Chapter 8: Membrane structure and Function

Abdalrhman Froukh
School of medicine
University of Jordan

Cellular membranes are fluid mosaics of lipids and proteins

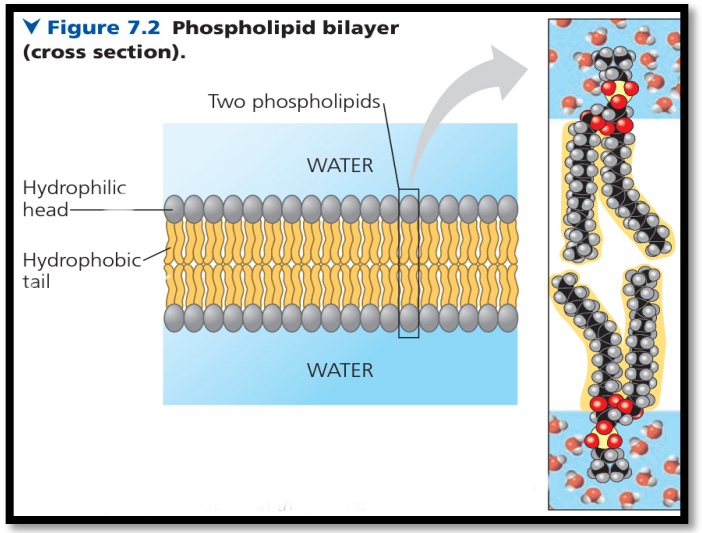
Lipids and **proteins** are the staple ingredients of membranes, although **carbohydrates** are also important. The most abundant **lipids** in most membranes are **phospholipids**.

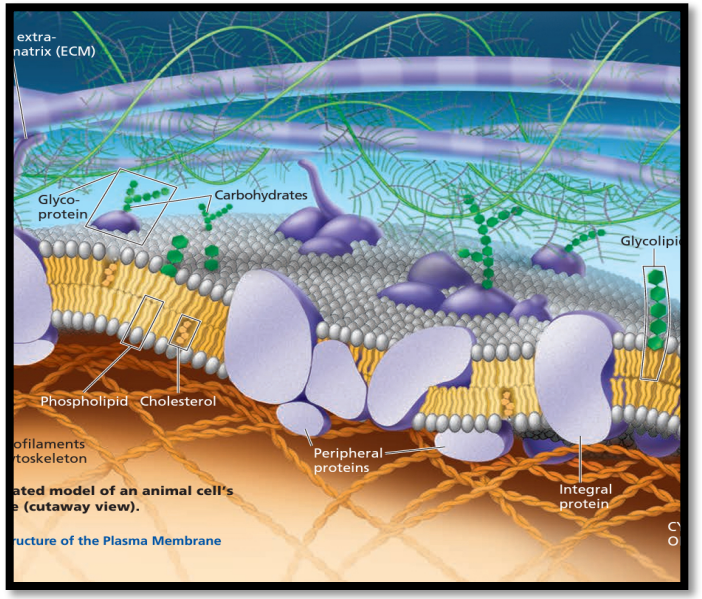
A phospholipid is an **amphipathic** molecule, meaning it has both a **hydrophilic** ("water-loving") region and a **hydrophobic** ("water-fearing") region.

Like membrane **lipids**, most membrane **proteins** are **amphipathic**. Such proteins can reside in the phospholipid bilayer with their hydrophilic regions protruding.

In the fluid mosaic model, the membrane is a mosaic of **protein** molecules bobbing in a fluid bilayer of **phospholipids**.

The **proteins** are not randomly distributed in the membrane, however. Groups of **proteins** are often associated with specific **lipids** in long-lasting, specialized patches called **lipid rafts.**





The Fluidity of Membranes

Membranes are not ***static*** sheets of molecules locked rigidly in place. A membrane is held together mainly by **hydrophobic interactions**, which are much weaker than **covalent bonds.**

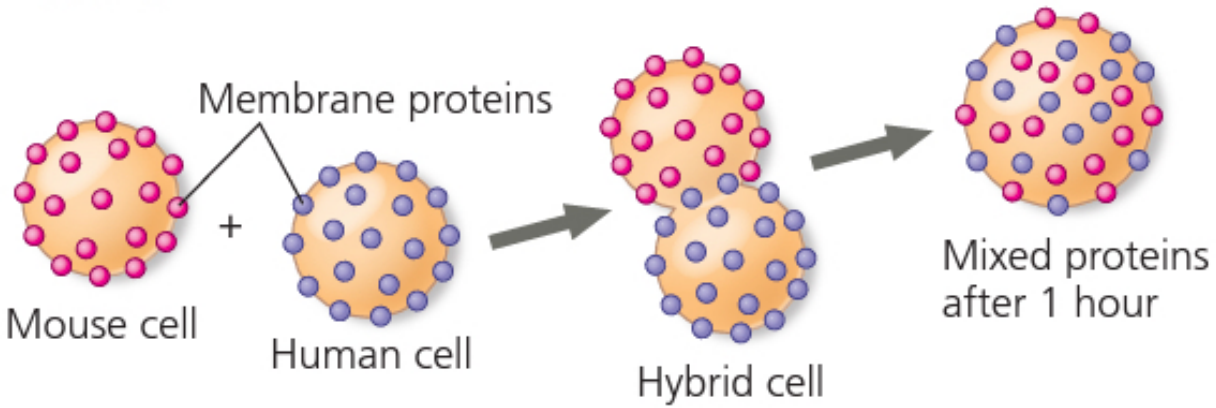
Most of the **lipids** and some **proteins** can shift about **sideways**, and Very rarely, also, a **lipid** may **flip-flop** across the membrane, switching from one phospholipid layer to the other.

The **sideways** movement of **phospholipids** within the membrane is rapid. **Proteins** are much larger than **lipids** and move more slowly, but some membrane proteins do drift.

Inquiry Do membrane proteins move?

Experiment Larry Frye and Michael Edidin, at Johns Hopkins University, labeled the plasma membrane proteins of a mouse cell and a human cell with two different markers and fused the cells. Using a microscope, they observed the markers on the hybrid cell.

Results



Conclusion The mixing of the mouse and human membrane proteins indicates that at least some membrane proteins move sideways within the plane of the plasma membrane.

The Fluidity of Membranes

Some membrane **proteins** seem to move in a highly directed manner, perhaps driven along **cytoskeletal fibers** in the cell by **motor proteins** connected to the membrane proteins' cytoplasmic regions.

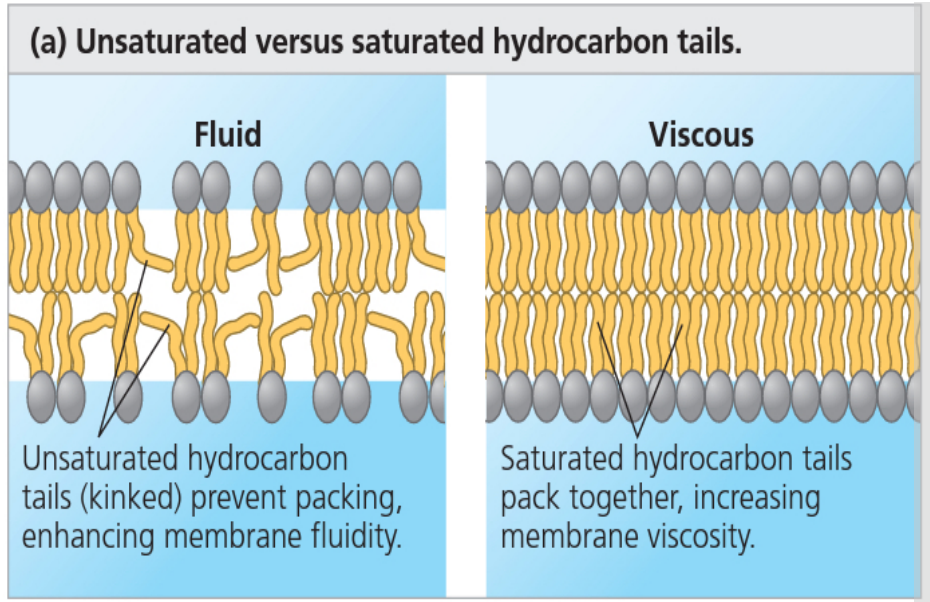
However, many other **membrane proteins** seem to be held immobile by their attachment to the **cytoskeleton** or to the **extracellular matrix.**

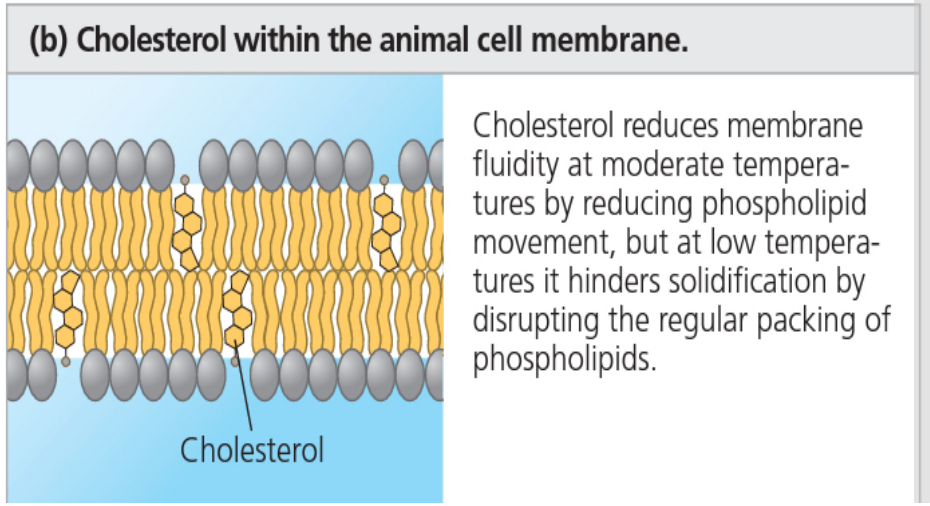
A membrane remains fluid as **temperature** decreases until the **phospholipids** settle into a closely packed arrangement and the membrane solidifies, As the **temperature** decreases, the membrane remains **fluid** to a lower temperature if it is rich in **phospholipids** with **unsaturated hydrocarbon tails.**

Because of **kinks** in the tails where double bonds are located, **unsaturated hydrocarbon tails** cannot pack together as closely as **saturated hydrocarbon tails**, making the membrane more fluid **.**

At relatively high temperatures— at 37°C, the body temperature of humans, for example— **cholesterol** makes the **membrane** less fluid by restraining **phospholipid** movement.

