

## 5.1 | Components and Structure

By the end of this section, you will be able to do the following:

- Understand the cell membrane fluid mosaic model
- Describe phospholipid, protein, and carbohydrate functions in membranes
- Discuss membrane fluidity

A cell's plasma membrane defines the cell, outlines its borders, and determines the nature of its interaction with its environment (see **Table 5.1** for a summary). Cells exclude some substances, take in others, and excrete still others, all in controlled quantities. The plasma membrane must be very flexible to allow certain cells, such as red and white blood cells, to change shape as they pass through narrow capillaries. These are the more obvious plasma membrane functions. In addition, the plasma membrane's surface carries markers that allow cells to recognize one another, which is vital for tissue and organ formation during early development, and which later plays a role in the immune response's "self" versus "non-self" distinction.

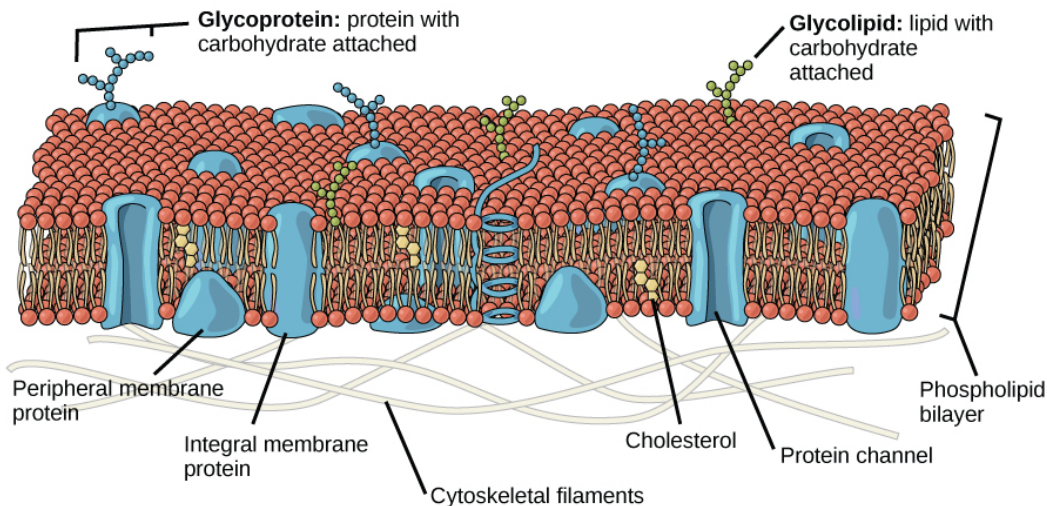
Among the most sophisticated plasma membrane functions is the ability for complex, integral proteins, receptors to transmit signals. These proteins act both as extracellular input receivers and as intracellular processing activators. These membrane receptors provide extracellular attachment sites for effectors like hormones and growth factors, and they activate intracellular response cascades when their effectors are bound. Occasionally, viruses hijack receptors (HIV, human immunodeficiency virus, is one example) that use them to gain entry into cells, and at times, the genes encoding receptors become mutated, causing the signal transduction process to malfunction with disastrous consequences.

### Fluid Mosaic Model

Scientists identified the plasma membrane in the 1890s, and its chemical components in 1915. The principal components they identified were lipids and proteins. In 1935, Hugh Davson and James Danielli proposed the plasma membrane's structure. This was the first model that others in the scientific community widely accepted. It was based on the plasma membrane's "railroad track" appearance in early electron micrographs. Davson and Danielli theorized that the plasma membrane's structure resembles a sandwich. They made the analogy of proteins to bread, and lipids to the filling. In the 1950s, advances in microscopy, notably transmission electron microscopy (TEM), allowed researchers to see that the plasma membrane's core consisted of a double, rather than a single, layer. In 1972, S.J. Singer and Garth L. Nicolson proposed a new model that provides microscopic observations and better explains plasma membrane function.

The explanation, the **fluid mosaic model**, has evolved somewhat over time, but it still best accounts for plasma membrane structure and function as we now understand them. The fluid mosaic model describes the plasma membrane structure as a mosaic of components—including phospholipids, cholesterol, proteins, and carbohydrates—that gives the membrane a fluid character. Plasma membranes range from 5 to 10 nm in thickness. For comparison, human red blood cells, visible via light microscopy, are approximately 8  $\mu\text{m}$  wide, or approximately 1,000 times wider than a plasma membrane. The membrane does look a bit like a sandwich (**Figure 5.2**).





**Figure 5.2** The plasma membrane fluid mosaic model describes the plasma membrane as a fluid combination of phospholipids, cholesterol, and proteins. Carbohydrates attached to lipids (glycolipids) and to proteins (glycoproteins) extend from the membrane's outward-facing surface.

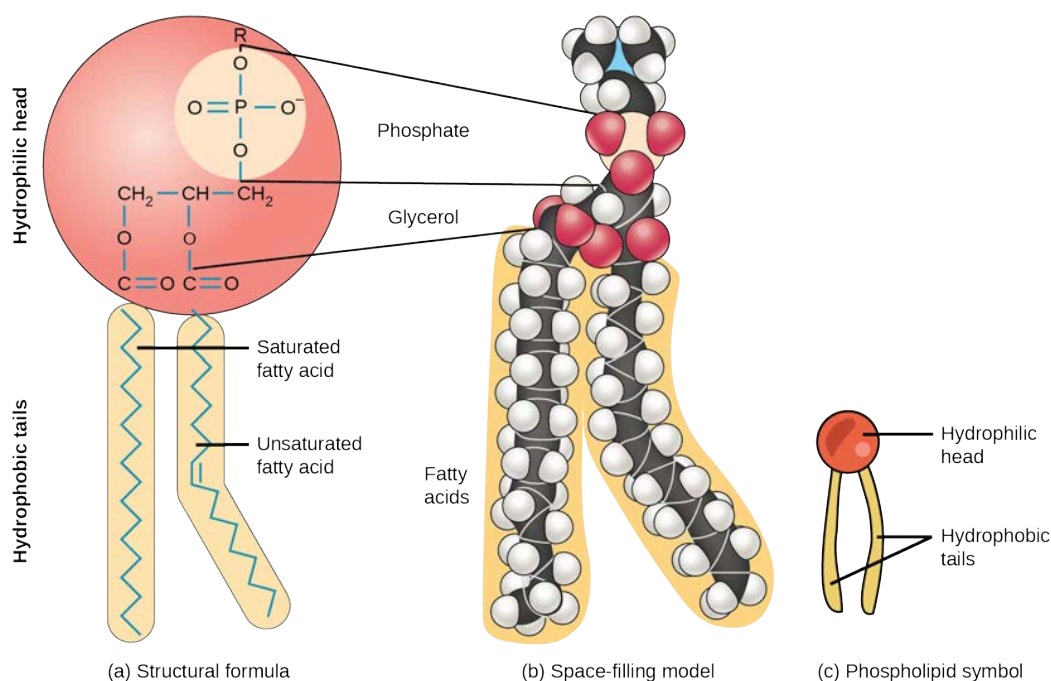
A plasma membrane's principal components are lipids (phospholipids and cholesterol), proteins, and carbohydrates attached to some of the lipids and proteins. A phospholipid is a molecule consisting of glycerol, two fatty acids, and a phosphate-linked head group. Cholesterol, another lipid comprised of four fused carbon rings, is situated alongside the phospholipids in the membrane's core. The protein, lipid, and carbohydrate proportions in the plasma membrane vary with cell type, but for a typical human cell, protein accounts for about 50 percent of the composition by mass, lipids (of all types) account for about 40 percent, and carbohydrates comprise the remaining 10 percent. However, protein and lipid concentration varies with different cell membranes. For example, myelin, an outgrowth of specialized cells' membrane that insulates the peripheral nerves' axons, contains only 18 percent protein and 76 percent lipid. The mitochondrial inner membrane contains 76 percent protein and only 24 percent lipid. The plasma membrane of human red blood cells is 30 percent lipid. Carbohydrates are present only on the plasma membrane's exterior surface and are attached to proteins, forming **glycoproteins**, or attached to lipids, forming **glycolipids**.

### Phospholipids

The membrane's main fabric comprises amphiphilic, phospholipid molecules. The **hydrophilic** or “water-loving” areas of these molecules (which look like a collection of balls in an artist's rendition of the model) (**Figure 5.2**) are in contact with the aqueous fluid both inside and outside the cell. **Hydrophobic**, or water-hating molecules, tend to be non-polar. They interact with other non-polar molecules in chemical reactions, but generally do not interact with polar molecules. When placed in water, hydrophobic molecules tend to form a ball or cluster. The phospholipids' hydrophilic regions form hydrogen bonds with water and other polar molecules on both the cell's exterior and interior. Thus, the membrane surfaces that face the cell's interior and exterior are hydrophilic. In contrast, the cell membrane's interior is hydrophobic and will not interact with water. Therefore, phospholipids form an excellent two-layer cell membrane that separates fluid within the cell from the fluid outside the cell.

A phospholipid molecule (**Figure 5.3**) consists of a three-carbon glycerol backbone with two fatty acid molecules attached to carbons 1 and 2, and a phosphate-containing group attached to the third carbon. This arrangement gives the overall molecule a head area (the phosphate-containing group), which has a polar character or negative charge, and a tail area (the fatty acids), which has no charge. The head can form hydrogen bonds, but the tail cannot. Scientists call a molecule with a positively or negatively charged area and an uncharged, or non-polar, area **amphiphilic** or “dual-loving.”

