The Plasma Membrane

ALL CELLS-BOTH PROKARYOTIC AND EUKARYOTIC-are surrounded by a plasma membrane, which defines the boundary of the cell and separates its internal contents from the environment.

Selective barrier to the passage of molecules, it determines the composition of the cytoplasm.

The first cell is thought to have arisen by the enclosure of self-replicating RNA in a membrane of phospholipids.

The basic structure of the PM is the phospholipid bilayer, which is impermeable to most water-soluble molecules.

The passage of ions and most biological molecules across PM is mediated by proteins, responsible for the selective traffic of molecules into and out of the cell.

The plasma membrane thus plays a dual role: It both isolates the cytoplasm and mediates interactions between the cell and its environment.

Structure of the Plasma Membrane

consists of both lipids and proteins.

The fundamental structure of the membrane is the phospholipid bilayer, which forms a stable barrier between two aqueous compartments.

Proteins embedded within the phospholipid bilayer carry out the specific functions of the PM, including selective transport of molecules and cell-cell recognition.

The Phospholipid Bilayer

The PM of mammalian red blood cells (erythrocytes) have been particularly useful as a model for studies of membrane structure.

The first evidence that biological membranes consist of lipid bilayers was in 1925, two Dutch scientists (Edwin Gorter and F. Grendel) conclusion that the membranes consisted of lipid bilayers rather than monolayers.

The morphology of PM frequently referred to as a "railroad track" appearance.

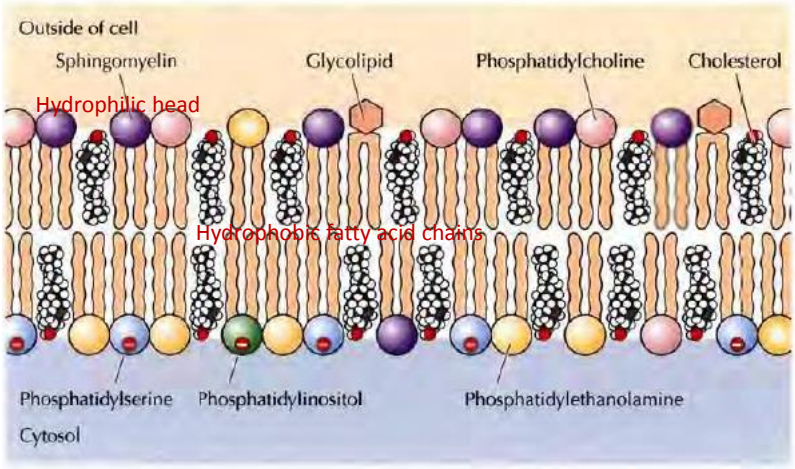


FIGURE 1 Lipid components of the plasma membrane The outer leaflet consists predominantly of phosphatidylcholine, sphingomyelin, and glycolipids, whereas the inner leaflet contains phosphatidylethanolamine, phosphatidylserine, and phosphatidylinositol. Cholesterol is distributed in both leaflets. The net negative charge of the head groups of phosphatidylserine and phosphatidylinositol is indicated.

The fatty acids of most natural phospholipids have one or more double bonds, which introduce kinks into the hydrocarbon chains and make them difficult to pack together.

The long hydrocarbon chains of the fatty acids therefore move freely in the interior of the membrane, so the membrane itself is soft and flexible.

Both phospholipids and proteins are free to diffuse laterally within the membrane that is critical for many membrane functions.

Cholesterol has distinct effects on membrane fluidity. At high temperatures, cholesterol interferes with the movement of the phospholipid fatty acid chains, making the outer part of the membrane less fluid and reducing its permeability to small molecules.

At low temperatures, however, cholesterol has the opposite effect: By interfering with interactions between fatty acid chains, cholesterol prevents membranes from freezing and maintains membrane fluidity.

Plant cells also lack cholesterol, but they contain related compounds (sterols) that fulfill a similar function.

