in its own section later on.

Proteins allow membrane diffusion to be selective

Many important molecules required by cells cannot easily cross the plasma membrane. These molecules can still enter the cell by diffusion through specific channel proteins or carrier proteins embedded in the plasma membrane, provided there is a higher concentration of the molecule outside the cell than inside. We call this process of diffusion mediated by a membrane protein **facilitated diffusion. Channel proteins** have a hydrophilic interior that provides an aqueous channel through which polar molecules can pass when the channel is open. **Carrier proteins,** in contrast to channels, bind specifically to the molecule they assist, much like an enzyme binds to its substrate. These channels and carriers are usually selective for one type of molecule, and thus the cell membrane is said to be **selectively permeable.**

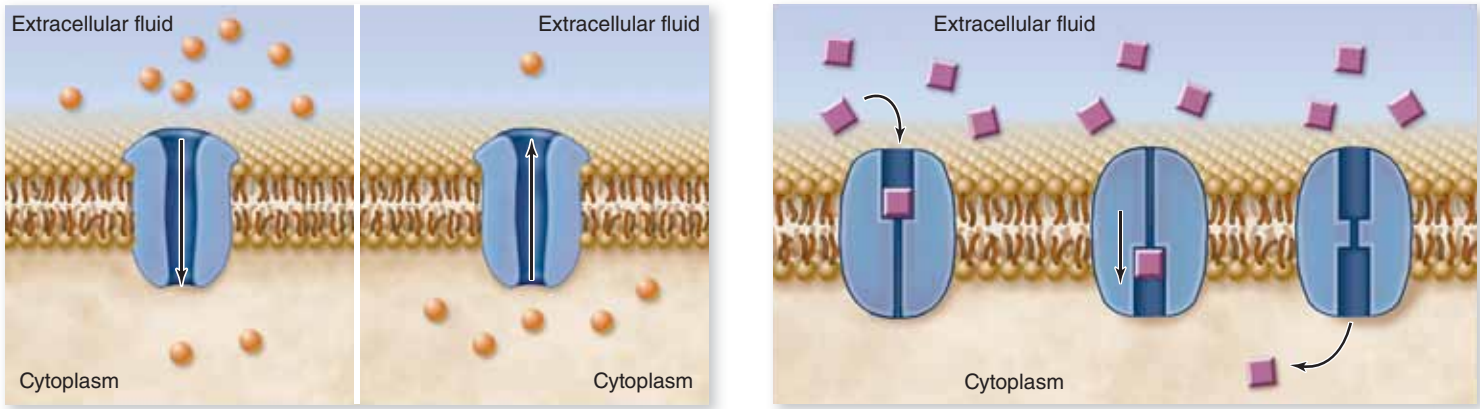
Facilitated diffusion of ions through channels

You saw in chapter 2 that atoms with an unequal number of protons and electrons have an electric charge and are called ions. Those that carry a positive charge are called *cations* and those that carry a negative charge are called *anions.*

Because of their charge, ions interact well with polar molecules such as water, but are repelled by nonpolar molecules such as the interior of the plasma membrane. 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, depending on their relative concentration across the membrane (figure 5.10). Some channel proteins can be opened or closed in response to a stimulus. These channels are called *gated channels,* and depending on the nature of the channel, the stimulus can be either chemical or electrical.

Three conditions determine the direction of net movement of the ions: (1) their relative concentrations on either side of the membrane, (2) the voltage difference across the membrane and for the gated channels, and (3) the state of the gate (open or



a. *b.*

Figure 5.10 Facilitated diffusion. Diffusion can be facilitated by membrane proteins. ***a.*** The movement of ions through a channel is shown. On the left the concentration is higher outside the cell, so the ions move into the cell. On the right the situation is reversed. In both cases, transport continues until the concentration is equal on both sides of the membrane. At this point, ions continue to cross the membrane in both directions, but there is no net movement in either direction. ***b.*** Carrier proteins bind specifically to the molecules they transport. In this case, the concentration is higher outside the cell, so molecules bind to the carrier on the outside. The carrier's shape changes, allowing the molecule to cross the membrane. This is reversible, so net movement continues until the concentration is equal on both sides of the membrane.

closed). A voltage difference is an electrical potential difference across the membrane called a *membrane potential.* Changes in membrane potential form the basis for transmission of signals in the nervous system and some other tissues. (We discuss this topic in detail in chapter 43.) Each type of channel is specific for a particular ion, such as calcium (Ca^{2+}), sodium (Na^{+}), potassium (K^{+}), or chloride (Cl^{-}), or in some cases, for more than one cation or anion. Ion channels play an essential role in signaling by the nervous system.

Facilitated diffusion by carrier proteins

Carrier proteins can help transport both ions and other solutes, such as some sugars and amino acids, across the membrane. Transport through a carrier is still a form of diffusion and therefore requires a concentration difference across the membrane.

Carriers must bind to the molecule they transport, so the relationship between concentration and rate of transport differs from that due to simple diffusion. As concentration increases, transport by simple diffusion shows a linear increase in rate of transport. But when a carrier protein is involved, a concentration increase means that more of the carriers are bound to the transported molecule. At high enough concentrations all carriers will be occupied, and the rate of transport will be constant. This means that the carrier exhibits *saturation.*

This situation is somewhat like that of a stadium (the cell) where a crowd must pass through turnstiles to enter. If there are unoccupied turnstiles, you can go right through, but when all are occupied, you must wait. When ticket holders are passing through the gates at maximum speed, the rate at which they enter cannot increase, no matter how many are waiting outside.

Facilitated diffusion in red blood cells

Several examples of facilitated diffusion can be found in the plasma membrane of vertebrate red blood cells (RBCs). One RBC carrier protein, for example, transports a different molecule in each direction: chloride ion (Cl^{-}) in one direction and bicarbonate ion (HCO_3^{-}) in the opposite direction. As you will learn in chapter 48, this carrier is important in the uptake and release of carbon dioxide.

The glucose transporter is a second vital facilitated diffusion carrier in RBCs. 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 can no longer bind to the glucose transporter, and therefore cannot pass back across the membrane. This maintains a steep concentration gradient for unphosphorylated glucose, favoring its entry into the cell.