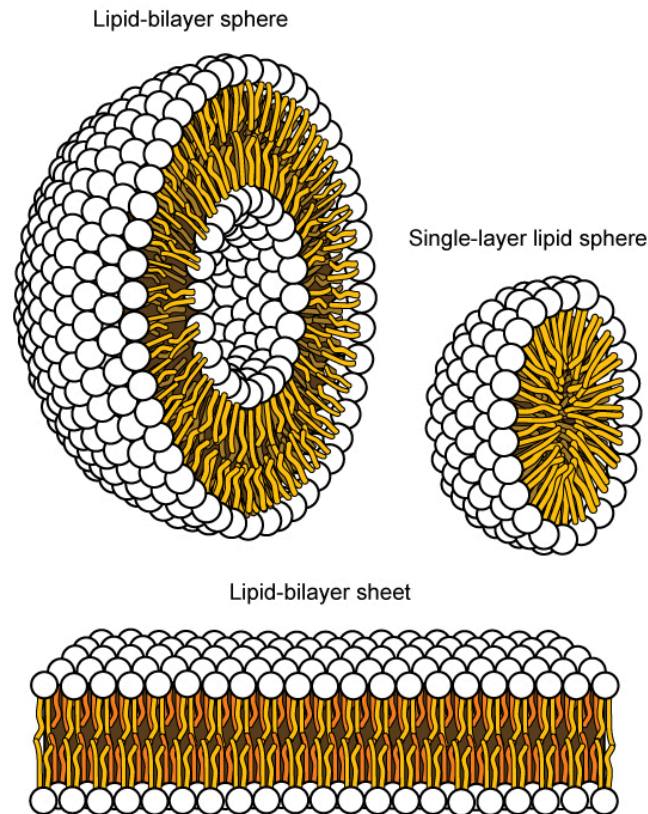




**Figure 5.3** A hydrophilic head and two hydrophobic tails comprise this phospholipid molecule. The hydrophilic head group consists of a phosphate-containing group attached to a glycerol molecule. The hydrophobic tails, each containing either a saturated or an unsaturated fatty acid, are long hydrocarbon chains.

This characteristic is vital to the plasma membrane's structure because, in water, phospholipids arrange themselves with their hydrophobic tails facing each other and their hydrophilic heads facing out. In this way, they form a lipid bilayer—a double layered phospholipid barrier that separates the water and other materials on one side from the water and other materials on the other side. Phospholipids heated in an aqueous solution usually spontaneously form small spheres or droplets (micelles or liposomes), with their hydrophilic heads forming the exterior and their hydrophobic tails on the inside (**Figure 5.4**).

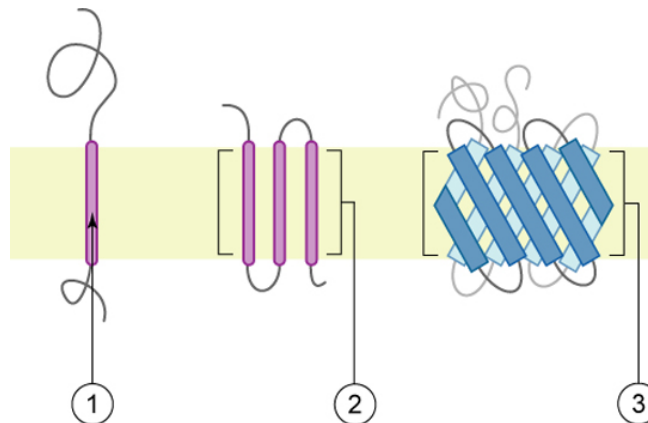




**Figure 5.4** In an aqueous solution, phospholipids usually arrange themselves with their polar heads facing outward and their hydrophobic tails facing inward. (credit: modification of work by Mariana Ruiz Villareal)

### Proteins

Proteins comprise the plasma membranes' second major component. **Integral proteins**, or integrins, as their name suggests, integrate completely into the membrane structure, and their hydrophobic membrane-spanning regions interact with the phospholipid bilayer's hydrophobic region (**Figure 5.2**). Single-pass integral membrane proteins usually have a hydrophobic transmembrane segment that consists of 20–25 amino acids. Some span only part of the membrane—associating with a single layer—while others stretch from one side to the other, and are exposed on either side. Up to 12 single protein segments comprise some complex proteins, which are extensively folded and embedded in the membrane (**Figure 5.5**). This protein type has a hydrophilic region or regions, and one or several mildly hydrophobic regions. This arrangement of protein regions orients the protein alongside the phospholipids, with the protein's hydrophobic region adjacent to the phospholipids' tails and the protein's hydrophilic region or regions protruding from the membrane and in contact with the cytosol or extracellular fluid.



**Figure 5.5** Integral membrane proteins may have one or more alpha-helices that span the membrane (examples 1 and 2), or they may have beta-sheets that span the membrane (example 3). (credit: "Foobar"/Wikimedia Commons)



**Peripheral proteins** are on the membranes' exterior and interior surfaces, attached either to integral proteins or to phospholipids. Peripheral proteins, along with integral proteins, may serve as enzymes, as structural attachments for the cytoskeleton's fibers, or as part of the cell's recognition sites. Scientists sometimes refer to these as “cell-specific” proteins. The body recognizes its own proteins and attacks foreign proteins associated with invasive pathogens.

### Carbohydrates

Carbohydrates are the third major plasma membrane component. They are always on the cells' exterior surface and are bound either to proteins (forming glycoproteins) or to lipids (forming glycolipids) (**Figure 5.2**). These carbohydrate chains may consist of 2–60 monosaccharide units and can be either straight or branched. Along with peripheral proteins, carbohydrates form specialized sites on the cell surface that allow cells to recognize each other. These sites have unique patterns that allow for cell recognition, much the way that the facial features unique to each person allow individuals to recognize him or her. This recognition function is very important to cells, as it allows the immune system to differentiate between body cells (“self”) and foreign cells or tissues (“non-self”). Similar glycoprotein and glycolipid types are on the surfaces of viruses and may change frequently, preventing immune cells from recognizing and attacking them.

We collectively refer to these carbohydrates on the cell's exterior surface—the carbohydrate components of both glycoproteins and glycolipids—as the glycocalyx (meaning “sugar coating”). The glycocalyx is highly hydrophilic and attracts large amounts of water to the cell's surface. This aids in the cell's interaction with its watery environment and in the cell's ability to obtain substances dissolved in the water. As we discussed above, the glycocalyx is also important for cell identification, self/non-self determination, and embryonic development, and is used in cell to cell attachments to form tissues.

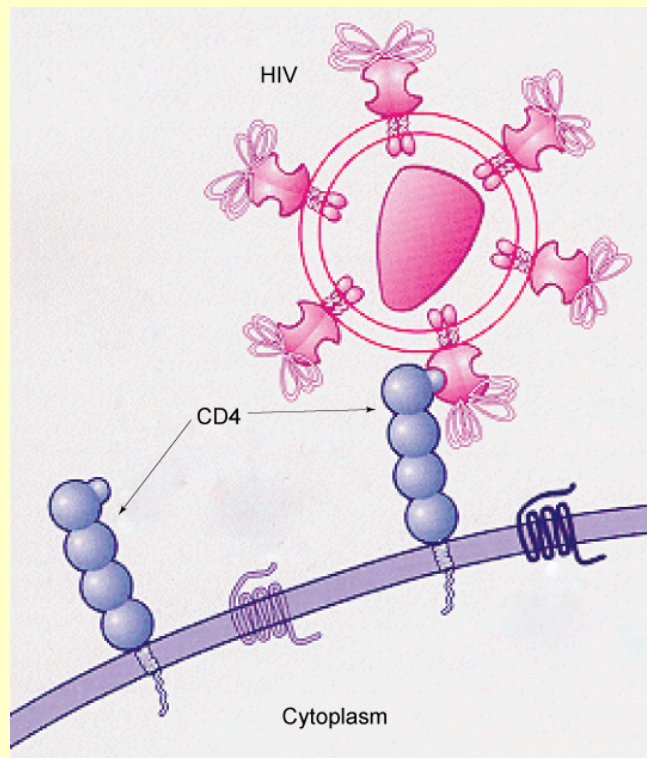


## evolution CONNECTION

### How Viruses Infect Specific Organs

Glycoprotein and glycolipid patterns on the cells' surfaces give many viruses an opportunity for infection. HIV and hepatitis viruses infect only specific organs or cells in the human body. HIV is able to penetrate the plasma membranes of a subtype of lymphocytes called T-helper cells, as well as some monocytes and central nervous system cells. The hepatitis virus attacks liver cells.

These viruses are able to invade these cells, because the cells have binding sites on their surfaces that are specific to and compatible with certain viruses (**Figure 5.6**). Other recognition sites on the virus's surface interact with the human immune system, prompting the body to produce antibodies. Antibodies are made in response to the antigens or proteins associated with invasive pathogens, or in response to foreign cells, such as might occur with an organ transplant. These same sites serve as places for antibodies to attach and either destroy or inhibit the virus' activity. Unfortunately, these recognition sites on HIV change at a rapid rate because of mutations, making an effective vaccine against the virus very difficult, as the virus evolves and adapts. A person infected with HIV will quickly develop different populations, or variants, of the virus that differences in these recognition sites distinguish. This rapid change of surface markers decreases the effectiveness of the person's immune system in attacking the virus, because the antibodies will not recognize the surface patterns' new variations. In the case of HIV, the problem is compounded because the virus specifically infects and destroys cells involved in the immune response, further incapacitating the host.



**Figure 5.6** HIV binds to the CD4 receptor, a glycoprotein on T cell surfaces. (credit: modification of work by NIH, NIAID)

### Membrane Fluidity

The membrane's mosaic characteristic helps to illustrate its nature. The integral proteins and lipids exist in the membrane as separate but loosely attached molecules. These resemble the separate, multicolored tiles of a mosaic picture, and they float, moving somewhat with respect to one another. The membrane is not like a balloon, however, that can expand and contract; rather, it is fairly rigid and can burst if penetrated or if a cell takes in too much water. However, because of its mosaic nature, a very fine needle can easily penetrate a plasma



membrane without causing it to burst, and the membrane will flow and self-seal when one extracts the needle.

The membrane's mosaic characteristics explain some but not all of its fluidity. There are two other factors that help maintain this fluid characteristic. One factor is the nature of the phospholipids themselves. In their saturated form, the fatty acids in phospholipid tails are saturated with bound hydrogen atoms. There are no double bonds between adjacent carbon atoms. This results in tails that are relatively straight. In contrast, unsaturated fatty acids do not contain a maximal number of hydrogen atoms, but they do contain some double bonds between adjacent carbon atoms. A double bond results in a bend in the carbon string of approximately 30 degrees (**Figure 5.3**).