Membrane Proteins

Most PM consist of approximately 50% lipid and 50% protein by weight, with the carbohydrate portions of glycolipids and glycoproteins constituting 5 to 10% of the membrane mass

In 1972 Jonathan Singer and Garth Nicolson proposed the fluid mosaic model of membrane structure

In this model, membranes are viewed as two-dimensional fluids in which proteins are inserted into lipid bilayers.

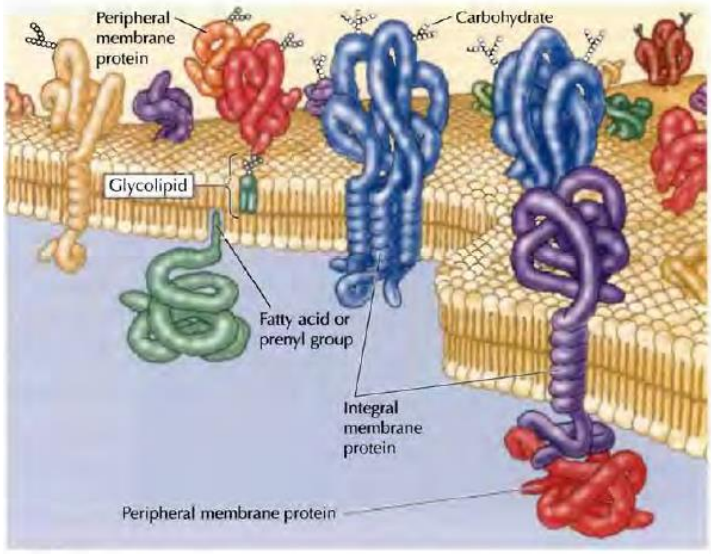
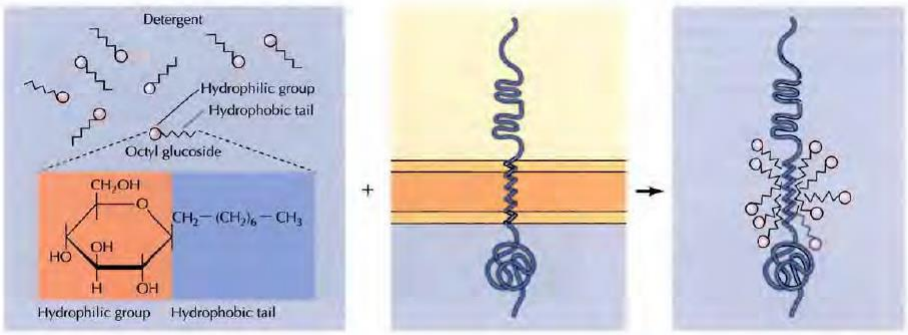


FIGURE 2 Fluid mosaic model of the plasma membrane integral membrane proteins are inserted into the lipid bilayer, whereas peripheral proteins are bound to the membrane indirectly by protein-protein interactions. Most integral membrane proteins are transmembrane proteins with portions exposed on both sides of the lipid bilayer. The extracellular portions of these proteins are usually glycosylated, as are the peripheral membrane proteins bound to the external face of the membrane.



Peripheral membrane proteins that dissociate from the membrane following treatments with polar reagents, such as solutions of extreme pH or high salt concentration that do not disrupt the phospholipid bilayer. These are indirectly associated with membranes through protein-protein interactions.

Integral membrane proteins can be released only by treatments that disrupt the phospholipid bilayer. They can be dissociated only by reagents that disrupt hydrophobic interactions. The detergents, which are small amphipathic molecules containing both hydrophobic and hydrophilic groups.

Many integral proteins are transmembrane proteins, which span the lipid bilayer with portions exposed on both sides of the membrane.

