Advanced Cell Biology

Biological Membranes Transport

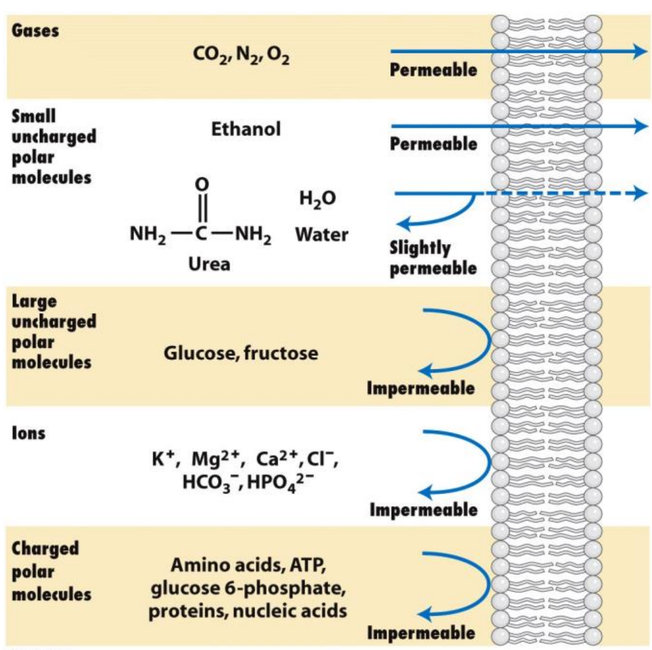
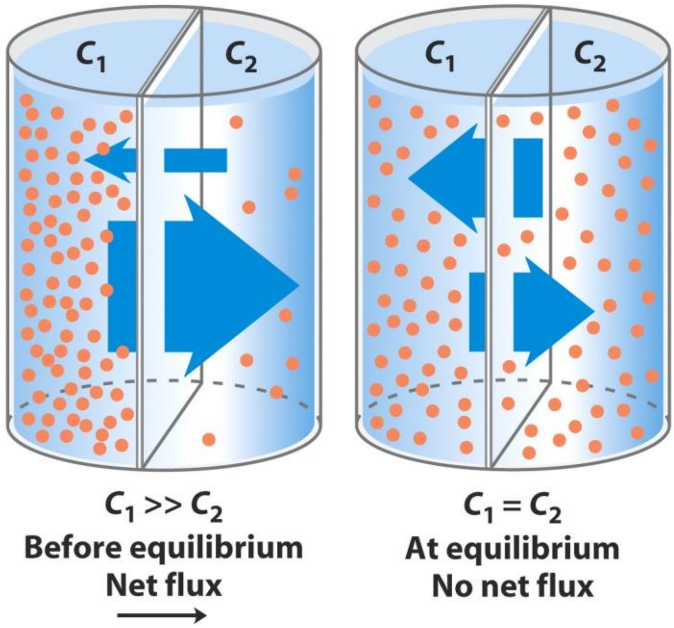
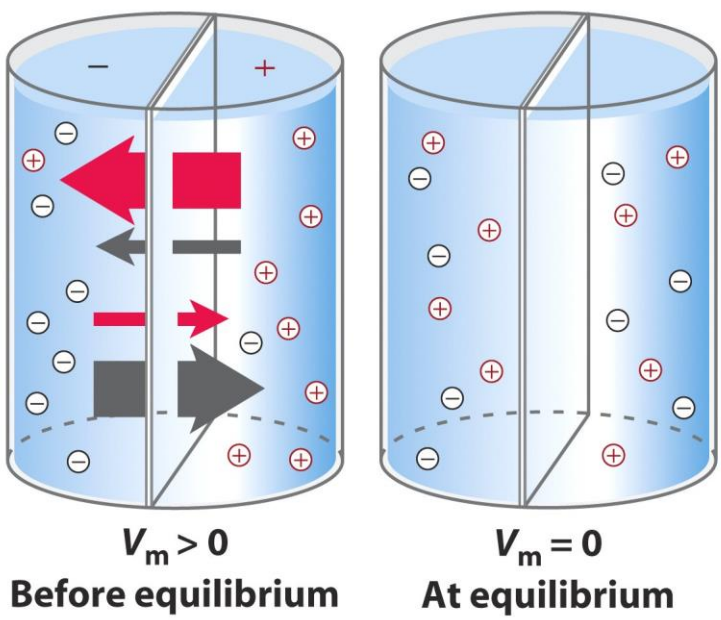


Figure 11-1
Molecular Cell Biology, Sixth Edition


C_1
C_2
C_1
C_2
$C_1 >> C_2$
Before equilibrium
Net flux
$C_1 = C_2$
At equilibrium
No net flux

3


−
+
$V_m > 0$
Before equilibrium
$V_m = 0$
At equilibrium

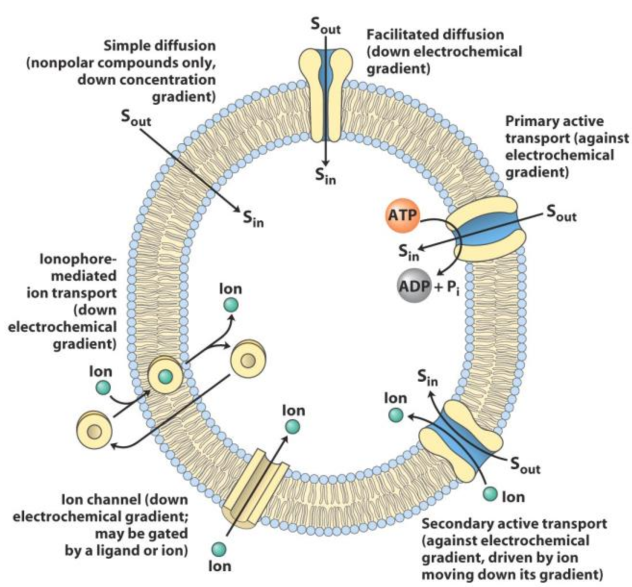
4

Transport through cell membranes

- The phospholipid bilayer is a good barrier around cells, especially to water soluble molecules. However, for the cell to survive some materials need to be able to enter and leave the cell.
- There are 4 basic mechanisms:

1. DIFFUSION and FACILITATED DIFFUSION
2. OSMOSIS
3. ACTIVE TRANSPORT
4. BULK TRANSPORT

11.3 Solute Transport across Membranes



Passive Transport Is Facilitated by Membrane Proteins

Energy changes accompanying passage of a hydrophilic solute through the lipid bilayer of a biological membrane

