5 A CLOSER LOOK AT CELL MEMBRANES

One Bad Transporter and Cystic Fibrosis

Each living cell is engaged in risky business. Think of how it has to move something as ordinary as water in one direction or the other across its plasma membrane. If all goes well, it takes in or sends out water in just the right amounts—not too little, not too much. But who is to say life always goes well?

CFTR is one of the protein channels across the plasma membrane of epithelial cells. Sheets of these cells line sweat glands, airways and sinuses, and ducts in the digestive and reproductive systems. Chloride ions move through them, and water follows to form a thin film on the free surface of the linings. Mucus, which lubricates tissues and helps prevent infection, slides freely on the watery film.

Sometimes mutation changes how CFTR works. Not enough chloride and water reach the lining's free surface, so the film does not form. Mucus dries out and thickens. Among other things, it clogs ducts from the pancreas, so digestive enzymes cannot get to the small intestine where most food is digested and absorbed. Weight loss follows. Sweat glands secrete too much salt and alter the water–salt balance for the internal environment, which affects the heart and other organs. Males become sterile.

Problems also develop in airways to the lungs, where ciliated cells are supposed to sweep away bacteria and other particles stuck in mucus. Now the mucus makes cilia too sticky, and **biofilms** form. Biofilms are microbial populations anchored to one epithelial lining or another by stiff, sticky polysaccharides of their own making. They resist the body's defenses and antibiotics. *Pseudomonas aeruginosa,* the most efficient of the colonizers, cause low-grade infections that may last for years. Most patients can expect to live no longer than thirty years, at which time their lungs usually fail. At present there is no cure.

These symptoms—outcomes of mutation in the CFTR protein—characterize *cystic fibrosis* (CF), the most common fatal genetic disorder in the United States. More than 10 million people carry a mutant form of the gene. CF develops when they inherited a mutated gene from both parents. This happens in about 1 of every 3,300 live births (Figure 5.1).

CFTR is one of the ABC transporters in all prokaryotic and eukaryotic cells (Figure 5.2). Some of these proteins, including CFTR, are channels that let hydrophobic substances cross a membrane. Others pump substances across. By their action, some types affect what other membrane proteins are doing.

In all but 10 percent of CF patients, loss of a single amino acid during protein synthesis causes the disorder. Before a new CFTR protein is shipped to the plasma membrane, it is supposed to be modified in that endomembrane system you read about in Chapter 4. Copies of the mutant protein do enter the ER, but enzymes destroy 99 percent of them before they reach Golgi bodies. Thus few chloride channels reach their normal destinations.

Mutant CFTR may also contribute to the sinus problems of an estimated 30 million people in the United States

Figure 5.1 Child affected by cystic fibrosis, or CF, who each day endures chest thumps, back thumps, and repositionings to dislodge thick mucus that collects in airways to the lungs. Symptoms vary from one affected individual to the next, partly because the abnormal protein that causes CF has mutated in more than 500 ways. Environmental factors and a person's genetic makeup also affect the outcome.

IMPACTS, ISSUES

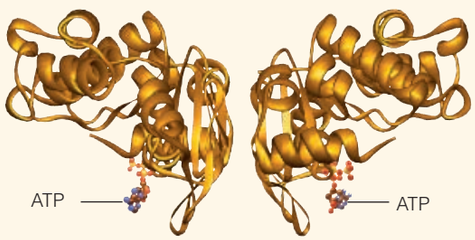


Figure 5.2 Model for part of an ABC transporter, a category of membrane proteins that includes CFTR. The parts shown here are ATP-driven motors that can widen an ion channel across the plasma membrane.

alone. In *sinusitis*, the linings of cavities inside the skull (around the nose) are chronically inflamed. In one study at Johns Hopkins University, researchers found a single copy of a mutant CFTR gene in 10 of 147 sinusitis patients. And they were only looking for 16 of more than 500 known mutant forms of the CFTR gene!

Think about it. A startling percentage of the human population can develop problems when the copies of even one kind of membrane protein don't work.

Your life depends on the functions of thousands of kinds of proteins and other molecules. Breathing, eating, moving, sleeping, crying, thinking—whatever you might be doing starts at the level of individual cells. And each cell functions properly only if it can be responsive to conditions in the microenvironments on both sides of its plasma membrane. Each eukaryotic cell also has to be responsive to conditions on both sides of its organelle membranes. *Cell membranes*—these thin boundary layers make the difference between organization and chaos.

How Would You Vote?

The ability to detect mutant genes that cause severe disorders raises bioethical questions. Should we encourage the mass screening of prospective parents for mutant genes that cause cystic fibrosis? Should society encourage women to give birth only if their child will not develop severe medical problems? See BiologyNow for details, then vote online.

Key Concepts

MEMBRANE STRUCTURE AND FUNCTION

Cell membranes have a thin, oily, water-insoluble lipid bilayer that functions as a boundary between the outside environment and the cell interior.

The lipid bilayer consists primarily of phospholipids. Many diverse proteins are embedded in the bilayer or are positioned at one of its surfaces. The proteins carry out most membrane functions, such as transport across the bilayer and cell-to-cell recognition. Sections 5.1, 5.2

DIFFUSION ACROSS MEMBRANES

Metabolism requires concentration gradients that drive the directional movements of substances. Cells have built-in mechanisms for increasing or decreasing water and solute concentrations across the plasma membrane and internal cell membranes. Section 5.3

TRANSPORT ACROSS MEMBRANES

In passive transport, a solute crosses a membrane by diffusing through a channel inside a transport protein. In active transport, a different kind of transport protein pumps the solute across a membrane, against its concentration gradient. An input of energy, typically from ATP, jump-starts active transport. Section 5.4

OSMOSIS

By a molecular behavior called osmosis, water diffuses across any selectively permeable membrane to a region where its concentration is lower. Section 5.5

MEMBRANE TRAFFIC

Larger packets of substances and, in some cases, engulfed cells move across the plasma membrane by processes of endocytosis and exocytosis. Membrane cycling pathways extend from the plasma membrane to organelles of the endomembrane system. Section 5.6

Links to Earlier Concepts

Reflect again on the road map in Section 1.1. Here you will see how complex lipids and proteins become organized in cell membranes (3.4, 4.1). Remember the different levels of protein organization? You will consider some examples of how protein structure translates into specific functions (3.6). You will be applying your knowledge of the properties of water molecules to the movement of water across membranes (2.5). You will see how the endomembrane system (4.6) helps cycle membranes.

5.1 Organization of Cell Membranes

LINKS TO SECTIONS 3.4, 4.1

Cell membranes consist of a lipid bilayer in which many different kinds of proteins are embedded. The membrane is a continuous boundary layer that selectively controls the flow of substances across it.

REVISITING THE LIPID BILAYER

Think back on the phospholipids, the most abundant components of cell membranes (Section 3.4 and Figure 5.3*a*). Each has a phosphate-containing head and two fatty acid tails attached to one glycerol backbone. The head is hydrophilic, meaning it dissolves fast in water. The tails are hydrophobic; water repels them.

Immerse a lot of phospholipids in water, and they interact with water molecules and with one another until they spontaneously cluster into a sheet or film at the water's surface. Some line up as two layers, with all fatty acid tails sandwiched between the outward-facing hydrophilic heads. This is a **lipid bilayer**, the basic framework for cell membranes (Figure 5.3*c*).

THE FLUID MOSAIC MODEL

By the **fluid mosaic model**, every cell membrane has a mixed composition—or a *mosaic*—of phospholipids, glycolipids, sterols, and proteins. The lipids form an oily bilayer that serves as a barrier to water-soluble substances. Diverse proteins are either embedded in the bilayer or attached to one of its surfaces. They carry out most membrane functions.

The membrane is *fluid* because of interactions and motions of its components. The phospholipids differ in their heads and the length of their fatty acid tails. At least one of the tails is usually kinked, or unsaturated. Remember, an unsaturated fatty acid has one or more double covalent bonds in its carbon backbone; a fully saturated type has none. Also, most phospholipids drift sideways, spin around their long axis, and flex their tails, so they do not bunch up as a solid layer.

Figure 5.4 shows the fluid mosaic model. Section 5.2 is an overview of the membrane proteins that you will be reading about in many chapters to come.

DO MEMBRANE PROTEINS STAY PUT?

