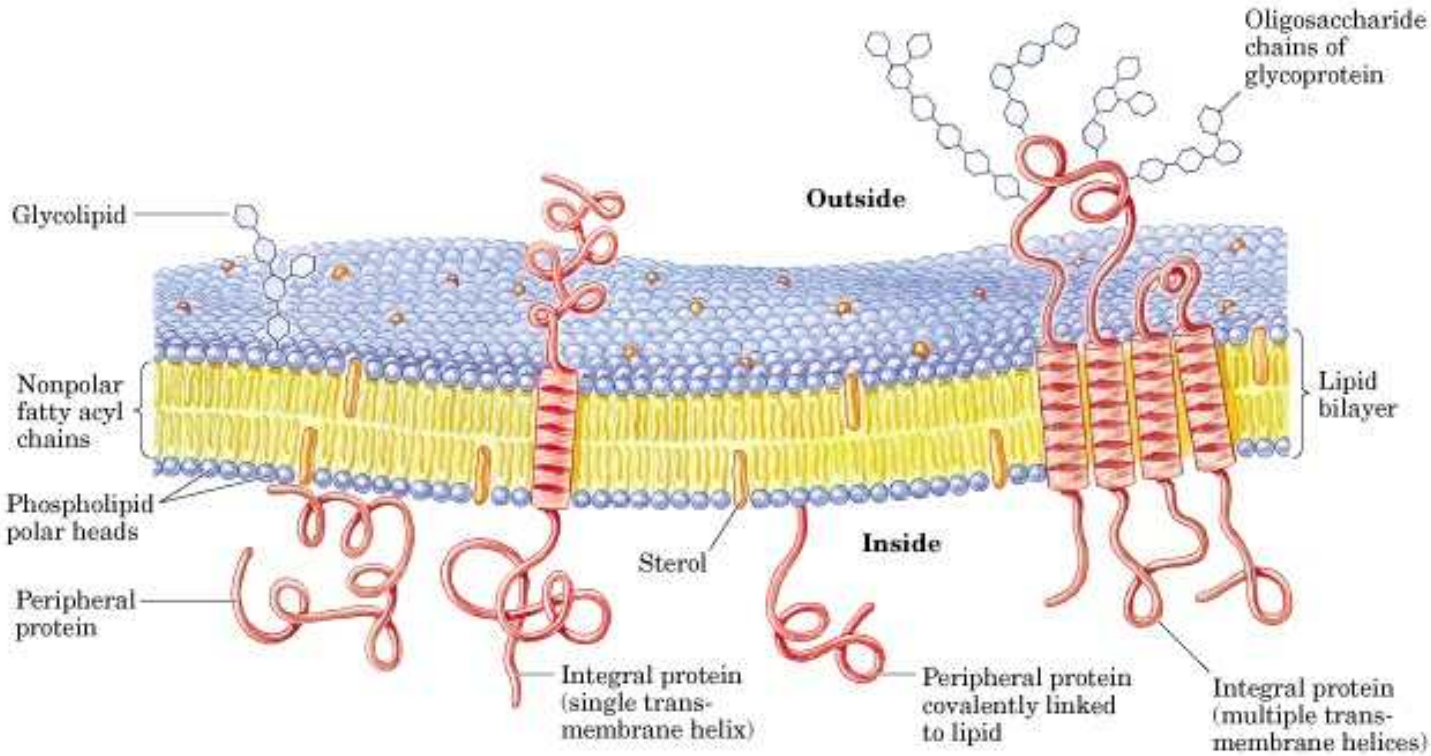
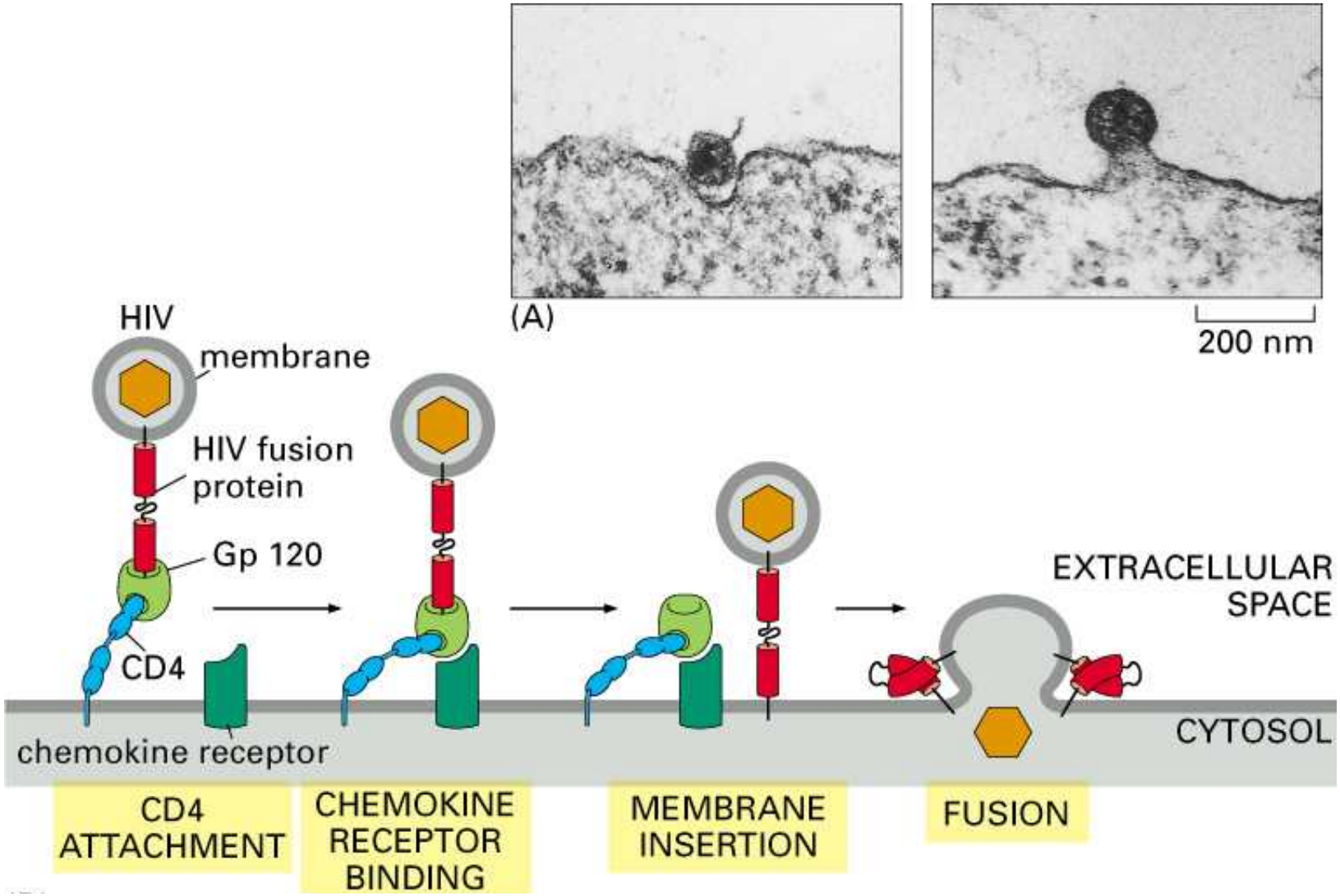
# Chpt. 11

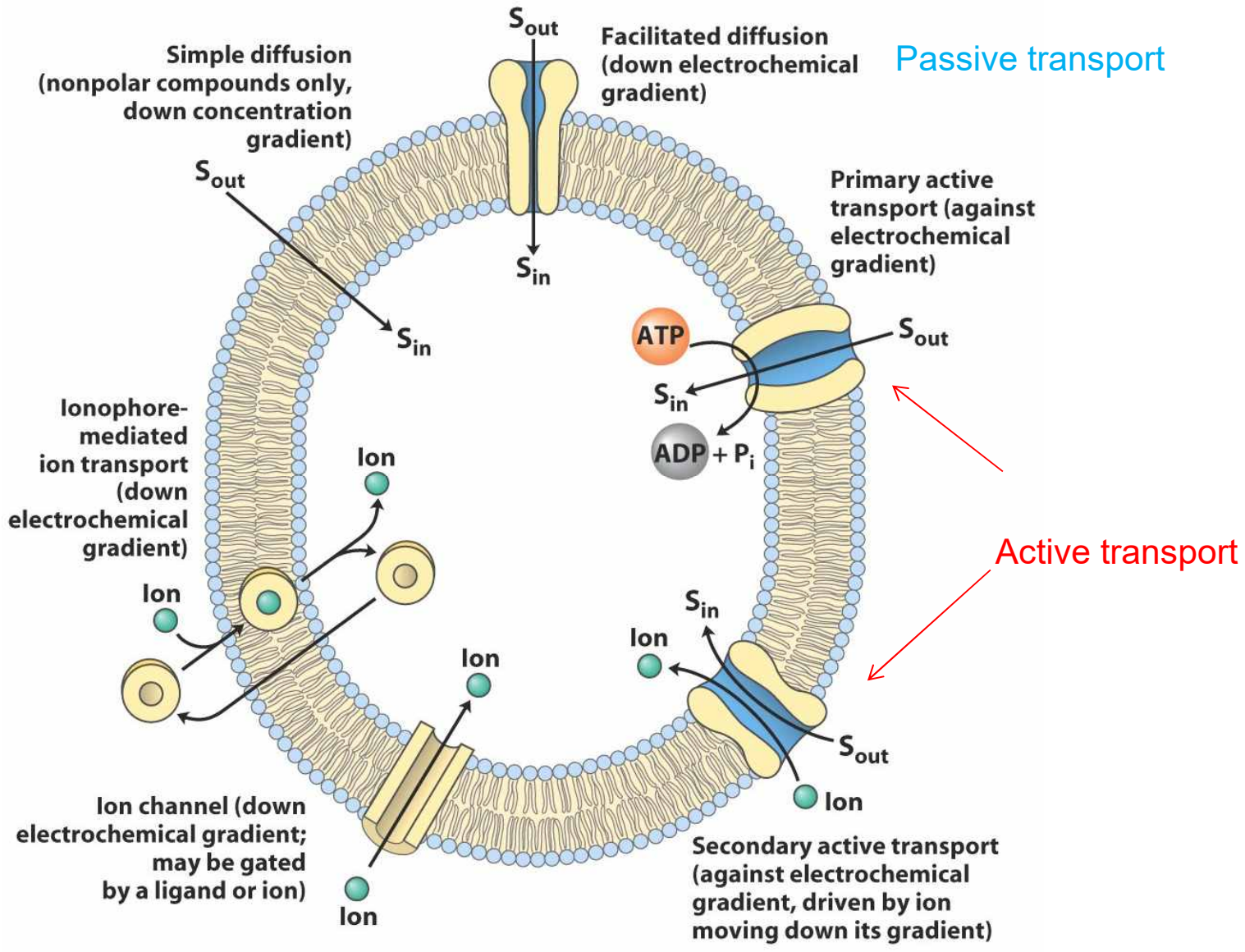
# Biological Membranes and Transport



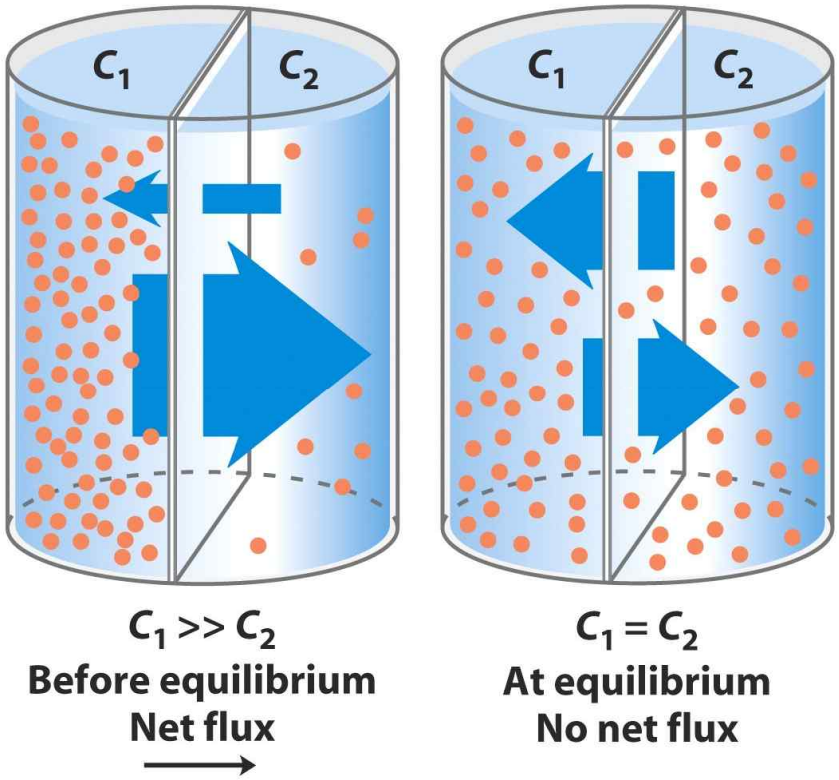
# The entry of enveloped viruses into cells