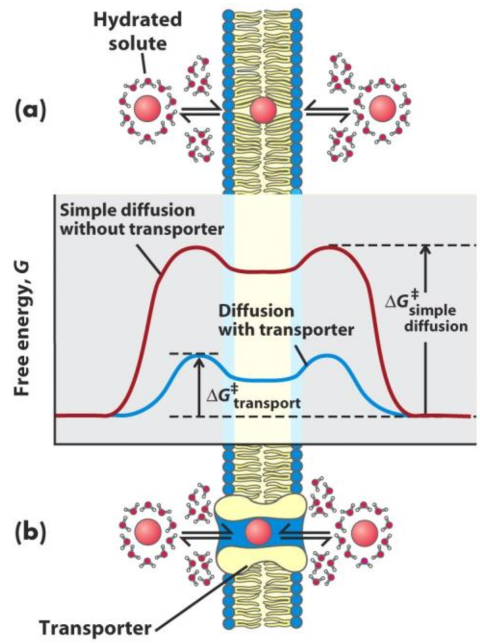


Figure 11.2 **Overview of membrane transport proteins.**

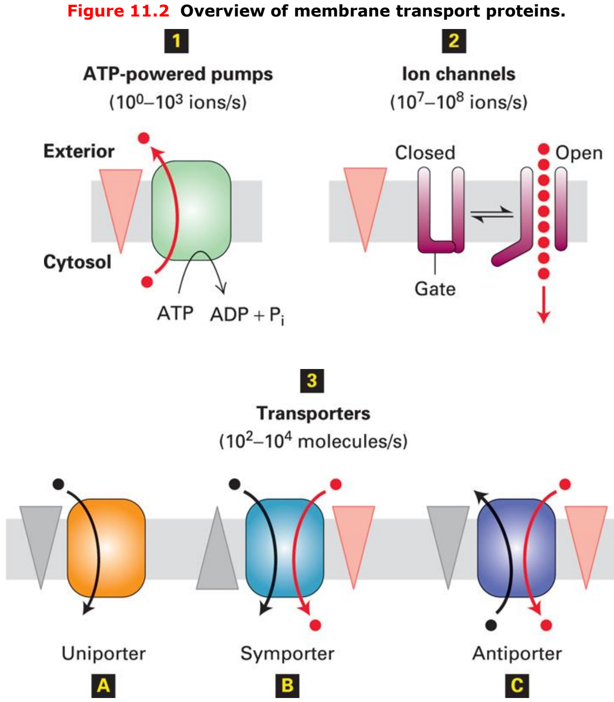


Figure 11.3 Multiple membrane transport proteins function together in the plasma membrane of metazoan cells.

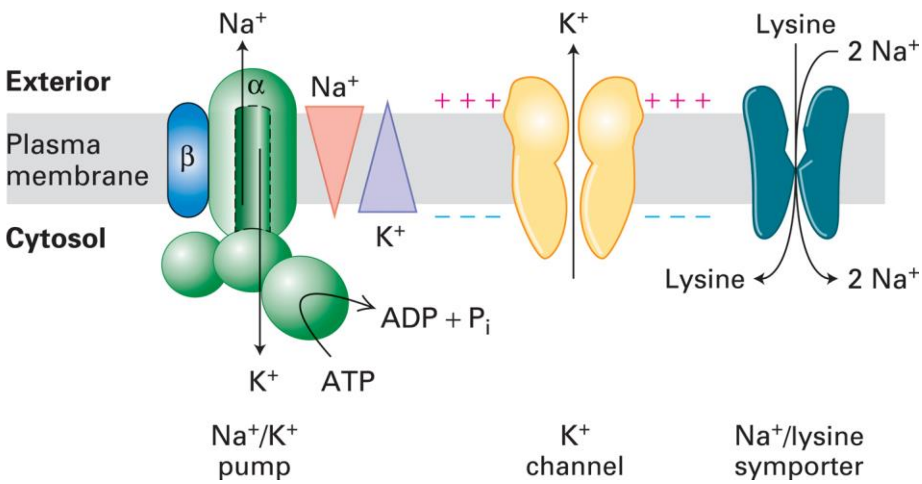


TABLE 11-1 Mechanisms for Transporting Ions and Small Molecules across Cell Membranes

PROPERTY	SIMPLE DIFFUSION	FACILITATED TRANSPORT	ACTIVE TRANSPORT	COTRANSPORT*
Requires specific protein	−	+	+	+
Solute transported against its gradient	−	−	+	+
Coupled to ATP hydrolysis	−	−	+	−
Driven by movement of a cotransported ion down its gradient	−	−	−	+
Examples of molecules transported	O_2, CO_2, steroid hormones, many drugs	Glucose and amino acids (uniporters); ions and water (channels)	Ions, small hydrophilic molecules, lipids (ATP-powered pumps)	Glucose and amino acids (symporters); various ions and sucrose (antiporters)

*Also called *secondary active transport.*

Table 11-1
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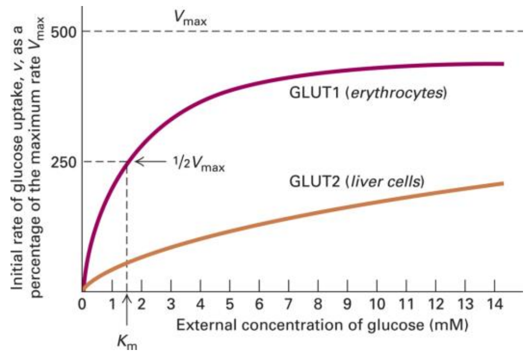
- Facilitated transport
  - Passive transport
  - Glucose – GLUT



Cellular uptake of glucose mediated by GLUT proteins exhibits simple enzyme kinetics

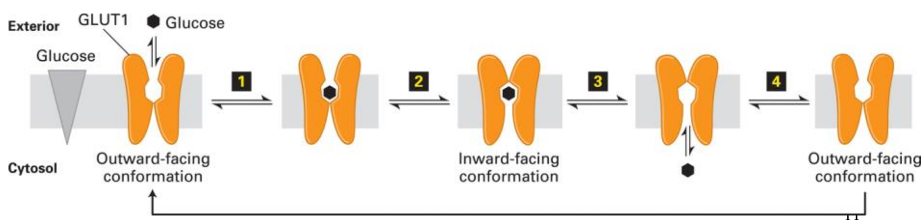


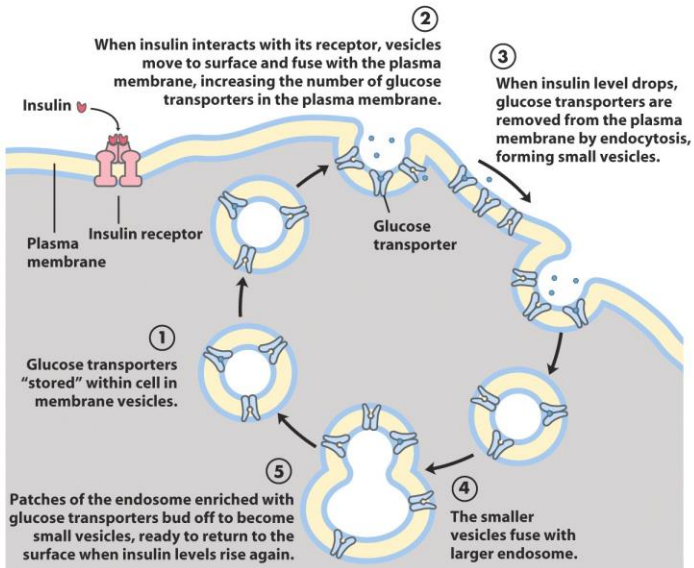
TABLE 11-4 Glucose Transporters in the Human Genome

Transporter	*Tissue(s) where expressed*	*Gene*	*Role**
GLUT1	Ubiquitous	*SLC2A1*	Basal glucose uptake
GLUT2	Liver, pancreatic islets, intestine	*SLC2A2*	In liver, removal of excess glucose from blood; in pancreas, regulation of insulin release
GLUT3	Brain (neuronal)	*SLC2A3*	Basal glucose uptake
GLUT4	Muscle, fat, heart	*SLC2A4*	Activity increased by insulin
GLUT5	Intestine, testis, kidney, sperm	*SLC2A5*	Primarily fructose transport
GLUT6	Spleen, leukocytes, brain	*SLC2A6*	Possibly no transporter function
GLUT7	Liver microsomes	*SLC2A7*	–
GLUT8	Testis, blastocyst, brain	*SLC2A8*	–
GLUT9	Liver, kidney	*SLC2A9*	–
GLUT10	Liver, pancreas	*SLC2A10*	–
GLUT11	Heart, skeletal muscle	*SLC2A11*	–
GLUT12	Skeletal muscle, adipose, small intestine	*SLC2A12*	–

*Dash indicates role uncertain.

