

# Cell and Molecular Biology

**Ninth Edition**

Gerald Karp, Janet Iwasa, Wallace Marshall

## Chapter 4

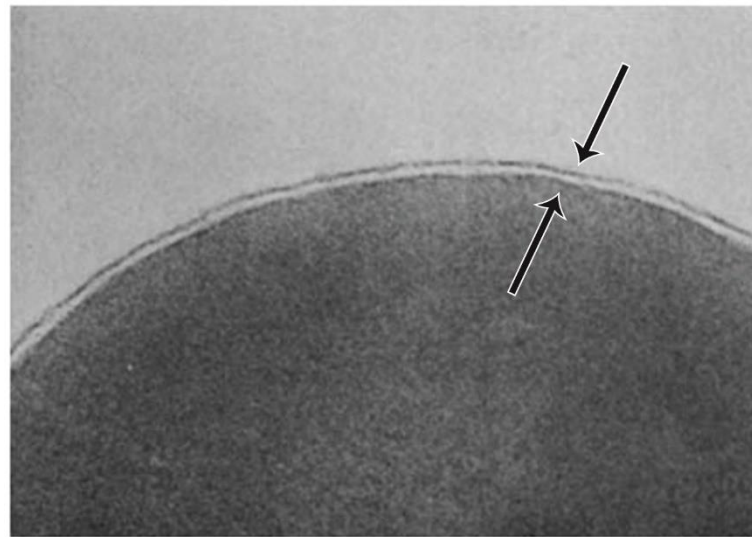
### The Structure and Function of the Plasma Membrane

## 4.0 | Nerve Gas

- Sarin is a type of **nerve gas**—a chemical weapon that interferes with the nervous system.
- This chapter will demonstrate how proteins in the cell membrane convert chemical signals to electrical signals that are required for many physiological activities.

# 4.1 | Introduction to the Plasma Membrane (1 of 3)

- **Plasma membrane:** The outer boundary of the cell that separates it from the world is a thin, fragile structure about 5–10 nm thick.
- Need electron microscope to examine.
- All membranes examined closely from plants, animals or microorganisms have the same ultrastructure.



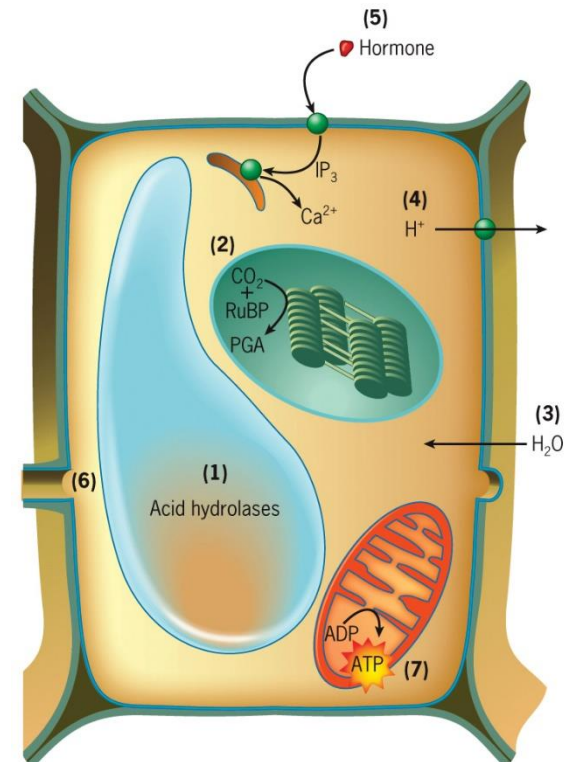
Source: © 1981 J.D. Robertson. Originally published in *The Journal of Cell Biology*. <https://doi.org/10.1083/jcb.91.3.185>

50 nm

# 4.1 | Introduction to the Plasma Membrane (2 of 3)

## An Overview of Some of Membrane Functions

- Transporting solutes
- Responding to external signals
- Intracellular interaction
- Selectively permeable barrier
- Energy transduction

