Biological Membranes: membrane permeability: pumps and channels, action potential.

Introduction

Membranes define the boundaries of the cell and its various internal compartments.
Their functions include:

- Define the boundaries of the cell and its organelles and act as permeability barriers.
- Sites for specific biochemical functions, such as electron transport during mitochondrial respiration or protein processing in the ER.
- Allow transport and have transport proteins that regulate the movement of substances into and out of the cell and its organelles.
- They provide mechanisms for cell-to-cell contact, adhesion, and communication.

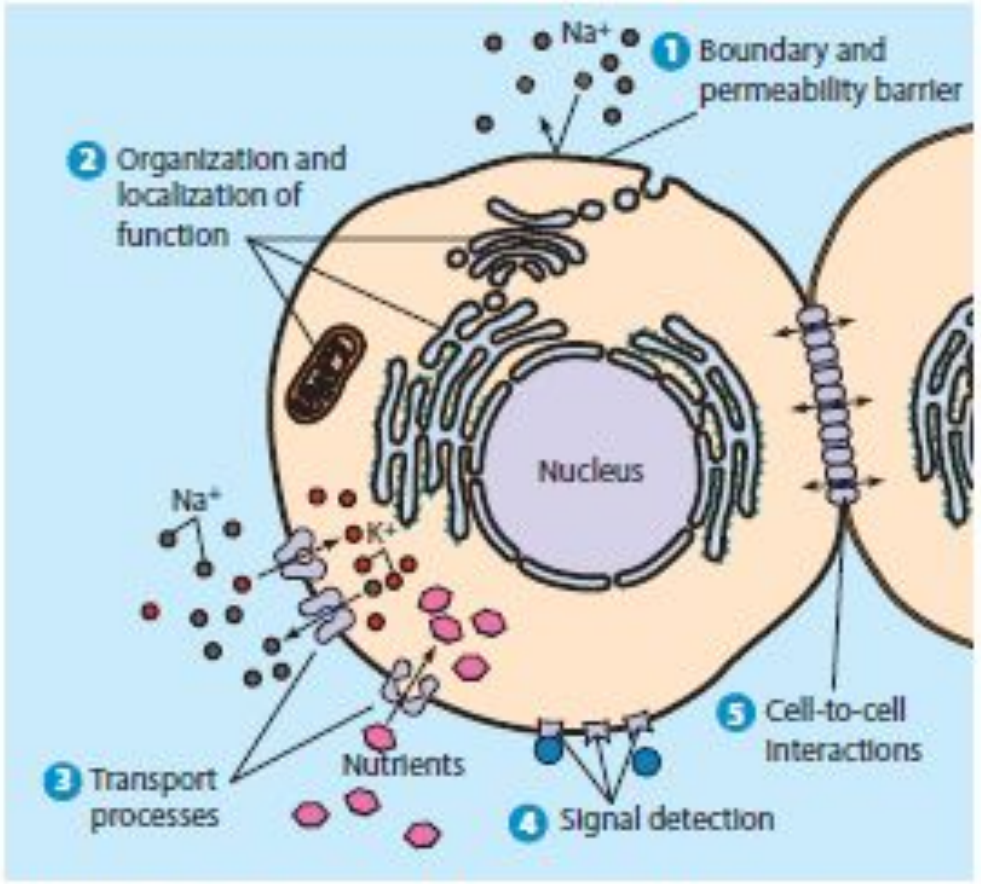
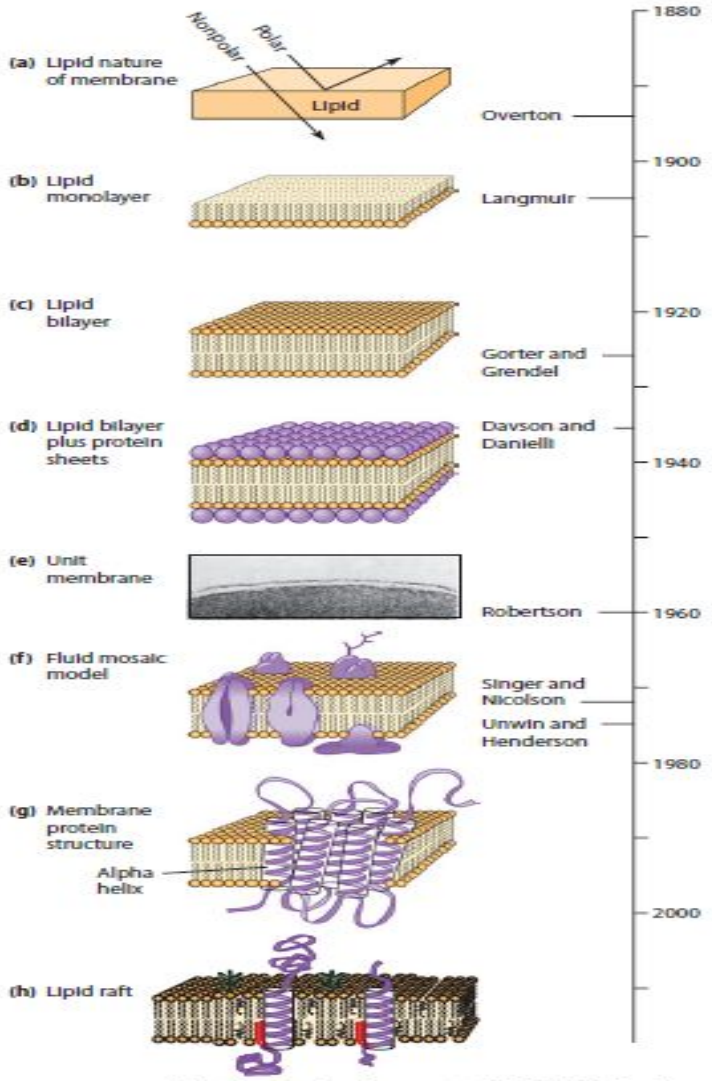


FIGURE 7-2 Functions of Membranes. Membranes not only define the cell and its organelles but also have a number of important functions, including transport, signaling, and adhesion.

What are membranes made up of ?