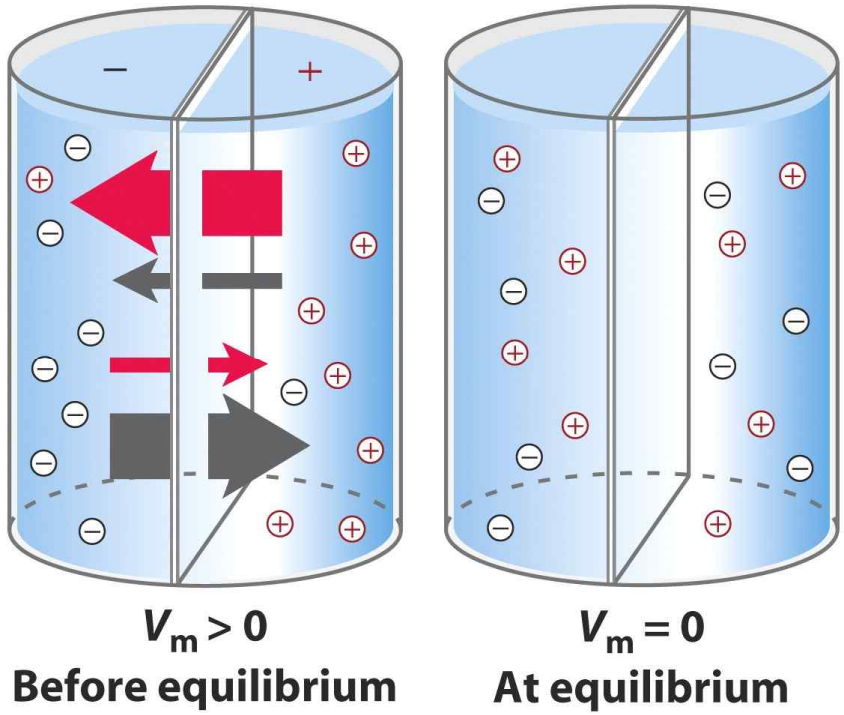


# Solute transport across membrane

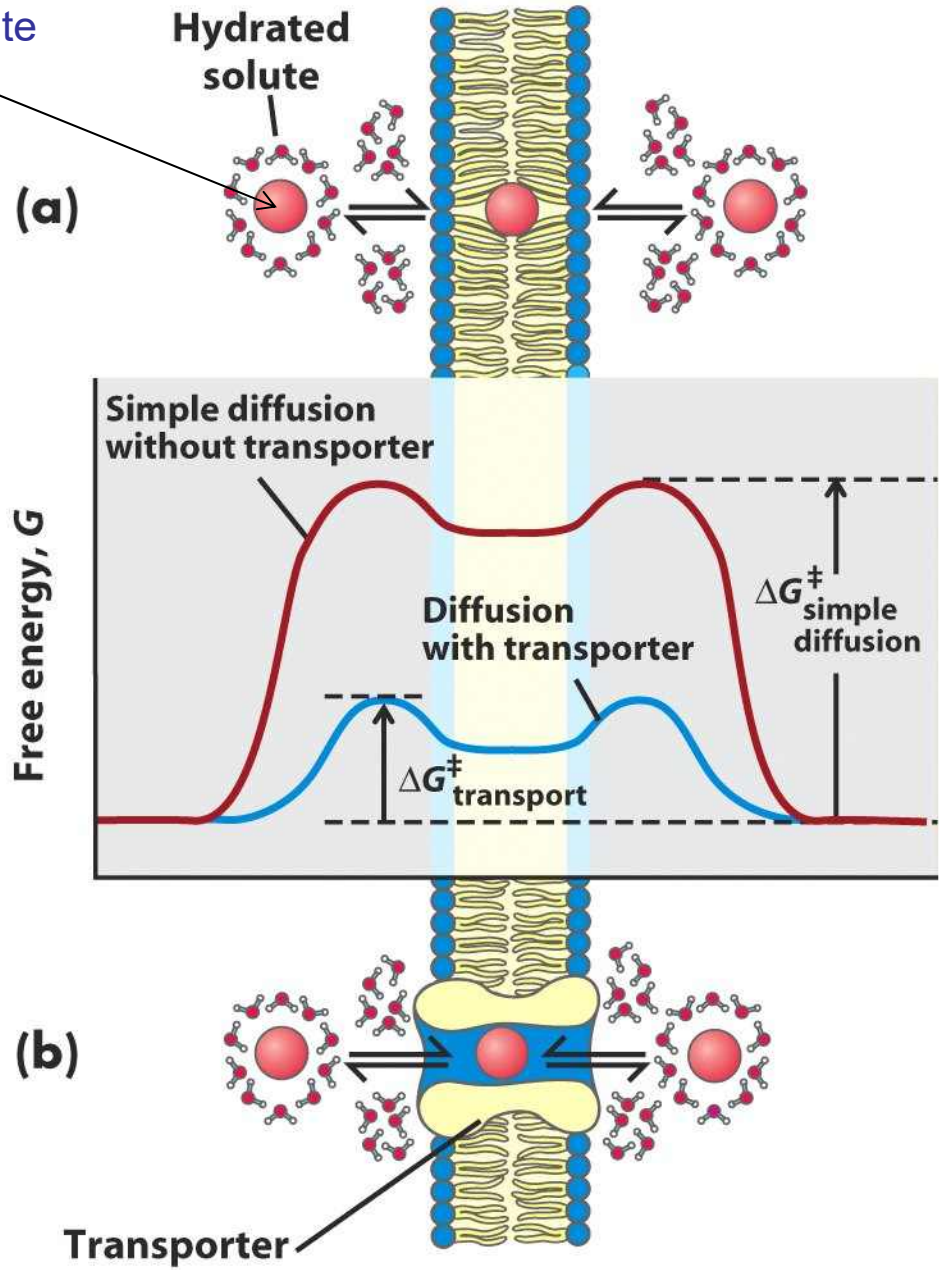


# Movement of solutes across a permeable membrane



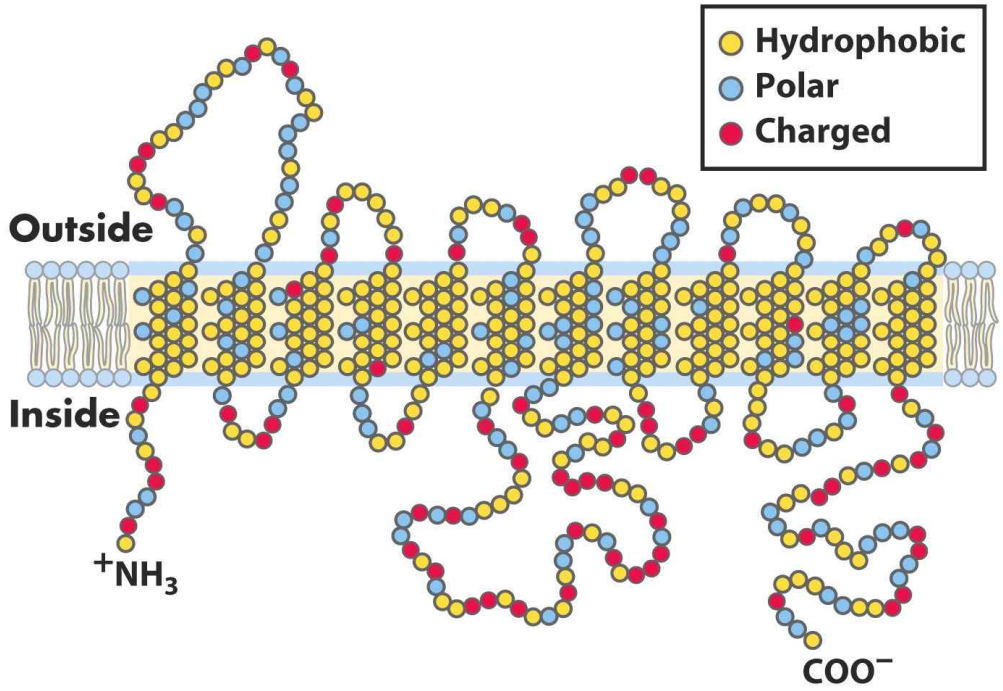



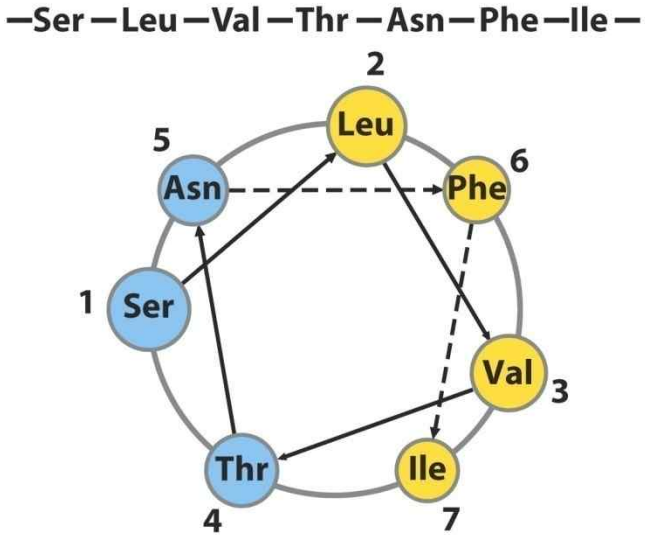
polar or charged solute

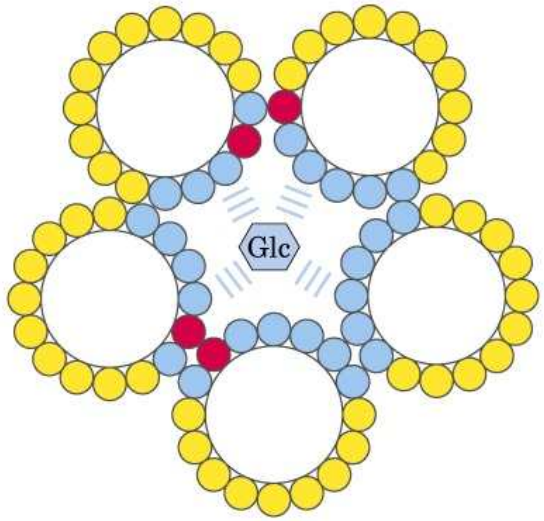


# GluT1

(passive transport)

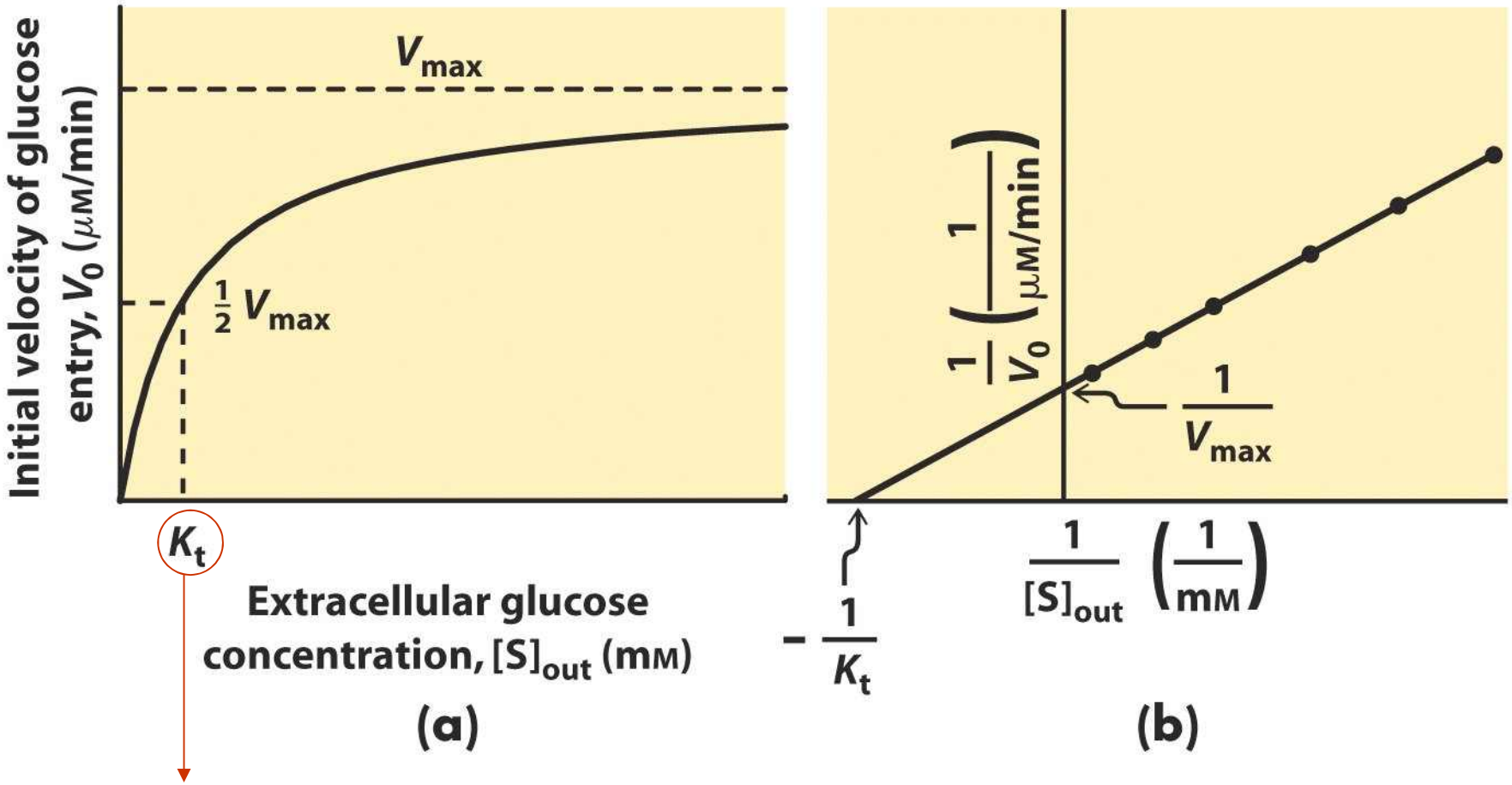



(c)

# **GluT1 :** high stereospecificity




GluT1: 1.5 mM for D-glucose
20, 30 mM for D-mannose, D-galactose
3000 mM for L-glucose