However, because **cholesterol** also hinders the close packing of **phospholipids**, it lowers the **temperature** required for the membrane to solidify. Thus, **cholesterol** can be thought of as a "**fluidity buffer**" for the membrane, resisting changes in membrane fluidity that can be caused by changes in **temperature**.



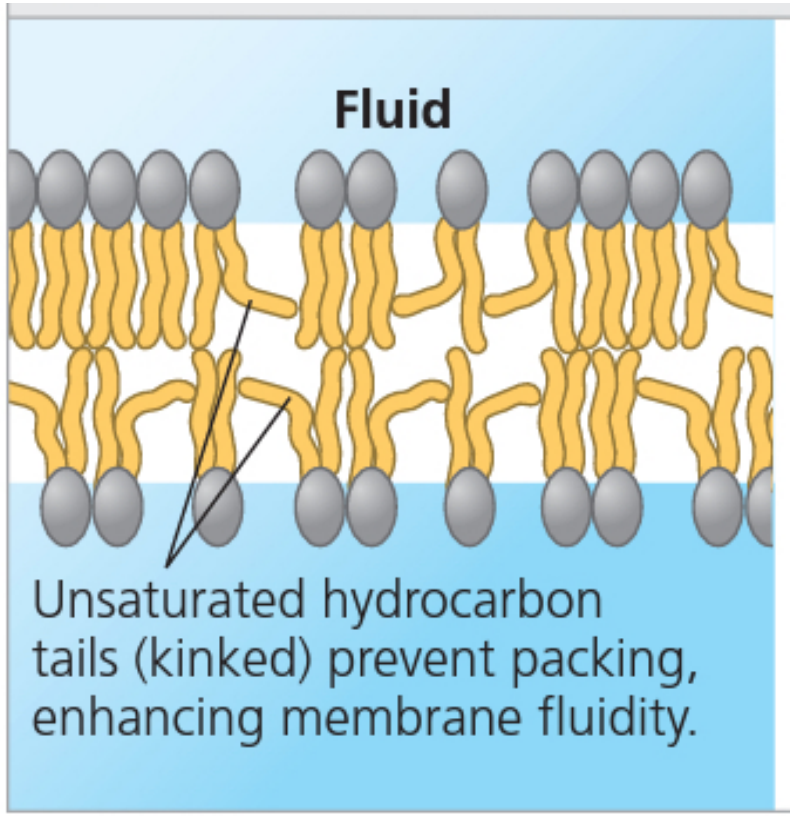


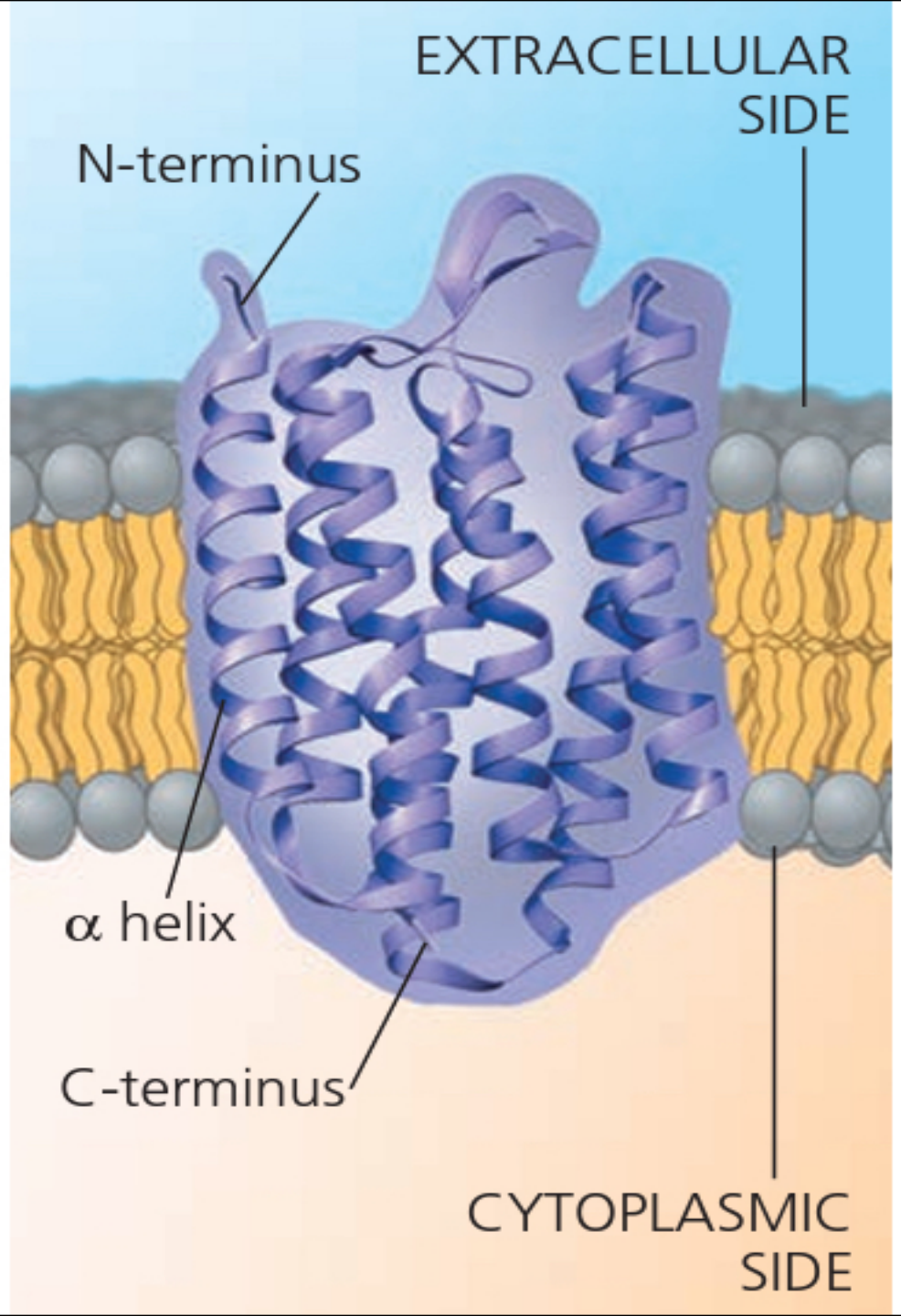
Importance of membrane fluidity

the fluidity of a **membrane** affects both its **permeability** and the ability of **membrane proteins** to move to where their function is needed.

When a **membrane** solidifies, its **permeability** changes, and **enzymatic proteins** in the **membrane** may become inactive if their activity requires movement within the **membrane**.

However, **membranes** that are too fluid cannot support **protein** function either.

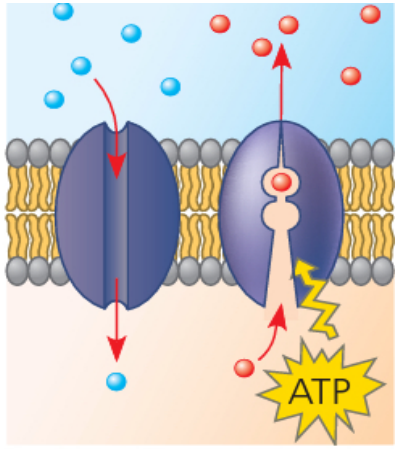




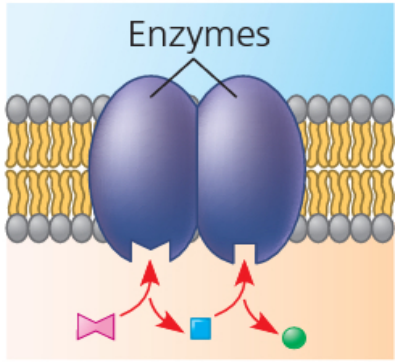
Membrane Proteins and Their Functions

- **Phospholipids** form the main fabric of the **membrane,** but **proteins** determine most of the **membrane's functions.** Different types of cells contain different sets of **membrane proteins,** and the various **membranes** within a **cell** each have a unique collection of **proteins**.
- There are two major populations of membrane proteins: **integral proteins** and **peripheral proteins**.
- **Integral proteins** penetrate the hydrophobic interior of the lipid bilayer. The majority are **transmembrane proteins,** which span the membrane; other **integral proteins** extend only partway into the hydrophobic interior.
- The hydrophobic regions consist of one or more stretches of **nonpolar amino acids** usually coiled into **α helices.** The hydrophilic parts of the molecule are exposed to the aqueous solutions on either side of the **membrane**.
- Some proteins also have one or more **hydrophilic channels** that allow passage through the membrane of **hydrophilic substances.**
- **Peripheral proteins** are not embedded in the **lipid bilayer** at all; they are loosely bound to the surface of the **membrane,** often to exposed parts of **integral proteins.**

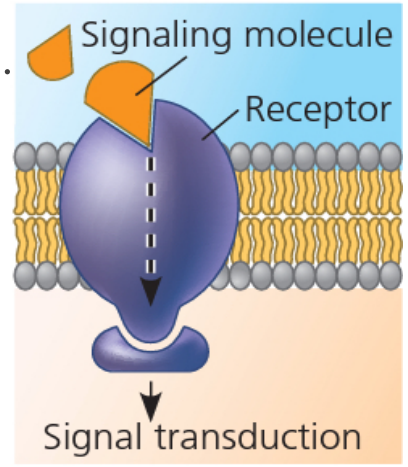
(a) Transport. *Left:* A protein that spans the membrane may provide a hydrophilic channel across the membrane that is selective for a particular solute. *Right:* Other transport proteins shuttle a substance from one side to the other by changing shape (see Figure 7.14b). Some of these proteins hydrolyze ATP as an energy source to actively pump substances across the membrane.