Some time ago, researchers figured out how to split a frozen plasma membrane down the middle of its bilayer. They found that proteins were not spread like a coat on the bilayer, as some had thought, but rather that many were embedded in it (Figure 5.5*a*). Were those proteins rigidly positioned in the membrane? No one knew until researchers designed an ingenious

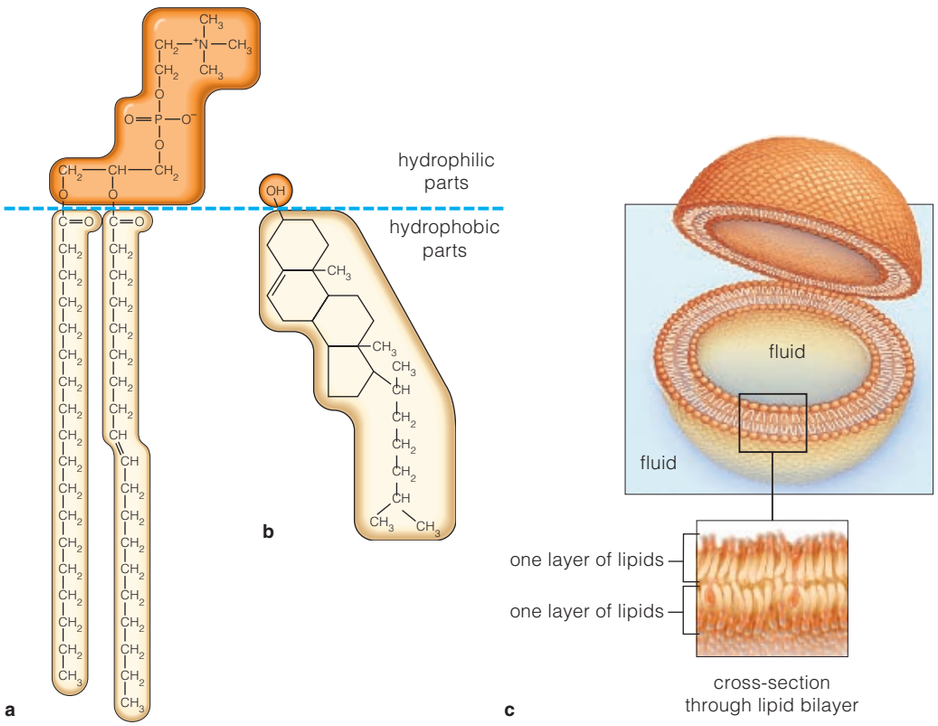


Figure 5.3 (**a**) Structural formula for phosphatidylcholine. This phospholipid is one of the most common molecules of animal cell membranes. *Orange* signifies its hydrophilic head, and *yellow*, its hydrophobic tails.

(**b**) Structural formula for cholesterol, the main sterol in animal tissues. Phytosterols are its equivalent in plant tissues.

(**c**) Spontaneous organization of lipid molecules into two layers (a bilayer structure). When immersed in liquid water, their hydrophobic tails become sandwiched between their hydrophilic heads, which dissolve in the water.

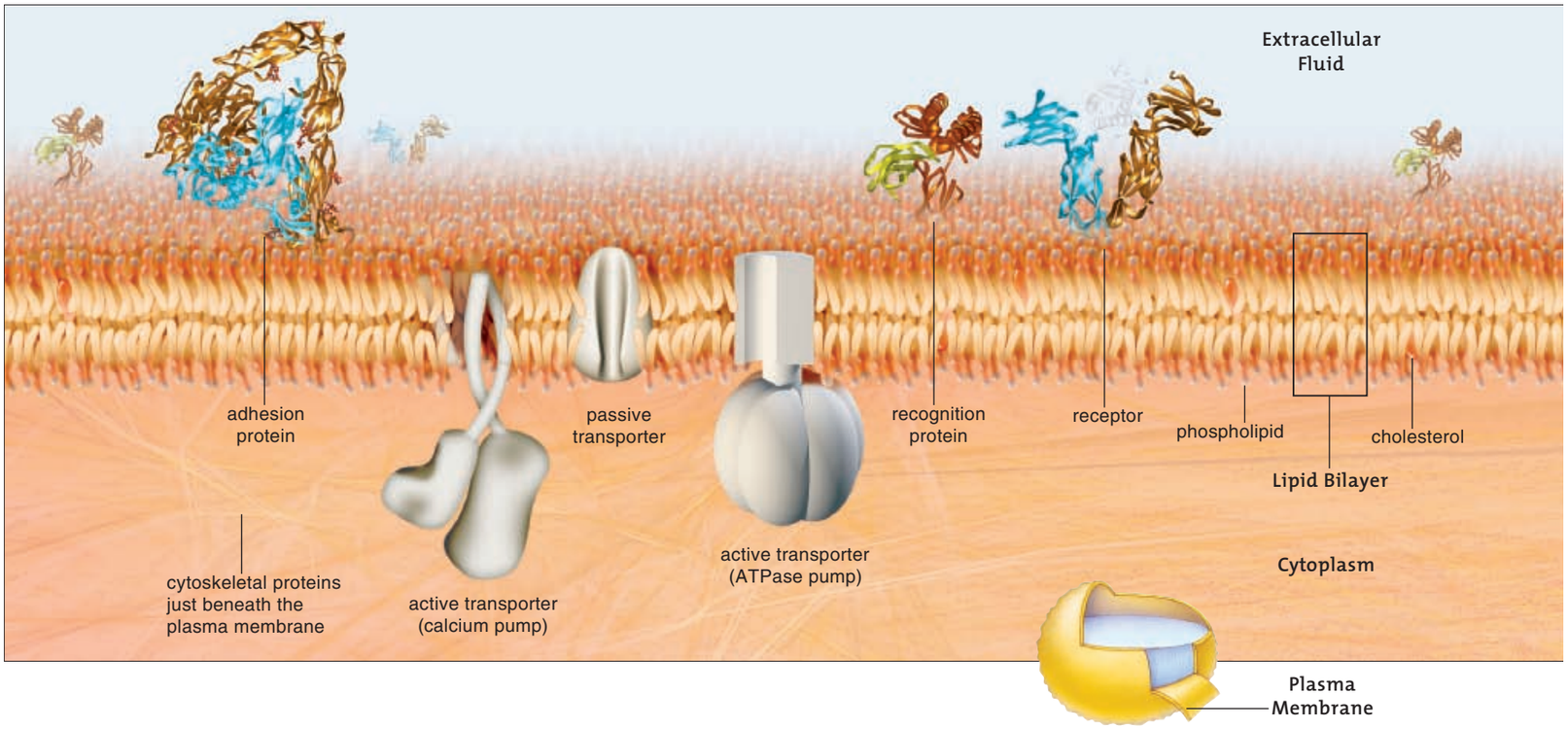


Figure 5.4 ***Animated!*** Fluid mosaic model for the plasma membrane of an animal cell.

experiment. They induced an isolated human cell and an isolated mouse cell to fuse. The plasma membranes from the two species merged to form one continuous membrane in a new, hybrid cell. Most of the proteins mixed together in less than an hour (Figure 5.5*b*).

As we now know, many proteins are free to move laterally through the lipid bilayer, but others stay put. Some unite in complexes and do not move relative to one another. Receptors for acetylcholine, a signaling molecule, are like this. Cytoskeletal elements tether other proteins and restrict their lateral movements. For instance, a mesh of cross-lined spectrin proteins anchor glycophorin, a type of recognition protein, to the surface of all red blood cells. A transport protein that moves chloride one way and bicarbonate the other across the plasma membrane is similarly anchored.

All cell membranes consist of two layers of lipids—mainly phospholipids—and diverse proteins. Hydrophobic parts of the lipids are sandwiched between hydrophilic parts, which are dissolved in cytoplasmic fluid or in extracellular fluid.

All cell membranes have protein receptors, transporters, and enzymes. The plasma membrane also incorporates adhesion, communication, and recognition proteins.

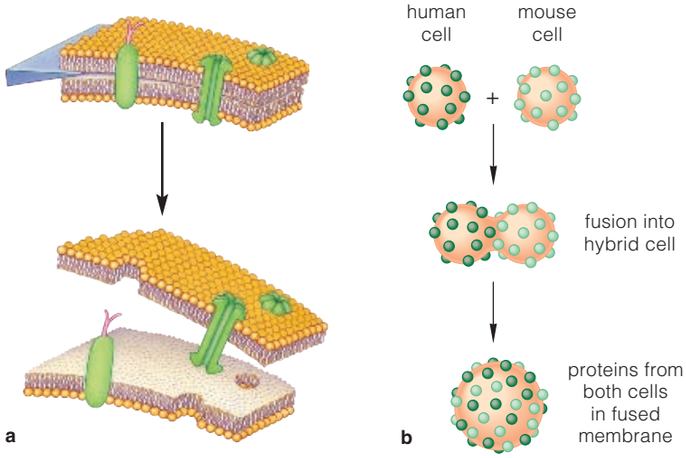


Figure 5.5 ***Animated!*** Studying membranes. (**a**) Researchers split the two layers of a cell membrane's lipid bilayer apart, which revealed that proteins are embedded in the bilayer. (**b**) Result of an experiment in which plasma membranes from cells of two species were induced to fuse. Membrane proteins from both drifted laterally and became mixed.

5.2 Overview of the Membrane Proteins

LINK TO SECTION 3.6

Cells interact with their surroundings through plasma membrane components. In membrane proteins, we see how structural diversity translates into functional diversity.

HOW ARE THE PROTEINS ORIENTED?

The fluid mosaic model is a good starting point for exploring membranes. But membranes differ in their composition and organization. Even the two surfaces of the same bilayer differ. For instance, many proteins (and lipids) of a plasma membrane have side chains of oligosaccharides and other carbohydrates, but only on the outward-facing surface (Figure 5.6). The kinds and number of side chains differ from one species to the next, even among cells of the same individual.

Integral proteins interact with hydrophobic parts of a bilayer's phospholipids. Most span the bilayer, with hydrophilic domains projecting beyond both surfaces. *Peripheral* proteins are located at one of the bilayer's surfaces. They interact weakly with integral proteins and with polar regions of membrane lipids.