# Model for glucose transport by GLUT1

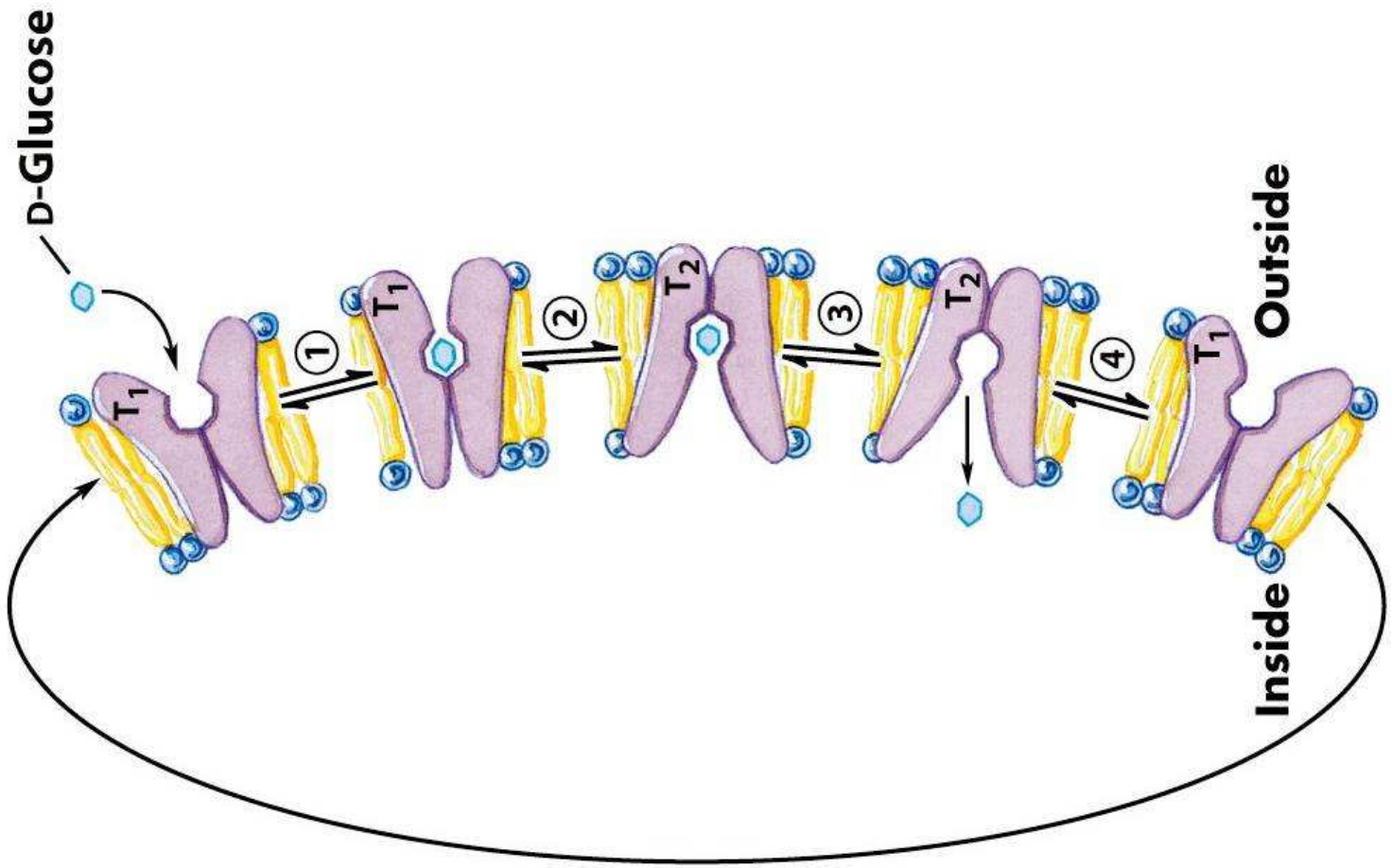


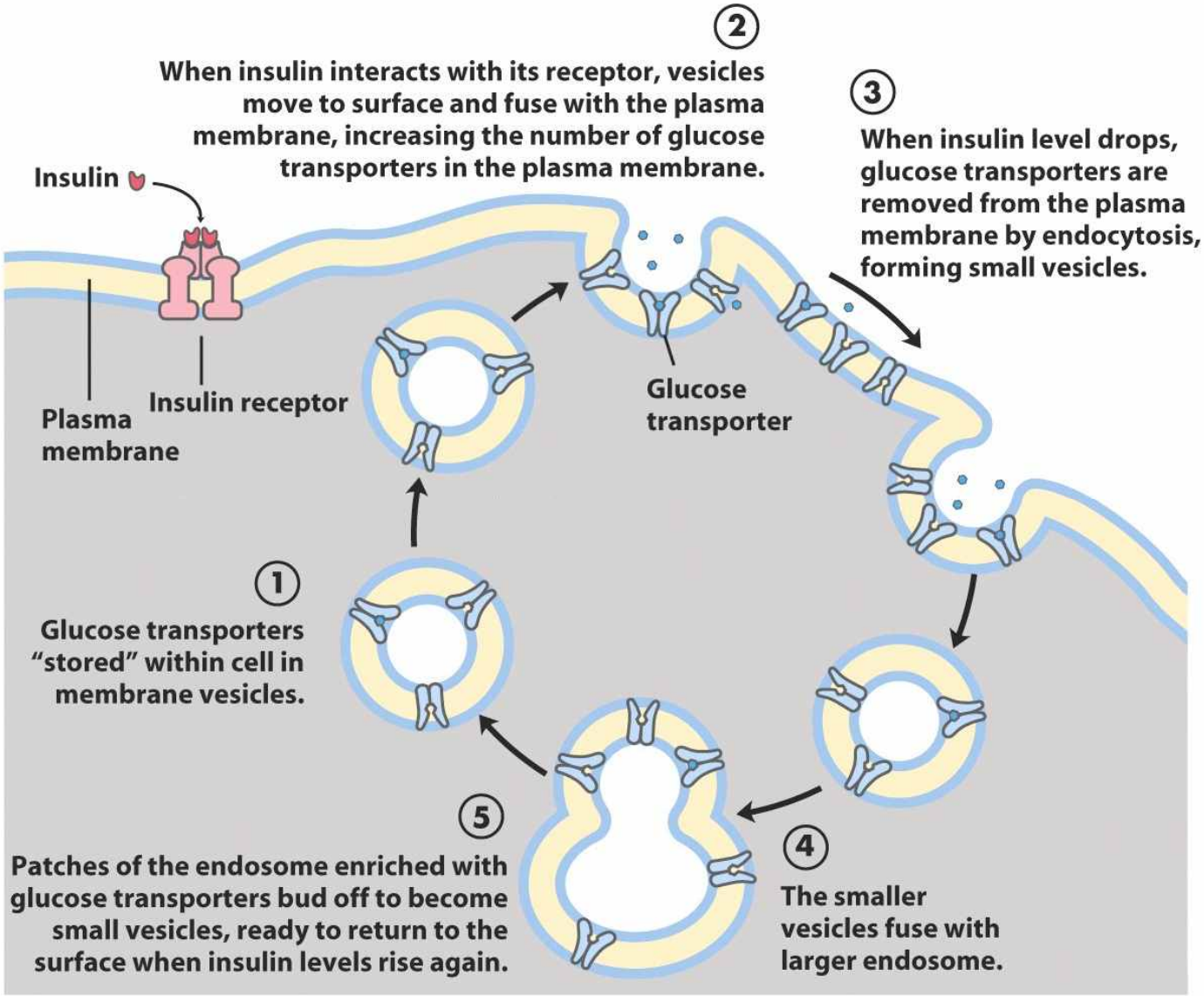
**TABLE 11–4** Glucose Transporters in the Human Genome

| *Transporter* | *Tissue(s) where expressed* | *Gene* | *Role*[*] |
|---|---|---|---|
| GLUT1 | Ubiquitous | *SLC2A1* | Basal glucose uptake |
| GLUT2 | Liver, pancreatic islets, intestine ($K_t$ : 66 mM) | *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* | – |

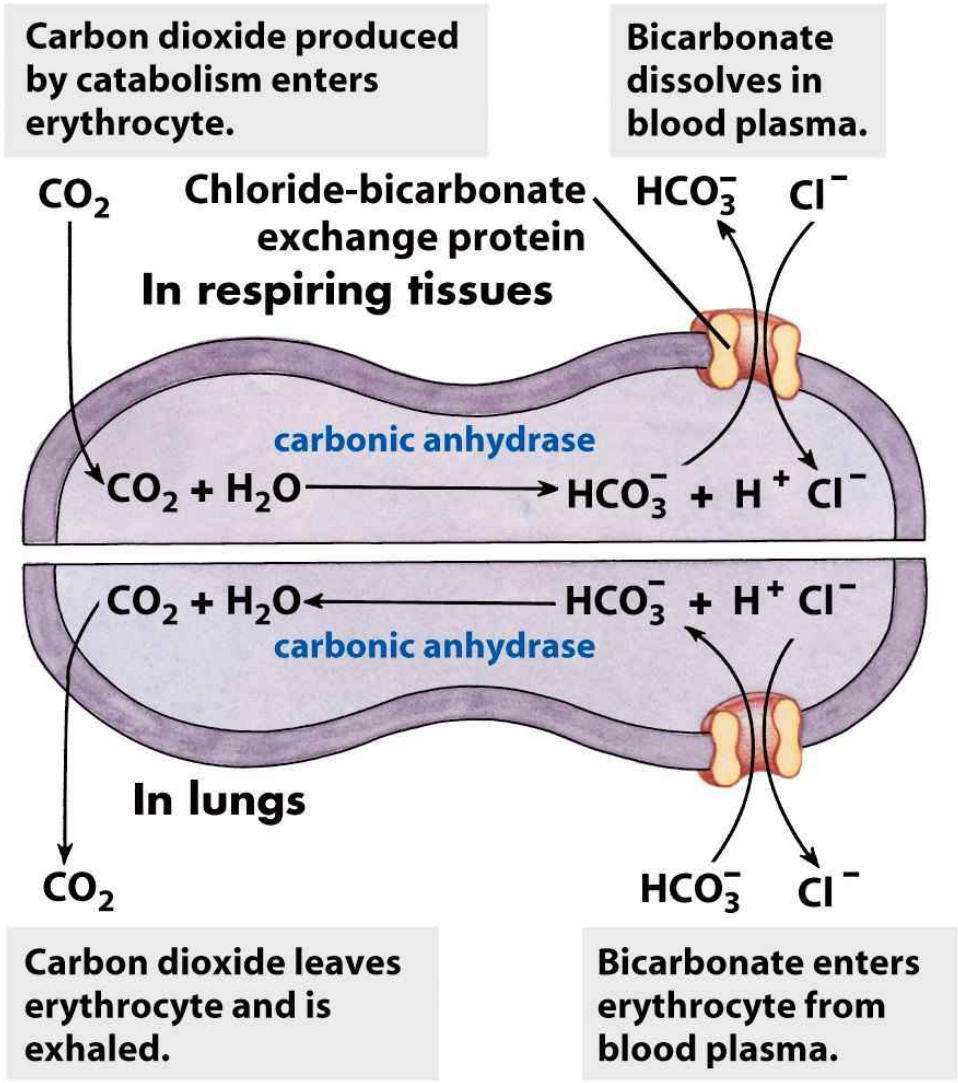
[*]Dash indicates role uncertain.

# Regulation by insulin of glucose transport

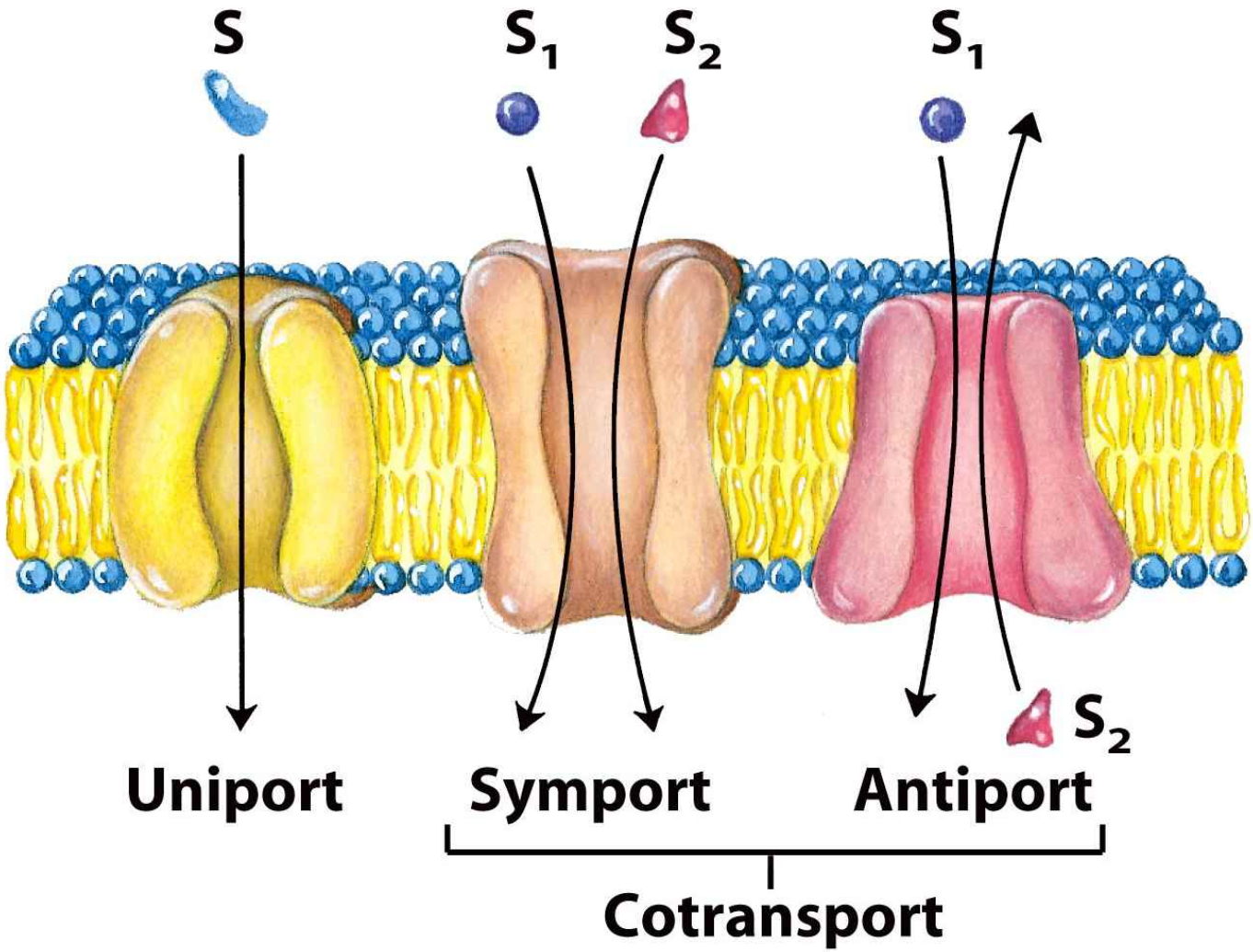
(by GLUT4 into a myocyte)