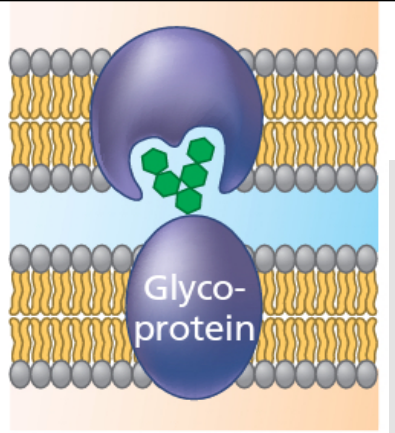
(b) Enzymatic activity. A protein built into the membrane may be an enzyme with its active site (where the reactant binds) exposed to substances in the adjacent solution. In some cases, several enzymes in a membrane are organized as a team that carries out sequential steps of a metabolic pathway.



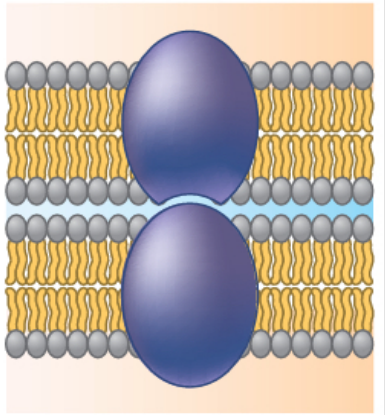
(c) Signal transduction. A membrane protein (receptor) may have a binding site with a specific shape that fits the shape of a chemical messenger, such as a hormone. The external messenger (signaling molecule) may cause the protein to change shape, allowing it to relay the message to the inside of the cell, usually by binding to a cytoplasmic protein (see Figure 11.6).



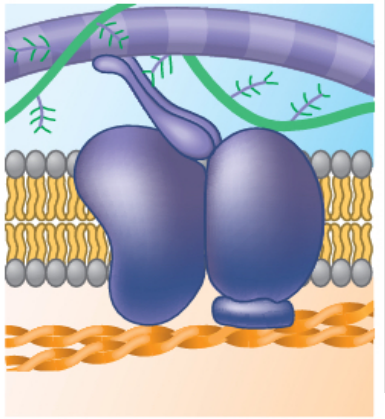
(d) Cell-cell recognition. Some glycoproteins serve as identification tags that are specifically recognized by membrane proteins of other cells. This type of cell-cell binding is usually short-lived compared to that shown in (e).



(e) Intercellular joining. Membrane proteins of adjacent cells may hook together in various kinds of junctions, such as gap junctions or tight junctions (see Figure 6.30). This type of binding is more long-lasting than that shown in (d).



(f) Attachment to the cytoskeleton and extracellular matrix (ECM). Microfilaments or other elements of the cytoskeleton may be noncovalently bound to membrane proteins, a function that helps maintain cell shape and stabilizes the location of certain membrane proteins. Proteins that can bind to ECM molecules can coordinate extracellular and intracellular changes (see Figure 6.28).



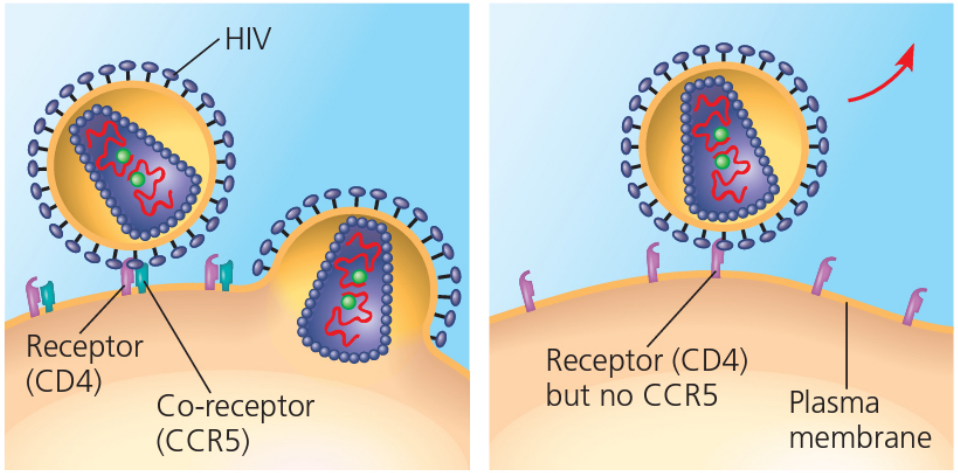
HIV Virus

Proteins on a cell's surface are important in the medical field. For example, a protein called **CD4** on the surface of immune cells helps the **human immunodeficiency virus (HIV)** infect these cells, leading to **acquired immune deficiency syndrome (AIDS).**

Further work showed that although **CD4** is the **main HIV receptor,** HIV must also bind to **CCR5** as a "**co-receptor**" to infect most cells.

Despite multiple exposures to **HIV,** however, a small number of people do not develop **AIDS** and show no evidence of **HIV-infected cells**. Comparing their genes with the genes of infected individuals, researchers learned that resistant people have an unusual form of a gene that codes for an immune cell-surface protein called **CCR5**.

Discovery of the **CCR5** co-receptor provided a safer target for development of drugs that mask this protein and block HIV entry. One such drug, **maraviroc** (brand name **Selzentry**), was approved for treatment of HIV in 2007 and is now being tested to determine whether this drug might also work to prevent HIV infection in uninfected, at-risk patients.



(a) HIV can infect a cell with CCR5 on its surface, as in most people.

(b) HIV cannot infect a cell lacking CCR5 on its surface, as in resistant individuals.

The Role of Membrane Carbohydrates in Cell-Cell Recognition

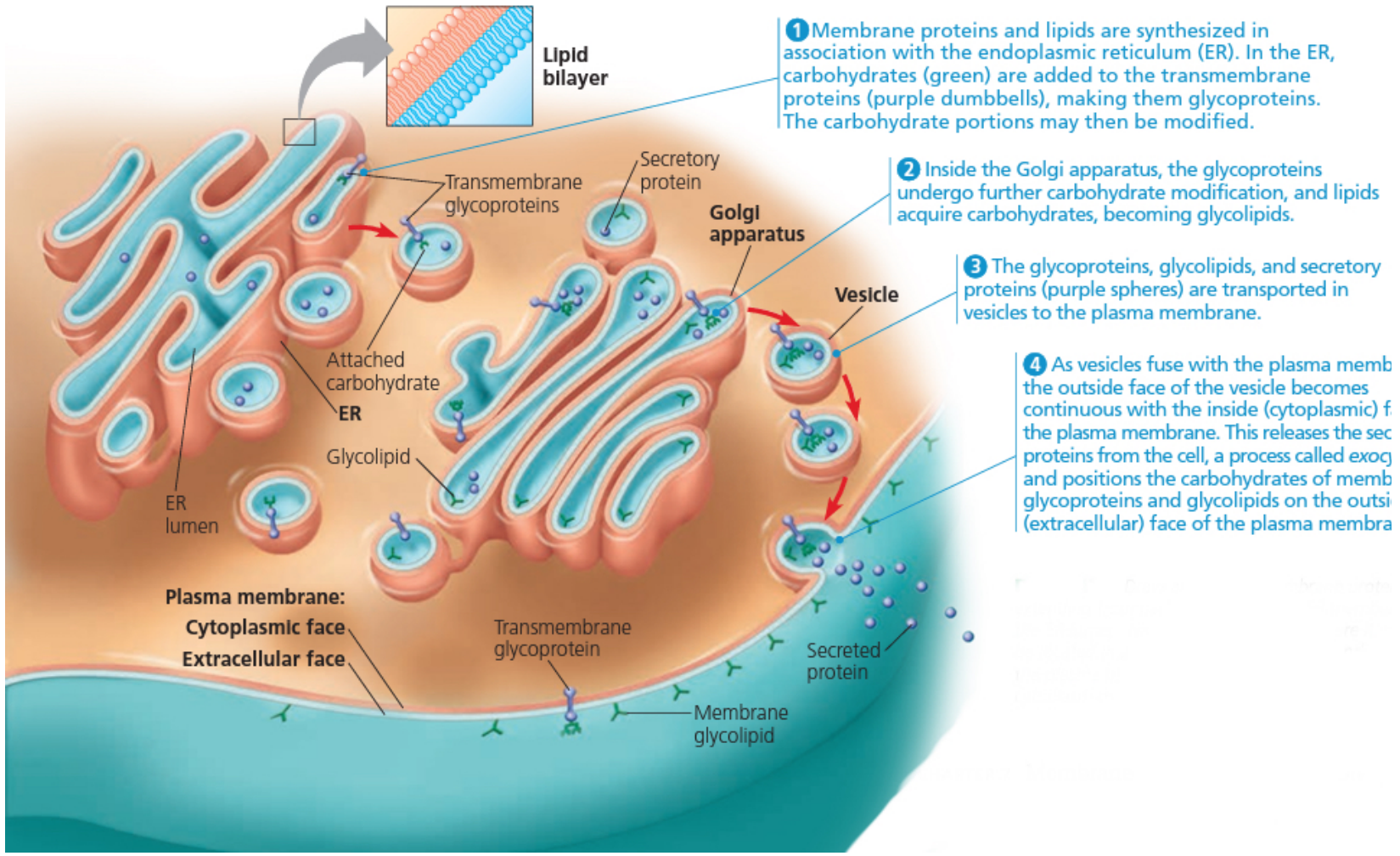
- **Cell-cell recognition**, a cell's ability to distinguish one type of neighboring cell from another, is crucial to the functioning of an organism. It is important, for example, in the sorting of **cells** into **tissues** and **organs** in an **animal embryo.**
- It is also the basis for the rejection of **foreign cells** by the **immune system**, an important line of defense in vertebrate **animals** .
- Membrane **carbohydrates** are usually short, branched chains of fewer than 15 sugar units. Some are covalently bonded to lipids, forming molecules called **glycolipids**. However, most are covalently bonded to proteins, which are thereby **glycoproteins.**
- The **carbohydrates** on the extracellular side of the plasma membrane vary from **species** to species, among **individuals** of the same **species**, and even from one cell type to another in a single **individual**.
- For example, the **four human blood types** designated A, B, AB, and O reflect variation in the carbohydrate part of **glycoproteins** on the surface of **red blood cells.**

Synthesis and Sidedness of Membranes

Membranes have distinct inside and outside faces. The two **lipid layers** may differ in **lipid** composition, and each **protein** has directional orientation in the membrane.