The glucose transporter that assists the entry of glucose into the cell does not appear to form a channel in the membrane. Instead, this transmembrane protein appears to bind to a glucose molecule and then to flip its shape, dragging the glucose through the bilayer and releasing it on the inside of the plasma membrane. After it releases the glucose, the transporter reverts to its original shape and is then available to bind the next glucose molecule that comes along outside the cell.

Osmosis is the movement of water across membranes

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 is termed the **solvent,** and the substances dissolved in the water are **solutes.** Both water and solutes tend to diffuse from regions of high concentration to ones of low concentration; that is, they diffuse down their concentration gradients.

When two regions are separated by a membrane, what happens depends on whether 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. The concentration gradient of these solutes can lead to the movement of water.

Osmosis

Water molecules interact with dissolved solutes by forming hydration shells around the charged solute molecules. When a membrane separates two solutions with different concentrations of solutes, the concentrations of *free* water molecules on the two sides of the membrane also differ. The side with higher solute concentration has tied up more water molecules in hydration shells and thus has fewer free water molecules.

As a consequence of this difference, free water molecules move down their concentration gradient, toward the higher solute concentration. This net diffusion of water across a membrane toward a higher solute concentration is called **osmosis** (figure 5.11).

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 **hypertonic** (Greek *hyper,* "more than"), and the solution with the lower concentration is **hypotonic** (Greek *hypo,* "less than"). When two solutions have the same osmotic concentration, the solutions are **isotonic** (Greek *iso,* "equal"). The terms *hyperosmotic, hypoosmotic,* and *isosmotic* are also used to describe these conditions.

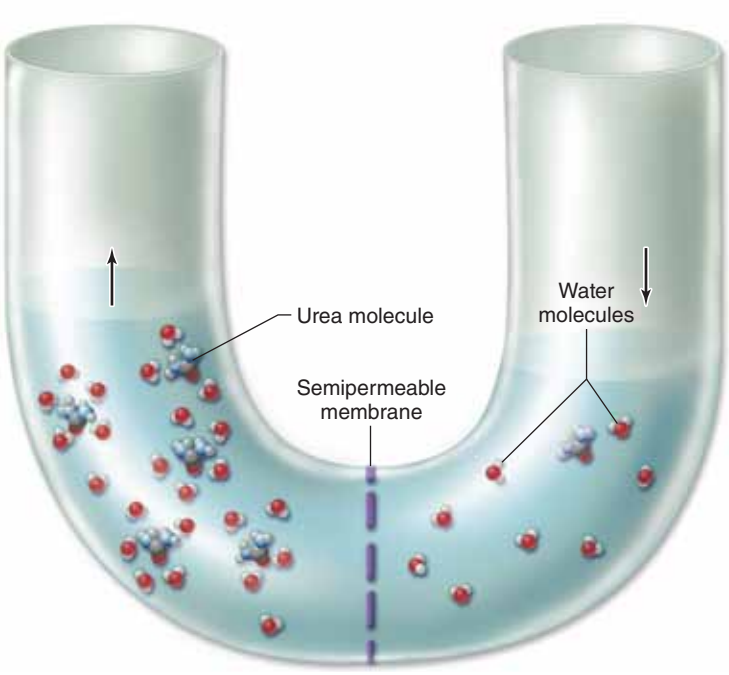


Figure 5.11 Osmosis. Concentration differences in charged or polar molecules that cannot cross a semipermeable membrane result in movement of water, which can cross the membrane. Water molecules form hydrogen bonds with charged or polar molecules creating a hydration shell around them in solution. A higher concentration of polar molecules (urea) shown on the left side of the membrane leads to water molecules gathering around each urea molecule. These water molecules are no longer free to diffuse across the membrane. The polar solute has reduced the concentration of free water molecules, creating a gradient. This causes a net movement of water by diffusion from right to left in the U-tube, raising the level on the left and lowering the level on the right.

A cell in any environment can be thought of as a plasma membrane separating two solutions: the cytoplasm and the extracellular fluid. The direction and extent of any diffusion of water across the plasma membrane is determined by comparing the osmotic strength of these solutions. Put another way, water diffuses out of a cell in a hypertonic solution (that is, the cytoplasm of the cell is hypotonic, compared with the extracellular fluid). This loss of water causes the cell to shrink until the osmotic concentrations of the cytoplasm and the extracellular fluid become equal.

Aquaporins: Water channels

The transport of water across the membrane is complex. Studies on artificial membranes show that water, despite its polarity, can cross the membrane, but this flow is limited. Water flow in living cells is facilitated by **aquaporins,** which are specialized channels for water.

A simple experiment demonstrates this. If an amphibian egg is placed in hypotonic spring water (the solute concentration in the cell is higher than that of the surrounding water), it does not swell. If aquaporin mRNA is then injected into the egg, the channel proteins are expressed and appear in the egg's plasma membrane. Water can now diffuse into the egg, causing it to swell.

More than 11 different kinds of aquaporins have been found in mammals. These fall into two general classes: those that are specific for only water, and those that allow other small hydrophilic molecules, such as glycerol or urea, to cross the membrane as well. This latter class explains how some membranes allow the easy passage of small hydrophilic substances.

The human genetic disease, hereditary (nephrogenic) diabetes insipidus (NDI), has been shown to be caused by a nonfunctional aquaporin protein. This disease causes the excretion of large volumes of dilute urine, illustrating the importance of aquaporins to our physiology.

Osmotic pressure

What happens to a cell in a hypotonic solution? (That is, the cell's cytoplasm is hypertonic relative to the extracellular fluid.) In this situation, water diffuses 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, increases. The amount of water that enters the cell depends on the difference in solute concentration between the cell and the extracellular fluid. This is measured as **osmotic pressure,** defined as the force needed to stop osmotic flow.

If the membrane is strong enough, the cell reaches 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 (figure 5.12).

Accordingly, it is important for animal cells, which only have plasma membranes, to maintain osmotic balance. In contrast, the cells of prokaryotes, fungi, plants, and many protists are surrounded by strong cell walls, which can withstand high internal pressures without bursting.

