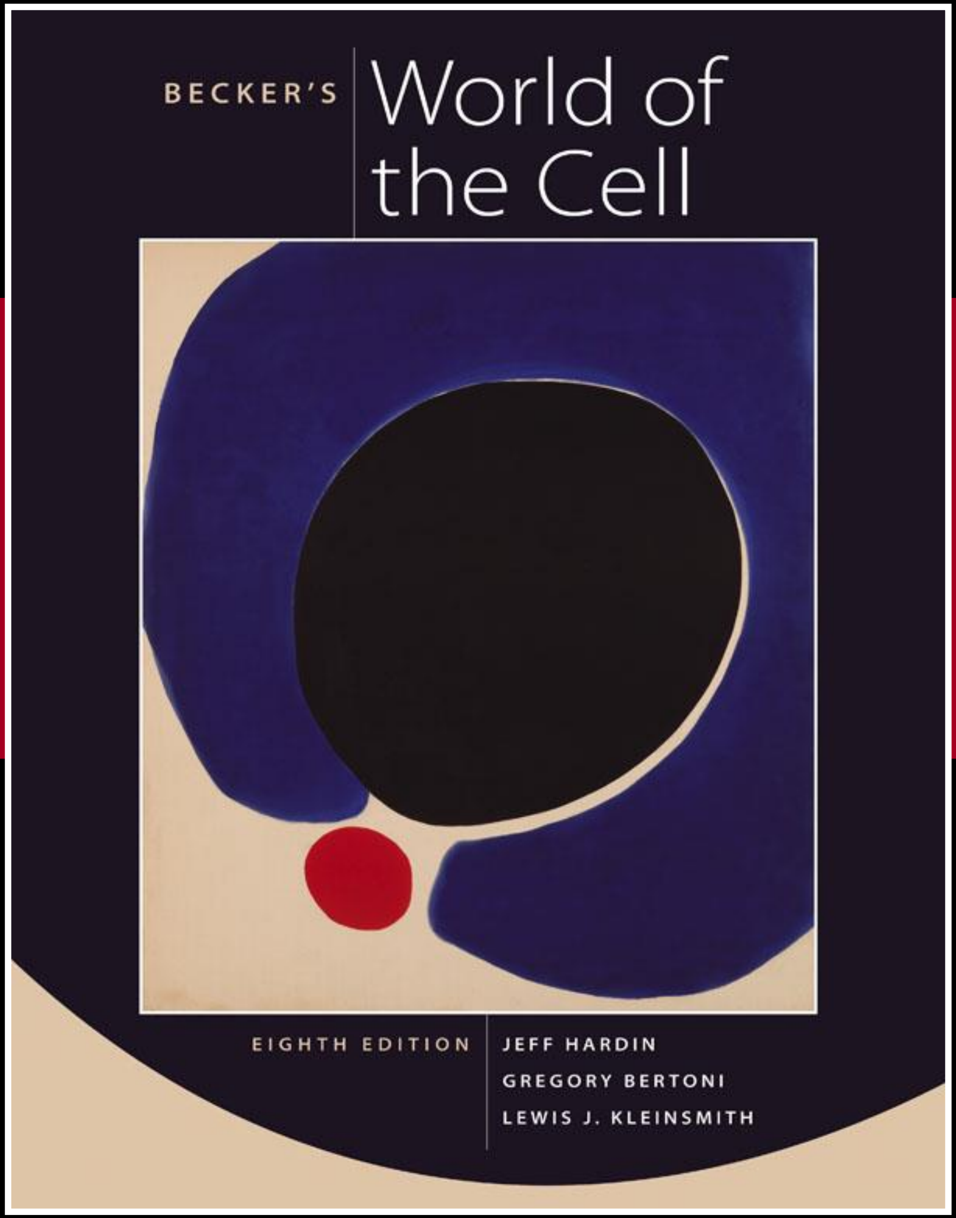


Chapter 8

Transport Across Membranes

Lectures by
Kathleen Fitzpatrick
Simon Fraser University

Transport Across Membranes: Overcoming the Permeability Barrier

- Overcoming the permeability barrier of cell membranes is crucial to proper functioning of the cell
- Specific molecules and ions need to be selectively moved into and out of the cell or organelle
- Membranes are *selectively permeable*

Cells and Transport Processes

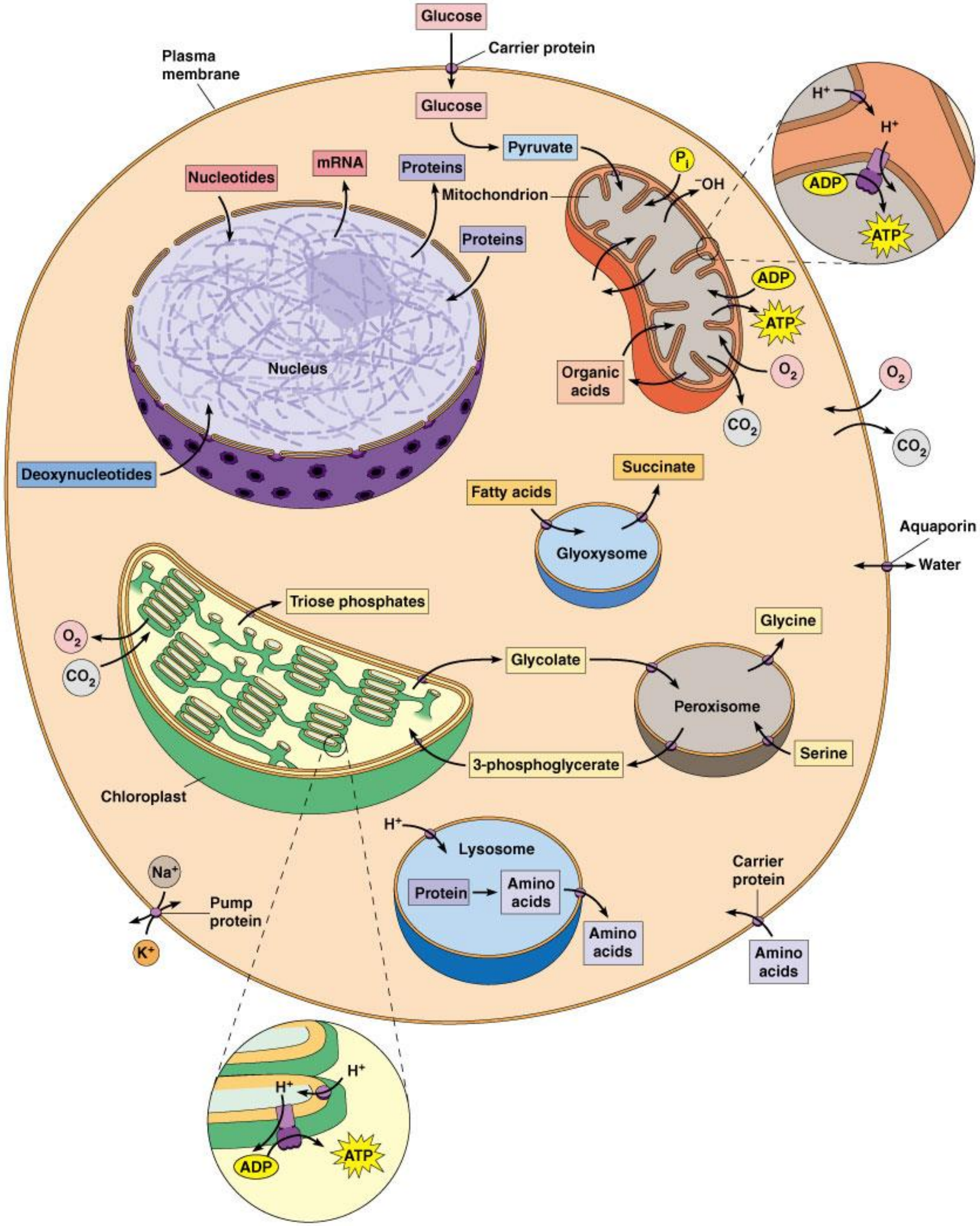
- Cells and cellular compartments are able to **accumulate** a variety of substances in concentrations that are very different from those of the surroundings

- Most of the substances that move across membranes are dissolved gases, ions, and small organic molecules; *solutes*

Transport is central to cell function

- A central aspect of cell function is selective **transport,** the movement of ions or small organic molecules (*metabolites*; components of metabolic pathways)

Figure 8-1



Glucose
Carrier protein
Plasma membrane
Glucose
Pyruvate
Nucleotides
mRNA
Proteins
Mitochondrion
Proteins
P_i
^-OH
H^+
H^+
ADP
ATP
ADP
ATP
Nucleus
Organic acids
O_2
O_2
CO_2
CO_2
Deoxynucleotides
Succinate
Fatty acids
Glyoxysome
Aquaporin
Water
Triose phosphates
O_2
CO_2
Glycine
Glycolate
Peroxisome
3-phosphoglycerate
Serine
Chloroplast
H^+
Lysosome
Carrier protein
Na^+
Pump protein
Protein
Amino acids
Amino acids
Amino acids
K^+
H^+
H^+
ADP
ATP

Solutes Cross Membranes by Diffusion (Simple or Facilitated), Active Transport and vesicular transport

- Quite different mechanisms are involved in moving solutes across membranes
- A few molecules cross membranes by *simple diffusion*, the direct unaided movement dictated by differences in concentration of the solute on the two sides of the membrane
- However, most solutes cannot cross the membrane this way

Transport proteins

- *Transport proteins* assist most solute across membranes

- These **integral membrane proteins** recognize the substances to be transported with great **specificity**

- Some move solutes to regions of lower concentration; this *facilitated diffusion* (or *passive transport)* uses no energy

Active transport

- In other cases, transport proteins move solutes against the concentration gradient; this is called *active transport*
- Active transport requires energy such as that released by the hydrolysis of ATP or by the simultaneous transport of another solute down an energy gradient

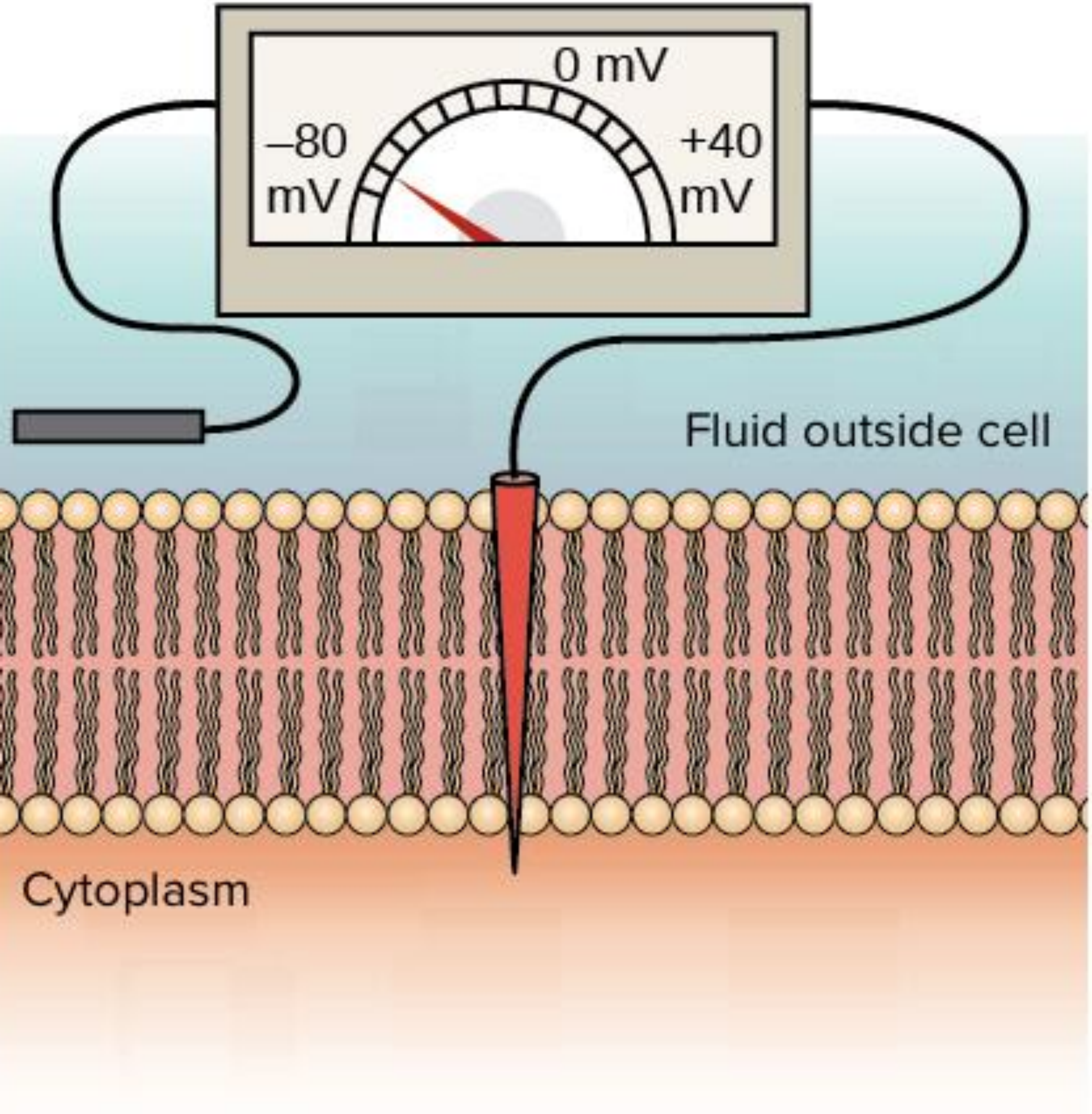
The Movement of a Solute Across a Membrane Is Determined by Its Concentration Gradient or Its Electrochemical Potential

- The movement of a molecule that has no net charge is determined by its **concentration gradient**
- Simple or facilitated diffusion involve **exergonic movement** "down" the concentration gradient (negative ΔG)
- Active transport involves **endergonic movement** "up" the concentration gradient (positive ΔG)

The electrochemical potential

- The movement of an **ion** is determined by its **electrochemical potential**, the combined effect of its concentration gradient and the charge gradient across the membrane

- The active transport of ions across a membrane creates a charge gradient or **membrane potential** (V_m) across the membrane


0 mV
–80
mV
+40
mV
Fluid outside cell
Cytoplasm

Active transport of ions

- Most cells have an excess of negatively charged solutes inside the cell
- This charge difference favors the inward movement of cations such as Na^+ and outward movement of anions such as Cl^-
- In all organisms, active transport of ions across the plasma membrane results in **asymmetric distribution of ions inside and outside the cell**

The Erythrocyte Plasma Membrane Provides Examples of Transport Mechanisms

- The transport proteins of the **erythrocyte** plasma membrane are among the best understood of all such proteins
- The membrane potential is maintained by active transport of **potassium ions inward and sodium ions outward**
- Special pores or *channels* allow **water** and **ions** to enter or leave the cell rapidly as needed

Simple Diffusion: Unassisted Movement Down the Gradient

- The most straightforward way for a solute to cross a membrane is through **simple diffusion**, the unassisted net movement of a solute from high to lower concentration

- Typically this is only possible for gases, nonpolar molecules, or small polar molecules such as water, glycerol, or ethanol

Oxygen and the function of erythrocytes

- Oxygen gas traverses the lipid bilayer readily by simple diffusion

- Erythrocytes take up oxygen in the lungs, where oxygen concentration is high, and release it in the body tissues, where oxygen concentration is low

Figure 8-3A

(a) In the capillaries of body tissues (low [O_2] and high [CO_2] relative to the erythrocytes), O_2 is released by hemoglobin within the erythrocytes and diffuses outward to meet tissue needs. CO_2 diffuses inward and is converted to bicarbonate by carbonic anhydrase in the cytosol. Bicarbonate ions are transported outward by the anion exchange protein, accompanied by the inward movement of chloride ions to maintain charge balance. Carbon dioxide therefore returns to the lungs as bicarbonate ions.