12

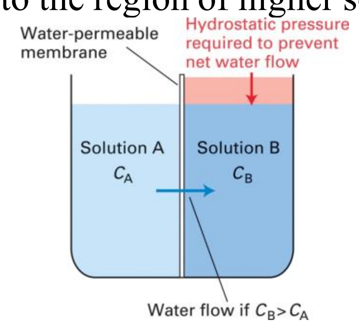
Regulation by insulin of glucose transport by GLUT4 into a myocyte



13

Effects of Osmosis on Water Balance

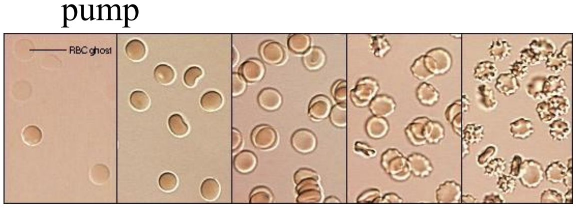
- **Osmosis** is the diffusion of water across a selectively permeable membrane
- The direction of osmosis is determined only by a difference in *total* solute concentration
- Water diffuses across a membrane from the region of lower solute concentration to the region of higher solute concentration

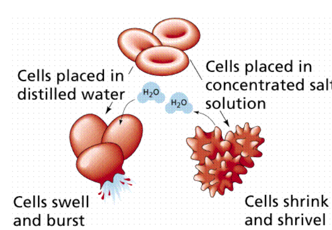


Water Balance of Cells Without Walls

- **Tonicity** is the ability of a 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
- **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

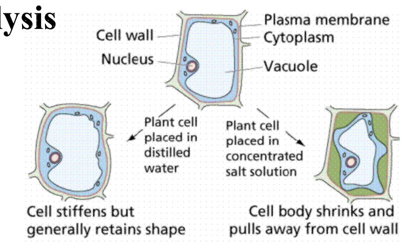
- Animals and other organisms without rigid cell walls have osmotic problems in either a **hypertonic** or **hypotonic** environment
- To maintain their internal environment, such organisms must have adaptations for **osmoregulation**, the control of water balance
- The protist *Paramecium,* which is hypertonic to its pond water environment, has a **contractile vacuole** that acts as a pump





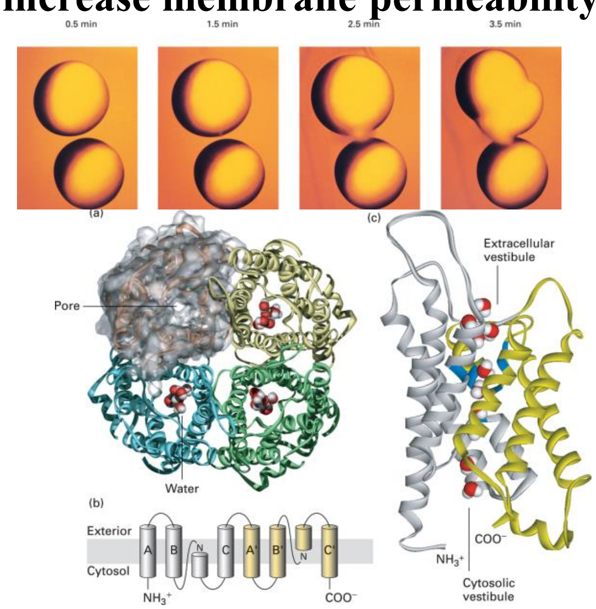
Water Balance of Cells with Walls

- **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), and the plant may wilt
- In a hypertonic environment, plant cells lose water; eventually, the membrane pulls away from the wall, a usually lethal effect called **plasmolysis**



Aquaporin increase membrane permeability to water

Frog oocytes



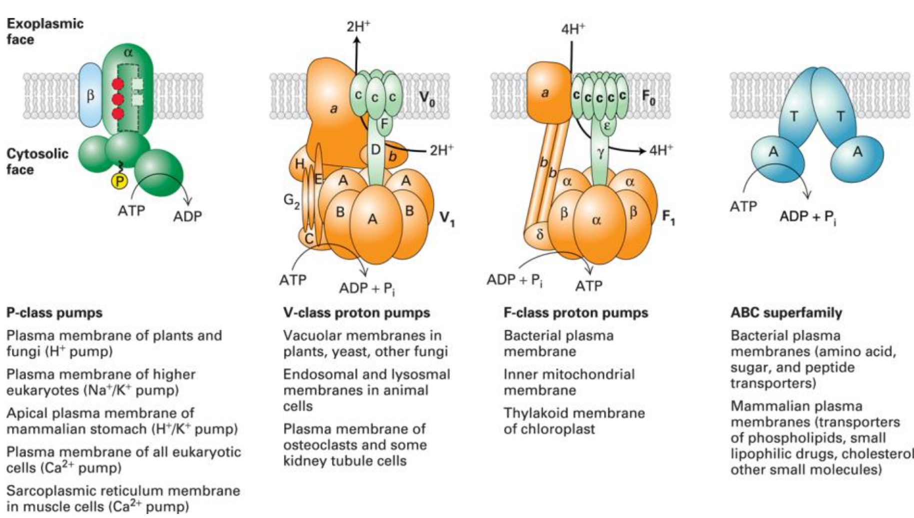
Structure of the water-channel protein aquaporin.

TABLE 11-6 Aquaporins

Aquaporin	*Roles and/or location*
AQP-1	Fluid reabsorption in proximal renal tubule; secretion of aqueous humor in eye and cerebrospinal fluid in central nervous system; water homeostasis in lung
AQP-2	Water permeability in renal collecting duct (mutations produce nephrogenic diabetes insipidus)
AQP-3	Water retention in renal collecting duct
AQP-4	Cerebrospinal fluid reabsorption in central nervous system; regulation of brain edema
AQP-5	Fluid secretion in salivary glands, lachrymal glands, and alveolar epithelium of lung
AQP-6	Kidney
AQP-7	Renal proximal tubule, intestine
AQP-8	Liver, pancreas, colon, placenta
AQP-9	Liver, leukocytes
TIP	Regulation of turgor pressure in plant tonoplast
PIP	Plant plasma membrane
AQY	Yeast plasma membrane

19

ATP-Powered Pumps



The four classes of ATP-powered transport proteins

TABLE 11-2	Typical Intracellular and Extracellular Ion Concentrations	
Ion	Cell (mM)	Blood (mM)
Squid Axon (invertebrate)*		
K^+	400	20
Na^+	50	440
Cl^-	40–150	560
Ca^{2+}	0.0003	10
$X^{-\dagger}$	300–400	5–10
Mammalian Cell (vertebrate)		
K^+	139	4
Na^+	12	145
Cl^-	4	116
HCO_3^-	12	29
X^-	138	9
Mg^{2+}	0.8	1.5
Ca^{2+}	<0.0002	1.8

*The large nerve axon of the squid has been widely used in studies of the mechanism of conduction of electric impulses.
†X^- represents proteins, which have a net negative charge at the neutral pH of blood and cells.

