

Chapter 8

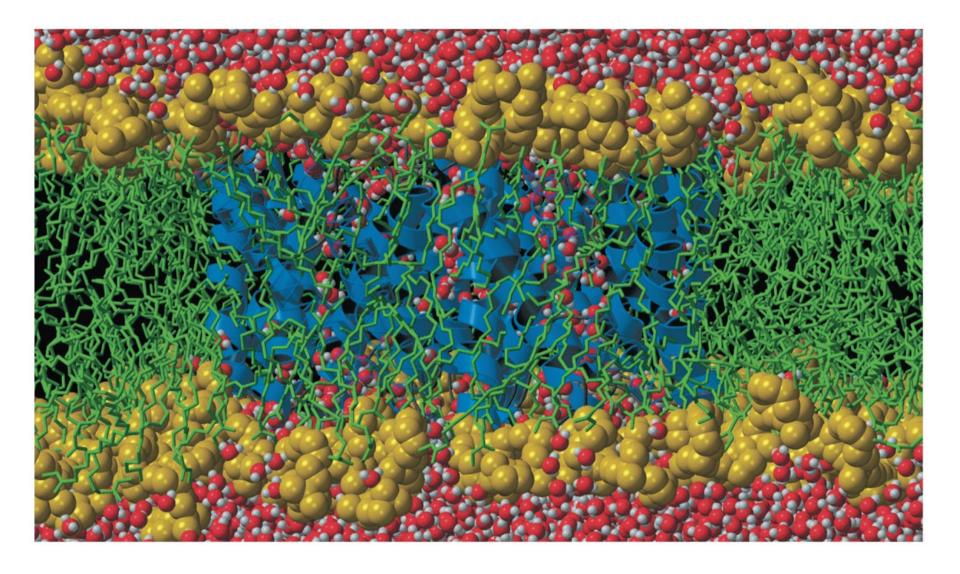
Cell Membranes

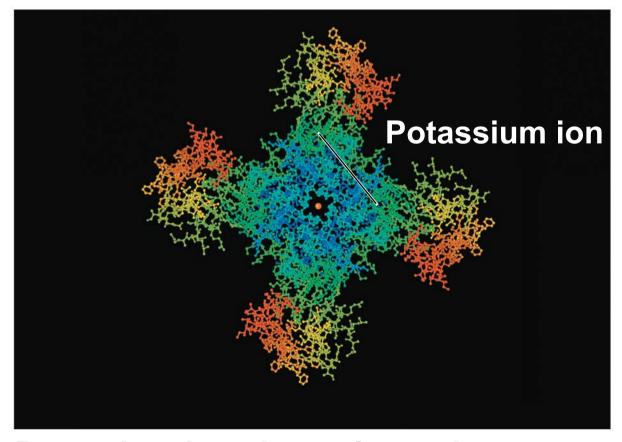
Lecture Presentations by Nicole Tunbridge and Kathleen Fitzpatrick

ife 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
- Transport proteins are often responsible for controlling passage across cellular membranes

Figure 8.1

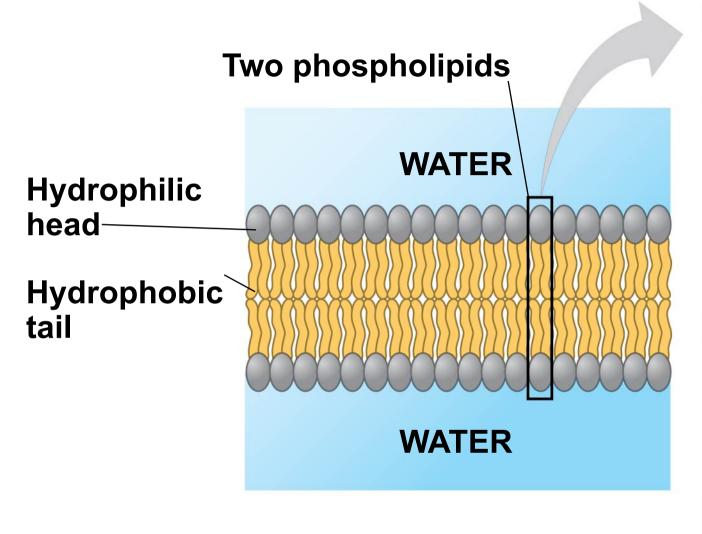


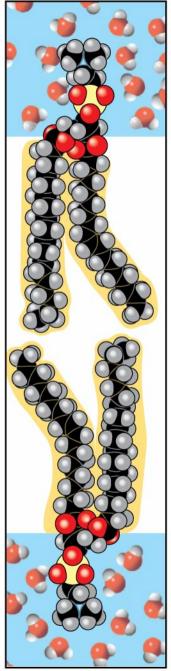


Potassium ion channel protein

oncept 8.1: Cellular membranes are fluid mosaics of lipids and proteins

- Phospholipids are the most abundant lipid in the plasma membrane
- Phospholipids are amphipathic molecules, containing hydrophobic ("water-fearing") and hydrophilic ("water-loving") regions
- The hydrophobic tails of the phospholipids are sheltered inside the membrane, while the hydrophilic heads are exposed to water on either side
- A) some proteins are amphipathic as well—having polar parts to the outer sides are hydrophobic parts to the interior.





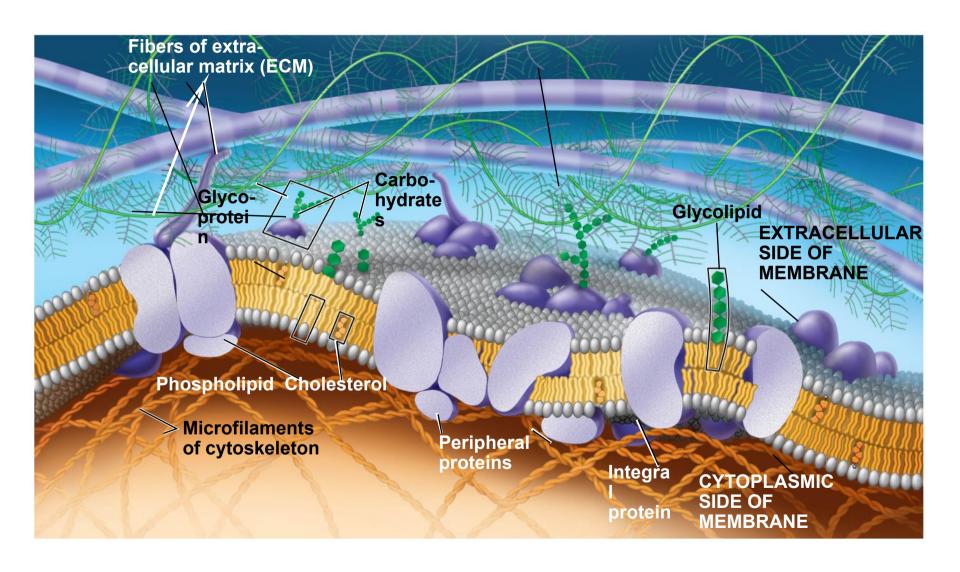
- In the fluid mosaic model, the membrane is a mosaic of protein molecules bobbing in a fluid bilayer of phospholipids
- Proteins are not randomly distributed in the membrane
- They are associated in long-lesting specialized patches where they carry out common functions.
- potches [similar to the above)

