General Biology

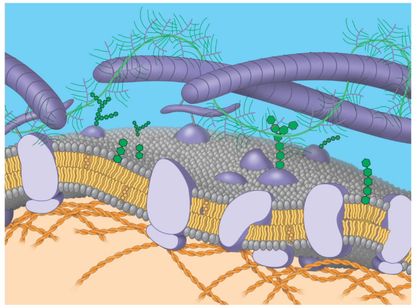
Course No: BNG2003
Credits: 3.00

4. Cell Membrane Structure and Function

Prof. Dr. Klaus Heese

- Life at the Edge
- ***The plasma membrane*** is the boundary that separates the living cell from its 'nonliving' surroundings

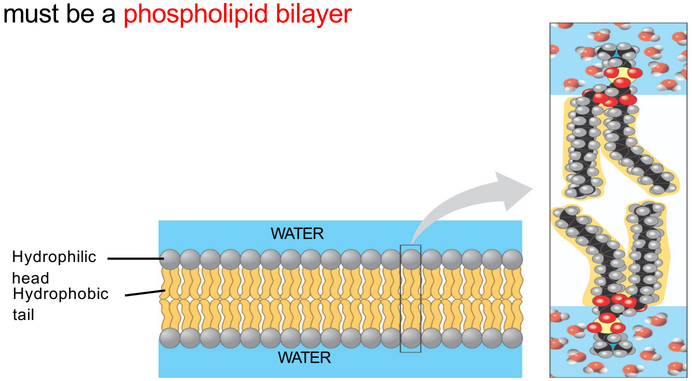
- The plasma membrane exhibits selective permeability - it allows some substances to cross it more easily than others



- **Cellular membranes** are fluid mosaics of **lipids** and **proteins**
- Phospholipids
  - are the most abundant lipid(s) in the plasma membrane
  - are amphipathic, containing both hydrophobic and hydrophilic regions
- The ***fluid mosaic model of membrane structure***
  - states that a membrane is a fluid structure with a "mosaic" of various proteins embedded in it

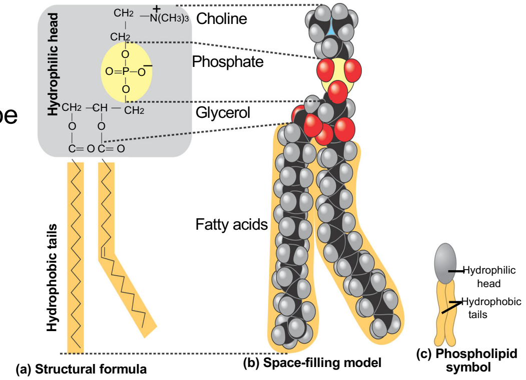
Membrane Models: Scientific Inquiry

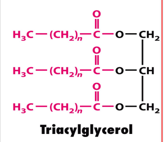
- Membranes have been chemically analyzed and found to be composed of proteins and lipids
- Scientists studying the plasma membrane reasoned that it must be a phospholipid bilayer



- The Davson-Danielli sandwich model of membrane structure
  - stated that the membrane was made up of a phospholipid bilayer sandwiched between two protein layers, and this

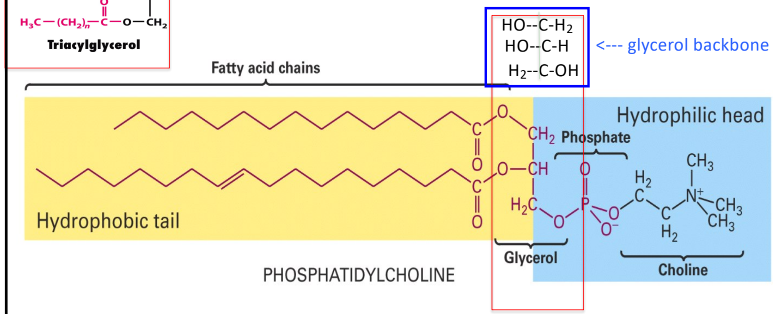
was supported by electron microscope pictures of membranes





Phosphatidylcholine, a typical phosphoglyceride

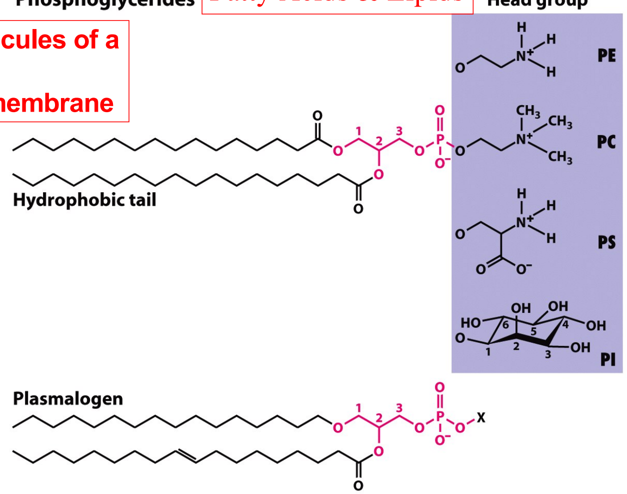
Lipids



All phosphoglycerides are amphipathic – having a hydrophobic tail (yellow) and a hydrophilic head (blue) in which glycerol is linked via a phosphate group to an alcohol. Either of or both the fatty acyl side chains in a phosphoglyceride may be saturated or unsaturated. In phosphatidic acid (red), the simplest phospholipid, the phosphate is not linked to an alcohol.