Thus, if decreasing temperatures compress saturated fatty acids with their straight tails, they press in on each other, making a dense and fairly rigid membrane. If unsaturated fatty acids are compressed, the “kinks” in their tails elbow adjacent phospholipid molecules away, maintaining some space between the phospholipid molecules. This “elbow room” helps to maintain fluidity in the membrane at temperatures at which membranes with saturated fatty acid tails in their phospholipids would “freeze” or solidify. The membrane's relative fluidity is particularly important in a cold environment. A cold environment usually compresses membranes comprised largely of saturated fatty acids, making them less fluid and more susceptible to rupturing. Many organisms (fish are one example) are capable of adapting to cold environments by changing the proportion of unsaturated fatty acids in their membranes in response to lower temperature.



Visit this **site** ([http://openstaxcollege.org//biological\\_memb](http://openstaxcollege.org//biological_memb)) to see animations of the membranes' fluidity and mosaic quality.

Animals have an additional membrane constituent that assists in maintaining fluidity. Cholesterol, which lies alongside the phospholipids in the membrane, tends to dampen temperature effects on the membrane. Thus, this lipid functions as a buffer, preventing lower temperatures from inhibiting fluidity and preventing increased temperatures from increasing fluidity too much. Thus, cholesterol extends, in both directions, the temperature range in which the membrane is appropriately fluid and consequently functional. Cholesterol also serves other functions, such as organizing clusters of transmembrane proteins into lipid rafts.

### Plasma Membrane Components and Functions

Component	Location
Phospholipid	Main membrane fabric
Cholesterol	Attached between phospholipids and between the two phospholipid layers
Integral proteins (for example, integrins)	Embedded within the phospholipid layer(s); may or may not penetrate through both layers
Peripheral proteins	On the phospholipid bilayer's inner or outer surface; not embedded within the phospholipids
Carbohydrates (components of glycoproteins and glycolipids)	Generally attached to proteins on the outside membrane layer

**Table 5.1**



## career CONNECTION

### Immunologist

The variations in peripheral proteins and carbohydrates that affect a cell's recognition sites are of prime interest in immunology. In developing vaccines, researchers have been able to conquer many infectious diseases, such as smallpox, polio, diphtheria, and tetanus.

Immunologists are the physicians and scientists who research and develop vaccines, as well as treat and study allergies or other immune problems. Some immunologists study and treat autoimmune problems (diseases in which a person's immune system attacks his or her own cells or tissues, such as lupus) and immunodeficiencies, whether acquired (such as acquired immunodeficiency syndrome, or AIDS) or hereditary (such as severe combined immunodeficiency, or SCID). Immunologists also help treat organ transplantation patients, who must have their immune systems suppressed so that their bodies will not reject a transplanted organ. Some immunologists work to understand natural immunity and the effects of a person's environment on it. Others work on questions about how the immune system affects diseases such as cancer. In the past, researchers did not understand the importance of having a healthy immune system in preventing cancer.

To work as an immunologist, one must have a PhD or MD. In addition, immunologists undertake at least two to three years of training in an accredited program and must pass the American Board of Allergy and Immunology exam. Immunologists must possess knowledge of the human body's function as they relate to issues beyond immunization, and knowledge of pharmacology and medical technology, such as medications, therapies, test materials, and surgical procedures.

## 5.2 | Passive Transport

By the end of this section, you will be able to do the following:

- Explain why and how passive transport occurs
- Understand the osmosis and diffusion processes
- Define tonicity and its relevance to passive transport

Plasma membranes must allow certain substances to enter and leave a cell, and prevent some harmful materials from entering and some essential materials from leaving. In other words, plasma membranes are **selectively permeable**—they allow some substances to pass through, but not others. If they were to lose this selectivity, the cell would no longer be able to sustain itself, and it would be destroyed. Some cells require larger amounts of specific substances. They must have a way of obtaining these materials from extracellular fluids. This may happen passively, as certain materials move back and forth, or the cell may have special mechanisms that facilitate transport. Some materials are so important to a cell that it spends some of its energy, hydrolyzing adenosine triphosphate (ATP), to obtain these materials. Red blood cells use some of their energy doing just that. Most cells spend the majority of their energy to maintain an imbalance of sodium and potassium ions between the cell's interior and exterior, as well as on protein synthesis.

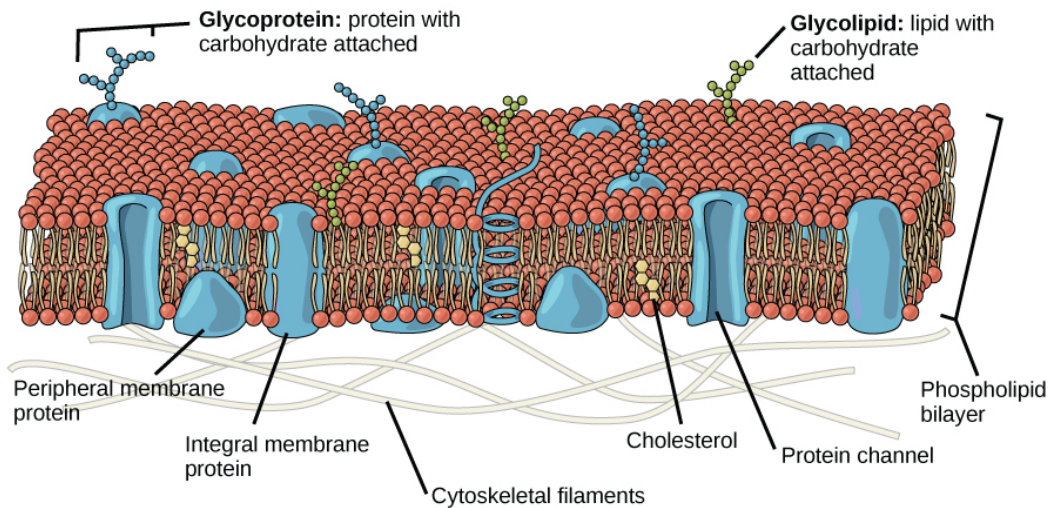
The most direct forms of membrane transport are passive. **Passive transport** is a naturally occurring phenomenon and does not require the cell to exert any of its energy to accomplish the movement. In passive transport, substances move from an area of higher concentration to an area of lower concentration. A physical space in which there is a single substance concentration range has a **concentration gradient**.

### Selective Permeability

Plasma membranes are asymmetric: the membrane's interior is not identical to its exterior. There is a considerable difference between the array of phospholipids and proteins between the two leaflets that form a membrane. On the membrane's interior, some proteins serve to anchor the membrane to cytoskeleton's fibers. There are peripheral proteins on the membrane's exterior that bind extracellular matrix elements. Carbohydrates,



attached to lipids or proteins, are also on the plasma membrane's exterior surface. These carbohydrate complexes help the cell bind required substances in the extracellular fluid. This adds considerably to plasma membrane's selective nature (**Figure 5.7**).



**Figure 5.7** The plasma membrane's exterior surface is not identical to its interior surface.

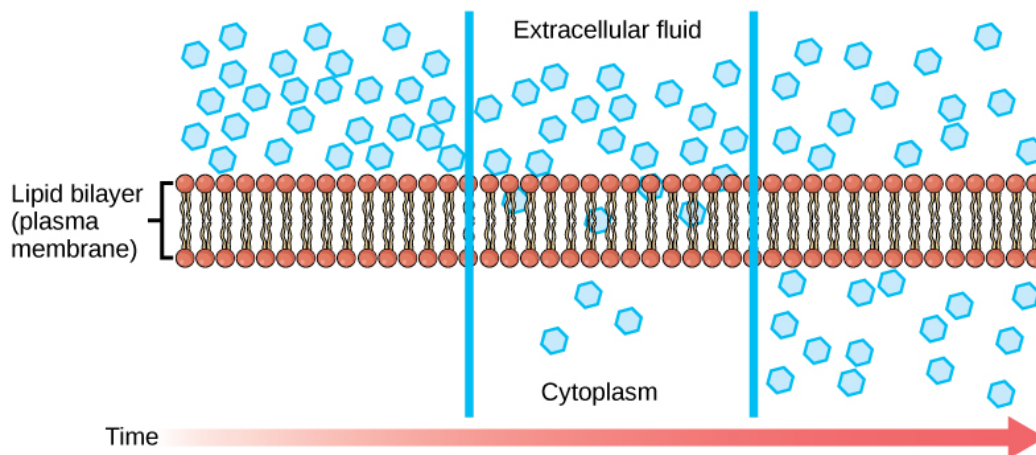
Recall that plasma membranes are amphiphilic: They have hydrophilic and hydrophobic regions. This characteristic helps move some materials through the membrane and hinders the movement of others. Non-polar and lipid-soluble material with a low molecular weight can easily slip through the membrane's hydrophobic lipid core. Substances such as the fat-soluble vitamins A, D, E, and K readily pass through the plasma membranes in the digestive tract and other tissues. Fat-soluble drugs and hormones also gain easy entry into cells and readily transport themselves into the body's tissues and organs. Oxygen and carbon dioxide molecules have no charge and pass through membranes by simple diffusion.

Polar substances present problems for the membrane. While some polar molecules connect easily with the cell's outside, they cannot readily pass through the plasma membrane's lipid core. Additionally, while small ions could easily slip through the spaces in the membrane's mosaic, their charge prevents them from doing so. Ions such as sodium, potassium, calcium, and chloride must have special means of penetrating plasma membranes. Simple sugars and amino acids also need the help of various transmembrane proteins (channels) to transport themselves across plasma membranes.

## Diffusion

**Diffusion** is a passive process of transport. A single substance moves from a high concentration to a low concentration area until the concentration is equal across a space. You are familiar with diffusion of substances through the air. For example, think about someone opening a bottle of ammonia in a room filled with people. The ammonia gas is at its highest concentration in the bottle. Its lowest concentration is at the room's edges. The ammonia vapor will diffuse, or spread away, from the bottle, and gradually, increasingly more people will smell the ammonia as it spreads. Materials move within the cell's cytosol by diffusion, and certain materials move through the plasma membrane by diffusion (**Figure 5.8**). Diffusion expends no energy. On the contrary, concentration gradients are a form of potential energy, which dissipates as the gradient is eliminated.