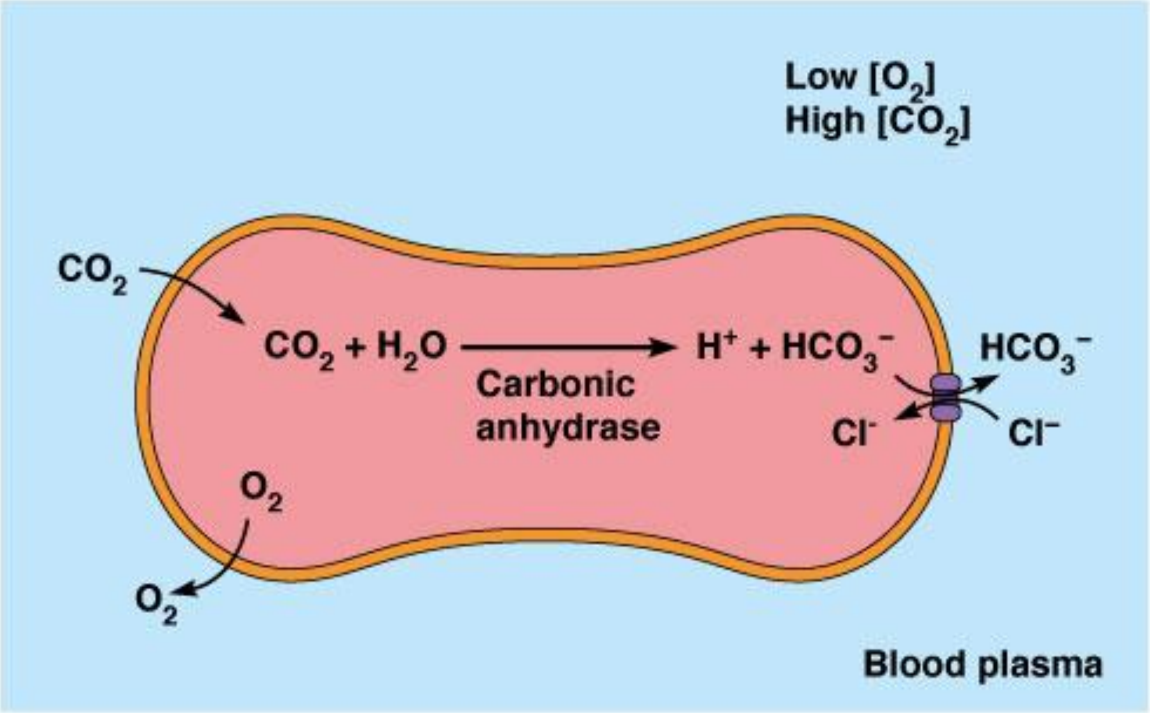
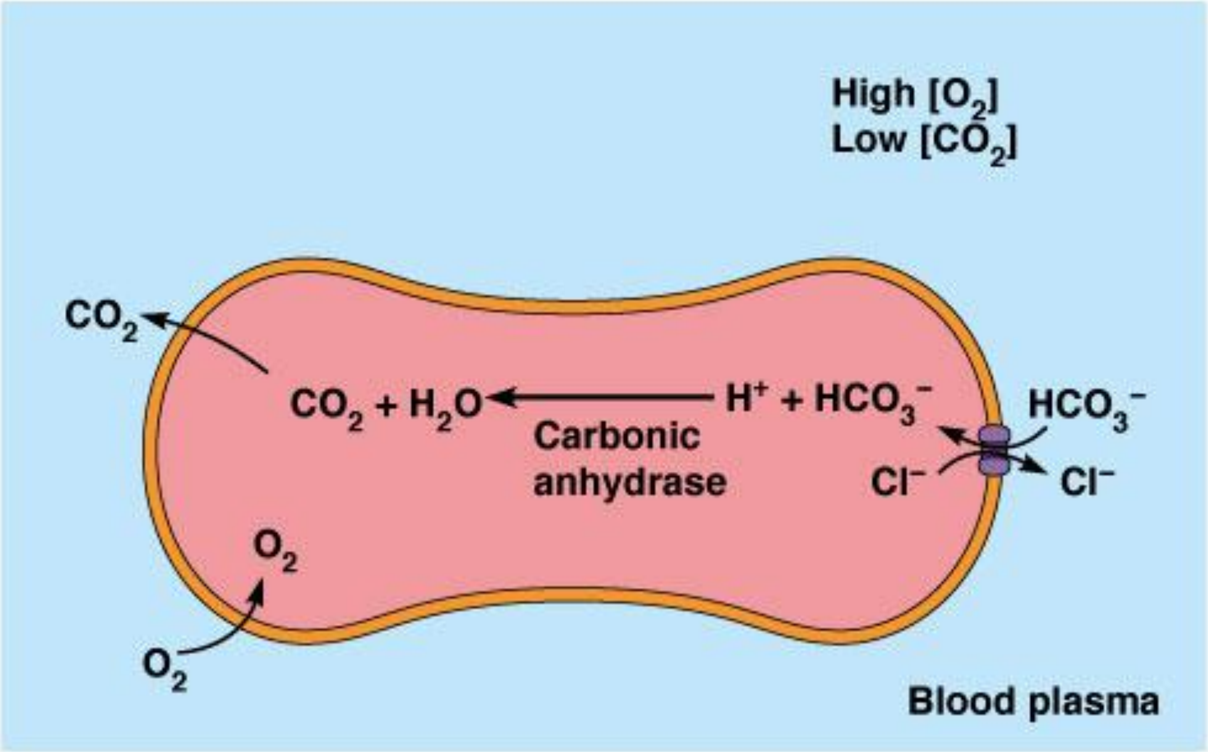


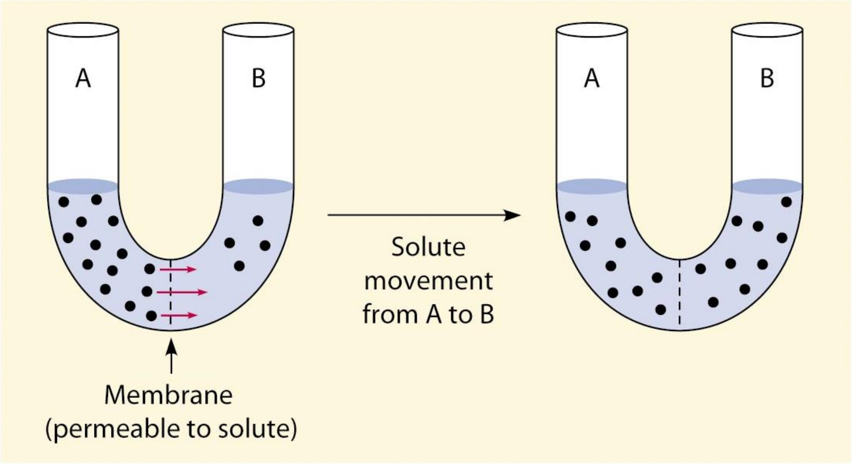
Figure 8-3B



(b) In the capillaries of the lungs (high $[O_2]$ and low $[CO_2]$ relative to the erythrocytes), O_2 diffuses inward and binds to hemoglobin. Bicarbonate moves inward from the blood plasma, accompanied by an outward movement of chloride ions. Incoming bicarbonate is converted into CO_2, which diffuses out of the erythrocytes and into the cells lining the capillaries of the lungs. The CO_2 is now ready to be expelled from the body.

Diffusion Always Moves Solutes Toward Equilibrium

- Diffusion always tends to create a random solution in which the concentration is the same everywhere



- Solutes will move toward regions of lower conc until the concs are equal

- Thus diffusion is always *movement toward equilibrium*

Osmosis Is the Diffusion of Water Across a Selectively Permeable Membrane

- Water diffuses from areas of **lower solute concentration** to areas of **higher solute concentration**
- In cells, water tends to move inward in a **controlled** manner
- Water molecules are **uncharged** and so are not affected by the membrane potential

Osmosis

- If two solutions are separated by a *selectively permeable membrane*, permeable to the water but not the solutes, the water will move toward the region of higher solute concentration
- For most cells, water tends to move inward

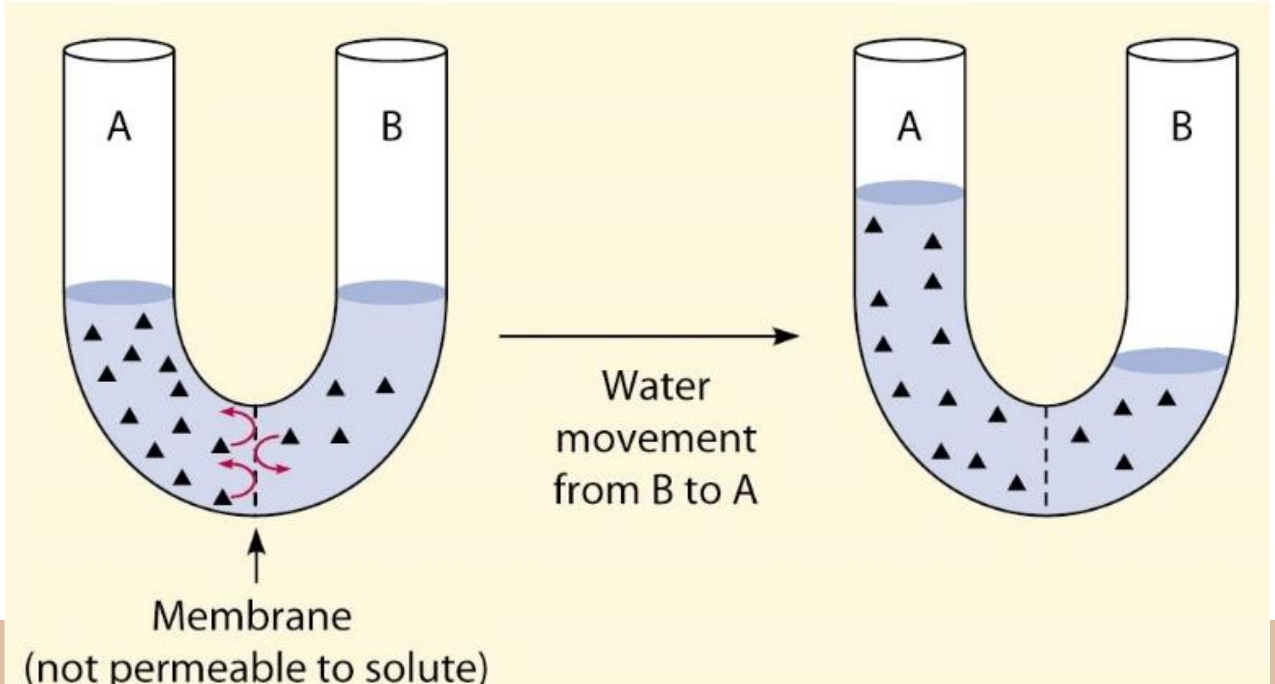
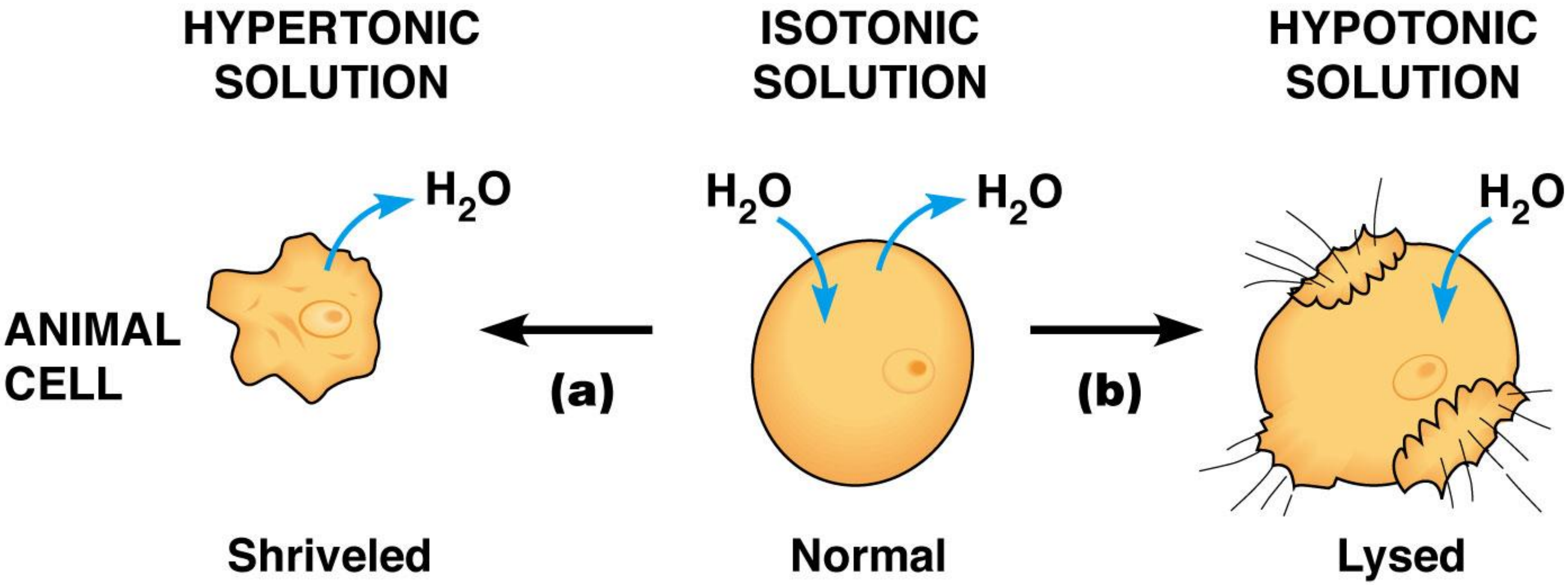
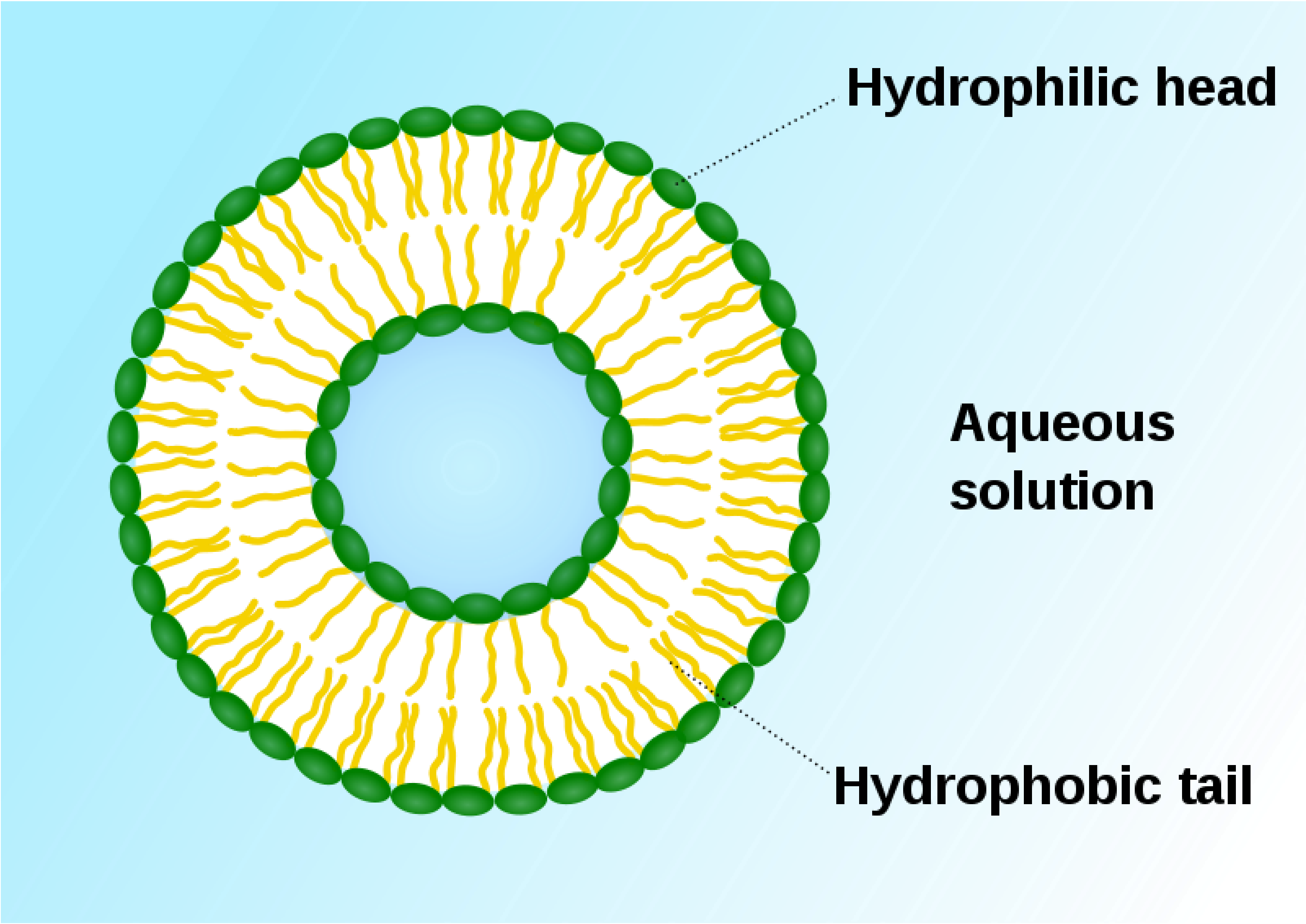


Figure 8-8A-1


HYPERTONIC SOLUTION
ISOTONIC SOLUTION
HYPOTONIC SOLUTION
ANIMAL CELL
H_2O
H_2O
H_2O
H_2O
(a)
(b)
Shriveled
Normal
Lysed

Simple Diffusion Is Limited to Small, Nonpolar Molecules

Liposomes – extracted lipids from membranes tend to form small vesicles consisting of spherical lipid bilayer


Hydrophilic head
Aqueous
solution
Hydrophobic tail

Simple Diffusion Is Limited to Small, Nonpolar Molecules

Liposomes ➔ trapping solutes and examining escape rates

Entrapped K^+ and Na^+ ions → lasted for days,
O_2 → escaped rapidly (couldn't be measured)

Three main factors affecting diffusion of solutes:
1. size
2. polarity
3. charge

Table 8-2 Factors Governing the Rate of Diffusion Across Lipid Bilayers

Factor	Examples: More Permeable	Examples: Less Permeable	Permeability Ratio*
1. Size: bilayer more permeable to smaller molecules	H_2O (Water)	$H_2N—CO—NH_2$ (Urea)	10^2:1
2. Polarity: bilayer more permeable to nonpolar molecules	$CH_3—CH_2—CH_2—OH$ (Propanol)	$HO—CH_2—CHOH—CH_2—OH$ (Glycerol)	10^3:1
3. Charge: bilayer highly impermeable to ions	O_2 (Oxygen)	OH^- (Hydroxide ion)	10^9:1

*Ratio of diffusion rate for the more permeable solute to the less permeable solute.