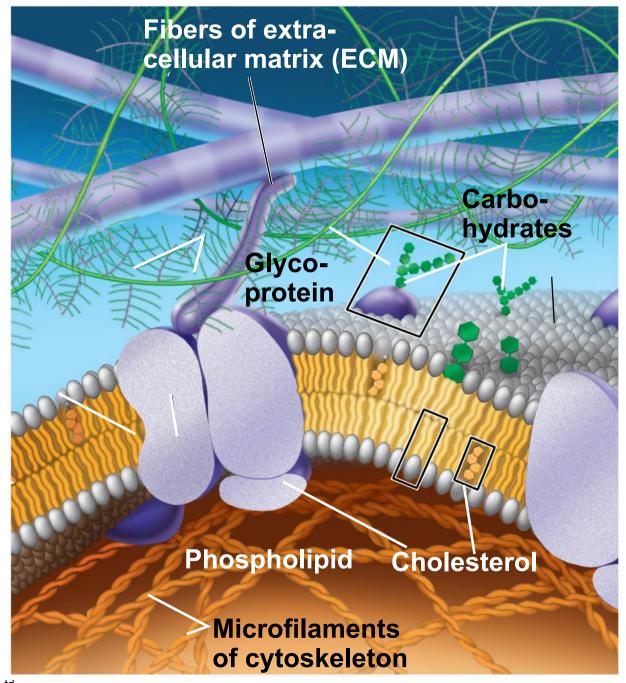
 Still not sure about whether they are really

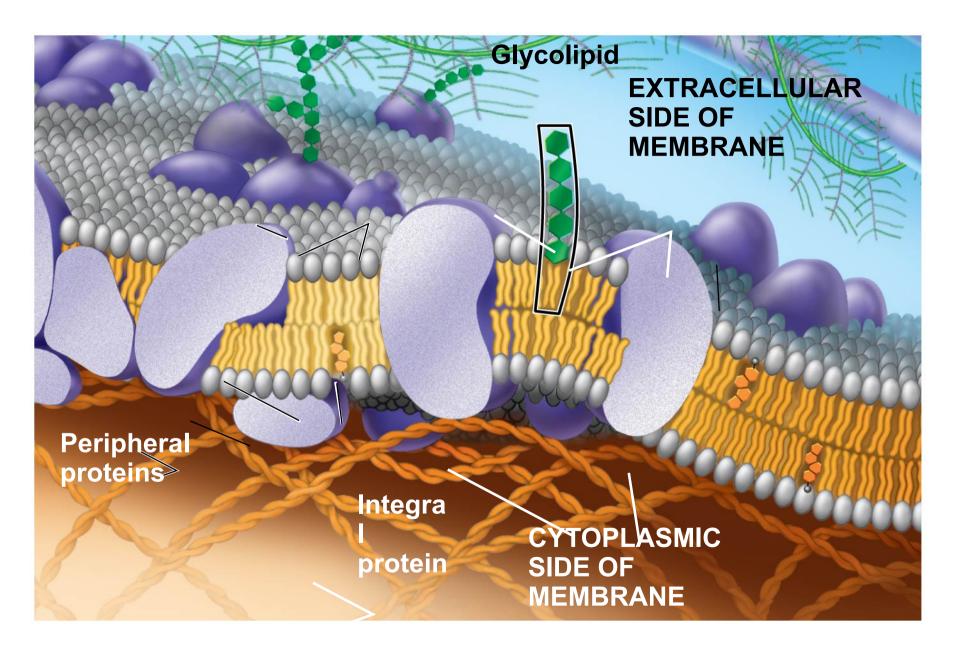
 Biochemical

 Biochemical

 Hechiniques.







he Fluidity of Membranes

- Membranes are held together mainly by weak hydrophobic interactions
- Most of the lipids and some proteins can move sideways within the membrane
- Rarely, a lipid may flip-flop across the membrane, from one phospholipid layer to the other
- Dide-way movement of phospholipids is rapid.

 They can Switch positions about 10⁷ times/second.

 Difference protein movement is slower about 2 μm and sometimes restricted by ≈ a bacterial length.

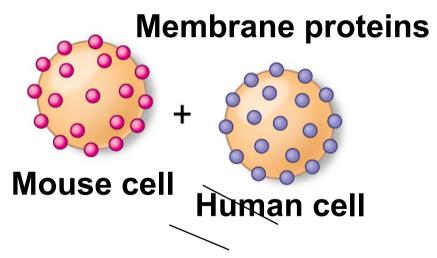
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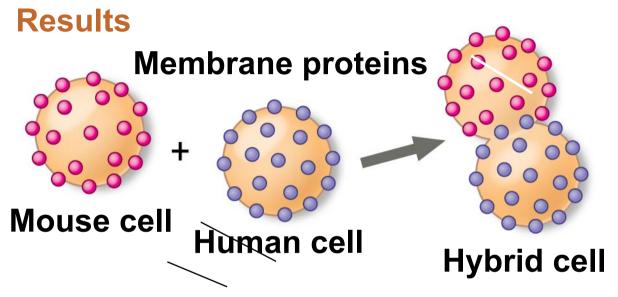
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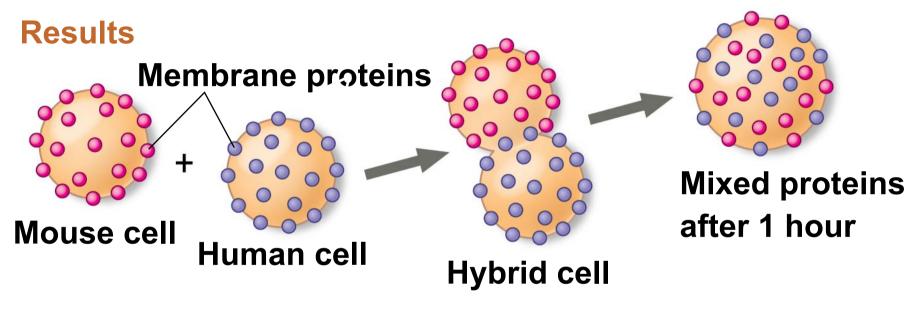
Results



Data from L. D. Frye and M. Edidin, The rapid intermixing of cell surface antigens after formation of mouse-human heterokaryons, *Journal of Cell Science* 7:319 (1970).



Data from L. D. Frye and M. Edidin, The rapid intermixing of cell surface antigens after formation of mouse-human heterokaryons, *Journal of Cell Science* 7:319 (1970).



Data from L. D. Frye and M. Edidin, The rapid intermixing of cell surface antigens after formation of mouse-human heterokaryons, *Journal of Cell Science* 7:319 (1970).

- Some proteins in the membrane are chiven along cytoslebetal fibers in an ordered manner.