**Figure 5.8** Diffusion through a permeable membrane moves a substance from a high concentration area (extracellular fluid, in this case) down its concentration gradient (into the cytoplasm). (credit: modification of work by Mariana Ruiz Villareal)

Each separate substance in a medium, such as the extracellular fluid, has its own concentration gradient, independent of other materials' concentration gradients. In addition, each substance will diffuse according to that gradient. Within a system, there will be different diffusion rates of various substances in the medium.

### Factors That Affect Diffusion

Molecules move constantly in a random manner, at a rate that depends on their mass, their environment, and the amount of thermal energy they possess, which in turn is a function of temperature. This movement accounts for molecule diffusion through whatever medium in which they are localized. A substance moves into any space available to it until it evenly distributes itself throughout. After a substance has diffused completely through a space, removing its concentration gradient, molecules will still move around in the space, but there will be no *net* movement of the number of molecules from one area to another. We call this lack of a concentration gradient in which the substance has no net movement dynamic equilibrium. While diffusion will go forward in the presence of a substance's concentration gradient, several factors affect the diffusion rate.

- **Extent of the concentration gradient:** The greater the difference in concentration, the more rapid the diffusion. The closer the distribution of the material gets to equilibrium, the slower the diffusion rate.
- **Mass of the molecules diffusing:** Heavier molecules move more slowly; therefore, they diffuse more slowly. The reverse is true for lighter molecules.
- **Temperature:** Higher temperatures increase the energy and therefore the molecules' movement, increasing the diffusion rate. Lower temperatures decrease the molecules' energy, thus decreasing the diffusion rate.
- **Solvent density:** As the density of a solvent increases, the diffusion rate decreases. The molecules slow down because they have a more difficult time passing through the denser medium. If the medium is less dense, diffusion increases. Because cells primarily use diffusion to move materials within the cytoplasm, any increase in the cytoplasm's density will inhibit the movement of the materials. An example of this is a person experiencing dehydration. As the body's cells lose water, the diffusion rate decreases in the cytoplasm, and the cells' functions deteriorate. Neurons tend to be very sensitive to this effect. Dehydration frequently leads to unconsciousness and possibly coma because of the decrease in diffusion rate within the cells.
- **Solubility:** As we discussed earlier, nonpolar or lipid-soluble materials pass through plasma membranes more easily than polar materials, allowing a faster diffusion rate.
- **Surface area and plasma membrane thickness:** Increased surface area increases the diffusion rate; whereas, a thicker membrane reduces it.
- **Distance travelled:** The greater the distance that a substance must travel, the slower the diffusion rate. This places an upper limitation on cell size. A large, spherical cell will die because nutrients or waste cannot reach or leave the cell's center, respectively. Therefore, cells must either be small in size, as in the case of many prokaryotes, or be flattened, as with many single-celled eukaryotes.

A variation of diffusion is the process of filtration. In filtration, material moves according to its concentration



gradient through a membrane. Sometimes pressure enhances the diffusion rate, causing the substances to filter more rapidly. This occurs in the kidney, where blood pressure forces large amounts of water and accompanying dissolved substances, or **solutes**, out of the blood and into the renal tubules. The diffusion rate in this instance is almost totally dependent on pressure. One of the effects of high blood pressure is the appearance of protein in the urine, which abnormally high pressure "squeezes through".

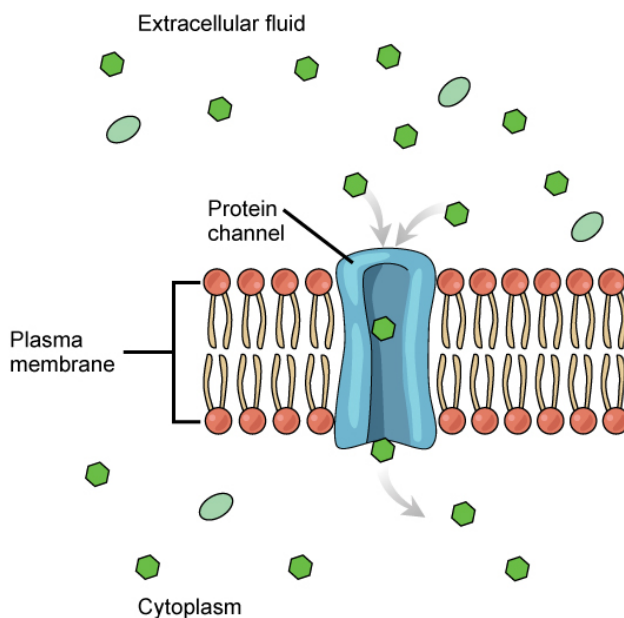
## Facilitated transport

In **facilitated transport**, or facilitated diffusion, materials diffuse across the plasma membrane with the help of membrane proteins. A concentration gradient exists that would allow these materials to diffuse into the cell without expending cellular energy. However, these materials are polar molecule ions that the cell membrane's hydrophobic parts repel. Facilitated transport proteins shield these materials from the membrane's repulsive force, allowing them to diffuse into the cell.

The transported material first attaches to protein or glycoprotein receptors on the plasma membrane's exterior surface. This allows removal of material from the extracellular fluid that the cell needs. The substances then pass to specific integral proteins that facilitate their passage. Some of these integral proteins are collections of beta-pleated sheets that form a pore or channel through the phospholipid bilayer. Others are carrier proteins which bind with the substance and aid its diffusion through the membrane.

### Channels

The integral proteins involved in facilitated transport are **transport proteins**, and they function as either channels for the material or carriers. In both cases, they are transmembrane proteins. Channels are specific for the transported substance. **Channel proteins** have hydrophilic domains exposed to the intracellular and extracellular fluids. In addition, they have a hydrophilic channel through their core that provides a hydrated opening through the membrane layers (**Figure 5.9**). Passage through the channel allows polar compounds to avoid the plasma membrane's nonpolar central layer that would otherwise slow or prevent their entry into the cell. **Aquaporins** are channel proteins that allow water to pass through the membrane at a very high rate.



**Figure 5.9** Facilitated transport moves substances down their concentration gradients. They may cross the plasma membrane with the aid of channel proteins. (credit: modification of work by Mariana Ruiz Villareal)

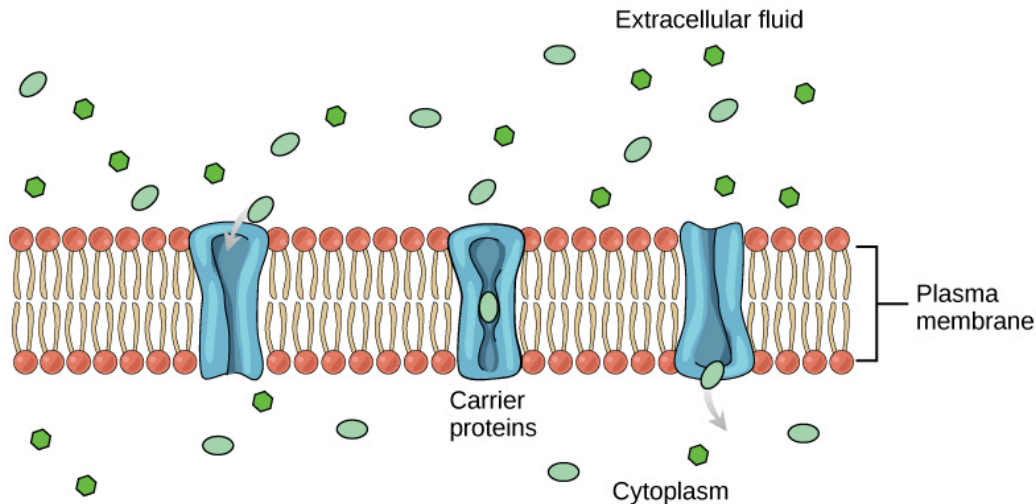
Channel proteins are either open at all times or they are "gated," which controls the channel's opening. When a particular ion attaches to the channel protein it may control the opening, or other mechanisms or substances may be involved. In some tissues, sodium and chloride ions pass freely through open channels; whereas, in other tissues a gate must open to allow passage. An example of this occurs in the kidney, where there are both channel forms in different parts of the renal tubules. Cells involved in transmitting electrical impulses, such as nerve and muscle cells, have gated channels for sodium, potassium, and calcium in their membranes. Opening and closing these channels changes the relative concentrations on opposing sides of the membrane of these ions, resulting in facilitating electrical transmission along membranes (in the case of nerve cells) or in muscle



contraction (in the case of muscle cells).

### Carrier Proteins

Another type of protein embedded in the plasma membrane is a **carrier protein**. This aptly named protein binds a substance and, thus triggers a change of its own shape, moving the bound molecule from the cell's outside to its interior (**Figure 5.10**). Depending on the gradient, the material may move in the opposite direction. Carrier proteins are typically specific for a single substance. This selectivity adds to the plasma membrane's overall selectivity. Scientists poorly understand the exact mechanism for the change of shape. Proteins can change shape when their hydrogen bonds are affected, but this may not fully explain this mechanism. Each carrier protein is specific to one substance, and there are a finite number of these proteins in any membrane. This can cause problems in transporting enough material for the cell to function properly. When all of the proteins are bound to their ligands, they are saturated and the rate of transport is at its maximum. Increasing the concentration gradient at this point will not result in an increased transport rate.



**Figure 5.10** Some substances are able to move down their concentration gradient across the plasma membrane with the aid of carrier proteins. Carrier proteins change shape as they move molecules across the membrane. (credit: modification of work by Mariana Ruiz Villareal)

An example of this process occurs in the kidney. In one part, the kidney filters glucose, water, salts, ions, and amino acids that the body requires. This filtrate, which includes glucose, then reabsorbs in another part of the kidney. Because there are only a finite number of carrier proteins for glucose, if more glucose is present than the proteins can handle, the excess is not transported and the body excretes this through urine. In a diabetic individual, the term is “spilling glucose into the urine.” A different group of carrier proteins, glucose transport proteins, or GLUTs, are involved in transporting glucose and other hexose sugars through plasma membranes within the body.

Channel and carrier proteins transport material at different rates. Channel proteins transport much more quickly than carrier proteins. Channel proteins facilitate diffusion at a rate of tens of millions of molecules per second; whereas, carrier proteins work at a rate of a thousand to a million molecules per second.