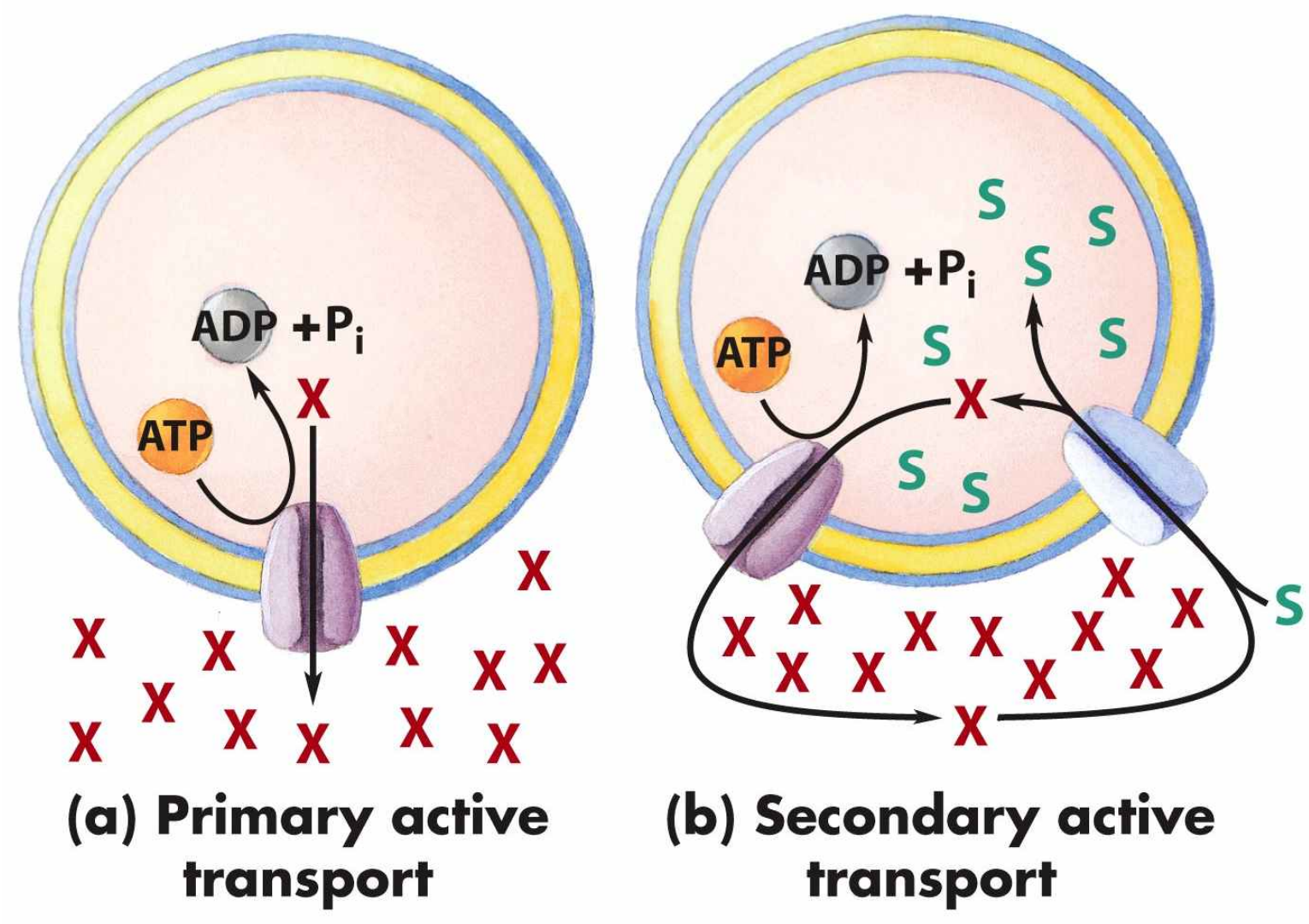
# Chloride-bicarbonate exchanger of the erythrocyte memb.



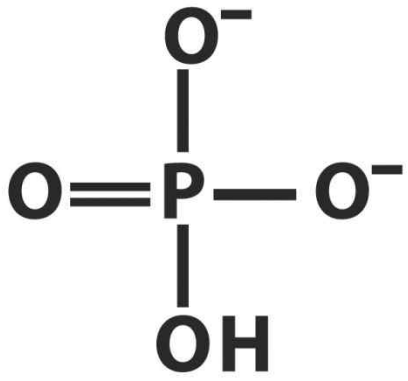
# Three general classes of transport systems



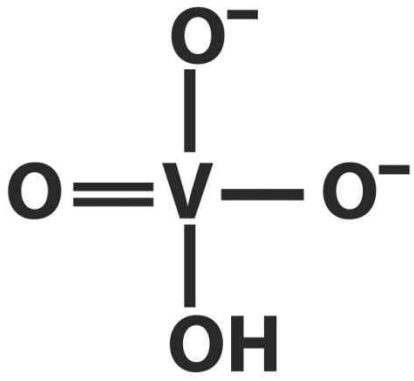
# Two types of active transport



**P-type ATPase:** ATP-driven cation transporters that are reversibly phosphorylated by ATP



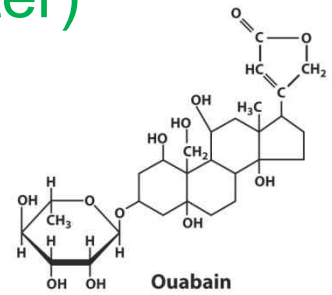

Phosphate



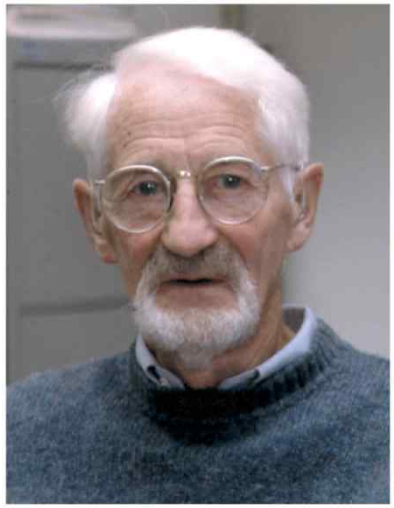

Vanadate

$Na^+$ $K^+$ ATPase (antiporter)

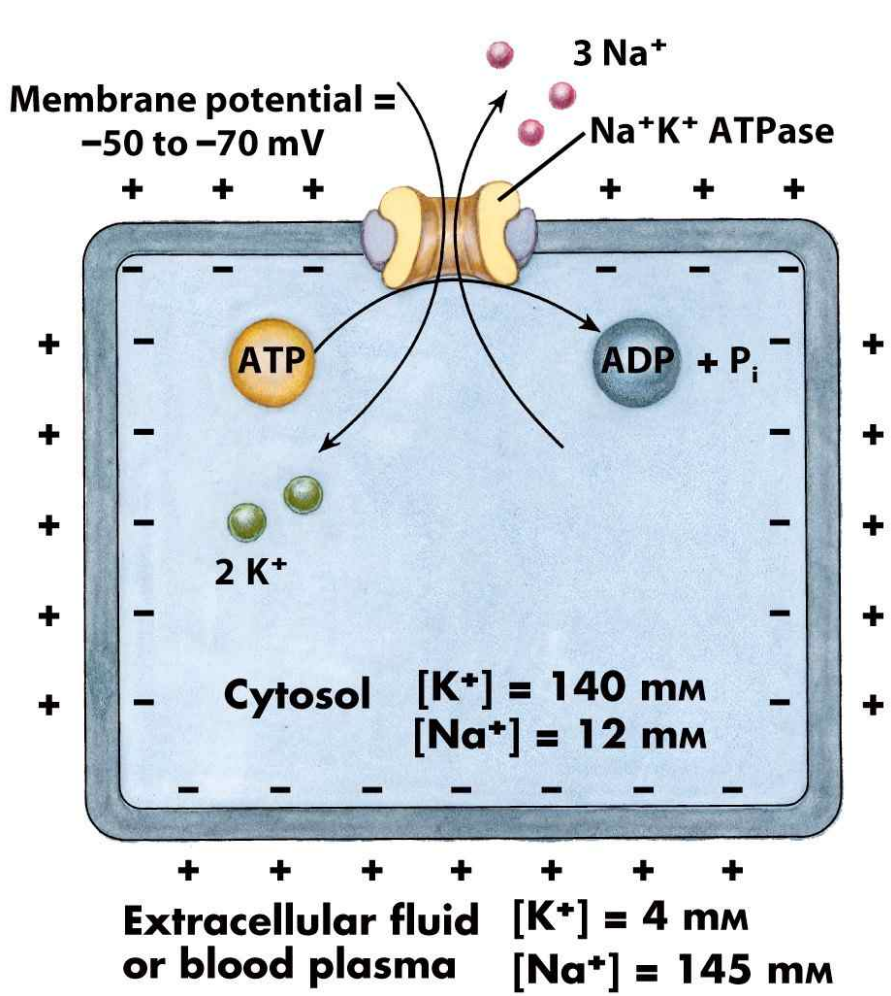
$Ca^+$ ATPase (uniporter)

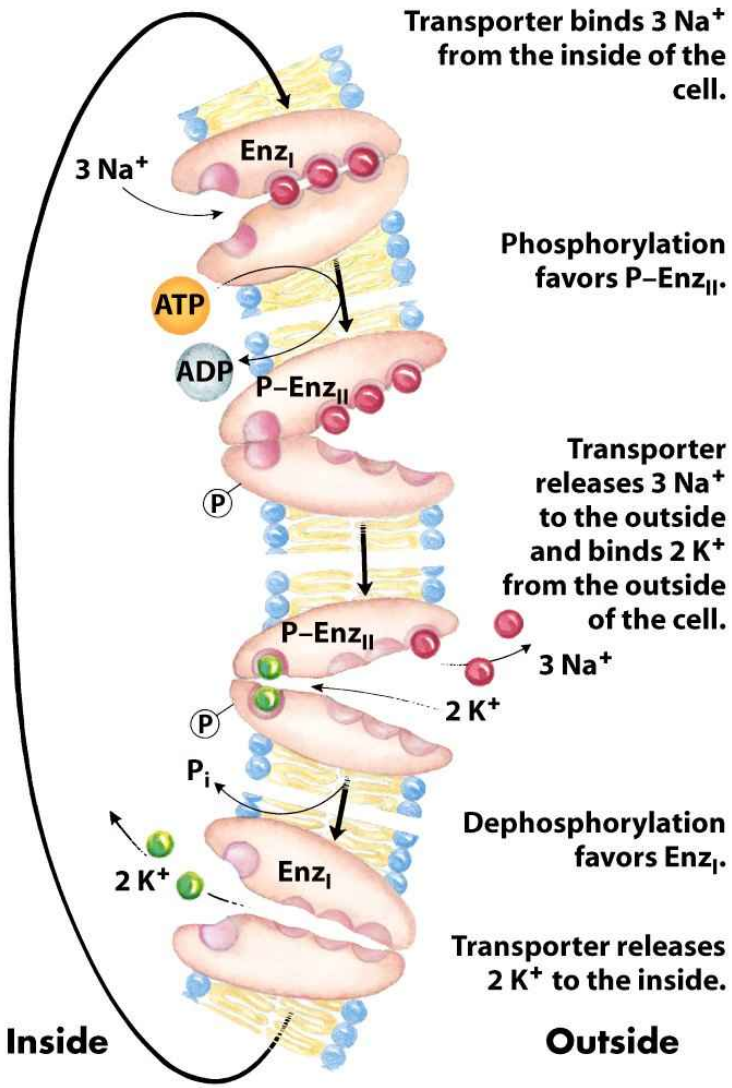


Ouabain

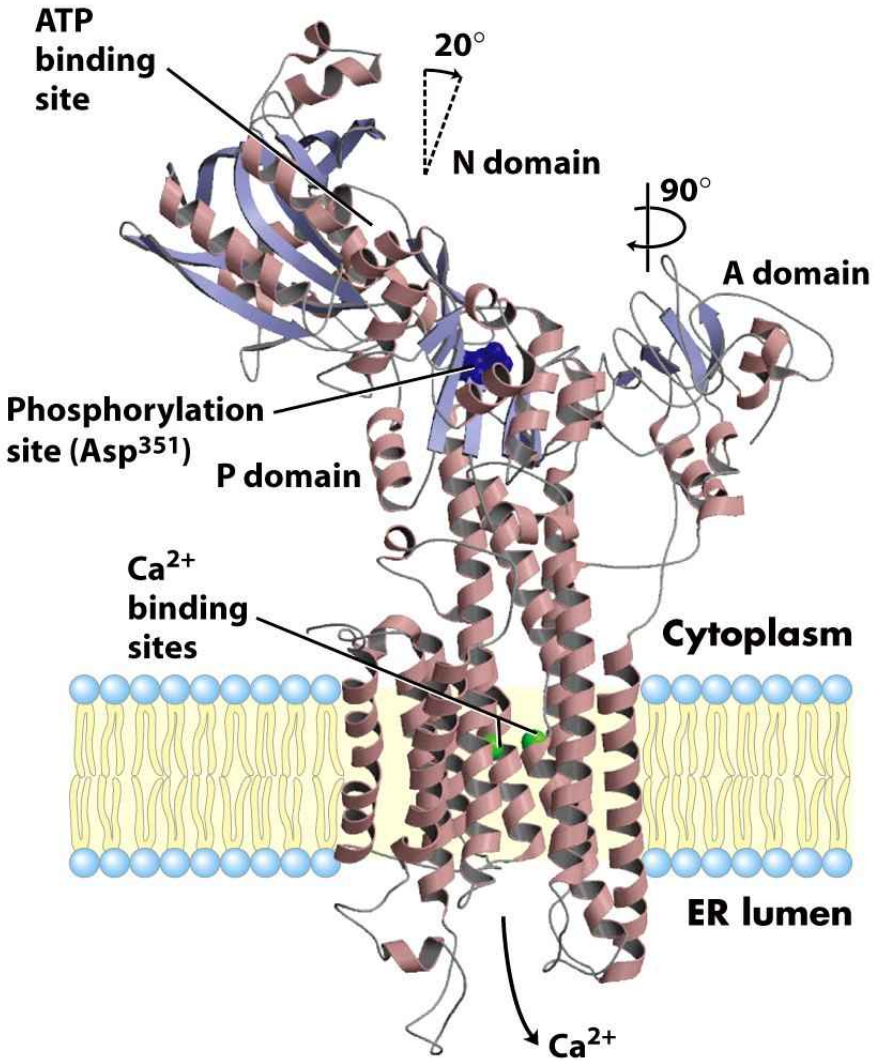


Jens Skou


3 Na+
Membrane potential =
−50 to −70 mV
Na+K+ ATPase
ATP
ADP + Pi
2 K+
Cytosol [K+] = 140 mM
[Na+] = 12 mM
Extracellular fluid [K+] = 4 mM
or blood plasma [Na+] = 145 mM


Transporter binds 3 Na+ from the inside of the cell.
3 Na+
Enz I
Phosphorylation favors P–Enz II.
ATP
ADP
P–Enz II
P
Transporter releases 3 Na+ to the outside and binds 2 K+ from the outside of the cell.
P–Enz II
3 Na+
2 K+
P
Pi
Dephosphorylation favors Enz I.
2 K+
Enz I
Transporter releases 2 K+ to the inside.
Inside
Outside