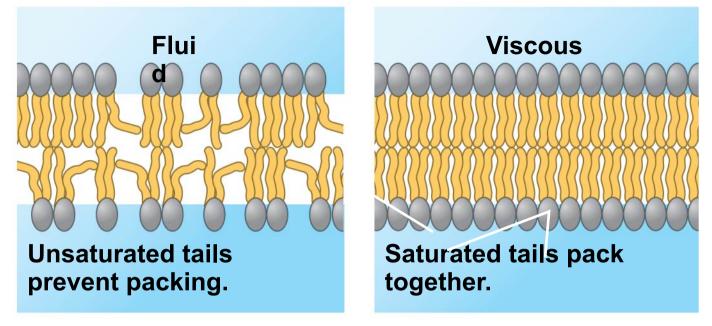
 To others simply drift in the numbrane.
- As temperatures cool, membranes switch from a fluid state to a solid state
- The temperature at which a membrane solidifies depends on the types of lipids
- Membranes rich in unsaturated fatty acids are more fluid than those rich in saturated fatty acids
- Membranes must be fluid to work properly;
 membranes are usually about as fluid as salad oil
- Demeability

 mobility of protein their functioning spots.

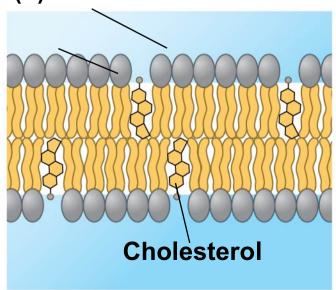
 Over-fluidity is no good either.

- The steroid cholesterol has different effects on the membrane fluidity of animal cells at different temperatures
- At warm temperatures (such as 37°C), cholesterol restrains movement of phospholipids
- At cool temperatures, it maintains fluidity by preventing tight packing
- Though cholesterol is present in plants, they use related steroid lipids to buffer membrane fluidity

(a) Unsaturated versus saturated hydrocarbon tails



(b) Cholesterol within the animal cell membrane



Cholesterol reduces membrane fluidity at moderate temperatures, but at low temperatures hinders solidification.

volution of Differences in Membrane Lipid Composition

- Variations in lipid composition of cell membranes of many species appear to be adaptations to specific environmental conditions
- Ability to change the lipid compositions in response to temperature changes has evolved in organisms that live where temperatures vary

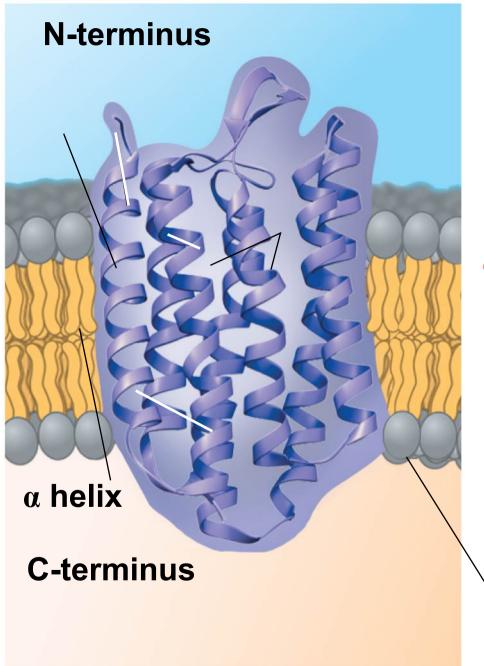
lembrane Proteins and Their Functions

- Somewhat like a tile mosaic, a membrane is a collage of different proteins, often clustered in groups, embedded in the fluid matrix of the lipid bilayer
- Phospholipids form the main fabric of the membrane
- Proteins determine most of the membrane's functions



often to the exposed parts of integral proteins.

- Peripheral proteins are bound to the surface of the membrane single—side penetration no "special" name.
- Integral proteins penetrate the hydrophobic core
- Integral proteins that span the membrane are called transmembrane proteins
- The hydrophobic regions of an integral protein consist of one or more stretches of nonpolar amino acids, often coiled into α helices



EXTRACELLULAR SIDE

@ To support the membrane framework:

Some membrane proteins are bound to:

(a) cytoskeletal fibers

(b) entracellular matrix

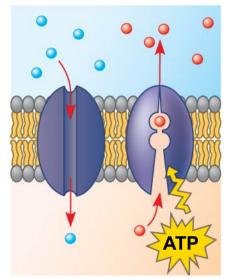
e.g. integrins (integral, transmembrane proteins)
bond to ECM e.g. fibromaterials in the necting

(see ch. 7.6)

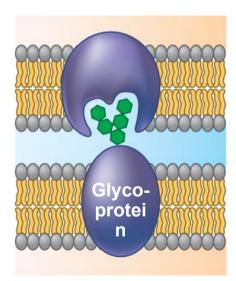
CYTOPLASMIC SIDE

- Cell-surface membranes can carry out several functions:
 - Transport
 - Enzymatic activity
 - Signal transduction
 - Cell-cell recognition
 - Intercellular joining
 - Attachment to the cytoskeleton and extracellular matrix (ECM)