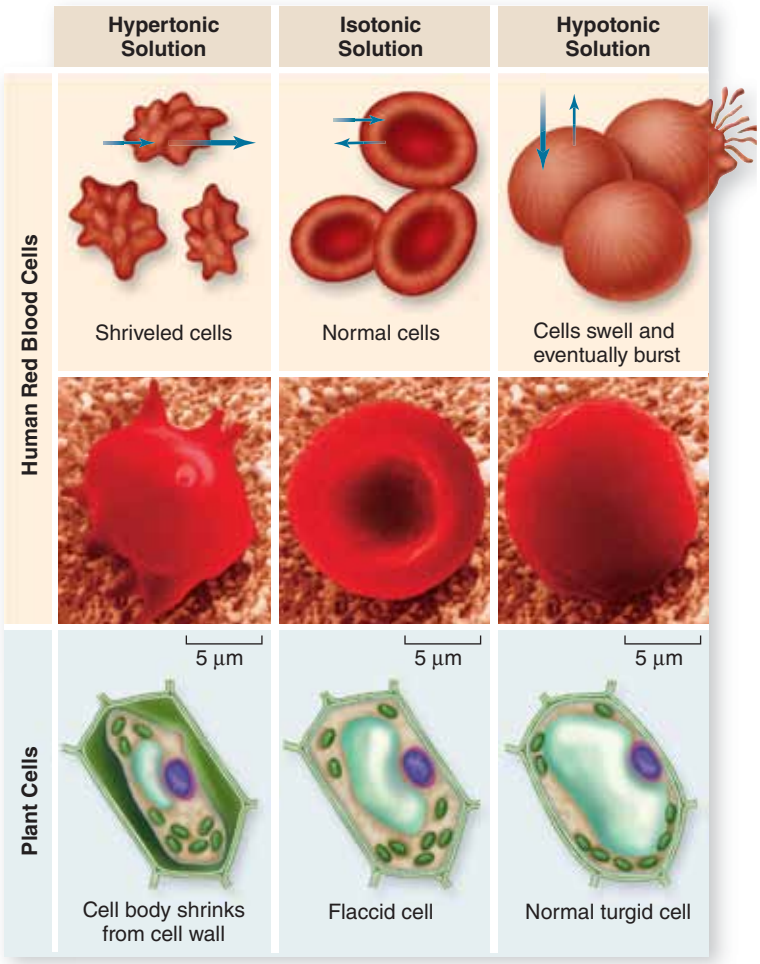


Figure 5.12 How solutes create osmotic pressure. In a hypertonic solution, water moves out of the cell, causing the cell to shrivel. In an isotonic solution, water diffuses into and out of the cell at the same rate, with no change in cell size. In a hypotonic solution, water moves into the cell. Direction and amount of water movement is shown with blue arrows *(top)*. As water enters the cell from a hypotonic solution, pressure is applied to the plasma membrane until the cell ruptures. Water enters the cell due to osmotic pressure from the higher solute concentration in the cell. Osmotic pressure is measured as the force needed to stop osmosis. The strong cell wall of plant cells can withstand the hydrostatic pressure to keep the cell from rupturing. This is not the case with animal cells.

Maintaining osmotic balance

Organisms have developed many strategies for solving the dilemma posed by being hypertonic to their environment and therefore having a steady influx of water by osmosis.

Extrusion. Some single-celled eukaryotes, such as 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 out (extrudes) through this pore the water that is continuously drawn into the cell by osmotic forces.

Isosmotic Regulation. Some organisms that live in the ocean adjust their internal concentration of solutes to match that of the surrounding seawater. Because they are isosmotic with respect to their environment, no net flow of water occurs 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 isotonic 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 that of your cells' cytoplasm.

Turgor. Most plant cells are hypertonic 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. Most green plants depend on turgor pressure to maintain their shape, and thus they wilt when they lack sufficient water.

Learning Outcomes Review 5.4

Passive transport involves diffusion, which requires a concentration gradient. Hydrophobic molecules can diffuse directly through the membrane (simple diffusion). Polar molecules and ions can also diffuse through the membrane, but only with the aid of a channel or carrier protein (facilitated diffusion). Channel proteins assist by forming a hydrophilic passageway through the membrane, whereas carrier proteins bind to the molecule they assist. Water passes through the membrane and through aquaporins in response to solute concentration differences inside and outside the cell. This process is called osmosis.

- ***If you require intravenous (IV) medication in the hospital, what should the concentration of solutes in the IV solution be relative to your blood cells?***

5.5 *Active Transport Across Membranes*

Learning Outcomes

1. ***Differentiate between active transport and diffusion.***
2. ***Describe the function of the Na^+/K^+ pump.***
3. ***Explain the energetics of coupled transport.***

Diffusion, facilitated diffusion, and osmosis are passive transport processes that move materials down their concentration gradients, but cells can also actively move substances across a cell membrane *up* their concentration gradients. This process requires the expenditure of energy, typically from ATP, and is therefore called **active transport.**

Active transport uses energy to move materials against a concentration gradient

Like facilitated diffusion, active transport involves highly selective protein carriers within the membrane that bind to the transported substance, which could be an ion or a simple molecule, such as a sugar, an amino acid, or a nucleotide. These carrier proteins are called **uniporters** if they transport a single type of molecule and symporters or antiporters if they transport two different molecules together. **Symporters** transport two molecules in the same direction, and **antiporters** transport two molecules in opposite directions. These terms can also be used to describe facilitated diffusion carriers.

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. Active transport also enables a cell to move substances out of its cytoplasm and into the extracellular fluid, despite higher external concentrations.

The use of energy from ATP in active transport may be direct or indirect. Let's first consider how ATP is used directly to move ions against their concentration gradients.

The sodium–potassium pump runs directly on ATP

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.