Timeline of experiments carried out for understanding the membrane structure

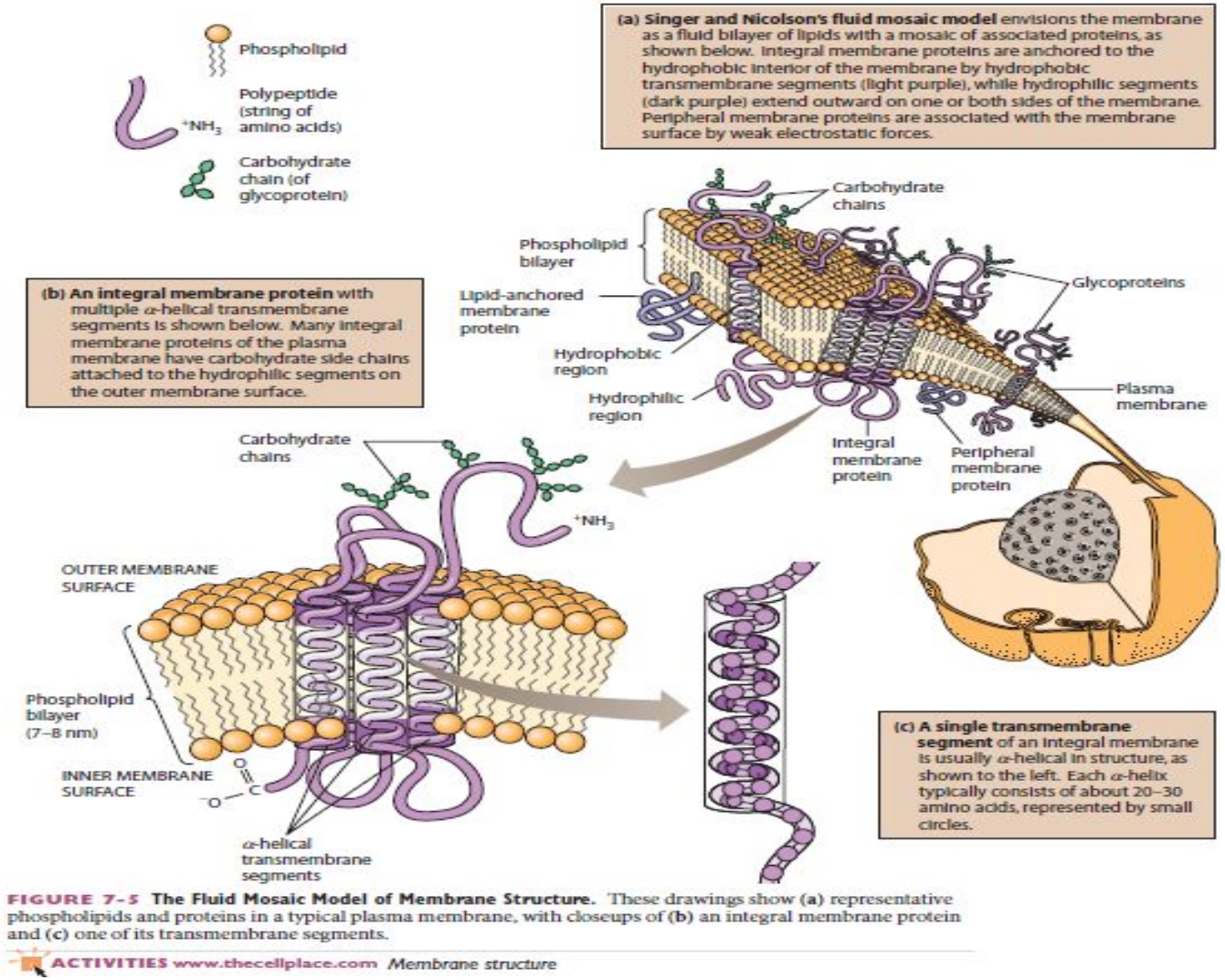


FIGURE 7-5 **The Fluid Mosaic Model of Membrane Structure.** These drawings show (a) representative phospholipids and proteins in a typical plasma membrane, with closeups of (b) an integral membrane protein and (c) one of its transmembrane segments.

ACTIVITIES www.thecellplace.com *Membrane structure*

Membranes are made up of a lipid bilayer, peripheral membrane proteins, integral membrane proteins and carbohydrates: all of which contributes to membrane permeability

Transport across membranes

- **Simple diffusion**: direct, unaided transport of small molecules
- **Facilitated diffusion**: Movement with help of channel proteins and carrier proteins
- **Active transport**: Energy driven transport

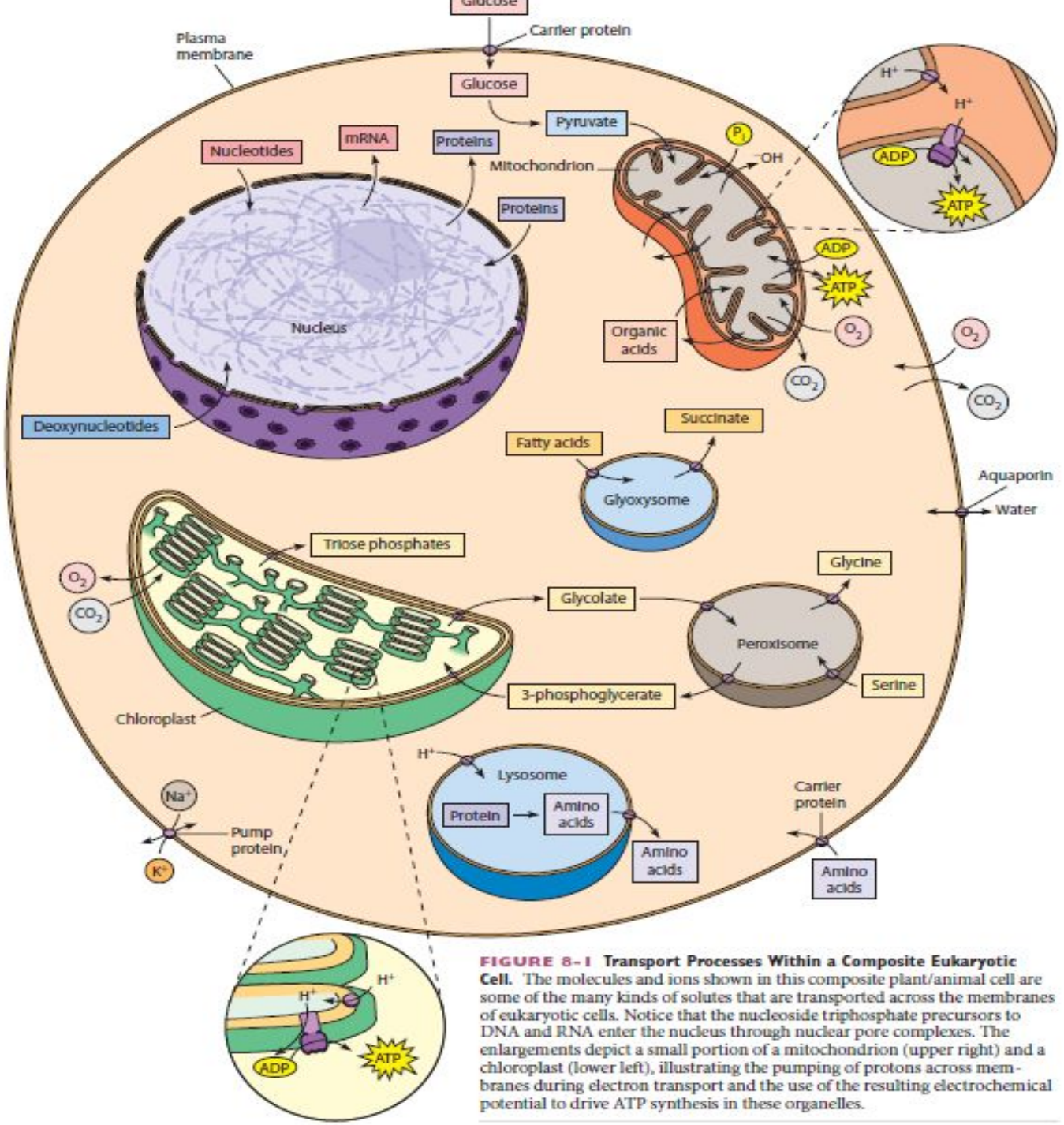


FIGURE 8-1 Transport Processes Within a Composite Eukaryotic Cell. The molecules and ions shown in this composite plant/animal cell are some of the many kinds of solutes that are transported across the membranes of eukaryotic cells. Notice that the nucleoside triphosphate precursors to DNA and RNA enter the nucleus through nuclear pore complexes. The enlargements depict a small portion of a mitochondrion (upper right) and a chloroplast (lower left), illustrating the pumping of protons across membranes during electron transport and the use of the resulting electrochemical potential to drive ATP synthesis in these organelles.