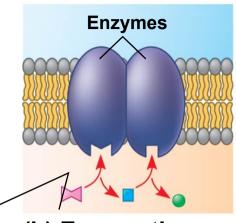
Figure 8.7



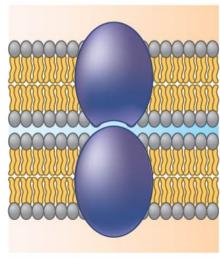
(a) Transport



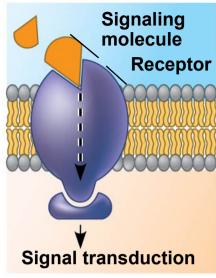
(d) Cell-cell recognition



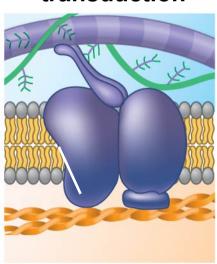
(b) Enzymatic activity



(e) Intercellular joining

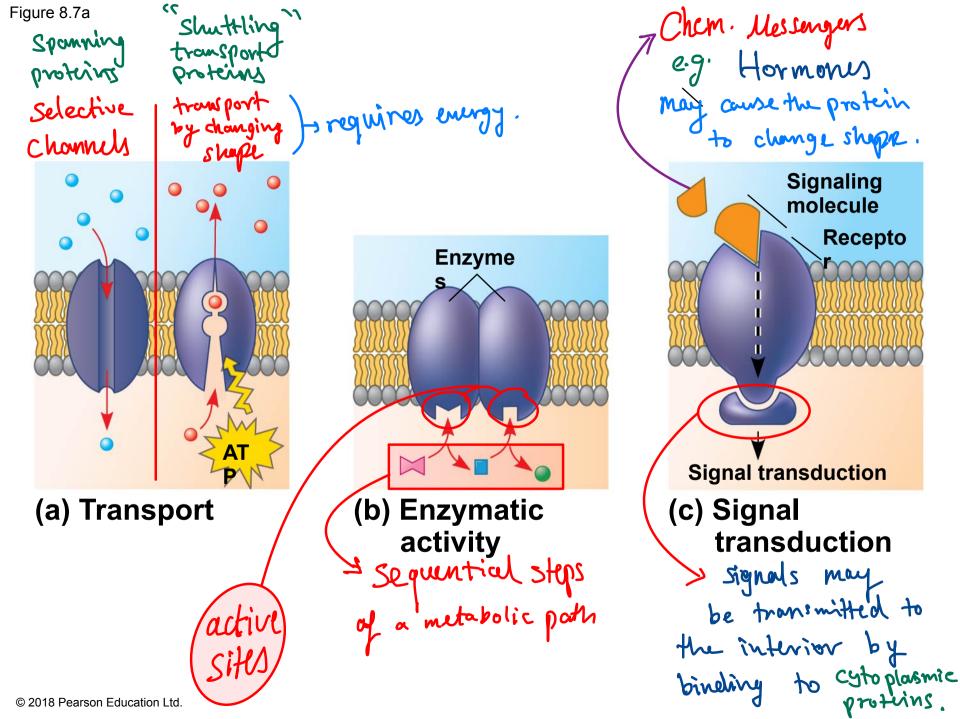


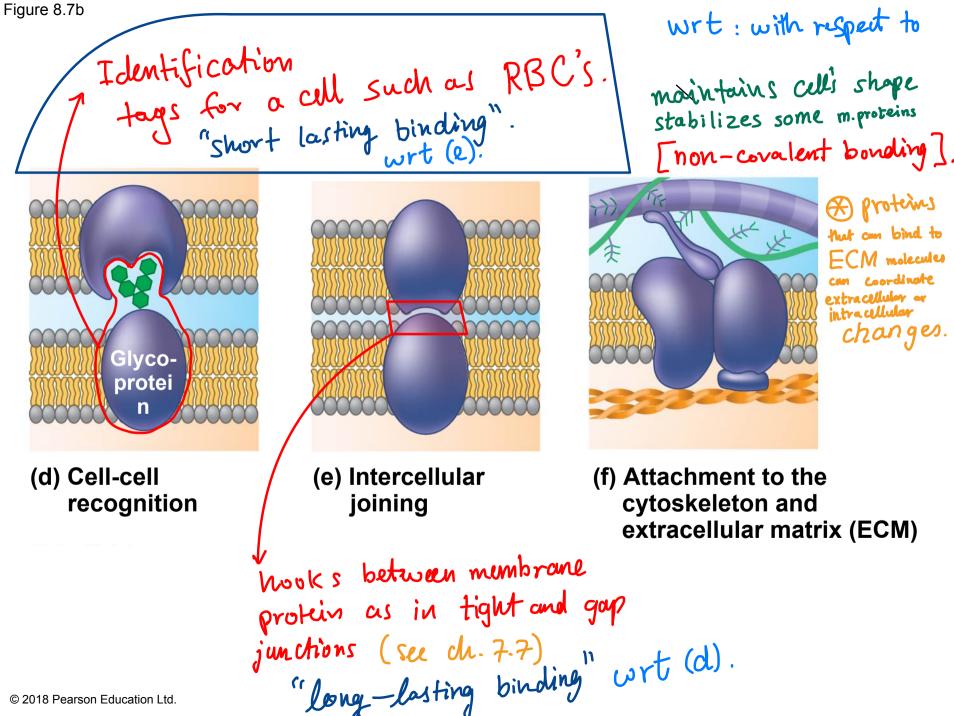
(c) Signal transduction



(f) Attachment to the cytoskeleton and extracellular matrix (ECM)

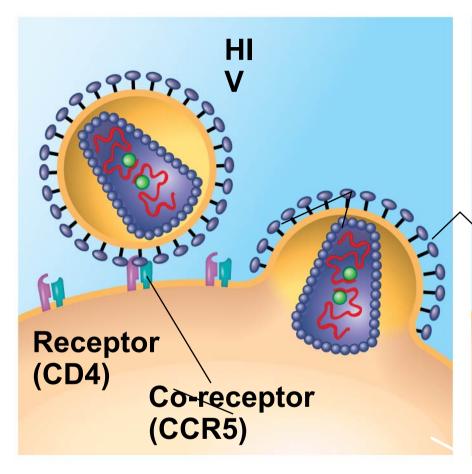






- Cell-surface proteins are important in the medical field
 - For example, HIV must bind to the immune cellsurface protein CD4 and a "co-receptor" CCR5 in order to infect a cell
 - HIV cannot enter the cells of resistant individuals who lack CCR5
 - Drugs are now being developed to mask the CCR5 protein

e.g. maravivoc (by Selzentry) approved in 2007.



Receptor (CD4) but no CCR5 **Plasma** membrane

(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.

Let gue alteration.

he Role of Membrane Carbohydrates in Cell-Cell Recognition in an embryonic animal an important eg is in the differentiation of cells into tissues

- Cells recognize each other by binding to molecules, often containing carbohydrates, on the extracellular surface of the plasma membrane
- Membrane carbohydrates may be covalently bonded to lipids (forming glycolipids) or, more commonly to proteins (forming glycoproteins)
- Carbohydrates on the extracellular side of the plasma membrane vary among species, individuals, and even cell types in an individual

RBC'S O,A,B,AB

ynthesis 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 ER and Golgi apparatus

▼ Figure 8.9 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. Lipid bilayer Transmembrane glycoprotein Glycolipid 1 Secretory proteins, membrane proteins, and lipids are synthesized in the endoplasmic reticulum (ER). In the ER, Secretory Attached carbohydrates (green) are added to the transmembrane protein carbohydrate proteins (purple dumbbells), making them glycoproteins. The carbohydrate portions may then be modified. Materials are transported in vesicles to the Golgi apparatus. 2 Inside the Golgi apparatus, the glycoproteins undergo further carbohydrate modification, and Golgi lipids acquire carbohydrates, becoming glycolipids. apparatus The glycoproteins, glycolipids, and secretory Vesicle proteins (purple spheres) 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 Glycolipid the plasma membrane. This releases the secretory proteins from the cell, a process called exocytosis, and positions the carbohydrates of membrane glycoproteins and glycolipids on the outside (extracellular) face of the plasma membrane. Plasma membrane: DRAW IT Draw an integral membrane protein Transmembrane Cytoplasmic face extending from partway through the ER membrane Secrete Extracellular face into the ER lumen. Next, draw the protein where it would be located in a series of numbered steps ending Membrane at the plasma membrane. Would the protein contact

the cytoplasm or the extracellular fluid? Explain.

oncept 8.2: 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
 - take in materials such as O_2 , sugars, A.acids...

 expell waste products such as CO_2 ...

 regulate the concentrations of inorganic ions such as Na^+ , CI^- , K^+ , Ca^{2+} ...