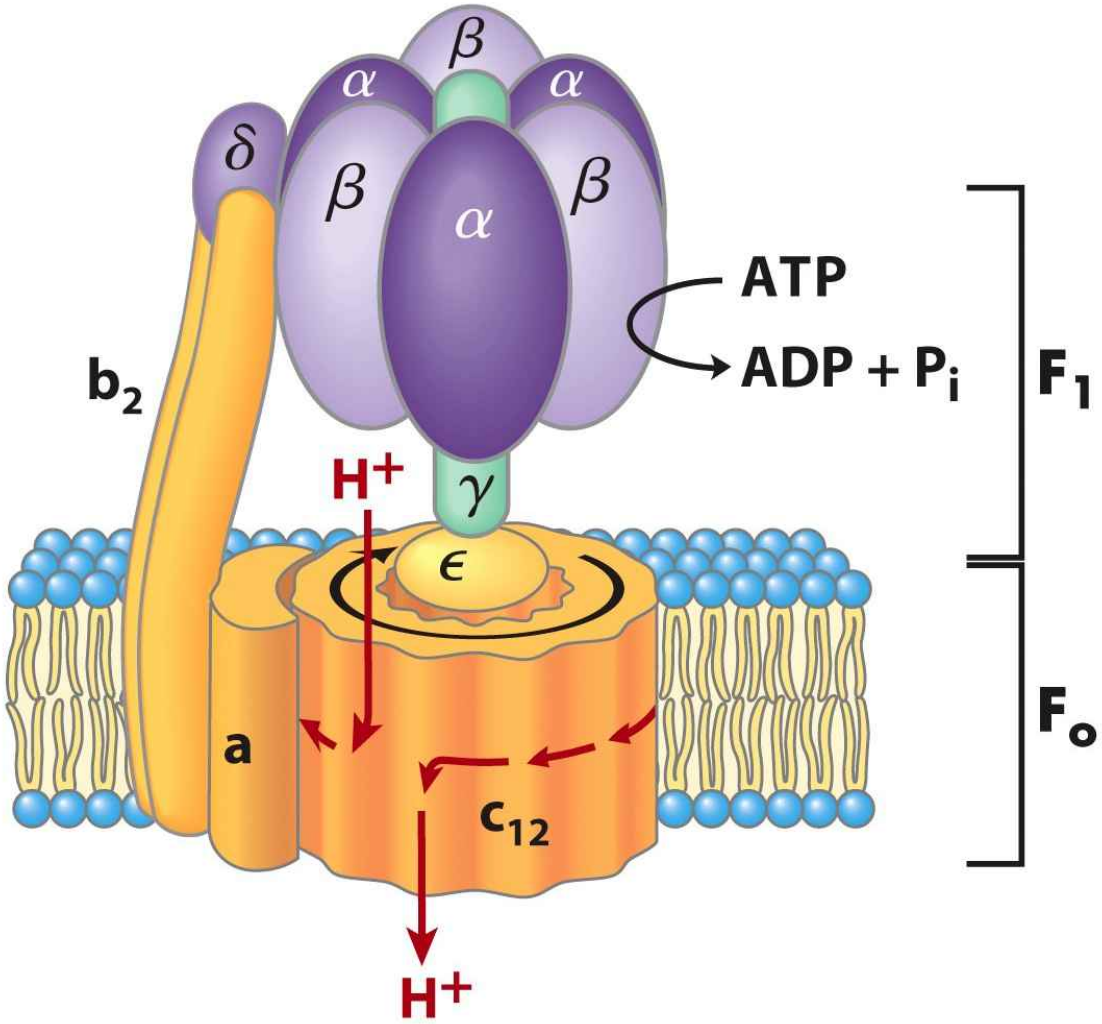
# Structure of the $Ca^{+}$ pump in SR

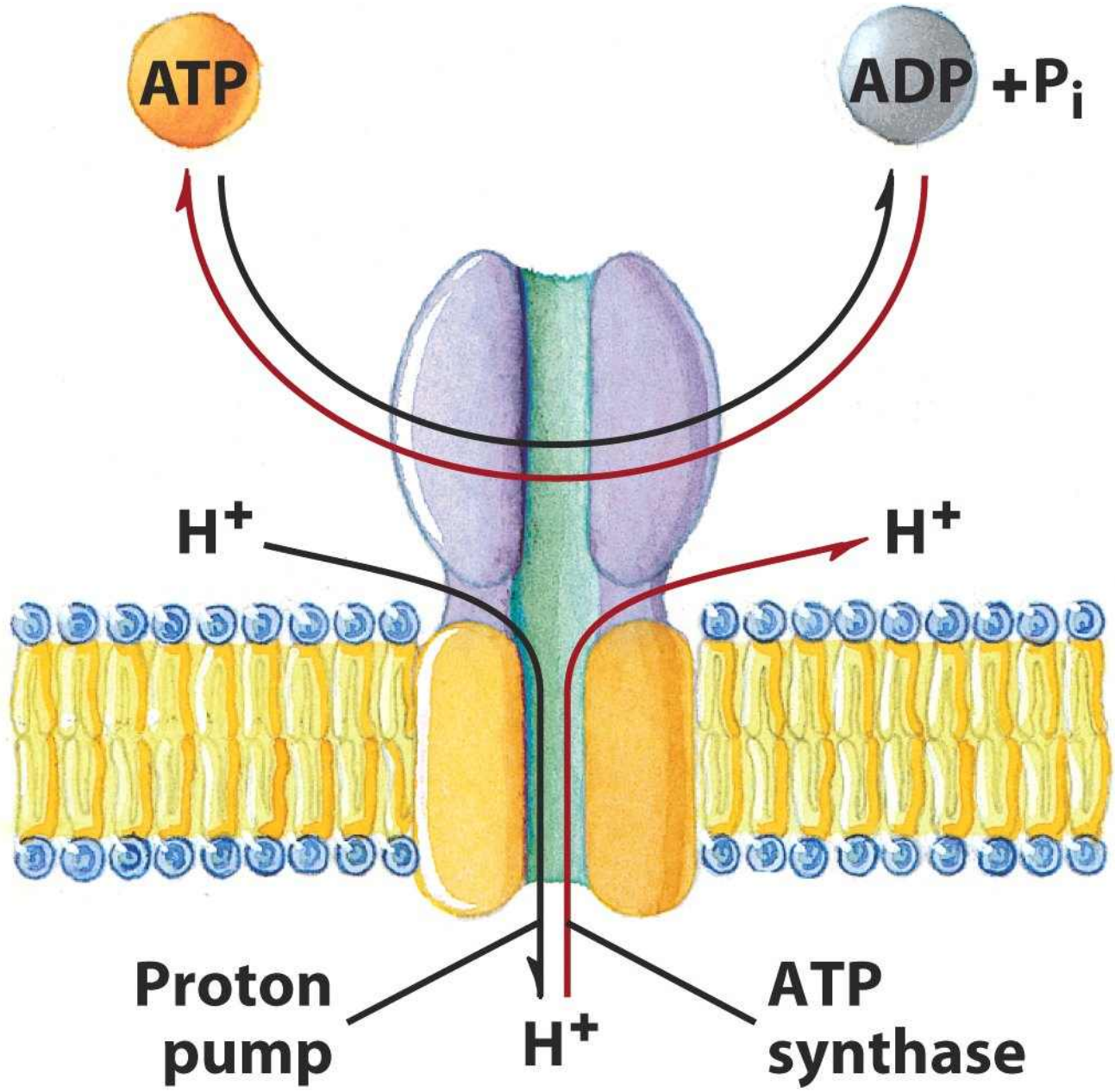



$[Ca^{+}] < 100$ nM

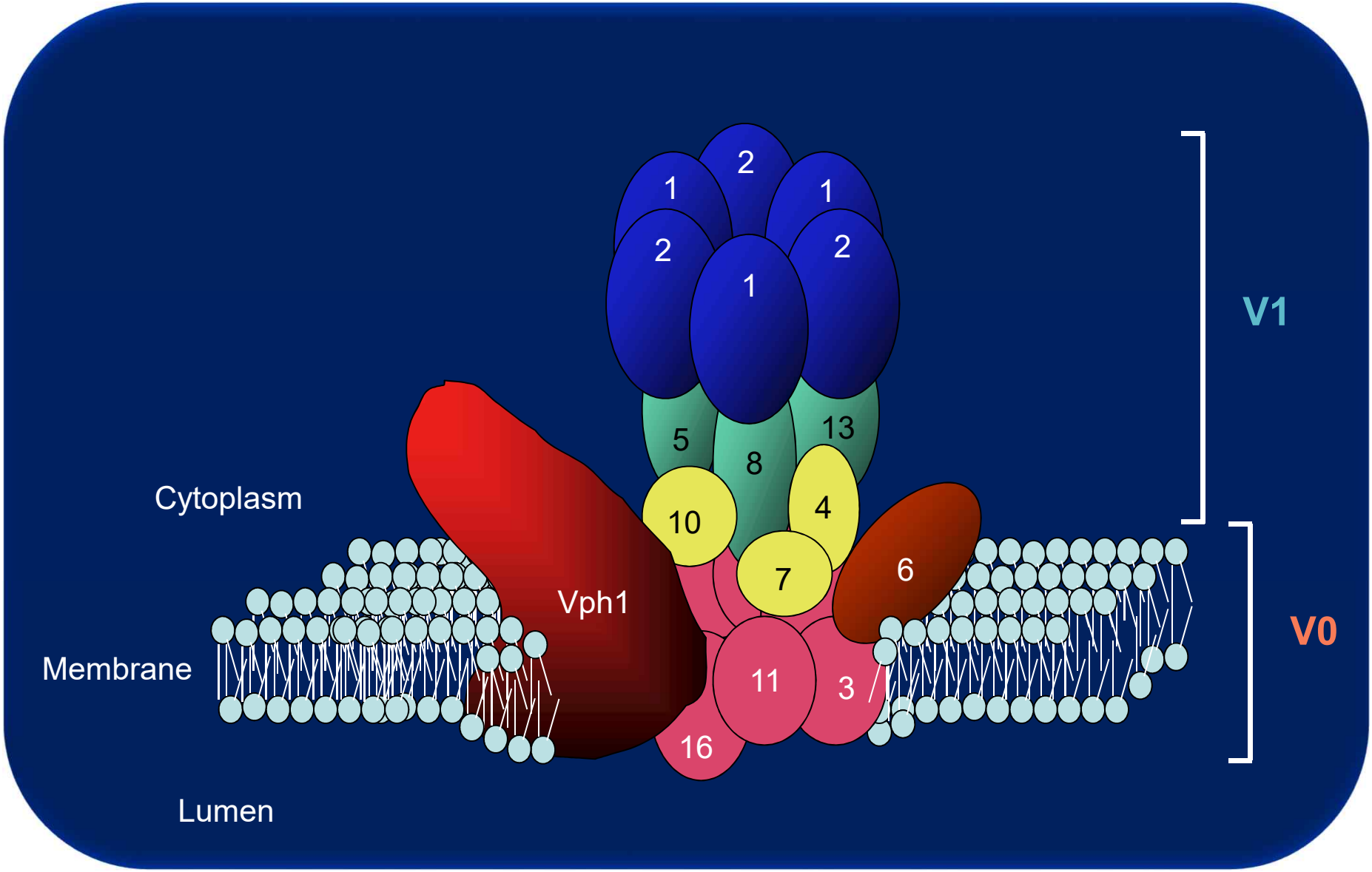
**F-type ATPase:** reversible ATP-driven proton pump