## Osmosis

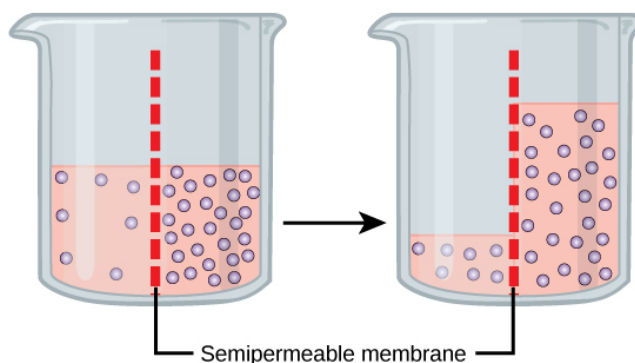
**Osmosis** is the movement of water through a semipermeable membrane according to the water's concentration gradient across the membrane, which is inversely proportional to the solutes' concentration. While diffusion transports material across membranes and within cells, osmosis transports *only water* across a membrane and the membrane limits the solutes' diffusion in the water. Not surprisingly, the aquaporins that facilitate water movement play a large role in osmosis, most prominently in red blood cells and the membranes of kidney tubules.

### Mechanism

Osmosis is a special case of diffusion. Water, like other substances, moves from an area of high concentration to one of low concentration. An obvious question is what makes water move at all? Imagine a beaker with a semipermeable membrane separating the two sides or halves (**Figure 5.11**). On both sides of the membrane the water level is the same, but there are different dissolved substance concentrations, or **solute**, that cannot



cross the membrane (otherwise the solute crossing the membrane would balance concentrations on each side). If the solution's volume on both sides of the membrane is the same, but the solute's concentrations are different, then there are different amounts of water, the solvent, on either side of the membrane.



**Figure 5.11** In osmosis, water always moves from an area of higher water concentration to one of lower concentration. In the diagram, the solute cannot pass through the selectively permeable membrane, but the water can.

To illustrate this, imagine two full water glasses. One has a single teaspoon of sugar in it; whereas, the second one contains one-quarter cup of sugar. If the total volume of the solutions in both cups is the same, which cup contains more water? Because the large sugar amount in the second cup takes up much more space than the teaspoon of sugar in the first cup, the first cup has more water in it.

Returning to the beaker example, recall that it has a solute mixture on either side of the membrane. A principle of diffusion is that the molecules move around and will spread evenly throughout the medium if they can. However, only the material capable of getting through the membrane will diffuse through it. In this example, the solute cannot diffuse through the membrane, but the water can. Water has a concentration gradient in this system. Thus, water will diffuse down its concentration gradient, crossing the membrane to the side where it is less concentrated. This diffusion of water through the membrane—osmosis—will continue until the water's concentration gradient goes to zero or until the water's hydrostatic pressure balances the osmotic pressure. Osmosis proceeds constantly in living systems.

## Tonicity

**Tonicity** describes how an extracellular solution can change a cell's volume by affecting osmosis. A solution's tonicity often directly correlates with the solution's osmolarity. **Osmolarity** describes the solution's total solute concentration. A solution with low osmolarity has a greater number of water molecules relative to the number of solute particles. A solution with high osmolarity has fewer water molecules with respect to solute particles. In a situation in which a membrane permeable to water, though not to the solute separates two different osmolarities, water will move from the membrane's side with lower osmolarity (and more water) to the side with higher osmolarity (and less water). This effect makes sense if you remember that the solute cannot move across the membrane, and thus the only component in the system that can move—the water—moves along its own concentration gradient. An important distinction that concerns living systems is that osmolarity measures the number of particles (which may be molecules) in a solution. Therefore, a solution that is cloudy with cells may have a lower osmolarity than a solution that is clear, if the second solution contains more dissolved molecules than there are cells.

### Hypotonic Solutions

Scientists use three terms—hypotonic, isotonic, and hypertonic—to relate the cell's osmolarity to the extracellular fluid's osmolarity that contains the cells. In a **hypotonic** situation, the extracellular fluid has lower osmolarity than the fluid inside the cell, and water enters the cell. (In living systems, the point of reference is always the cytoplasm, so the prefix *hypo-* means that the extracellular fluid has a lower solute concentration, or a lower osmolarity, than the cell cytoplasm.) It also means that the extracellular fluid has a higher water concentration in the solution than does the cell. In this situation, water will follow its concentration gradient and enter the cell.

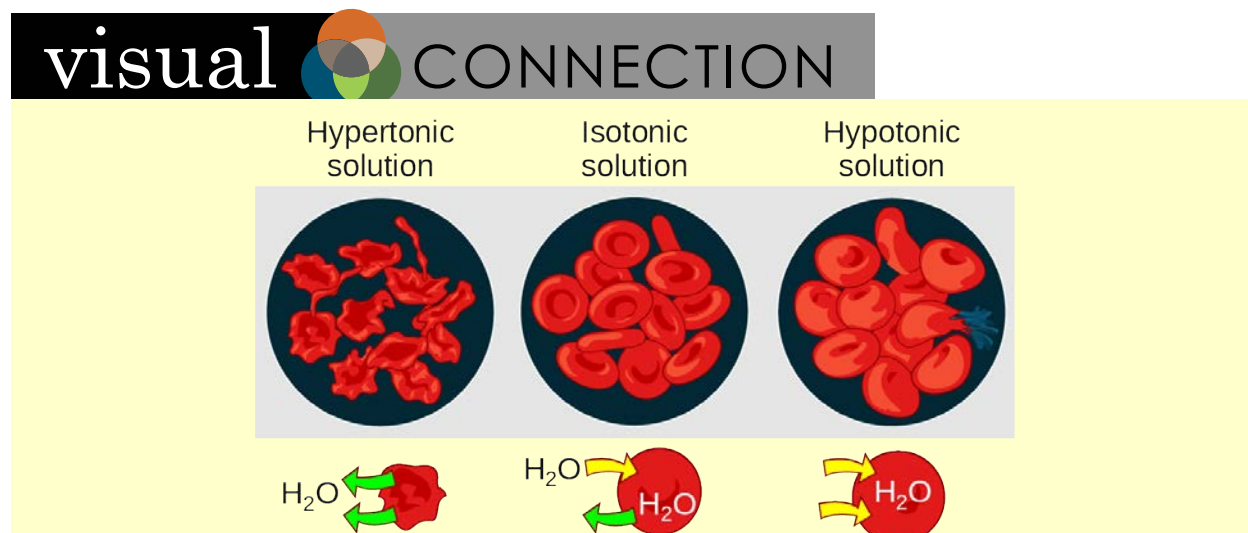
### Hypertonic Solutions

As for a **hypertonic** solution, the prefix *hyper-* refers to the extracellular fluid having a higher osmolarity than the cell's cytoplasm; therefore, the fluid contains less water than the cell does. Because the cell has a relatively higher water concentration, water will leave the cell.



### Isotonic Solutions

In an **isotonic** solution, the extracellular fluid has the same osmolarity as the cell. If the cell's osmolarity matches that of the extracellular fluid, there will be no net movement of water into or out of the cell, although water will still move in and out. Blood cells and plant cells in hypertonic, isotonic, and hypotonic solutions take on characteristic appearances (**Figure 5.12**).



**Figure 5.12** Osmotic pressure changes red blood cells' shape in hypertonic, isotonic, and hypotonic solutions. (credit: Mariana Ruiz Villareal)

A doctor injects a patient with what the doctor thinks is an isotonic saline solution. The patient dies, and an autopsy reveals that many red blood cells have been destroyed. Do you think the solution the doctor injected was really isotonic?

### LINK TO LEARNING

For a video illustrating the diffusion process in solutions, visit this [site \(http://openstaxcollege.org//dispersion\)](http://openstaxcollege.org//dispersion).

### Tonicity in Living Systems

In a hypotonic environment, water enters a cell, and the cell swells. In an isotonic condition, the relative solute and solvent concentrations are equal on both membrane sides. There is no net water movement; therefore, there is no change in the cell's size. In a hypertonic solution, water leaves a cell and the cell shrinks. If either the hypo- or hyper- condition goes to excess, the cell's functions become compromised, and the cell may be destroyed.

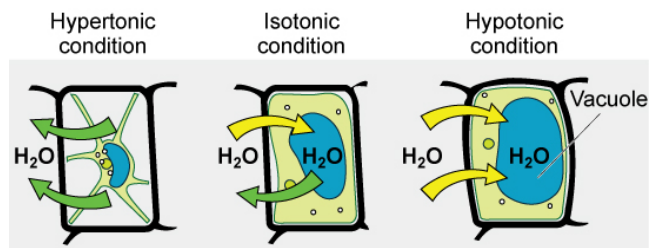
A red blood cell will burst, or lyse, when it swells beyond the plasma membrane's capability to expand. Remember, the membrane resembles a mosaic, with discrete spaces between the molecules comprising it. If the cell swells, and the spaces between the lipids and proteins become too large, the cell will break apart.

In contrast, when excessive water amounts leave a red blood cell, the cell shrinks, or crenates. This has the effect of concentrating the solutes left in the cell, making the cytosol denser and interfering with diffusion within the cell. The cell's ability to function will be compromised and may also result in the cell's death.

Various living things have ways of controlling the effects of osmosis—a mechanism we call osmoregulation. Some organisms, such as plants, fungi, bacteria, and some protists, have cell walls that surround the plasma membrane and prevent cell lysis in a hypotonic solution. The plasma membrane can only expand to the



cell wall's limit, so the cell will not lyse. The cytoplasm in plants is always slightly hypertonic to the cellular environment, and water will always enter a cell if water is available. This water inflow produces turgor pressure, which stiffens the plant's cell walls (**Figure 5.13**). In nonwoody plants, turgor pressure supports the plant. Conversely, if you do not water the plant, the extracellular fluid will become hypertonic, causing water to leave the cell. In this condition, the cell does not shrink because the cell wall is not flexible. However, the cell membrane detaches from the wall and constricts the cytoplasm. We call this **plasmolysis**. Plants lose turgor pressure in this condition and wilt (**Figure 5.14**).