Nuclear localization signal and transport of proteins into nucleus

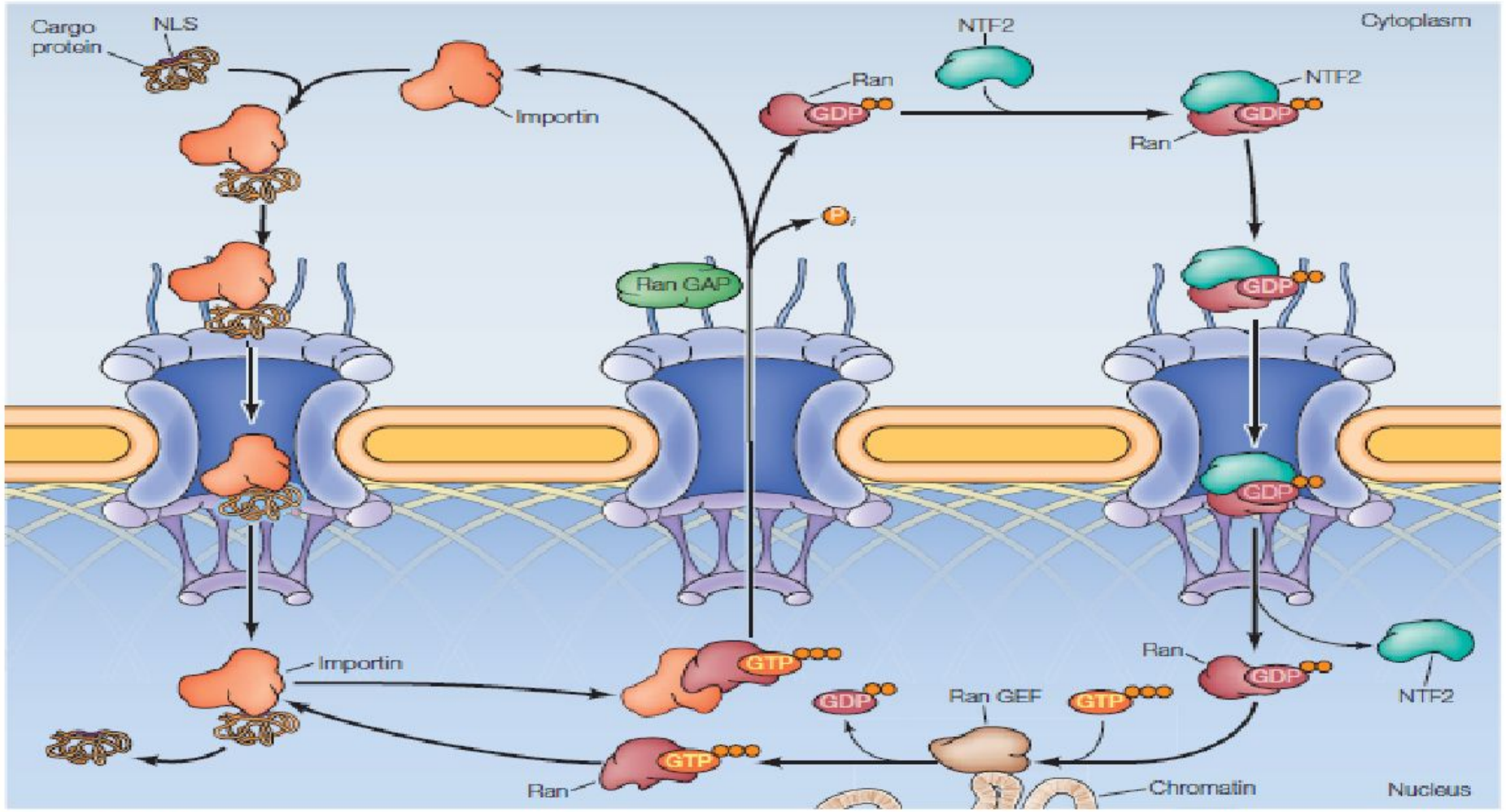


Figure 11.10 Protein import through the nuclear pore complex Transport begins when the nuclear localization sequence (NLS) of a cargo protein is recognized by an importin. The cargo/importin complex binds to nuclear pore proteins in the cytoplasmic filaments and is transported through the pore. At the nuclear side of the envelope, Ran/GTP binds to the importin, disrupting the cargo/importin complex and releasing the cargo protein into the nucleus. The importin-Ran/GTP complex is re-exported through the nuclear pore and the GTPase-activating protein (Ran GAP) associated with cytoplasmic filaments stimulates hydrolysis of the GTP to GDP, releasing the importin. Ran/GDP is then transported back to the nucleus in association with its own import receptor, NTF2. In the nucleus, Ran GEF (bound to chromatin) stimulates the exchange of GDP bound to Ran for GTP, leading to the conversion of Ran/GDP to Ran/GTP and maintaining a high concentration of Ran/GTP within the nucleus.

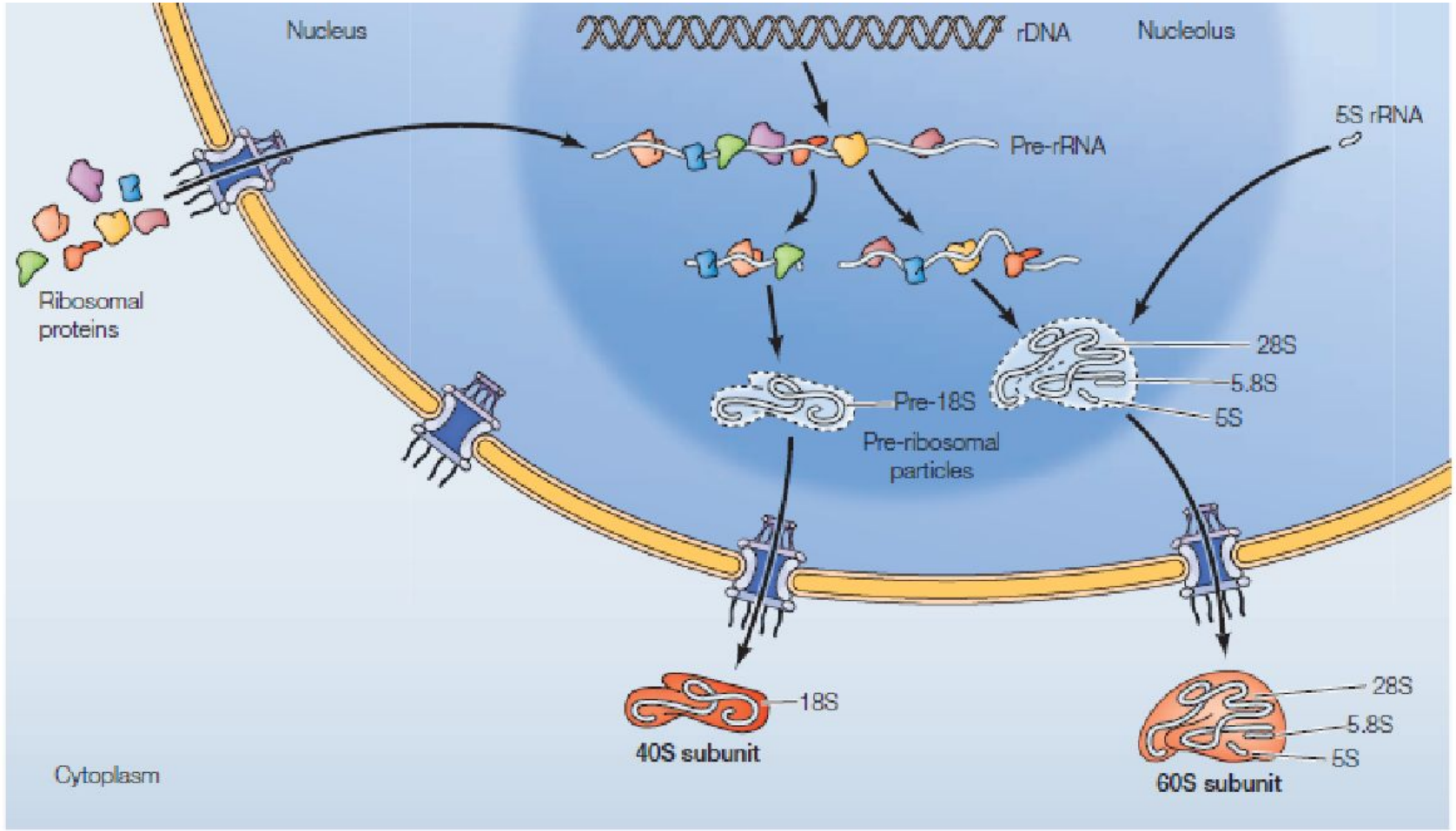
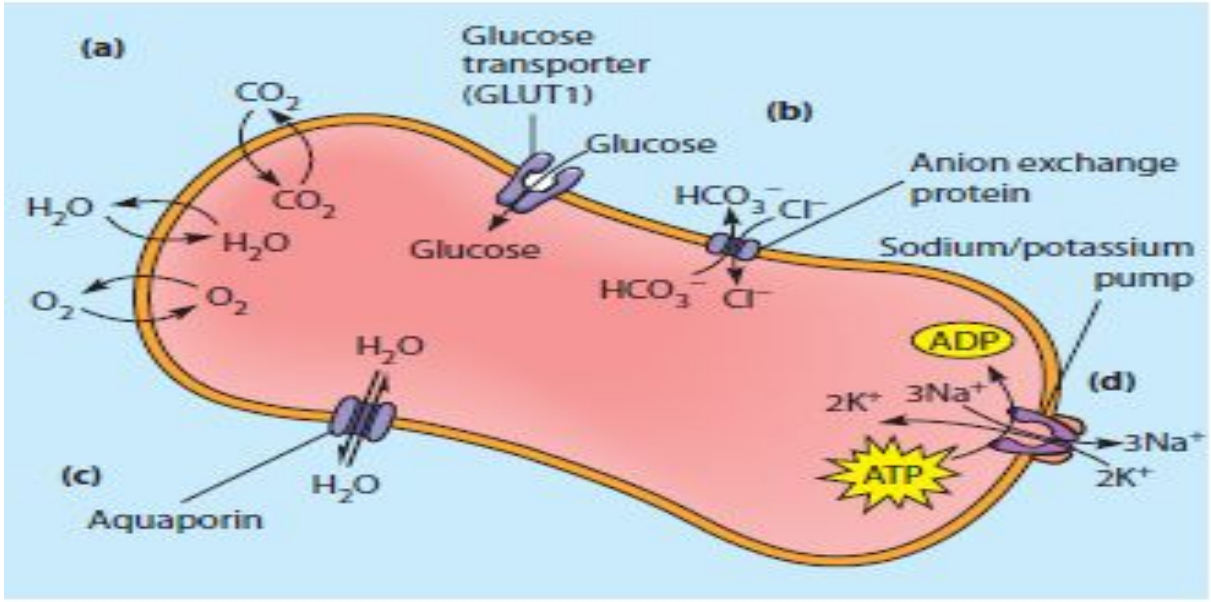