$F_0 F_1$ ATPase/ATP synthase

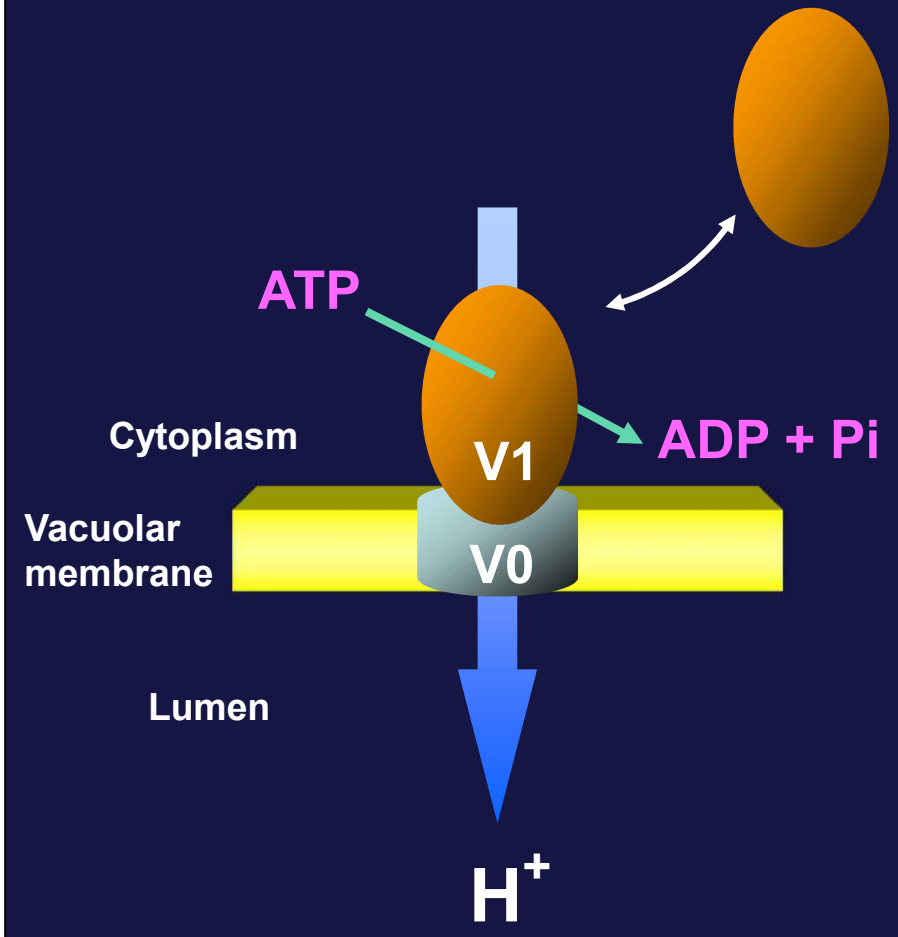



ATP
ADP +Pi
H+
H+
Proton pump
H+
ATP synthase

# **V-type ATPase:** ATP-driven proton pump

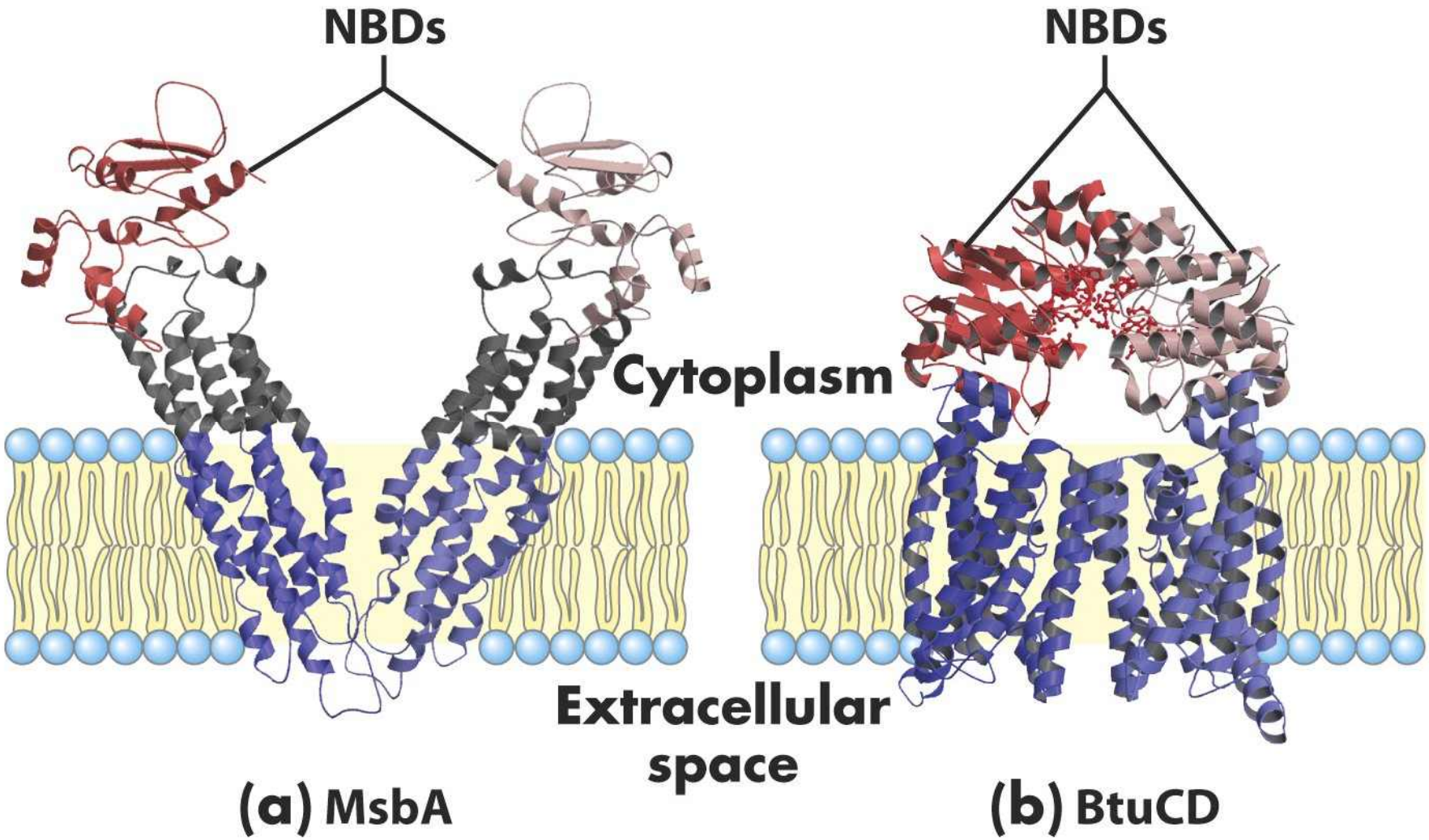


# Physiological function of V-ATPase




- Receptor-mediated endocytosis
- Intracellular targeting of lysosomal enzymes
- Protein processing, degradation and viral entry
- Coupled transport of small molecules (eg. Neurotransmitters)
- Bone resorption and renal acidification
- Tumour metastasis and multidrug resistance

# **ABC transporters** (ATP-dependent transporter)




Lipid A flippase

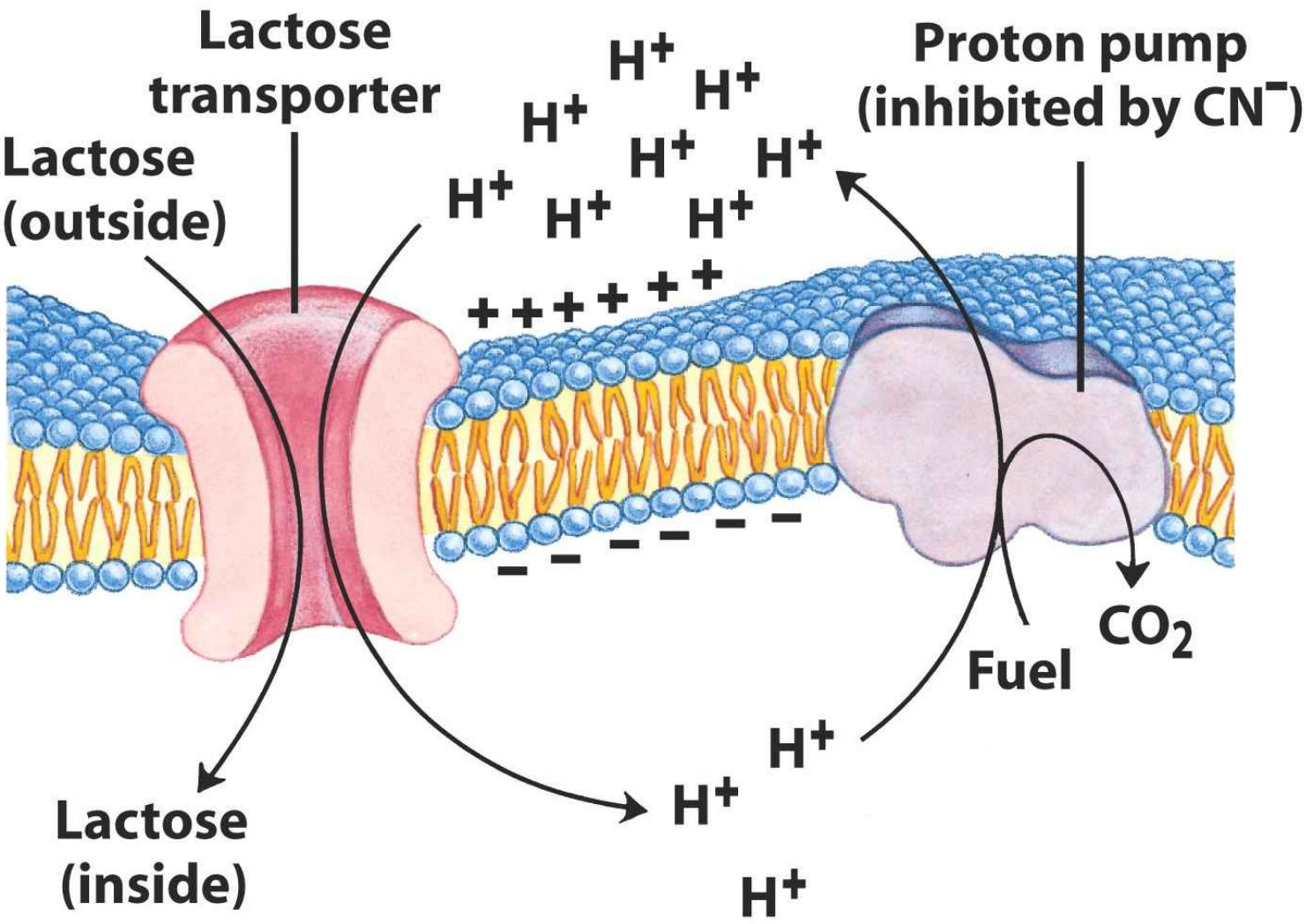
Vitamin $B_{12}$ importer

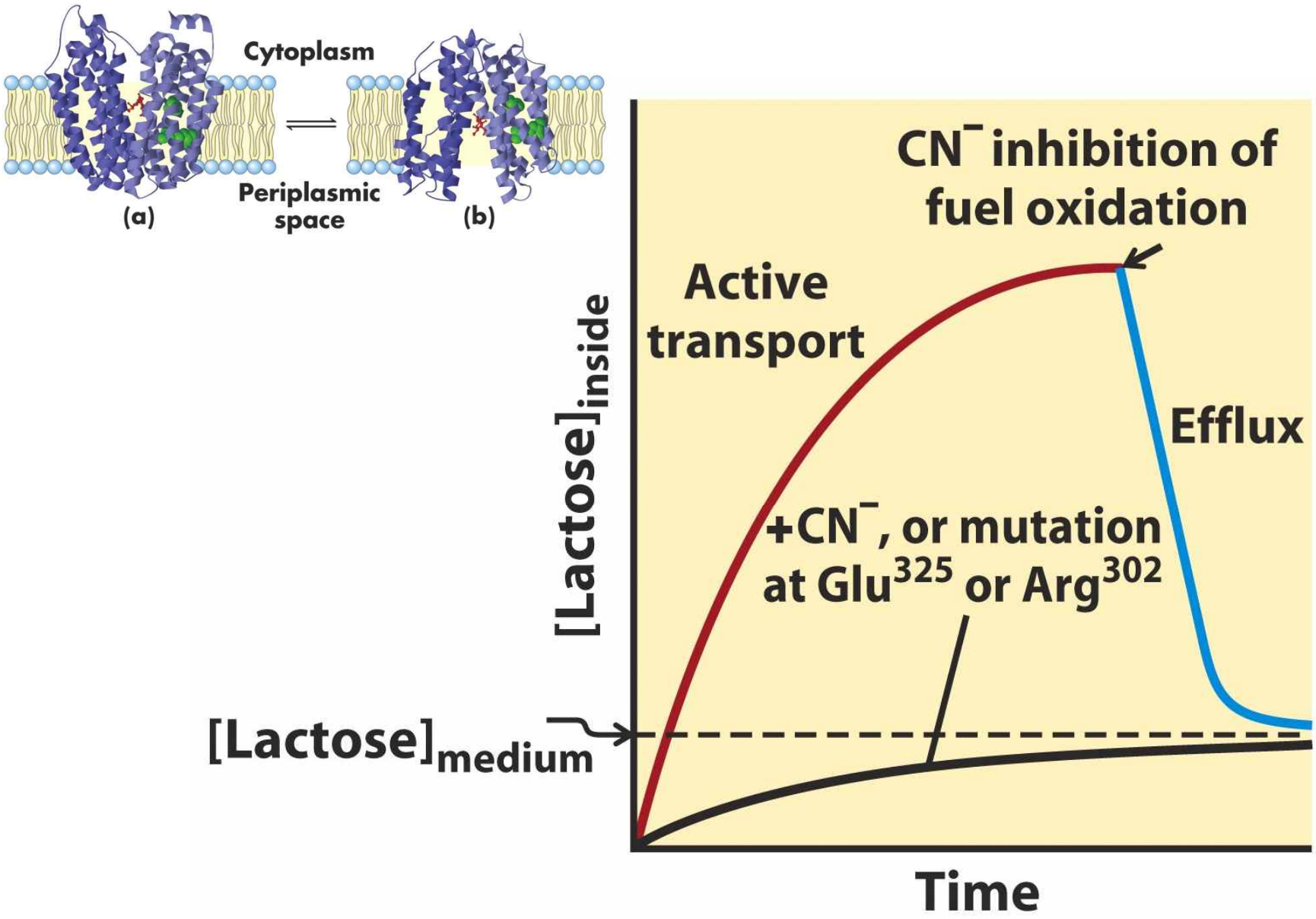
# Cotransport system

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

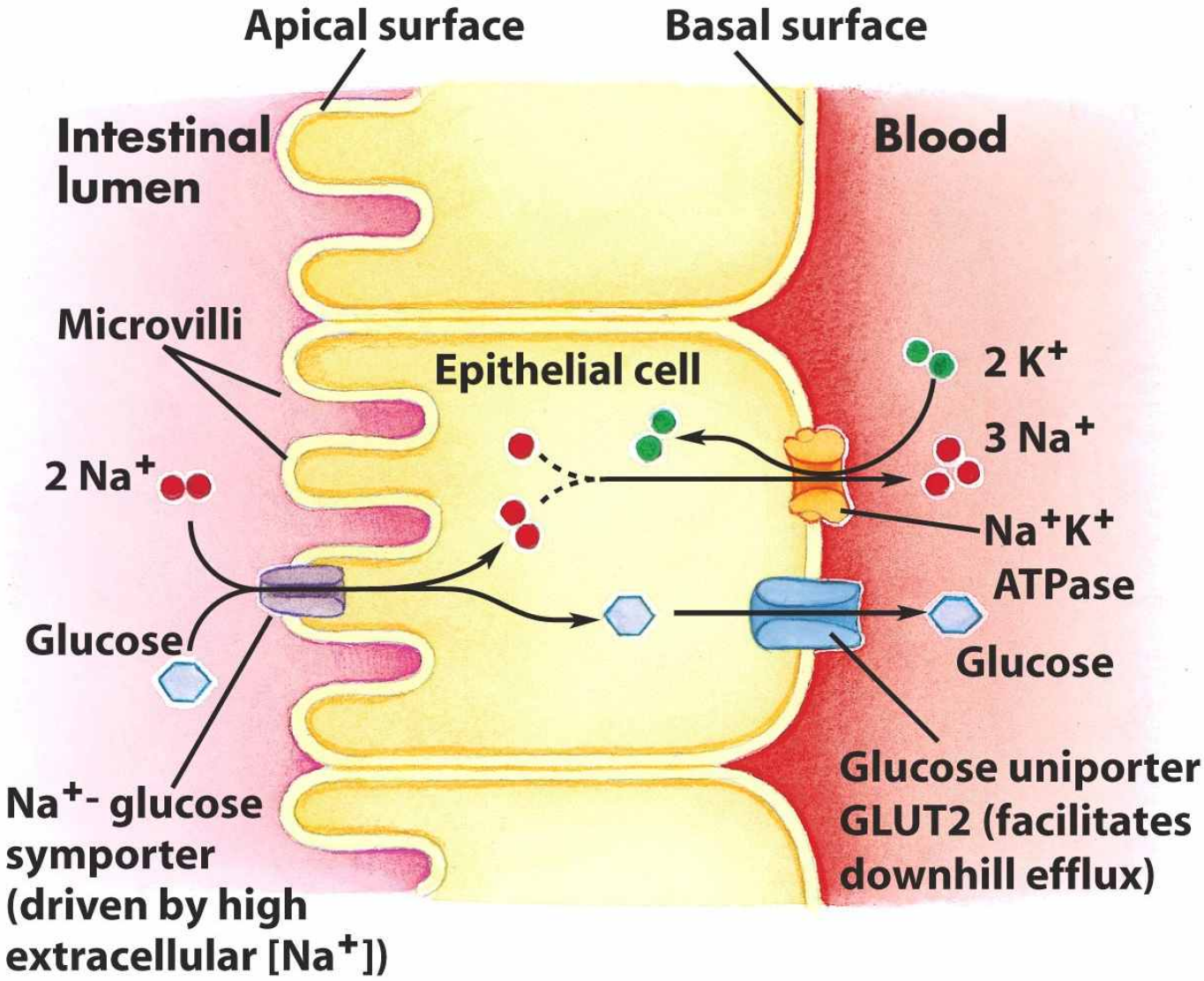
| *Organism/tissue/cell type* | *Transported solute (moving against its gradient)* | *Cotransported solute (moving down its gradient)* | *Type of transport* |
|---|---|---|---|
| *E. coli* | Lactose | $H^+$ | Symport |
| | Proline | $H^+$ | Symport |
| | Dicarboxylic acids | $H^+$ | Symport |
| Intestine, 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 |