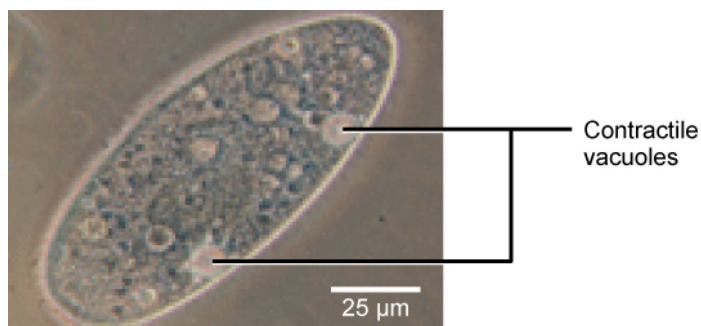


**Figure 5.13** The turgor pressure within a plant cell depends on the solution's tonicity in which it is bathed. (credit: modification of work by Mariana Ruiz Villareal)



**Figure 5.14** Without adequate water, the plant on the left has lost turgor pressure, visible in its wilting. Watering the plant (right) will restore the turgor pressure. (credit: Victor M. Vicente Selvas)

Tonicity is a concern for all living things. For example, paramecia and amoebas, which are protists that lack cell walls, have contractile vacuoles. This vesicle collects excess water from the cell and pumps it out, keeping the cell from lysing as it takes on water from its environment (**Figure 5.15**).



**Figure 5.15** A paramecium's contractile vacuole, here visualized using bright field light microscopy at 480x magnification, continuously pumps water out of the organism's body to keep it from bursting in a hypotonic medium. (credit: modification of work by NIH; scale-bar data from Matt Russell)

Many marine invertebrates have internal salt levels matched to their environments, making them isotonic with the water in which they live. Fish, however, must spend approximately five percent of their metabolic energy maintaining osmotic homeostasis. Freshwater fish live in an environment that is hypotonic to their cells. These



fish actively take in salt through their gills and excrete diluted urine to rid themselves of excess water. Saltwater fish live in the reverse environment, which is hypertonic to their cells, and they secrete salt through their gills and excrete highly concentrated urine.

In vertebrates, the kidneys regulate the water amount in the body. Osmoreceptors are specialized cells in the brain that monitor solute concentration in the blood. If the solute levels increase beyond a certain range, a hormone releases that slows water loss through the kidney and dilutes the blood to safer levels. Animals also have high albumin concentrations, which the liver produces, in their blood. This protein is too large to pass easily through plasma membranes and is a major factor in controlling the osmotic pressures applied to tissues.

## 5.3 | Active Transport

By the end of this section, you will be able to do the following:

- Understand how electrochemical gradients affect ions
- Distinguish between primary active transport and secondary active transport

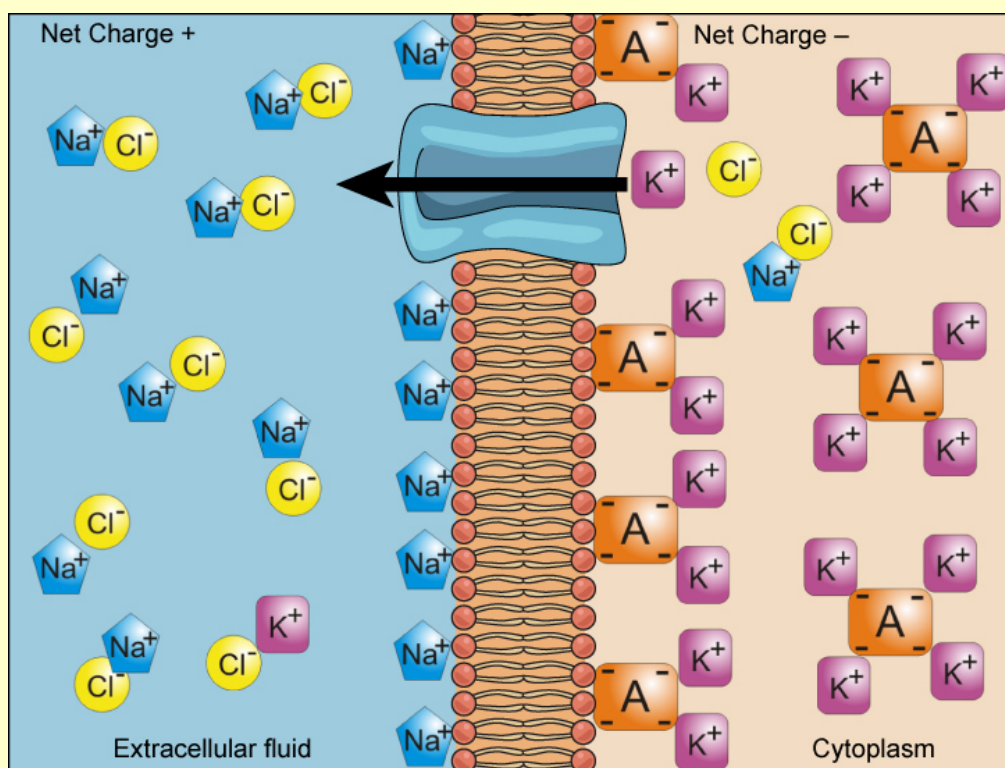
**Active transport** mechanisms require the cell's energy, usually in the form of adenosine triphosphate (ATP). If a substance must move into the cell against its concentration gradient—that is, if the substance's concentration inside the cell is greater than its concentration in the extracellular fluid (and vice versa)—the cell must use energy to move the substance. Some active transport mechanisms move small-molecular weight materials, such as ions, through the membrane. Other mechanisms transport much larger molecules.

### Electrochemical Gradient

We have discussed simple concentration gradients—a substance's differential concentrations across a space or a membrane—but in living systems, gradients are more complex. Because ions move into and out of cells and because cells contain proteins that do not move across the membrane and are mostly negatively charged, there is also an electrical gradient, a difference of charge, across the plasma membrane. The interior of living cells is electrically negative with respect to the extracellular fluid in which they are bathed, and at the same time, cells have higher concentrations of potassium ( $K^+$ ) and lower concentrations of sodium ( $Na^+$ ) than the extracellular fluid. Thus in a living cell, the concentration gradient of  $Na^+$  tends to drive it into the cell, and its electrical gradient (a positive ion) also drives it inward to the negatively charged interior. However, the situation is more complex for other elements such as potassium. The electrical gradient of  $K^+$ , a positive ion, also drives it into the cell, but the concentration gradient of  $K^+$  drives  $K^+$  out of the cell (**Figure 5.16**). We call the combined concentration gradient and electrical charge that affects an ion its **electrochemical gradient**.



# visual CONNECTION



**Figure 5.16** Electrochemical gradients arise from the combined effects of concentration gradients and electrical gradients. Structures labeled A represent proteins. (credit: "Synaptitude"/Wikimedia Commons)

Injecting a potassium solution into a person's blood is lethal. This is how capital punishment and euthanasia subjects die. Why do you think a potassium solution injection is lethal?

## Moving Against a Gradient

To move substances against a concentration or electrochemical gradient, the cell must use energy. This energy comes from ATP generated through the cell's metabolism. Active transport mechanisms, or **pumps**, work against electrochemical gradients. Small substances constantly pass through plasma membranes. Active transport maintains concentrations of ions and other substances that living cells require in the face of these passive movements. A cell may spend much of its metabolic energy supply maintaining these processes. (A red blood cell uses most of its metabolic energy to maintain the imbalance between exterior and interior sodium and potassium levels that the cell requires.) Because active transport mechanisms depend on a cell's metabolism for energy, they are sensitive to many metabolic poisons that interfere with the ATP supply.

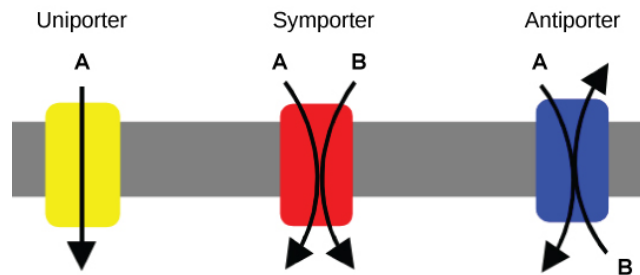
Two mechanisms exist for transporting small-molecular weight material and small molecules. **Primary active transport** moves ions across a membrane and creates a difference in charge across that membrane, which is directly dependent on ATP. **Secondary active transport** does not directly require ATP: instead, it is the movement of material due to the electrochemical gradient established by primary active transport.

## Carrier Proteins for Active Transport

An important membrane adaption for active transport is the presence of specific carrier proteins or pumps to facilitate movement: there are three protein types or **transporters** (Figure 5.17). A **uniporter** carries one specific ion or molecule. A **symporter** carries two different ions or molecules, both in the same direction. An **antiporter** also carries two different ions or molecules, but in different directions. All of these transporters can also transport small, uncharged organic molecules like glucose. These three types of carrier proteins are also in facilitated diffusion, but they do not require ATP to work in that process. Some examples of pumps for active transport are  $\text{Na}^+/\text{K}^+$  ATPase, which carries sodium and potassium ions, and  $\text{H}^+/\text{K}^+$  ATPase, which carries



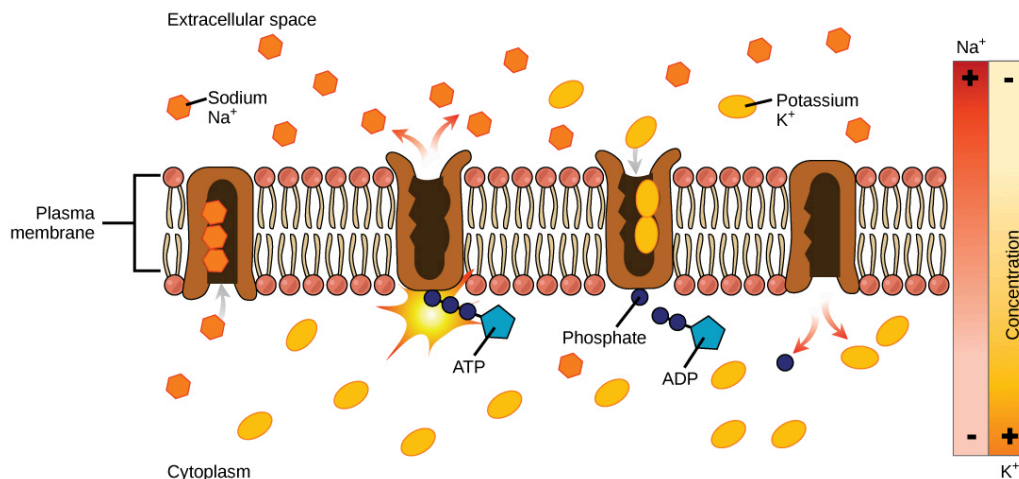
hydrogen and potassium ions. Both of these are antiporter carrier proteins. Two other carrier proteins are  $\text{Ca}^{2+}$  ATPase and  $\text{H}^{+}$  ATPase, which carry only calcium and only hydrogen ions, respectively. Both are pumps.