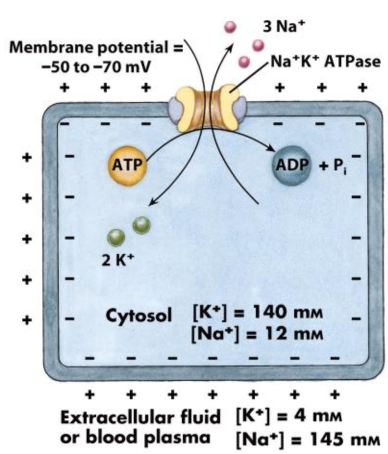
Maintenance of Membrane Potential by Ion Pumps

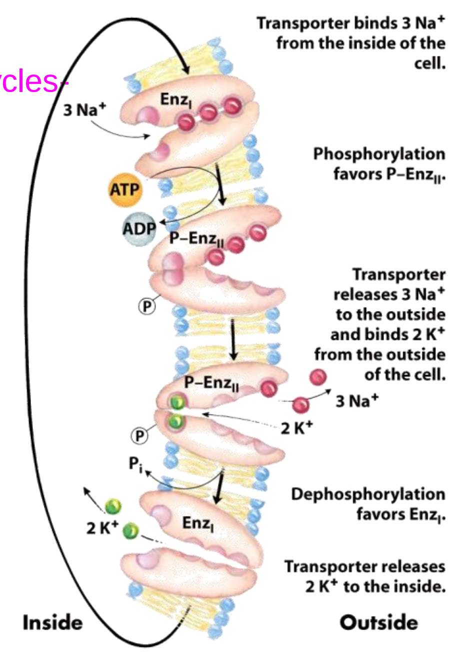
- **Membrane potential is the voltage difference across a membrane**
- Two combined forces, collectively called the **electrochemical gradient**, drive the diffusion of ions across a membrane:
  - **A chemical force** (the ion's concentration gradient)
  - **An electrical force** (the effect of the membrane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

- An **electrogenic pump** is a transport protein that **generates the voltage** across a membrane
- The main electrogenic pump of plants, fungi, and bacteria is a **proton pump**

P-Type ATPases Undergo Phosphorylation during Catalytic Cycles-

Na^+K^+ ATPase





24

P-Type Ca^{2+} Pumps Maintain a Low Concentration of Calcium in the Cytosol-

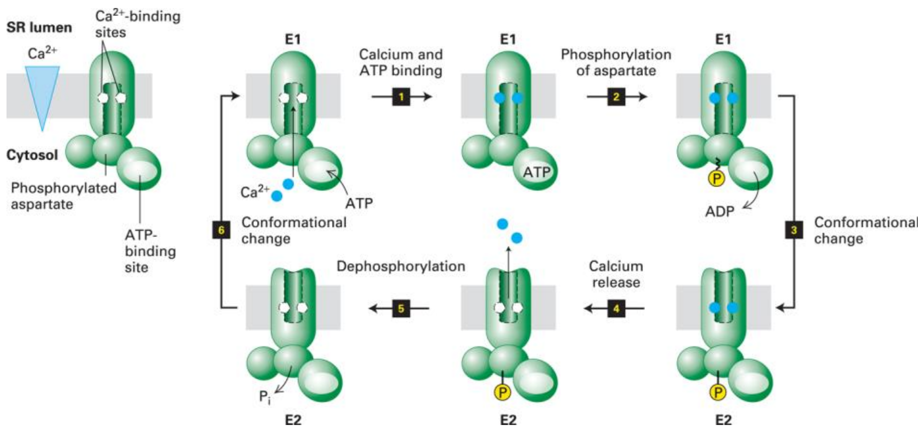
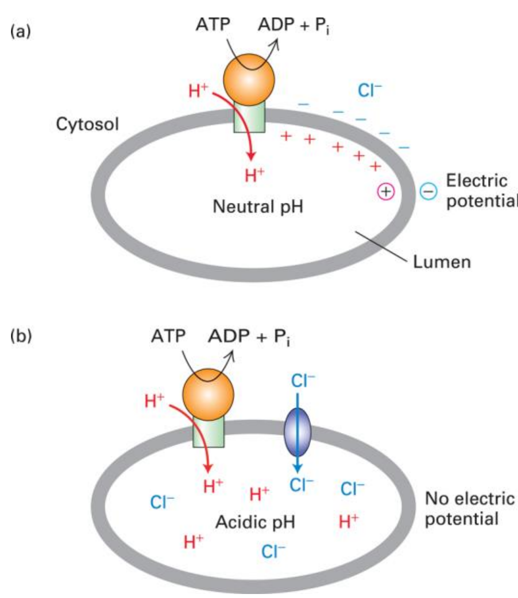


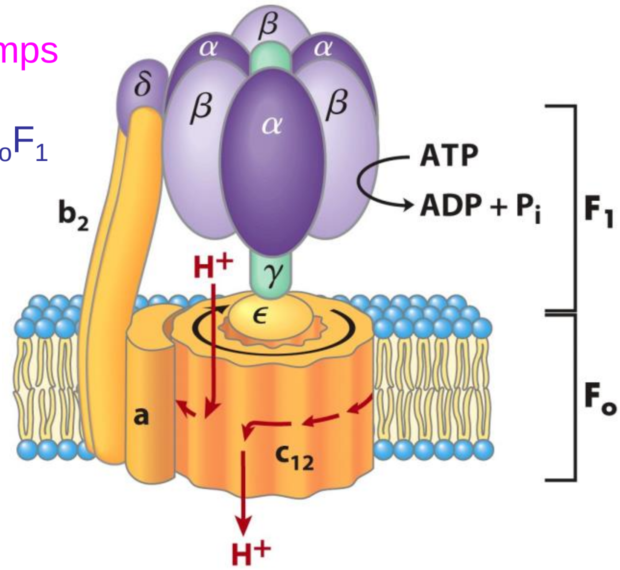
Figure 11.10 Operational model of the Ca^{2+} ATPase in the SR membrane of skeletal muscle cells.



Effect of V-class H^+ pumps on H^+ concentration gradients and electric potential gradients across cellular

F-Type ATPase Are Reversible, ATP-driven Proton Pumps

Structure of the F_oF_1 ATPase/ATP synthase



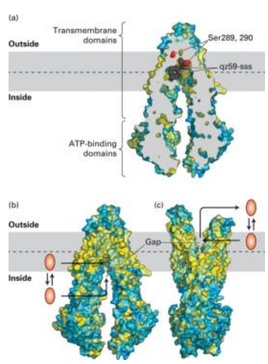
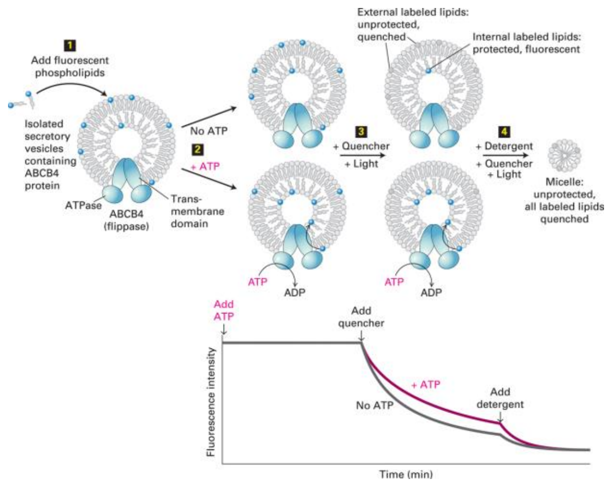


Figure 11.15 The multidrug transporter ABCB1 (MDR1): structure and model of ligand export.