# Lactose uptake in *E. coli*



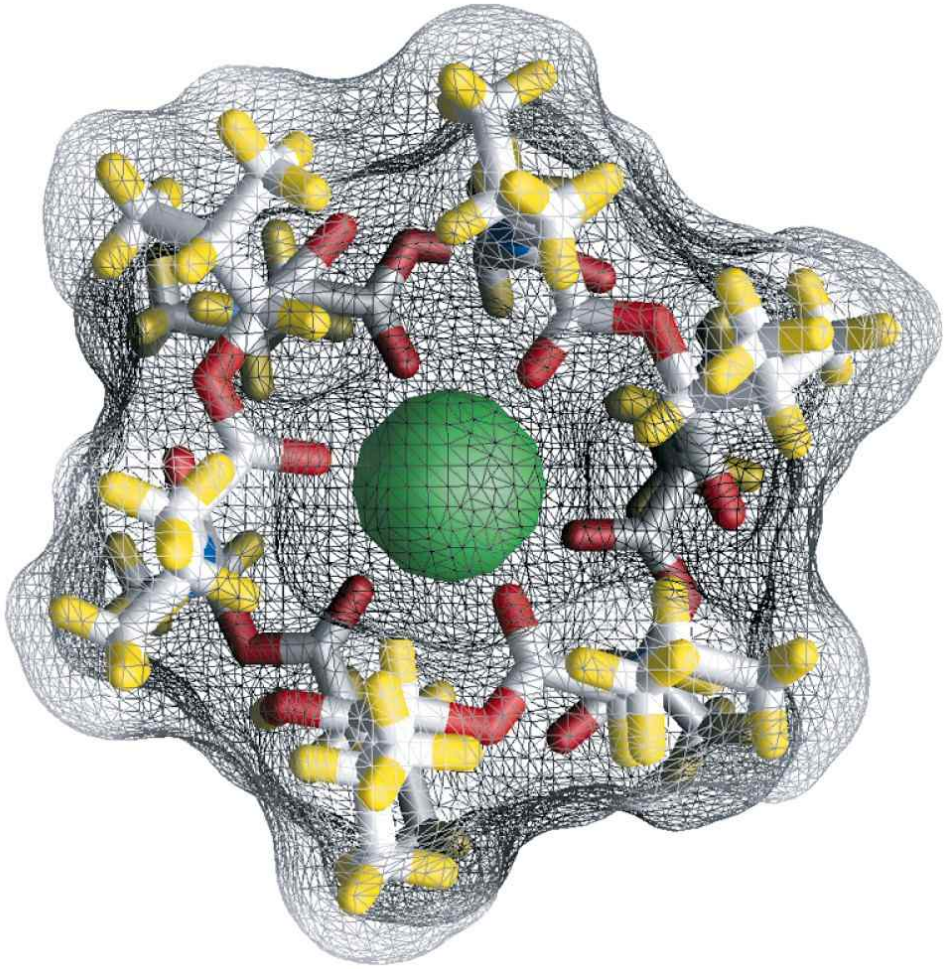

Cytoplasm
Periplasmic space
(a)
(b)
CN⁻ inhibition of fuel oxidation
Active transport
Efflux
+CN⁻, or mutation at Glu325 or Arg302
[Lactose]inside
[Lactose]medium
Time

# Glucose transport in intestinal epithelial cells



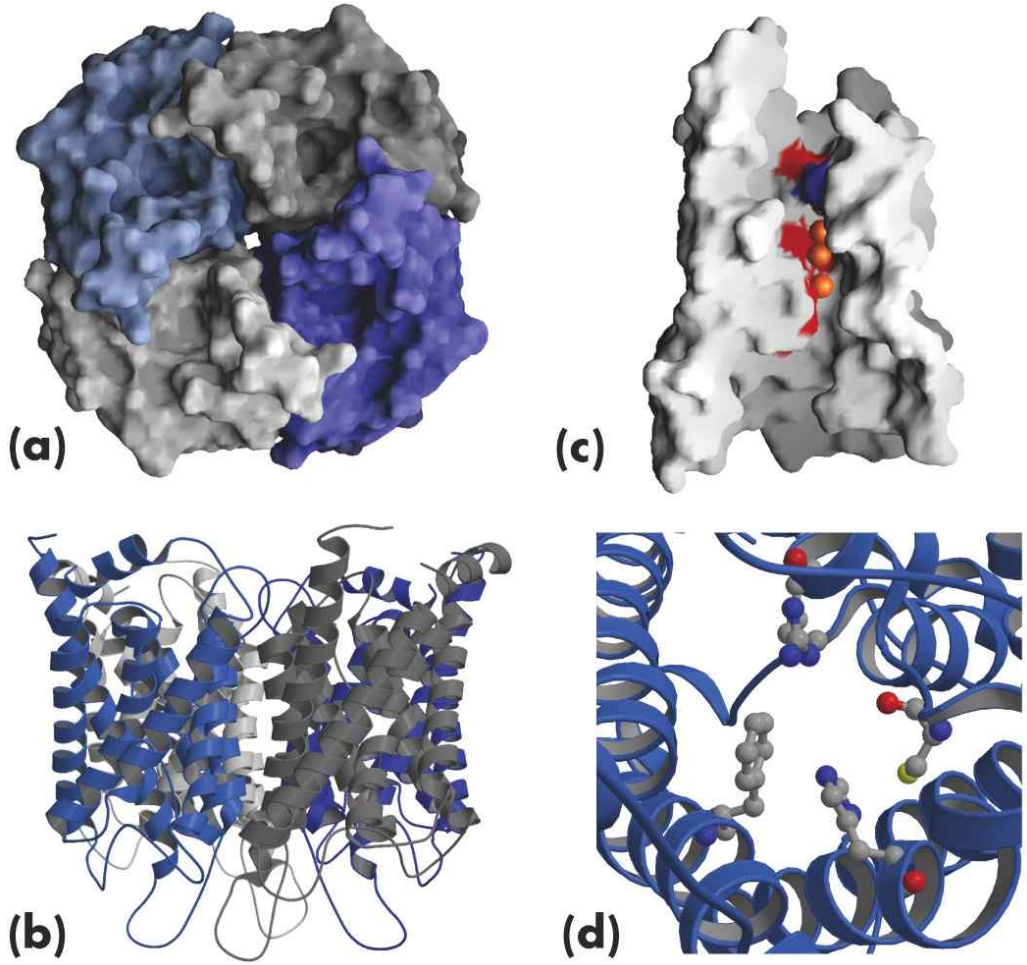
# **Valinomycin,** a peptide ionophore that binds $K^+$

- potent antibiotics



# Aquaporins

- provide channels for rapid movement of water molecules ($10^9$ $s^{-1}$)
- 2 x $10^5$ copies of AQP-1 per cell

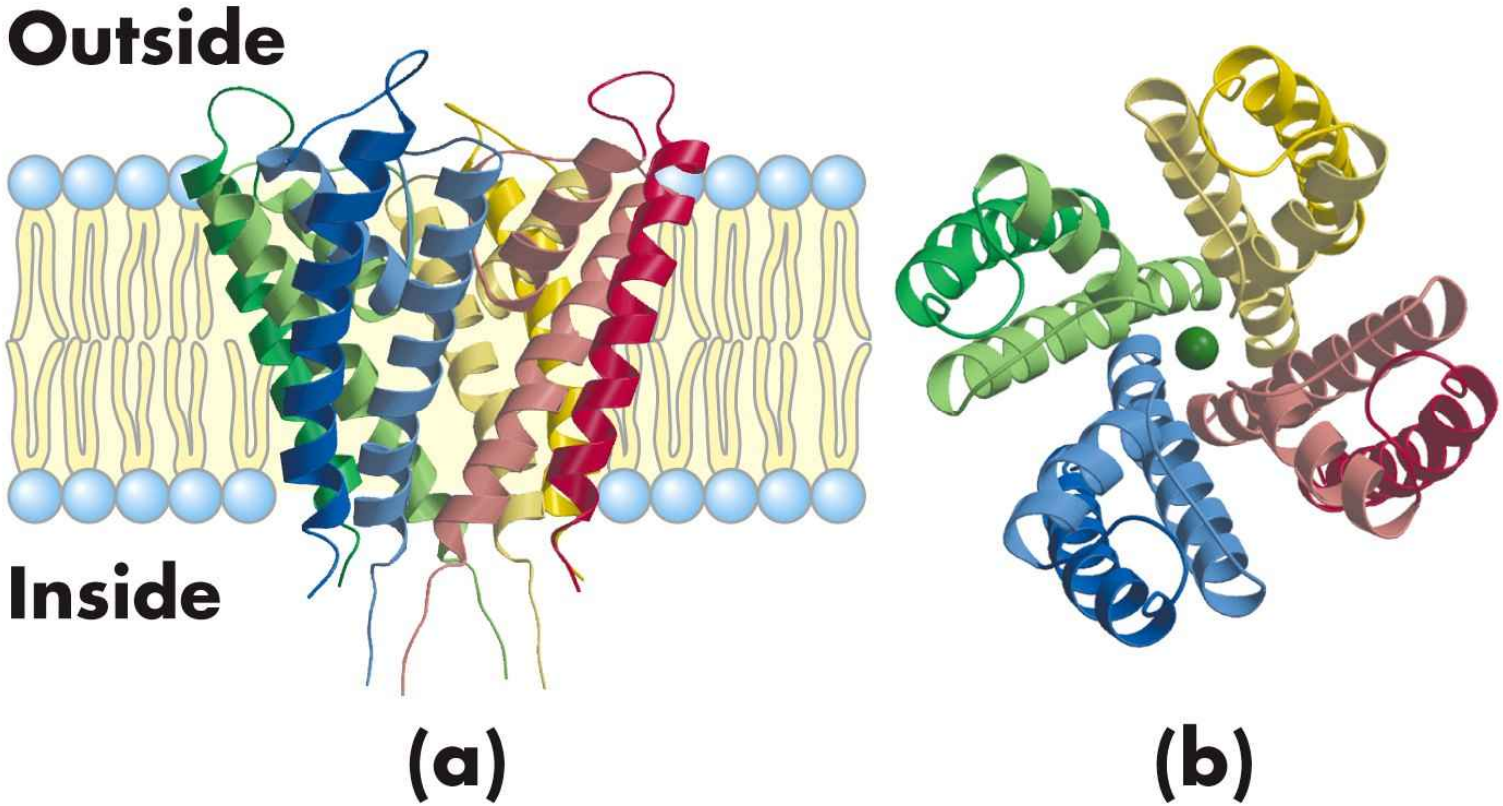


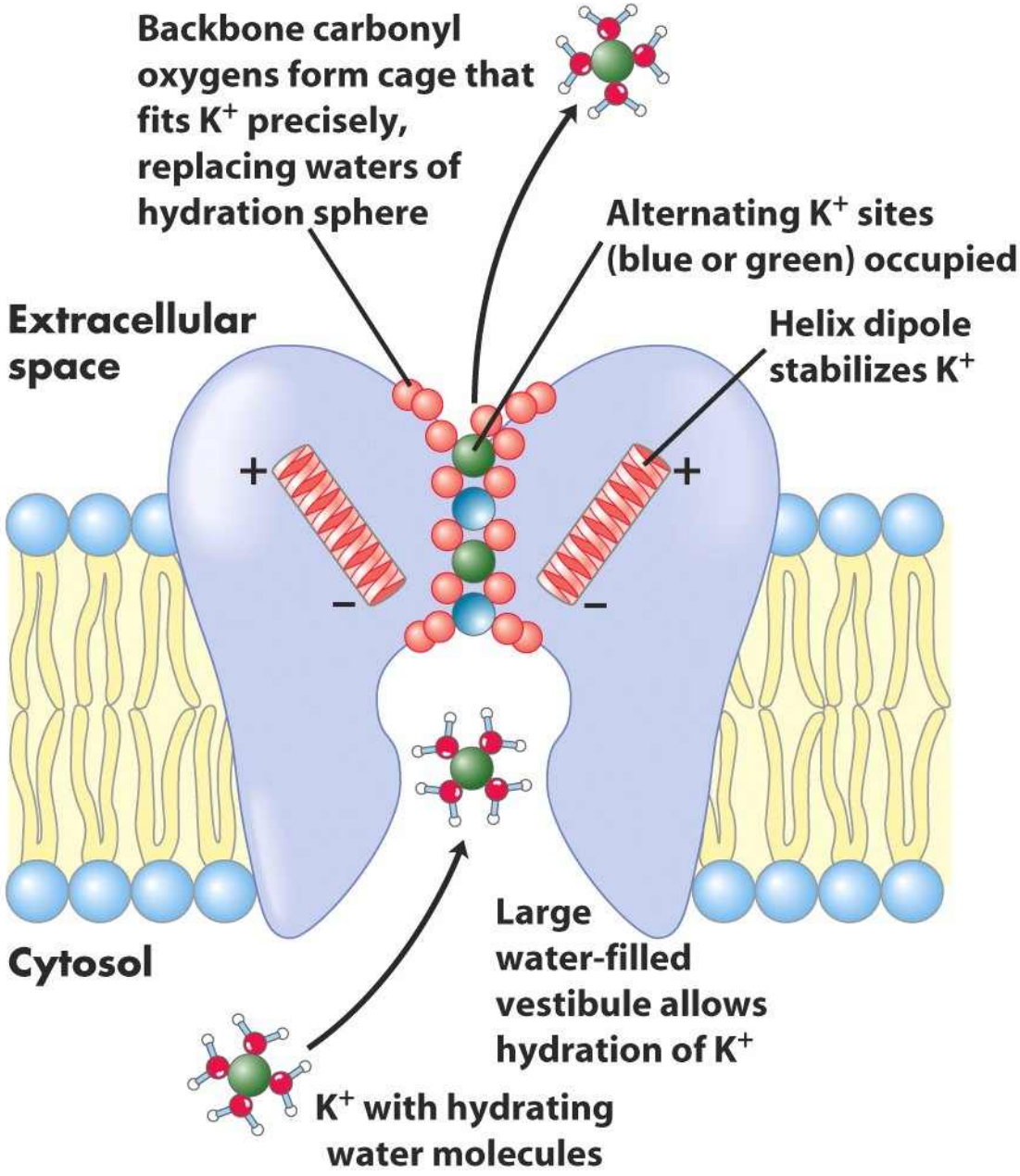
## TABLE 11–6 Aquaporins

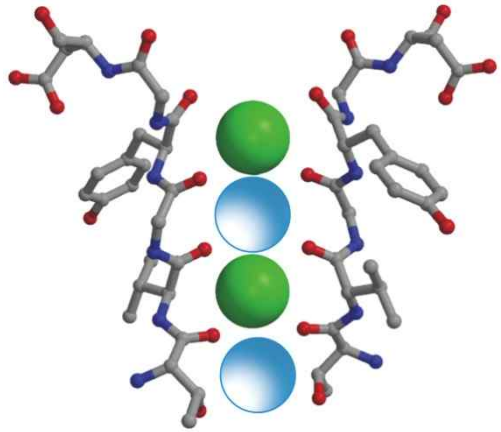
| *Aquaporin* | *Roles and/or location* |
|---|---|
| AQP-1 | Fluid reabsorption in proximal renal tubule; secretion of aqueous humor in eye and cerebrospinal fluid in central nervous system; water homeostasis in lung |
| AQP-2 | Water permeability in renal collecting duct (mutations produce nephrogenic 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 |