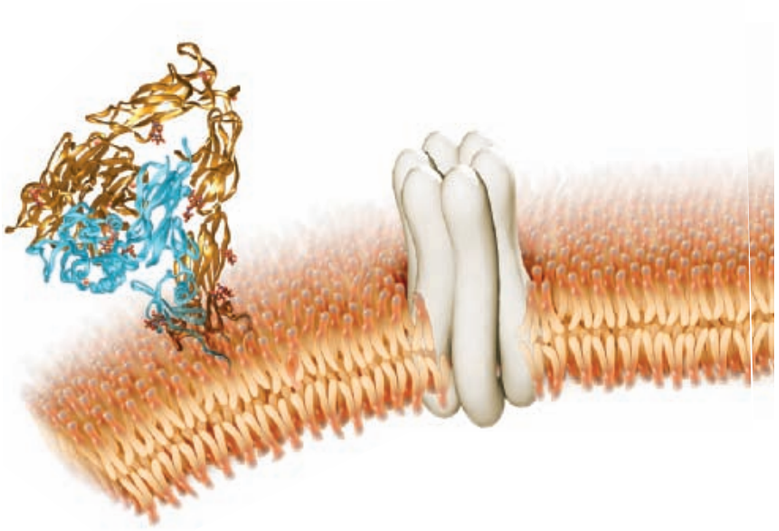
WHAT ARE THEIR FUNCTIONS?

Figure 5.6 shows the main membrane proteins, lists their defining features, and gives some examples. The **transport proteins** either passively let specific solutes diffuse through a membrane-spanning channel in their interior or actively pump them through. Transporters are incorporated into all cell membranes.

The other proteins shown are typical of the plasma membrane. The **receptor proteins** bind extracellular substances, such as hormones, that can trigger change in cell activities. For example, certain enzymes control cell growth and division. They are switched on when somatotropin binds with receptors for it. Cells differ in their combinations of receptors.

Multicelled organisms have **recognition proteins** that are unique identity tags for each species; they are like molecular fingerprints. **Adhesion proteins** help cells of the same type locate each other and remain in the proper tissues. The **communication proteins** form channels that match up across the plasma membranes of two cells. They let signals and substances rapidly flow from the cytoplasm of one into the other.

All cell membranes have transporters that passively and actively assist water-soluble substances across the lipid bilayer. The plasma membrane, especially of multicelled species, has diverse receptors and proteins that function in self-recognition, adhesion, and communication.



Adhesion Proteins

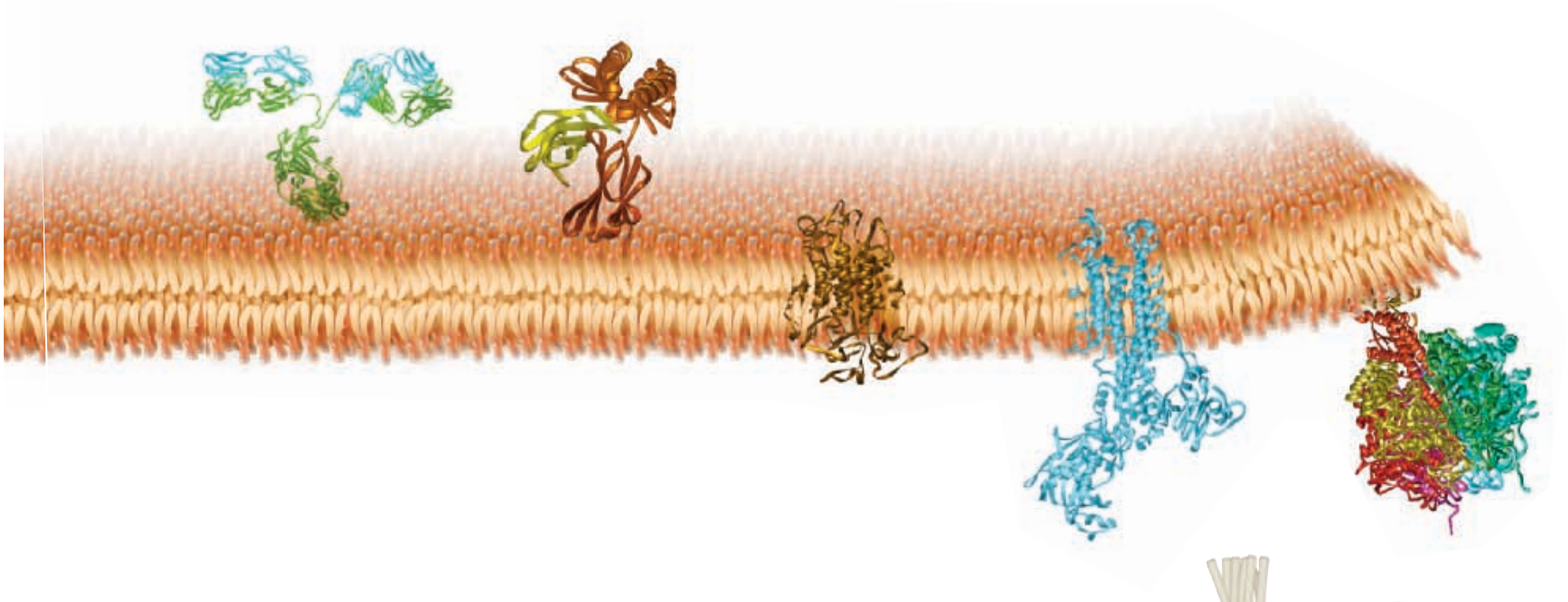
These proteins are embedded in the plasma membrane. They help one cell adhere to another or to a protein, such as collagen, that is part of an extracellular matrix.

Integrins, including this one, relay signals across the cell membrane. Cadherins of one cell bind with identical cadherins in adjoining cells. Selectins, which hold cells together, are abundant in endothelium, the special lining of blood vessels and the heart.

Communication Proteins

Communication proteins of one cell match up with identical proteins in the plasma membrane of an adjoining cell. Fingerlike projections of both intertwine in the space between the two cells. The result is a channel that directly connects the cytoplasm of both. Chemical and electrical signals flow fast through the channel.

This protein is one-half of a cardiac gap junction in heart muscle. The other half is in the lipid bilayer of another heart muscle cell (not shown) positioned above it. Signals flow so fast across such channels that heart muscle cells contract as a single functional unit.



Receptor Proteins

Receptors embedded in a membrane are docks for hormones and other signaling molecules that may cause target cells to change their activities.

A signal might make a cell synthesize a certain protein, block or speed a reaction, secrete a substance, or get ready to divide.

Shown above, an antibody, a type of receptor made only by the type of white blood cell known as the B lymphocytes. These receptors are vital for all immune responses (Chapter 39).

Recognition Proteins

Certain glycoproteins (and glycolipids) project above the plasma membrane and identify a cell as *nonself* (foreign) or *self* (belonging to one's own body or a tissue).

Some, such as the HLAs (page 49), function in tissue defense. Foreign fragments bound to HLA sound the alarm for cells that defend the body. Other recognition proteins help cells stick to one another in tissues.

Passive Transporters

Passive transporters have a channel through their interior. Different kinds assist solutes or water simply by letting them diffuse through the channel, down concentration or electric gradients (Section 5.4). They do not require activation by energy inputs.

Shown here, GluT1; when its channel changes shape, glucose can cross a membrane. Aquaporins are open channels for water (page 89).

One cotransporter helps chloride and bicarbonate ions across a membrane at the same time, in opposite directions.

Ion-selective channels have molecular gates. Some gates open or close fast if a small molecule binds to them or if the charge distribution across the membrane shifts. Nerve and muscle cells have gated channels for sodium, calcium, potassium, and chloride ions.

Active Transporters

Active transport proteins pump a solute across the membrane to the side where it is more concentrated and less likely to move on its own. They require energy inputs to do this. Some are cotransporters that let one kind of solute flow passively "downhill" even as they pump a different kind "uphill."

Left, a calcium pump. Like the sodium–potassium pump, it is one of the ATPases.

Right, a type of ATPase that pumps H^+ through its interior channel, against gradients. It also can let H^+ diffuse back through the channel in a way that drives ATP synthesis. Hence its more precise name, ATP synthase (Chapters 7 and 8).

Figure 5.6 ***Animated!*** Major categories of membrane proteins. Included are simple icons and descriptions for membrane proteins that you will encounter in later chapters. The transporters span the lipid bilayer of all cell membranes. The other proteins shown are components of plasma membranes. Bear in mind, cell membranes also incorporate additional kinds of proteins, including some enzymes.

5.3 Diffusion, Membranes, and Metabolism

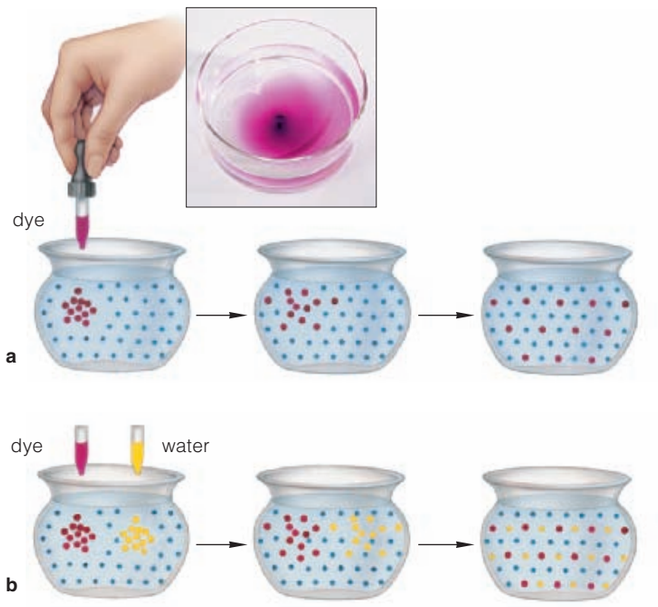
LINKS TO SECTIONS 2.3, 2.5, 3.4

What determines whether a substance will move one way or another to and from a cell, across that cell's membranes, or through the cell itself? Diffusion down concentration gradients is part of the answer.

WHAT IS A CONCENTRATION GRADIENT?