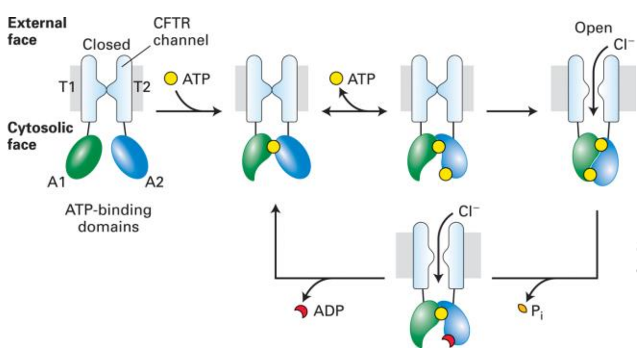
TABLE 11-3 Selected Human ABC Proteins

Protein	Tissue Expression	Function	Disease Caused by Defective Protein
ABCB1 (MDR1)	Adrenal, kidney, brain	Exports lipophilic drugs	
ABCB4 (MDR2)	Liver	Exports phosphatidylcholine into bile	
ABCB11	Liver	Exports bile salts into bile	
CFTR	Exocrine tissue	Transports Cl ions	Cystic fibrosis
ABCDI	Ubiquitous in peroxisomal membrane	Influences activity of peroxisomal enzyme that oxidizes very long chain fatty acids	Adrenoleukodystrophy (ADL)
ABCG5/8	Liver, intestine	Exports cholesterol and other sterols	β-Sitosterolemia
ABCA1	Ubiquitous	Exports cholesterol and phospholipid for uptake into high-density lipoprotein (HDL)	Tangier's disease



In vitro fluorescence-quenching assay can detect phospholipid flippase activity of ABCB4.

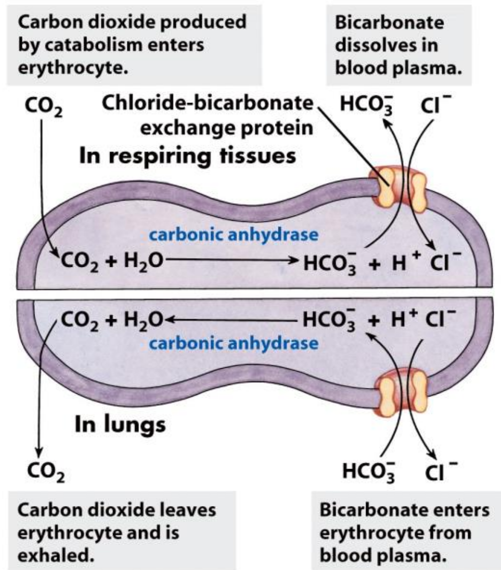
- Certain ABC proteins flip phospholipids and other lipid-soluble substrates from one membrane leaflet to the other
- i.e. ABCB1 – liver cell plasma membrane



Structure and function of the cystic fibrosis transmembrane regulator (CFTR).

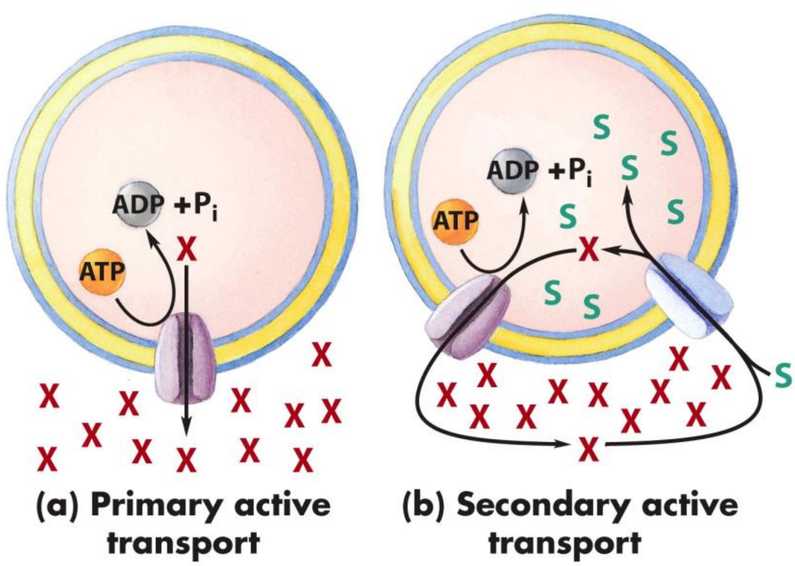
- CFTR – ABCC7 : Cl^- channel
- Reuptake Cl^- lost by sweating

The Chloride-Bicarbonate Exchanger Catalyzes Electrochemical Cotransport of Anions across the Plasma Membrane



31

Active Transport Results in Solute Movement against a Concentration or Electrochemical Gradient



Ion Gradients Provide the Energy for Secondary Active Transport

TABLE 11–5 Cotransport Systems Driven by Gradients of Na^+ or H^+

Organism/tissue/cell type	*Transported solute (moving against its gradient)*	*Cotransported solute (moving down its gradient)*	*Type of transport*
E. coli	Lactose	H^+	Symport
	Proline	H^+	Symport
	Dicarboxylic acids	H^+	Symport
Intestine, kidney (vertebrates)	Glucose	Na^+	Symport
	Amino acids	Na^+	Symport
Vertebrate cells (many types)	Ca^{2+}	Na^+	Antiport
Higher plants	K^+	H^+	Antiport
Fungi (*Neurospora*)	K^+	H^+	Antiport

33

Lactose uptake in *E. coli*

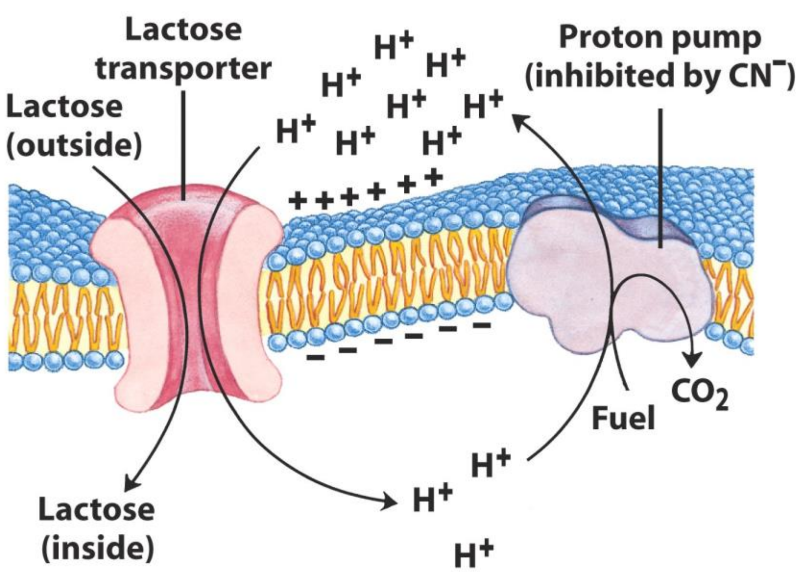


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Figure 11.29 Concentration of ions and sucrose by the plant vacuole.