Fatty Acids & Lipids

Molecules of a Biomembrane

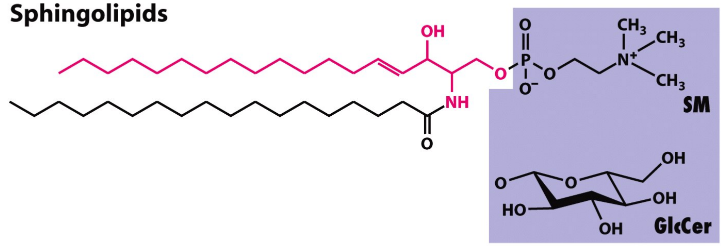


PC = phosphatidylcholine; PE = phosphatidylethanol; PS = phosphatidylserine; SM = sphingomyelin; PI = phosphoinositol

Molecules of a Biomembrane

Fatty Acids & Lipids

Sphingolipids



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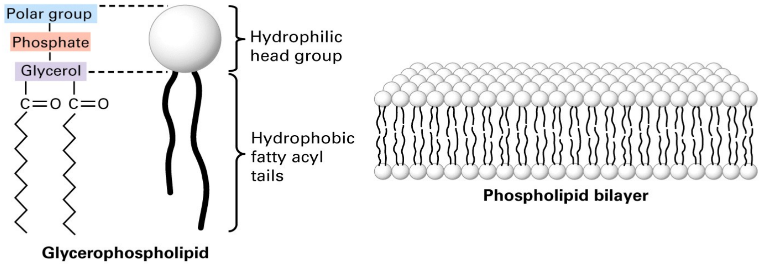
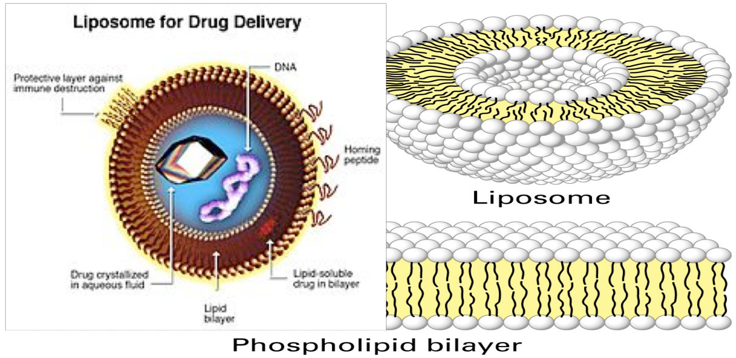
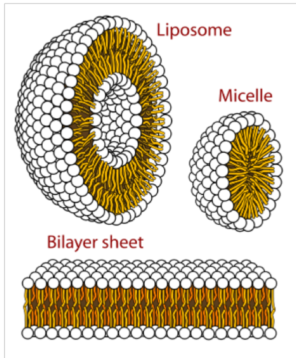
Essential Cell Membrane Molecules



Cross-sectional views of the three structures formed by phospholipids in aqueous solutions



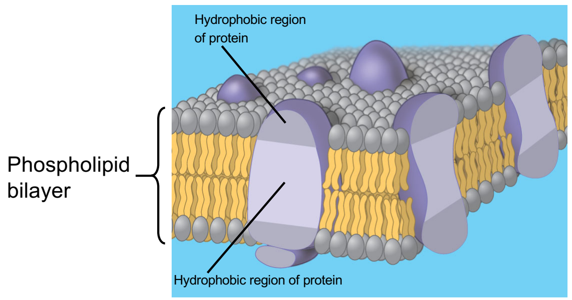
The white spheres depict the hydrophilic heads of the phospholipids, and the squiggly black lines (in the yellow regions) represent the hydrophobic tails. Shown are a spherical micelle with a hydrophobic interior composed entirely of fatty acyl chains; a spherical liposome, which has two phospholipid layers and an aqueous center; and a two-molecule-thick sheet of phospholipids, or bilayer, the basic structural unit of bio-membranes.



A micelle is an aggregate of surfactant molecules dispersed in a liquid colloid

Micelles are approximately spherical in shape.

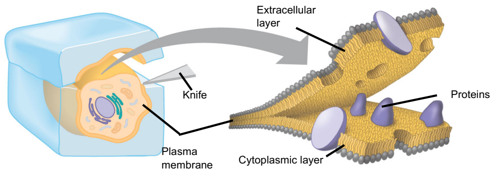
- In 1972, Singer and Nicolson
  - proposed that membrane proteins are dispersed and individually inserted into the phospholipid bilayer



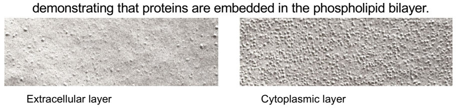
- Freeze-fracture studies of the plasma membrane
  - supported the fluid mosaic model of membrane structure

APPLICATION A cell membrane can be split into its two layers, revealing the ultrastructure of the membrane's interior.

TECHNIQUE A cell is frozen and fractured with a knife. The fracture plane often follows the hydrophobic interior of a membrane, splitting the phospholipid bilayer into two separated layers. The membrane proteins go wholly with one of the layers.

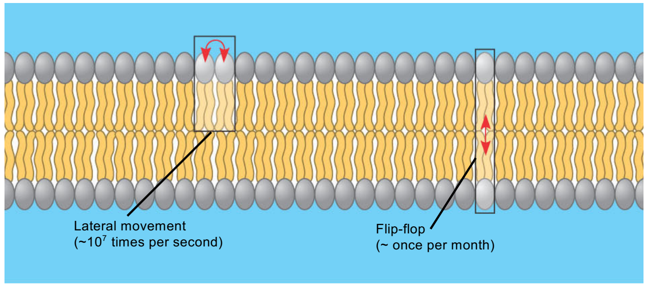


RESULTS These SEMs show membrane proteins (the "bumps") in the two layers, demonstrating that proteins are embedded in the phospholipid bilayer.



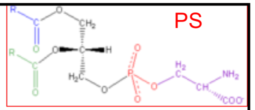
The Fluidity of Membranes

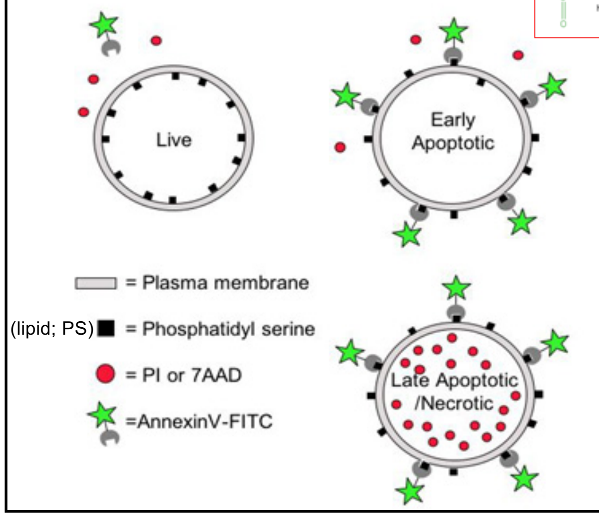
- Phospholipids in the plasma membrane
  - can move within the bilayer



Movement of phospholipids

Apoptosis Assay



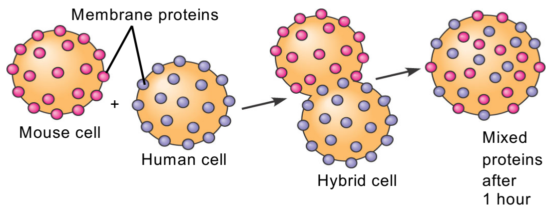


propidium iodide (PI) lables DNA; **Propidium iodide** is used as a DNA stain in flow cytometry to evaluate dead or dying cells.