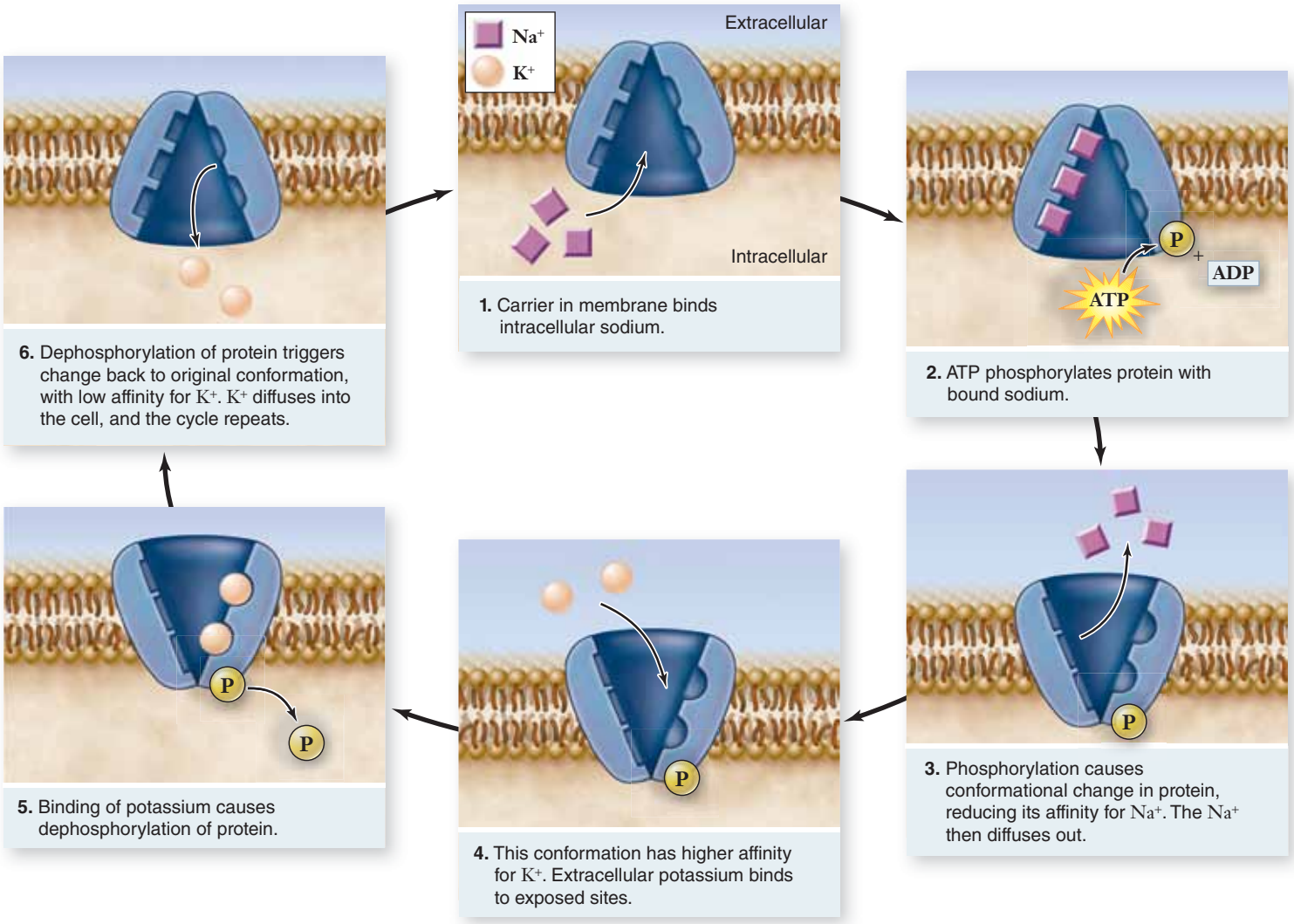


Figure 5.13 The sodium–potassium pump. The protein carrier known as the sodium–potassium pump transports sodium (Na^+) and potassium (K^+) across the plasma membrane. For every three Na^+ transported out of the cell, two K^+ are transported into it. The sodium–potassium pump is fueled by ATP hydrolysis. The affinity of the pump for Na^+ and K^+ is changed by adding or removing phosphate (P), which changes the conformation of the protein.

The remarkable protein that transports these two ions across the cell membrane is known as the **sodium–potassium pump** (Na^+/K^+ pump) (figure 5.13). This carrier protein uses the energy stored in ATP to move these two ions. In this case, the energy is used to change the conformation of the carrier protein, which changes its affinity for either Na^+ ions or K^+ ions. This is an excellent illustration of how subtle changes in the structure of a protein affect its function.

The important characteristic of the Na^+/K^+ pump is that it is an active transport mechanism, transporting Na^+ and K^+ from areas of low concentration to areas of high concentration. This transport is the opposite of passive transport by diffusion; it is achieved only by the constant expenditure of metabolic energy. The Na^+/K^+ pump works through the following series of conformational changes in the transmembrane protein (summarized in figure 5.13):

Step 1. Three Na^+ bind to the cytoplasmic side of the protein, causing the protein to change its conformation.

Step 2. In its new conformation, the protein binds a molecule of ATP and cleaves it into adenosine diphosphate (ADP) and phosphate (P_i). ADP is released, but the phosphate group is covalently linked 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, so they now face the exterior. In this new conformation, the protein has a low affinity for Na^+, and the three bound Na^+ break away 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 hydrolysis of the bound phosphate group.

Step 6. Freed of the phosphate group, the protein reverts to its original shape, 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.

In every cycle, three Na^+ leave the cell and two K^+ enter. 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 Na^+/K^+ pump appears to exist in all animal cells, although cells vary widely in the number of pump proteins they contain.

Coupled transport uses ATP indirectly

Some molecules are moved against their concentration gradient by using the energy stored in a gradient of a different molecule. In this process, called *coupled transport,* the energy released as one molecule moves down its concentration gradient is captured and used to move a different molecule against its gradient. As you just saw, the energy stored in ATP molecules can be used to create a gradient of Na^+ and K^+ across the membrane. These gradients can then be used to power the transport of other molecules across the membrane.

As one example, let's consider the active transport of glucose across the membrane in animal cells. Glucose is such an important molecule that there are a variety of transporters for it, one of which was discussed earlier under passive transport. In a multicellular organism, intestinal epithelial cells can have a higher concentration of glucose inside the cell than outside, so these cells need to be able to transport glucose against its concentration gradient. This requires energy and a different transporter than the one involved in facilitated diffusion of glucose.

The active glucose transporter uses the Na^+ gradient produced by the Na^+/K^+ pump as a source of energy to power the movement of glucose into the cell. In this system, both glucose and Na^+ bind to the transport protein, which allows Na^+ to pass into the cell down its concentration gradient, capturing the energy and using it to move glucose into the cell. In this kind of cotransport, both molecules are moving in the same direction across the membrane; therefore the transporter is a symporter (figure 5.14).