Figure 11.24 Ribosome assembly Ribosomal proteins are imported to the nucleolus from the cytoplasm and begin to assemble on pre-rRNA prior to its cleavage. As the pre-rRNA is processed, additional ribosomal proteins and the 5S rRNA (which is synthesized elsewhere in the nucleus) assemble to form pre-ribosomal particles. The final steps of maturation follow the export of pre-ribosomal particles to the cytoplasm, yielding the 40S and 60S ribosomal subunits.

(a) **Simple diffusion.** Oxygen, carbon dioxide, and water diffuse directly across the plasma membrane in response to their relative concentrations inside and outside the cell.

(b) **Facilitated diffusion mediated by carrier proteins.** The movement of glucose across the plasma membrane is facilitated by a specific glucose transporter called GLUT1. An anion exchange protein facilitates the reciprocal transport of chloride (Cl^-) and bicarbonate (HCO_3^-).



(c) **Facilitated diffusion mediated by channel proteins.** Aquaporin channel proteins can facilitate the rapid inward or outward movement of water molecules.

(d) **Active transport.** Driven by the hydrolysis of ATP, the Na^+/K^+ pump moves three sodium ions outward for every two potassium ions moved inward, establishing an electrochemical potential across the plasma membrane for both ions.

Important Transport Processes of the Erythrocyte

Table 8-1 Comparison of Simple Diffusion, Facilitated Diffusion, and Active Transport

Properties	Simple Diffusion	Facilitated Diffusion	Active Transport
Solutes transported			
	Small polar (H_2O, glycerol)	Small polar (H_2O, glycerol)	
	Small nonpolar (O_2, CO_2)	Large polar (glucose)	Large polar (glucose)
	Large nonpolar (oils, steroids)	Ions (Na^+, K^+, Ca^{2+})	Ions (Na^+, K^+, Ca^{2+})
Thermodynamic properties			
Direction relative to electrochemical gradient	Down	Down	Up
Metabolic energy required	No	No	Yes
Intrinsic directionality	No	No	Yes
Kinetic properties			
Membrane protein required	No	Yes	Yes
Saturation kinetics	No	Yes	Yes
Competitive inhibition	No	Yes	Yes

Simple diffusion

- Simple diffusion is that the net rate of transport for a specific substance is directly proportional to the concentration difference for that substance across the membrane over a broad concentration range.

- For the diffusion of solute S from the outside to the inside of a cell, the expression for the rate, or velocity, of inward diffusion through the membrane:

$$V_{inward} = P A [S]$$

where V_{inward} is the rate of inward diffusion (in moles/square cm second of membrane surface), and $\Delta[S]$ is the concentration gradient of the solute across the membrane and P is the permeability coefficient

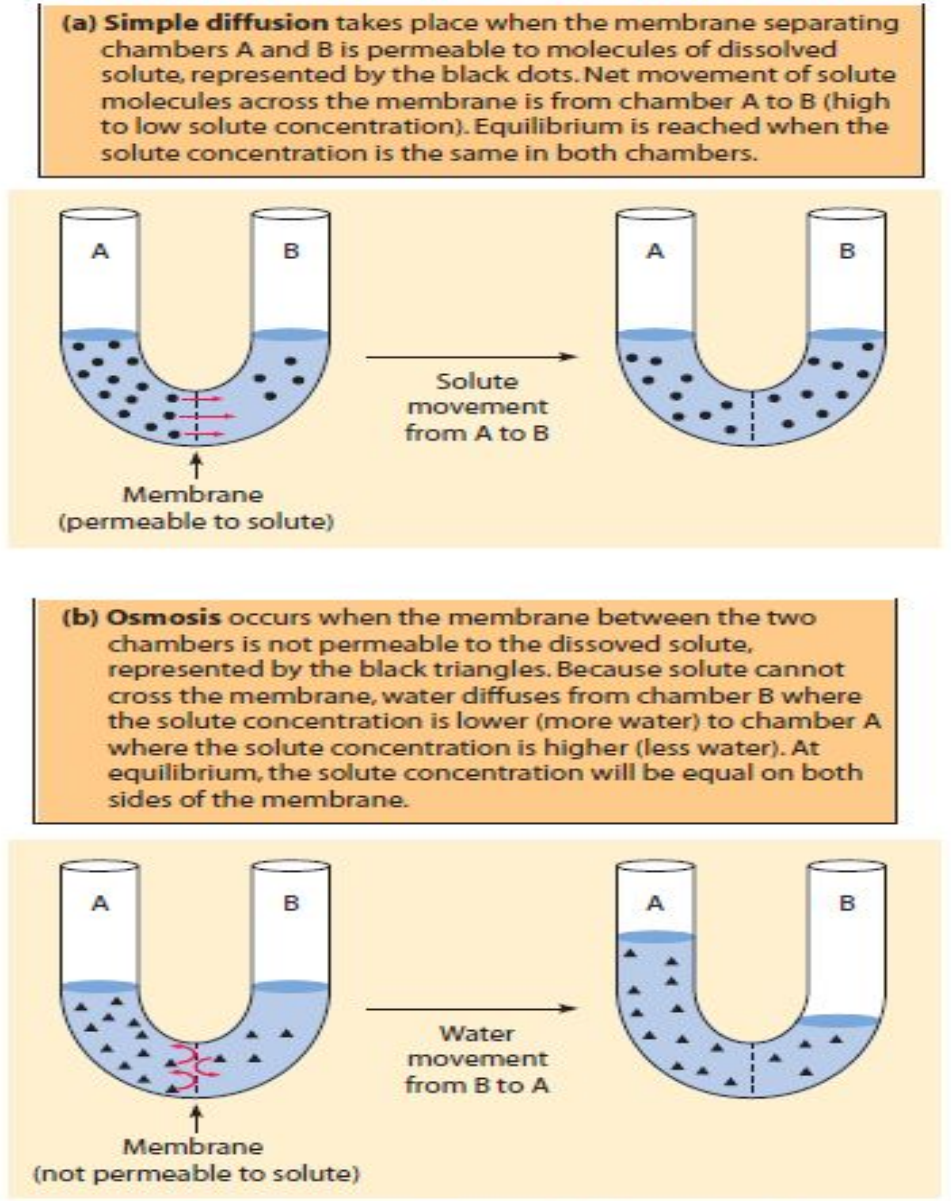


FIGURE 8-4 Comparison of Simple Diffusion and Osmosis. In both examples shown, there is initially more solute in chamber A than in chamber B. The membrane in example **(a)** is permeable to the solute and the membrane in example **(b)**, like a typical cell membrane, is not.

Facilitated diffusion

Facilitated 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 electrical potential across the membrane

Two classes of proteins that mediate facilitated diffusion have generally been distinguished: **carrier proteins and channel proteins**.

Carrier proteins bind specific molecules to be transported on one side of the membrane. They then undergo conformational changes that allow the molecule to pass through the membrane and be released on the other side.