The membrane-spanning portions of transmembrane proteins are usually *a helices of 20 to 25 hydrophobic amino acids that are inserted into the* membrane of the ER during synthesis of the polypeptidte chain

The two major integral membrane proteins of red blood cells-glycophorin and band 3-provide well-studied examples of transmembrane protein structure

Because of their amphipathic character, transmembrane proteins have proved difficult to crystallize

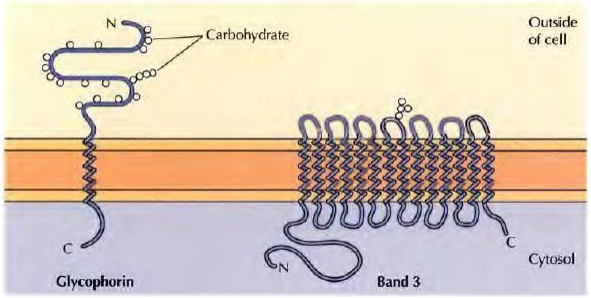


FIGURE 3 Integral membrane proteins of red blood cells Glycophorin (131 amino acids) contains a single transmembrane *a helix. It is* heavily glyocosylated, with oligosaccharides attached to 16 sites on the extracellular portion of the polypeptide chain.
Band 3 (929 amino acids) has multiple transmembrane *a helices* and is thought to cross the membrane 14 times.

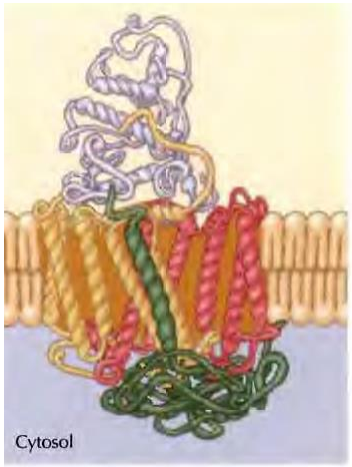


FIGURE 4: A bacterial photosynthetic reaction center The reaction center consists of three transmembrane proteins designated L (red), M (yellow), and H (green). The Land M subunits each have five transmembrane *a helices, whereas* the H subunit has only one. The fourth subunit of the reaction center is a cytochrome (white), which is a peripheral membrane protein.

Although most transmembrane proteins span the membrane by alpha-helical regions, this is not always the case. A well-characterized exception is provided by the **Porins**-a class of proteins that form channels in the outer membranes of some bacteria.

Structural analysis shows that the porins do not contain hydrophobic beta-helical regions. Instead, they cross the membrane as beta barrels in which 8-22 beta sheets fold up into a barrel-like structure enclosing an aqueous pore.

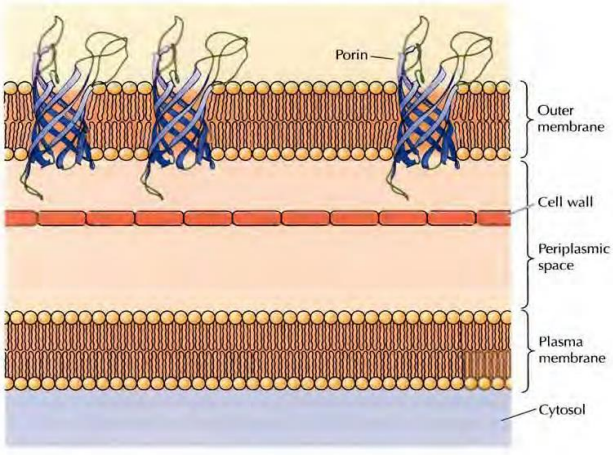


FIGURE 4 Bacterial outer membranes The plasma membrane of some bacteria is surrounded by a cell wall and a distinct outer membrane. The outer membrane contains porins, which form aqueous channels allowing the free passage of ions and small molecules. Porins cross the membrane as beta-barrels.