A **concentration gradient** is a difference in the number per unit volume of molecules (or ions) of a substance between two adjoining regions. In the absence of other forces, the molecules move from a region where they are more concentrated to a region where they are not as concentrated. Why? Their inherent thermal energy keeps them in constant motion, so that they collide at random and bounce off one another millions of times each second. This happens more in regions where the molecules are most concentrated, and when you add it all up, the *net* movement is toward the region where they are not colliding and bouncing around as much. The molecules flow down their concentration gradient.

Diffusion is the name for the net movement of like molecules or ions down a concentration gradient. It is a factor in how substances move into, through, and out of cells. In multicelled species, it moves substances between body regions and between the body and its environment. For instance, when photosynthesis is going on in leaf cells, oxygen builds up and diffuses out of the cells and into air spaces in the leaf, where its concentration is lower. It then diffuses into the air outside the leaf, where its concentration is lower still.



Like other substances, oxygen tends to diffuse in a direction set by its *own* concentration gradient, not by gradients of other solutes. You can see the outcome by squeezing a drop of dye into water. The dye molecules diffuse slowly into the region where they are not as concentrated, and the water molecules move into the region where *they* are not as concentrated. Figure 5.7 shows simple examples of diffusion.

WHAT DETERMINES DIFFUSION RATES?

How fast a particular solute diffuses depends on the steepness of its concentration gradient, its size, the temperature, and electric or pressure gradients that may be present.

First, rates are high with steep gradients, because more molecules are moving out of a region of greater concentration compared with the number moving into it. Second, more heat energy makes molecules move faster and collide more often in warmer regions. Third, smaller molecules diffuse faster than large ones do.

Fourth, an electric gradient may alter the rate and direction of diffusion. An **electric gradient** is simply a difference in electric charge between adjoining regions. For example, each ion dissolved in fluids bathing a cell membrane contributes to a local electric charge. Opposite charges attract. Therefore, the fluid having more negative charge overall exerts the greatest pull on positively charged substances, such as sodium ions. Later chapters explain how many cell activities, such as ATP formation and the sending and receiving of signals in nervous systems, require the driving force of electric and concentration gradients.

Fifth, diffusion also may be affected by a **pressure gradient**. This is a difference in pressure exerted per unit volume (or area) between two adjoining regions.

MEMBRANE CROSSING MECHANISMS

Now think about the water bathing the surfaces of a cell membrane. Plenty of substances are dissolved in it, but the kinds and amounts close to its two surfaces

Figure 5.7 ***Animated!*** Two examples of diffusion. (**a**) A drop of dye enters a bowl of water. Gradually, the dye molecules become evenly dispersed through the molecules of water. (**b**) The same thing happens with the water molecules. Here, dye (*red*) and water (*yellow*) are added to the same bowl. Each substance will show a net movement down its own concentration gradient.

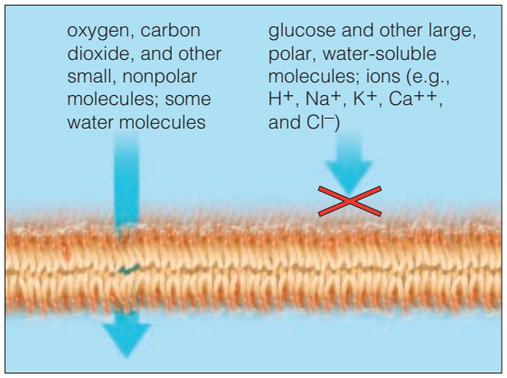


Figure 5.8 ***Animated!*** Selective permeability of cell membranes. Small, nonpolar molecules and some water molecules cross the lipid bilayer. Ions and large, polar, water-soluble molecules and the water dissolving them cross with the help of transport proteins. Also, proteins called aquaporins specifically enhance the diffusion of water across the plasma membrane of certain cells.

differ. The membrane itself helps set up and maintain these differences. How? Its diverse lipid and protein components show **selective permeability**. They allow some substances but not others to enter and leave a cell. They also control when each substance can cross and how much crosses at a given time (Figure 5.8).

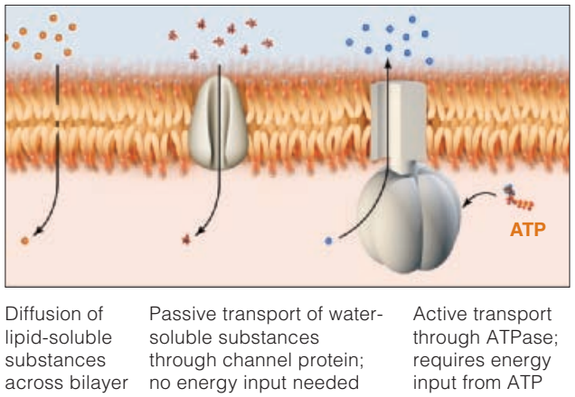
Membrane barriers and crossings are vital, because metabolism depends on the cell's capacity to increase, decrease, and maintain concentrations of substances required for reactions. That capacity also supplies the cell or organelles with raw materials, removes wastes, and maintains the cell volume and pH within ranges that favor reactions.

Lipids of a membrane's bilayer are mostly nonpolar, so they let small, nonpolar molecules such as O_2 and CO_2 slip across. Water molecules are polar, but some can slip through gaps that form when hydrophobic tails of lipids flex and bend (Section 5.1).

The lipid bilayer is impermeable to ions and large, polar molecules, including glucose. These substances cross a membrane by diffusing through the interior of transport proteins that span the bilayer. In many cells, proteins called aquaporins allow molecules of water to quickly cross the plasma membrane.

The passive transporters help specific solutes move down their concentration gradients but do not expend energy doing so. The mechanism, described shortly, is called *passive transport* or "facilitated" diffusion.

The active transporters help specific solutes diffuse across membranes, but they are not passive about it.



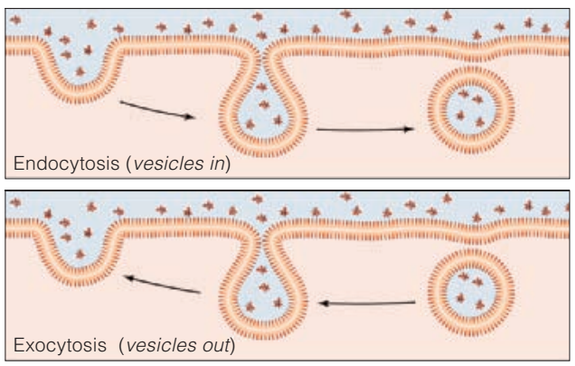


Figure 5.9 Overview of membrane crossing mechanisms.

They move solutes against concentration and electric gradients, and they require an input of energy to do so. We call this mechanism *active transport*.

Other mechanisms move large particles into or out of cells. In *endocytosis* a vesicle forms around particles when a patch of plasma membrane sinks inward and seals back on itself. In *exocytosis*, a vesicle that formed in the cytoplasm fuses with the plasma membrane, so that its contents are released to the outside.

Before getting into these diverse mechanisms, you may wish to study the overview in Figure 5.9.

Diffusion is the net movement of molecules or ions of a substance into an adjoining region where they are not as concentrated. The steepness of such a concentration gradient as well as temperature, molecular size, and electric and pressure gradients affect diffusion rates.

Cellular mechanisms increase and decrease concentration gradients across cell membranes.

5.4 Working With and Against Gradients

LINK TO SECTION 4.6

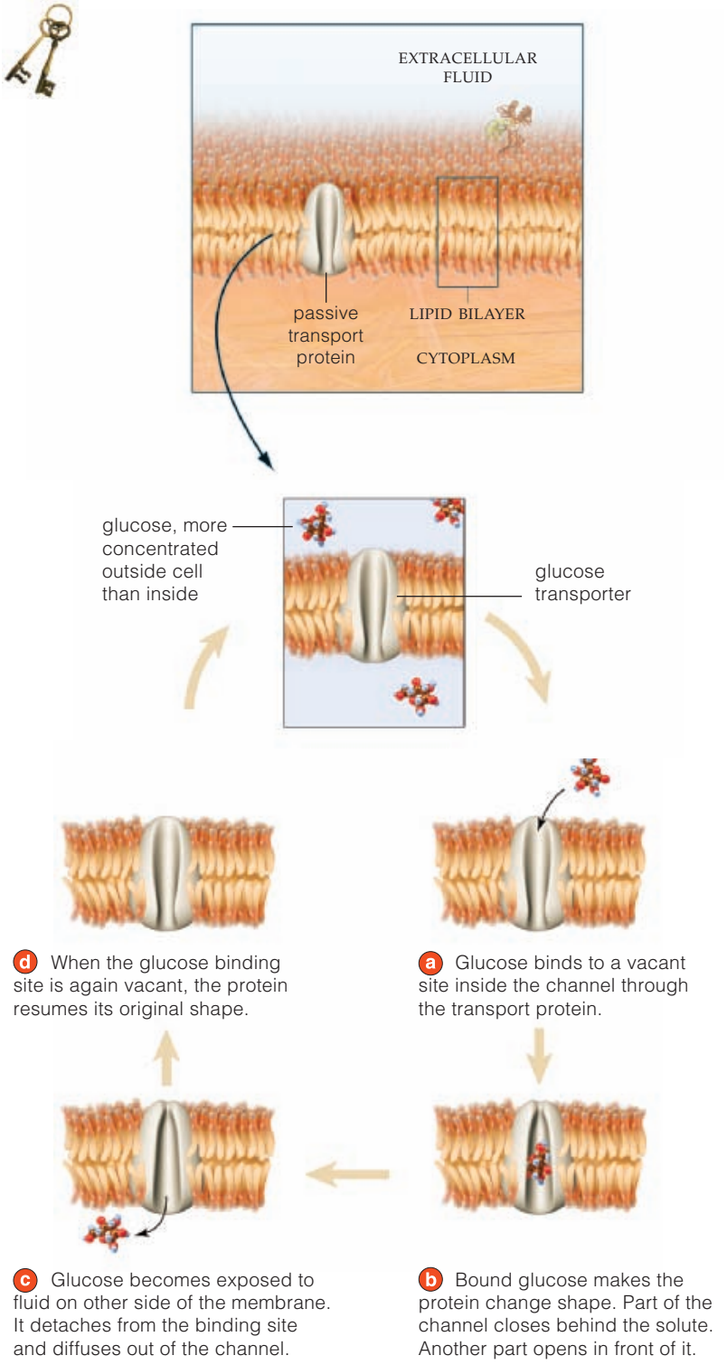


Figure 5.10 ***Animated!*** Passive transport. This model shows one of the glucose transporters that span the plasma membrane. Glucose crosses in both directions. The *net* movement of this solute is down its concentration gradient.