- Proteins in the plasma membrane can drift within the bilayer

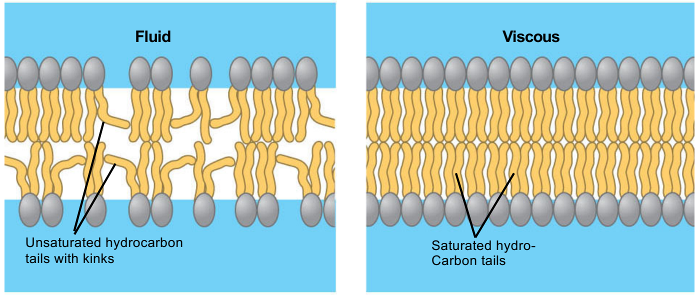
EXPERIMENT Researchers labeled the plasma mambrane proteins of a mouse cell and a human cell with two different markers and fused the cells. Using a microscope, they observed the markers on the hybrid cell.

RESULTS



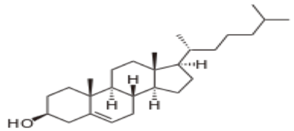
CONCLUSION The mixing of the mouse and human membrane proteins indicates that at least some membrane proteins move sideways within the plane of the plasma membrane.

- The type of hydrocarbon tails in phospholipids
  - affects the fluidity of the plasma membrane

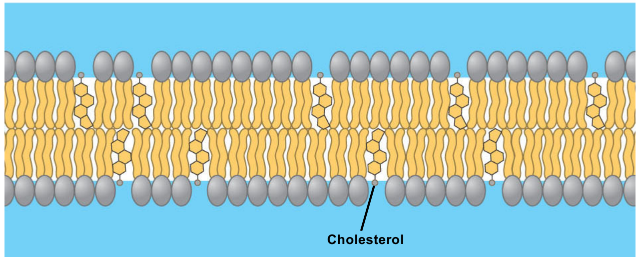


Membrane fluidity

- The steroid **cholesterol**



has different effects on membrane fluidity at different temperatures

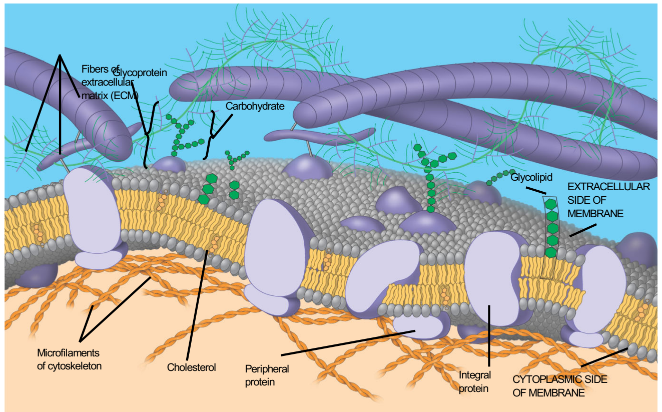


Cholesterol within the animal cell membrane

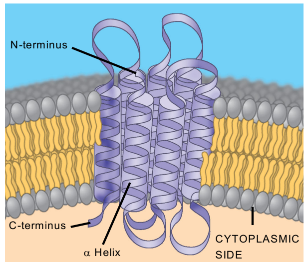
Adding Cholesterol to a cell membrane reduces fluidity, therefore, making the cell membrane more rigid reducing phospholipid movement. Without cholesterol, cell membranes would be too fluid, not firm enough, and too permeable to some molecules. While cholesterol adds firmness and integrity to the plasma membrane and prevents it from becoming overly fluid, it also helps to maintain its fluidity. At the high concentrations as it is found in our cell's plasma membranes cholesterol helps to separate the phospholipids so that the fatty acid chains can't come together and crystallize. Therefore, cholesterol helps to prevent extremes-- whether too fluid, or too firm -- in the consistency of the cell membrane.

Membrane Proteins and Their Functions

- A membrane is a collage of different proteins embedded in the fluid matrix of the lipid bilayer



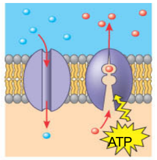
- *Integral proteins*
  - penetrate the hydrophobic core of the lipid bilayer
  - are often transmembrane proteins, completely spanning the membrane



- peripheral proteins are appendages, loosely bound to the surface of the membrane

An overview of six major functions of membrane proteins

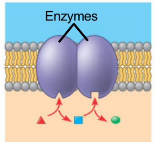
(a) **Transport. (left)** A protein that spans the membrane may provide a hydrophilic channel across the membrane that is selective for a particular solute. **(right)** Other transport proteins shuttle a substance from one side to the other by changing shape. Some of these proteins hydrolyze ATP as an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



e.g. ABC-transporter

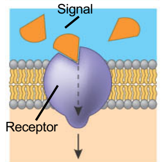
Na/K-ATPase, NMDAR

(b) **Enzymatic activity.** A protein built into the membrane may be an enzyme with its active site 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.



e.g. PLC
γ-secretase

(c) **Signal transduction.** A membrane protein may have a binding site with a specific shape that fits the shape of a chemical messenger, such as a hormone. The external messenger (signal) may cause a conformational change in the protein (receptor) that relays the message to the inside of the cell.