In contrast, **channel proteins** form open pores through the membrane, allowing the free diffusion of any molecule of the appropriate size and charge.

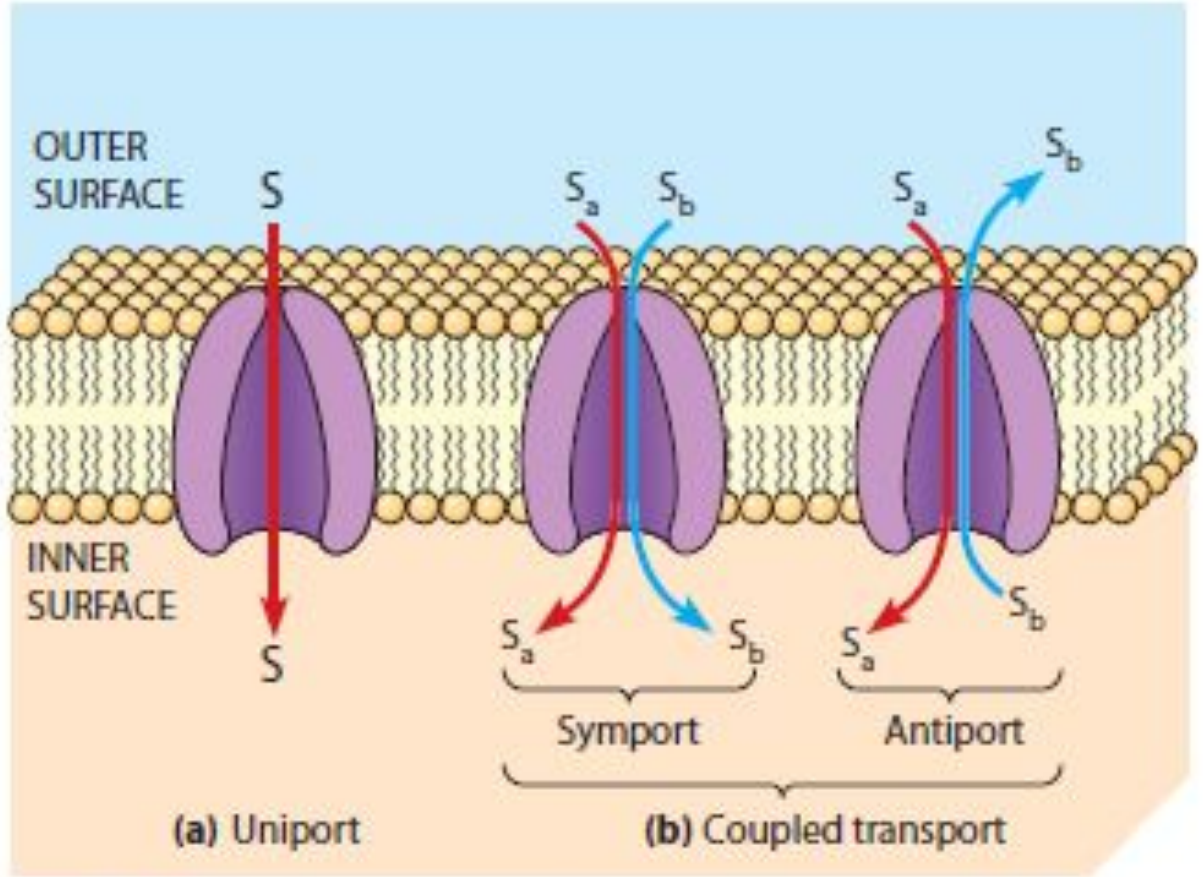


FIGURE 8-6 Comparison of Uniport, Symport, and Antiport Transport by Carrier Proteins. **(a)** In uniport, a membrane transport protein moves a single solute across a membrane. **(b)** Coupled transport involves the simultaneous transport of two solutes, S_a and S_b. Coupled transport may be either symport (both solutes moved in the same direction) or antiport (the two solutes moved in opposite directions). Note that transporters are not simply open channels, as depicted in this simplified illustration, but alternate between two conformations as solutes are transported.

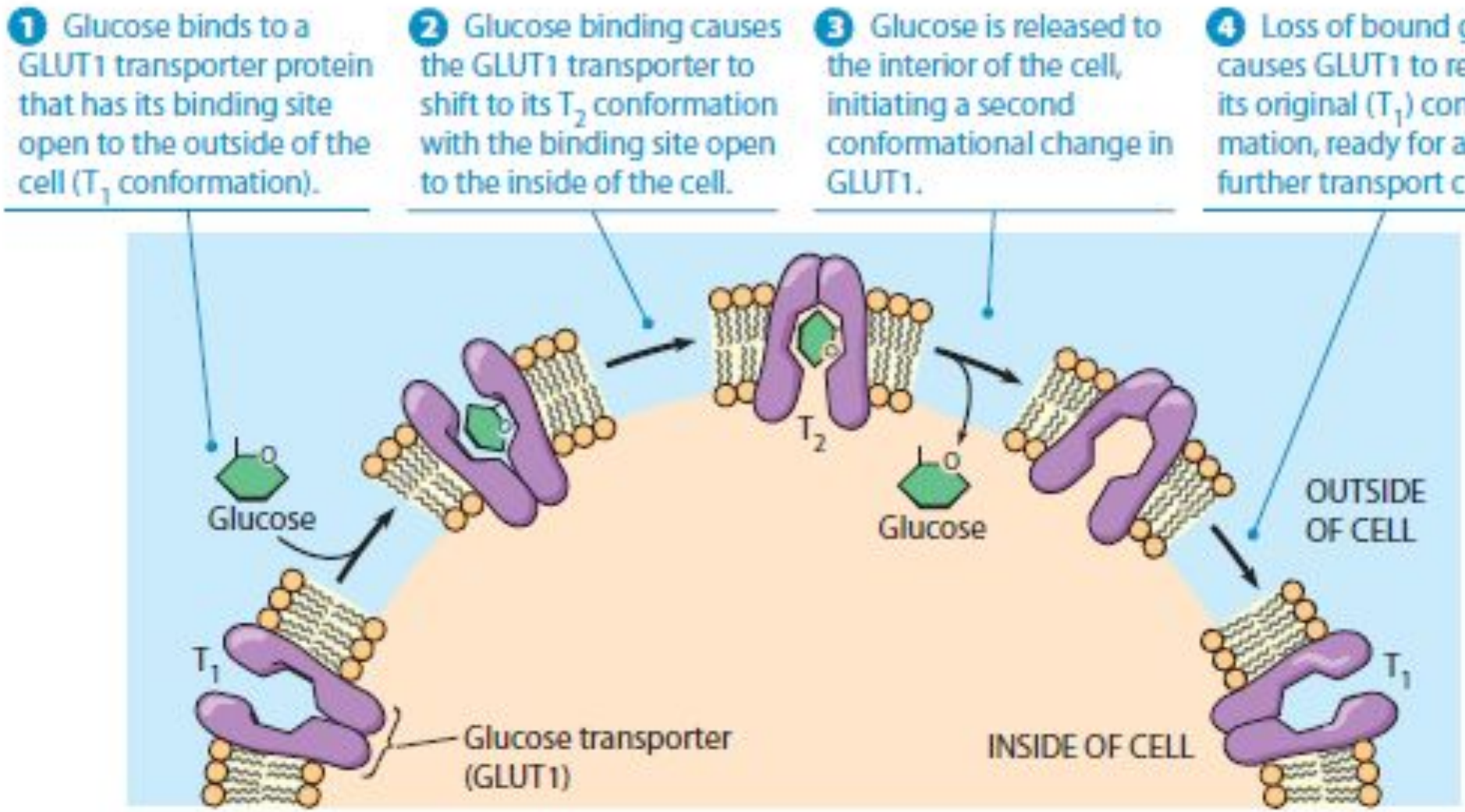


FIGURE 8-7 The Alternating Conformation Model for Facilitated Diffusion of Glucose by the Glucose Transporter GLUT1 in the Erythrocyte Membrane. The inward transport of glucose by GLUT1 is shown here in four steps, arranged at the periphery of a cell.

Channel proteins

One group of **channel proteins** discussed earlier is the porins, which permit the free passage of ions and small polar molecules through the outer membranes of bacteria, mitochondria, and chloroplasts. **Gap junctions**, contain channel proteins that permit the passage of molecules between connected cells.