Large, polar molecules and ions cannot diffuse across a lipid bilayer. They require the help of transport proteins.

Many kinds of solutes cross a membrane by diffusing through a channel or tunnel inside transport proteins. When one solute molecule or ion enters the channel and weakly binds to the protein, the protein's shape changes. The channel closes behind the solute and opens in front of it, which exposes the solute to fluid on the other side of the membrane. Now the solute is released; the binding site reverts to its original shape.

PASSIVE TRANSPORT

In **passive transport**, a concentration gradient, electric gradient, or both drive diffusion of a substance across a cell membrane, through the interior of a transport protein. The protein does not require an energy input to assist the directional movement. That is why this mechanism is also known as facilitated diffusion.

Some passive transporters are open channels; others open or close as conditions change. Figure 5.10 shows how a glucose transporter works. When one end of its channel is shut, the other is open and invites glucose in. The channel closes behind the glucose and opens in front of it, on the other side of the membrane.

The *net* direction of a solute's movement depends on how many of its molecules or ions are randomly colliding with the transporters. Encounters simply are more frequent on the side of the membrane where its concentration is greatest. The solute's *net* movement tends to be toward the side of the membrane where it is less concentrated.

If nothing else were going on, passive transport would continue until concentrations on both sides of a membrane were equal. However, other events affect the outcome. For example, the bloodstream moves glucose to all tissues. There, glucose transporters help molecules of glucose get into cells. But as fast as some glucose molecules are diffusing into the cells, others are being used as building blocks and energy sources. By *using* glucose, then, cells help maintain a gradient that favors the uptake of *more* glucose molecules.

ACTIVE TRANSPORT

Solute concentrations continually shift across the cell membrane. Living cells never stop expending energy to pump solutes into and out of their interior. With **active transport**, energy-driven protein motors help a particular kind of solute cross a cell membrane *against* its concentration gradient.

Only specific solutes can bind to functional groups that line the interior channel of an active transporter, which is activated by a phosphate group from an ATP molecule. The phosphate-group transfer changes the transporter's shape in a way that releases the solute on the other side of the membrane.

Figure 5.11 focuses on a **calcium pump**. This active transporter helps keep the concentration of calcium in a cell at least a thousand times lower than outside. What is so great about that? You will find out later, but for now think of how one of your muscle moves. The nervous system commands calcium ions to flood out from a specialized ER compartment that threads around muscle fibers inside the muscle. Calcium ions clear the way for trillions of motor proteins (myosins) to interact with actin filaments in ways that bring about contraction (Section 37.7). That muscle will go on contracting until staggering numbers of calcium pumps move those ions back inside the compartment, against their concentation gradient.

The **sodium–potassium pump** is a cotransporter that moves two kinds of ions in opposite directions. Sodium ions (Na^+) from the cytoplasm diffuse into the pump's channel and bind to functional groups. A phosphate-group transfer by ATP activates the pump, which changes shape. The change opens the channel on other side of the membrane, where Na^+ is released and potassium (K^+) diffuses in—down *its* gradient. The phosphate group is released. The channel closes behind the K^+, which is released to the other side of the membrane. As you will see, the nervous, digestive, and urinary systems of vertebrates cannot function without cellular pumps that respond to signals and to chemical changes (Sections 34.3, 41.5, and 42.3).

All cells incorporate membrane pumps. In Section 32.3, you will read about an H^+ pump that controls the transport of a hormone in growing plant parts.

Many membrane transport proteins act as open or gated channels across cell membranes. They undergo reversible changes in shape that assist solutes across the membrane.

In passive transport, a transporter allows a solute to cross a cell membrane simply by diffusing through its interior.

In active transport, the net diffusion of a specific solute is against its gradient. The transporter must be activated, usually by an energy input from ATP, which counters the force inherent in the gradient.

Passive and active transport continually help lower or raise gradients across a membrane, which helps the cell respond to signals and to chemical changes.

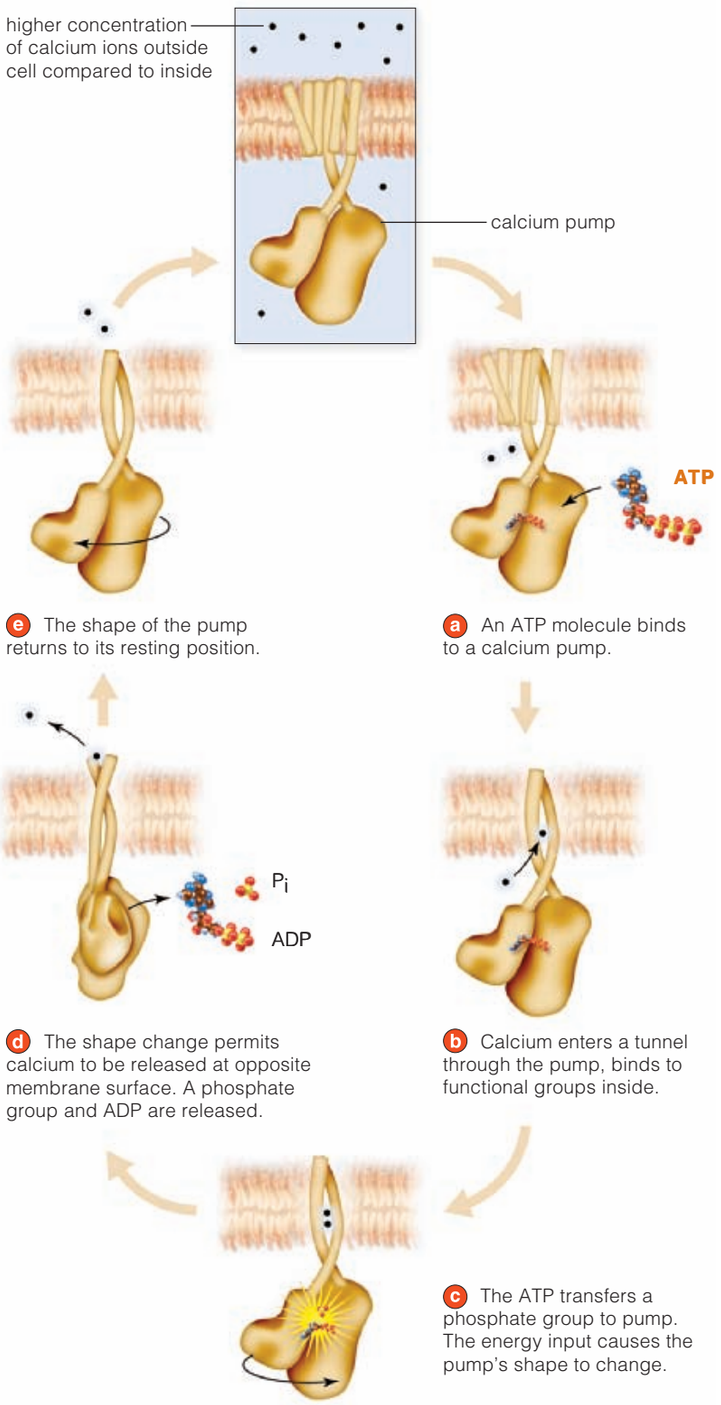


Figure 5.11 ***Animated!*** Active transport. This example uses a calcium pump that spans the plasma membrane. This sketch shows its channel for calcium ions. After two calcium ions bind to the pump, ATP transfers a phosphate group to it, thus providing energy that drives the movement of calcium *against* a concentration gradient across the cell membrane.

5.5 Which Way Will Water Move?

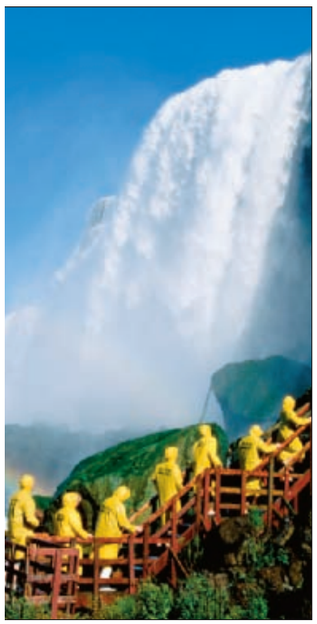
LINKS TO SECTIONS 2.5, 4.8, 4.9

By far, more water diffuses across cell membranes than any other substance, so the main factors that influence its directional movement deserve special attention.