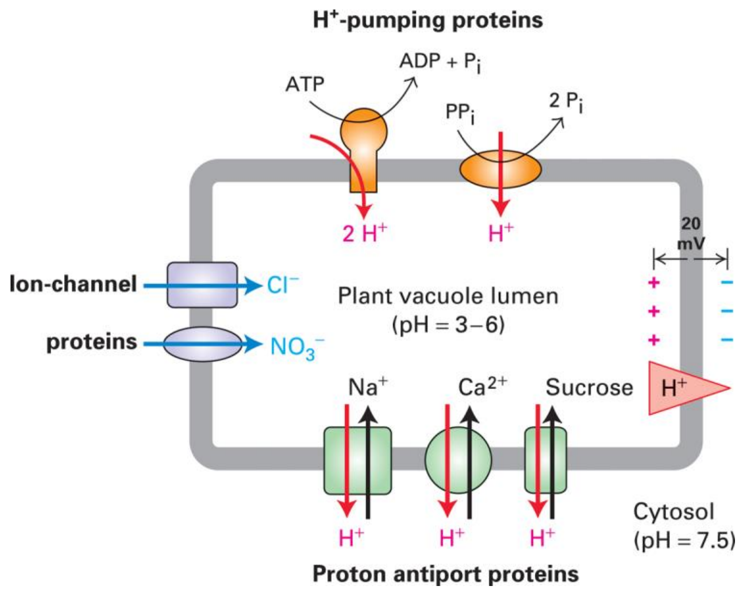
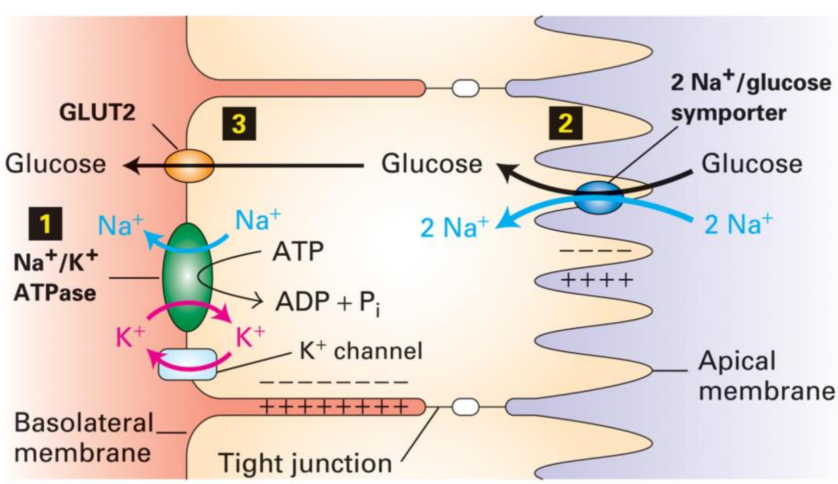


Figure 11.30 Transcellular transport of glucose from the intestinal lumen into the blood.



Blood	Cytosol	Intestinal lumen
High Na^+	Low Na^+	Dietary glucose
Low K^+	High K^+	High dietary Na^+Cl^-

Figure 11.31 Acidification of the stomach lumen by parietal cells in the gastric lining.

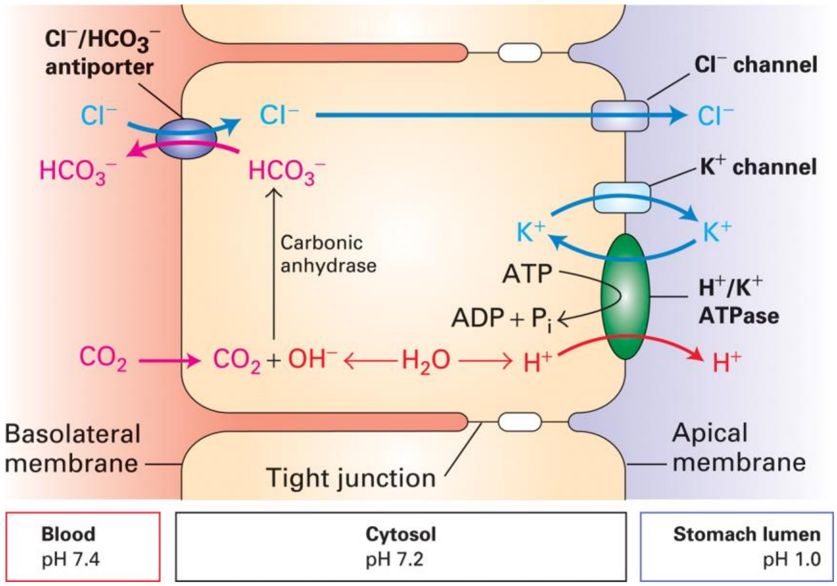
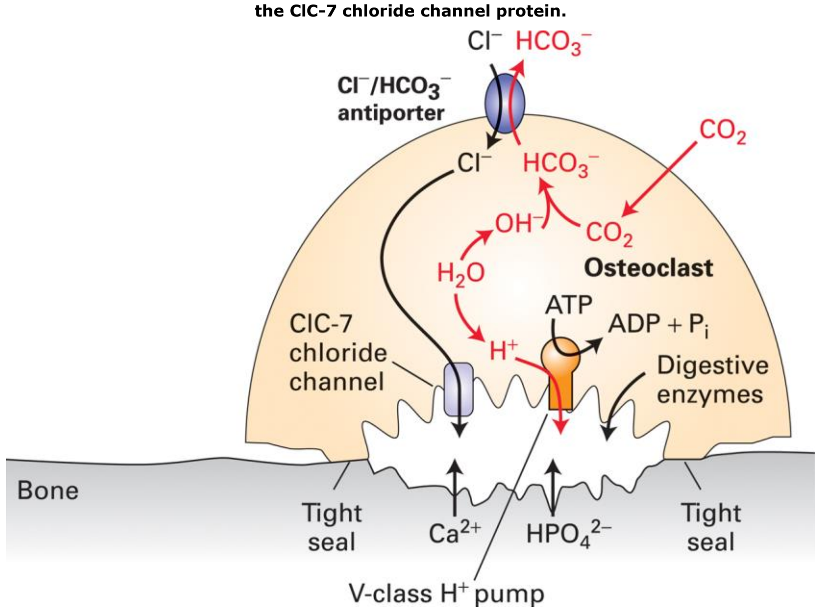
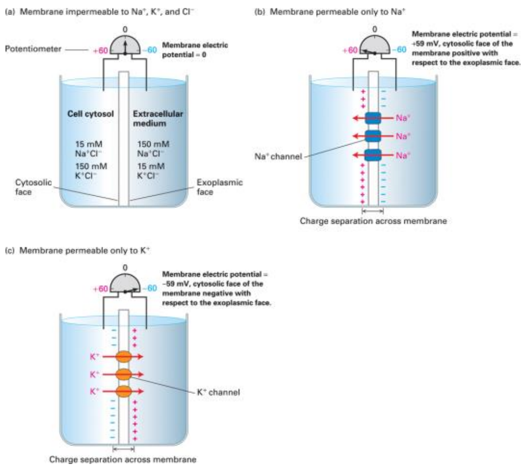


Figure 11.32 Dissolution of bone by polarized osteoclast cells requires a V-class proton pump and the ClC-7 chloride channel protein.