he Permeability of the Lipid Bilayer

+ {02,002}

- Hydrophobic (nonpolar) molecules, such as hydrocarbons, can dissolve in the lipid bilayer and pass through the membrane rapidly, selective permeability (1).
- Hydrophilic molecules including ions and polar molecules do not cross the membrane easily
- Proteins built into the membrane play key roles in regulating transport

ransport Proteins

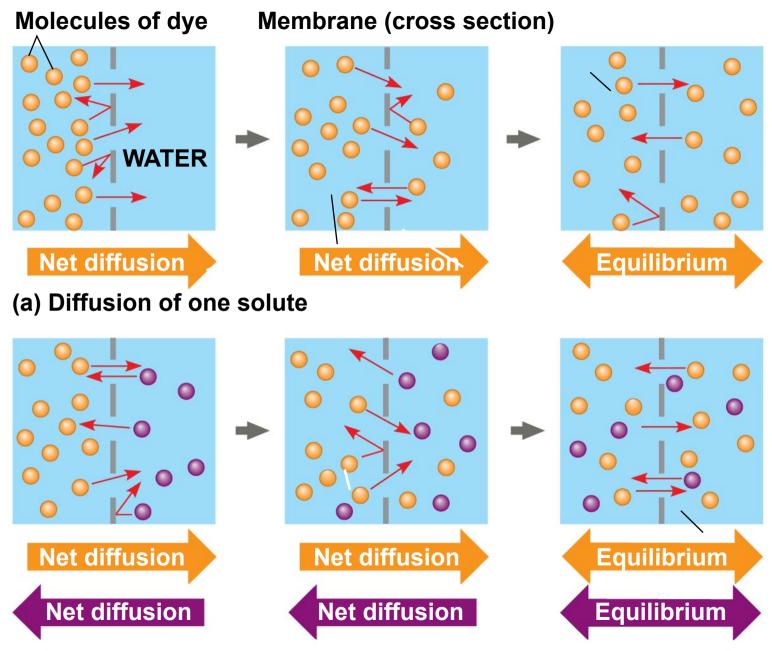
- Transport proteins allow passage of hydrophilic substances across the membrane
- Some transport proteins, called channel proteins, have a hydrophilic channel that certain molecules or ions can use as a tunnel
- Channel proteins called aquaporins greatly facilitate the passage of water molecules
 - Aguaporins => Quoternary (4 identical Submits)
 each having a channel for water passage
 Allowing = 3 billion H20 molecules per second.

- 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

oncept 8.3: Passive transport is diffusion of a substance across a membrane with no energy investment

- 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
- At dynamic equilibrium, as many molecules cross the membrane in one direction as in the other

Figure 8.10



(b) Diffusion of two solutes

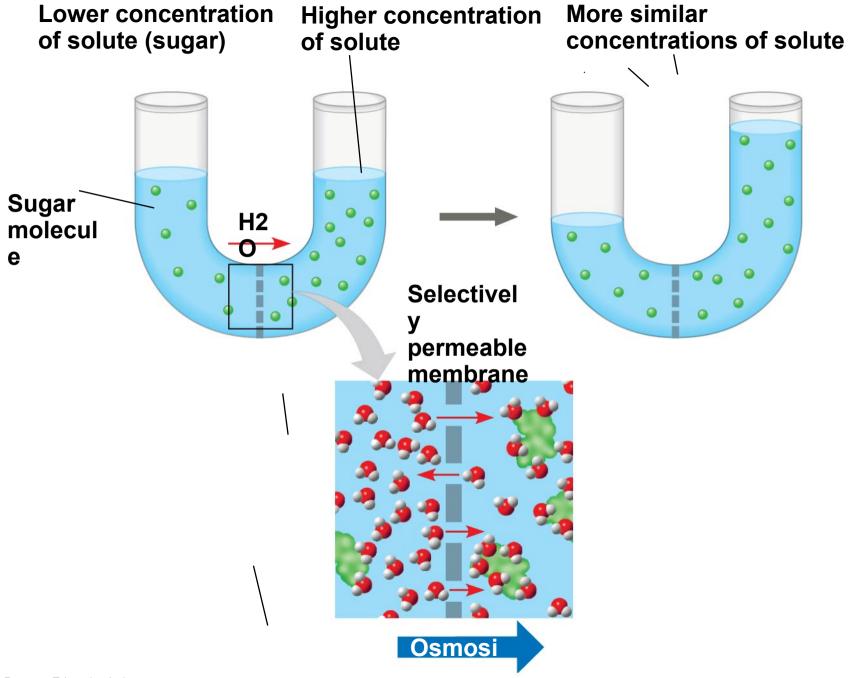
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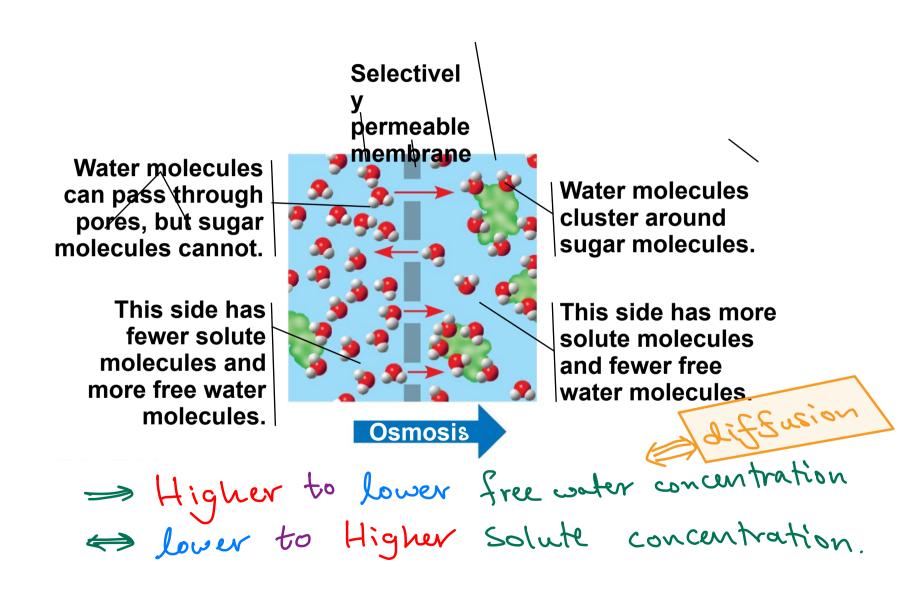
- Substances diffuse down their concentration gradient, the region along which the density of a chemical substance increases or decreases
- No work must be done to move substances down the concentration gradient
- The diffusion of a substance across a biological membrane is passive transport because no energy is expended by the cell to make it happen

ffects of Osmosis on Water Balance

- Osmosis is the diffusion of water across a selectively permeable membrane
- Water diffuses across a membrane from the region of lower solute concentration to the region of higher solute concentration until the solute concentration is equal on both sides