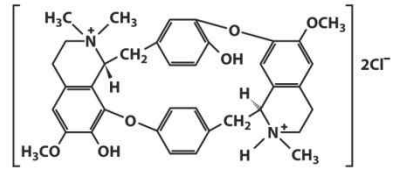
# Ion selective channels

## $K^+$ channels



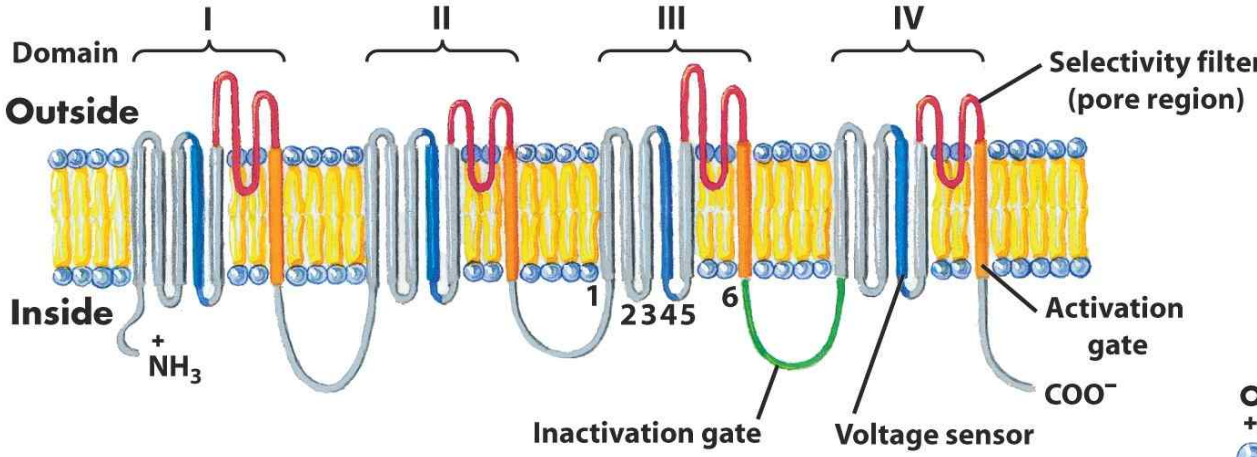


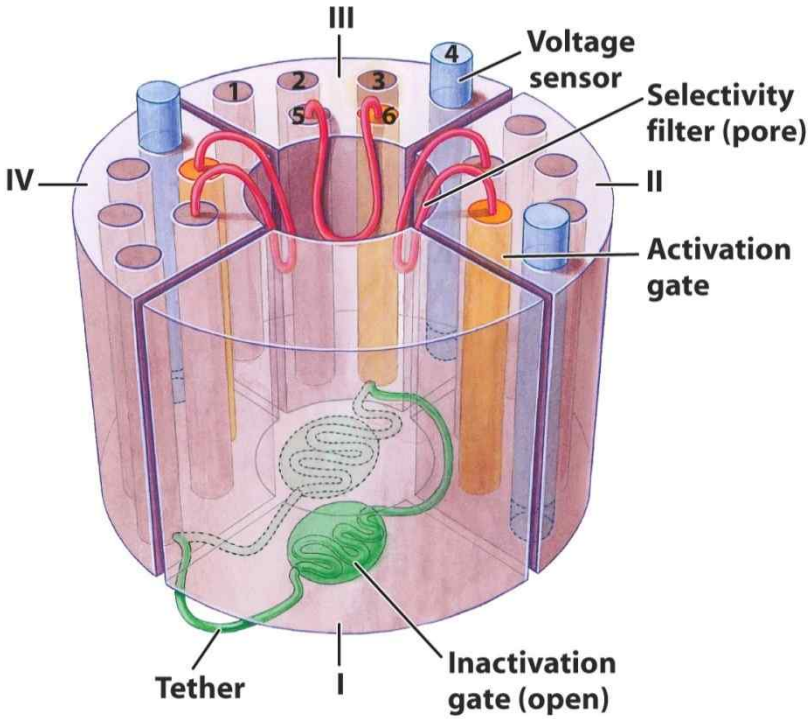



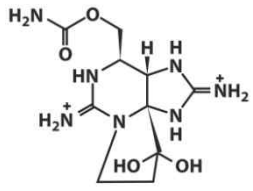


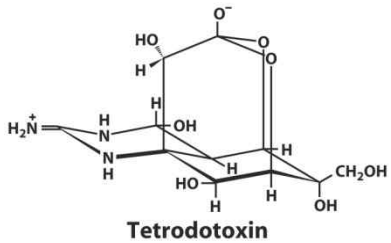

D-Tubocurarine chloride

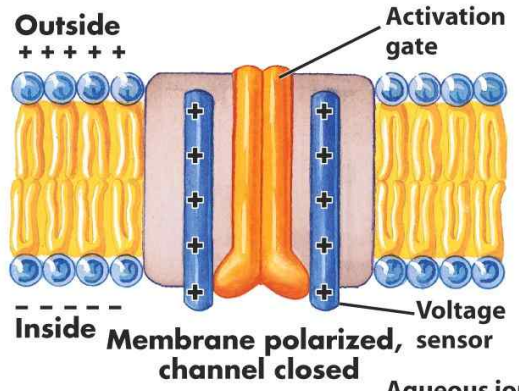
# Voltage-gated $Na^+$ channels of neurons

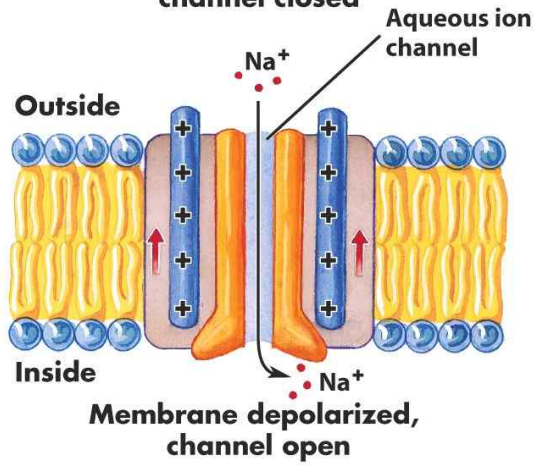


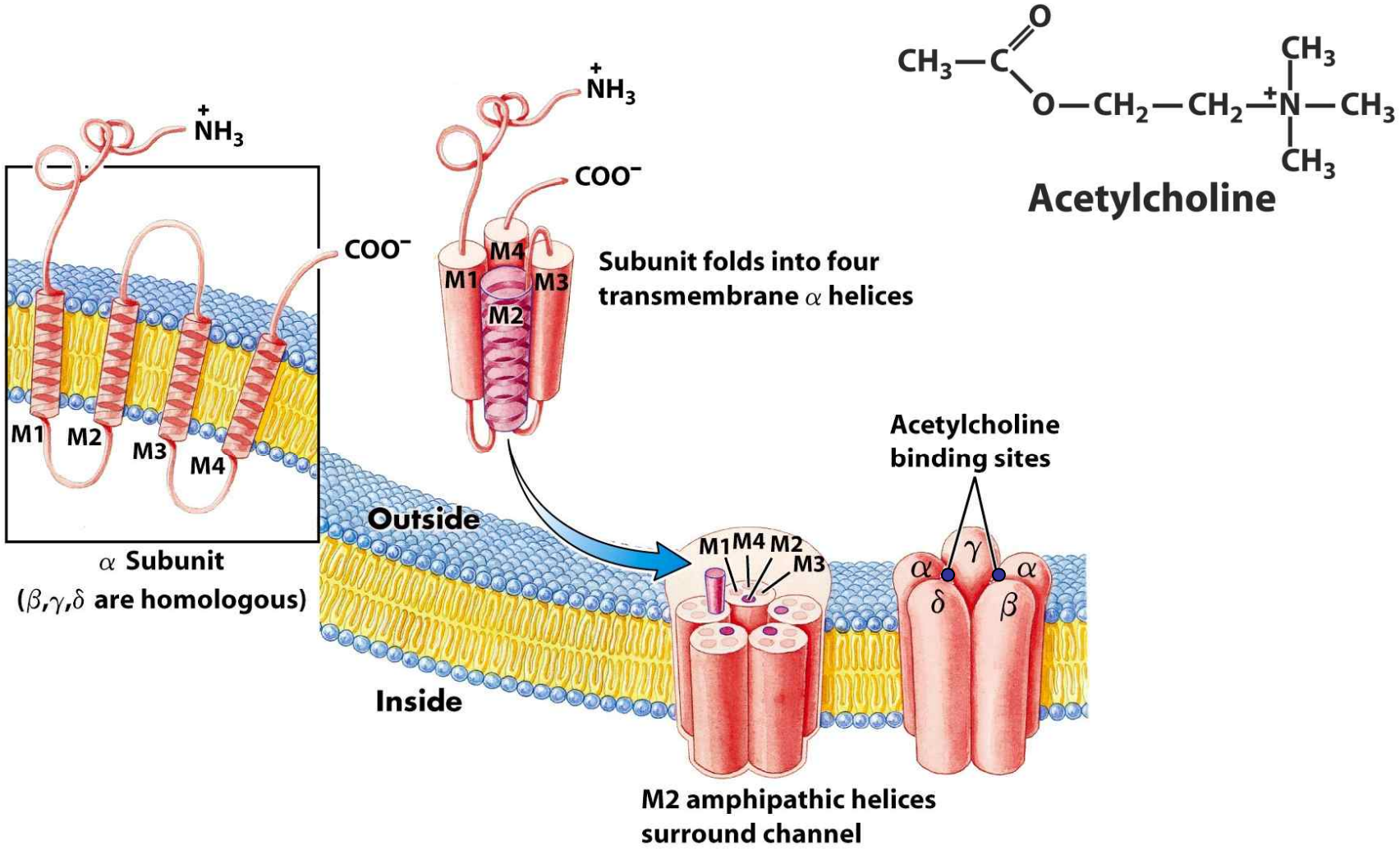



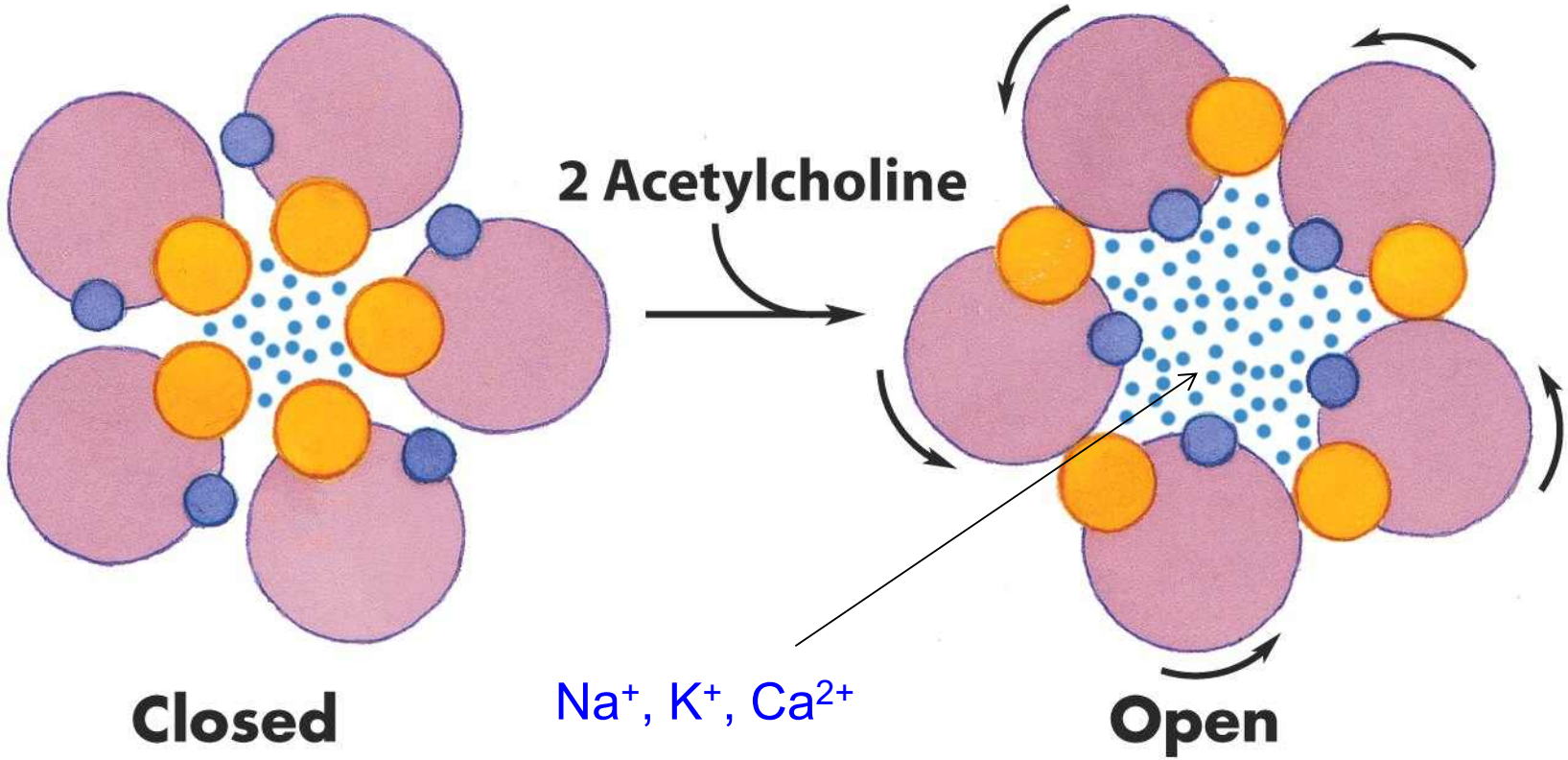
# Acetylcholine receptor ion channel



Bulky hydrophobic Leu side chains of M2 helices close the channel.

Binding of two acetylcholine molecules causes twisting of the M2 helices.

M2 helices now have smaller, polar residues lining the channel.



# “Patch clamps”