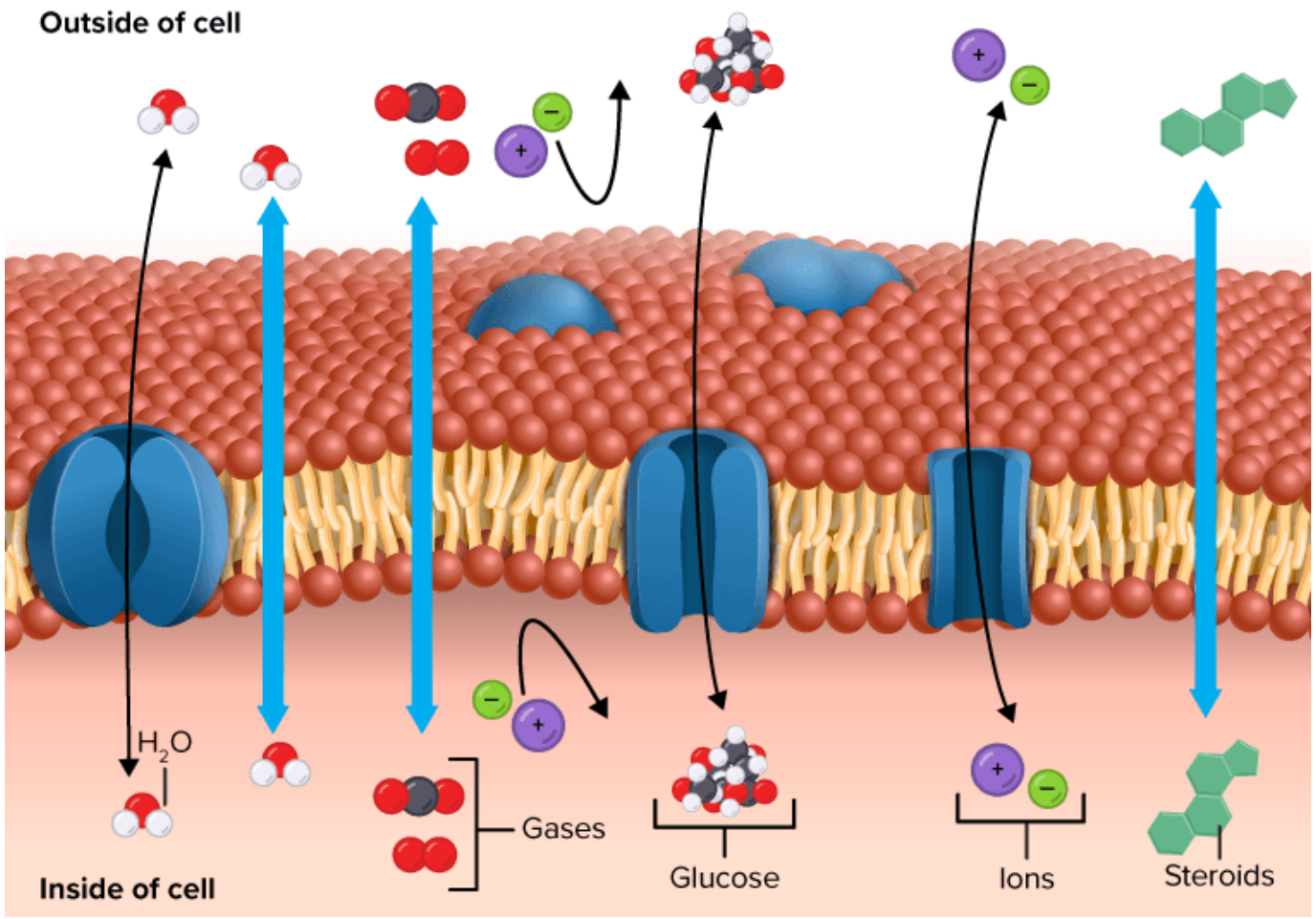
The asymmetrical arrangement of **proteins, lipids,** and their associated **carbohydrates** in the plasma membrane is determined as the membrane is being built by the **endoplasmic reticulum (ER)** and **Golgi apparatus,** components of the endomembrane system.

Figure 7.9 Synthesis of membrane components and their orientation in the membrane. The cytoplasmic (orange) face of the plasma membrane differs from the extracellular (aqua) face. The latter arises from the inside face of ER, Golgi, and vesicle membranes.



Membrane structure results in selective permeability

- A steady traffic of **small molecules** and **ions** moves across the **plasma membrane** in both directions. Consider the **chemical exchanges** between a **muscle cell** and the **extracellular fluid** that bathes it. **Sugars**, **amino acids**, and other **nutrients** enter the **cell**, and metabolic waste products leave it.
- Although the heavy traffic through them may seem to suggest otherwise, cell **membranes** are **selectively permeable**, and **substances** do not cross the barrier indiscriminately. The **cell** is able to take up some **small molecules** and **ions** and exclude others.



The Permeability of the Lipid Bilayer

Nonpolar molecules, such as **hydrocarbons**, **CO_2** , and **O_2** , are hydrophobic, as are **lipids**. They can all therefore dissolve in the **lipid bilayer** of the **membrane** and cross it easily, without the aid of **membrane proteins.**

Polar molecules such as **glucose** and other sugars pass only slowly through a lipid bilayer, and even **water**, a very small **polar** molecule, does not cross rapidly relative to **nonpolar** molecules.

Proteins built into the **membrane** play key roles in regulating **transport**.

Transport Proteins

- Some transport proteins, called **channel proteins,** function by having a **hydrophilic** channel that certain **molecules** or **atomic ions** use as a tunnel through the **membrane.**
- For example, the passage of **water** molecules through the **membrane** in certain **cells** is greatly **facilitated** by **channel proteins** known as **aquaporins.**
- Other transport proteins, called **carrier proteins,** hold onto their passengers and change shape in a way that **shuttles** them across the **membrane.**
- A **transport protein** is specific for the **substance** it translocates (moves), allowing only a certain **substance** (or a small group of related **substances**) to cross the **membrane**.
- For example, **glucose** transporter is so selective that it even rejects **fructose**, a structural isomer of **glucose**.

Concept Check 8.2

1. What property allows o2 and co2 to cross a lipid bilayer without the aid of membrane proteins?

2. VIsUAL sKILLs examine Figure 7.2. Why is a transport protein needed to move many water molecules rapidly across a membrane?

3. MAKe ConneCtIons Aquaporins exclude passage of hydronium ions (h3 o+), but some aquaporins allow passage of glycerol, a three-carbon alcohol (see Figure 5.9), as well as h2 o. Since h3 o+ is closer in size to water than glycerol is, yet cannot pass through, what might be the basis of this selectivity?

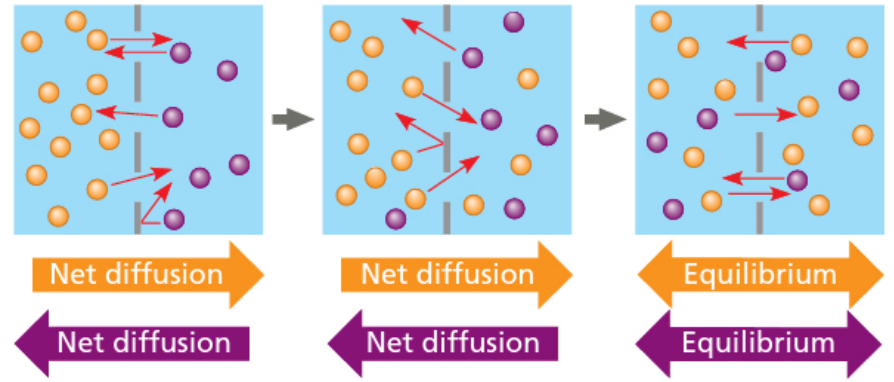
Passive transport is diffusion of a substance across a membrane with no energy investment

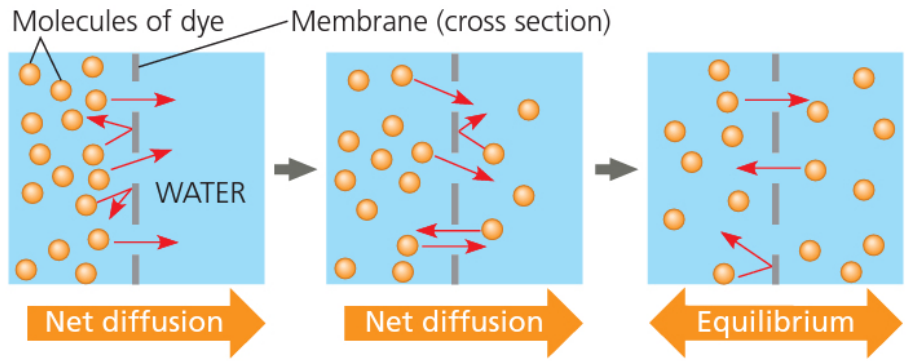
Molecules have a type of energy called **thermal energy,** due to their **constant motion**. One result of this **motion** is **diffusion,** the movement of particles of any **substance** so that they spread out into the available space.