Figure 8.11



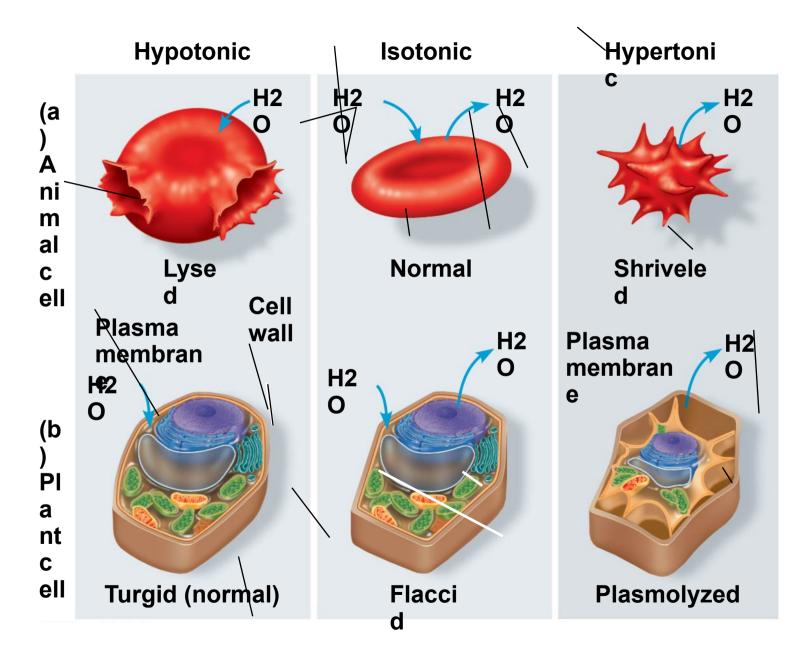


later Balance of Cells Without Cell Walls

- Tonicity is the ability of a surrounding solution to cause a cell to gain or lose water
- The tonicity of a solution depends on its concentration of solutes that cannot cross the membrane relative to that inside the cell
 - (x) aka. non-penetrating solutes.

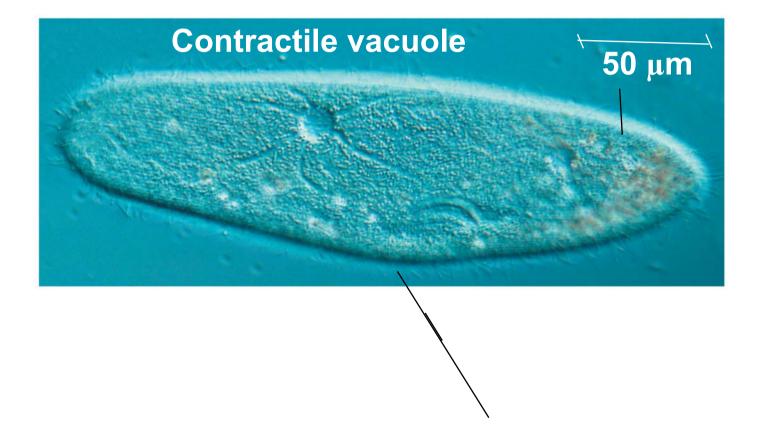
 (x) Osmosis is not affected by concentrations of "penetrating" solutes they can diffuse evenly.

- Isotonic solution: Solute concentration is the same as that inside the cell; no net water movement across the plasma membrane
- Hypertonic solution: Solute concentration is greater than that inside the cell; cell loses water
- Hypotonic solution: Solute concentration is less than that inside the cell; cell gains water
- Cells without cell walls will shrivel in hypertonic solution and lyse (burst) in a hypotonic solution
 - O seawater is ISOTONIC to most marine vertebrates.



Cells of most terrestrial animals are bothed in an entracellular fuid the is ISOTONIC to the cells.

- Hypertonic or hypotonic environments create osmotic problems for organisms that have cells without rigid walls
- Osmoregulation, the control of solute concentrations and water balance, is a necessary adaptation for life in such environments
 - For example, the unicellular eukaryote Paramecium, which is hypertonic to its pond water environment, has a contractile vacuole that acts as a pump
 - Deparameciums' membranes are less permentle to water, which slows osmosis but does not them many other cells' stop it.



 Bacteria and archaea that live in hypersaline (excessively salty) environments have cellular mechanisms to balance internal and external solute concentrations

later Balance of Cells with Cell Walls

- Cell walls on the interior is
- Cell walls help maintain water balance
- A plant cell in a hypotonic solution swells until the wall opposes uptake; the cell is now turgid (firm)
- If a plant cell and its surroundings are isotonic, there
 is no net movement of water into the cell; the cell
 becomes flaccid (limp)

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- In a hypertonic environment, plant cells lose water
- The membrane pulls away from the cell wall, causing the plant to wilt, a potentially lethal effect called plasmolysis

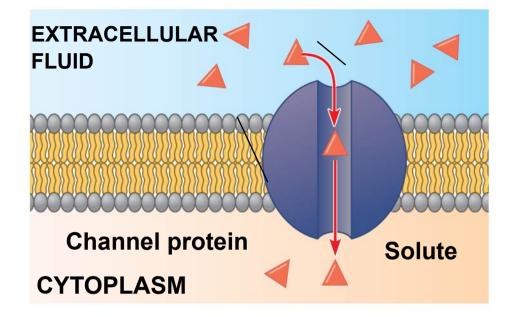
acilitated Diffusion: Passive Transport Aided by Proteins

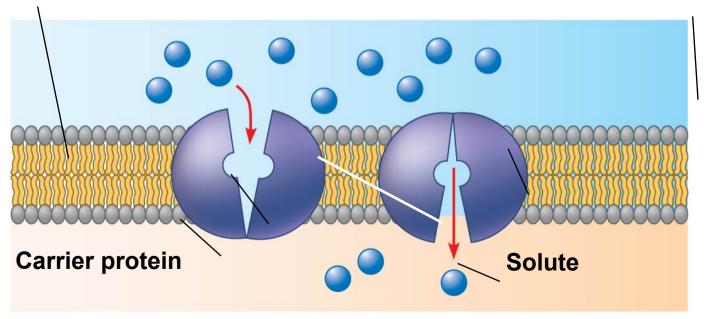
- In facilitated diffusion, transport proteins speed the passive movement of molecules across the plasma membrane
- Transport proteins include channel proteins and carrier proteins



- Channel proteins provide corridors that allow a specific molecule or ion to cross the membrane
- Aquaporins facilitate the diffusion of water
- Ion channels facilitate the transport of ions
- Some ion channels, called gated channels, open or close in response to a stimulus Chemical stimulus by Chemical stimulus b
 - response to electrical stimulus

(a) A channel protein





(b) A carrier protein

- Carrier proteins undergo a subtle change in shape that translocates the solute-binding site across the membrane
- This change in shape can be triggered by the binding and release of the transported molecule

All methods of transport up to this point Do Not require energy; as they are down the concentration gradient]

oncept 8.4: Active transport uses energy to move solutes against their gradients

- Facilitated diffusion is still passive because the solute moves down its concentration gradient, and the transport requires no energy
- Some transport proteins, however, can move solutes against their concentration gradients

he Need for Energy in Active Transport

- Active transport requires energy, usually in the form of ATP hydrolysis, to move substances against their concentration gradients
- All proteins involved in active transport are carrier proteins → Important.

- Active transport allows cells to maintain concentration gradients that differ from their surroundings
 - For example, an animal cell has a much higher potassium (K+) and a much lower sodium (Na+) concentration compared to its surroundings
 - This is controlled by the sodium-potassium pump, a transport protein that is energized by transfer of a phosphate group from the hydrolysis of ATP

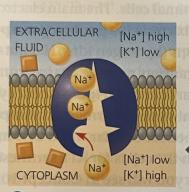
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Status (0): non-phosphorylated -> High affinity for Nat (3 ions) [open to the inside]
Status (1): Phosphorylated -> High affinity for Kt (2 ions) [open to the outside].
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► Figure 8.16 The sodium-potassium pump: a specific case of active transport.