Solute Size

- In general, lipid bilayers are more permeable to small molecules—water, oxygen, carbon dioxide—than larger ones (size up to 100 Da)

- But without a transporter even these small molecules move more slowly than in the absence of a membrane

- Still, water diffuses more rapidly than would be expected for a **polar molecule**

Solute Polarity

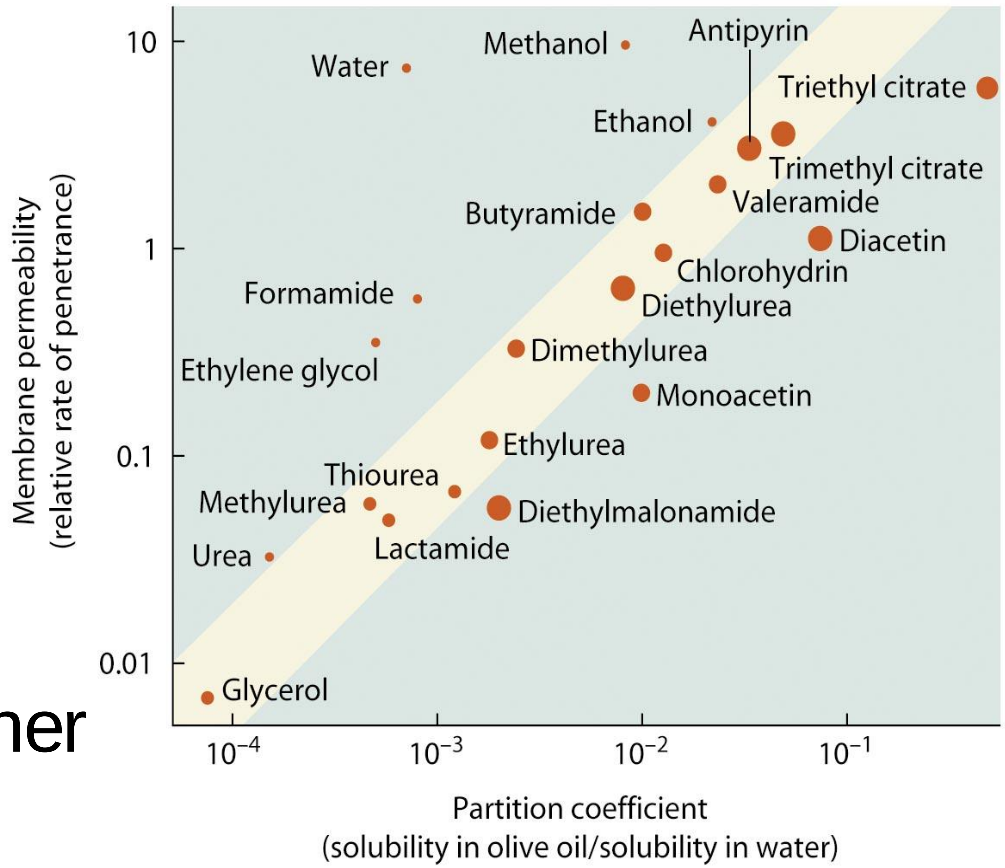
- Lipid bilayers are more permeable to nonpolar substances than to polar ones

- Nonpolar substances dissolve readily into the hydrophobic region of the bilayer

- Large nonpolar molecules such as estrogen and testosterone cross membranes easily, despite their large size

A measure of solute polarity

- Polarity of a solute can be measured by the ratio of its solubility in an organic solvent to its solubility in water
- This is called the *partition coefficient*
- In general, the more nonpolar (hydrophobic) a substance is, the higher the partition coefficient

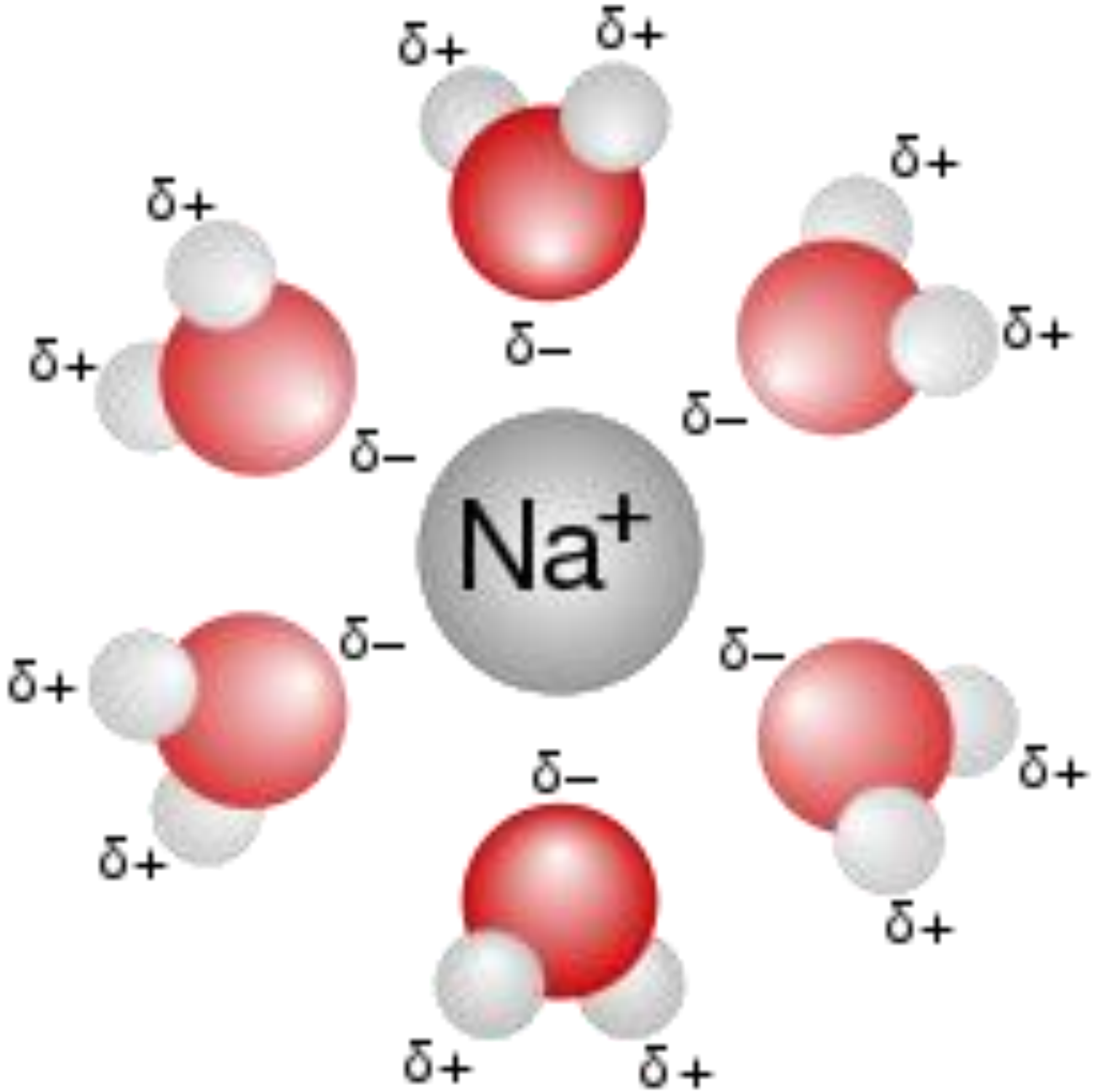


Solute Charge

- The relative impermeability of polar substances, especially ions, is due to their association with water molecules

- The molecules of water form a *shell of hydration* around polar substances

- In order for these substances to move into a membrane, the water molecules must be removed, which requires energy


Na+
δ+
δ–

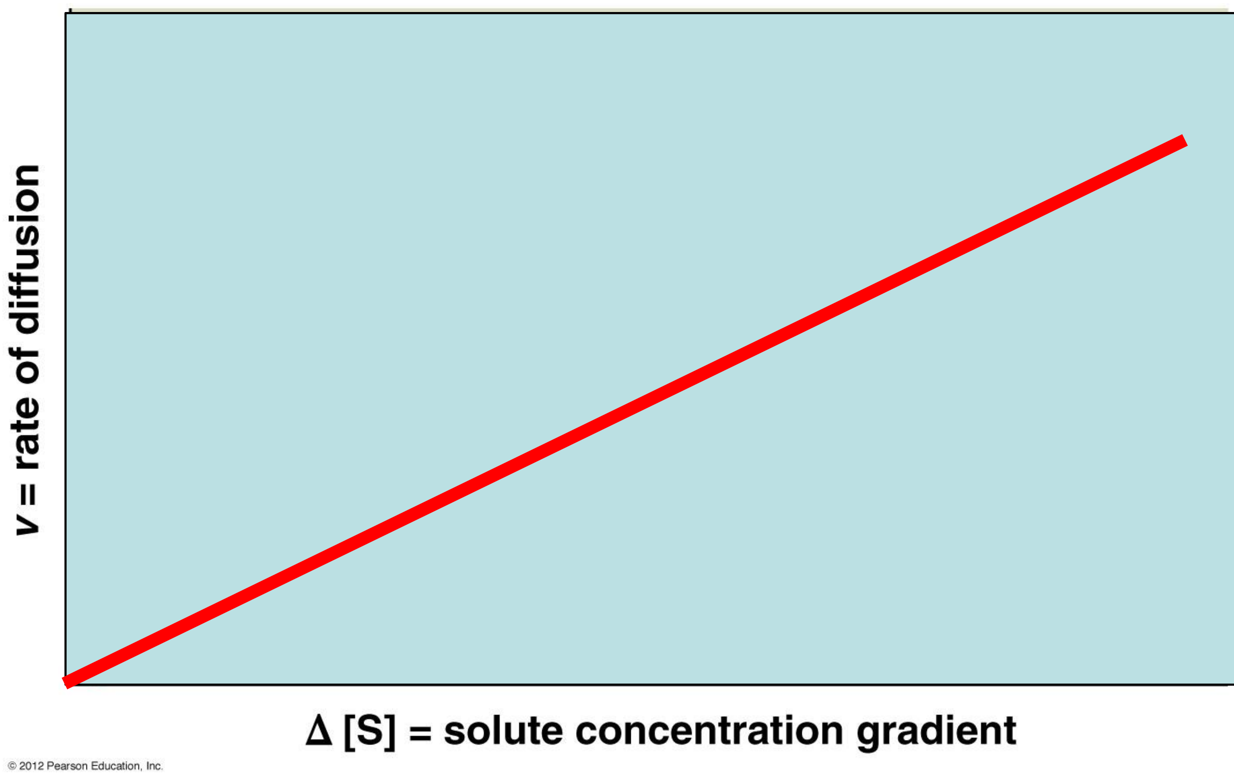
The Rate of Simple Diffusion Is Directly Proportional to the Concentration Gradient

- Thermodynamically, simple diffusion is always an exergonic process, requiring no input of energy

- Kinetically, the net rate of transport for a substance is proportional to its concentration difference across the membrane

- V_{inward} = rate of diffusion in moles/sec.cm^2
- $\Delta[S] = [S]_{outside} - [S]_{inside}$

- Simple diffusion has a linear relationship between inward flux of solute and solute concn



Facilitated Diffusion: Protein-Mediated Movement Down the Gradient

- Most substances in the cell are too large or too polar to cross membranes by simple diffusion
- These can only move in and out of cells with the assistance of **transport proteins**
- If the process is exergonic, it is called **facilitated diffusion;** the solute diffuses as dictated by its concentration gradient

Transport proteins in facilitated diffusion

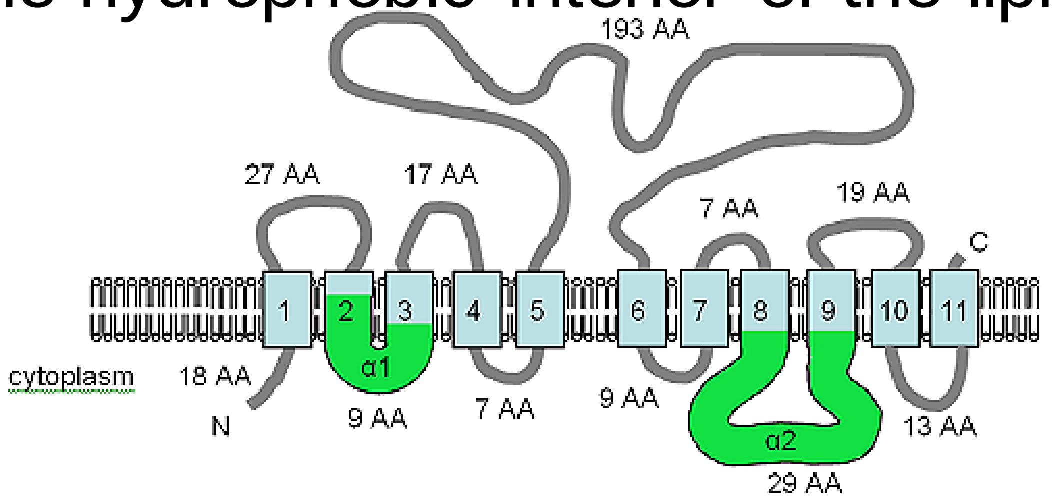
- No input of energy is needed in facilitated diffusion

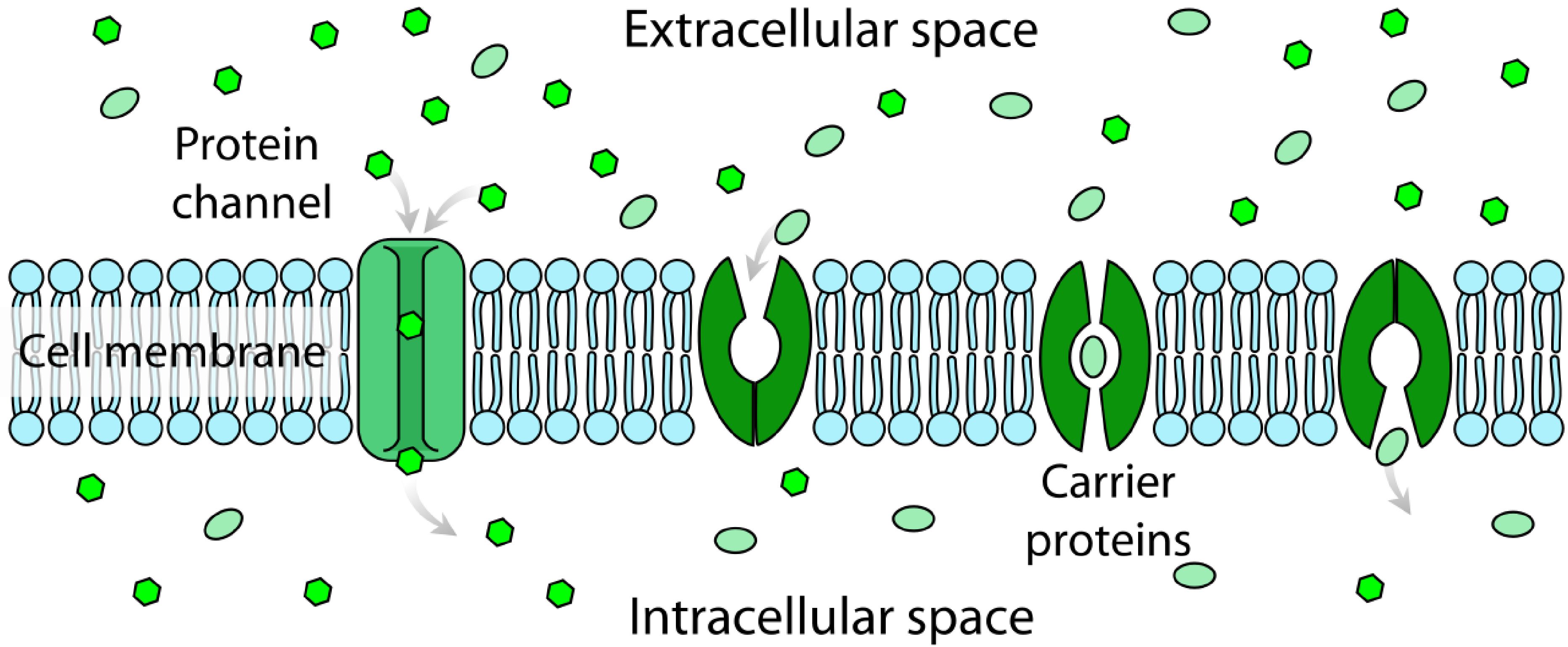
- The role of the transport proteins is just to provide a path through the lipid bilayer, allowing the "downhill" movement of a polar or charged solute

Transport proteins in facilitated diffusion structure

- All membrane transport proteins have been found to be multipass transmembrane proteins.

- These proteins enable specific hydrophilic solutes to cross the membrane without coming into direct contact with the hydrophobic interior of the lipid bilayer.




Extracellular space
Protein
channel
Cell membrane
Carrier
proteins
Intracellular space

Carrier Proteins and Channel Proteins Facilitate Diffusion by Different Mechanisms

- **Channel proteins** form hydrophilic *channels* through the membrane to provide a passage route for solutes
- **Carrier proteins** (*transporters* or *permeases*) bind solute molecules on one side of a membrane, **undergo a conformation change**, and release the solute on the other side of the membrane

Channels

- Some channels are large and nonspecific, such as the *pores* on the outer membranes of bacteria, mitchondria, and chloroplasts

- Pores are formed by transmembrane proteins called *porins* that allow passage of solutes up to a certain size to pass (600 Da)

- Most channels are smaller and highly selective

Ion channels

- Most of the smaller channels are involved in ion transport and are called *ion channels*

- *The movement of solutes through ion channels is much faster than transport by carrier proteins*

- This is likely because conformation changes are not required

A channel protein provides a hydrophilic pore or channel into the membrane, allowing ions to pass through without coming into contact with the membrane's hydrophobic interior.

However, channels cannot be coupled to an energy source to perform active transport so the transport that they mediate is always passive (“downhill”).