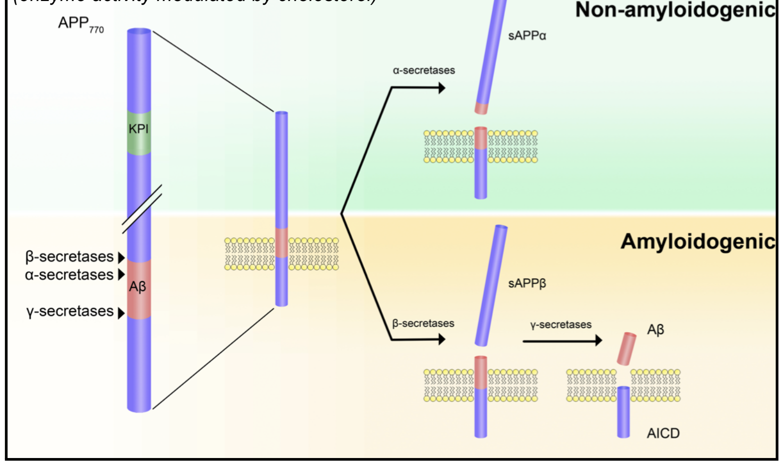


Receptors:
e.g. TRKA
p75NTR
NMDR

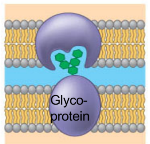
Regulated Intramembrane Proteolysis / RIP-tide mechanism

APP (Amyloid Precursor Protein) processing by secretases

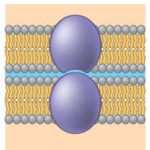
(enzyme activity modulated by cholesterol)



(d) **Cell-cell recognition.** Some glyco-proteins serve as identification tags that are specifically recognized by other cells.



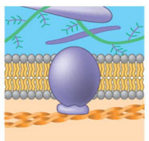
(e) **Intercellular joining.** Membrane proteins of adjacent cells may hook together in various kinds of junctions, such as gap junctions or tight junctions.



inter-cell-signalling: e.g.

Notch-Delta

(f) **Attachment to the cytoskeleton and extracellular matrix (ECM).** Microfilaments or other elements of the cytoskeleton may be bonded to membrane proteins, a function that helps maintain cell shape and stabilizes the location of certain membrane proteins. Proteins that adhere to the ECM can coordinate extracellular and intracellular changes.



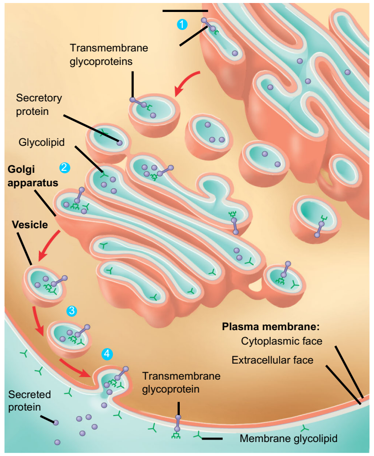
The Role of Membrane Carbohydrates in Cell-Cell Recognition

- Cell-cell recognition is a cell's ability to distinguish one type of neighboring cell from another
- Membrane carbohydrates interact with the surface molecules of other cells, facilitating cell-cell recognition

Synthesis and Sidedness of Membranes

- Membranes have distinct inside and outside faces
- This affects the movement of proteins synthesized in the endomembrane system

- Membrane proteins and lipids are synthesized in the ER and Golgi apparatus

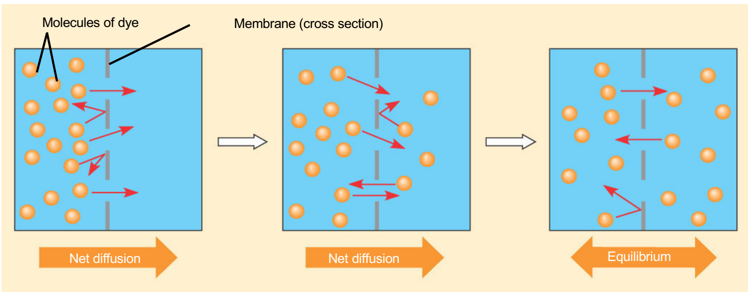


- Membrane structure results in selective permeability
- A cell must exchange materials with its surroundings, a process controlled by the plasma membrane

The Permeability of the Lipid Bilayer

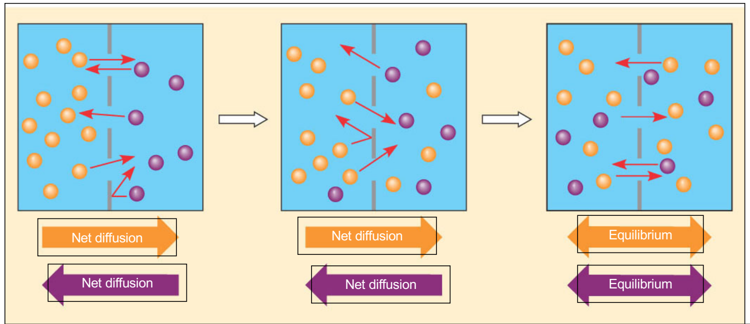
- Hydrophobic molecules are lipid soluble and can pass through the membrane rapidly
- Polar molecules do not cross the membrane rapidly
- *Transport proteins* allow passage of hydrophilic substances across the membrane
- Passive transport is diffusion of a substance across a membrane with no energy investment

Diffusion is the tendency for molecules of any substance to spread out evenly into the available space



Diffusion of one solute. The membrane has pores large enough for molecules of dye to pass through. Random movement of dye molecules will cause some to pass through the pores; this will happen more often on the side with more molecules. The dye diffuses from where it is more concentrated to where it is less concentrated (called diffusing down a concentration gradient). This leads to a dynamic equilibrium: The solute molecules continue to cross the membrane, but at equal rates in both directions.

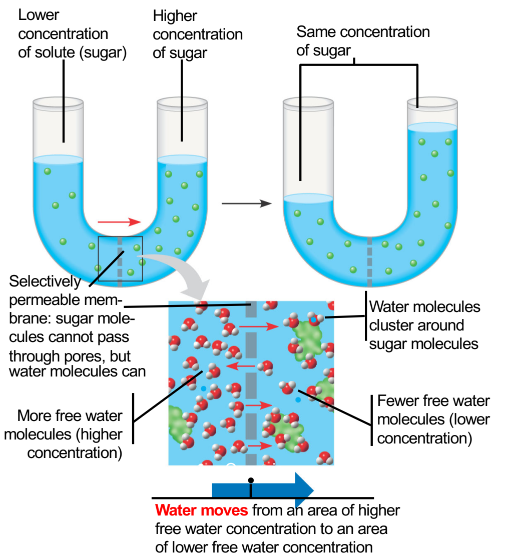
Substances diffuse down their concentration gradient, the difference in concentration of a substance from one area to another



Diffusion of two solutes. Solutions of two different dyes are separated by a membrane that is permeable to both. Each dye diffuses down its own concentration gradient. There will be a net diffusion of the purple dye toward the left, even though the *total* solute concentration was initially greater on the left side.