MOVEMENT OF WATER

Something as gentle as a running faucet or as mighty as Niagara Falls demonstrates **bulk flow**, or the mass movement of one or more substances in response to pressure, gravity, or another external force. Bulk flow accounts for some movement of water in multicelled organisms. A beating heart generates fluid pressure that pumps blood, which is mostly water. Sap flows inside tubes in trees, and this, too, is bulk flow.

What about the movement of water into and out of cells and organelles? If the concentration of water is not equal on both sides of a membrane, osmosis will probably occur. **Osmosis** is the diffusion of water across a selectively permeable membrane, to a region where the water concentration is lower.



You might be wondering: How can water —a liquid—be more or less concentrated? For the answer, you have to think of water in terms of its concentration relative to the amounts of solutes that may be dissolved in it. The greater the solute concentration, the lower the water concentration.

Visualize yourself pouring some glucose or another solute to a glass of water, so that you increase the volume of liquid. The glass has the same number of water molecules but in a greater volume of liquid.

Now visualize yourself using a membrane to divide the inside of another glass of water into two compartments. The membrane lets water but not glucose diffuse across it. Next, add glucose on one side of the membrane. Water follows its concentration gradient into the glucose solution until its concentration is the same on both sides of the membrane (Figure 5.12).

In cases of osmosis, "solute concentration" refers to the total number of molecules or ions in a volume of a solution. It does not matter whether the dissolved substance is glucose, urea, or anything else. The type of solute does not dictate water concentration.

EFFECTS OF TONICITY

Suppose you decide to test the statement that water tends to move into a region where solutes are more concentrated. You make three sacs from a membrane that water but not sucrose can cross, and fill each one with a solution that is 2 percent sucrose. You immerse the first sac in a liter of distilled water, the second sac in a solution that is 10 percent sucrose, and the third sac in a solution that is 2 percent sucrose.

In each experiment, tonicity dictates the extent and direction of water movement across the membrane, as Figure 5.13 shows. *Tonicity* refers to the relative solute concentrations of two fluids. When two fluids that are on opposing sides of a membrane differ in their solute concentrations, the **hypotonic solution** is the one with fewer solutes. The one having more solutes is a **hypertonic solution**. Water tends to diffuse from a hypotonic fluid into a hypertonic fluid. **Isotonic solutions** show no net osmotic movement.

Most cells have built-in mechanisms that counter shifts in tonicity. Red blood cells do not. Figure 5.13 shows what would happen to them if tonicity were to change. Normally, fluid in red blood cells is isotonic with tissue fluid. If the tissue fluid became hypotonic, too much water would diffuse into the cells, which would burst. If that tissue fluid became hypertonic, water would diffuse out, and the cells would shrivel.

EFFECTS OF FLUID PRESSURE

Most cells do not swell and burst from an influx of water by osmosis. For one thing, they can selectively transport solutes out. For another thing, the cells of plants and many protists, fungi, and bacteria have a

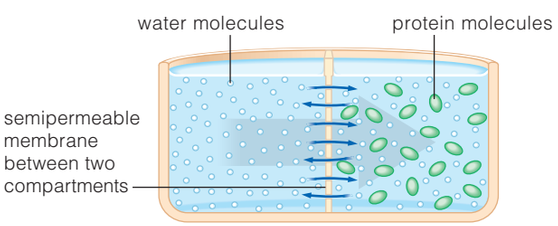


Figure 5.12 Solute concentration gradients and osmosis. A membrane divides this container into two compartments. Water but not proteins can cross it. Pour 1 liter of water in the left compartment and 1 liter of a protein-rich solution in the right compartment. The proteins occupy some of the space available, and the net diffusion of water in this case is from left to right (large *gray* arrow).

wall that helps keep them from rupturing when they become turgid, or swollen with fluid.

In later chapters, you will see how osmosis affects the water and solutes inside plants and animals. For now, just think about the hypotonic and hypertonic solutions in Figure 5.14. Water molecules move back and forth until the water concentration is equal on both sides of a membrane that separates them. But the volume of the formerly hypertonic solution has now increased, because its solutes cannot diffuse out.

The same thing happens in plant cells, which tend to be hypertonic relative to soil water. When a young plant cell grows, water moves into it by osmosis and exerts fluid pressure on its primary wall (Section 4.9). Up to a point, this pliable wall expands under fluid pressure, and the cell increases in volume. Continued expansion ends when the wall shows enough resistance to stop the further inward movement of water.

Any volume of fluid exerts **hydrostatic pressure**, or *turgor* pressure, against the wall or membrane that contains it. The **osmotic pressure** of any fluid is one measure of the tendency of water to follow its water concentration gradient and move into that fluid. When hydrostatic pressure and osmotic pressure are equal in magnitude, osmosis stops completely.

Plant cells also are vulnerable to the loss of water, which can occur when soil dries or becomes too salty. Water stops diffusing in and starts diffusing out, so hydrostatic pressure falls and the cytoplasm shrinks.

Osmosis is a net diffusion of water between two solutions that differ in solute concentration and are separated by a selectively permeable membrane. The greater the number of molecules and ions dissolved in a given amount of water, the lower the water concentration will be.

Water tends to move osmotically to regions of greater solute concentration (from hypotonic to hypertonic solutions). There is no net diffusion between isotonic solutions.

Fluid pressure that a solution exerts against a membrane or wall influences the osmotic movement of water.

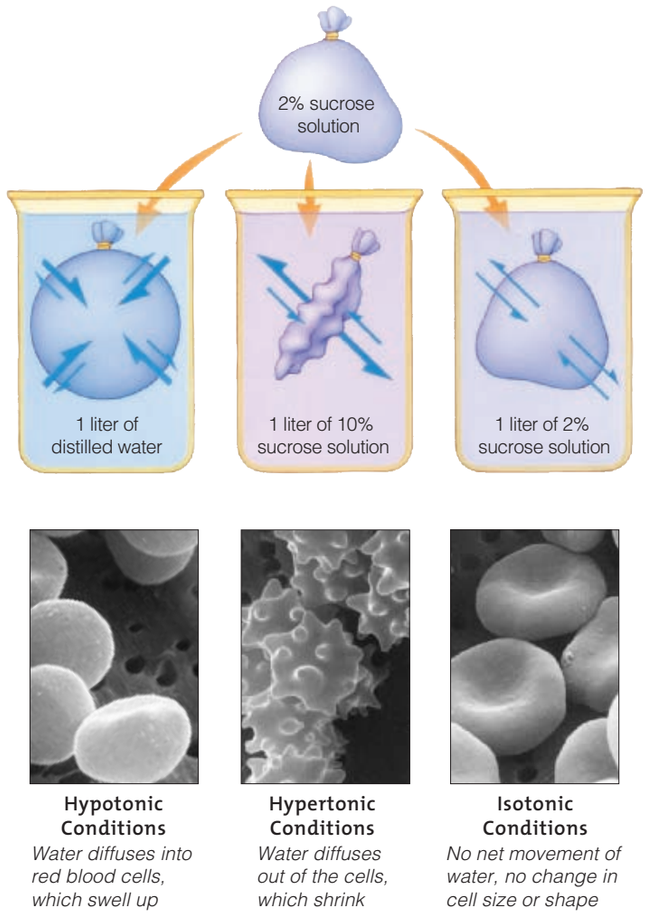


Figure 5.13 ***Animated!*** Tonicity and the direction of water movement between two adjoining regions. In each of three containers, arrow widths signify the direction and the relative amounts of flow. The micrographs below each sketch show the shape of a human red blood cell that is immersed in fluids of higher, lower, or equal concentrations of solutes. The solutions inside and outside red blood cells are normally balanced. This type of cell has no way to adjust to drastic change in solute levels in its fluid surroundings.

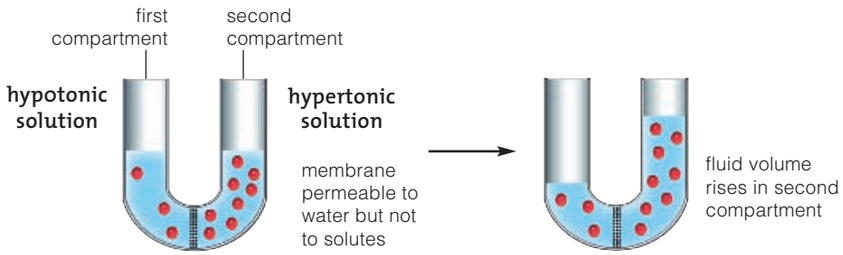


Figure 5.14 ***Animated!*** Experiment showing an increase in fluid volume as an outcome of osmosis. A selectively permeable membrane separates two compartments. Over time, the net diffusion will be the same in both directions across the membrane, but the fluid volume in the second compartment will be greater because there are more solute molecules in it.

5.6 Membrane Traffic To and From the Cell Surface

LINKS TO SECTIONS 4.6, 4.11

We leave this chapter with another look at exocytosis and endocytosis. By these mechanisms, vesicles move substances to and from the plasma membrane. Vesicles help the cell take in and expel materials in larger packets than transport proteins would be able to handle.

ENDOCYTOSIS AND EXOCYTOSIS

Think back on the lipid bilayer and how it minimizes the number of hydrophobic groups exposed to water. When the arrangement is disrupted—as when part of the plasma membrane or an organelle pinches off as a vesicle—the bilayer becomes self-sealing. Why? The disruption exposes too many of hydrophobic groups to the surroundings. When a patch of membrane is budding off, its phospholipids are being repelled by water on both sides of it. The water molecules "push" the phospholipids together, which rounds off the bud as a vesicle and also seals the rupture.