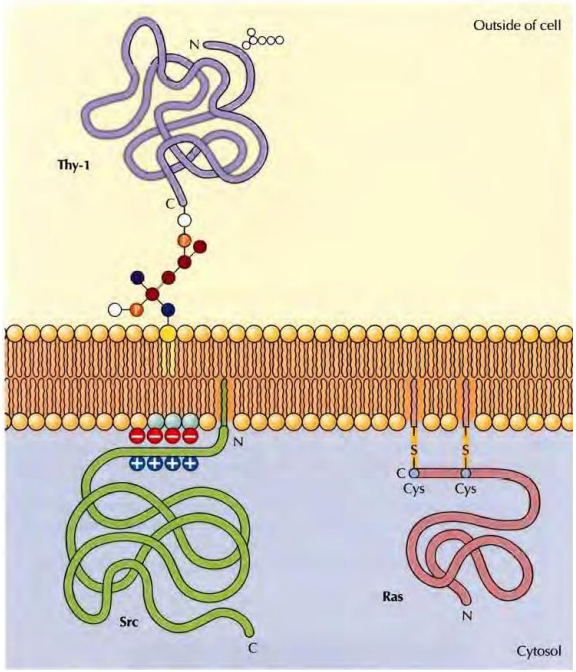
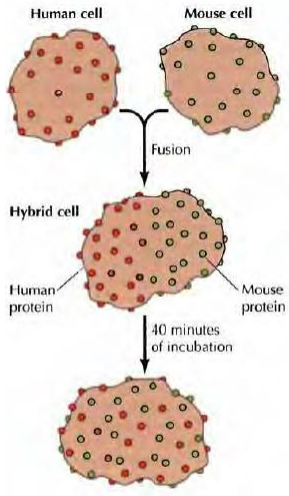


FIGURE 5: Examples of proteins anchored in the plasma membrane by lipids and glycolipids Some proteins (e.g., the lymphocyte protein Thy-1) are anchored in the outer leaflet of the plasma membrane by glycosylphosphatidylinositol (GPI) anchors added to their C terminus in the endoplasmic reticulum. These proteins are glycosylated and exposed on the cell surface. Other proteins are anchored in the inner leaflet of the plasma membrane following their translation on free cytosolic ribosomes. The Ras protein illustrated is anchored by a prenyl group attached to the side chain of a C-terminal cysteine and by a palrnitoyl group attached to a cysteine located five amino acids upstream. The Src protein is anchored by a myristoyl group attached to its N terminus. A positively charged region of Src also plays a role in membrane association, perhaps by interacting with the negatively charged head groups of phosphatidylserine.

Mobility of Membrane Proteins



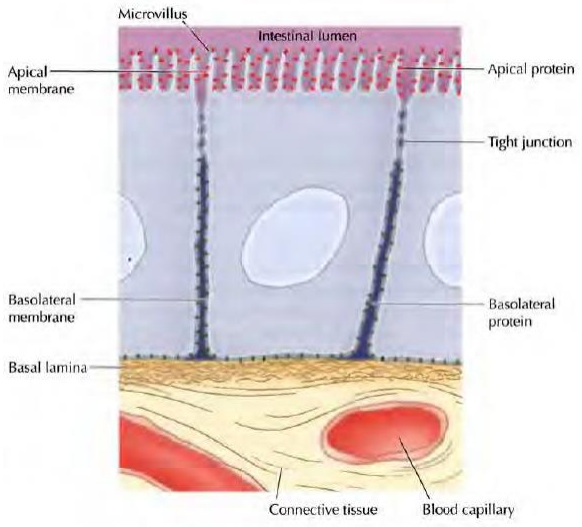


FIGURE 7 A polarized intestinal epithelial cell The apical surface of the cell contains microvilli and is specialized for absorption of nutrients from the intestinal lumen. The basolateral surface is specialized for the transfer of absorbed nutrients to the underlying connective tissue, which contains blood capillaries. Tight junctions separate the apical and basolateral domains of the plasma membrane. Membrane proteins are free to diffuse within each domain but are not able to cross from one domain to the other.