Effects of Osmosis on Water Balance

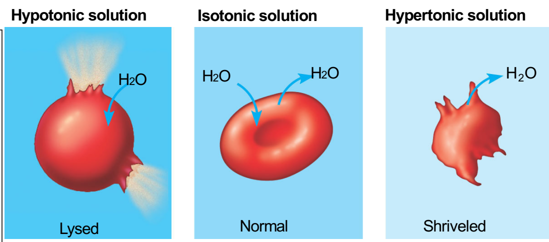
Osmosis is the movement of water across a semipermeable membrane; it is affected by the concentration gradient of dissolved substances



Water Balance of Cells Without Walls

- Tonicity is the ability of a solution to cause a cell to gain or lose water; it has a great impact on cells without walls
- If a solution is isotonic
  - the concentration of solutes is the same as it is inside the cell
  - there will be no net movement of water
- If a solution is hypertonic
  - the concentration of solutes is greater than it is inside the cell
  - the cell will lose water
- If a solution is hypotonic
  - the concentration of solutes is less than it is inside the cell
  - the cell will gain water

- Water balance in cells without walls
- Animals and other organisms without rigid cell walls living in hypertonic or hypotonic environments
  - must have special adaptations for **osmoregulation**

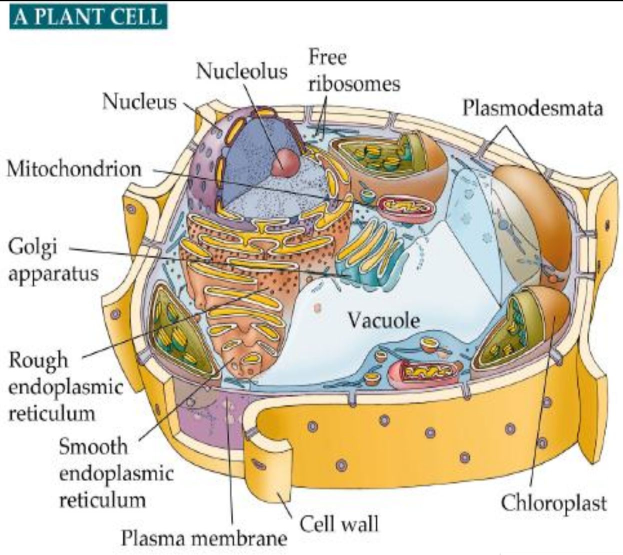


Animal cell. An animal cell fares best in an isotonic environment unless it has special adaptations to offset the osmotic uptake or loss of water.

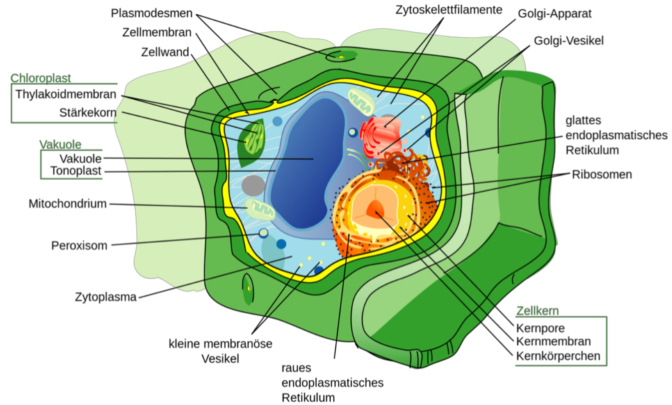
An increase in the salinity (saltiness; salt concentration) of a lake can kill animals there; if the lake water becomes hypertonic to the animal's cells, the cells might shrivel and die. Hypotonic environment is hazardous as well.

Water Balance of Cells with Walls

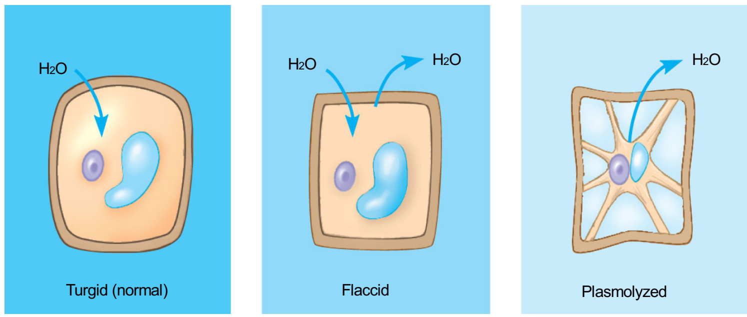
- Cell walls help maintain water balance
- If a plant cell is turgid
  - it is in a hypotonic environment
  - it is very firm, a healthy state in most plants
- If a plant cell is flaccid
  - it is in an isotonic or hypertonic environment



Plant - Cell

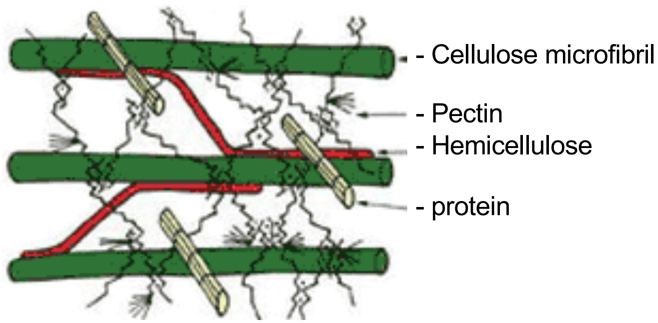


- **Water balance in cells with walls**

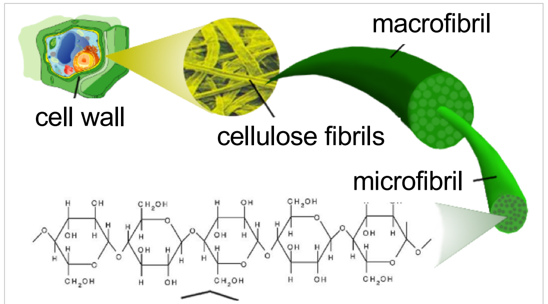


Plant cell. Plant cells are turgid (firm) and generally healthiest in a hypotonic environment, where the uptake of water is eventually balanced by the elastic wall pushing back on the cell.