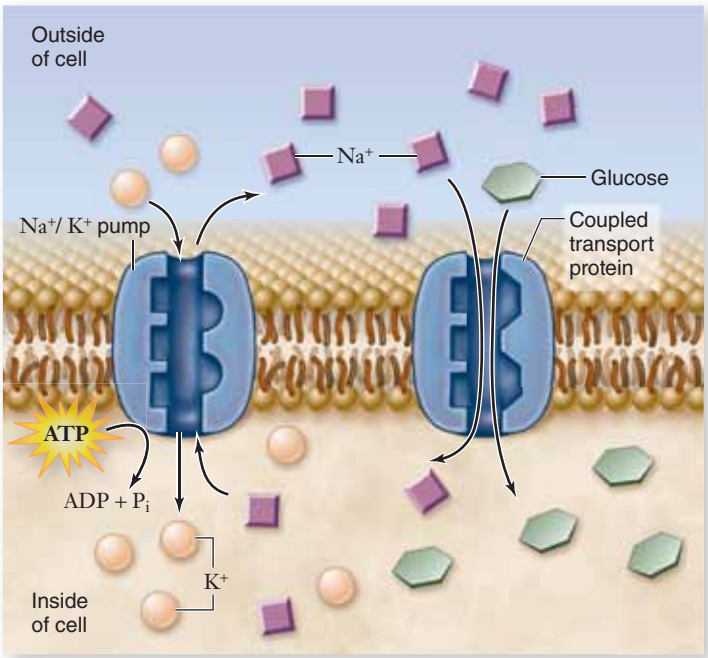


Figure 5.14 Coupled transport. A membrane protein transports Na^+ into the cell, down its concentration gradient, at the same time it transports a glucose molecule into the cell. The gradient driving the Na^+ entry allows sugar molecules to be transported against their concentration gradient. The Na^+ gradient is maintained by the Na^+/K^+ pump. ADP = adenosine diphosphate; ATP = adenosine triphosphate; P_i = inorganic phosphate

In a related process, called *countertransport,* the inward movement of Na^+ is coupled with the outward movement of another substance, such as Ca^{2+} or H^+. As in cotransport, both Na^+ and the other substance bind to the same transport protein, which in this case is an antiporter, as the substances 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 eject a substance against its concentration gradient. In both cotransport and countertransport, the potential energy in the concentration gradient of one molecule is used to transport another molecule against its concentration gradient. They differ only in the direction that the second molecule moves relative to the first.

Learning Outcomes Review 5.5

Active transport requires both a carrier protein and energy, usually in the form of ATP, to move molecules against a concentration gradient. The Na^+/K^+ pump uses ATP to moved Na^+ in one direction and K^+ in the other to create and maintain concentration differences of these ions. In coupled transport, a favorable concentration gradient of one molecule is used to move a different molecule against its gradient, such as in the transport of glucose by Na^+.

- ***Can active transport involve a channel protein? Why or why not?***

5.6 Bulk Transport by Endocytosis and Exocytosis

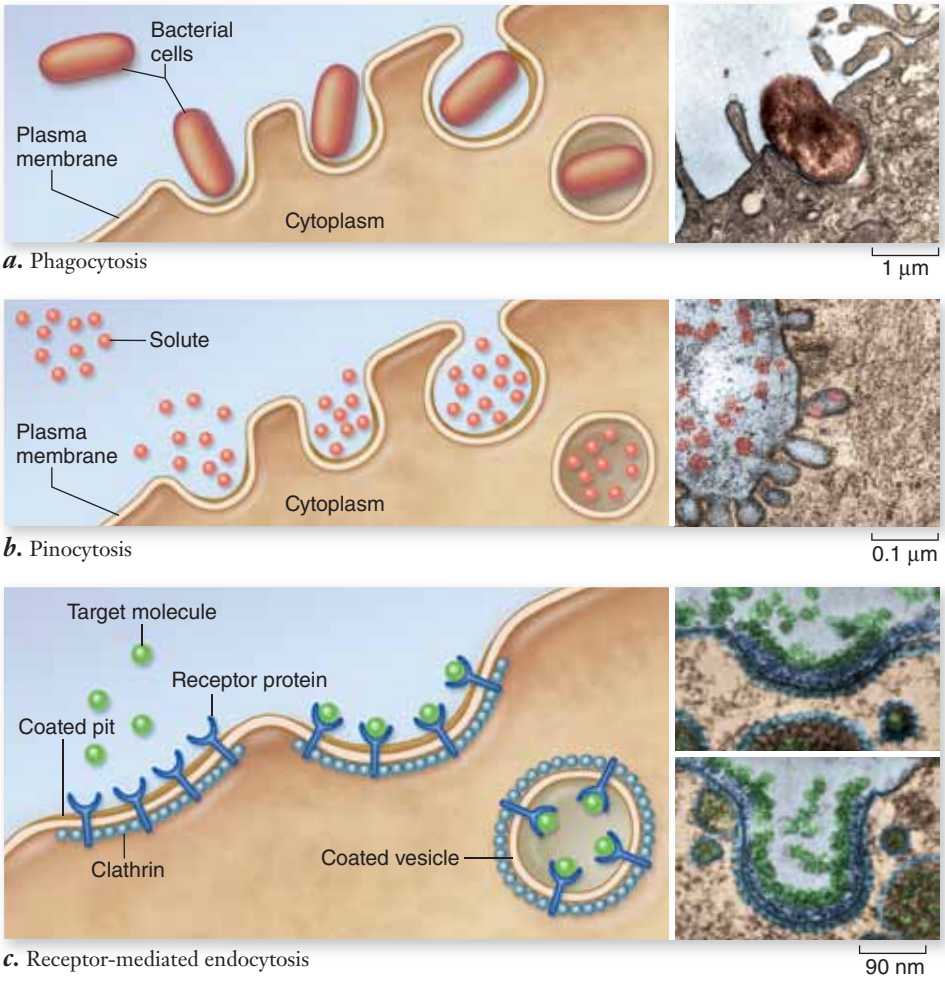
Learning Outcomes

1. ***Distinguish between endocytosis and exocytosis.***
2. ***Illustrate how endocytosis can be specific.***

The lipid nature of cell plasma membranes raises a second problem. The substances cells require for growth are mostly large, polar molecules that cannot cross the hydrophobic barrier a lipid bilayer creates. How do these substances get into cells? Two processes are involved in this **bulk transport:** *endocytosis* and *exocytosis.*