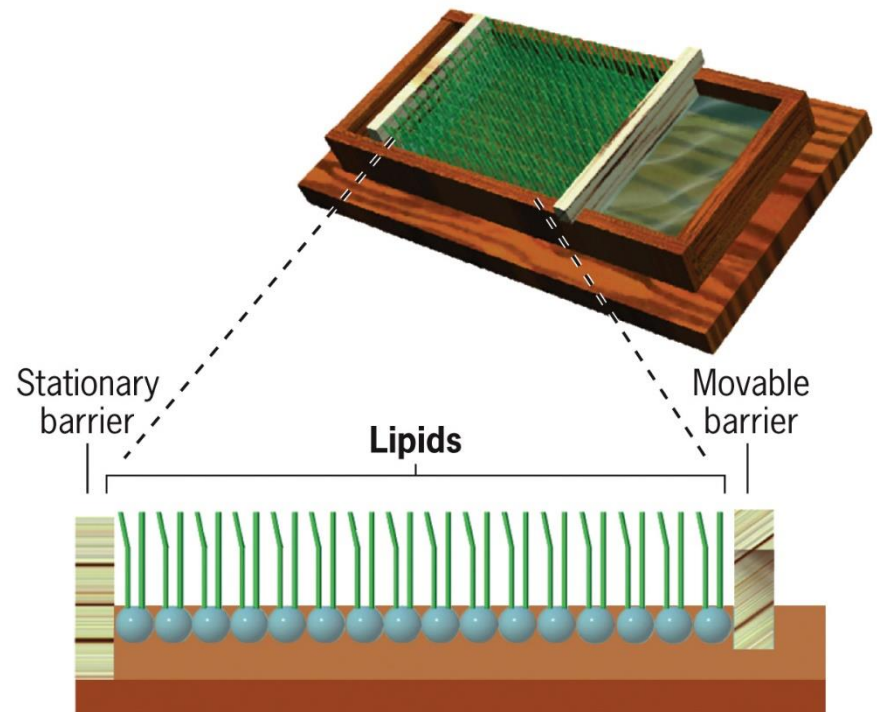


A summary of membrane functions in a plant cell

# 4.1 | Introduction to the Plasma Membrane (3 of 3)

## A Brief History of Studies on Plasma Membrane Structure

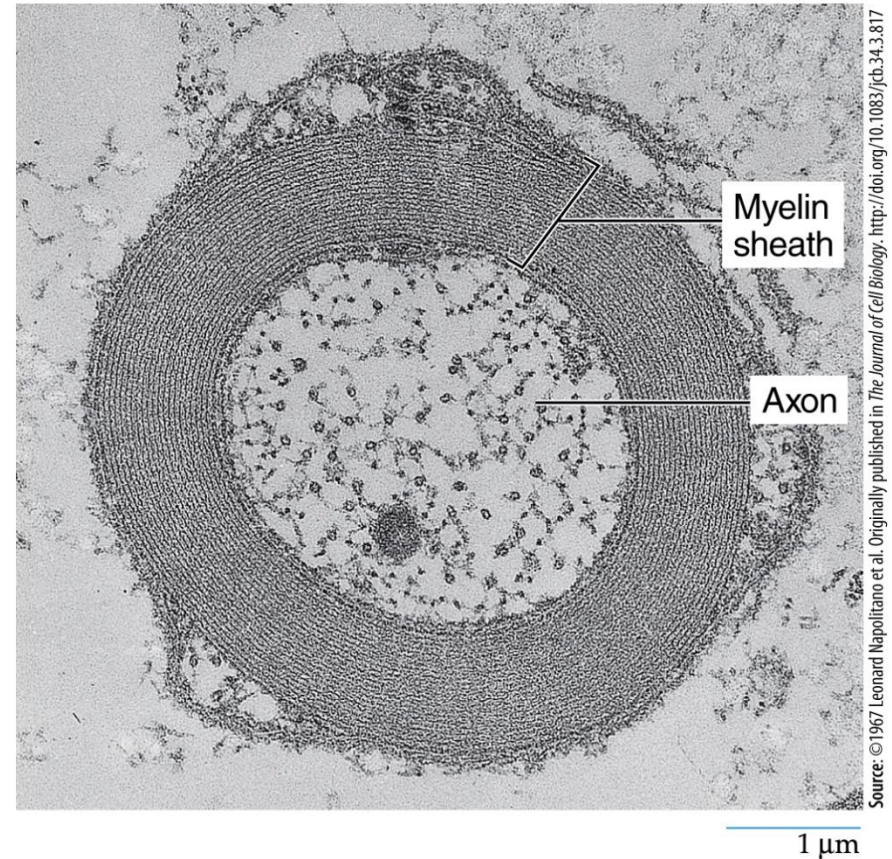
- Membranes were found to be mostly composed of oil.
- The **lipid bilayer** accounted for the 2:1 ratio of lipid to cell surface area.



Calculating the surface area of a lipid preparation

## 4.2 | The Chemical Composition of Membranes (1 of 6)

- Membranes are made of lipid–protein assembly
- The ratio of lipid to protein varies
- The myelin sheath acts as electrical insulation for the nerve cell