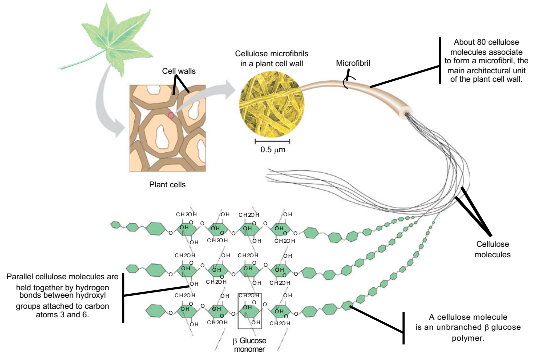
plant-cell wall details



plant-cell wall details

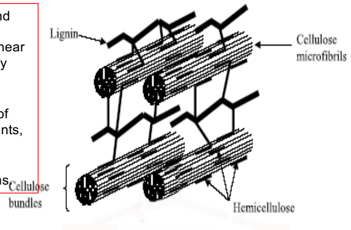


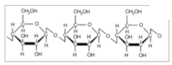
– Cellulose is a major component of the tough walls that enclose plant cells



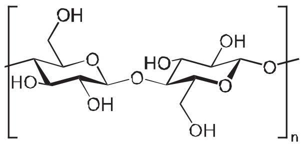
- Cellulose is a major component of the tough walls that enclose plant cells

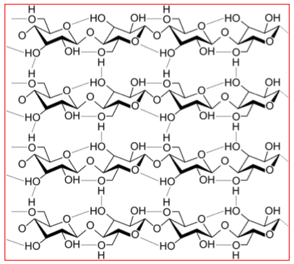
Cellulose is an organic compound with the formula $(C_6H_{10}O_5)_n$, a polysaccharide consisting of a linear chain of several hundred to many thousands of β(1→4) linked D-glucose units. Cellulose is an important structural component of the primary cell wall of green plants, many forms of algae and the oomycetes. Some species of bacteria secrete it to form biofilms.

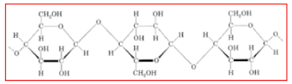




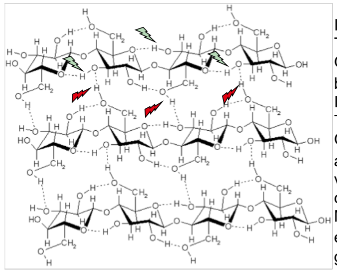
Cellulose





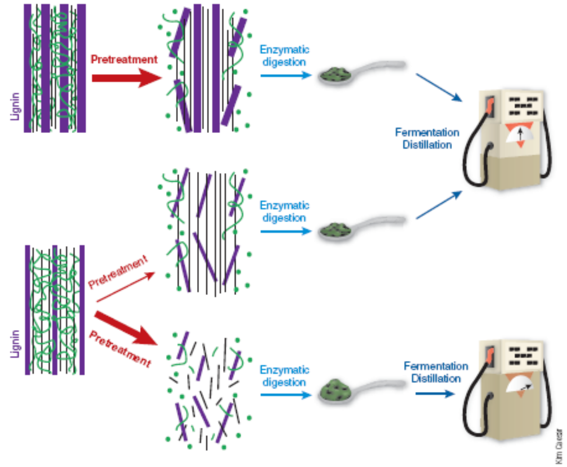


The crystalline regions of cellulose have intramolecular and intermolecular hydrogen bonds, allowing the linear glucan chains to form crystalline structures that exclude water and enzymes.

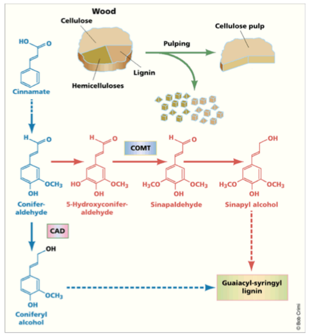


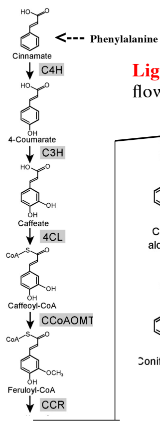
Intramolecular:
The H of the OH on C3 to the O that makes the glycosidic bonds.
Intermolecular:
The H of the OH on C6 to the O of the OH on C3. These are the bonds that make the very tight structure of cellulose microfibrils.
Microfibrils have 30-40 chains each with 2000 to 10,000 glucose units.

Lignin modification may decrease the need for pretreatment

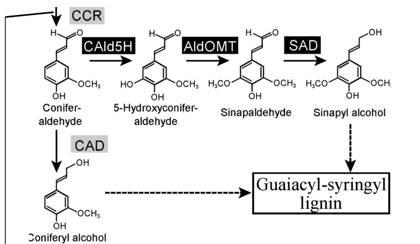


Lignin biosynthetic pathway in woody angiosperms (e.g. aspen or poplar)



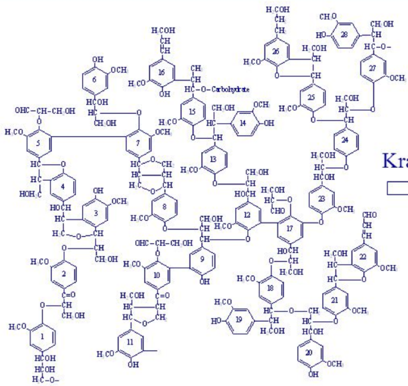


Lignin biosynthetic pathway in woody angiosperms (the flowering plants) (e.g. aspen or poplar)



Secretion is followed by oxidative polymerization catalyzed by peroxidase

The Goal of Lignin Reactions in Kraft Pulping



Kraft Pulping → Soluble Fragments

The goal in kraft pulping is to take large insoluble lignin and turn it into small alkali soluble fragments.