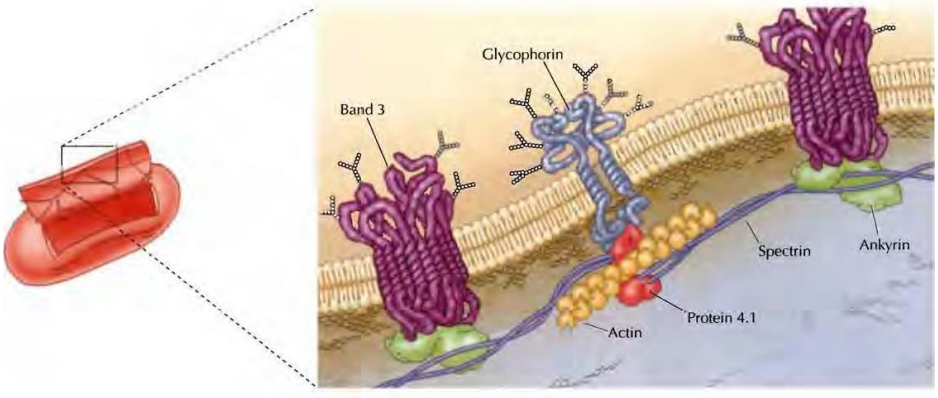


FIGURE 8: Association of the erythrocyte cortical cytoskeleton with the plasma membrane
The plasma membrane is associated with a network of spectrin tetramers cross-linked by short actin filaments in association with protein 4.1. The spectrin-actin network is linked to the membrane by ankyrin, which binds to both spectrin and the abundant transmembrane protein, band 3. An additional link is provided by the binding of protein 4.1 to glycophorin.

Transport of Small Molecules

FIGURE : The glycocalyx An electron micrograph of intestinal epithelium illustrating the glycocalyx (arrows).

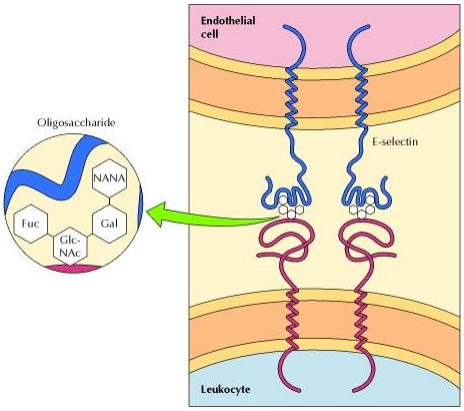


FIGURE: **Binding of selectins to oligosaccharides** E-selectin is a transmembrane protein expressed by endothelial cells that binds to an oligosaccharide expressed on the surface of leukocytes. The oligosaccharide recognized by E-selectin contains N-acetylglucosamine (GlcNAc), fucose (Fuc), galactose (Gal), and sialic acid (N-acetylneuraminic acid, NANA).

Passive Diffusion

The simplest mechanism by which molecules can cross the PM.

During passive diffusion, a molecule simply dissolves in the phospholipid bilayer, diffuses across it, and then dissolves in the aqueous solution at the other side of the membrane.

No membrane proteins are involved and the direction of transport is determined simply by the relative concentrations of the molecule inside and outside of the cell.

Nonselective process any molecule able to dissolve in the phospholipid bilayer is able to cross the plasma membrane and equilibrate between the inside and outside of the cell.

Importantly, only small, relatively hydrophobic molecules are able to diffuse across a phospholipid bilayer at significant rates

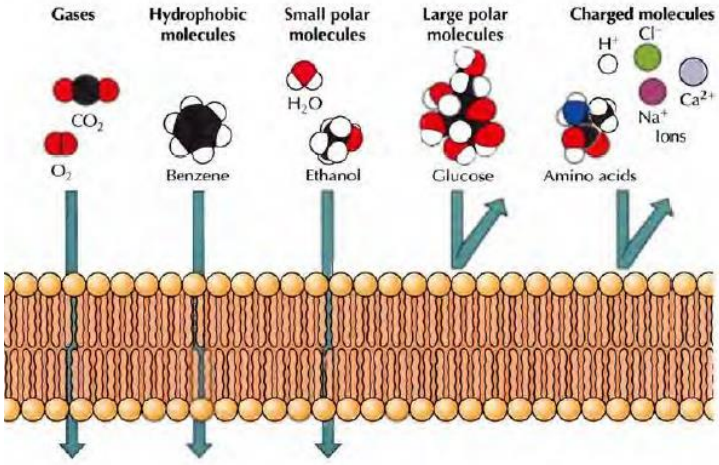


FIGURE Permeability of phospholipid bilayers Gases, hydrophobic molecules, and small polar uncharged molecules can passively diffuse through phospholipid bilayers. Larger polar molecules and charged molecules cannot.

Facilitated Diffusion and Carrier Proteins

Facilitated diffusion, like passive diffusion, involves the movement of molecules in the direction determined by their relative concentrations inside and outside of the cell.