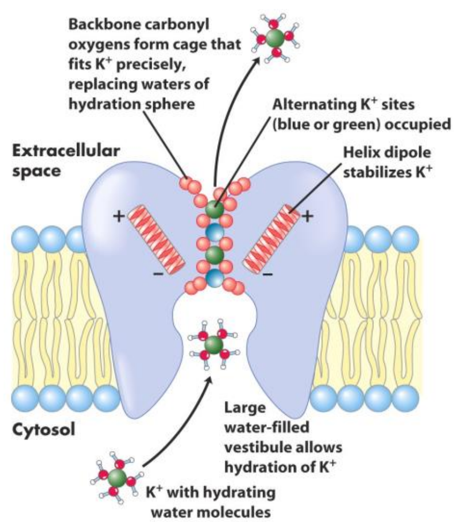
Ion channel

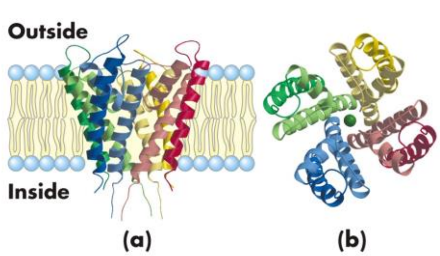


- Movement of ions through Ion channel generate transmembrane electric potential

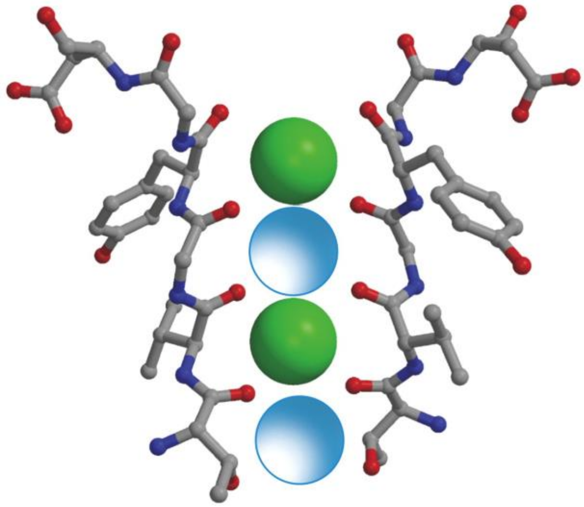
Structure and function of the K^+ channel of *Streptomyces lividans* -

Diagram of the K^+ channel in cross section



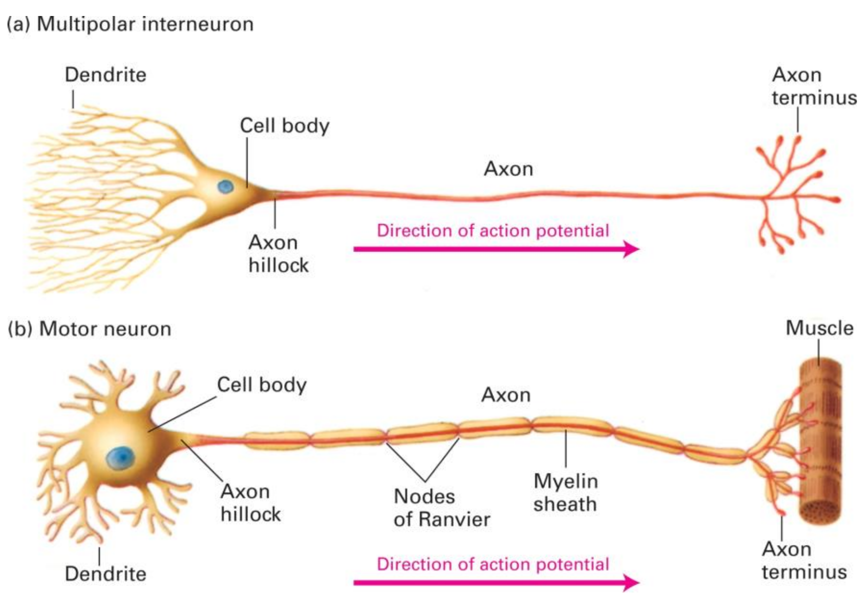


K^+ binding sites in the selectivity pore of the K^+ channel

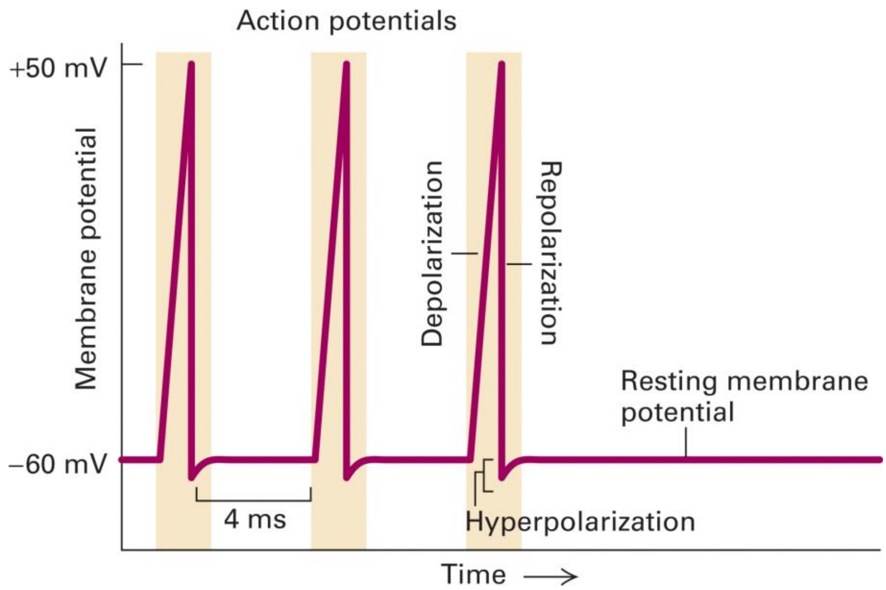


41

Figure 22.1 Typical morphology of two types of mammalian neurons.

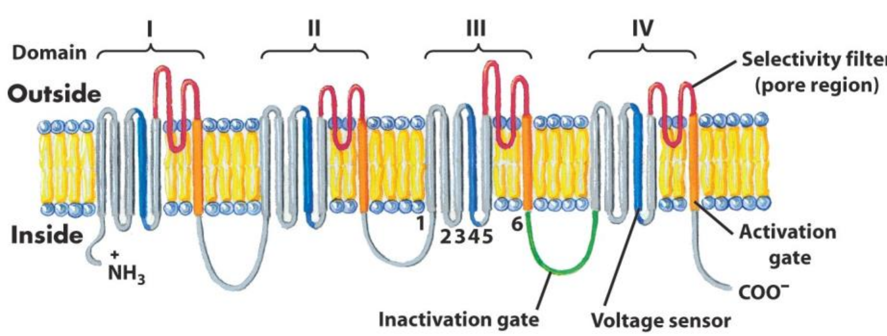


Experimental Figure 22.2 **Recording of an axonal membrane potential over time reveals the amplitude and frequency of action potentials.**



The Neuronal Na^+ Channel Is a Voltage-Gated Ion Channel

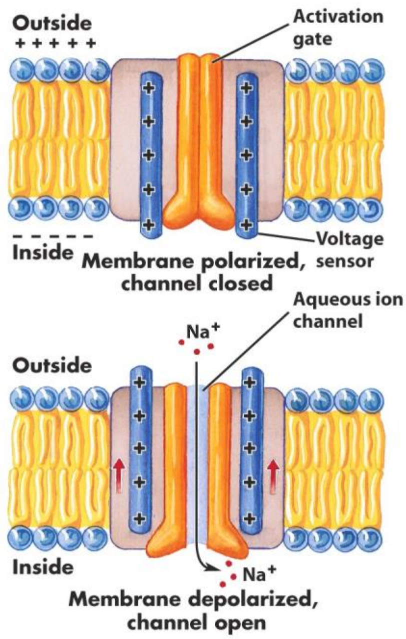
Voltage-gated Na^+ channel of neurons



44

Voltage-gated Na^+ channel of neurons-

The voltage-sensing mechanism involves movement of helix 4 perpendicular to the plane of the membrane in response to a change in potential