Ion Channels: Transmembrane Proteins That Allow Rapid Passage of Specific Ions

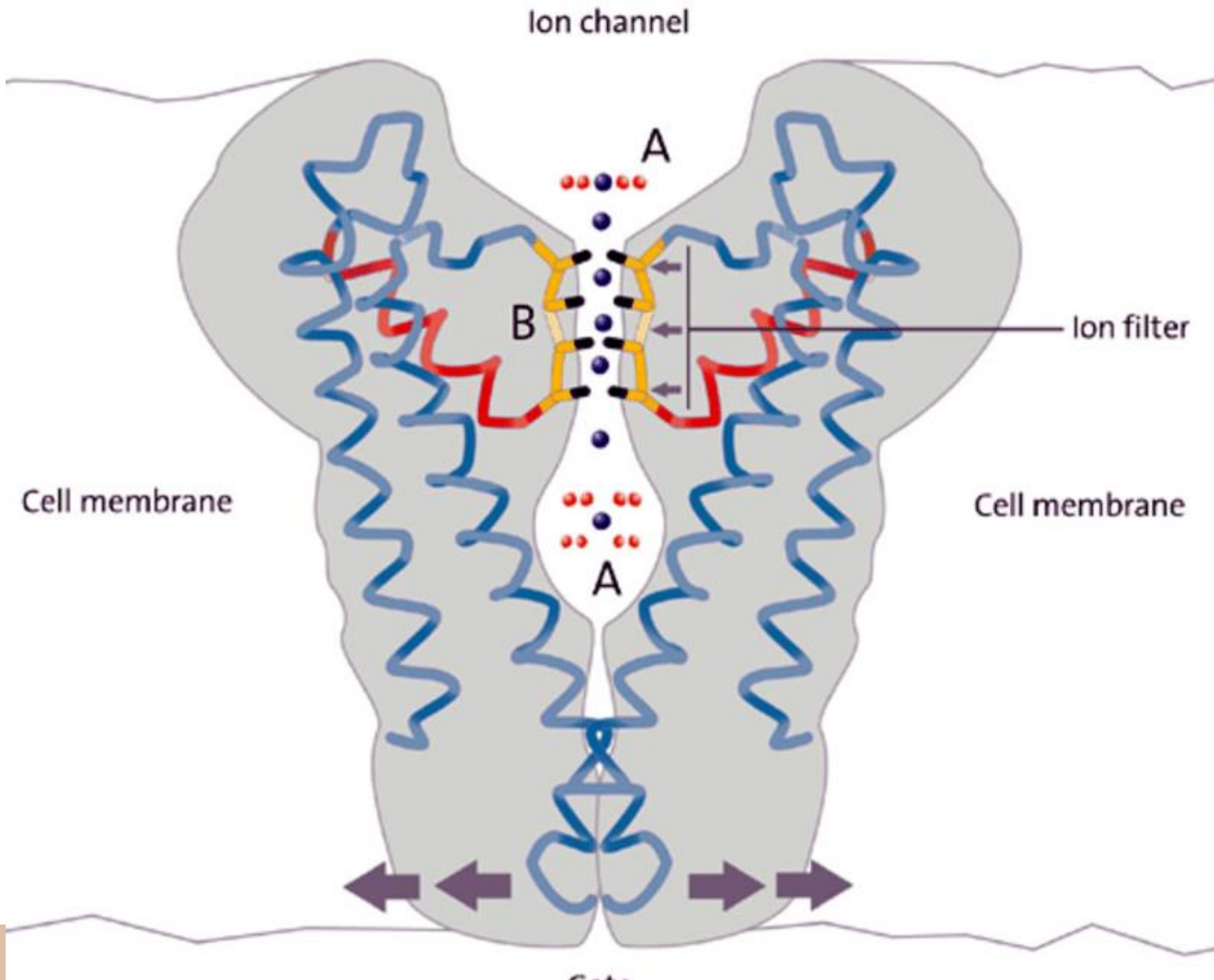
- Because most allow passage of just **one ion**, there are separate proteins needed to transport Na^+, K^+, Ca^{2+}, and $Cl^–$, etc.

- Selectivity is based on

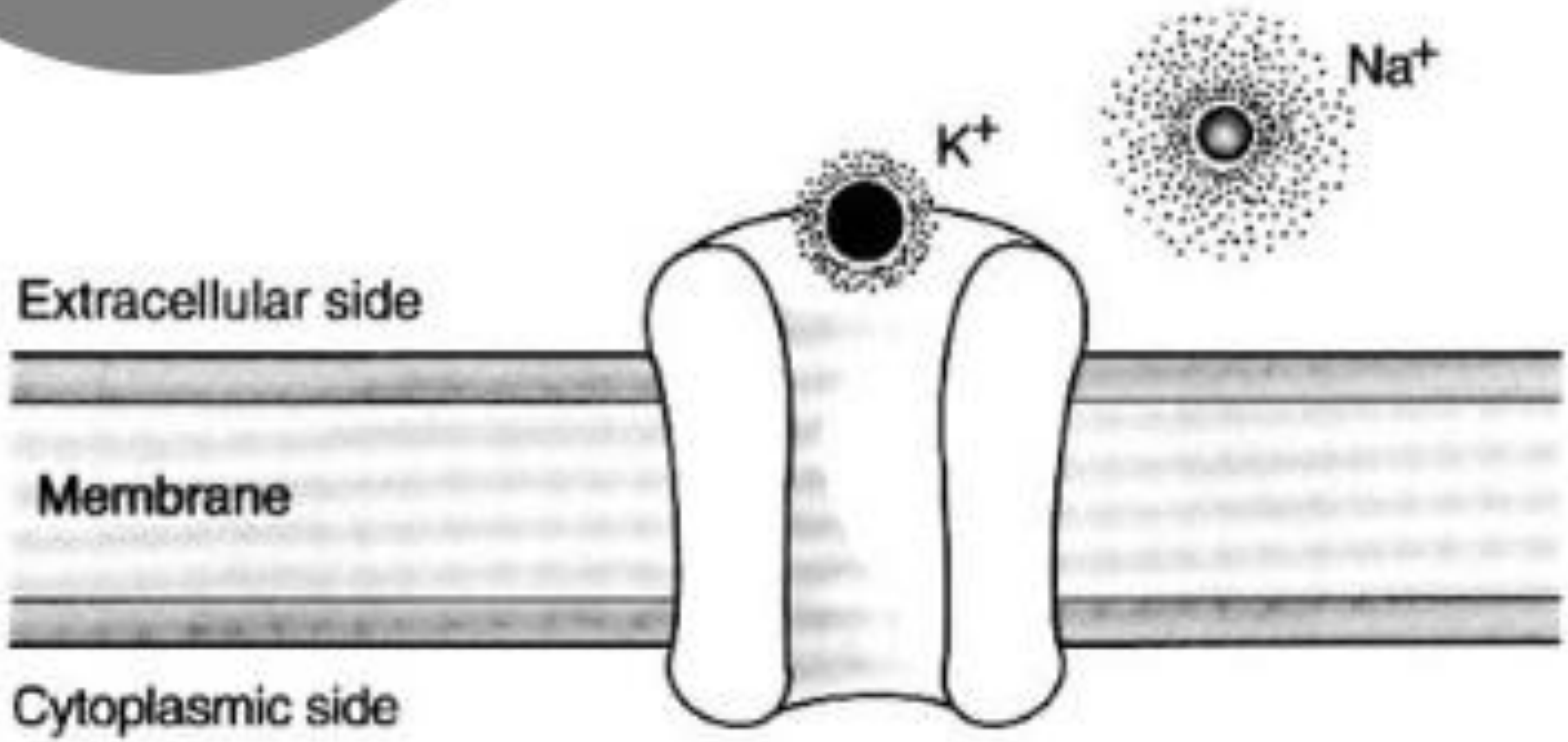
a. binding sites involving amino acid side chains

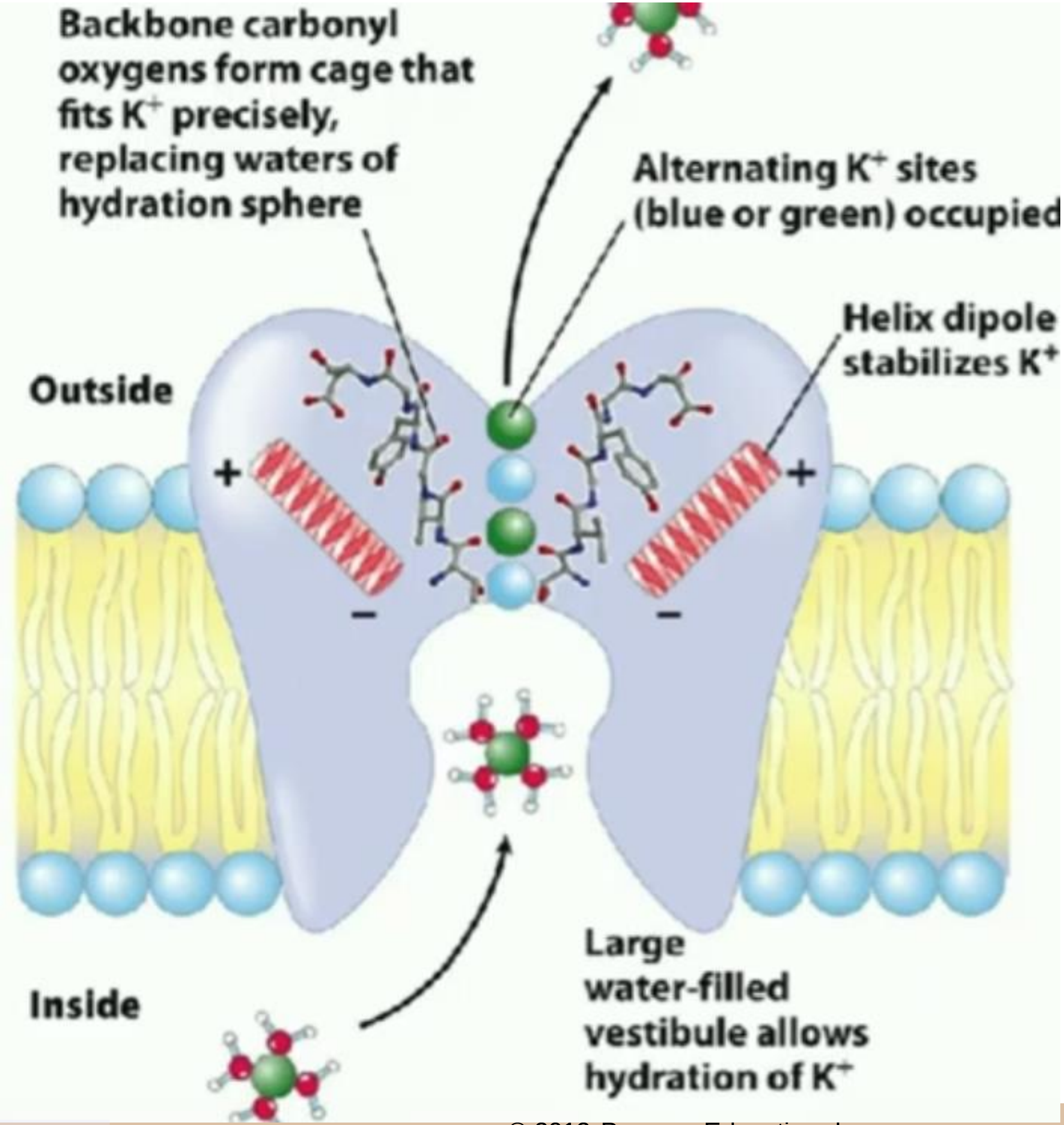
b. a size filter

Ion channels show *ion selectivity,* permitting some inorganic ions to pass, but not others through a **selectivity filter**



size filter that allows K+ to enter but not Na+





binding sites involving amino acid side chains

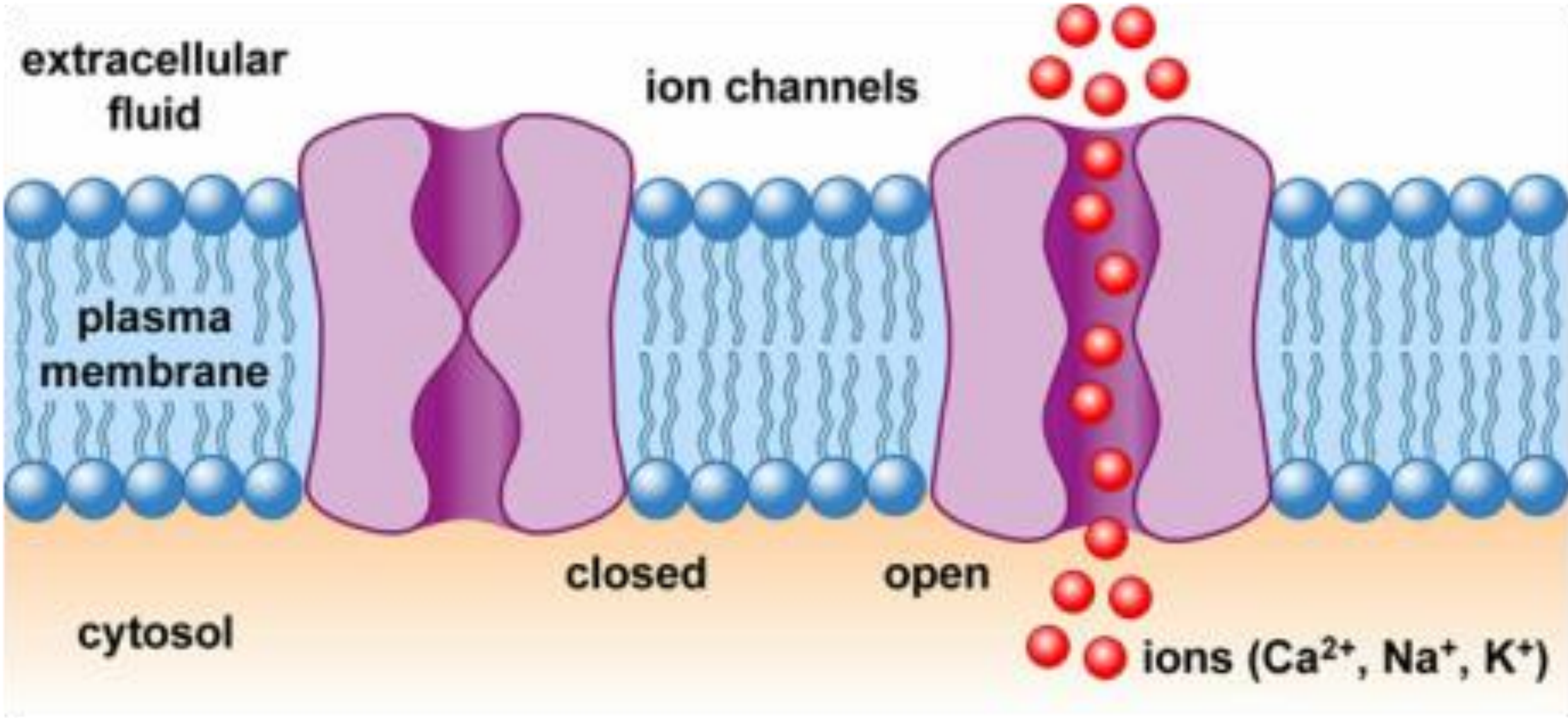
Channels are gated

- Most ion channels are ***gated***, meaning that they **open** and **close** in response to some stimulus

  - *Voltage-gated channels* open and close in response to changes in membrane potential

  - *Ligand-gated channels* are triggered by the binding of certain substances to the channel protein

  - *Mechanosensitive channels* respond to mechanical forces acting on the membrane ex. Piezo channels


extracellular fluid
ion channels
plasma membrane
closed
open
cytosol
ions (Ca^{2+}, Na^{+}, K^{+})

Do channel proteins undergo **any** conformational changes?

Yes/NO

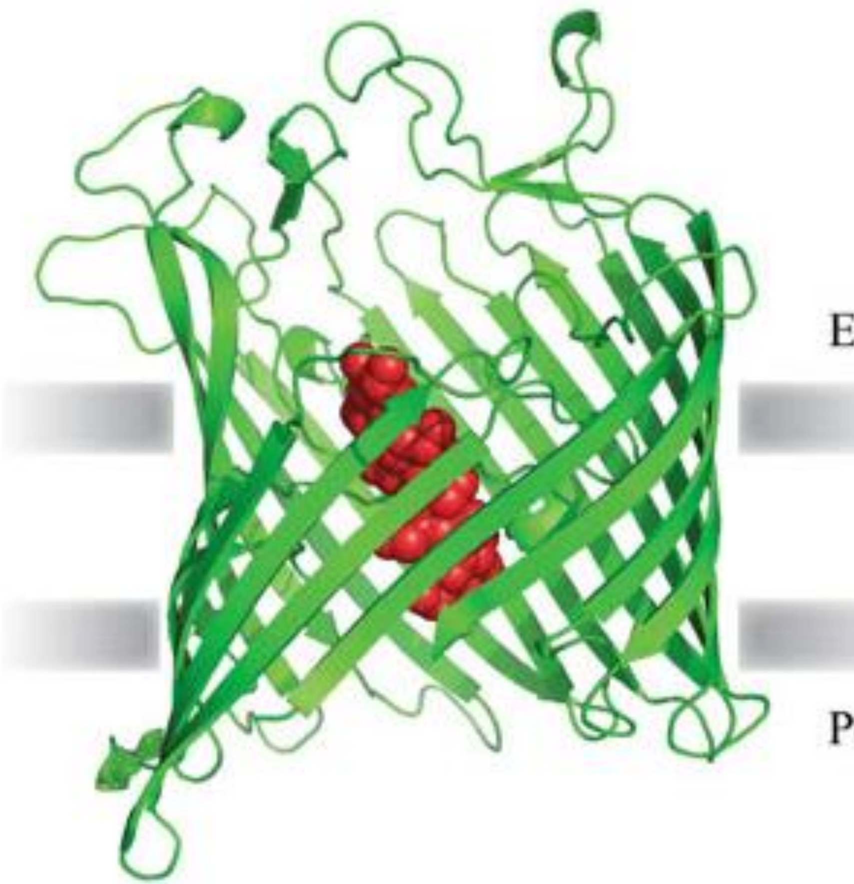
Yes till a certain degree

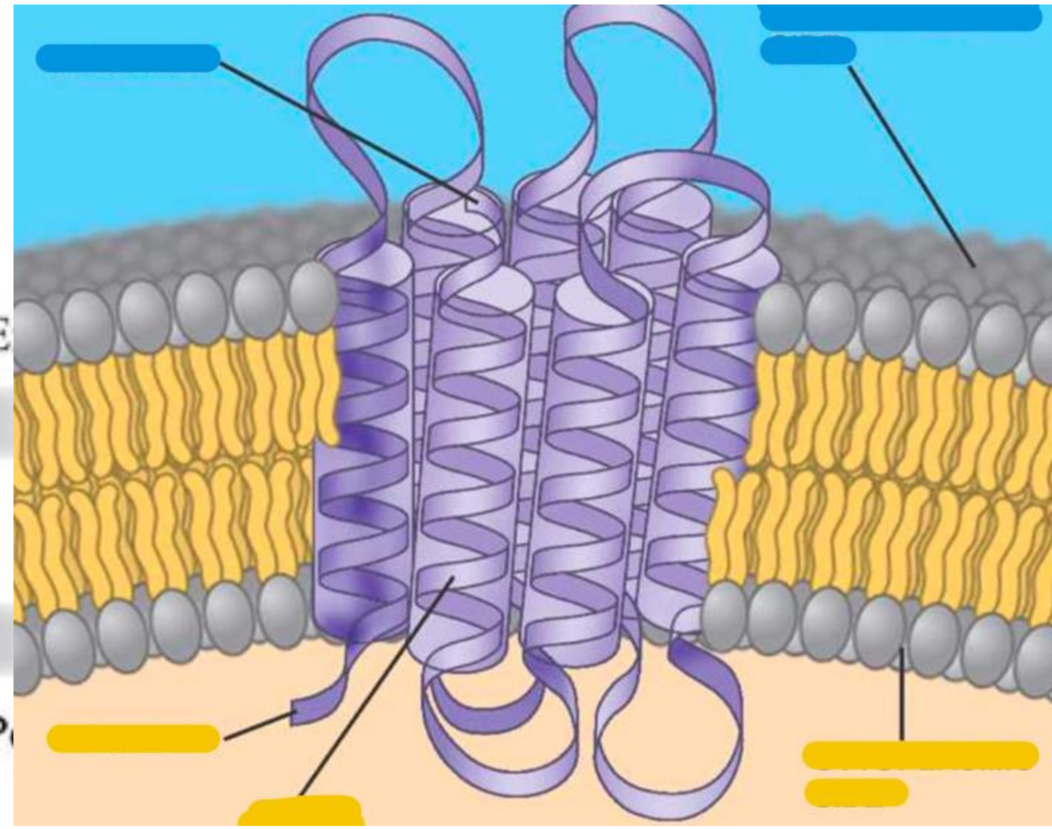
Closed state → open state (Gated)