After this **constant motion** across the **membrane,** there will be equal **concentrations** in both sides, and this is called **dynamic equilibrium, ,** in which **roughly** the same number of **molecules** crossing the **membrane** each second in one direction as in the other.

A substance will diffuse from where it is **more** concentrated to where it is **less** concentrated. Put another way, any substance will **diffuse down** its **concentration gradient** (assuming that the **membrane** is **permeable** to that substance).

One important example is the uptake of **oxygen** by a **cell** performing **cellular respiration**. Dissolved **oxygen** diffuses into the **cell** across the **plasma membrane.** As long as **cellular respiration** consumes the **O2** as it enters, diffusion into the **cell** will continue because the **concentration gradient** favors movement in that direction.



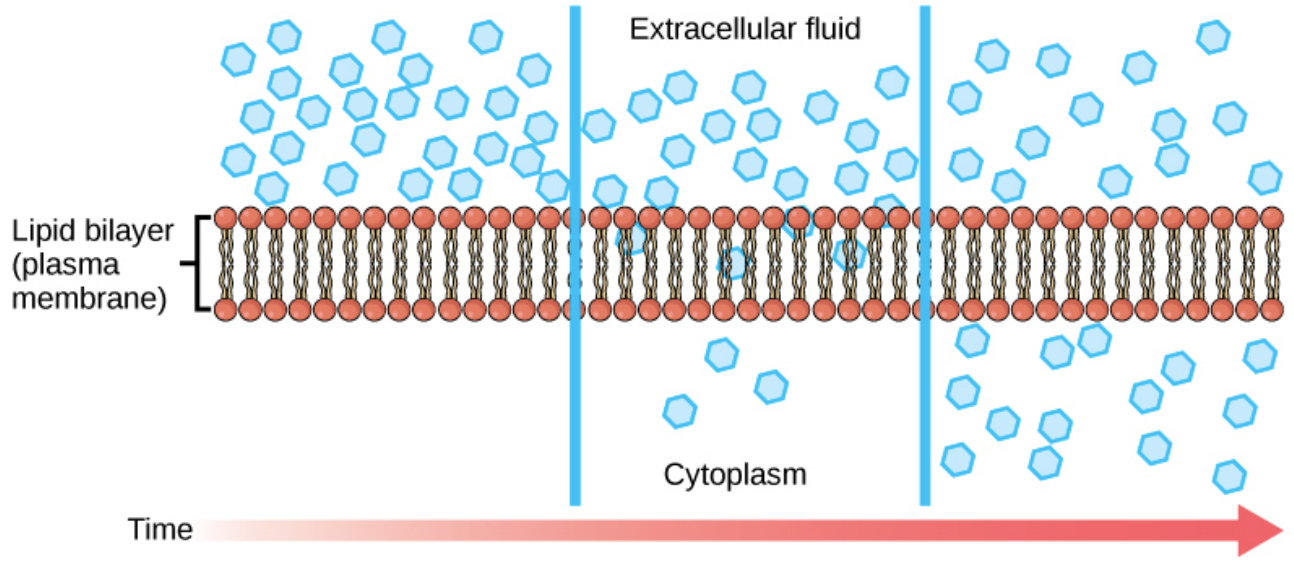


Passive transport

The **diffusion** of a substance across a biological **membrane** is called **passive transport** because the **cell** does not have to expend **energy** to make it happen. The **concentration gradient** itself represents **potential energy** and drives **diffusion**.

However, **membranes** are **selectively permeable** and therefore have different effects on the rates of **diffusion** of various **molecules**.

Water diffuses across the membrane from the region of higher free **water** concentration (lower solute concentration) to that of lower free **water** concentration (higher solute concentration) until the solute concentrations on both sides of the **membrane** are more nearly equal. The diffusion of free **water** across a selectively permeable membrane, whether artificial or cellular, is called **osmosis**.



Water Balance of Cells Without Cell Walls

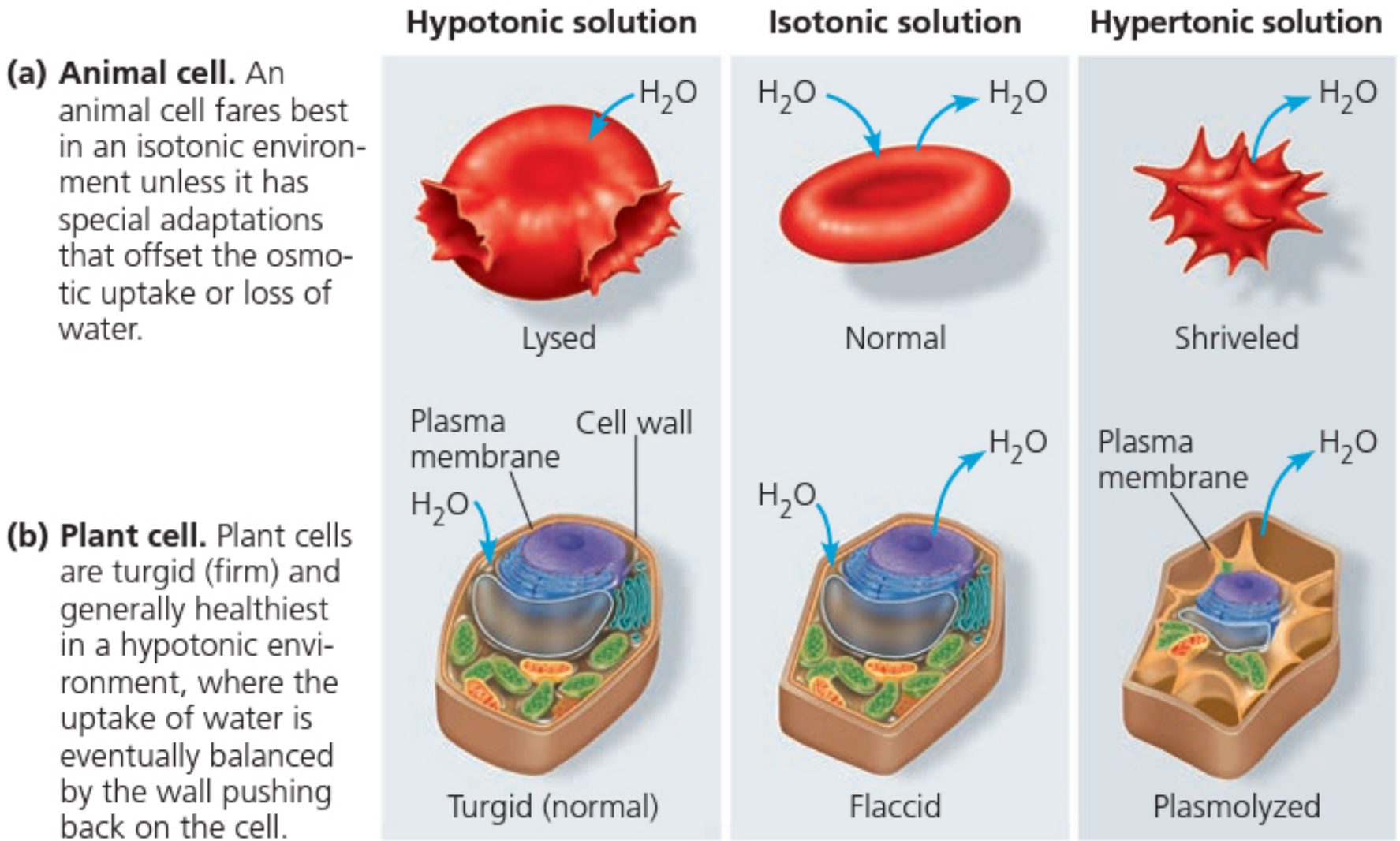
- **Tonicity** is the ability of a surrounding solution to cause a **cell** to gain or lose **water**.
- The tonicity of a solution depends in part on its **concentration** of **solutes** that cannot cross the membrane (**nonpenetrating solutes**) relative to that inside the **cell**.
- **Isotonic solution** means that there is no net movement of **water** across the **plasma membrane.**
- **Hypertonic solution** means that The cell will lose water, shrivel, and probably die. This is why an increase in the salinity (saltiness) of a lake can kill the animals there.
- **Hypotonic solution** means thatvwater will enter the cell faster than it leaves, and the cell will swell and lyse (burst) like an overfilled water balloon.
- A **cell** without rigid cell walls can tolerate neither excessive **uptake** nor excessive **loss** of **water**.

Adaptations for osmoregulation

- he unicellular **eukaryote Paramecium** lives in pond water, which is hypotonic to the cell. **Paramecium** has a **plasma membrane** that is much less permeable to water than the **membranes** of most other cells, but this only slows the uptake of **water**, which continually enters the cell.
- The **Paramecium** cell doesn't burst because it is also equipped with a **contractile vacuole**, an **organelle** that functions as a bilge pump to force **water** out of the cell as fast as it enters by **osmosis**.
- In contrast, the **bacteria** and **archaea** that live in **hypersaline** (excessively salty) environments have cellular mechanisms that balance the **internal** and **external solute concentrations** to ensure that **water** does not move out of the **cell**.