The best-characterized channel proteins are the **ion channels**, which mediate the passage of ions across plasma membranes. Three properties of ion channels are central to their function:

- Transport through channels is **extremely rapid**.
- Ion channels are **highly selective** because narrow pores in the channel restrict passage to ions of the appropriate size and charge
- Most ion channels are **not permanently open**. Instead, the opening of ion channels is regulated by "gates" that transiently open in response to specific stimuli. Some channels (called ligand-gated channels) open in response to the binding of neurotransmitters or other signaling molecules; others (voltage-gated channels) open in response to changes in electric potential across the plasma membrane.

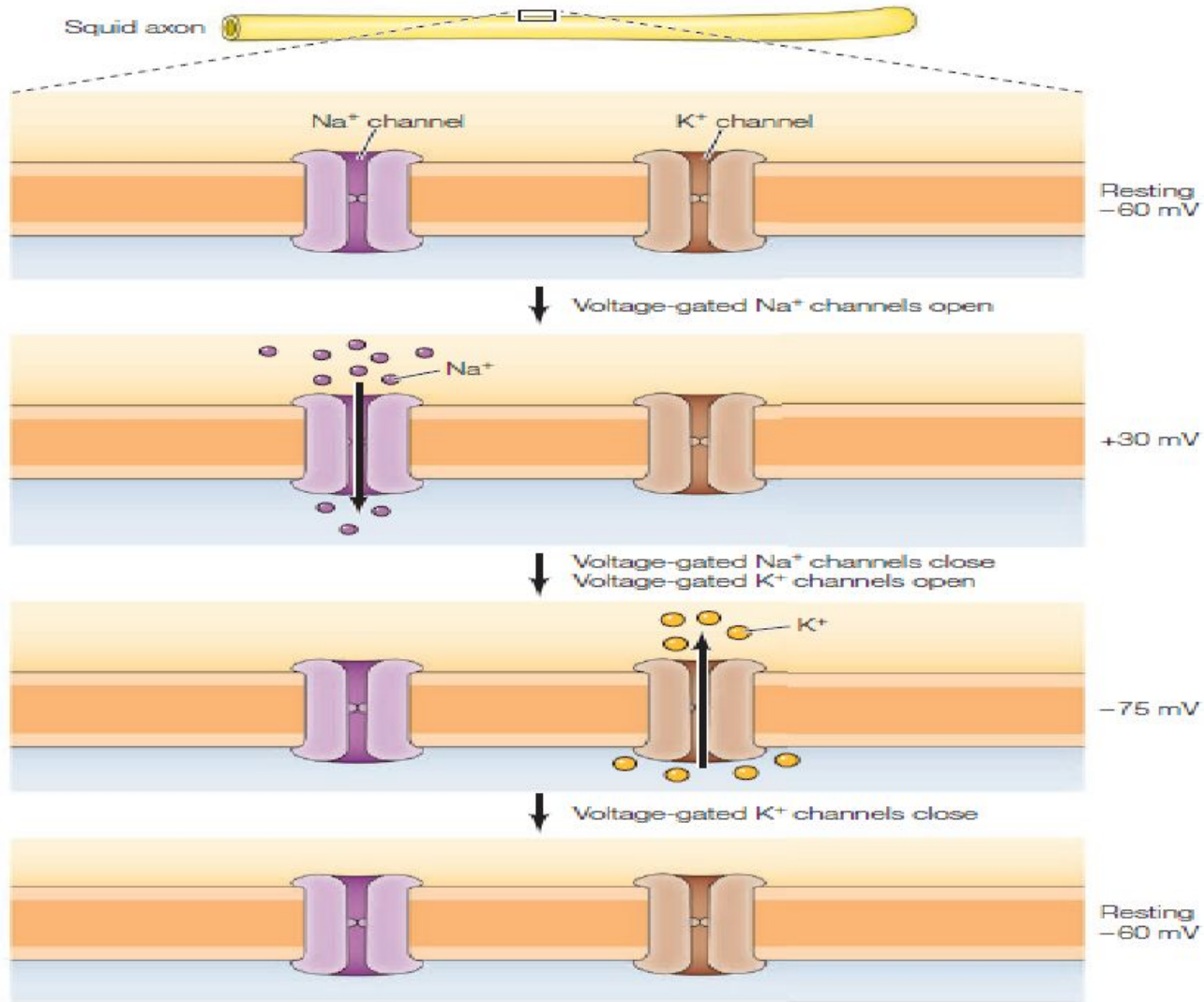


Figure 15.18 Membrane potential and ion channels during an action potential The membrane potential first increases as voltage-gated Na^+ channels open. The membrane potential then falls below its resting value as the Na^+ channels are inactivated and voltage-gated K^+ channels open. The voltage-gated K^+ channels are then inactivated, and the membrane potential returns to its resting value.

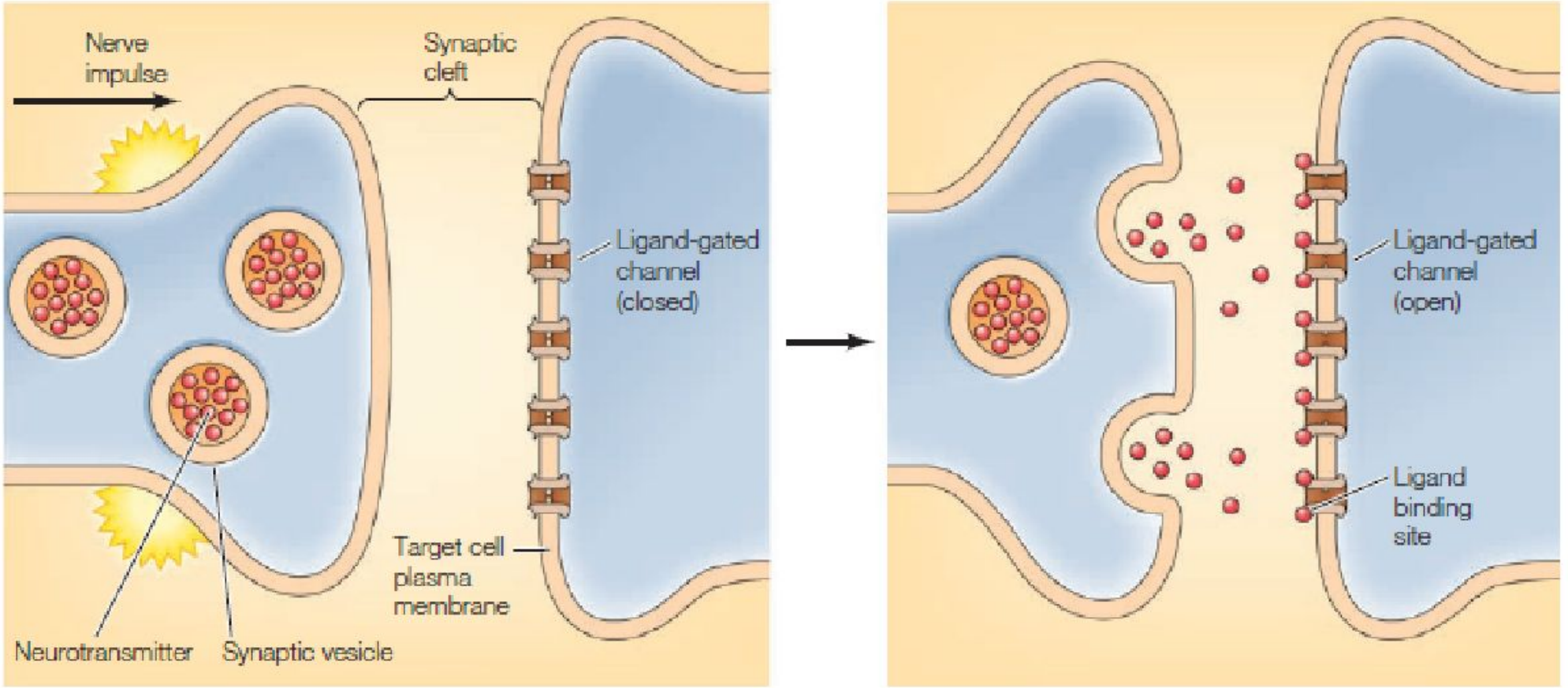


Figure 15.19 Signaling by neurotransmitter release at a synapse
The arrival of a nerve impulse at the terminus of the neuron signals the fusion of synaptic vesicles with the plasma membrane, resulting in the release of neurotransmitters from the presynaptic cell into the synaptic cleft. The neurotransmitter binds to receptors and opens ligand-gated ion channels in the target cell plasma membrane.