No external source of energy is provided, so molecules travel across the membrane in the direction determined by their concentration gradients and, in the case of charged molecules, by the electric potential across the membrane.

Facilitated diffusion allows polar and charged molecules, such as carbohydrates, amino acids, nucleosides, and ions, to cross the plasma membrane.

The facilitated diffusion mediated by two classes of proteins carrier proteins and channel proteins .

The glucose transporter provides a well-studied example of a carrier protein.

The glucose transporter was initially identified as a 55-kd protein in human red blood cells in which it represents approximately 5% of total membrane protein.

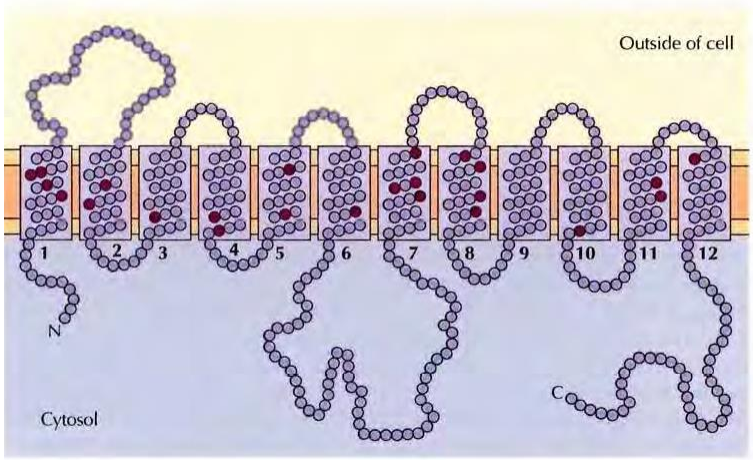


FIGURE Structure of the glucose transporter The glucose transporter has 12 transmembrane *a* helices. Polar amino acid residues located within the phospholipid bilayer are indicated as dark purple circles.

Polar amino acid residues that are thought to form the glucose-binding site in the interior of the protein.

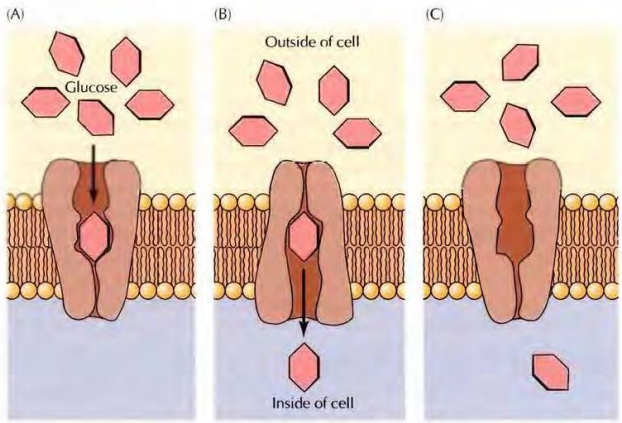
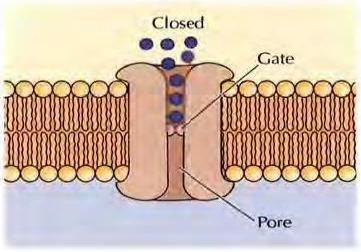


FIGURE Model for the facilitated diffusion of glucose The glucose transporter alternates between two conformations in which a glucose binding site is alternately exposed on the outside and the inside of the cell. In the first conformation shown (A), glucose binds to a site exposed on the outside of the plasma membrane. The transporter then undergoes a conformational change such that the glucose binding site faces the inside of the cell and glucose is released into the cytosol (B). The transporter then returns to its original conformation (C).

Ion Channels

channel proteins



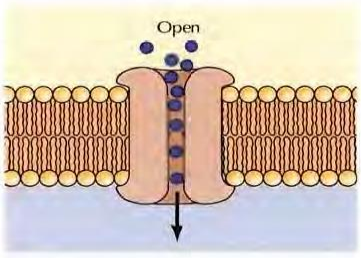


FIGURE: Model of an ion channel In the closed conformation, the flow of ions is blocked by a gate. Opening of the gate allows ions to flow rapidly through the channel. The channel contains a narrow pore that restricts passage to ions of the appropriate size and charge.