Water Balance of Cells with Cell Walls

- The cells of **plants, prokaryotes, fungi,** and some **unicellular eukaryotes** are surrounded by **cell walls.**
- When such a cell is immersed in a **hypotonic** solution the **cell wall** helps maintain the **cell's water** balance. The **plant cell** swells as **water** enters by **osmosis,** however, the relatively inelastic **cell wall** will expand only so much before it exerts a back pressure on the **cell,** called **turgor pressure,** that opposes further **water** uptake.
- At this point, the cell is **turgid** (very firm), the healthy state for most **plant cells.**
- If a plant's cells and surroundings are **isotonic,** there is no net tendency for water to enter and the cells become **flaccid** (limp); the plant **wilts**.
- If the cell is immersed in a **hypertonic** environment, it will lose water to its surroundings and shrink. As the plant cell shrivels, its **plasma membrane** pulls away from the cell wall at multiple places. This phenomenon, called **plasmolysis,** causes the plant to wilt and can lead to **plant death.**


Hypotonic solution
Isotonic solution
Hypertonic solution
(a) Animal cell. An animal cell fares best in an isotonic environment unless it has special adaptations that offset the osmotic uptake or loss of water.
H_2O
Lysed
H_2O
H_2O
Normal
H_2O
Shriveled
(b) Plant cell. Plant cells are turgid (firm) and generally healthiest in a hypotonic environment, where the uptake of water is eventually balanced by the wall pushing back on the cell.
Plasma membrane
Cell wall
H_2O
Turgid (normal)
H_2O
H_2O
Flaccid
Plasma membrane
H_2O
Plasmolyzed

Facilitated Diffusion: Passive Transport Aided by Proteins

Facilitated diffusion means that the polar molecules and ions diffuse passively with the help of transport **proteins** that span the **membrane**.

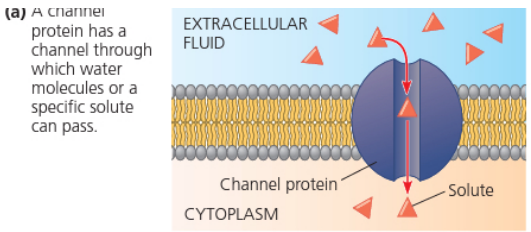
Channel proteins simply provide corridors that allow specific **molecules** or **ions** to cross the **membrane.**

Channel proteins that transport ions are called **ion channels.**

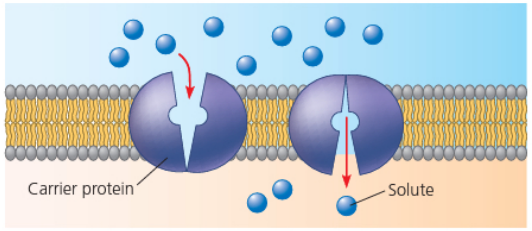
Many ion channels function as **gated channels**, which open or close in response to a stimulus. For some gated channels, the **stimulus** is electrical.

Other **gated channels** open or close when a specific substance other than the one to be transported binds to the channel.

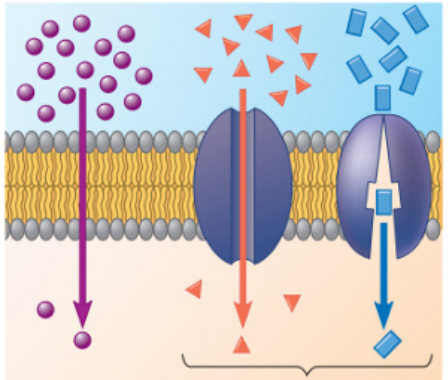
Carrier proteins involved in **facilitated diffusion** result in the net **movement** of a substance down its **concentration gradient.** For example, glucose transporter, seem to undergo a subtle change in shape that somehow translocates the solute-binding site across the **membrane.**



(a) A channel protein has a channel through which water molecules or a specific solute can pass.



(b) A carrier protein alternates between two shapes, moving a solute across the membrane during the shape change.



Diffusion. Hydrophobic molecules and (at a slow rate) very small uncharged polar molecules can diffuse through the lipid bilayer.

Facilitated diffusion. Many hydrophilic substances diffuse through membranes with the assistance of transport proteins, either channel proteins (left) or carrier proteins (right).

Concept Check 8.3

1. how do you think a cell performing cellular respiration rids itself of the resulting co2 ?

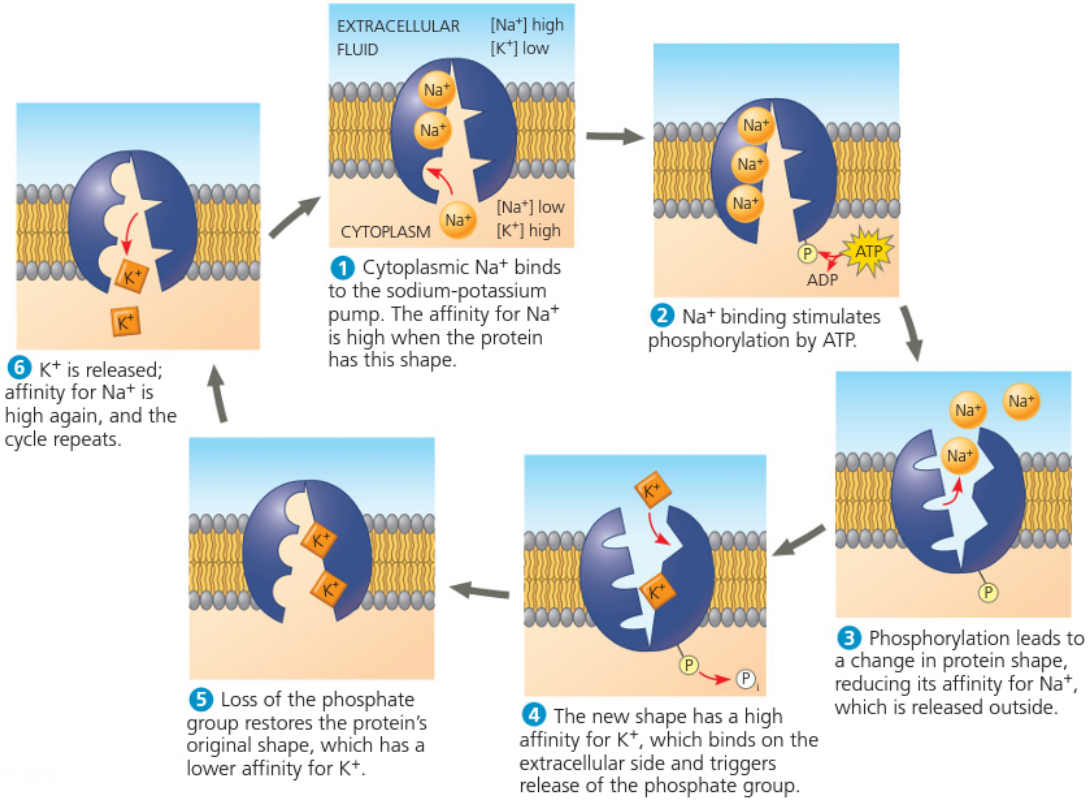
2. WHAt IF? if a Paramecium swims from a hypotonic to an isotonic environment, will its contractile vacuole become more active or less? Why?

Active transport uses energy to move solutes against their gradients

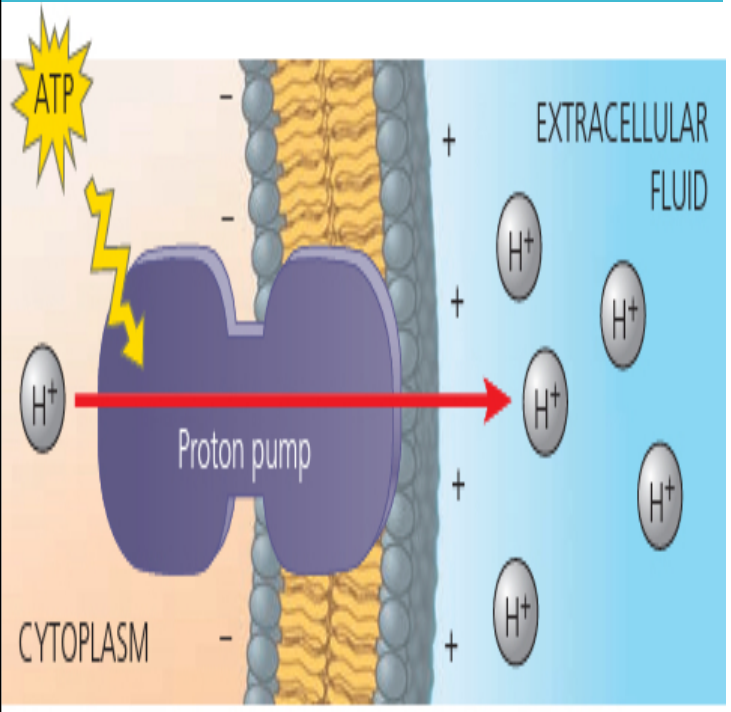
To pump a solute across a **membrane** against its **gradient** requires work; the cell must expend **energy**. Therefore, this type of **membrane** traffic is called **active transport**.