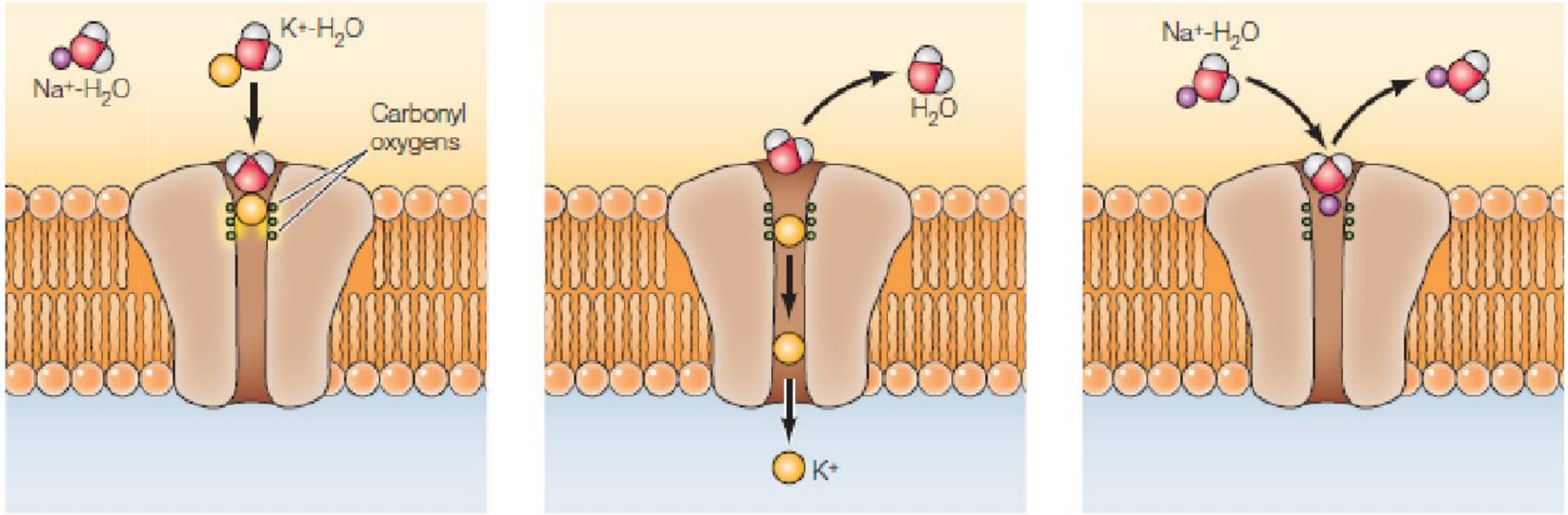


Figure 15.22 Selectivity of K^+ channels The K^+ channel contains a narrow selectivity filter lined with carbonyl oxygen (C=O) atoms. The pore is just wide enough to allow the passage of dehydrated K^+ from which all associated water molecules have been displaced as a result of interactions between K^+ 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.

Active transport driven by ATP hydrolysis

- In active transport, energy provided by another coupled reaction (such as the hydrolysis of ATP) is used to drive the uphill transport of molecules in the energetically unfavorable direction.
- The ion pumps responsible for maintaining gradients of ions across the plasma membrane provide important examples of active transport driven directly by ATP hydrolysis.
- These ion gradients are maintained by the Na_+-K_+ pump (also called the Na_+-K_+ ATPase), which uses energy derived from ATP hydrolysis to transport Na_+ and K_+ against their electrochemical gradients.
- This process is a result of **ATP-driven conformational changes in the pump**

(a) Direct active transport involves a transport system coupled to an exergonic chemical reaction, most commonly the hydrolysis of ATP. As shown here, ATP hydrolysis drives the outward transport of protons, thereby establishing an electro-chemical potential for protons across the membrane.

(b) Indirect active transport involves the coupled transport of a solute S and ions—protons, in this case. The exergonic inward movement of protons provides the energy to move the transported solute, S, against its concentration gradient or electrochemical potential.

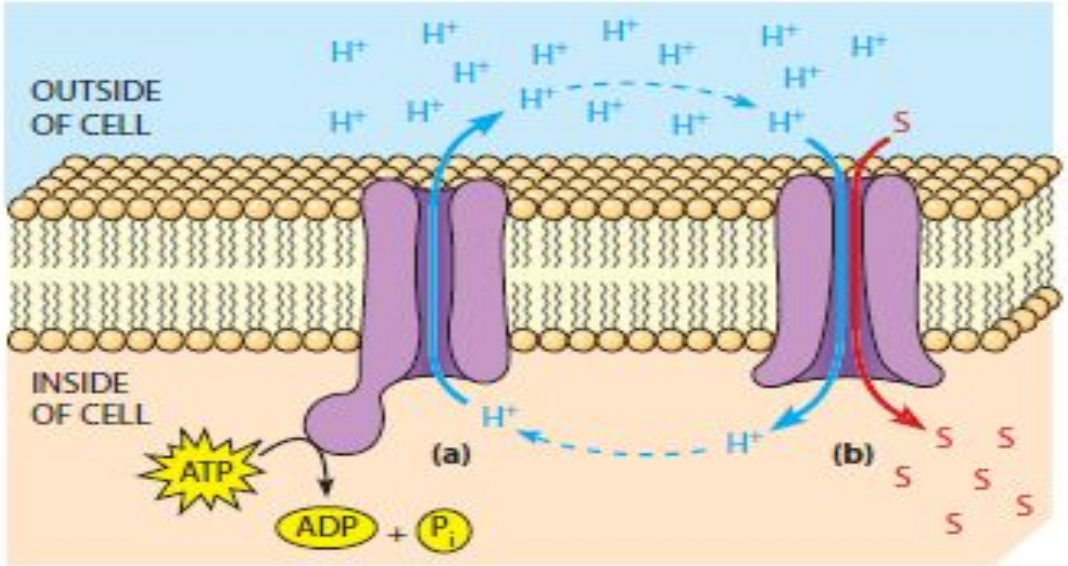


FIGURE 8-9 Comparison of Direct and Indirect Active Transport. Note the circulation of protons across the membrane that results from the coupling of direct and indirect mechanisms of active transport. Note also that transporters are not simply open channels, as depicted in the simplified illustration.