Bulk material enters the cell in vesicles

In **endocytosis,** the plasma membrane envelops food particles and fluids. Cells use three major types of endocytosis: phagocytosis, pinocytosis, and receptor-mediated endocytosis (figure 5.15). Like active transport, these processes also require energy expenditure.



a. Phagocytosis

b. Pinocytosis

c. Receptor-mediated endocytosis

Figure 5.15 Endocytosis. Both ***(a)*** phagocytosis and ***(b)*** pinocytosis are forms of endocytosis. ***c.*** In receptor-mediated endocytosis, cells have pits coated with the protein clathrin that initiate endocytosis when target molecules bind to receptor proteins in the plasma membrane. Photo inserts (false color has been added to enhance distinction of structures): ***(a)*** A TEM of phagocytosis of a bacterium, *Rickettsia tsutsugamushi,* by a mouse peritoneal mesothelial cell. The bacterium enters the host cell by phagocytosis and replicates in the cytoplasm. ***(b)*** A TEM of pinocytosis in a smooth muscle cell. ***(c)*** A coated pit appears in the plasma membrane of a developing egg cell, covered with a layer of proteins. When an appropriate collection of molecules gathers in the coated pit, the pit deepens and will eventually seal off to form a vesicle.

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 5.15*a*), the process is called **phagocytosis** (Greek *phagein,* "to eat," + *cytos,* "cell"). If the material the cell takes in is liquid (figure 5.15*b*), the process 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 endocytotic processes, 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 up to 25% of their cell volume each hour.

Receptor-mediated endocytosis

Molecules are often transported into eukaryotic cells through **receptor-mediated endocytosis.** These molecules first bind to specific receptors in the plasma membrane—they have a conformation that fits snugly into the receptor. Different cell types contain a characteristic battery of receptor types, each for a different kind of molecule in their membranes.

The portion of the receptor molecule that lies inside the membrane is trapped in an indented pit coated on the cytoplasmic side with the protein *clathrin.* Each pit acts like a molecular mousetrap, closing over to form an internal vesicle when the right molecule enters the pit (figure 5.15*c*). The trigger that releases the trap is the binding of the properly fitted target molecule to the embedded receptor. When binding occurs, the cell reacts by initiating endocytosis; the process is highly specific and very fast. The vesicle is now inside the cell carrying its cargo.

One type of molecule that is taken up by receptor-mediated endocytosis is low-density lipoprotein (LDL). LDL molecules bring cholesterol into the cell 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 familial hypercholesterolemia, the LDL receptors lack tails, so they are never fastened in the clathrin-coated pits and as a result, do not trigger vesicle formation. The cholesterol stays in the bloodstream of affected individuals, accumulating as plaques inside arteries and leading to heart attacks.

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.

Material can leave the cell by exocytosis

The reverse of endocytosis is **exocytosis**, the discharge of material from vesicles at the cell surface (figure 5.16). 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 considered a form of exocytosis. In animal cells, exocytosis provides a mechanism for secreting many hormones, neurotransmitters, digestive enzymes, and other substances.

The mechanisms for transport across cell membranes are summarized in table 5.2.

Learning Outcomes Review 5.6

Large molecules and other bulky materials can enter a cell by endocytosis and leave the cell by exocytosis. These processes require energy. Endocytosis may be mediated by specific receptor proteins in the membrane that trigger the formation of vesicles.

- ***What feature unites transport by receptor-mediated endocytosis, transport by a carrier, and catalysis by an enzyme?***

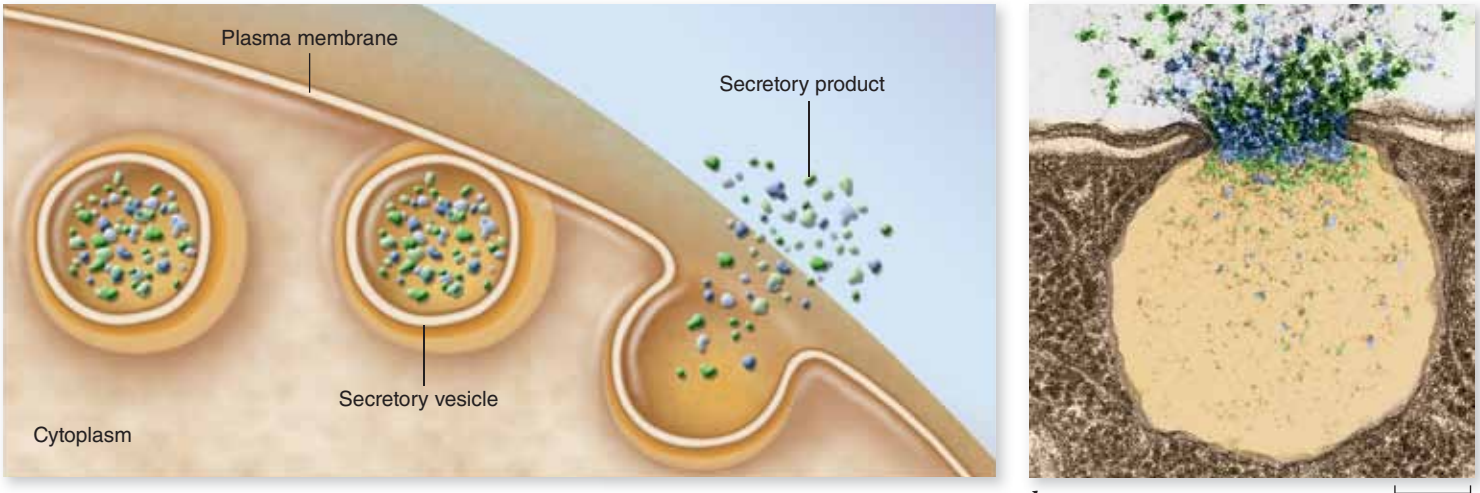
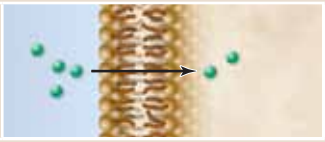
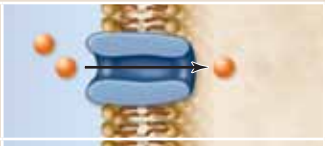
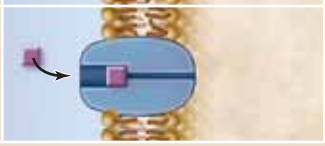
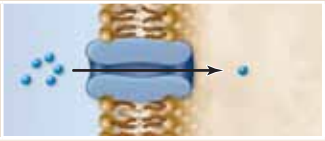
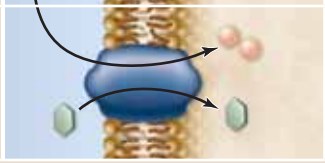
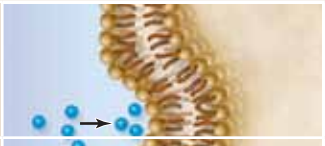
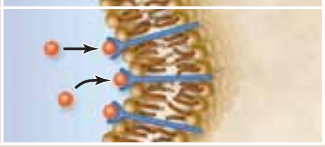
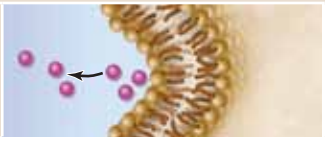
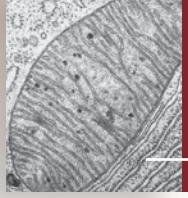