**Figure 5.17** A uniporter carries one molecule or ion. A symporter carries two different molecules or ions, both in the same direction. An antiporter also carries two different molecules or ions, but in different directions. (credit: modification of work by "Lupask"/Wikimedia Commons)

## Primary Active Transport

The primary active transport that functions with the active transport of sodium and potassium allows secondary active transport to occur. The second transport method is still active because it depends on using energy as does primary transport (**Figure 5.18**).



**Figure 5.18** Primary active transport moves ions across a membrane, creating an electrochemical gradient (electrogenic transport). (credit: modification of work by Mariana Ruiz Villareal)

One of the most important pumps in animal cells is the sodium-potassium pump ( $\text{Na}^{+}\text{-K}^{+}$  ATPase), which maintains the electrochemical gradient (and the correct concentrations of  $\text{Na}^{+}$  and  $\text{K}^{+}$ ) in living cells. The sodium-potassium pump moves  $\text{K}^{+}$  into the cell while moving  $\text{Na}^{+}$  out at the same time, at a ratio of three  $\text{Na}^{+}$  for every two  $\text{K}^{+}$  ions moved in. The  $\text{Na}^{+}\text{-K}^{+}$  ATPase exists in two forms, depending on its orientation to the cell's interior or exterior and its affinity for either sodium or potassium ions. The process consists of the following six steps.

1. With the enzyme oriented towards the cell's interior, the carrier has a high affinity for sodium ions. Three ions bind to the protein.
2. The protein carrier hydrolyzes ATP and a low-energy phosphate group attaches to it.
3. As a result, the carrier changes shape and reorients itself towards the membrane's exterior. The protein's affinity for sodium decreases and the three sodium ions leave the carrier.
4. The shape change increases the carrier's affinity for potassium ions, and two such ions attach to the protein. Subsequently, the low-energy phosphate group detaches from the carrier.
5. With the phosphate group removed and potassium ions attached, the carrier protein repositions itself towards the cell's interior.
6. The carrier protein, in its new configuration, has a decreased affinity for potassium, and the two ions moves



into the cytoplasm. The protein now has a higher affinity for sodium ions, and the process starts again.

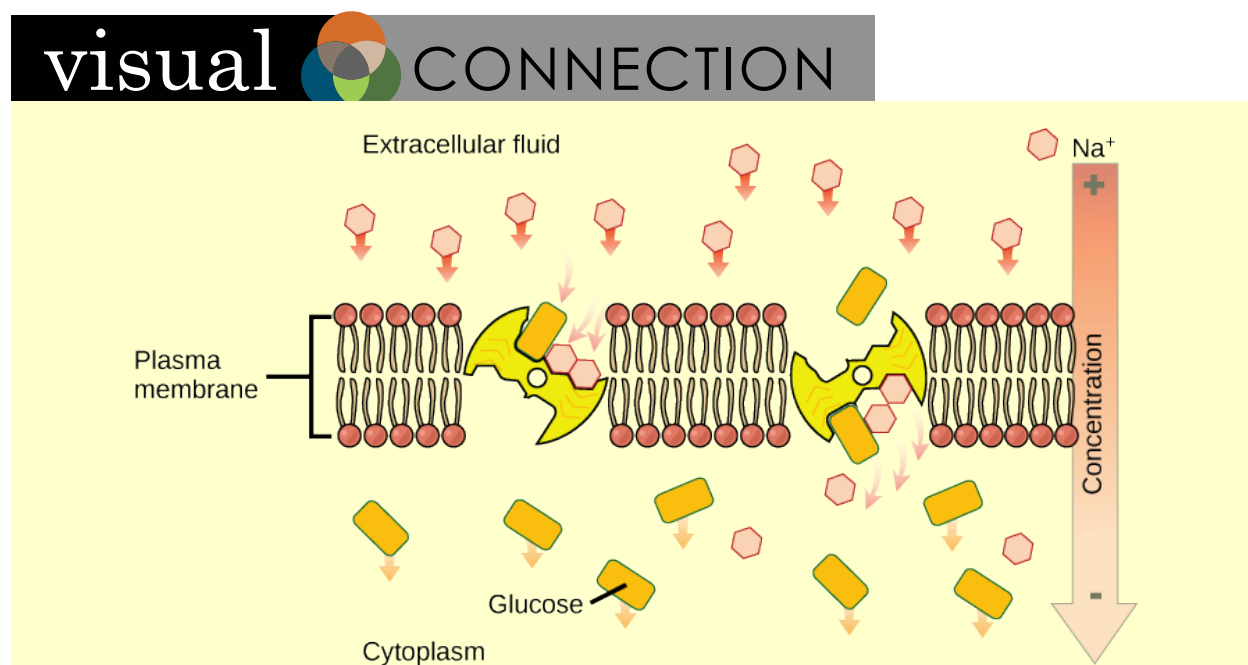
Several things have happened as a result of this process. At this point, there are more sodium ions outside the cell than inside and more potassium ions inside than out. For every three sodium ions that move out, two potassium ions move in. This results in the interior being slightly more negative relative to the exterior. This difference in charge is important in creating the conditions necessary for the secondary process. The sodium-potassium pump is, therefore, an **electrogenic pump** (a pump that creates a charge imbalance), creating an electrical imbalance across the membrane and contributing to the membrane potential.



Watch this [video \(https://openstax.org//Na\\_K\\_ATPase\)](https://openstax.org//Na_K_ATPase) to see an active transport simulation in a sodium-potassium ATPase.

## Secondary Active Transport (Co-transport)

Secondary active transport brings sodium ions, and possibly other compounds, into the cell. As sodium ion concentrations build outside of the plasma membrane because of the primary active transport process, this creates an electrochemical gradient. If a channel protein exists and is open, the sodium ions will pull through the membrane. This movement transports other substances that can attach themselves to the transport protein through the membrane (**Figure 5.19**). Many amino acids, as well as glucose, enter a cell this way. This secondary process also stores high-energy hydrogen ions in the mitochondria of plant and animal cells in order to produce ATP. The potential energy that accumulates in the stored hydrogen ions translates into kinetic energy as the ions surge through the channel protein ATP synthase, and that energy then converts ADP into ATP.



**Figure 5.19** An electrochemical gradient, which primary active transport creates, can move other substances against their concentration gradients, a process scientists call co-transport or secondary active transport. (credit: modification of work by Mariana Ruiz Villareal)

If the pH outside the cell decreases, would you expect the amount of amino acids transported into the cell to increase or decrease?



## 5.4 | Bulk Transport

By the end of this section, you will be able to do the following:

- Describe endocytosis, including phagocytosis, pinocytosis, and receptor-mediated endocytosis
- Understand the process of exocytosis

In addition to moving small ions and molecules through the membrane, cells also need to remove and take in larger molecules and particles (see **Table 5.2** for examples). Some cells are even capable of engulfing entire unicellular microorganisms. You might have correctly hypothesized that when a cell uptakes and releases large particles, it requires energy. A large particle, however, cannot pass through the membrane, even with energy that the cell supplies.

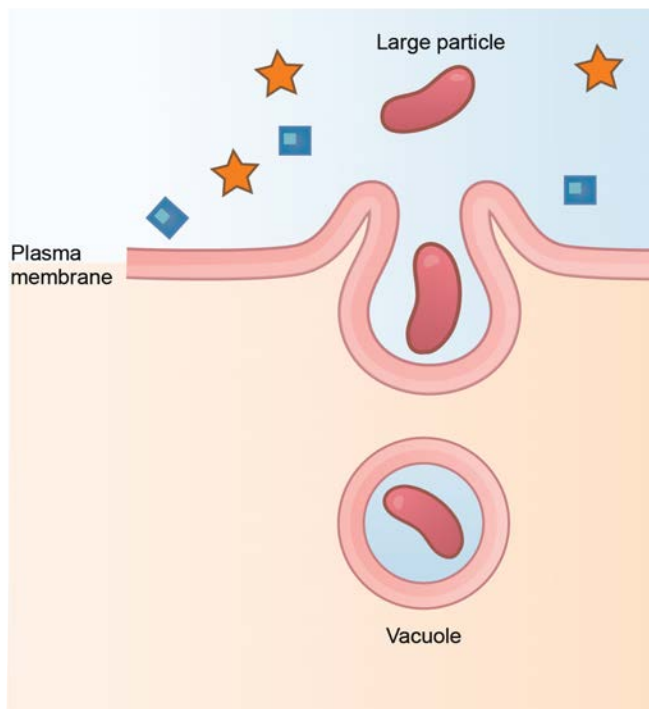
### Endocytosis

**Endocytosis** is a type of active transport that moves particles, such as large molecules, parts of cells, and even whole cells, into a cell. There are different endocytosis variations, but all share a common characteristic: the cell's plasma membrane invaginates, forming a pocket around the target particle. The pocket pinches off, resulting in the particle containing itself in a newly created intracellular vesicle formed from the plasma membrane.

#### Phagocytosis

Phagocytosis (the condition of “cell eating”) is the process by which a cell takes in large particles, such as other cells or relatively large particles. For example, when microorganisms invade the human body, a type of white blood cell, a neutrophil, will remove the invaders through this process, surrounding and engulfing the microorganism, which the neutrophil then destroys (**Figure 5.20**).