The lipid bilayer's self-sealing behavior is the basis of membrane traffic to and from a cell surface (Figure 5.15). That traffic moves in two directions.

By **endocytosis**, a small patch of plasma membrane balloons inward and pinches off inside the cytoplasm. It forms an endocytic vesicle that moves its contents to some organelle or stores them in a cytoplasmic region. By **exocytosis**, a vesicle moves to the cell surface, and then the protein-studded lipid bilayer of its membrane fuses with the plasma membrane. While this exocytic vesicle is losing its identity, its contents are released to the outside (Figure 5.15).

There are three endocytic pathways. With *receptor-mediated* endocytosis, a hormone, vitamin, mineral, or another substance binds to receptors at the plasma membrane. A slight depression, or pit, forms in the plasma membrane beneath the receptors. The pit sinks into the cytoplasm as hydrophobic interactions cause a vesicle to form (Figure 5.16).

Phagocytosis ("cell eating") is a common endocytic pathway. Phagocytes such as amoebas engulf microbes, food particles, or cellular debris. In multicelled species, macrophages and some other white blood cells engulf pathogenic viruses and bacteria, cancerous body cells, and other threats. Receptors play a different role in phagocytosis. When they bind to a specific substance, they cause microfilaments to become rearranged into a mesh just beneath the phagocyte's plasma membrane. The microfilaments contract and a bulging volume of cytoplasm is squeezed toward the cell periphery. The bulge, still enclosed in the plasma membrane, extends outward as a pseudopod (Section 4.11 and Figure 5.17).

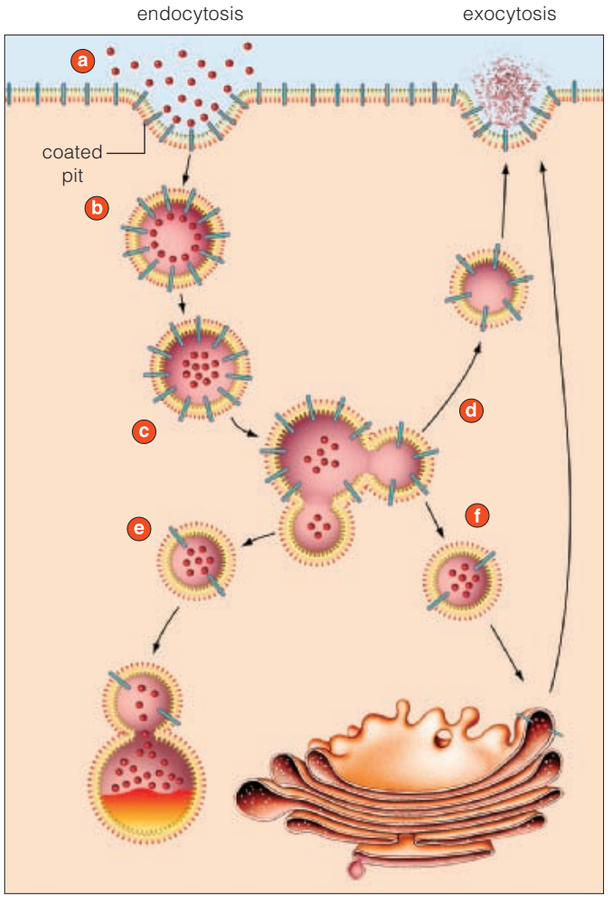


Figure 5.15 ***Animated!*** Endocytosis and exocytosis. This sketch starts with receptor-mediated endocytosis. (**a**) Molecules get concentrated inside coated pits at the plasma membrane. (**b**) The pits sink inward and become endocytic vesicles. (**c**) The vesicle contents are sorted and often released from receptors. (**d**) Many sorted molecules are cycled back to the plasma membrane. (**e**,**f**) Many others are delivered to lysosomes and stay there or are degraded. Still others are routed to spaces in the nuclear envelope and inside ER membranes, and others to Golgi bodies.

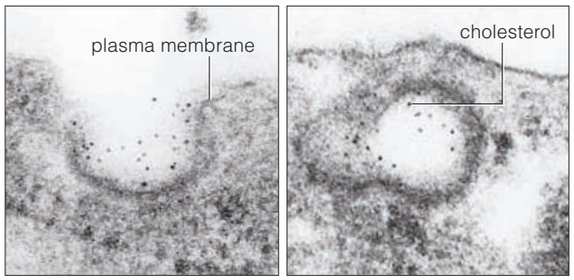


Figure 5.16 Endocytosis of cholesterol molecules.

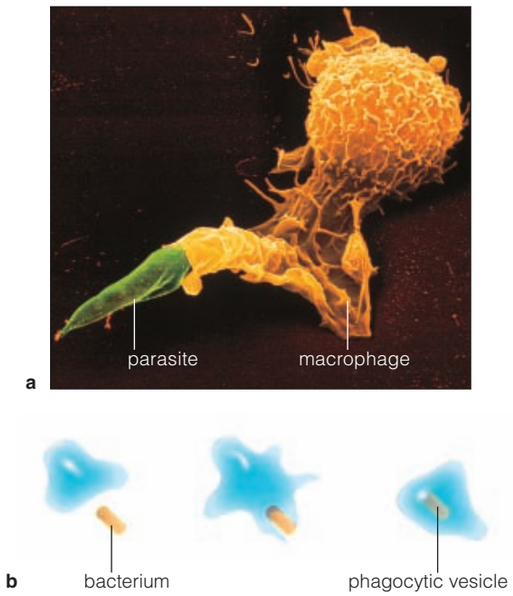


Figure 5.17 (**a**) A macrophage engulfing *Leishmania mexicana*. This parasitic protozoan causes leishmaniasis, an often-fatal disease. Bites from infected sandflies can transmit the parasite to humans. (**b**) Phagocytosis. Lobes of an amoeba's cytoplasm surround a target. The plasma membrane of the extensions fuses to form a phagocytic vesicle. In the cytoplasm, this endocytic vesicle fuses with lysosomes, which digest its contents.

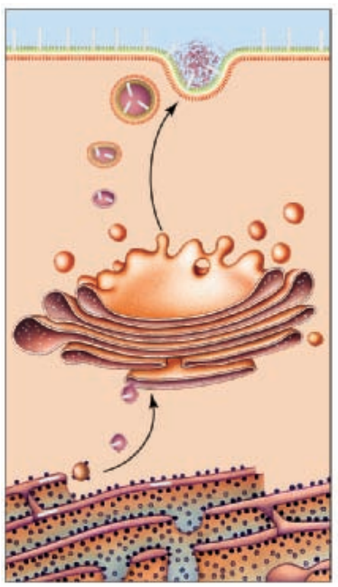


Figure 5.18 Example of how the asymmetric distribution of proteins, carbohydrates, and lipids in cell membranes originates. Proteins of the plasma membrane start out as new polypeptide chains, which become modified inside the channels of the ER and Golgi bodies. Many depart in vesicles that bud off, move to the plasma membrane, and fuse with it. The proteins inside automatically become oriented in the proper direction in the plasma membrane.

Pseudopods flow completely around their target and then form a cytoplasmic vesicle. The vesicle sinks into the cytoplasm and fuses with lysosomes (Section 4.6). Lysosomal enzymes digest the vesicle's contents into fragments and smaller, reusable molecules.

Bulk-phase endocytosis is not as selective. A vesicle forms around a small volume of the extracellular fluid regardless of the kinds of substances dissolved in it.

MEMBRANE CYCLING

As long as a cell is alive, exocytosis and endocytosis are continually replacing and withdrawing patches of its plasma membrane, as in Figure 5.15. Apparently they do so at rates that maintain the total surface area of the plasma membrane. Steady losses in the form of endocytic membranes are balanced by replacements in the form of exocytic membranes.

For example, neurons release neurotransmitters in bursts of exocytosis. Each neurotransmitter is a type of signaling molecule that acts on neighboring cells. An intense burst of endocytosis counterbalances each major burst of exocytosis.

The membranes are not shipped any which way. As an example, the composition and organization of the plasma membrane start inside the ER membranes, where many polypeptide chains become modified before being packaged and moved on to their final destinations (Section 4.6). Proteins that will become part of the plasma membrane are shipped in vesicles that fuse with a Golgi body. There, they are further modified, then sent off in other vesicles that fuse with the plasma membrane. As Figure 5.18 shows, fusion releases the proteins to the membrane surface that faces outside. There they will perform their functions.

Whereas transport proteins in a plasma membrane deal with ions and small molecules, exocytosis and endocytosis move large packets of materials in bulk across a plasma membrane.

By exocytosis, a cytoplasmic vesicle fuses with the plasma membrane, and its contents are released outside the cell.

By endocytosis, a small patch of plasma membrane sinks into the cytoplasm and pinches off as a vesicle. Membrane receptors often activate cytoskeletal elements that take part in endocytosis.

Phagocytosis is a form of endocytosis by which predatory amoebas engulf prey and certain white blood cells actively engulf tissue invaders, tissue debris, and cancer cells.

Summary

Section 5.1 Animal cell membranes consist mainly of phospholipids, along with glycolipids and sterols. The lipids are organized as a double layer, with all of their hydrophobic tails sandwiched between hydrophilic heads at both surfaces.

The lipid bilayer gives a cell membrane its primary structure and prevents uncontrolled movement of water-soluble substances across it. Diverse proteins embedded in the bilayer or associated with one of its surfaces carry out most membrane functions.

Biology Now

Learn about membrane structure and the experiments that elucidated it with the animation on BiologyNow.