Figure 5.16 Exocytosis. ***a.*** Proteins and other molecules are secreted from cells in small packets called vesicles, whose membranes fuse with the plasma membrane, releasing their contents outside the cell. ***b.*** A false-colored transmission electron micrograph showing exocytosis.

TABLE 5.2 Mechanisms for Transport Across Cell Membranes

Process		How It Works	Example
PASSIVE PROCESSES			
Diffusion			
Direct		Random molecular motion produces net migration of nonpolar molecules toward region of lower concentration	Movement of oxygen into cells
Facilitated Diffusion			
Protein channel		Polar molecules or ions move through a protein channel; net movement is toward region of lower concentration	Movement of ions in or out of cell
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			
Aquaporins		Diffusion of water across the membrane via osmosis; requires osmotic gradient	Movement of water into cells placed in a hypotonic solution
ACTIVE PROCESSES			
Active Transport			
Protein carrier			
Na^+/K^+ pump		Carrier uses energy to move a substance across a membrane against its concentration gradient	Na^+ and K^+ against their concentration gradients
Coupled transport		Molecules are transported across a membrane against their concentration gradients by the cotransport of sodium ions or protons down their concentration gradients	Coupled uptake of glucose into cells against its concentration gradient using a Na^+ gradient
Endocytosis			
Membrane vesicle			
Phagocytosis		Particle is engulfed by membrane, which folds around it and forms a vesicle	Ingestion of bacteria by white blood cells
Pinocytosis		Fluid droplets are engulfed by membrane, which forms vesicles around them	"Nursing" of human egg cells
Receptor-mediated endocytosis		Endocytosis triggered by a specific receptor, forming clathrin-coated vesicles	Cholesterol uptake
Exocytosis			
Membrane vesicle		Vesicles fuse with plasma membrane and eject contents	Secretion of mucus; release of neurotransmitters



Chapter Review

5.1 The Structure of Membranes

The fluid mosaic model shows proteins embedded in a fluid lipid bilayer.

Membranes are sheets of phospholipid bilayers with associated proteins (figure 5.3). Hydrophobic regions of a membrane are oriented inward and hydrophilic regions oriented outward. In the fluid mosaic model, proteins float on or in the lipid bilayer.

Cellular membranes consist of four component groups.

In eukaryotic cells, membranes have four components: a phospholipid bilayer, transmembrane proteins (integral membrane proteins), an interior protein network, and cell-surface markers. The interior protein network is composed of cytoskeletal filaments and peripheral membrane proteins, which are associated with the membrane but are not an integral part. Membranes contain glycoproteins and glycolipids on the surface that act as cell identity markers.

Cellular membranes have an organized substructure

Cholesterol and sphingolipid can associate to form microdomains. The two leaflets of the plasma membrane are also not identical.

Electron microscopy has provided structural evidence.

Transmission electron microscopy (TEM) and scanning electron microscopy (SEM) have confirmed the structure predicted by the fluid mosaic model.

5.2 Phospholipids: The Membrane's Foundation

Phospholipids are composed of two fatty acids and a phosphate group linked to a three-carbon glycerol molecule.

Phospholipids spontaneously form bilayers.

The phosphate group of a phospholipid is polar and hydrophilic; the fatty acids are nonpolar and hydrophobic, and they orient away from the polar head of the phospholipids. The nonpolar interior of the lipid bilayer impedes the passage of water and water-soluble substances.

The phospholipid bilayer is fluid.

Hydrogen bonding of water keeps the membrane in its bilayer configuration; however, phospholipids and unanchored proteins in the membrane are loosely associated and can diffuse laterally.

Membrane fluidity can change.

Membrane fluidity depends on the fatty acid composition of the membrane. Unsaturated fats tend to make the membrane more fluid because of the "kinks" of double bonds in the fatty acid tails. Temperature also affects fluidity. Some bacteria have enzymes that alter the fatty acids of the membrane to compensate for temperature changes.

5.3 Proteins: Multifunctional Components

Proteins and protein complexes perform key functions.

Transporters are integral membrane proteins that carry specific substances through the membrane. Enzymes often occur on the interior surface of the membrane. Cell-surface receptors respond to external chemical messages and change conditions inside the cell; cell identity markers on the surface allow recognition of the body's cells as "self." Cell-to-cell adhesion proteins glue cells together; surface proteins that interact with other cells anchor to the cytoskeleton.

Structural features of membrane proteins relate to function.

Surface proteins are attached to the surface by nonpolar regions that associate with polar regions of phospholipids. Transmembrane proteins may cross the bilayer a number of times, and each membrane-spanning region is called a transmembrane domain. Such a domain is composed of hydrophobic amino acids usually arranged in α helices. In certain proteins, β-pleated sheets in the nonpolar region form a pipelike passageway having a polar environment. An example is the porin class of proteins.

5.4 Passive Transport Across Membranes

Transport can occur by simple diffusion.

Simple diffusion is the passive movement of a substance along a chemical or electrical gradient. Biological membranes pose a barrier to hydrophilic polar molecules, while they allow hydrophobic substances to diffuse freely.

Proteins allow membrane diffusion to be selective.