The **transport proteins** that move solutes against their concentration gradients are all carrier **proteins** rather than **channel proteins.**

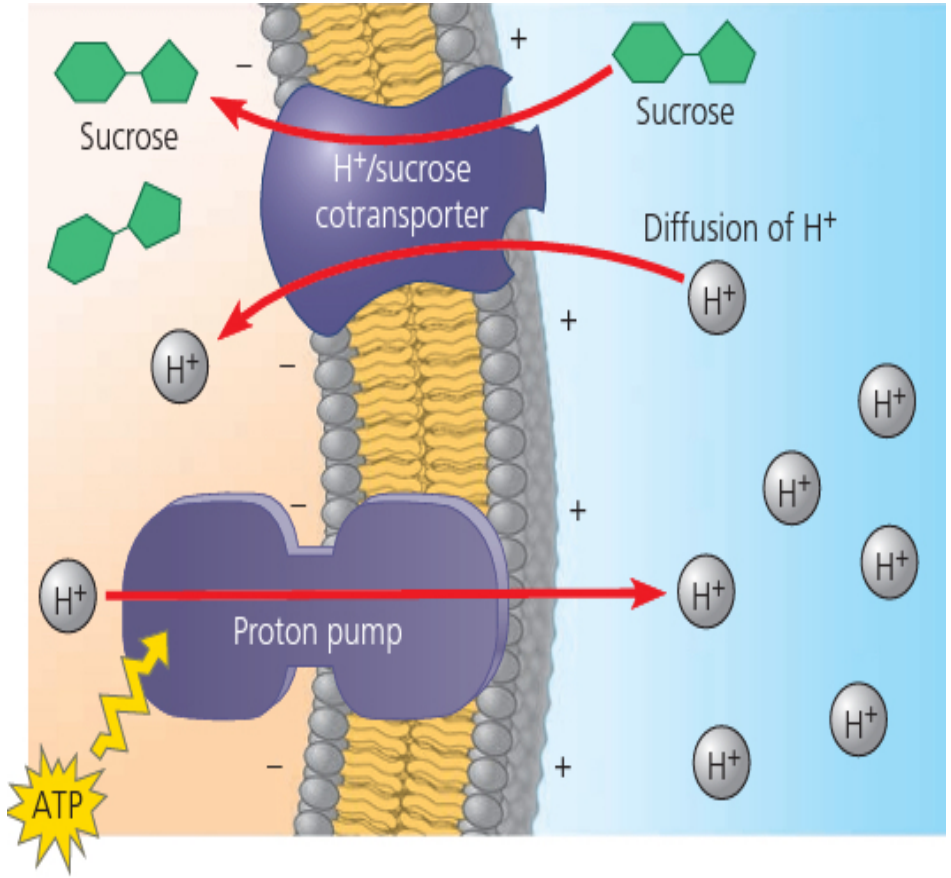
One transport system that works this way is the **sodium-potassium pump**, which exchanges **Na+** for **K+** across the **plasma membrane** of **animal cells.**



How Ion Pumps Maintain Membrane Potential



- The voltage across a membrane, called a **membrane potential,** ranges from about **-50 to -200** millivolts (**mV**). (The minus sign indicates that the **inside** of the cell is **negative** relative to the **outside**.)
- Because the **inside** of the cell is **negative** compared with the **outside,** the **membrane potential** favors the **passive transport** of **cations** into the cell and **anions** out of the cell.
- Thus, two forces drive the **diffusion** of **ions** across a **membrane**: **chemical force** and an **electrical force.** This combination of forces acting on an ion is called the **electrochemical gradient.**
- Some **membrane proteins** that **actively** transport **ions** contribute to the **membrane potential**. A transport protein that generates **voltage** across a **membrane** is called an **electrogenic pump.**
- The **sodium-potassium pump** appears to be the major electrogenic pump of **animal cells**. The main electrogenic pump of **plants, fungi, and bacteria** is a **proton pump,** which actively transports protons (hydrogen ions, H+) out of the cell.



Cotransport: Coupled Transport by a Membrane Protein

A solute that exists in **different concentrations** across a **membrane** can do work as it moves across that **membrane** by **diffusion** down its **concentration gradient.**

In a mechanism called **cotransport,** a transport protein (a cotransporter) can couple the "**downhill**" diffusion of the solute to the "**uphill**" transport of a second substance against its own **concentration gradient.**

For instance, a **plant cell** uses the gradient of **H+** generated by its ATP-powered proton pumps to drive the **active transport** of **amino acids, sugars,** and several other **nutrients** into the **cell**.

Plants use **H+/sucrose cotransport** to load sucrose produced by **photosynthesis** into cells in the **veins** of **leaves**.

Clinical Correlation

- Normally, sodium in waste is reabsorbed in the colon, maintaining constant levels in the body, but diarrhea expels waste so rapidly that reabsorption is not possible, and sodium levels fall precipitously.

- To treat this life-threatening condition, patients are given a solution to drink containing high concentrations of salt (NaCl) and glucose. The solutes are taken up by sodium glucose co-transporters on the surface of intestinal cells and passed through the cells into the blood. This simple treatment has lowered infant mortality worldwide.

Concept Check 8.4

1. Sodium-potassium pumps help nerve cells establish a voltage across their plasma membranes. Do these pumps use Atp or produce Atp? explain.

2. VIsUAL sKILLs compare the sodium-potassium pump in Figure 7.15 with the cotransporter in Figure 7.18. explain why the sodium-potassium pump would not be considered a cotransporter.

3. MAKe ConneCtIons review the characteristics of the lysosome in concept 6.4. Given the internal environment of a lysosome, what transport protein might you expect to see in its membrane?

Exocytosis

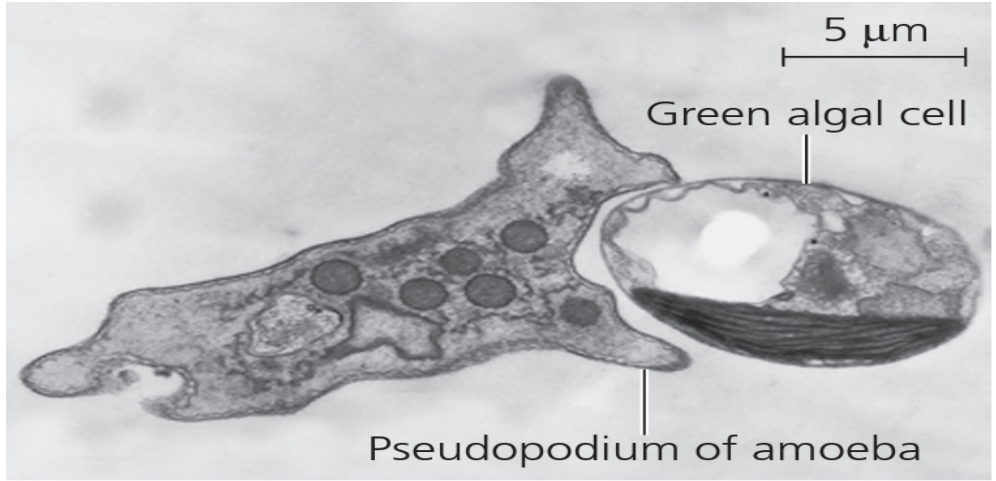
- Large molecules—such as proteins and polysaccharides, as well as larger particles—generally cross the membrane in bulk, packaged in vesicles. Like active transport, these processes require energy.
- A transport vesicle that has budded from the **Golgi apparatus** moves along microtubules of the cytoskeleton to the **plasma membrane**. When the vesicle membrane and plasma membrane come into contact, fusion occurs and the contents of the vesicle are spilled out of the cell. This process is called **exocytosis**.
- Many secretory cells use exocytosis to export products. For example, cells in the pancreas that make **insulin** secrete it into the extracellular fluid by **exocytosis**. In another example, nerve cells use **exocytosis** to release **neurotransmitters** that signal other **neurons** or **muscle** cells.

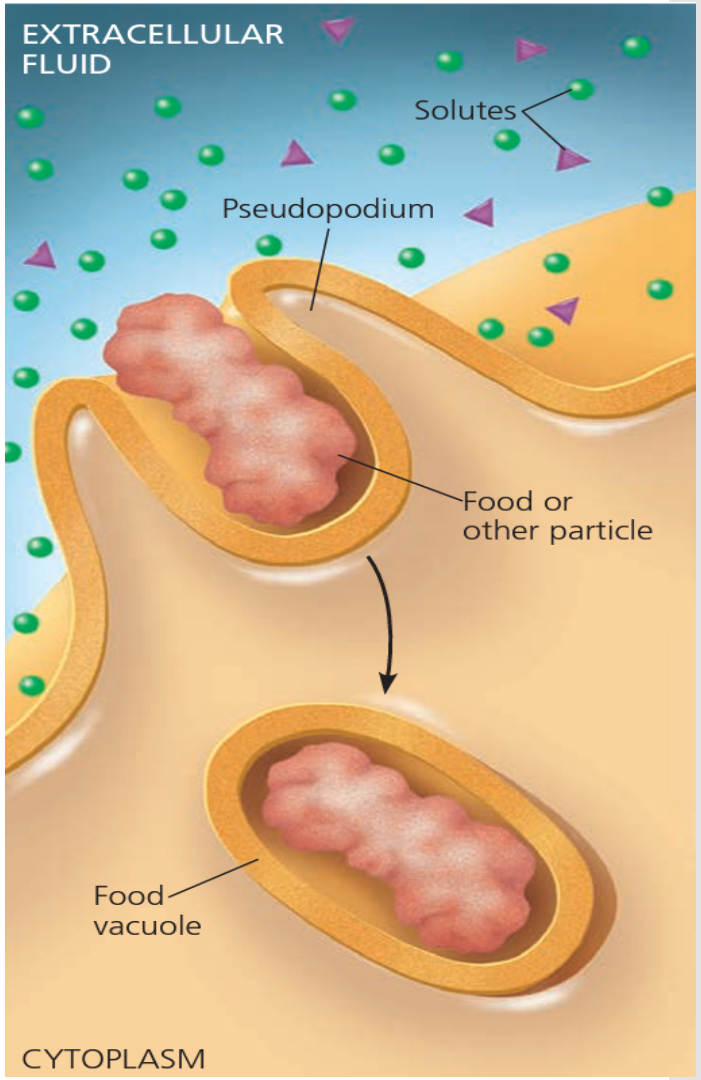
Endocytosis

- In endocytosis, the cell takes in molecules and particulate matter by forming new vesicles from the plasma membrane.
- First, a small area of the plasma membrane sinks inward to form a pocket. Then, as the pocket deepens, it pinches in, forming a vesicle containing material that had been outside the cell.
- There are three types of endocytosis: phagocytosis ("cellular eating"), pinocytosis ("cellular drinking"), and receptor-mediated endocytosis.