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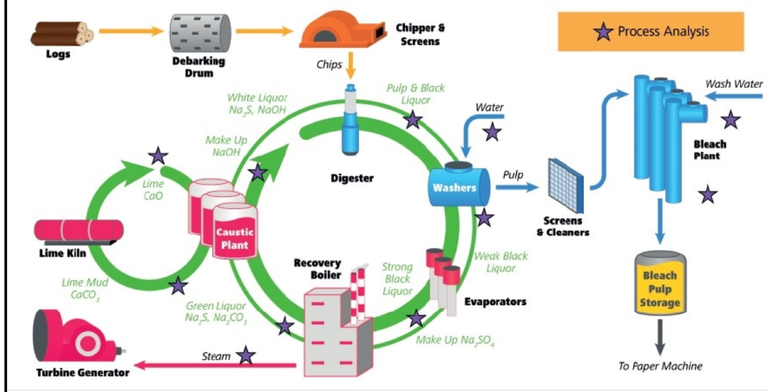
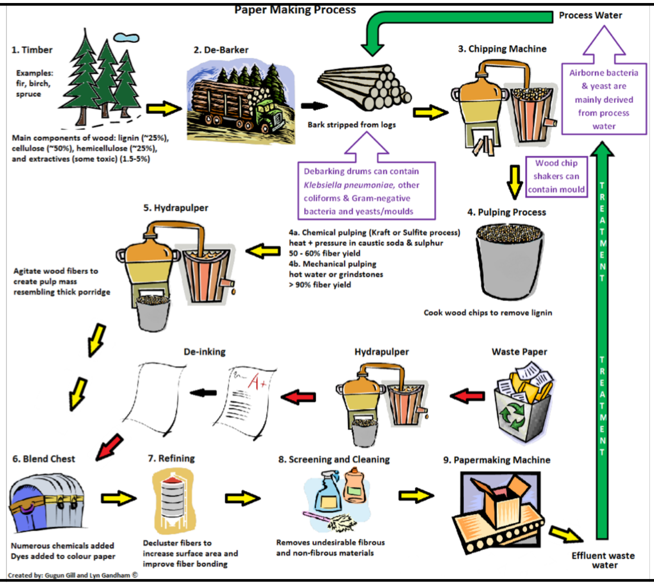
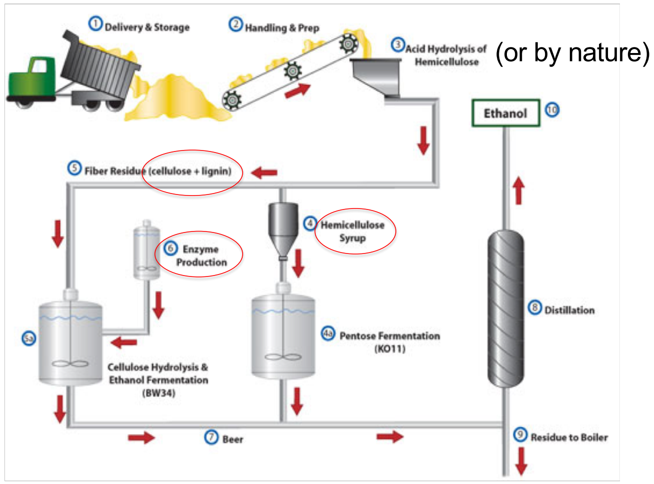




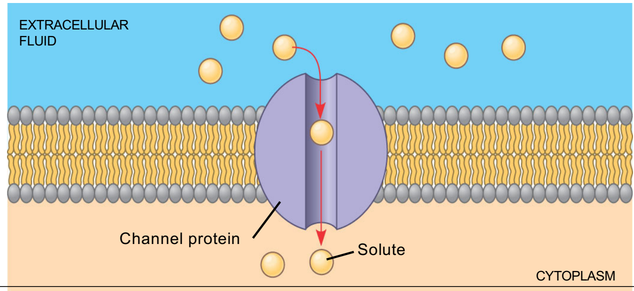
A simplified scheme for the processing of biomass into ethanol



Facilitated Diffusion: Passive Transport Aided by Proteins

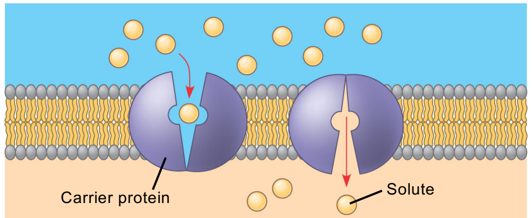
- In facilitated diffusion
  - *transport proteins* speed the movement of molecules across the plasma membrane

- Channel proteins (e.g. ion channels (various types such as voltage-gated or neurotransmitter receptors) in neurons)
  - provide corridors that allow a specific molecule or ion to cross the membrane



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

- Carrier proteins (various types)
  - undergo a subtle change in shape that translocates the solute-binding site across the membrane (also as 'Co-transporters')



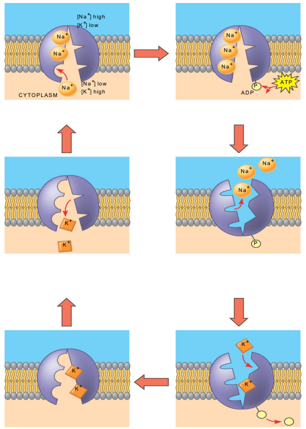
A carrier protein alternates between two conformations, moving a solute across the membrane as the shape of the protein changes. The protein can transport the solute in either direction, with the net movement being down the concentration gradient of the solute.

- Active transport uses energy to move solutes against their gradients

The Need for Energy in Active Transport

- Active transport
  - moves substances against their concentration gradient
  - requires energy, usually in the form of ATP

The sodium-potassium pump (Na/K-ATPase is one type of **active** transport system

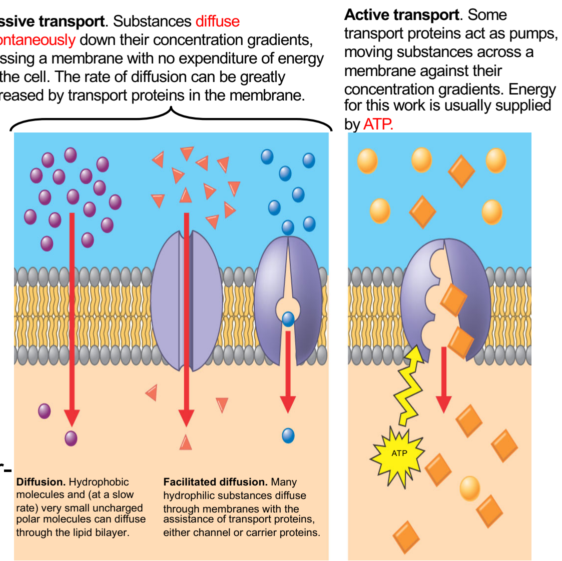


- Cytoplasmic Na^+ binds to the sodium-potassium pump.
- Na+ binding stimulates phosphorylation by ATP.
- Phosphorylation causes the protein to change its conformation, expelling Na^+ to the outside.
- Extracellular K^+ binds to the protein, triggering release of the Phosphate group.
- Loss of the phosphate restores the protein's original conformation.
- K^+ is released and Na^+ sites are receptive again; the cycle repeats.