1) Transport through channels is extremely rapid, approximately a thousand times greater than the rate of transport by carrier proteins.
2) Highly selective because narrow pores in the channel restrict passage to ions of the appropriate size and charge.

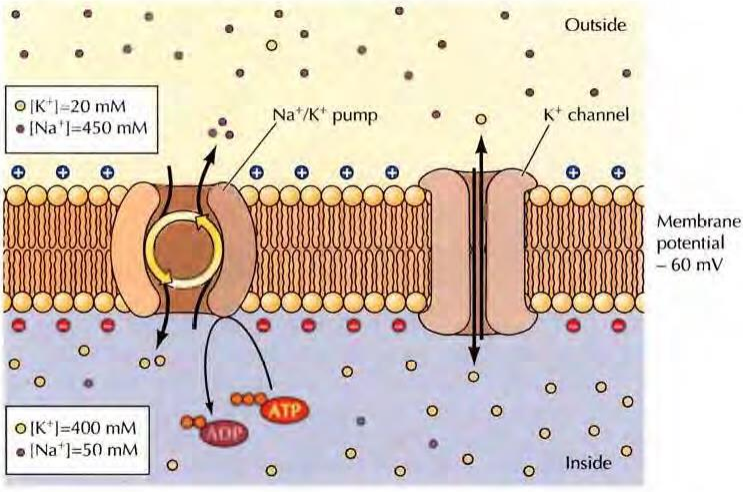


FIGURE Ion gradients and resting membrane potential of the giant squid axon Only the concentrations of Na+ and K+ are shown because these are the ions that function in the transmission of nerve impulses . Na+ is pumped out of the cell while K+ is pumped in, so the concentration of Na+ is higher outside than inside of the axon, whereas the concentration of K+ is higher inside than out. The resting membrane is more permeable to K+ than to Na+ or other ions because it contains open K+ channels. The flow of K+ through these channels makes the major contribution to the resting membrane potential of -60 mV, which is therefore close to the K+ equilibrium potential.

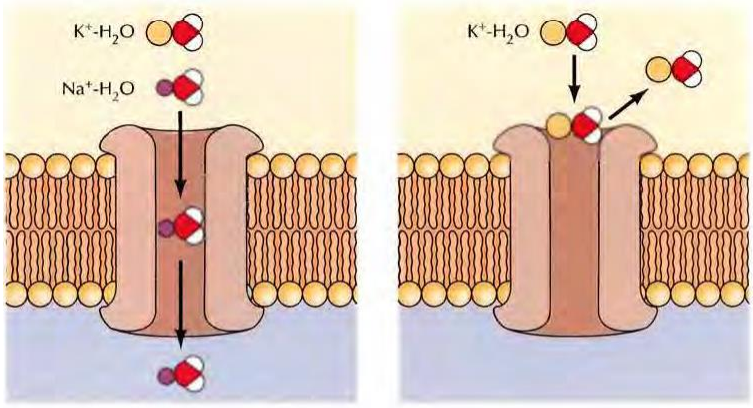


FIGURE 13.24 Ion selectivity of Na^+ channels A narrow pore permits the passage of Na^+ bound to a single water molecule but interferes with the passage of K^+ or larger ions.