Phagocytosis

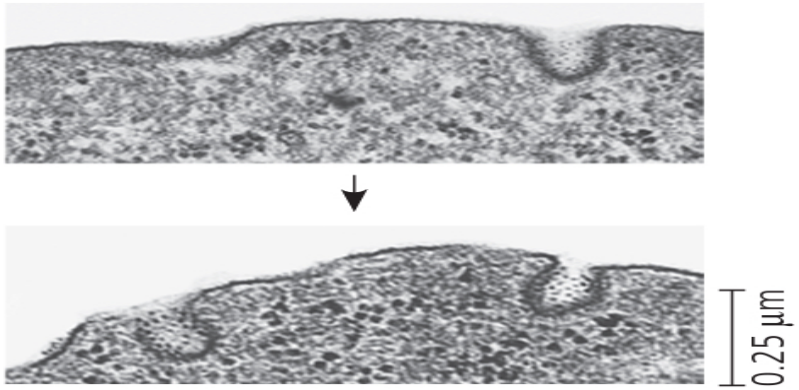
- In **phagocytosis**, a cell engulfs a particle by extending pseudopodia (singular, pseudopodium) around it and packaging it within a membranous sac called a food vacuole. The particle will be digested after the food vacuole fuses with a lysosome containing hydrolytic enzymes.
- An amoeba engulfing a green algal cell via phagocytosis (TEM).



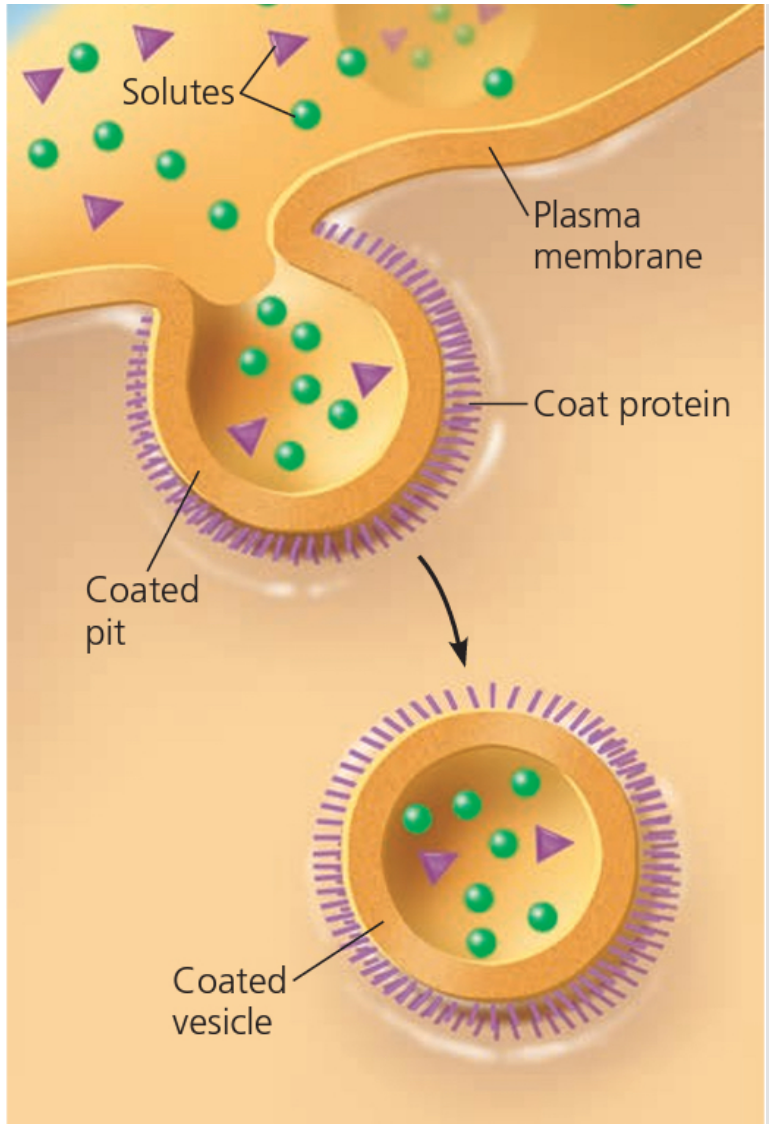


Pinocytosis

- In **pinocytosis**, a cell continually "gulps" droplets of extracellular fluid into tiny vesicles, formed by infoldings of the plasma membrane. In this way, the cell obtains molecules dissolved in the droplets. Because any and all solutes are taken into the cell, pinocytosis as shown here is nonspecific for the substances it transports. In many cases, as above, the parts of the plasma membrane that form vesicles are lined on their cytoplasmic side by a fuzzy layer of coat protein; the "pits" and resulting vesicles are said to be "coated."

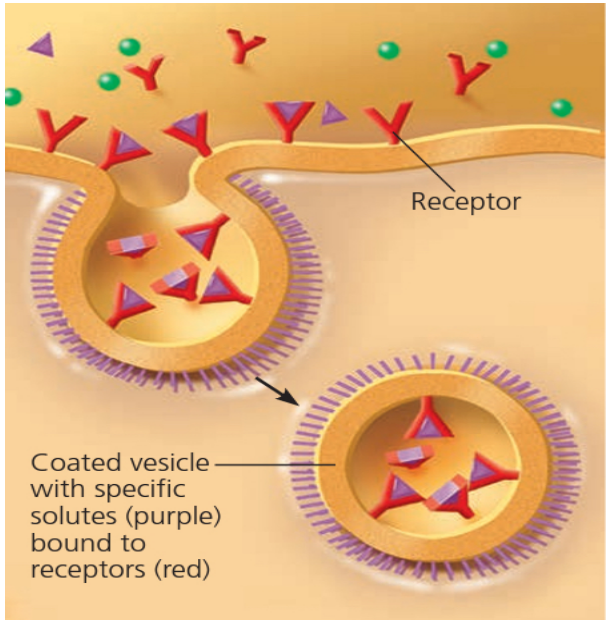


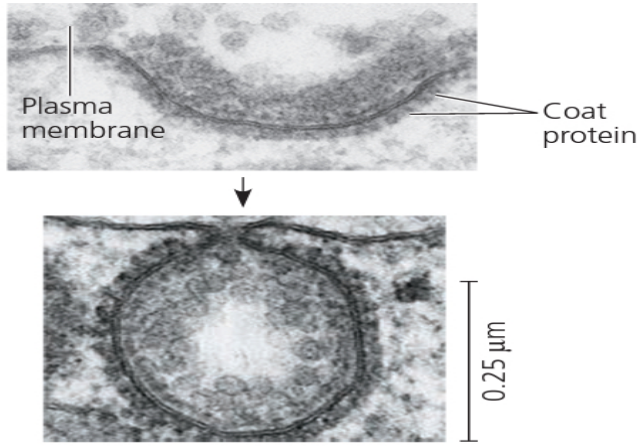
Pinocytotic vesicles forming (TEMs).



Receptor-Mediated Endocytosis

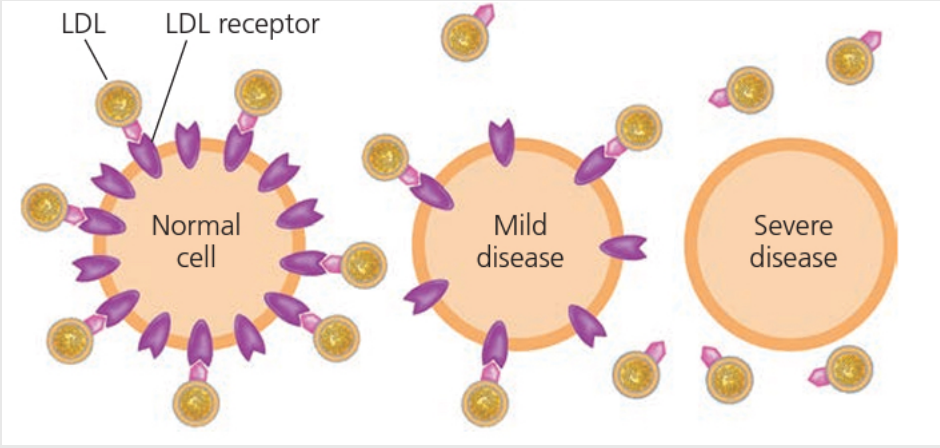
- Receptor-mediated endocytosis is a specialized type of pinocytosis that enables the cell to acquire bulk quantities of specific substances, even though those substances may not be very concentrated in the extracellular fluid. Embedded in the plasma membrane are proteins with receptor sites exposed to the extracellular fluid. Specific solutes bind to the receptors. The receptor proteins then cluster in coated pits, and each coated pit forms a vesicle containing the bound molecules.
- After the ingested material is liberated from the vesicle, the emptied receptors are recycled to the plasma membrane by the same vesicle.





Clinical Connection

- Human cells use receptor-mediated endocytosis to take in cholesterol for membrane synthesis and the synthesis of other steroids. Cholesterol travels in the blood in particles called low-density lipoproteins (LDLs), each a complex of lipids and a protein.
- LDLs bind to LDL receptors on plasma membranes and then enter the cells by endocytosis. In the inherited disease familial hypercholesterolemia, characterized by a very high level of cholesterol in the blood, LDLs cannot enter cells because the LDL receptor proteins are defective or missing.
- Consequently, cholesterol accumulates in the blood, where it contributes to early atherosclerosis, the buildup of lipid deposits within the walls of blood vessels. This buildup narrows the space in the vessels and impedes blood flow, potentially resulting in heart damage and stroke.



- Endocytosis and exocytosis also provide mechanisms for rejuvenating or remodeling the plasma membrane. These processes occur continually in most eukaryotic cells, yet the amount of plasma membrane in a nongrowing cell remains fairly constant. The addition of membrane by one process appears to offset the loss of membrane by the other.
- Energy and cellular work have figured prominently in our study of membranes. In the next three chapters, you will learn more about how cells acquire chemical energy to do the work of life.