Phagocytosis



**Figure 5.20** In phagocytosis, the cell membrane surrounds the particle and engulfs it. (credit: modification of work by Mariana Ruiz Villareal)

In preparation for phagocytosis, a portion of the plasma membrane's inward-facing surface becomes coated with the protein **clathrin**, which stabilizes this membrane's section. The membrane's coated portion then extends from the cell's body and surrounds the particle, eventually enclosing it. Once the vesicle containing the particle

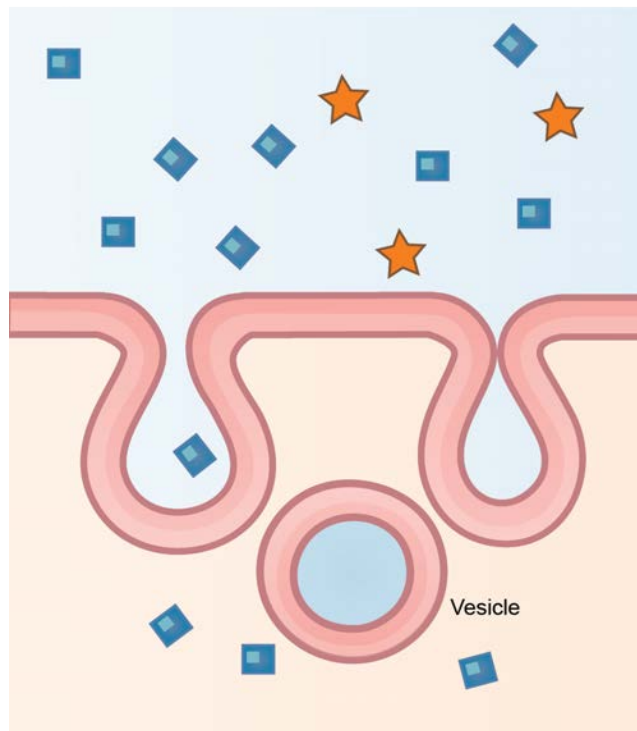


is enclosed within the cell, the clathrin disengages from the membrane and the vesicle merges with a lysosome for breaking down the material in the newly formed compartment (endosome). When accessible nutrients from the vesicular contents' degradation have been extracted, the newly formed endosome merges with the plasma membrane and releases its contents into the extracellular fluid. The endosomal membrane again becomes part of the plasma membrane.

### Pinocytosis

A variation of endocytosis is **pinocytosis**. This literally means “cell drinking”. Discovered by Warren Lewis in 1929, this American embryologist and cell biologist described a process whereby he assumed that the cell was purposefully taking in extracellular fluid. In reality, this is a process that takes in molecules, including water, which the cell needs from the extracellular fluid. Pinocytosis results in a much smaller vesicle than does phagocytosis, and the vesicle does not need to merge with a lysosome (**Figure 5.21**).

Pinocytosis



**Figure 5.21** In pinocytosis, the cell membrane invaginates, surrounds a small volume of fluid, and pinches off. (credit: modification of work by Mariana Ruiz Villareal)

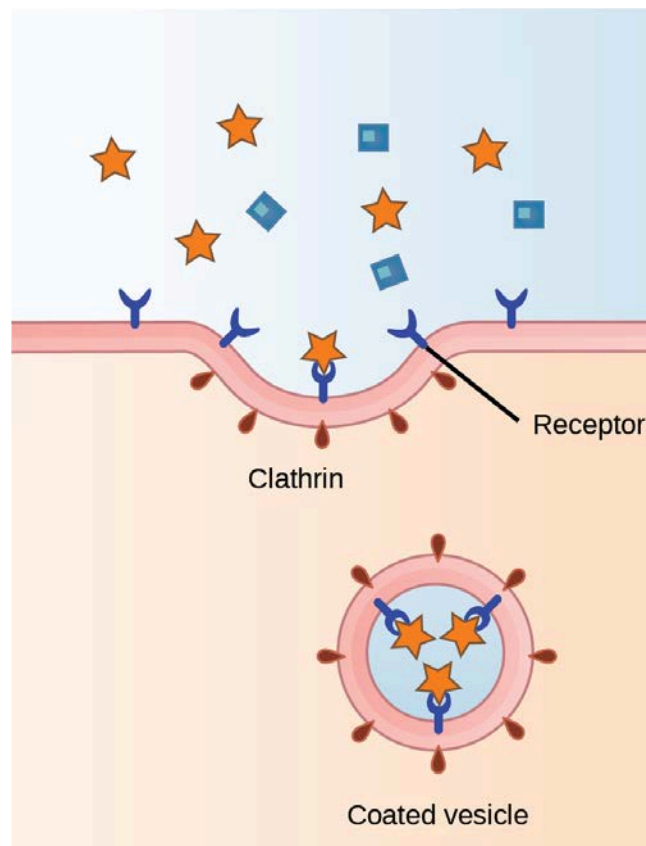
A variation of pinocytosis is **potocytosis**. This process uses a coating protein, **caveolin**, on the plasma membrane's cytoplasmic side, which performs a similar function to clathrin. The cavities in the plasma membrane that form the vacuoles have membrane receptors and lipid rafts in addition to caveolin. The vacuoles or vesicles formed in caveolae (singular caveola) are smaller than those in pinocytosis. Potocytosis brings small molecules into the cell and transports them through the cell for their release on the other side, a process we call transcytosis.

### Receptor-mediated Endocytosis

A targeted variation of endocytosis employs receptor proteins in the plasma membrane that have a specific binding affinity for certain substances (**Figure 5.22**).



### Receptor-mediated endocytosis



**Figure 5.22** In receptor-mediated endocytosis, the cell's uptake of substances targets a single type of substance that binds to the receptor on the cell membrane's external surface. (credit: modification of work by Mariana Ruiz Villareal)

In **receptor-mediated endocytosis**, as in phagocytosis, clathrin attaches to the plasma membrane's cytoplasmic side. If a compound's uptake is dependent on receptor-mediated endocytosis and the process is ineffective, the material will not be removed from the tissue fluids or blood. Instead, it will stay in those fluids and increase in concentration. The failure of receptor-mediated endocytosis causes some human diseases. For example, receptor mediated endocytosis removes low density lipoprotein or LDL (or "bad" cholesterol) from the blood. In the human genetic disease familial hypercholesterolemia, the LDL receptors are defective or missing entirely. People with this condition have life-threatening levels of cholesterol in their blood, because their cells cannot clear LDL particles.

Although receptor-mediated endocytosis is designed to bring specific substances that are normally in the extracellular fluid into the cell, other substances may gain entry into the cell at the same site. Flu viruses, diphtheria, and cholera toxin all have sites that cross-react with normal receptor-binding sites and gain entry into cells.



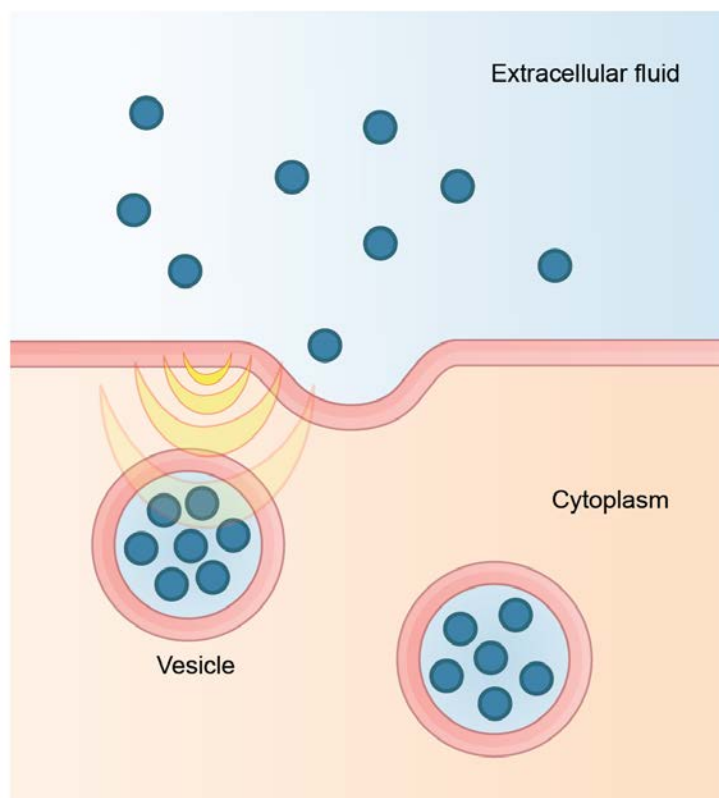
See receptor-mediated endocytosis in action, and click on different **parts** (<http://openstaxcollege.org//endocytosis>) for a focused animation.



## Exocytosis

The reverse process of moving material into a cell is the process of exocytosis. **Exocytosis** is the opposite of the processes we discussed above in that its purpose is to expel material from the cell into the extracellular fluid. Waste material is enveloped in a membrane and fuses with the plasma membrane's interior. This fusion opens the membranous envelope on the cell's exterior, and the waste material expels into the extracellular space (**Figure 5.23**). Other examples of cells releasing molecules via exocytosis include extracellular matrix protein secretion and neurotransmitter secretion into the synaptic cleft by synaptic vesicles.

Exocytosis



**Figure 5.23** In exocytosis, vesicles containing substances fuse with the plasma membrane. The contents then release to the cell's exterior. (credit: modification of work by Mariana Ruiz Villareal)

## Methods of Transport, Energy Requirements, and Types of Transported Material

Transport Method	Active/ Passive	Material Transported
Diffusion	Passive	Small-molecular weight material
Osmosis	Passive	Water
Facilitated transport/diffusion	Passive	Sodium, potassium, calcium, glucose
Primary active transport	Active	Sodium, potassium, calcium
Secondary active transport	Active	Amino acids, lactose
Phagocytosis	Active	Large macromolecules, whole cells, or cellular structures
Pinocytosis and potocytosis	Active	Small molecules (liquids/water)

**Table 5.2**



Methods of Transport, Energy Requirements, and Types of Transported Material

Transport Method	Active/ Passive	Material Transported
Receptor-mediated endocytosis	Active	Large quantities of macromolecules

Table 5.2