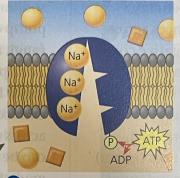
This transport system pumps ions against steep concentration gradients. The pump oscillates between two shapes in a cycle that moves Na⁺ out of the cell (steps 11 - 3) and K⁺ into the cell (steps 4 - 6). The two shapes have different binding affinities for Na+ and K+. ATP hydrolysis powers the shape change by transferring a phosphate group to the transport protein (phosphorylating the protein).

VISUAL SKILLS For each ion (Na⁺ and K⁺), describe its concentration inside the cell relative to outside. How many Na⁺ are moved out of the cell and how many K⁺ moved in per cycle?

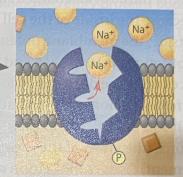
Mastering Biology
Animation: Active Transport



1 Cytoplasmic Na⁺ binds to the sodium-potassium pump with high affinity when the protein has this shape.



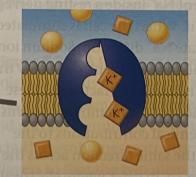
2 Binding of 3 Na⁺ ions stimulates phosphorylation by a kinase, using ATP.



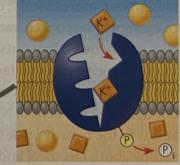
3 Phosphorylation leads to a change in protein shape, reducing its affinity for Na⁺; 3 Na⁺ are released outside.



6 2 K⁺ are released; affinity for Na⁺ is high again, and the cycle repeats.

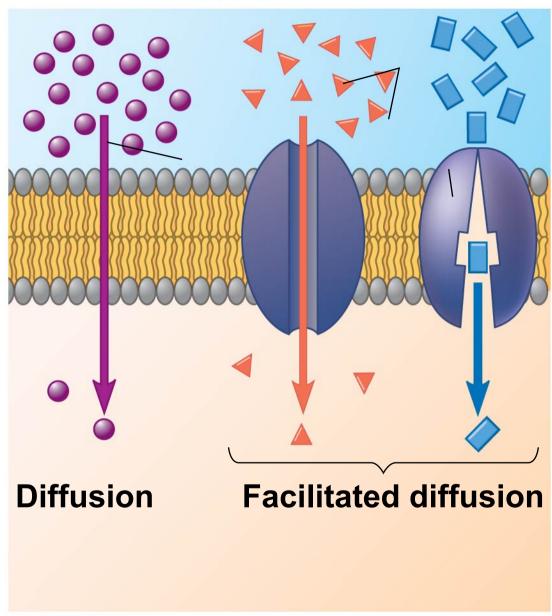


5 Loss of the phosphate group restores the protein's original shape, which has a lower affinity for K⁺.

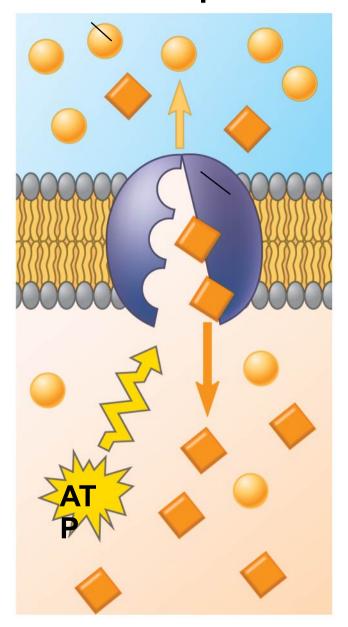


4 The new shape has a high affinity for K+; 2 K+ bind on the extracellular side, triggering release of the phosphate group.

Passive transport



Active transport



ow Ion Pumps Maintain Membrane Potential

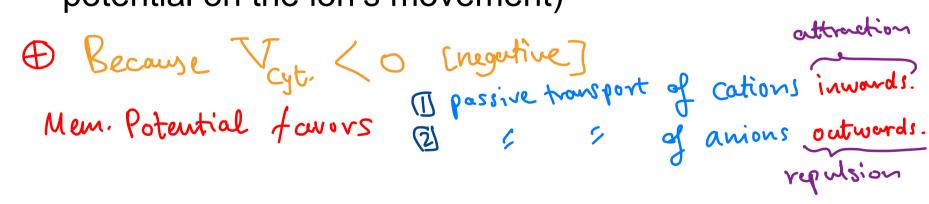
- Membrane potential is the voltage across a membrane
- Voltage is created by differences in the distribution of positive and negative ions across a membrane
- The cytoplasmic side of the membrane is negative in charge relative to the extracellular side

MEM. Potential
$$\in$$
 [-200,-50] mV.

MEM. Potential = $V_{\text{cytoplasm}}$ V_{ECSide}

The regative number indicates that $V_{\text{cyt.}} < V_{\text{ECSide}}$

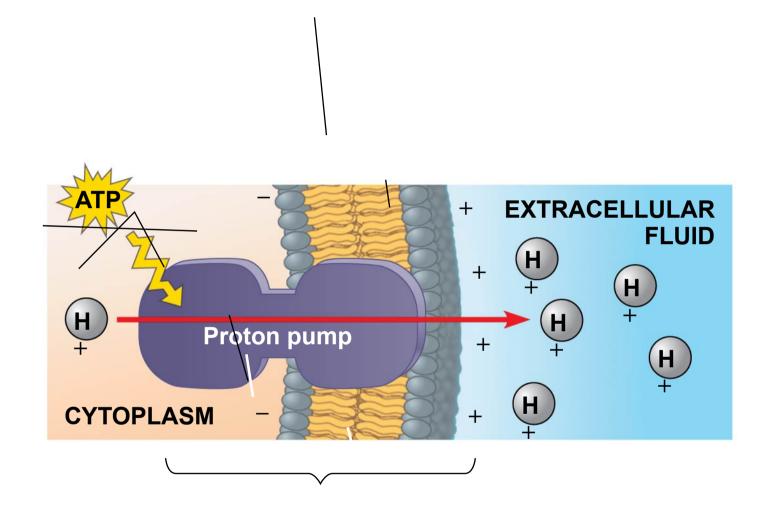
- Two combined forces, collectively called the electrochemical gradient, drive the diffusion of ions across a membrane
 - A chemical force (the ion's concentration gradient)
 - An electrical force (the effect of the membrane potential on the ion's movement)



Diffusion of ions (+/-) across the plasma membrane
Diffusion of ions (+/-) across the plasma membrane is Controlled by 2 gradients
Memical: Concentration (Simple aggression).
[Chemical: Concentration (simple diffusion). [Electrical: Wrt the membrane potential autwords
The combination of both gradients is colled
o solls.
The Electrochemical gradient. in verve cells.
El C con act together as in the case of Nat ions when the cell is stimulated (Fgoes inwords) & (Nat is much higher outside
cell is stimulated (+ goes inwords) & (Nat is much higher outside
or against each other
Live transport may be needed?
[active transport may be needed].