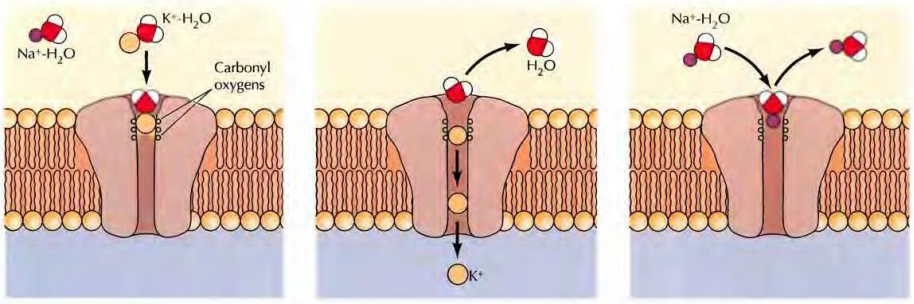


FIGURE: Selectivity of K+ channels

The K+ channel contains a narrow selectivity filter lined with carbonyl oxygen (C=O) atoms. The pore is just wide enough to allow the passage of dehydrated K+ from which all associated water molecules have been displaced as a result of interactions between K+ and these carbonyl oxygens. Na+ is too small to interact with the carbonyl oxygens of the selectivity filter, so it remains bound to water in a complex that is too large to pass through the channel pore.

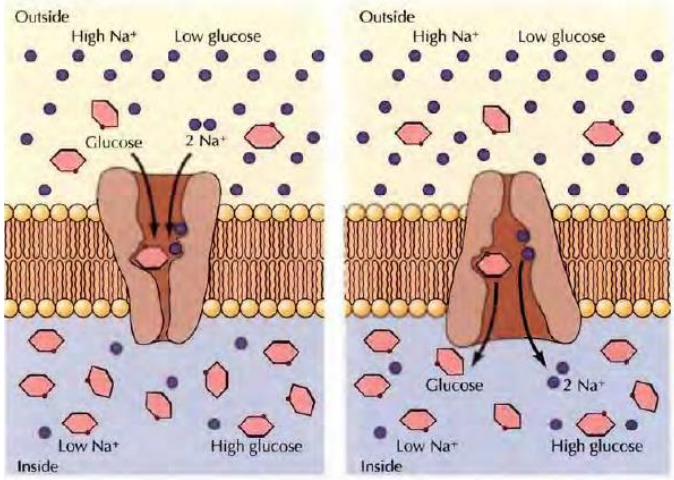


FIGURE: Active transport of glucose- Active transport driven by the Na+ gradient is responsible for the uptake of glucose from the intestinal lumen. The transporter coordinately binds and transports one glucose molecule and two Na+ ions into the cell. The transport of Na+ in the energetically favorable direction drives the uptake of glucose against its concentration gradient.

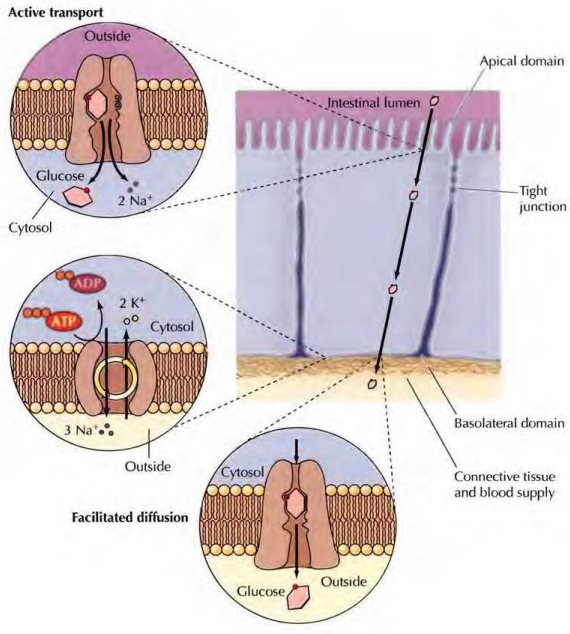


FIGURE Glucose transport by intestinal epithelial cells

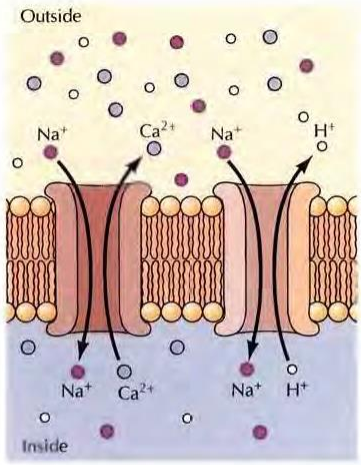


FIGURE 13.33 Examples of antiport
Ca^{2+} and H^+ are exported from cells by antiporters, which couple their export to the energetically favorable import of Na^+.