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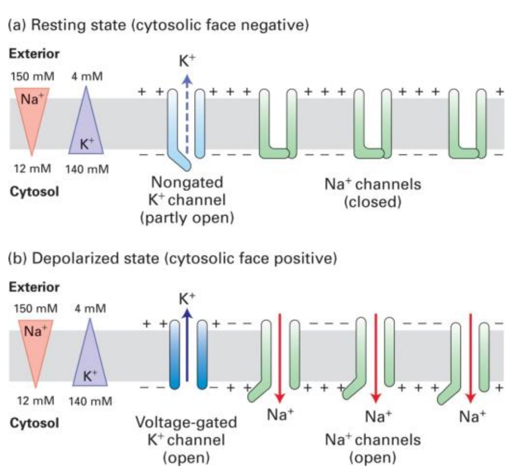
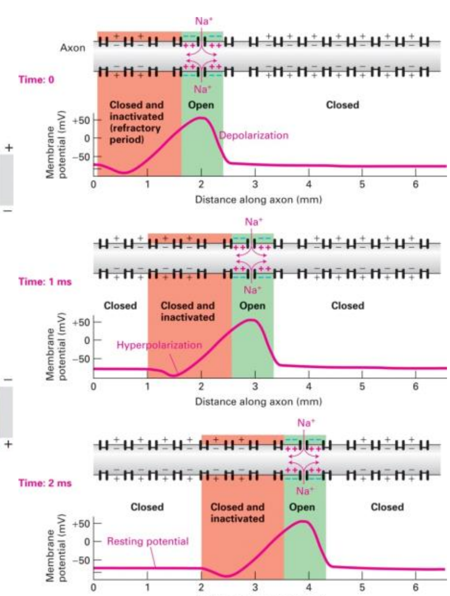
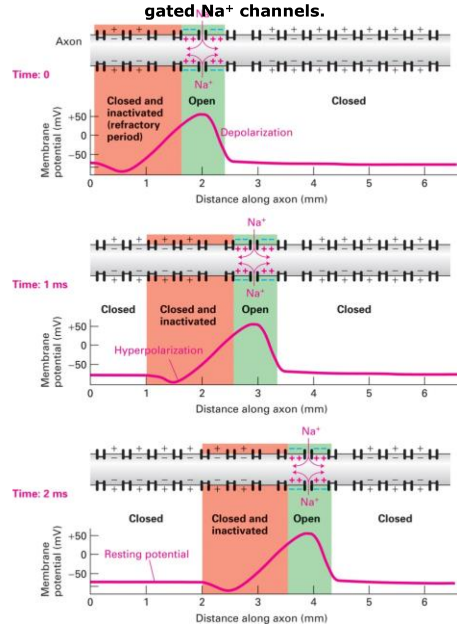


Figure 22.6 Depolarization of the plasma membrane due to opening of gated Na^+ channels.



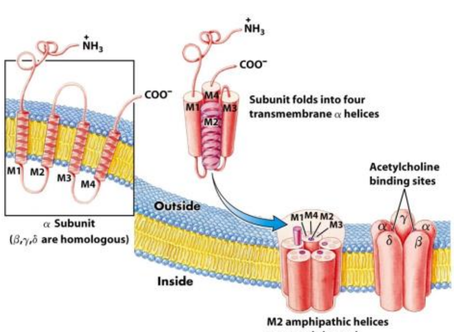
Unidirectional conduction of an action potential due to transient inactivation of voltage-gated Na^+ channels.

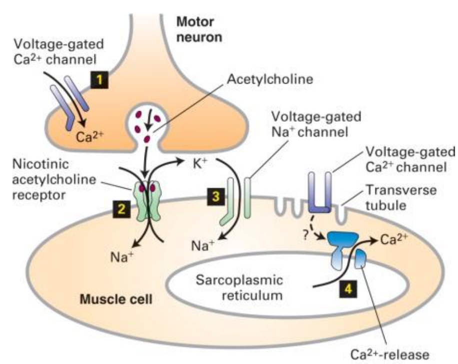
Figure 22.9 **Unidirectional conduction of an action potential due to transient inactivation of voltage-gated Na^+ channels.**

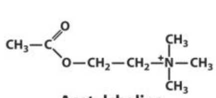


The Acetylcholine Receptor Is a Ligand-Gated Ion Channel

Structure of the acetylcholine receptor ion channel







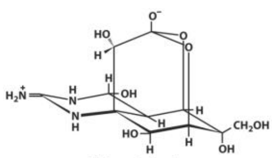
Acetylcholine

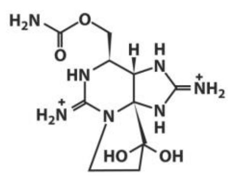
48

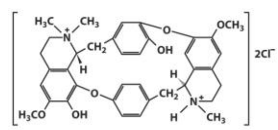
Defective Ion Channels Can Have Adverse Physiological Consequences

TABLE 11–8 Some Diseases Resulting from Ion Channel Defects

Ion channel	*Affected gene*	*Disease*
Na^+ (voltage-gated, skeletal muscle)	*SCN4A*	Hyperkalemic periodic paralysis (or paramyotonia congenita)
Na^+ (voltage-gated, neuronal)	*SCN1A*	Generalized epilepsy with febrile seizures
Na^+ (voltage-gated, cardiac muscle)	*SCN5A*	Long QT syndrome 3
Ca^{2+} (neuronal)	*CACNA1A*	Familial hemiplegic migraine
Ca^{2+} (voltage-gated, retina)	*CACNA1F*	Congenital stationary night blindness
Ca^{2+} (polycystin-1)	*PKD1*	Polycystic kidney disease
K^+ (neuronal)	*KCNQ4*	Dominant deafness
K^+ (voltage-gated, neuronal)	*KCNQ2*	Benign familial neonatal convulsions
Nonspecific cation (cGMP-gated, retinal)	*CNCG1*	Retinitis pigmentosa
Acetylcholine receptor (skeletal muscle)	*CHRNA1*	Congenital myasthenic syndrome
Cl^-	*CFTR*	Cystic fibrosis


Tetrodotoxin

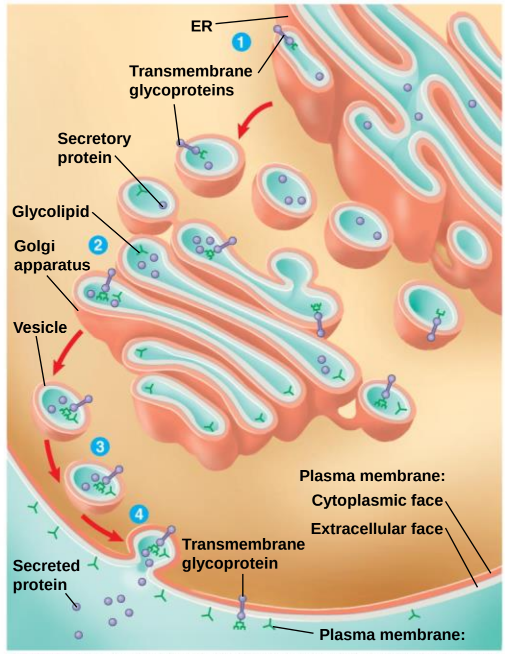

Saxitoxin


D-Tubocurarine chloride

49

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 by transport proteins
- Large molecules, such as polysaccharides and proteins, cross the membrane via vesicles


ER
1
Transmembrane glycoproteins
Secretory protein
Glycolipid
Golgi apparatus
2
Vesicle
3
4
Plasma membrane:
Cytoplasmic face
Extracellular face
Transmembrane glycoprotein
Secreted protein
Plasma membrane: