# Chapter 8: Membrane Structure and Function

## Overview: Life at the Edge

- The plasma membrane is the boundary that separates the living cell from its surroundings.
- The plasma membrane exhibits selective permeability, allowing some substances to cross it more easily than others.

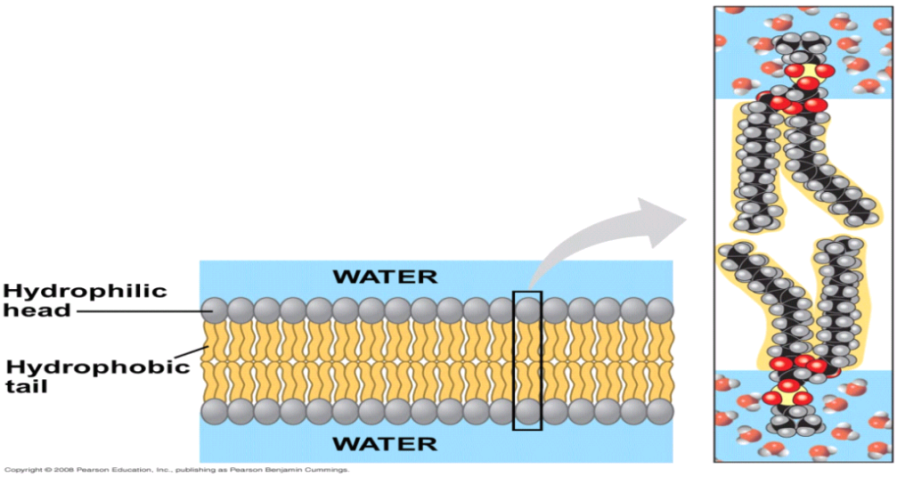
## Concept 7.1:Cellular membranes are fluid mosaics of lipids and proteins

- 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 region and a hydrophobic region.
- In the fluid mosaic model,the membrane is a fluid structure with a"mosaic" of various proteins embedded in or attached to a double layer(bilayer) of phospholipids.

### v Membrane Models: Scientific Inquiry

- Membranes have been chemically analysed and found to be made of proteins and lipids.
- Scientists studying the plasma membrane reasoned that it must be a phospholipid bilayer.

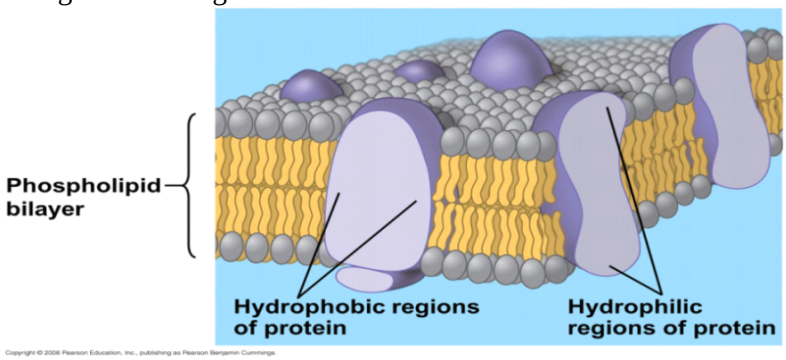
Fig. 7-2 phospholipid bilayer (cross section)




- In 1935, Hugh Davson and James Danielli suggested that the membrane might be coated on both sides with hydrophilic proteins, they proposed a sandwich model: phospholipid bilayer lies between two layers of globular proteins.

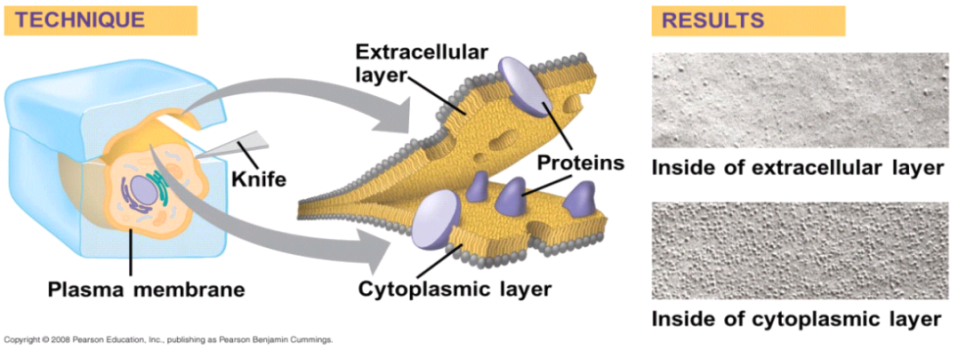
- Later studies found problems with this model, particularly the placement of membrane proteins, which have hydrophilic and hydrophobic regions.
- In 1972, J. Singer and G. Nicolson proposed that the membrane is a mosaic of proteins dispersed within the phospholipid bilayer, with only the hydrophilic regions exposed to water.

Fig. 7-3The original fluid mosaic model for membrane




- This molecular arrangement would a maximize contact of hydrophilic regions of proteins and phospholipids with water in the cytosol and extracellular fluid, while providing their hydrophobic parts with a non-aqueous environment.
- Freeze-Fracture is a method of preparing cells for electron microscopy.
- Freeze-fracture studies of the plasma membrane supported the fluid mosaic model.
- Freeze-fracture is a specialized preparation technique that splits a membrane along the middle of the phospholipid bilayer.

Fig. 7-4 Freeze-fracture

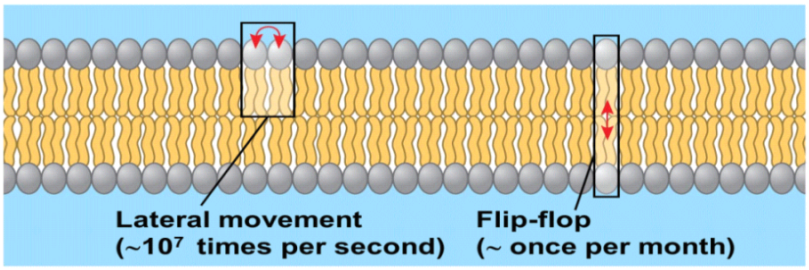



v The Fluidity of Membranes

- A membrane is held together primarily by hydrophobic interactions, which are much weaker than covalent bonds.
- Phospholipids in the plasma membrane can move within the bilayer.
- Most of the lipids and some of the proteins can shift about laterally.

- It is quite rare, for a molecule to flip-flop transversely across the membrane, switching from one phospholipid layer to the other; to do so , the hydrophilic part of the molecule must cross the hydrophobic interior of the membrane.
- The lateral movement of phospholipids is rapid.
- Proteins are much larger than lipids and move more slowly.

Fig.7.5 The movement of phospholipids

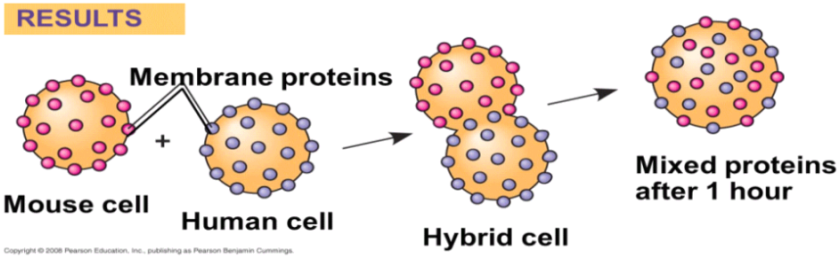



(a) Movement of phospholipids



Fig.7-7 Inquiry

Do membrane proteins move?



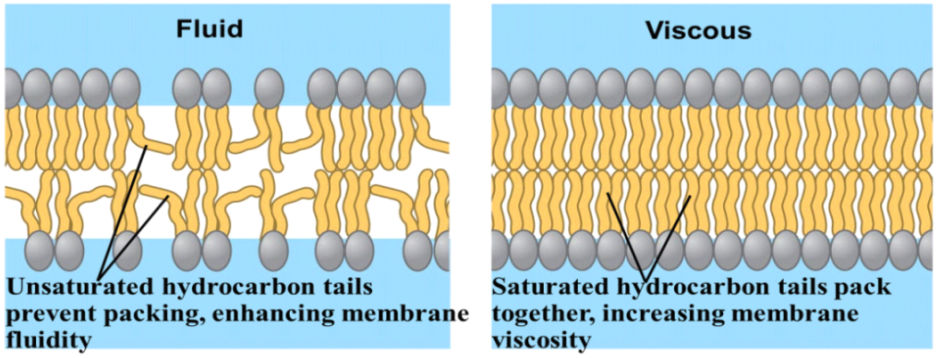



**CONCLUSION**

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.

- As temperatures cool, membranes switch from a fluid state to a solid state.
- The temperature at which a membrane solidifies depends on the types of lipids.
- Because of kinks in the tails where double bonds are located, unsaturated hydrocarbon tails cannot pack together as closely as saturated hydrocarbon tails,and this makes the membrane which rich in unsaturated fatty acids more fluid than those rich in saturated fatty acids.
- Membranes must be fluid to work properly; they are usually about as fluid as salad oil.

Fig.7.8 Factors that affect membrane fluidity.

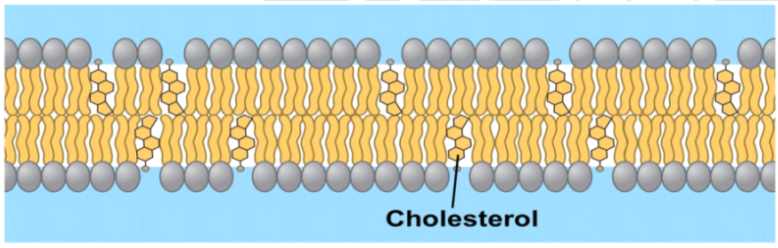





**(a) Unsaturated versus saturated hydrocarbon tails**

- The steroid cholesterol, which is wedged between phospholipid molecules in the plasma membranes of animal cells,has different effects on membrane fluidity at different temperature.
- At relatively high "warm" temperatures -at 37°C for example-cholesterol makes the membrane less fluid by restraining phospholipid movement.
- At cool temperatures, it maintains fluidity and hinders solidification by preventing tight packing.
- 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.

Fig.7.8Factors that affect membrane fluidity.




**(b) Cholesterol within the animal cell membrane**



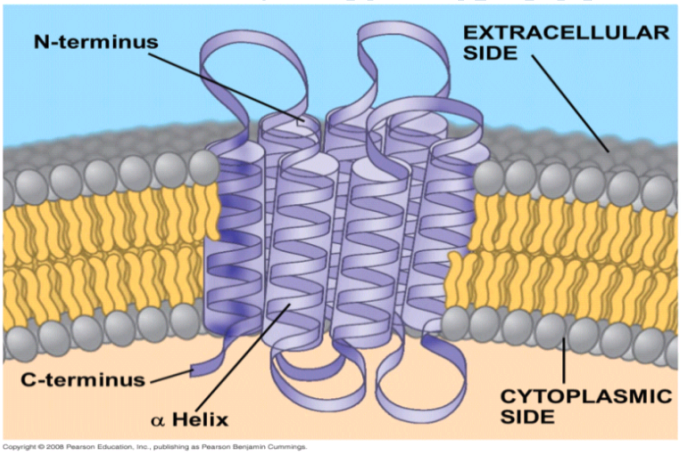
v Evolution Of Differences In Membrane Lipid Composition

- Variations in the cell membrane lipid compositions of many species appear to be evolutionary adaptations that maintain the appropriate membrane fluidity under specific environmental conditions, For instance, fishes that live in extreme cold have membranes with a high proportion of unsaturated hydrocarbon tails, enabling their membrane to remain fluid.
- The ability to change the lipid composition of cell membrane in response to changing temperatures has evolved in organisms that live where temperatures vary.

v Membrane Proteins and Their Functions

- A membrane is a collage of different proteins,often clustered together in groups, embedded in the fluid matrix of the lipid bilayer.
- Phospholipids form the main fabric of the membrane, but proteins determine most of the membrane's specific functions.
- There are two major populations of membrane proteins: integral proteins and peripheral proteins.
- Integral proteins :
  1/ penetrate the hydrophobic interior of the lipid bilayer.
  2/ the majority are transmembrane proteins, which span the membrane; other integral proteins extend only partway into the hydrophobic interior.
  3/The hydrophobic regions of an integral protein consist of one or more stretches of nonpolar amino acids, often coiled into alpha helices.
  4/ some proteins also have a hydrophilic channel through their center that allows passage of hydrophilic substances.
- Peripheral proteins are not embedded in the lipid bilayer at all; they are appendages loosely bound to the surface of the membrane, often to exposed parts of integral proteins.
- On the cytoplasmic side of the Plasma membrane, some membrane proteins are held in place by attachment to the cytoskeleton, And on the extracellular side, certain membrane proteins are attached to fibers of the extracellular matrix.
- These attachments combine to give animal cells a stronger framework than the plasma membrane alone could provide.

Fig.7.9 The structure of a transmembrane protein



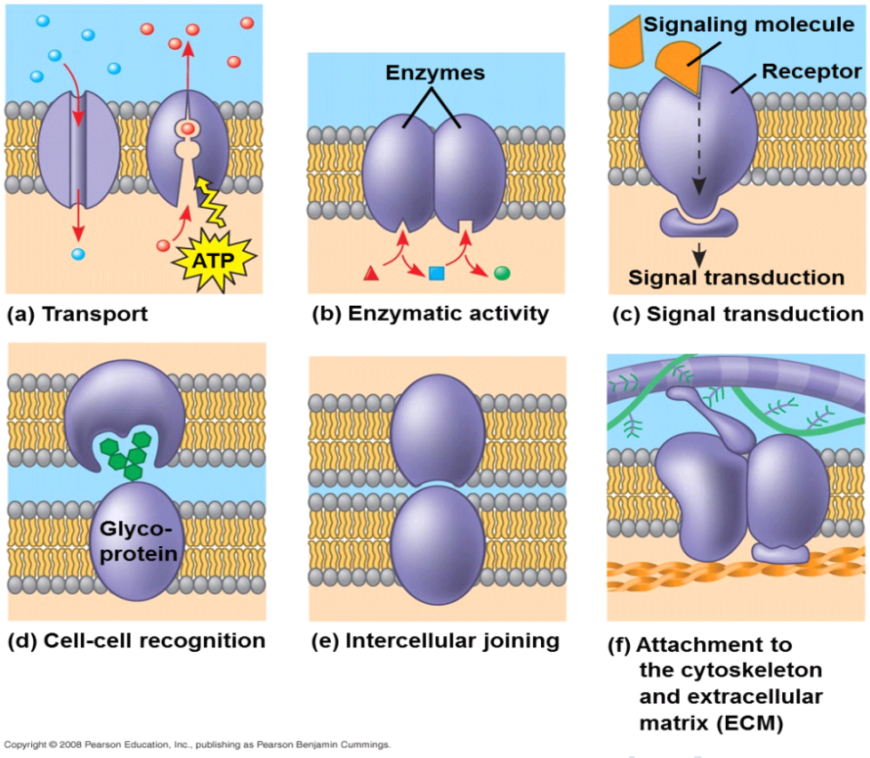

Explanation of figure 7.9

- Bacteriorhodopsin(a bacterial transport protein) has a distinct orientation in the membrane, with its N- terminus outside the cell and its C-terminus inside.
- The protein includes seven transmembrane helices.
- The non-helical hydrophilic segments are in contact with the aqueous solutions on the extracellular and cytoplasmic sides of the membrane.

- Six major functions of membrane proteins:

1.Transport
2.Enzymatic activity
3.Signal transduction
4.Cell-cell recognition
5.Intercellular joining
6.Attachment to the cytoskeleton and extracellular matrix (ECM)

Fig.7.10 functions of membrane proteins





- Proteins on the surface of a cell are important in the medical field because some proteins can help outside agents invade the cell, For example cell-surface proteins help the human immunodeficiency virus (HIV) infect immune system cells, leading to acquired immune deficiency syndrome (AIDS).

IMPACT
Blocking HIV Entry into Cells as a Treatment for HIV Infections
Despite multiple exposures to HIV, 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 discovered that resistant individuals have an unusual form of a gene that codes for an immune cell-surface protein called CCR5. Further work showed that HIV binds to a main protein receptor(CD4) on an immune cell, but most types of HIV also need to bind to CCR5 as a "co-receptor" to actually infect the cell. An absence of CCR5 on the cells of resistant individuals, due to the gene alteration, prevents the virus from entering the cells.

So HIV can infect a cell that has CCR5 on its surface, as in most people and cannot infect a cell lacking CCR5 on its surface,as in resistant individuals.

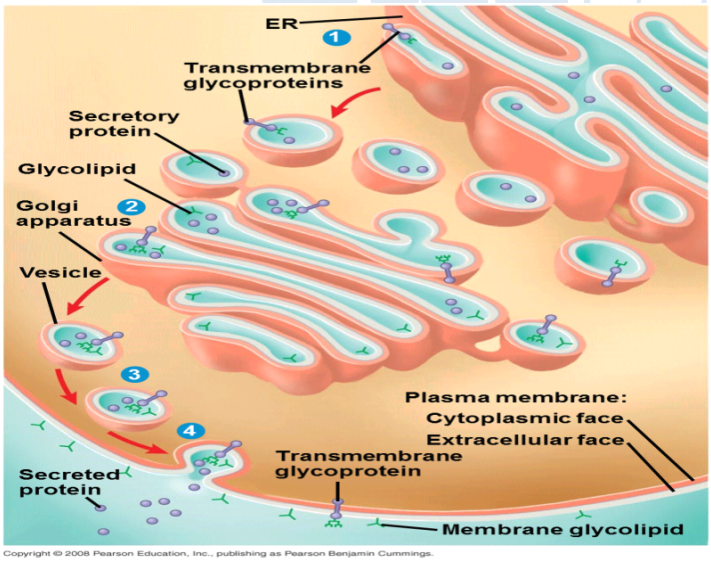
## v The Role of Membrane Carbohydrates in Cell-Cell Recognition

- Cell-Cell recognition, a cell's ability to distinguish one type of neighboring cell from another, is crucial to the functioning of an organism.
- Cell-cell recognition is the basis for the rejection of foreign cells by the immune system.
- Cells recognize other cells by binding to surface molecules, often containing carbohydrates, on the extracellular surface of the plasma membrane.
- Membrane carbohydrates are usually short,branched chains of fewer than 15 sugar units.
- Membrane carbohydrates may be covalently bonded to lipids (forming glycolipids) or more commonly to proteins (forming glycoproteins).
- Carbohydrates on the external side of the plasma membrane vary from species to species,among individuals of the same species , and even from one cell types to another in an 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.

## v Synthesis and Sidedness of Membranes.

- Membranes have distinct inside and outside faces.
- The asymmetrical distribution of proteins, lipids, and associated carbohydrates in the plasma membrane is determined when the membrane is built by the endoplasmic reticulum (ER) and Golgi apparatus.

Fig.7.12 Synthesis of membrane components and their orientation in the membrane. (The cytoplasmic face of the plasma membrane differs from the extracellular face)



Explanation of figure 7.12

1. Membrane proteins and lipids are synthesized in the endoplasmic reticulum (ER). Carbohydrates are added to the transmembrane proteins, making them glycoproteins. The carbohydrate portions may then be modified.
2. Inside the Golgi apparatus, the glycoproteins undergo further carbohydrate modification, and lipids acquire carbohydrates, becoming glycolipids.

3. The glycoproteins, glycolipids, and secretory proteins are transported in Vesicles to the plasma membrane.
4. As vesicles fuse with the plasma membrane, the outside face of the vesicle becomes continuous with the inside(cytoplasmic) face of the plasma membrane. This releases the secretory proteins from the cell , a process called exocytosis, and positions the carbohydrates of membrane glycoproteins and glycol-lipids on the outside (extracellular) face of the plasma membrane.

## Concept 7.2: Membrane structure results in selective permeability

- A cell must exchange materials with its surroundings, a process controlled by the plasma membrane.
- Plasma membranes are selectively permeable, regulating the cell's molecular traffic, and substances do not cross the barrier indiscriminately.

### v The Permeability of the Lipid Bilayer

- Nonpolar molecules, such as hydrocarbons, carbon dioxide and oxygen, are hydrophobic and can therefore dissolve in the lipid bilayer of the membrane and cross it easily, without the aid of membrane proteins.
- The hydrophobic interior of the membrane impedes the direct passage of ions and polar molecules,which are hydrophilic, through the membrane,thus Polar molecules such as glucose and other sugars pass only slowly "not easily" through a lipid bilayer,and even water, an extremely small polar molecule,doesn't cross very rapidly.
- A charged atom or molecule and its surrounding shell of water find the hydrophobic interior of the membrane even more difficult to penetrate.

### v Transport Proteins

- The hydrophilic substances can avoid contact with the lipid bilayer by passing through transport proteins that span the membrane.
- Some transport proteins, called channel proteins, have a hydrophilic channel that certain molecules or atomic ions can use as a tunnel through the membrane.
- Channel proteins called aquaporins, facilitate the passage of water through the membrane.
- Other transport proteins, called carrier proteins, bind to molecules and change shape to shuttle them across the membrane.
- A transport protein is specific for the substance it moves,allowing only a certain substance (or a small group of related substances) to cross the membrane.

- The selective permeability of a membrane depends on both the discriminating barrier of the lipid bilayer and the specific transport proteins built into the membrane.

ü Concept check

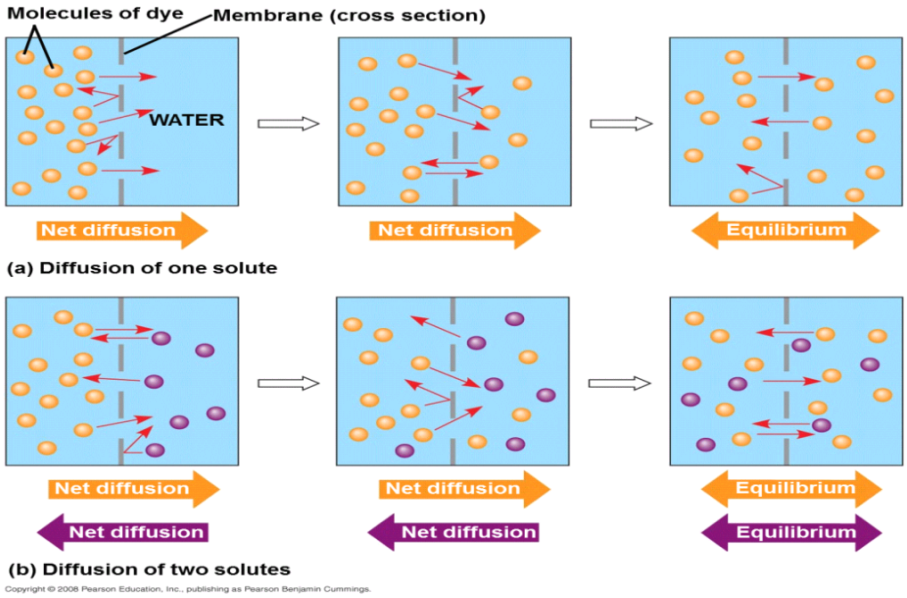
Why is a transport protein needed to move water molecule rapidly and in large quantities across a membrane?

water is a polar molecule, so it cannot pass very rapidly through the hydrophobic regions in the middle of a phospholipid bilayer.

## Concept 7.3: Passive transport is diffusion of a Substance across a Membrane with no Energy Investment

- Diffusion is the movement of molecules of any substance so that they spread out evenly into the available space (in other word diffusion is the tendency for molecules to spread out evenly into the available space).
- Although each molecule moves randomly,diffusion of a population of molecules may be directional "exhibit a net movement in one direction".
- At dynamic equilibrium,as many dye molecules crossing the membrane each second in one direction as in the other.
- Simple rule of diffusion:In the absence of other forces, a substance will diffuse down its concentration gradient "from where it is more concentrated to where it is less concentrated".
- Note that each substance diffuses down its own concentration gradient, unaffected by the concentration gradients of other substances.
- Concentration gradient means,the region along which the density of a chemical substance increases or decreases.
- No work must be done to move substances down the concentration gradient.
- Diffusion is a spontaneous process.
- The diffusion of a substance across a biological membrane is passive transport because it requires no energy from the cell to make it happen.

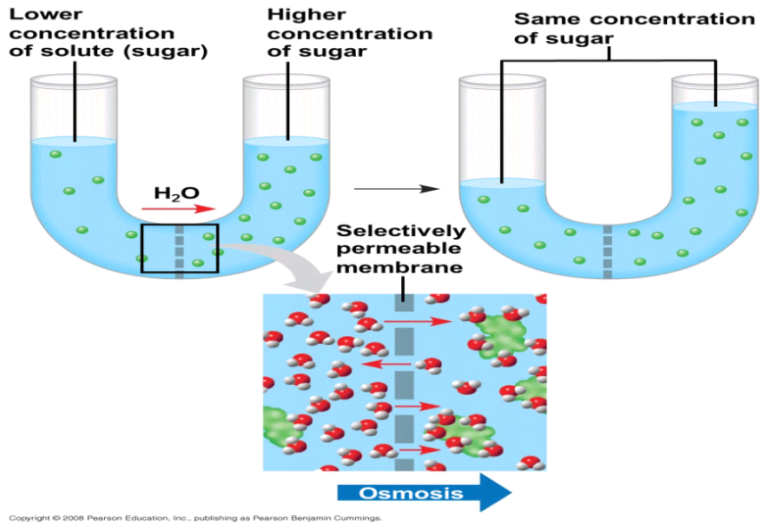
Fig.7.13 The diffusion of solutes across a synthetic membrane.




v Effects of Osmosis on Water Balance

- Water diffuses across the membrane from the region of lower solute concentration (higher free water concentration)to that of higher solute concentration (lower free water concentration) until the solute concentrations on both sides of the membrane are equal.
- The diffusion of free water across a selectively permeable membrane, whether artificial or cellular, is called osmosis.
- The movement of water across cell membranes and the balance of water between the cell and its environment are crucial to organisms.

Figure 7.14 Osmosis.




Explanation of figure 7.14

- Two sugar solutions of different concentrations are separated by a membrane that

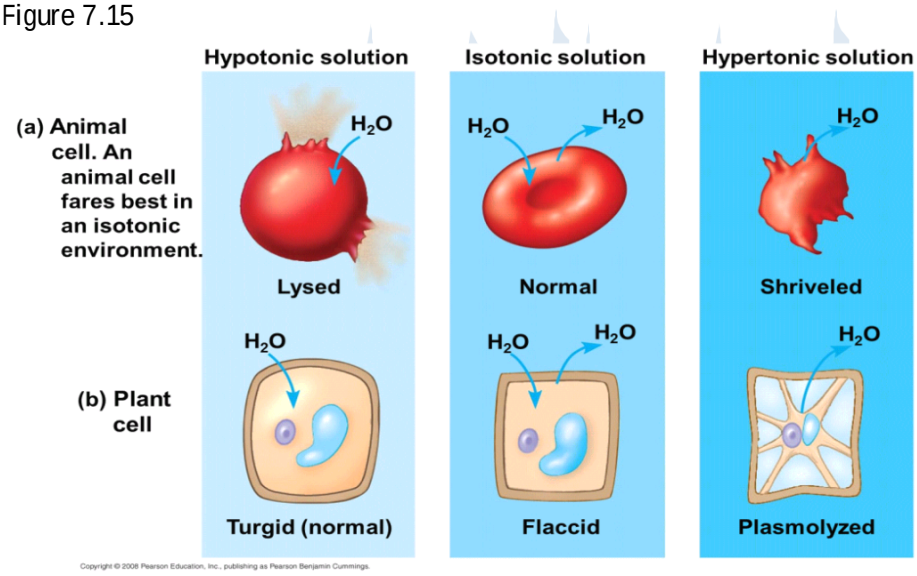
the solvent (water) can pass through but the solute (sugar) cannot.

- Water molecules move randomly and may cross in either direction, but overall, water diffuses from the solution with less concentrated solute to that with more concentrated solute.
- This diffusion of water, or osmosis, equalizes the sugar concentrations on both sides.

### v Water Balance of Cells without Walls

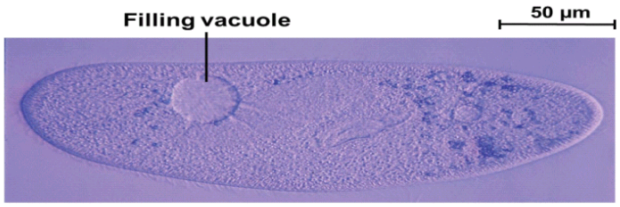
- Tonicity is the ability of a surrounding solution to cause a cell to gain or lose water.
- Isotonic solution:Solute concentration is the same as that inside the cell; no net water movement across the plasma membrane. Water diffuses across the membrane, but at the same rate in both directions.
- In an isotonic environment, the volume of an animal cell "cell without wall" is stable.
- Hypertonic solution: Solute concentration is greater than that inside the cell; cell loses water, shrivel, and probably die.
- Hypotonic solution: Solute concentration is less than that inside the cell; cell gains water, and the cell will swell and lyse (burst).

Figure 7.15

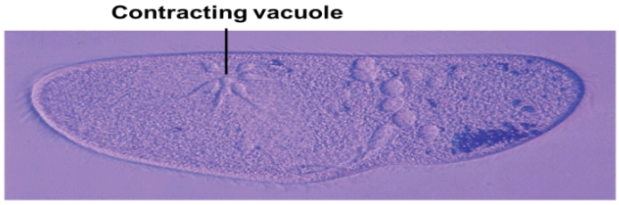



- Hypertonic or hypotonic environments create osmotic problems for organisms that lack rigid cell walls, so in these environment organisms that lack rigid cell walls must have other adaptations for osmoregulation. (Osmoregulation means the control of solute concentration and water balance).
- For example, The protist Paramecium caudatum, lives in pond water, which is hypotonic to the cell, has a plasma membrane that is much less permeable to water than the membranes of most other cells.
- The protist paramecium caudatum 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.

Fig.7.16 The contractile vacuole of Paramecium caudatum.




(a) A contractile vacuole fills with fluid that enters from a system of canals radiating throughout the cytoplasm.




(b) When full, the vacuole and canals contract, expelling fluid from the cell.



### v Water Balance of Cells with Walls

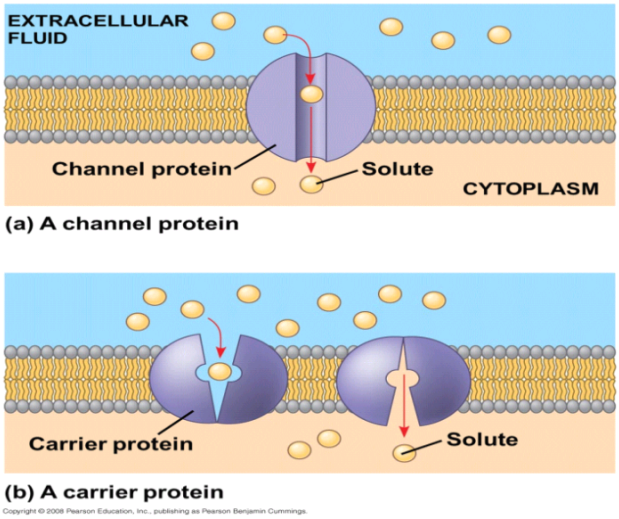
- When a cell is immersed in a hypotonic solution, the wall helps maintain the cell's water balance. A plant cell in a hypotonic solution swells as water enters by osmosis.However, the relatively inelastic wall will expand only so much before it exerts a back pressure on the cell, called turgor pressure, that opposes further water uptake.At this point cell is turgid(very firm), which is the healthy state for most plant cells.
- If a plant cell and its surroundings are isotonic, there is no net tendency for water to enter; the cell becomes flaccid (limp).
- In a hypertonic environment, plant cells lose water and shrink; eventually, the plasma membrane pulls away from the wall. This phenomenon, called plasmolysis, causes the plant to wilt and can lead to plant death.

### v Facilitated Diffusion: Passive Transport Aided by Proteins

- Many polar molecules and ions impeded by the lipid bilayer of the membrane diffuse passively with the help of transport proteins, This phenomenon is called Facilitated diffusion.
- Most transport proteins are very specific:They transport some substances but not others.
- In facilitated diffusion, transport proteins speed the passive movement of molecules across the plasma membrane.
- Remember that in passive transport the net movement of a substance is down its concentration gradient.
- Channel proteins provide corridors that allow a specific molecule or ion to cross the membrane.
- Channel proteins include:
  1/Aquaporins, for facilitated diffusion of water.
  2/Ion channels that open or close in response to a stimulus (gated channels).
- For some gated channels, the stimulus is electrical,for example, opens in response to an electrical stimulus, allowing potassium ions to leave the cell.
- Other gated channels open or close when a specific substance other than the one to be transported binds to the channel.

- Carrier proteins,such as the glucose transporter, undergo a subtle change in shape that translocates the solute-binding site across the membrane.
- In certain inherited diseases, specific transport systems are either defective or missing altogether, An example is cystinuria, a human disease characterized by the absence of a carrier protein that transports cysteine and some other amino acids across the membranes of kidney cells.

Fig.7.17 Two types of transport proteins that carry out facilitated diffusion



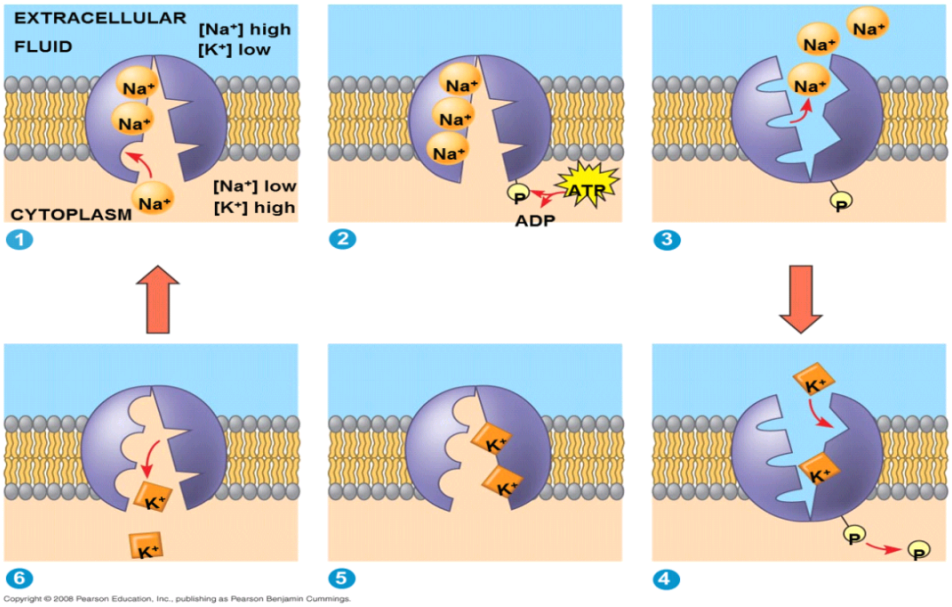

## Concept 7.4: Active transport uses energy to move solutes against their gradients

- Some transport proteins, can move solutes against their concentration gradients(from the side where they are less concentrated to the side where they are more concentrated), across the plasma membrane.

### v The Need for Energy in Active Transport

- 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.
- Active transport allows cells to maintain internal concentration of small solutes that differ from concentration in its environment.
- Energy for active transport is usually supplied by ATP.
- The sodium-potassium pump is one type of active transport system.

Figure 7.18Thesodium-potassium pump





Explanation of figure 7.18

1/Cytoplasmic Na+ binds to the sodium-potassium pump.The affinity for Na+ is high when the protein has this shape.

2/ Na+ binding stimulates phosphorylation by ATP.

3/ Phosphorylation leads to a change in protein shape, reducing its affinity for Na+,which is released outside.

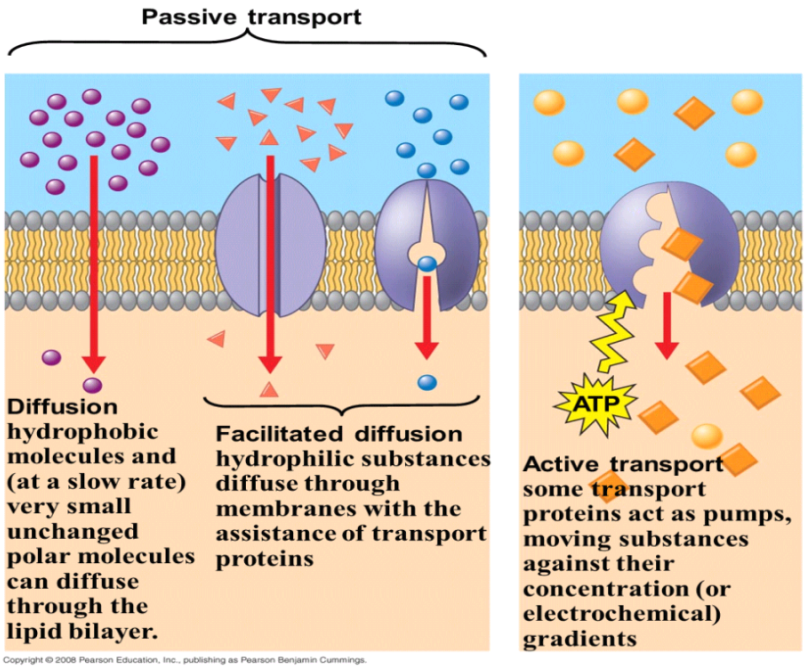
4/ The new shape has a high affinity for K+, which binds on the extracellular side and triggers release of the phosphate group.

5/Loss of the phosphate restores the protein s' original shape, which has a lower affinity for K+.

6/ K+ is released , affinity for Na+ is high again, and the cycle repeats.

- The pump oscillates between two shapes in a cycle that moves 3 Na+ out of the cell for every 2 K+ pumped into the cell.
- With each "crank" of the pump, there is a net transfer of one positive charge from the cytoplasm to the extracellular fluid, a process that stores energy as voltage.
- ATP powers the shape change by transferring a phosphate group to the transport protein (phosphorylating the protein).

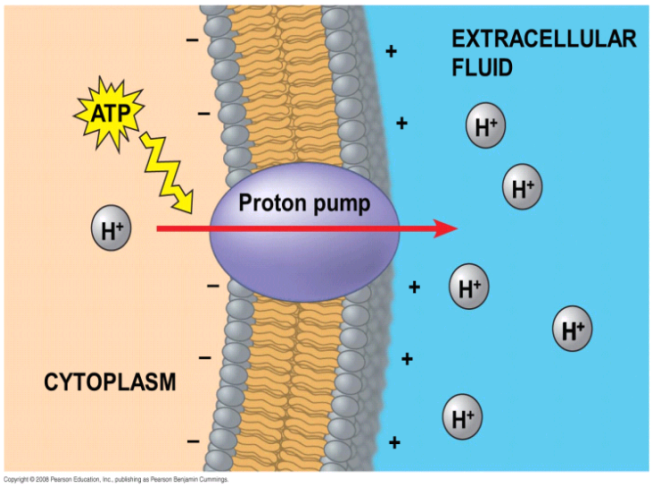
Figure 7.19 Passive and active transport




v How Ion Pumps Maintain Membrane Potential

- Voltage is electrical potential energy and created by differences in the distribution of positive and negative ions.
- The voltage difference 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).
- Two combined forces, collectively called the electrochemical gradient, drive the diffusion of ions across a membrane:
    1. A chemical force (the ion's concentration gradient).
    2. An electrical force (the effect of the membrane potential on the ion's movement).
- In the case of ions, then, we must refine our concept of passive transport: An ion diffuses not simply down its concentration gradient but, more exactly, down its electrochemical gradient.
- An electrogenic pump is a transport protein that generates voltage across a membrane.
- The sodium-potassium pump is 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.
- The pumping of H+ transfers positive charge from the cytoplasm to the extracellular solution.

Figure 7.20A proton pump



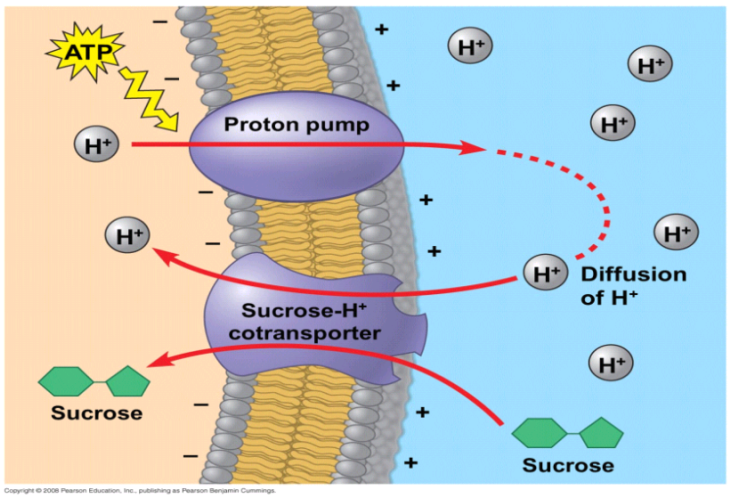

Explanation of figure 7.20

- A proton pump store energy by generating voltage (charge separation) across membranes.
- The voltage and H+ concentration gradient represent a dual energy source that can drive other processes such as the uptake of nutrients.
- One important use of proton gradients in the cell is for ATP synthesis during cellular reparation.
- Most proton pumps are powered by ATP.

v Cotransport: coupled transport by a membrane protein

- A single ATP powered pump that transports a specific solute can indirectly drive the active transport of several other solutes in a mechanism called cotransport (in other words:Cotransport occurs when active transport of a solute indirectly drives transport of another solute).
- Sucrose-H+cotransporter: transport protein couples the return of H+ to the transport of sucrose into the cells.
- This protein (Sucrose-H+cotransporter) can translocate sucrose into the cell against a concentration gradient, but only if the sucrose molecule travels in the company of hydrogen ion.
- The hydrogen ion uses the transport protein (Sucrose-H+cotransporter) as an avenue to diffuse down the electrochemical gradient maintained by the proton pump.

Figure 7.21




Explanation of figure 7.21

- A carrier protein, such as this sucrose- H+ cotransporter in a plant cell, is able to use the diffusion of H+ down its electrochemical gradient into the cell to drive the uptake of sucrose.
- The H+ gradient is maintained by an ATP-driven proton pump that concentrates H+ outside the cell, thus storing potential energy that can be used for active transport, in this case of sucrose.
- Thus, ATP indirectly provides the energy necessary for cotransport.

## Concept 7.5: Bulk transport across the plasma membrane occurs by exocytosis and endocytosis

- Water and small solutes enter and leave the cell by diffusing through the lipid bilayer of the plasma membrane or by being pumped or moved across the membrane by transport proteins.
- Large molecules, such as proteins and polysaccharides, as well as larger particle, generally cross the membrane in bulk by mechanisms that involve packaging in vesicles.
- Like active transport, these processes require energy.

### v Exocytosis

- The cell secrets certain biological molecules by the fusion of vesicles with the plasma membrane, this process is called exocytosis.
- A transport vesicle that hasbudded from the Golgi apparatus moves along microtubules of the cytoskeleton to the plasma membrane. when the vesicle membrane and plasma membrane come into contact, specific proteins rearrange the lipid molecules of the two bilayers so that the two membrane fuse.the contents of the vesicle then spill outside of the cell and the vesicle membrane becomes part of the plasma membrane.
- Many secretory cells use exocytosis to export products,for example, the cells in the pancreas that make insulin secrete it into the extracellular fluid by exocytosis.

v Endocytosis

- In endocytosis, the cell takes in biological molecules and particulate matter by forming new vesicles from the plasma membrane.
- There are three types of endocytosis: Phagocytosis, Pinocytosis and Receptor-Mediated Endocytosis.
- Human cells use receptor-mediated endocytosis to take cholesterol for membrane synthesis and the synthesis of other steroids.
- Ligand: a term for any molecule that binds specifically to a receptor site on another molecule.
- Vesicles not only transport substances between the cell and its surroundings, but also provide a mechanism for rejuvenating or remodeling the plasma membrane.
- Endocytosis and exocytosis occurs continually in the most eukaryotic cells, yet the amount of plasma membrane in a non-growing cell remains fairly constant.apparently the addition of membrane by one process offsets the loss of membrane by the other.

Figure 7.22 Exploring Endocytosis in animal cells

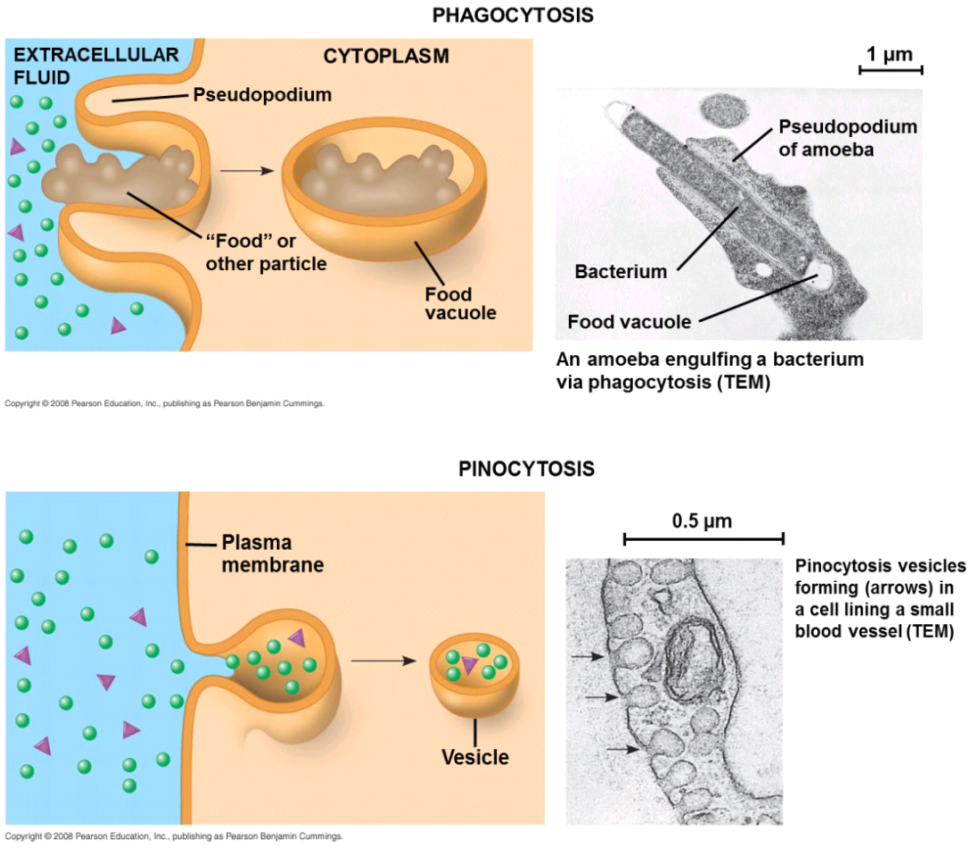
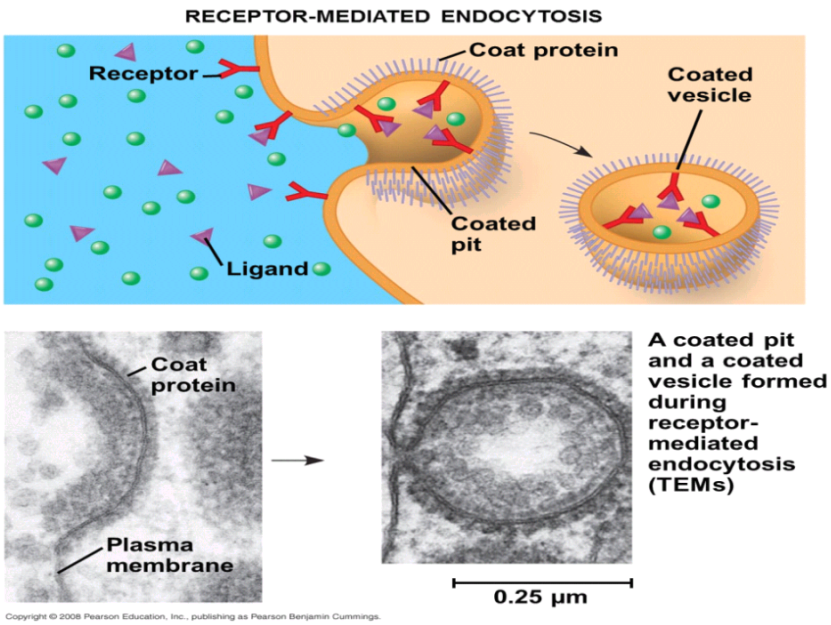



Fig.7.22 Exploring Endocytosis in animal cells




Explanation of figure 7.22

- Phagocytosis: a cell engulfs a particle by wrapping pseudopodia around it and packaging within a membrane sac called a food vacuole.the particle will be digested after the food vacuole fuses with a lysosome containing hydrolytic enzymes.
- Pinocytosis: the cell gulps droplets of extracellular fluid into tiny vesicles.it is not the fluid itself that is needed by the cell but the molecules dissolved in the droplets. Because any and all includes solutes are taken into the cell, pinocytosis is nonspecific in the substances it transports.
- Receptor-mediated endocytosis: enables the cell to acquire bulk quantities of specific substances, even though those substances may not be very concentrated in extracellular fluid. Embedded in the membrane are proteins with specific receptor sites exposed to the extracellular fluid, to which specific substances (ligands) bind. The receptor proteins then cluster in regions of the membrane called coated pits, which are lined on their cytoplasmic side by a fuzzy layer of coat proteins. Next, each coated pit forms a vesicle containing the ligand molecules. Notice that there are relatively more bound molecules inside the vesicle, but other molecules " nonbound molecules" are also present. After the ingested material is liberated from the vesicle, the emptied receptors are recycled to the plasma membrane by the same vesicle.