Porins: Transmembrane Proteins That Allow Rapid Passage of Various Solutes

- Pores on outer membranes of bacteria, mitochondria and chloroplasts are larger and less specific than ion channels
- The pores are formed by multipass transmembrane proteins called **porins**
- The transmembrane segments of porins cross the membrane as β barrels

Porin vs integral protein transmembrane segments





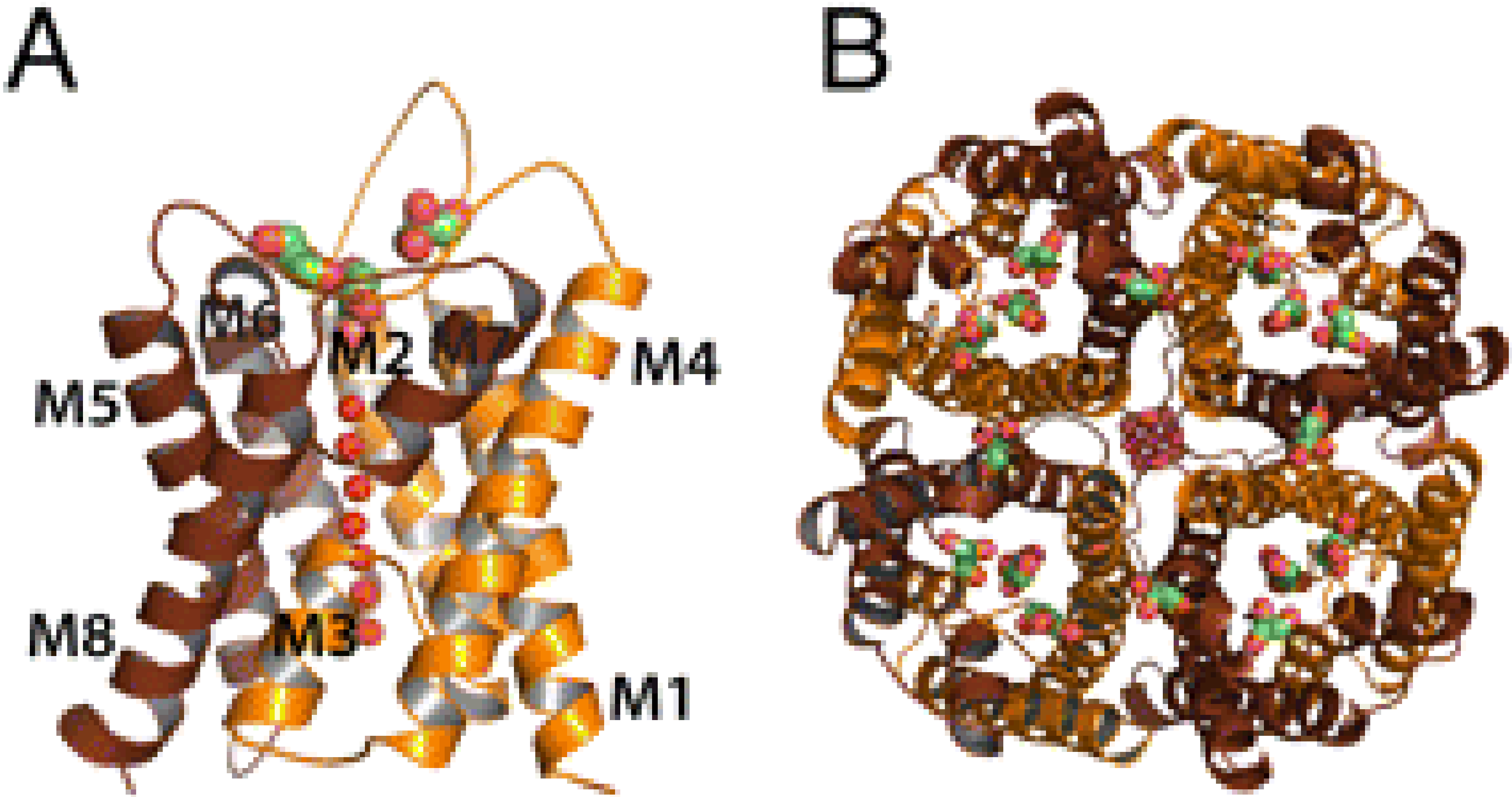
Aquaporins: Transmembrane Channels That Allow Rapid Passage of Water

- Movement of water across cell membranes in some tissues is faster than expected given the polarity of the water molecule

- **Aquaporin (AQP)** was discovered only in 1992

- Aquaporins allow rapid passage of water through membranes of erythrocytes and kidney cells in animals, and root cells and vacuolar membranes in plants

Structure of aquaporin



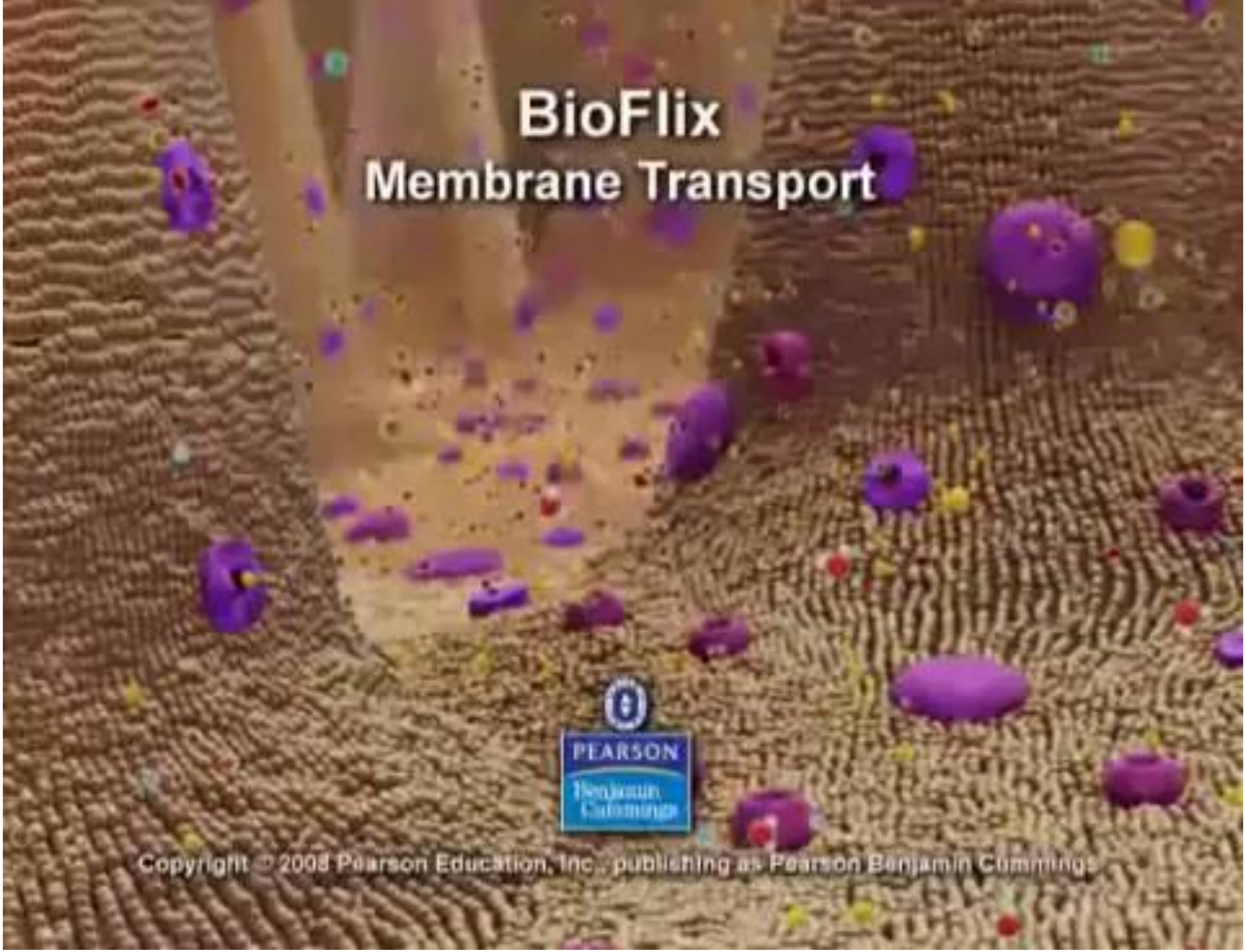
https://www.pnas.org/content/106/18/7437

Carrier Proteins Alternate Between Two Conformational States

- The **alternating conformation model** states that a carrier protein is allosteric protein and alternates between two conformational states

- In one state the solute binding site of the protein is accessible on one side of the membrane

- The protein shifts to the alternate conformation, with the solute binding site on the other side of the membrane, triggering solute release


BioFlix
Membrane Transport
PEARSON
Copyright © 2008 Pearson Education, Inc., publishing as Pearson Benjamin Cummings

Carrier Proteins Are Analogous to Enzymes in Their Specificity and Kinetics

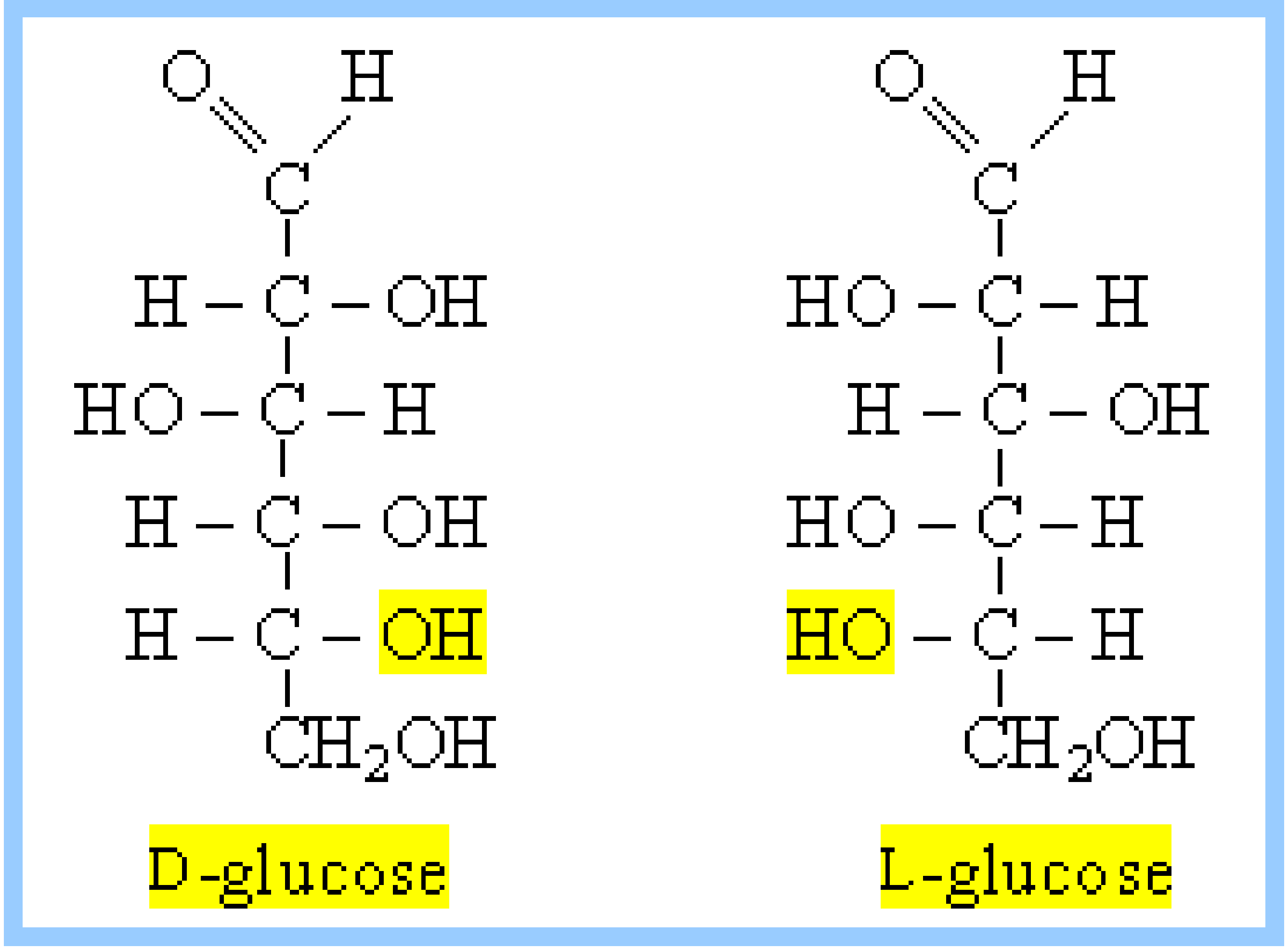
- Carrier proteins are analogous to enzymes
  - Facilitated diffusion involves binding a substrate, on a specific solute binding site
  - The carrier protein and solute form an intermediate
  - After conformational change, the "product" is released (the transported solute)
  - Carrier proteins are regulated by external factors

Specificity of Carrier Proteins

- Carrier proteins share the property of high specificity with enzymes, too

- Transport proteins are often highly specific for a single compound or a small group of closely related compounds

- The carrier protein for glucose in erythrocytes is specific to a few monosaccharides, and is *stereospecific* for only their *D*-isomers



O
H
C
H – C – OH
HO – C – H
H – C – OH
H – C – OH
CH2OH
D-glucose
O
H
C
HO – C – H
H – C – OH
HO – C – H
HO – C – H
CH2OH
L-glucose

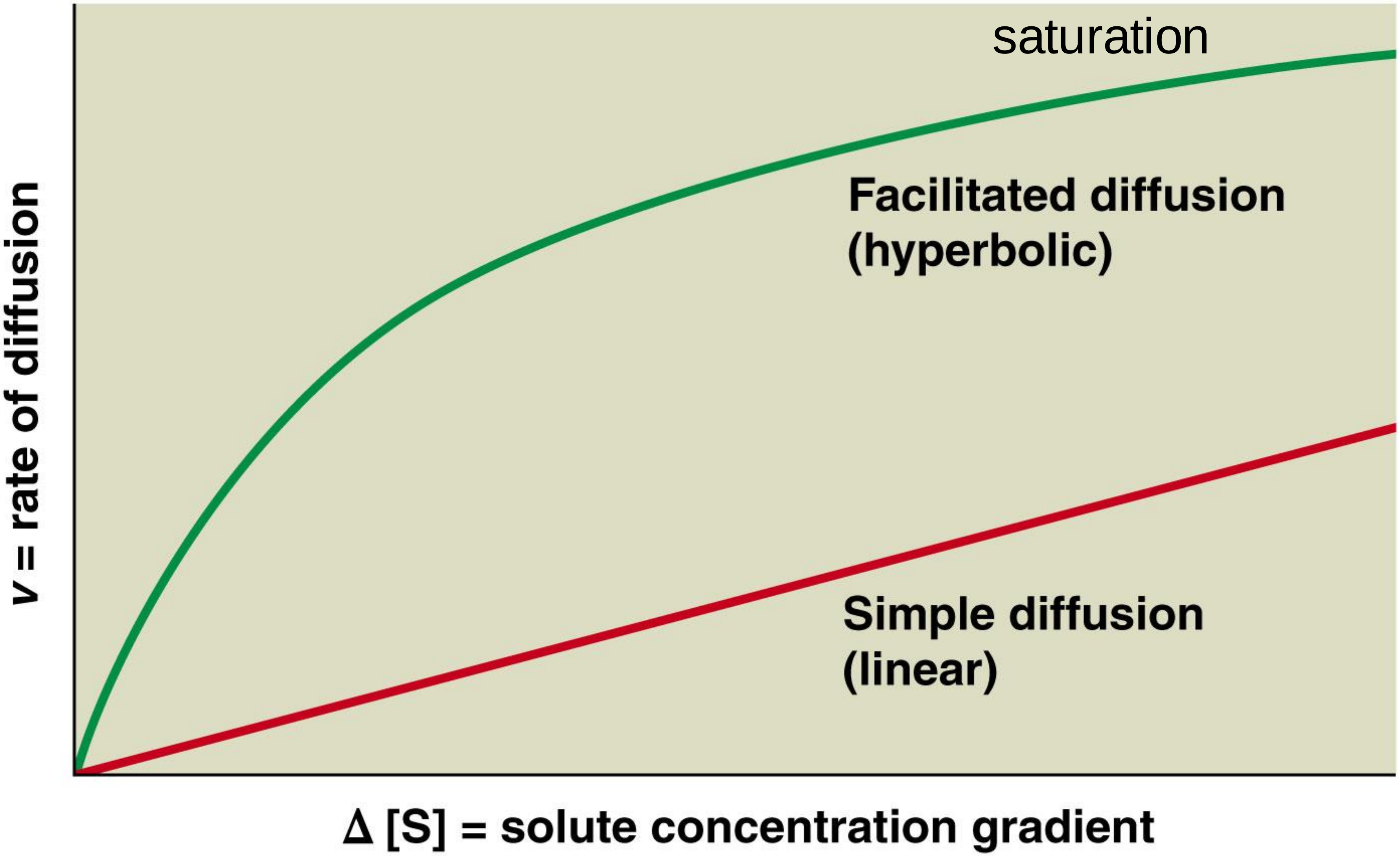
Kinetics of Carrier Protein Function

- Carrier proteins can become **saturated** as the concentration of the solute rises