- 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 hydrogen ions (H+) out of the cell
- Electrogenic pumps help store energy that can be used for cellular work in the form of Voltage différence.

eg. @ ATP synthesis 2) cotransport.

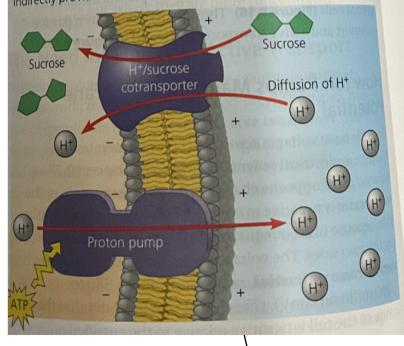


otransport: Coupled Transport by a Membrane Protein

- Cotransport occurs when active transport of a solute indirectly drives transport of other substances
- The diffusion of an actively transported solute down its concentration gradient is coupled with the transport of a second substance against its own concentration gradient \int Important.

plants load sucrose into cells in the veins of leaves to be transported "vascularily" into non-photosynthetic organs.

▼ Figure 8.19 Cotransport: active transport driven by a concentration gradient. A carrier protein, such as this H⁺/sucrose cotransporter in a plant cell (top), is able to use the diffusion of H⁺ cotransporter in a plant cell (top), is able to use the diffusion of H⁺ down its electrochemical gradient into the cell to drive the uptake of sucrose. (The cell wall is not shown.) Although not technically of sucrose. (The cell wall is not shown.) Although not technically part of the cotransport process, an ATP-driven proton pump is shown here (bottom), which concentrates H⁺ outside the cell. The resulting H⁺ gradient represents potential energy that can be used for active transport—of sucrose, in this case. Thus, ATP hydrolysis indirectly provides the energy necessary for cotransport.



A similar cotransporter in animals transports Na⁺ into intestinal cells together with glucose, which is moving down its concentration gradient into the cell. (The Na⁺ is then pumped out of the cell into the blood on the other side by Na⁺/K⁺ pumps; see Figure 8.16.) Our understanding of Na⁺/ glucose cotransporters has helped us find more effective treatments for diarrhea, a serious problem in developing countries. 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 Na⁺/glucose cotransporters on the surface of intestinal cells and passed through the cells into the blood. This simple treatment has lowered infant mortality worldwide.

oncept 8.5: Bulk transport across the plasma membrane occurs by exocytosis and endocytosis

- Small molecules and water enter or leave the cell through the lipid bilayer or via transport proteins
- Large molecules, such as polysaccharides and proteins, cross the membrane in bulk via vesicles

xocytosis

• In exocytosis, transport vesicles migrate to the membrane, fuse with it, and release their contents outside the cell specific with the change in photpholipid

• Many secretory cells use exocytosis to export their products)— Such as pancreatic cells

(secrete insulin).

2 release of neurotransmitters for signals.

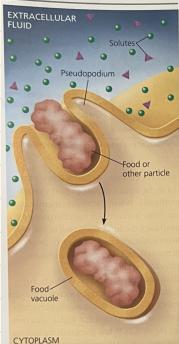
Telease of necessary carbohydrates and other meterials when building roll walls.

ndocytosis

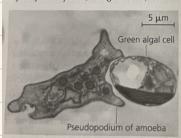
- In endocytosis, the cell takes in macromolecules by forming vesicles from the plasma membrane
- Endocytosis is a reversal of exocytosis, involving different proteins
- There are three types of endocytosis
 - Phagocytosis ("cellular eating")
 - Pinocytosis ("cellular drinking")
 - Receptor-mediated endocytosis

▼ Figure 8.21 Exploring Endocytosis in Animal Cells

Phagocytosis

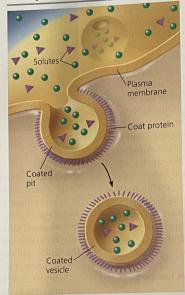


In phagocytosis, a cell engulfs a particle by extending pseudopodia (singular, pseudopodium) around it and packaging it within a membranous sac called a food vacuole. The particle will be digested after the food vacuole fuses with a lysosome containing a fuzzy layer of coat protein; the "pits" and hydrolytic enzymes (see Figure 7.13a).

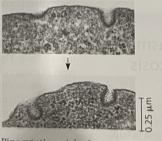


An amoeba engulfing a green algal cell via phagocytosis (TEM).

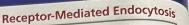
Pinocytosis

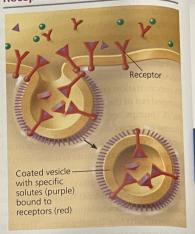


In pinocytosis, a cell continually "gulps" droplets of extracellular fluid into tiny vesicles, formed by infoldings of the plasma membrane. In this way, the cell obtains molecules dissolved in the droplets. Because any and all solutes are taken into the cell, pinocytosis as shown here is nonspecific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

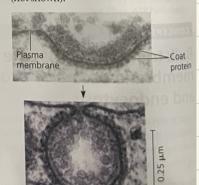


Pinocytotic vesicles forming (TEMs).





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. The diagram shows only bound molecules (purple triangles) inside the vesicle, but other molecules from the extracellular fluid 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 (not shown).



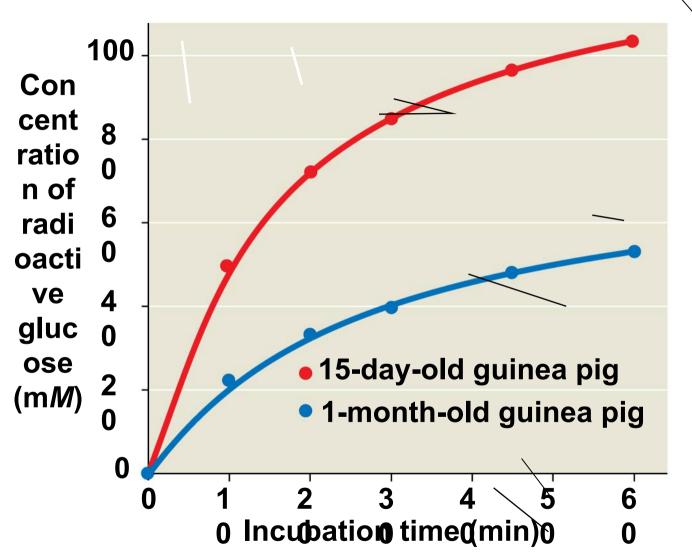
Plasma membrane SA loss by endocytosis is Balanced by exocytosis.

Phagocytosis
Pivocytosis
one not specific
unlike R.M. Endocytosis.

VISUAL SKILLS Use the scale bars to estimate the diameters of (a) the food vacuole that

- Human cells use receptor-mediated endocytosis to take in cholesterol, which is carried in particles called low-density lipoproteins (LDLs) & complex of lipids and protein.
- Individuals with the disease familial hypercholesterolemia have missing or defective LDL receptor proteins





Data from T. Kondo and E. Beutler, Developmental changes in glucose transport of guinea pig erythrocytes, *Journal of Clinical Investigation* 65:1–4 (1980).