Section 5.2 Each cell membrane associates with cytoplasmic proteins that structurally reinforce it. Each has receptors at its surface. The plasma membrane also contains adhesion proteins, communication proteins, recognition proteins, and diverse receptors (Figure 5.19). Differences in the number and types of proteins affect responsiveness to substances at the membrane, as well as cell metabolism, pH, and volume.

Water-soluble substances cross cell membranes by passing through the interior of transport proteins, which open to both sides of the membrane.

Receptor proteins bind extracellular substances, and binding triggers alterations in cell activities.

Recognition proteins are molecular fingerprints; they identify cells as being of a given type. Adhesion proteins help cells of tissues adhere to one another and to proteins of the extracellular matrix.

Communication junctions extend across the plasma membranes of adjoining cells; they let substances and signals travel swiftly from one into the other.

Biology Now

Use the animation on BiologyNow to familiarize yourself with the functions of receptor proteins.

Section 5.3 A concentration gradient is a difference in the number per unit volume of molecules (or ions) of a substance between two regions. The molecules tend to show a net movement down such a gradient, to the region where they are less concentrated. This behavior is called diffusion. The steepness of a concentration gradient, temperature, molecular size, and gradients in electrical charge and pressure influence diffusion rates.

Built-in cellular mechanisms work with and against gradients to move solutes across membranes.

Molecular oxygen, carbon dioxide, and other small, nonpolar molecules easily diffuse across a membrane's lipid bilayer. Ions and large, polar molecules such as glucose cross it through the interior of transport proteins that span the bilayer. Water molecules slip through gaps that briefly open in the bilayer. Aquaporins selectively assist water molecules across certain cell membranes.

Biology Now

Investigate diffusion across membranes with the interaction on BiologyNow.

Section 5.4 Many solutes cross membranes through transport proteins that act as open or gated channels or that reversibly change shape. Passive transport does not require energy input; a solute is free to follow its own concentration gradient across the membrane. Active transport requires an energy input from ATP to move a specific solute against its concentration gradient.

Biology Now

Compare the processes of passive and active transport, using the animation on BiologyNow.

Section 5.5 Osmosis is the diffusion of water across a selectively permeable membrane. The water molecules move down a water concentration gradient, which is influenced by solute concentrations and pressure.

Biology Now

Explore the effects of osmosis with the interaction and animation on BiologyNow.

Section 5.6 By exocytosis, a cytoplasmic vesicle fuses with the plasma membrane, and its contents are released outside. By endocytosis, a patch of plasma membrane forms a vesicle that sinks into the cytoplasm.

Biology Now

Use the animation on BiologyNow to discover how membrane components are cycled.

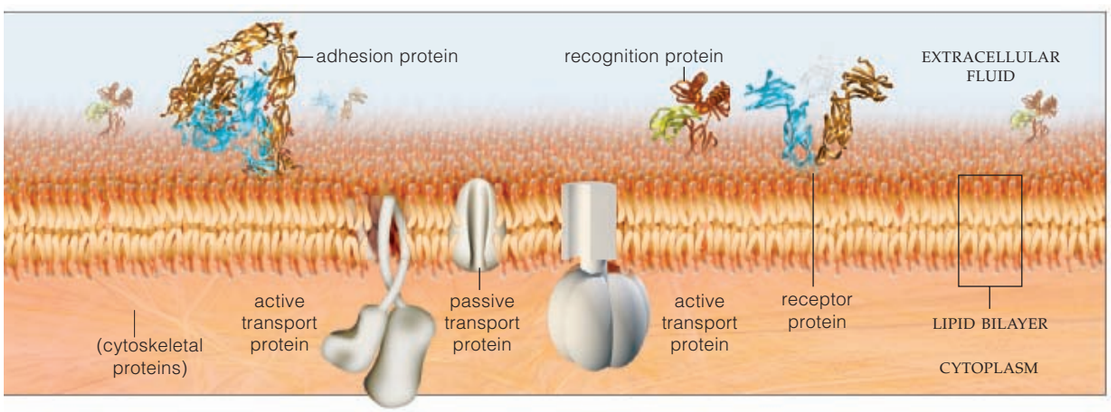


Figure 5.19 Summary of major types of membrane proteins.

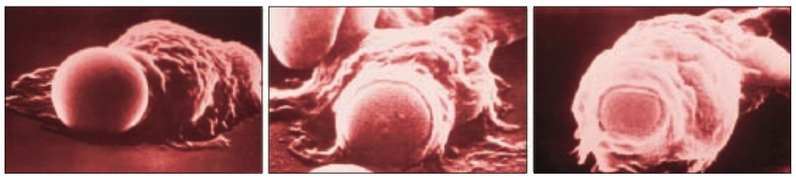


Figure 5.20 Go ahead, name the mystery membrane mechanism.

Self-Quiz

Answers in Appendix II

1. Cell membranes consist mainly of a _____ .
   a. carbohydrate bilayer and proteins
   b. protein bilayer and phospholipids
   c. lipid bilayer and proteins

2. In a lipid bilayer, _____ of all of the lipid molecules are sandwiched between all of the _____ .
   a. hydrophilic tails; hydrophobic heads
   b. hydrophilic heads; hydrophilic tails
   c. hydrophobic tails; hydrophilic heads
   d. hydrophobic heads; hydrophilic tails

3. Most membrane functions are carried out by _____ .
   a. proteins
   b. phospholipids
   c. nucleic acids
   d. hormones

4. Plasma membranes incorporate _____ .
   a. transport proteins
   b. adhesion proteins
   c. recognition proteins
   d. all of the above

5. Diffusion is the movement of ions or molecules from one region to another where they are less concentrated. The rate of diffusion is affected by _____ .
   a. temperature
   b. electrical gradients
   c. molecular size
   d. all of the above

6. _____ can readily diffuse across a lipid bilayer.
   a. Glucose
   b. Oxygen
   c. Carbon dioxide
   d. b and c

7. Some sodium ions cross a cell membrane through transport proteins that first must be activated by an energy boost. This is an example of _____ .
   a. passive transport
   b. active transport
   c. facilitated diffusion
   d. a and c

8. Immerse a living cell in a hypotonic solution, and water will tend to _____ .
   a. move into the cell
   b. move out of the cell
   c. show no net movement
   d. move in by endocytosis

9. Vesicles form by way of _____ .
   a. membrane cycling
   b. exocytosis
   c. phagocytosis
   d. halitosis
   e. a through c
   f. all of the above

10. Match the term with its most suitable description.

____ phagocytosis	a. molecular fingerprint
____ passive transport	b. basis of diffusion
____ recognition protein	c. big in membranes
____ active transport	d. one cell engulfs another
	e. requires energy boost
____ phospholipid	f. docks for signals and substances at cell surface
____ concentration gradient	g. no energy boost required to move solutes
____ receptors	

Additional questions are available on Biology Now™

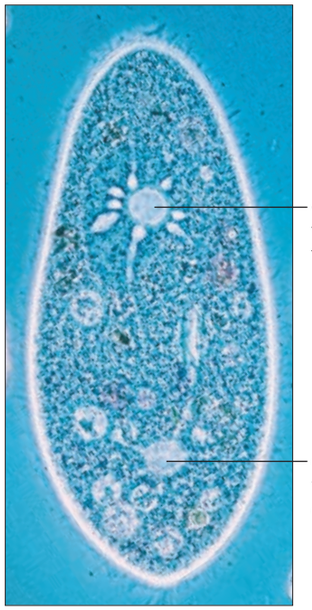


Figure 5.21 Light micrograph of one of the ciliated protozoans (*Paramecium*). This tiny single-celled body is crammed with diverse organelles, including contractile vacuoles.

Critical Thinking

1. Is the white blood cell shown in Figure 5.20 disposing of a worn-out red blood cell by endocytosis, phagocytosis, or both?

2. Water moves osmotically into *Paramecium*, a single-celled aquatic protist. If unchecked, the influx would bloat the cell and rupture its plasma membrane, and the cell would die. An energy-requiring mechanism that involves contractile vacuoles expels excess water (Figure 5.21). Water enters the vacuole's tubelike extensions and collects inside. A full vacuole contracts and squirts water out of the cell through a pore. Are *Paramecium*'s surroundings hypotonic, hypertonic, or isotonic?

3. Water crosses cell membranes by diffusing past lipids that are jostling apart from one another in the bilayer. In many tissues, it also crosses faster through the interior channels of *aquaporins* (*white* arrow in Figure 5.22). As many as 3 billion water molecules per second flow through an aquaporin. Researchers already have found similar aquaporins in bacteria, plants, and insects.

Different aquaporins help different tissues respond to shifting conditions in the internal environment. They have roles in how the kidneys conserve or get rid of excess water. They play a part in producing and maintaining the fluid that bathes the spinal cord and brain, in producing saliva and tears, in keeping the lining of the lungs moist, and in keeping red blood cells from bursting or shriveling as the body's water–solute balance shifts.

If the gene for one of these water channels mutates, the outcome may be serious. Mutation in *aquaporin–0* results in cataracts, and mutation in *aquaporin–2* leads to a form of diabetes insipidus. Yet *aquaporin–1* seems less essential. In its absence, affected adults tend to produce unusually dilute urine but remain in good health as long as they drink plenty of water. Even so, affected individuals are rare. Speculate on the reasons why.

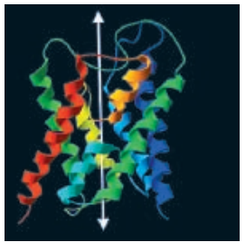


Figure 5.22 Model for one of the four aquaporin subunits.