- This is because the number of carrier proteins is limited and each functions at a finite maximum velocity

- So, carrier-facilitated transport (like enzyme catalysis) exhibits *saturation kinetics*

Figure 8-5


saturation
Facilitated diffusion
(hyperbolic)
Simple diffusion
(linear)
v = rate of diffusion
Δ [S] = solute concentration gradient

Competitive inhibition of carrier proteins

- *Competitive inhibition* of carrier proteins can occur in the presence of molecules or ions that are structurally related to the correct substrate

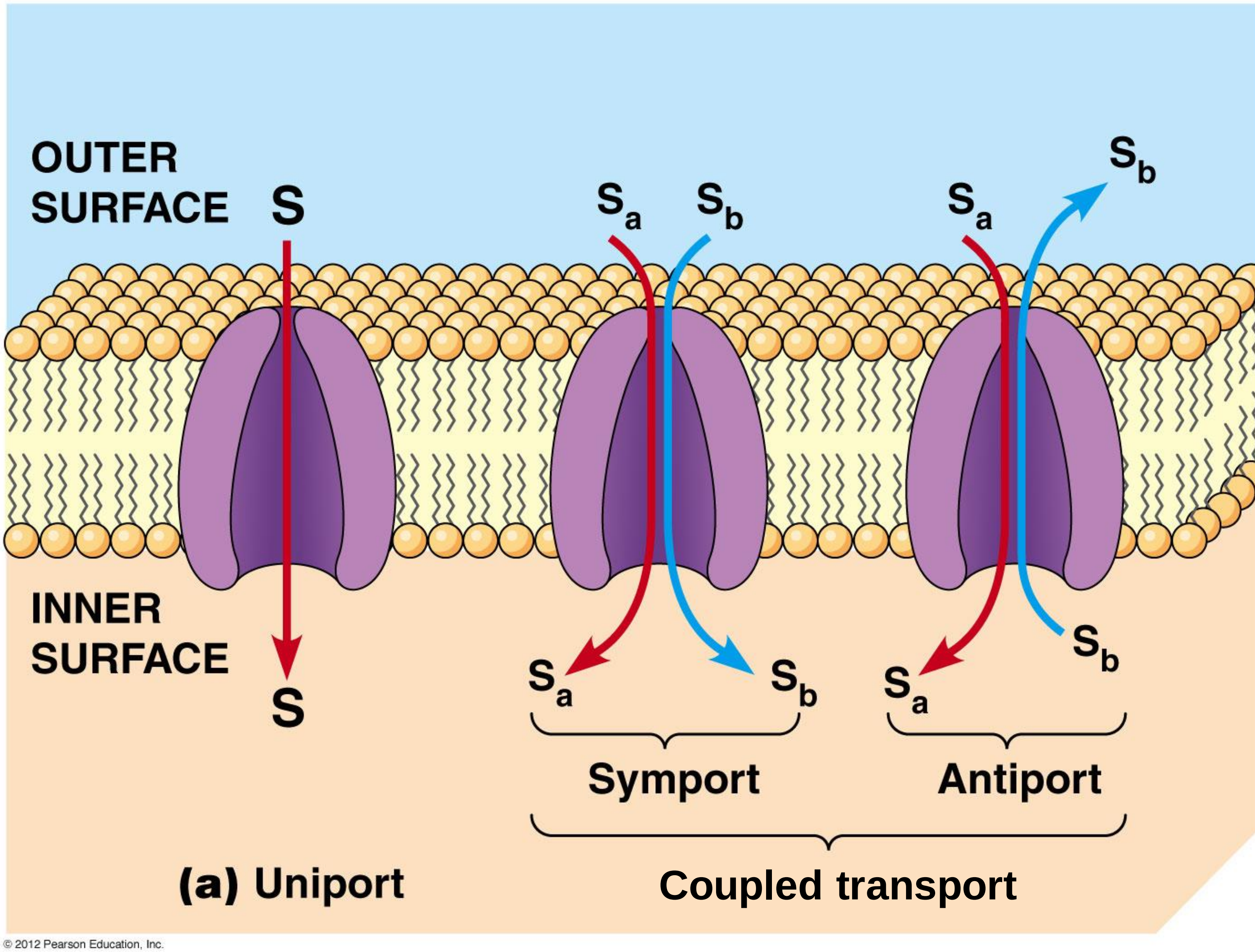
- For example, the transport of glucose by glucose carrier proteins can be inhibited by the other monosaccharides that the carrier accepts (such as mannose and galactose)

Carrier Proteins Transport Either One or Two Solutes

- When a carrier protein transports a single solute across the membrane, the process is called **uniport**

- A carrier protein that transports a single solute is called a *uniporter*

- When two solutes are transported simultaneously, and their transport is coupled, the process is called **coupled transport**


OUTER SURFACE
S
S_a
S_b
S_a
S_b
INNER SURFACE
S
S_a
S_b
S_b
S_a
Symport
Antiport
(a) Uniport
Coupled transport
© 2012 Pearson Education, Inc.

Coupled transport

- If the two solutes are moved across a membrane in the same direction, it is referred to as **symport** (or *cotransport*)

- If the solutes are moved in opposite directions, it is called **antiport** (or *countertransport*)

- Transporters that mediate these processes are *symporters* and *antiporters*

The Glucose Transporter: A Uniport Carrier

- The erythrocyte is capable of glucose uptake by facilitated diffusion because the level of blood glucose is much higher than that inside the cell
- Glucose is transported inward by a **glucose transporter** (**GLUT**; GLUT1 in erythrocytes)
- GLUT1 is an integral membrane protein with 12 transmembrane segments, which form a cavity with hydrophilic side chains

Mechanism of transport by GLUT1

- GLUT1 is thought to transport glucose through the membrane by the alternating conformation mechanism

- One conformational state, T_1, has the binding site for glucose open on the outside of the cell

- The other conformational state, T_2, has the binding site open to the inside of the cell

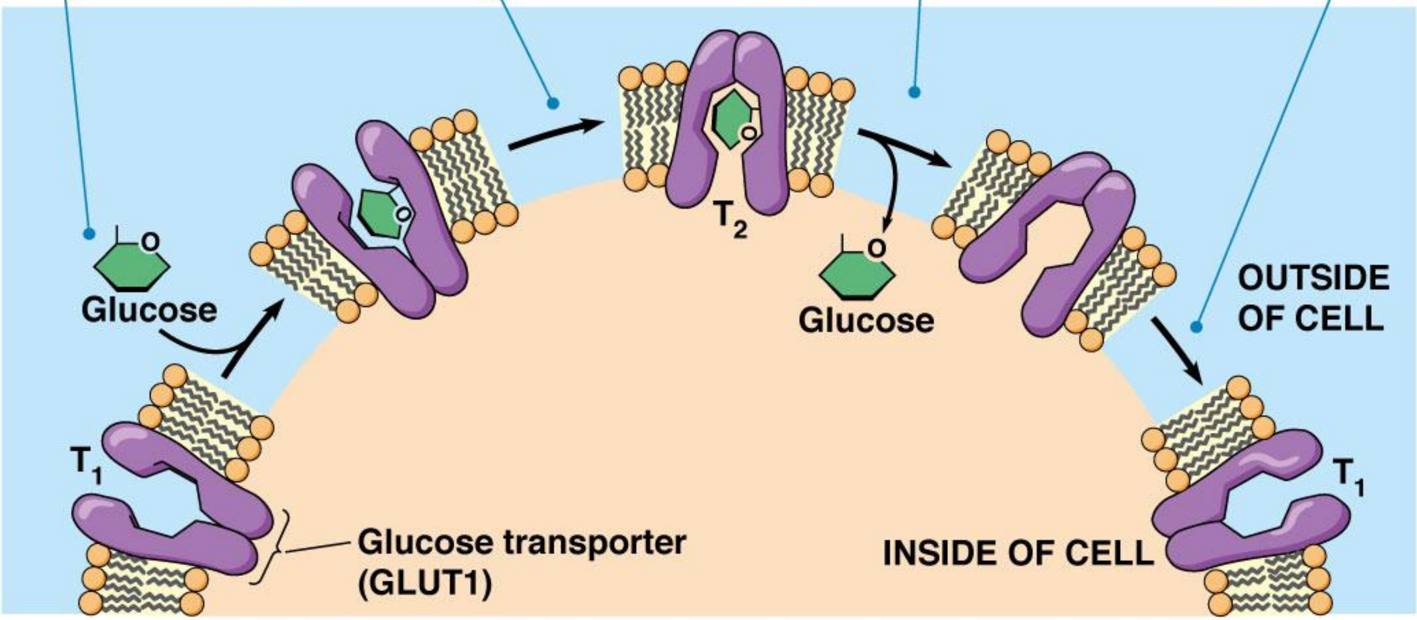
Figure 8-7

1 Glucose binds to a GLUT1 transporter protein that has its binding site open to the outside of the cell (T_1 conformation).

2 Glucose binding causes the GLUT1 transporter to shift to its T_2 conformation with the binding site open to the inside of the cell.

3 Glucose is released to the interior of the cell, initiating a second conformational change in GLUT1.

4 Loss of bound glucose causes GLUT1 to return to its original (T_1) conformation, ready for a further transport cycle.



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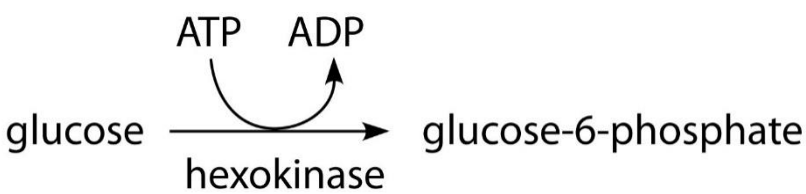
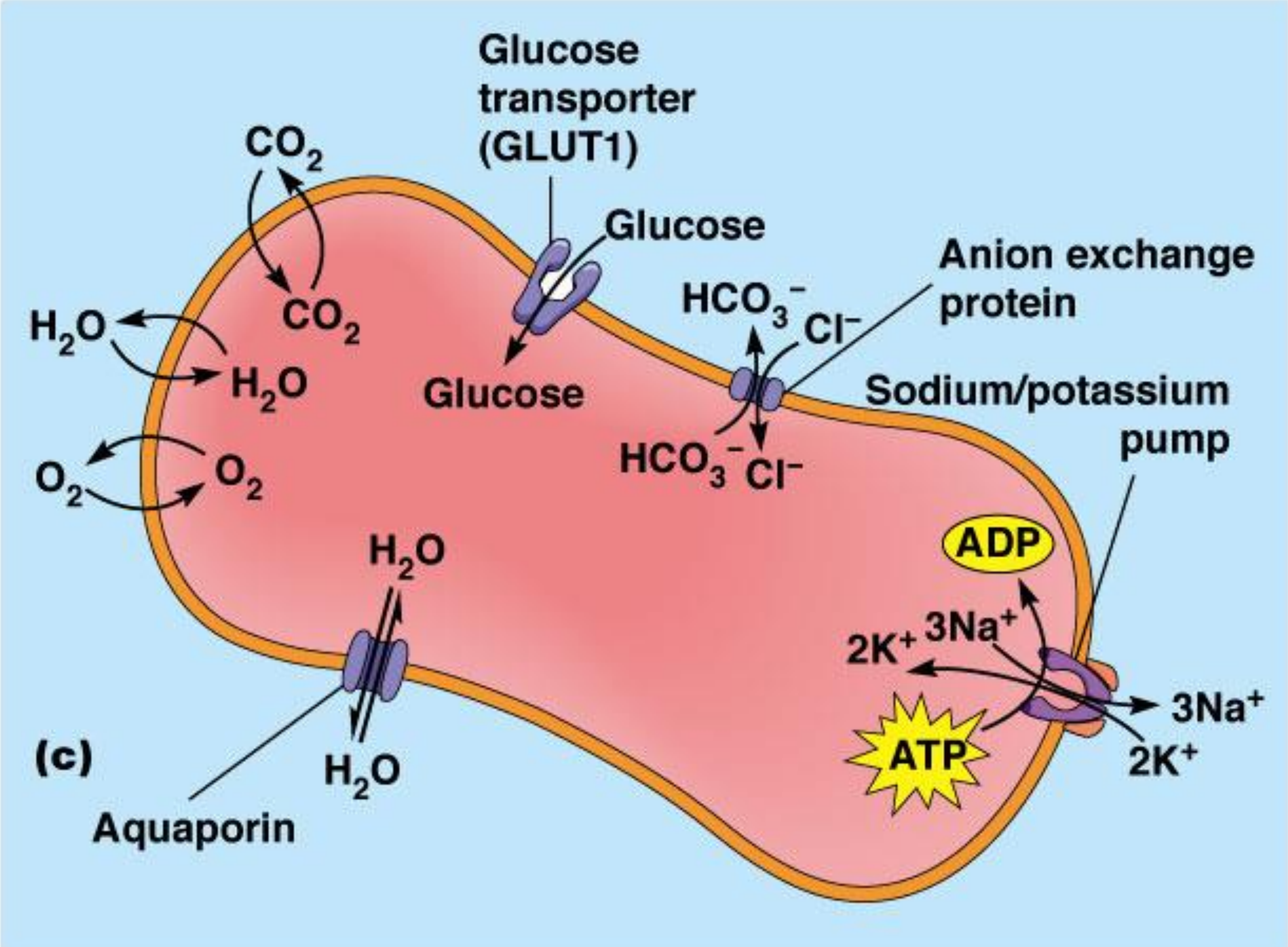
Transport by GLUT1 is reversible

- A carrier protein can facilitate transport in either direction

- The direction of transport is dictated by the relative solute concentrations outside and inside the cell



- Glucose concentration is kept low inside most animal cells (phosphorylation by hexokinase). Once phosporylated, glucose cannot bind the carrier protein any longer, and is effectively locked into the cell


Glucose transporter (GLUT1)
CO_2
CO_2
Glucose
Glucose
Anion exchange protein
HCO_3^-
Cl^-
HCO_3^-
Cl^-
H_2O
H_2O
O_2
O_2
Sodium/potassium pump
ADP
$3Na^+$
$2K^+$
$3Na^+$
$2K^+$
ATP
H_2O
H_2O
(c)
Aquaporin

The Erythrocyte Anion Exchange Protein: An Antiport Carrier

- The anion exchange protein (also called the chloride-bicarbonate exchanger) facilitates reciprocal exchange of Cl^- and HCO_3^- ions only
- Exchange will stop if either anion is absent
- The ions are exchanged in a strict 1:1 ratio

The "ping-pong" mechanism

- The anion exchange protein is thought to alternate between two conformational states

- In the first, it binds a chloride ion on one side of the membrane, which causes a change to the second state

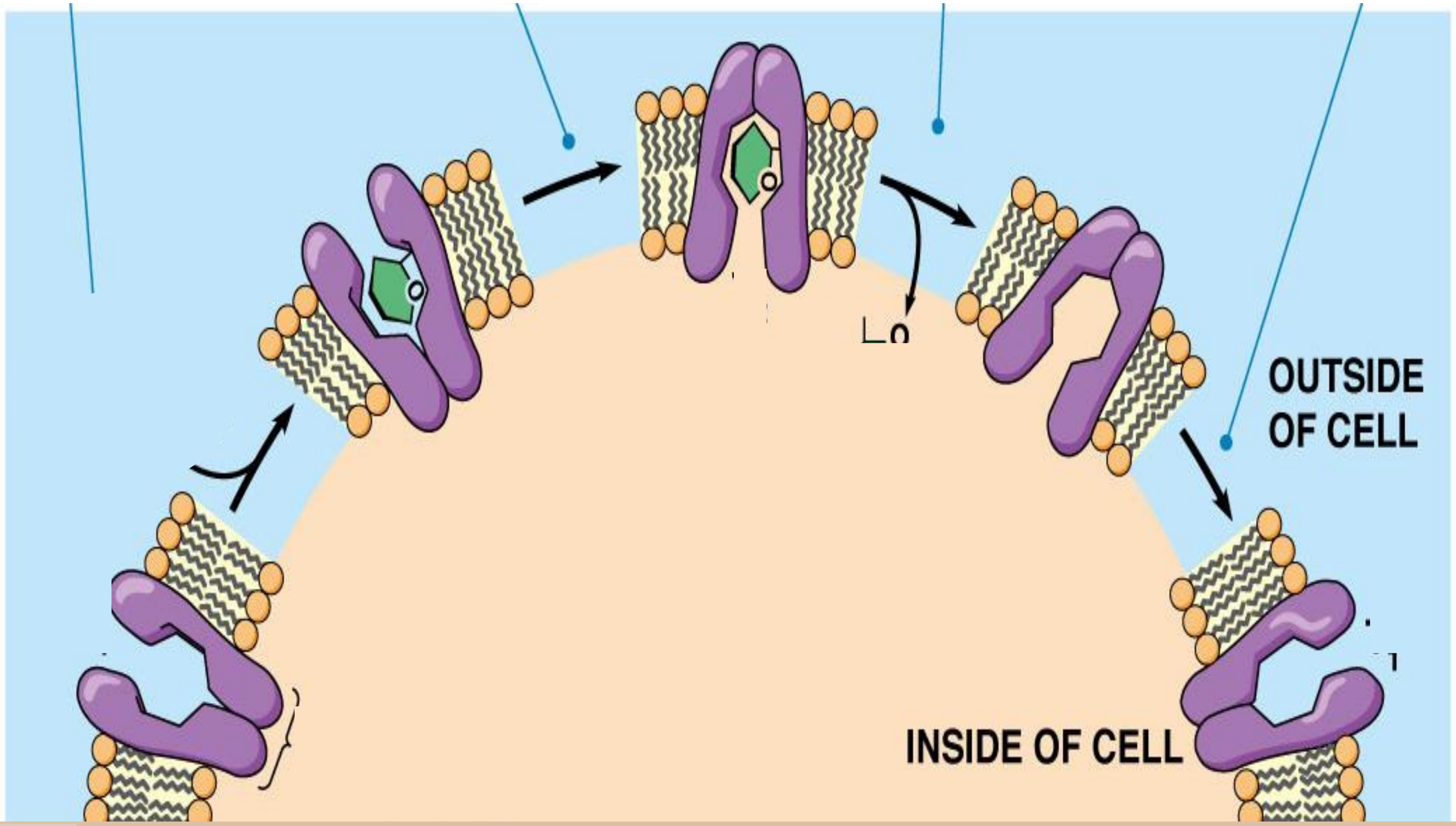
- In the second state, the chloride is moved across the membrane and released