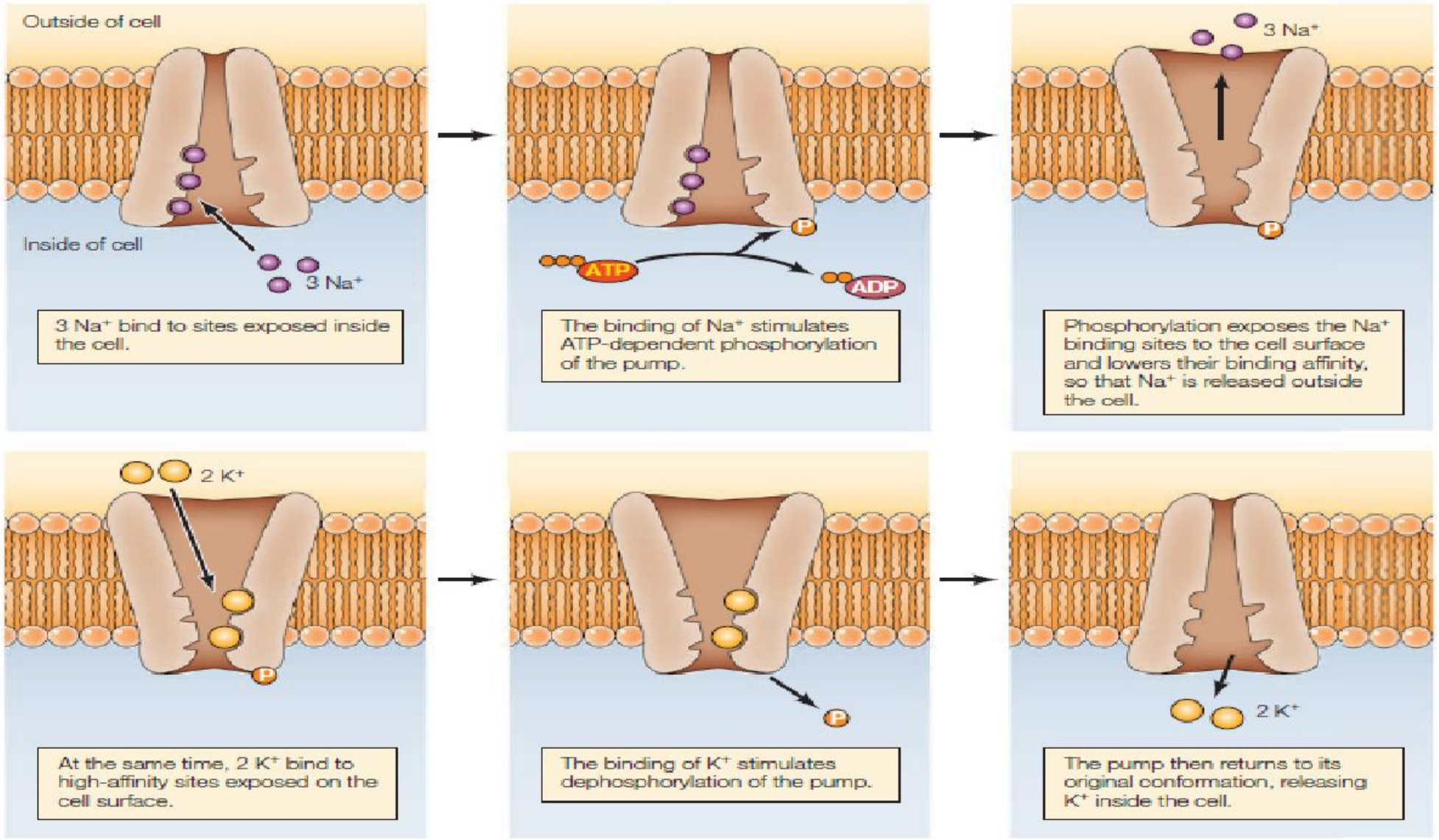


Figure 15.24 Model for operation of the Na^+-K^+ pump

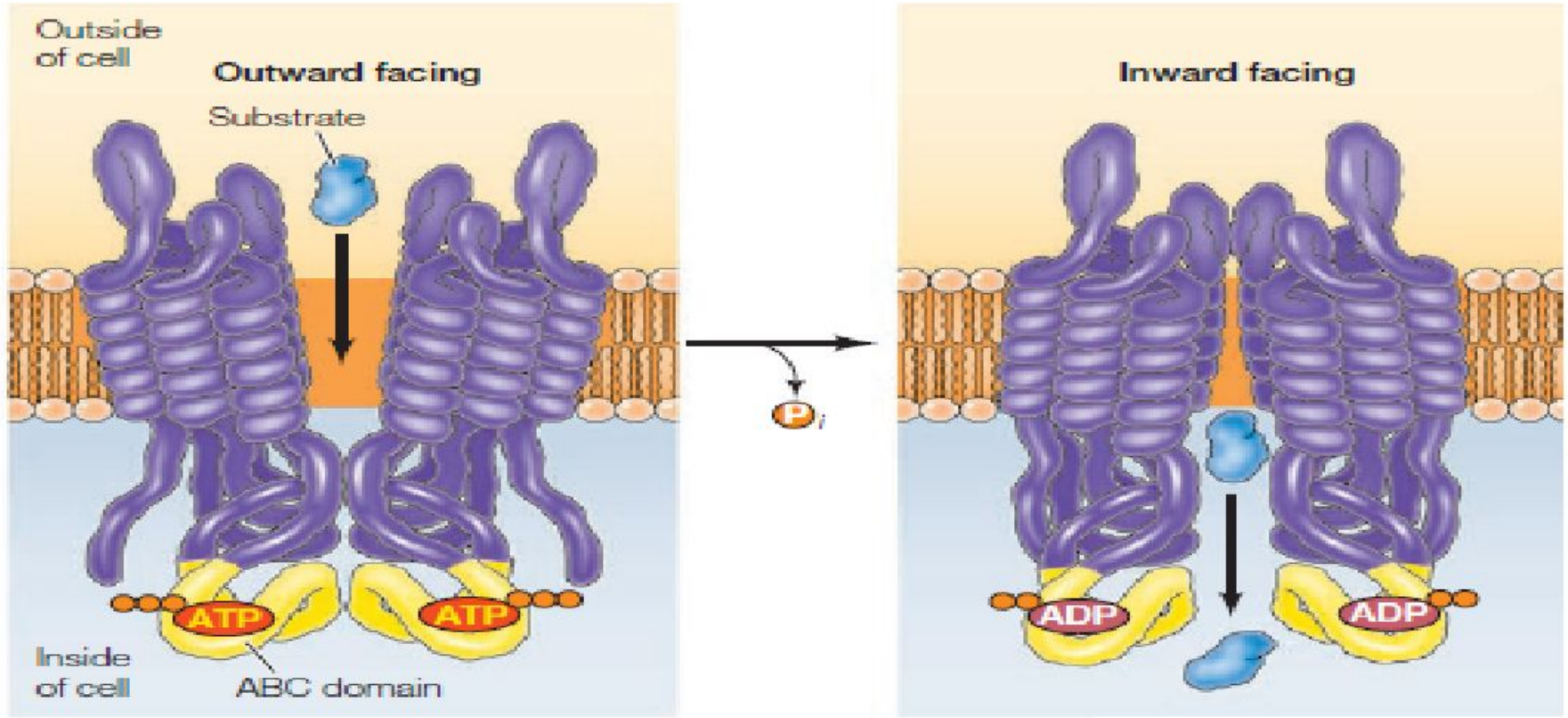


Figure 15.26 Model of active transport by an ABC transporter The transporter consists of two transmembrane domains (each containing six membrane-spanning α helices) and two cytosolic ATP-binding domains (ABC domains). The transporter illustrated is an importer, with its substrate-binding site facing outward with ATP bound to the ABC domain. Hydrolysis of ATP to ADP changes the conformation of the transporter, releasing its substrate inside the cell.

Table 8-2 Main Types of Transport ATPases (Pumps)

Solutes Transported	Kind of Membrane	Kind of Organisms	Example of ATPase function
P-type ATPases (P for "phosphorylation")			
P_1			
K^+, Cu^+, Zn^{2+}, Cd^{2+}, Pb^{2+}	Plasma membrane	Bacteria, archaea, plants, fungi, animals	Transport of potassium or heavy metal ions
P_2			
Ca^{2+}/H^+	SR* or plasma membrane	Eukaryotes	Keeps $[Ca^{2+}]$ low in cytosol
Na^+/K^+	Plasma membrane	Animals	Maintains membrane potential (−60 mV)
H^+/K^+	Plasma membrane	Animals	Pumps H^+ to acidify stomach
P_3			
H^+	Plasma membrane	Plants, fungi	Pumps protons out of cell to generate membrane potential (−180 mV)
P_4			
Phospholipids	Plasma membrane	Eukaryotes	Flippases that maintain asymmetry in the lipid bilayer
P_5			
Various cations	ER, vacuole, lysosome	Eukaryotes	Not well characterized
V-type ATPases (V for "vacuole")			
H^+	Lysosomes, secretory vesicles	Animals	Keeps pH of compartment low, which activates hydrolytic enzymes
	Vacuolar membrane	Plants, fungi	
F-type ATPases (F for "factor"); also called ATP synthases			
H^+	Inner mitochondrial membrane	Eukaryotes	Uses H^+ gradient to drive ATP synthesis
	Plasma membrane	Bacteria	
	Thylakoid membrane	Plants	
ABC-type ATPases (ABC for "ATP-binding cassette")			
Importers A variety of solutes**	Plasma membrane, organellar membranes	Bacteria	Nutrients such as vitamin B_{12}
Exporters Antitumor drugs, toxins, antibiotics, lipids	Plasma membrane	Bacteria, archaea, eukaryotes	Multidrug resistance transporter removes drugs and antibiotics from cell