Ions and large hydrophilic molecules cannot cross the phospholipid bilayer. Diffusion can still occur with the help of proteins, thus we call this facilitated diffusion. These proteins can be either channels, or carriers. Channels allow the diffusion of ions based on concentration and charge across the membrane. They are specific for different ions, but form an aqueous pore in the membrane. Carrier proteins bind to the molecules they transport, much like an enzyme. The rate of transport by a carrier is limited by the number of carriers in the membrane.

Osmosis is the movement of water across membranes.

The direction of movement due to osmosis depends on the solute concentration on either side of the membrane (figure 5.12). Solutions can be isotonic, hypotonic, or hypertonic. Cells in an isotonic solution are in osmotic balance; cells in a hypotonic solution will gain water; and cells in a hypertonic solution will lose water. Aquaporins are water channels that facilitate the diffusion of water.

5.5 Active Transport Across Membranes

Active transport uses energy to move materials against a concentration gradient.

Active transport uses specialized protein carriers that couple a source of energy to transport. They are classified based on the number of molecules and direction of transport. Uniporters transport a specific molecule in one direction; symporters transport two molecules in the same direction; and antiporters transport two molecules in opposite directions.

The sodium–potassium pump runs directly on ATP.

The sodium–potassium pump moves Na^+ out of the cell and K^+ into the cell against their concentration gradients using ATP. In every cycle of the pump, three Na^+ leave the cell and two K^+ enter it. This pump appears to be almost universal in animal cells.

Coupled transport uses ATP indirectly.

Coupled transport occurs when the energy released by a diffusing molecule is used to transport a different molecule against its concentration gradient in the same direction. Countertransport is similar to coupled transport, but the two molecules move in opposite directions.

5.6 Bulk Transport by Endocytosis and Exocytosis

Bulk transport moves large quantities of substances that cannot pass through the cell membrane.

Bulk material enters the cell in vesicles.

In endocytosis, the cell membrane surrounds material and pinches off to form a vesicle. In receptor-mediated endocytosis, specific molecules bind to receptors on the cell membrane.

Material can leave the cell by exocytosis.

In exocytosis, material in a vesicle is discharged when the vesicle fuses with the membrane.

Review Questions

UNDERSTAND

1. The fluid mosaic model of the membrane describes the membrane as
   a. containing a significant quantity of water in the interior.
   b. composed of fluid phospholipids on the outside and protein on the inside.
   c. composed of protein on the outside and fluid phospholipids on the inside.
   d. made of proteins and lipids that can freely move.
2. What chemical property characterizes the interior of the phospholipid bilayer?
   a. It is hydrophobic.
   b. It is hydrophilic.
   c. It is polar.
   d. It is saturated.
3. The transmembrane domain of an integral membrane protein
   a. is composed of hydrophobic amino acids.
   b. often forms an α-helical structure.
   c. can cross the membrane multiple times.
   d. All of the choices are correct.
4. The specific function of a membrane within a cell is determined by the
   a. degree of saturation of the fatty acids within the phospholipid bilayer.
   b. location of the membrane within the cell.
   c. presence of lipid rafts and cholesterol.
   d. type and number of membrane proteins.
5. The movement of water across a membrane is dependent on
   a. the solvent concentration.
   b. the solute concentration.
   c. the presence of carrier proteins.
   d. membrane potential.
6. If a cell is in an isotonic environment, then
   a. the cell will gain water and burst.
   b. no water will move across the membrane.
   c. the cell will lose water and shrink.
   d. osmosis still occurs, but there is no net gain or loss of cell volume.
7. Which of the following is NOT a mechanism for bringing material into a cell?
   a. Exocytosis
   b. Endocytosis
   c. Pinocytosis
   d. Phagocytosis

APPLY

1. A bacterial cell that can alter the composition of saturated and unsaturated fatty acids in its membrane lipids is adapted to a cold environment. If this cell is shifted to a warmer environment, it will react by
   a. increasing the amount of cholesterol in its membrane.
   b. altering the amount of protein present in the membrane.
   c. increasing the degree of saturated fatty acids in its membrane.
   d. increasing the percentage of unsaturated fatty acids in its membrane.
2. What variable(s) influence(s) whether a nonpolar molecule can move across a membrane by passive diffusion?
   a. The structure of the phospholipids bilayer
   b. The difference in concentration of the molecule across the membrane
   c. The presence of transport proteins in the membrane
   d. All of the choices are correct.
3. Which of the following does NOT contribute to the selective permeability of a biological membrane?
   a. Specificity of the carrier proteins in the membrane
   b. Selectivity of channel proteins in the membrane
   c. Hydrophobic barrier of the phospholipid bilayer
   d. Hydrogen bond formation between water and phosphate groups
4. How are *active* transport and *coupled* transport related?
   a. They both use ATP to move molecules.
   b. Active transport establishes a concentration gradient, but coupled transport doesn't.
   c. Coupled transport uses the concentration gradient established by active transport.
   d. Active transport moves one molecule, but coupled transport moves two.
5. A cell can use the process of facilitated diffusion to
   a. concentrate a molecule such as glucose inside a cell.
   b. remove all of a toxic molecule from a cell.
   c. move ions or large polar molecules across the membrane regardless of concentration.
   d. move ions or large polar molecules from a region of high concentration to a region of low concentration.

SYNTHESIZE

1. Figure 5.5 describes a classic experiment demonstrating the ability of proteins to move within the plane of the cell's plasma membrane. The following table outlines three different experiments using the fusion of labeled mouse and human cells.

Experiment	Conditions	Temperature (°C)	Result
1	Fuse human and mouse cells	37	Intermixed membrane proteins
2	Fuse human and mouse cells in presence of ATP inhibitors	37	Intermixed membrane proteins
3	Fuse human and mouse cells	4	No intermixing of membrane proteins

   What conclusions can you reach about the movement of these proteins?
2. Each compartment of the endomembrane system of a cell is connected to the plasma membrane. Create a simple diagram of a cell including the RER, Golgi apparatus, vesicle, and the plasma membrane. Starting with the RER, use two different colors to represent the inner and outer halves of the bilayer for each of these membranes. What do you observe?
3. The distribution of lipids in the ER membrane is symmetric, that is, it is the same in both leaflets of the membrane. The Golgi apparatus and plasma membrane do not have symmetric distribution of membrane lipids. What kinds of processes could achieve this outcome?

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