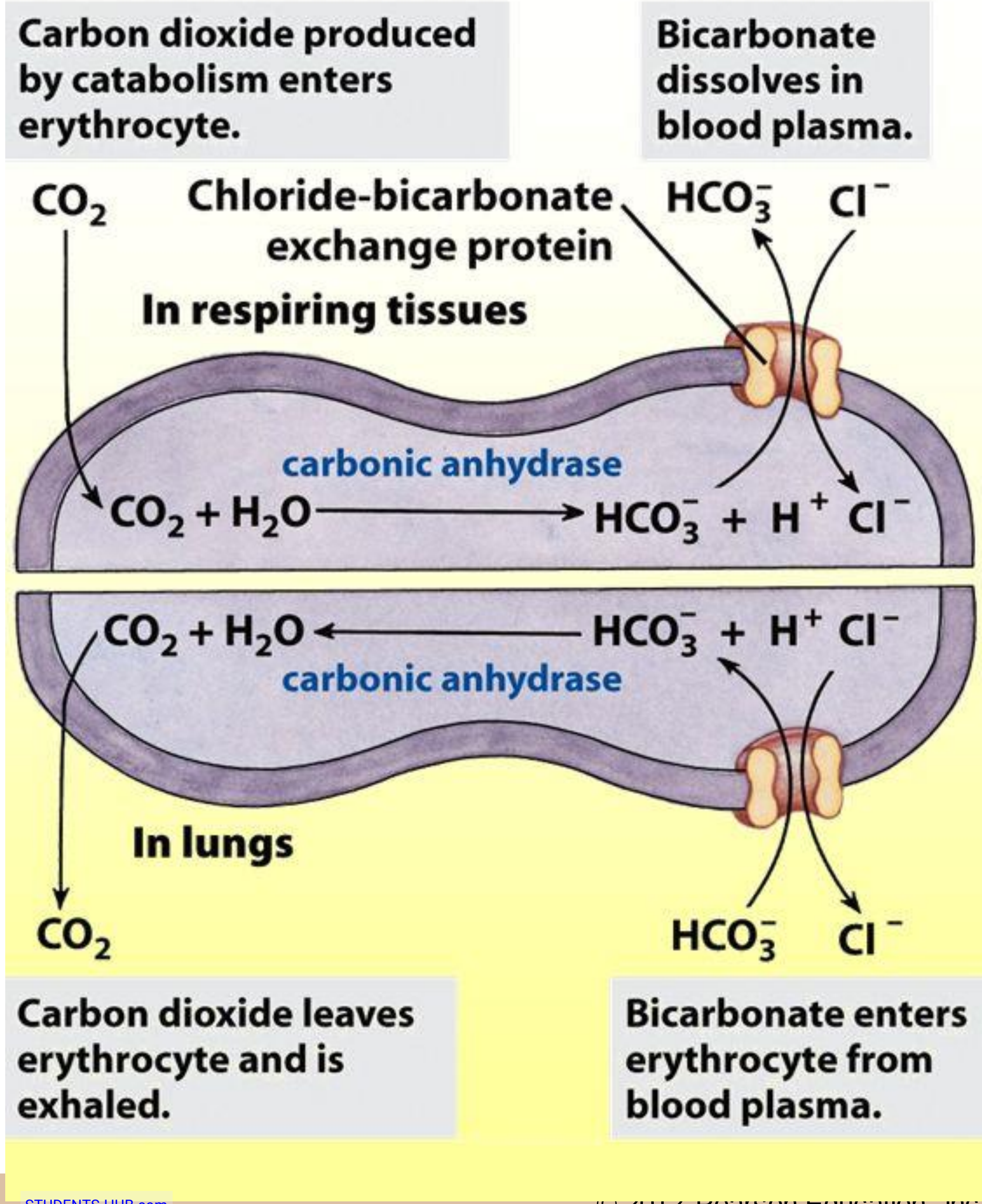
The "ping-pong" mechanism (continued)

- The release of chloride causes the protein to bind bicarbonate

- The binding of bicarbonate causes a shift back to the first conformation

- In this conformation, bicarbonate is moved out of the cell, allowing the carrier to bind chloride again


OUTSIDE OF CELL
INSIDE OF CELL


Carbon dioxide produced by catabolism enters erythrocyte.
Bicarbonate dissolves in blood plasma.
CO_2
Chloride-bicarbonate exchange protein
HCO_3^-
Cl^-
In respiring tissues
carbonic anhydrase
$CO_2 + H_2O \rightarrow HCO_3^- + H^+$ Cl^-
$CO_2 + H_2O \leftarrow HCO_3^- + H^+$ Cl^-
carbonic anhydrase
In lungs
CO_2
HCO_3^-
Cl^-
Carbon dioxide leaves erythrocyte and is exhaled.
Bicarbonate enters erythrocyte from blood plasma.

Biological relevance of anion exchange

- In tissues, waste CO_2 diffuses into the erythrocytes where it is converted to HCO_3^- by the enzyme *carbonic anhydrase*

- As the concentration of bicarbonate rises it moves out of the cell, coupled with uptake of Cl^- to prevent a net charge imbalance

- In the lungs, the entire process is reversed

Active Transport: Protein-Mediated Movement Up the Gradient

- Facilitated diffusion is important, but only accounts for movement of molecules down a concentration gradient, toward equilibrium

- Sometimes a substance must be transported *against* a concentration gradient

- In this case active transport is used to move solutes *up* a concentration gradient, *away* from equilibrium

Functions of active transport

- Active transport couples endergonic transport to an exergonic process, usually ATP hydrolysis

- Active transport performs three important cellular functions

  - Uptake of essential nutrients
  - Removal of wastes
  - Maintenance of non-equilibrium concentrations of certain ions

Nonequilibrium conditions

- Active transport allows the creation and maintenance of an internal cellular environment that differs greatly from the surrounding environment

- Many membrane proteins involved in active transport are called **pumps**, because energy is required to move substances against their concentration gradients

Active transport is *unidirectional*

- Active transport differs from diffusion (both simple and facilitated) in the direction of transport
- Diffusion is ***nondirectional*** with respect to the membrane and proceeds as directed by the concentrations of the transported substances
- Active transport has an intrinsic **directionality**

The Coupling of Active Transport to an Energy Source May Be Direct or Indirect

- Active transport mechanisms can be divided based on the **sources of energy** and whether or not two solutes are transported at **the same time**

- Active transport is categorized as *direct* or *indirect*

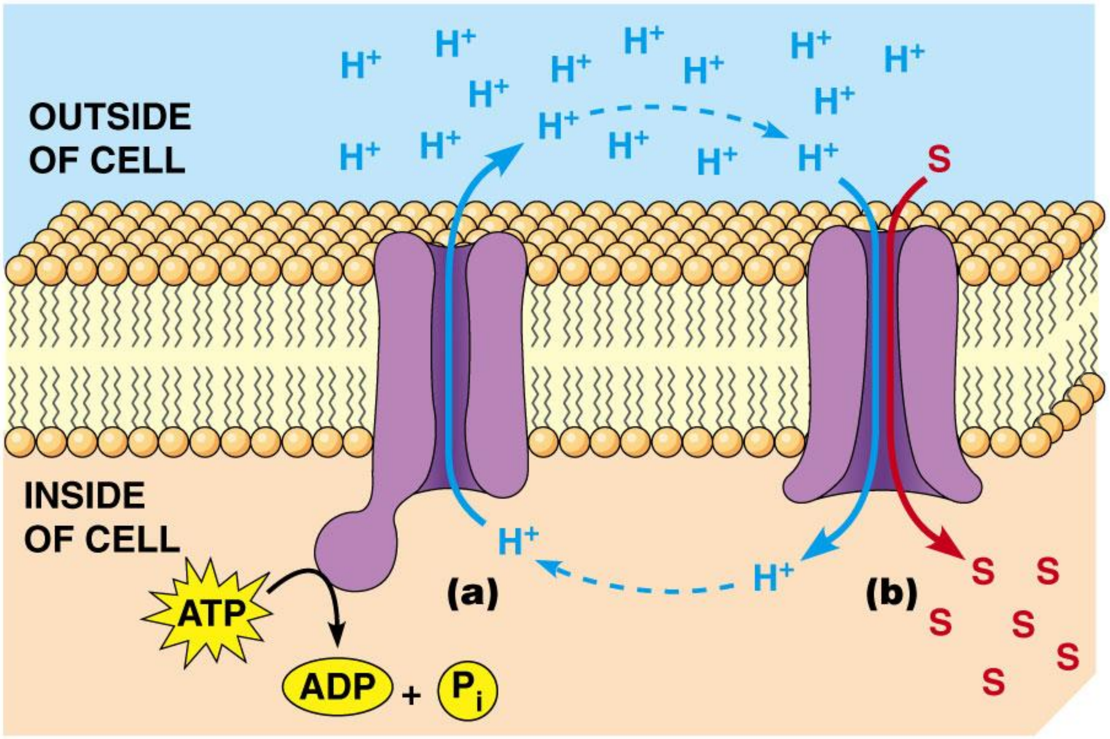
Direct active transport

- In **direct active transport** (or *primary active transport*), the accumulation of solute molecules on one side of the membrane is coupled *directly* to an exergonic chemical reaction
- This is usually hydrolysis of ATP
- Transport proteins driven by ATP hydrolysis are called *transport ATPases* or *ATPase pumps*

Figure 8-9A

(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 electrochemical 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.



Indirect active transport

- Indirect active transport depends on the **simultaneous transport of two solutes**

- Favorable movement of one solute *down* its gradient drives the unfavorable movement of the other *up* its gradient

- This can be a ***symport or an antiport***, depending on whether the two molecules are transported in the same or different directions

Figure 8-9A

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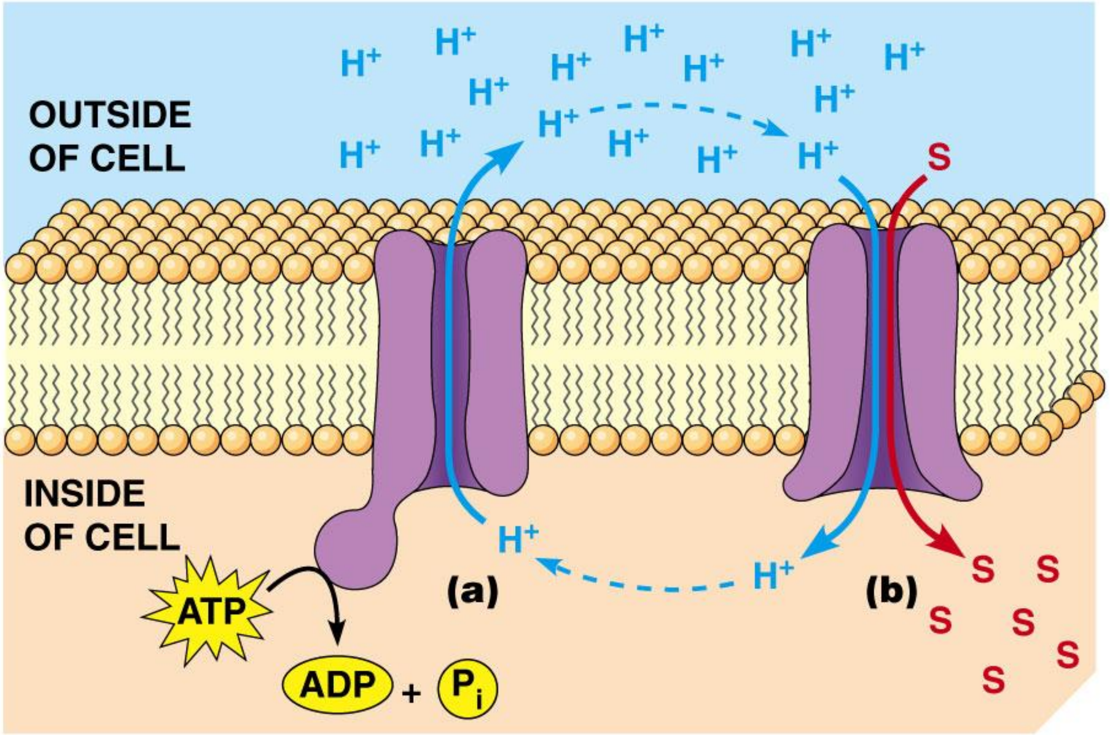


Indirect Active Transport Is Driven by Ion Gradients

- Indirect active transport (or *secondary active transport*) is not powered by ATP hydrolysis

- The inward transport of molecules *up* their electrochemical gradients is often **coupled** to and driven by simultaneous inward movement of Na^+ (animals) or protons (plant, fungi, bacteria) *down* their gradients

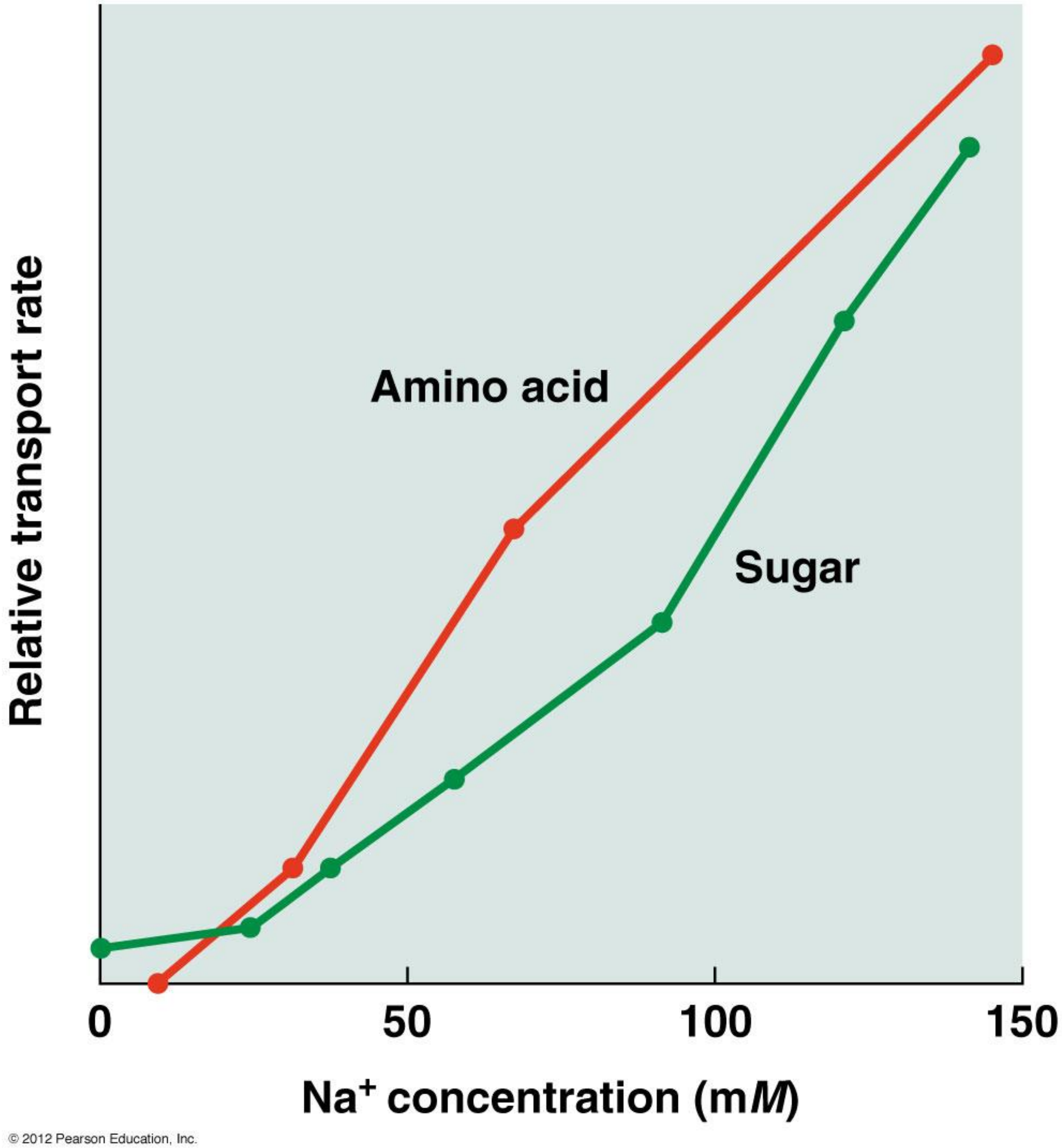
Symport mechanisms of indirect active transport

- Most cells continuously pump either sodium ions or protons out of the cell (e.g., the Na^+/K^+ pump in animals)

- The resulting high extracellular concentration of Na^+ is a driving force for the **uptake of sugars and amino acids**

- This is indirectly related to ATP because the pump that maintains the sodium ion gradient is driven by ATP

Figure 8-10


Relative transport rate
Amino acid
Sugar
0
50
100
150
Na⁺ concentration (mM)
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Proton gradients drive indirect active transport in many organisms

- Most organisms rely on proton gradients rather than the Na^+ gradients used by animals
- For example, fungi and plants use proton symport for the uptake of organic solutes, with ATP driving the proton pump that creates and maintains the proton electrochemical potential
- Proton or ion gradients can be used for *export* as well as *import*