Review passive and active transport compared

Ion-channels

Neurotransmitter-Receptors



Maintenance of Membrane Potential by Ion Pumps (as the Na/K ATPase; proton pump)

Membrane potential is the voltage difference across a membrane

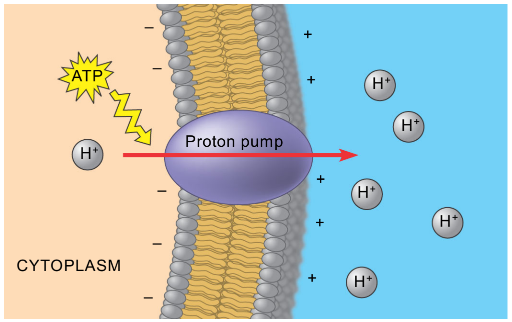
An electrochemical gradient

is caused by the concentration electrical gradient of ions across a membrane

Co-transport: Coupled Transport by a Membrane Protein

Cotransport occurs when active transport of a specific solute indirectly drives the active transport of another solute

- An electrogenic pump
  - is a transport protein that generates the voltage across a membrane



H^+ gradient is either created by ATP or H^+ gradient is used to make ATP

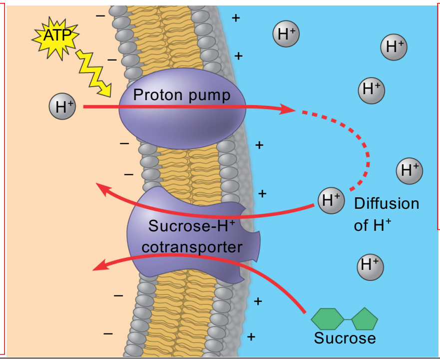
- An electrogenic pump is a transport protein that generates the voltage across a membrane
- Cotransport: active transport driven by a concentration gradient

See also
F-class H⁺-pump:

Mitochondria:
ATP generation

Chloroplasts:
Photosynthesis

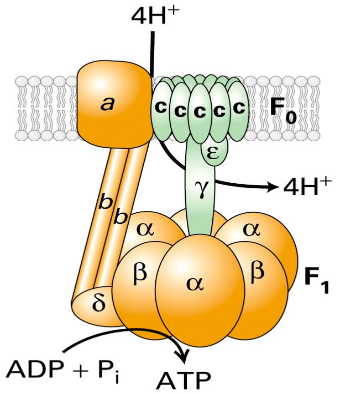
compare with:
Na/K ATPase



e.g.: V-class proton pumps at vacuolar membranes in plants, yeast, other fungi; at endosomal and lysosomal membranes in animal cells; at plasma membrane of osteoclasts and some kidney tubule cells.

H^+ gradient is either created by ATP, or H^+ gradient is used to make/synthesize ATP (as in choroplasts or mitochondria)

ATP-synthesis: F-class H^+-pump



F-class proton pumps

Bacterial plasma membrane

Inner mitochondrial membrane

Thylakoid membrane of chloroplast

electromotive force (emf)

F-class pumps do not form phosphoprotein intermediates and transport only protons. V/F-class structures are similar and contain similar proteins, but none of their subunits are related to the P-class pumps. F-class pumps *operate in the reverse directions* (compared to V-class) to utilize energy in a proton concentration or electrochemical gradient to synthesize ATP.

- Bulk transport across the plasma membrane occurs by exocytosis and endocytosis
- Large proteins cross the membrane by different mechanisms

Exocytosis

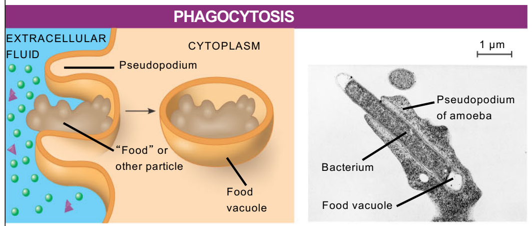
- In exocytosis transport vesicles migrate to the plasma membrane, fuse with it, and release their contents (neurotransmitter release)

Endocytosis

- In endocytosis the cell takes in macromolecules by forming new vesicles from the plasma membrane

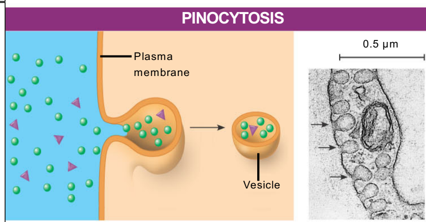
- Three types of endocytosis

In **phagocytosis,** a cell engulfs a particle by Wrapping pseudopodia around it and packaging it within a membrane-enclosed sac large enough to be classified as a vacuole. The particle is digested after the vacuole fuses with a lysosome containing hydrolytic enzymes.



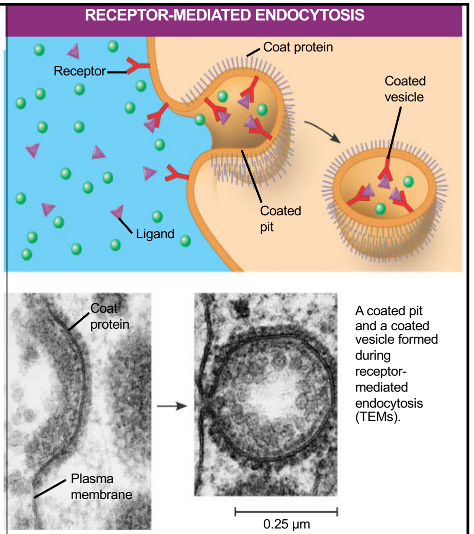
An amoeba engulfing a bacterium via phagocytosis (TEM).

In **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 droplet. Because any and all included solutes are taken into the cell, pinocytosis is nonspecific in the substances it transports.



Pinocytosis vesicles forming (arrows) in a cell lining a small blood vessel (TEM).

Receptor-mediated endocytosis 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 membrane are proteins with specific receptor sites exposed to the extracellular fluid. The receptor proteins are usually already clustered in regions of the membrane called coated pits, which are lined on their cytoplasmic side by a fuzzy layer of coat proteins. Extracellular substances (ligands) bind to these receptors. When binding occurs, the coated pit forms a vesicle containing the ligand molecules. Notice that there are relatively more bound molecules (purple) inside the vesicle, other molecules (green) are also present. After this ingested material is liberated from the vesicle, the receptors are recycled to the plasma membrane by the same vesicle.



A coated pit and a coated vesicle formed during receptor-mediated endocytosis (TEMs).

Cell signalling

Retrograde NGF (Nerve Growth Factor) Signalling