Direct Active Transport: The Na^+/K^+ Pump Maintains Electrochemical Ion Gradients

- In a typical mammalian neuron, $[K^+]_{inside}/[K^+]_{outside}$ is about 35:1 and $[Na^+]_{inside}/[Na^+]_{outside}$ is around 0.08:1

- The electrochemical potentials for sodium and potassium are essential as a driving force for coupled transport and for transmission of nerve impulses

Requirement for energy

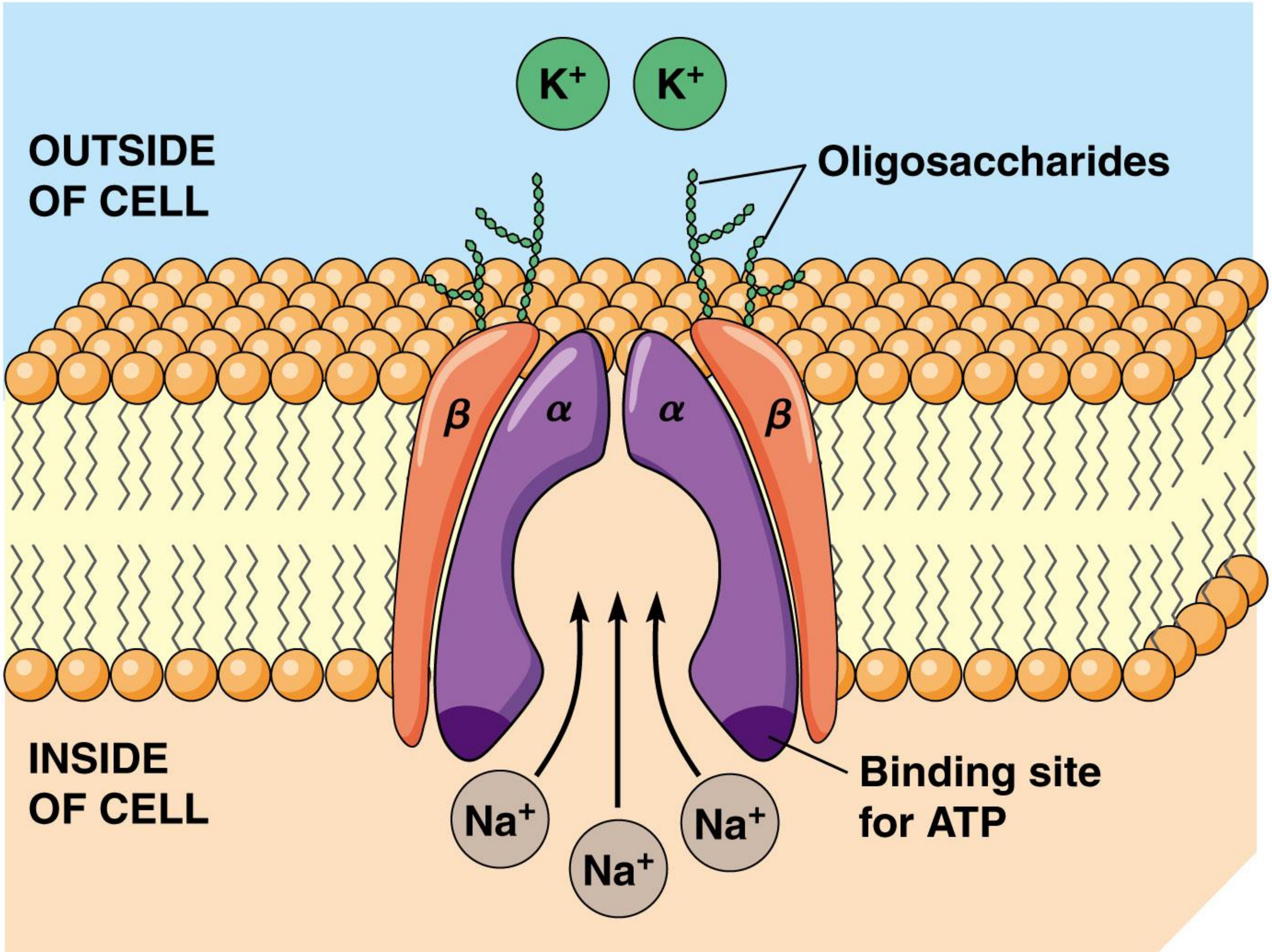
- The pumping of both Na^+ and K^+ ions against their gradients requires energy

- The pump that is responsible, the **Na^+/K^+ ATPase** (or **pump**), uses the **hydrolysis of ATP** to drive the transport of both ions

- It is responsible for the asymmetric distribution of ions across the plasma membrane of animal cells

- Three sodium ions are moved out and two potassium ions moved in per molecule of ATP hydrolysed

Figure 8-11



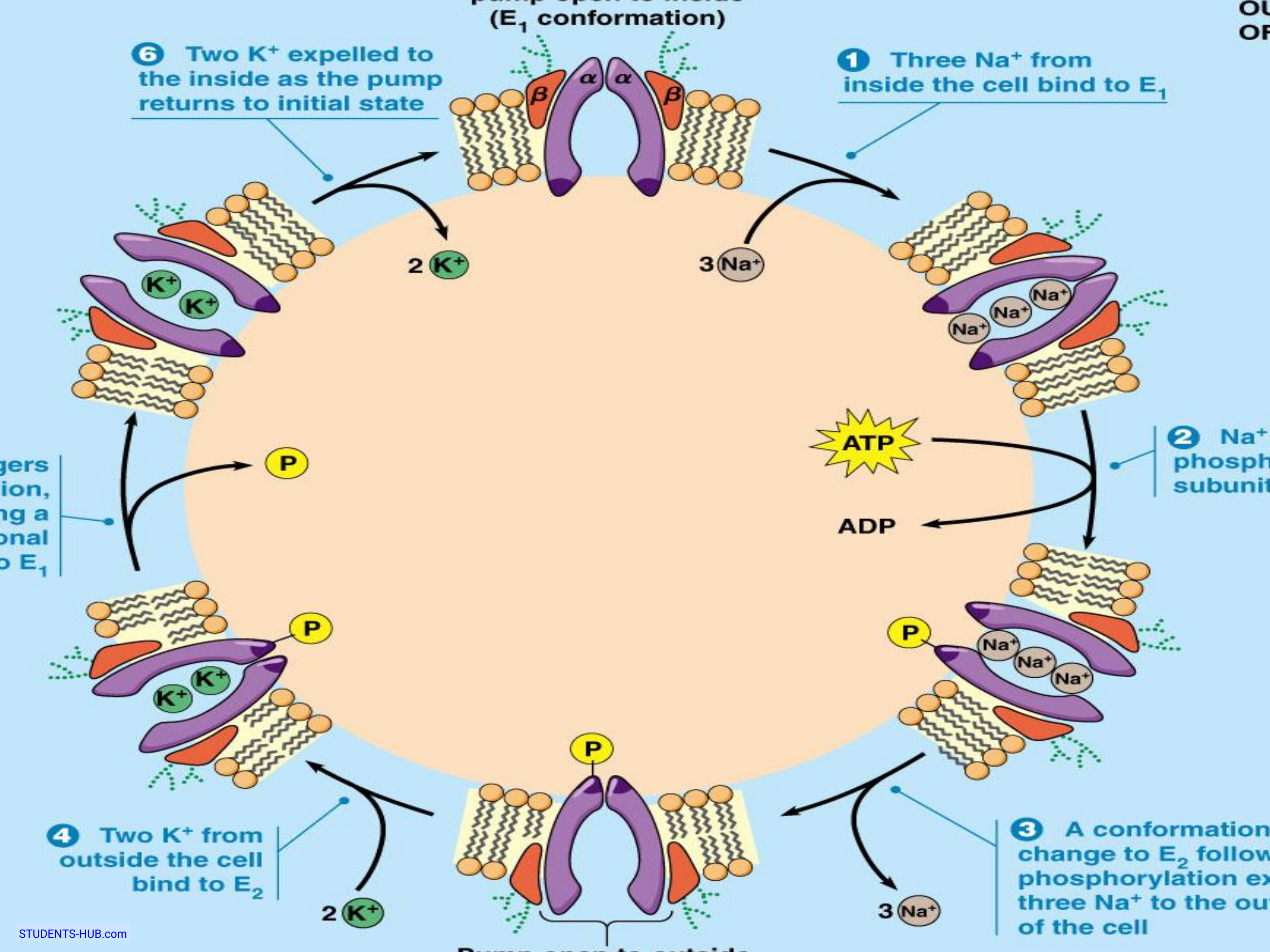
OUTSIDE OF CELL
K^+
K^+
Oligosaccharides
β
α
α
β
INSIDE OF CELL
Na^+
Na^+
Na^+
Binding site for ATP

The Na^+/K^+ pump is an allosteric protein

- The Na^+/K^+ pump has two alternative conformational states, E_1 and E_2

- The E_1 conformation is open to the inside of the cell and has high affinity for Na^+ ions

- The E_2 conformation is open to the outside of the cell and has high affinity for K^+ ions



(E$_1$ conformation)
6 Two K$^+$ expelled to the inside as the pump returns to initial state
1 Three Na$^+$ from inside the cell bind to E$_1$
α
β
2 K$^+$
3 Na$^+$
Na$^+$
K$^+$
ATP
ADP
P
4 Two K$^+$ from outside the cell bind to E$_2$

The Na^+/K^+ pump

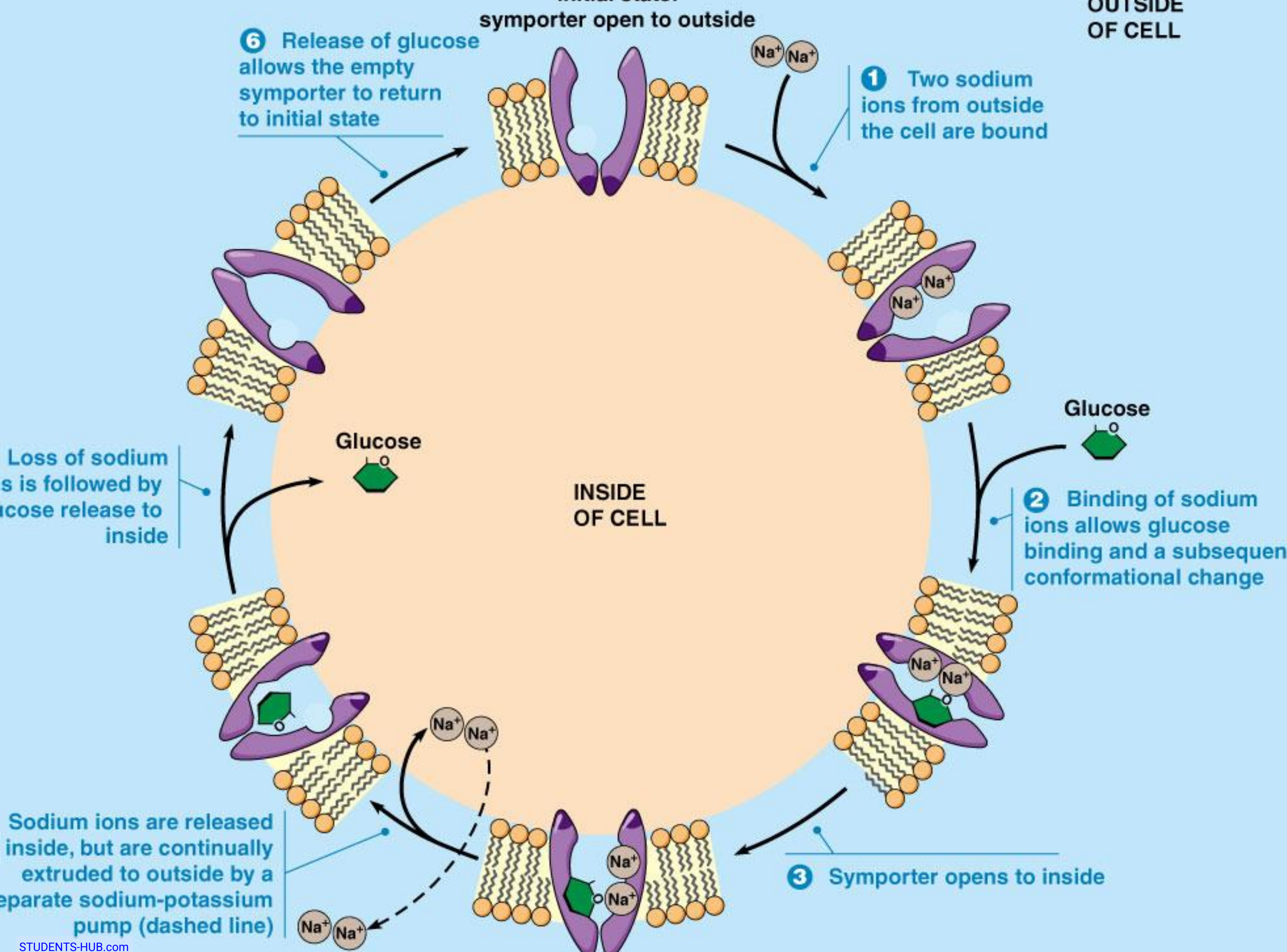
3 Na+ outside
2 K+ inside

1+ charge difference to the outside

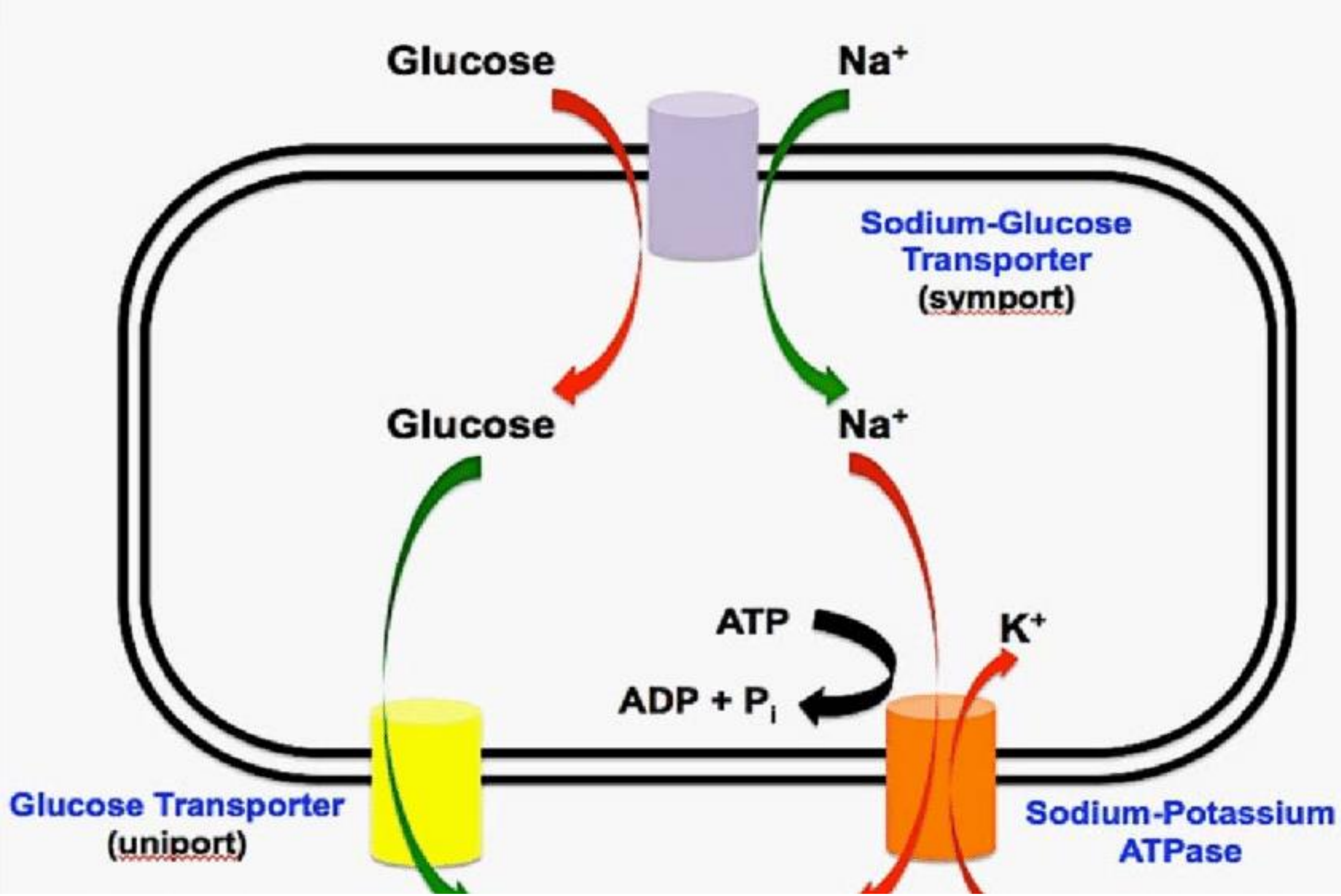
MAINTAIN THE MEMBRANE POTENTIAL

Indirect Active Transport: Sodium Symport Drives the Uptake of Glucose

- Although most glucose into and out of our cells occurs by facilitated diffusion, some cells use a **Na^+/glucose symporter**
- For example, the cells lining the intestine take up glucose and some amino acids even when their concentrations are much lower outside than inside the cells
- A steep Na^+ gradient that is maintained across the plasma membrane (via the Na^+/K^+ pump) is used to provide the energy needed



symporter open to outside
OUTSIDE
OF CELL
6 Release of glucose allows the empty symporter to return to initial state
Na+ Na+
1 Two sodium ions from outside the cell are bound
Glucose
2 Binding of sodium ions allows glucose binding and a subsequen conformational change
INSIDE
OF CELL
Glucose
Loss of sodium s is followed by ucose release to inside
3 Symporter opens to inside
Sodium ions are released inside, but are continually extruded to outside by a eparate sodium-potassium pump (dashed line)



Glucose
Na+
Sodium-Glucose Transporter (symport)
Glucose
Na+
ATP
ADP + Pi
K+
Glucose Transporter (uniport)
Sodium-Potassium ATPase