Electron micrograph of a nerve cell axon

## 4.2 | The Chemical Composition of Membranes (2 of 6)

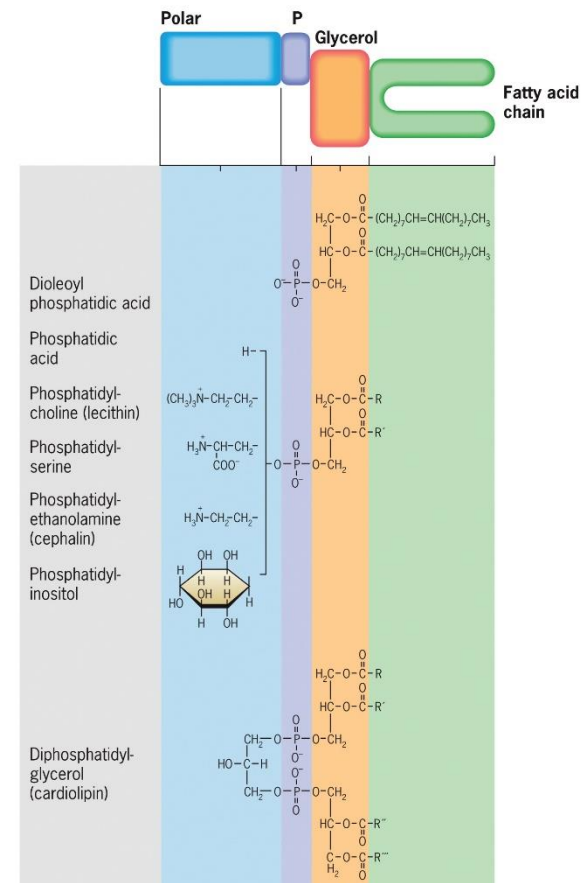
### Membrane Lipids

- Membrane lipids are **amphipathic** which contain both hydrophilic and hydrophobic regions.
- Phosphoglycerides, sphingolipids and cholesterol are types of this.

# 4.2 | The Chemical Composition of Membranes (3 of 6)

## Membrane Lipids: Phosphoglycerides

- Lipids with a phosphate group are **phospholipids**.
- Phospholipids built on a glycerol backbone are called **phosphoglycerides**.
- Fatty acyl chains are hydrophobic
- A fatty acid may be fully saturated, monounsaturated, or polyunsaturated.



## 8.2 | The Lipid Composition of Membranes

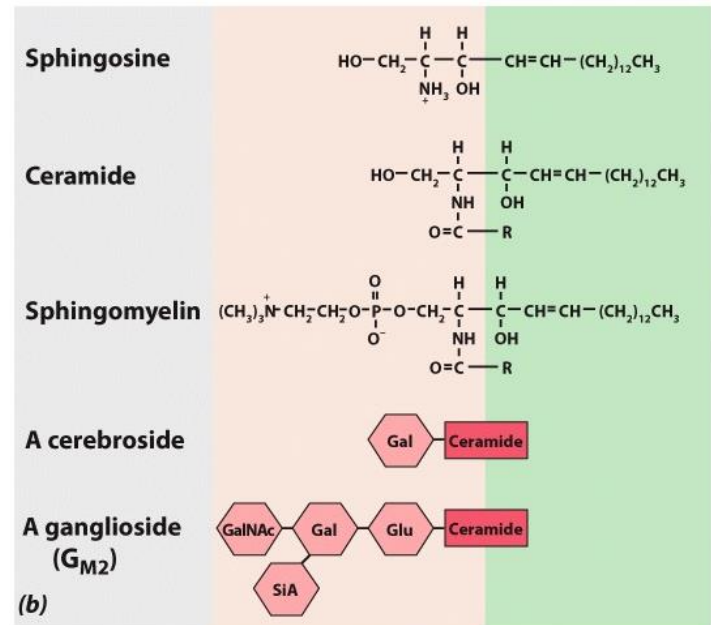
### Membrane Lipids: Sphingolipids

Sphingolipids are derivatives of **sphingosine**, an amino alcohol that contains a long hydrocarbon chain.

Sphingolipids consist of sphingosine linked to a fatty acid by its amino group, called a ceramide.

If the substitution is phosphorylcholine, the molecule is **sphingomyelin**. If the substitution is a carbohydrate, the molecule is a **glycolipid**.

If the carbohydrate is a simple sugar, the glycolipid is a **cerebroside**; if it is a small cluster of sugars that includes sialic acid, the glycolipid is a **ganglioside**.

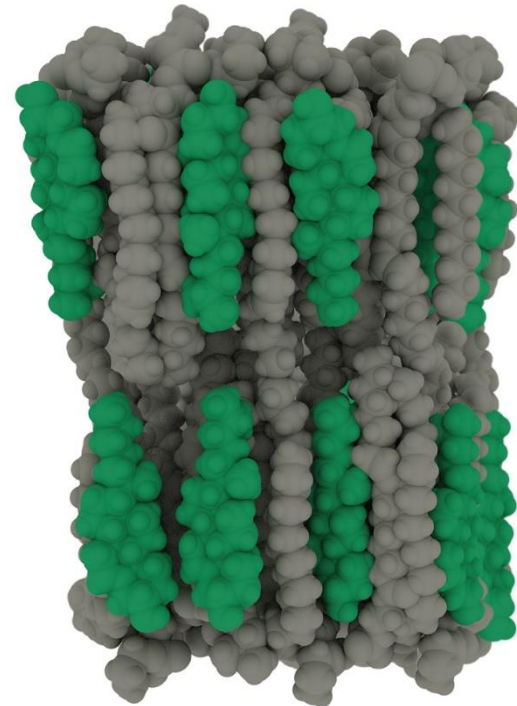


The chemical structure of membrane lipids

## 4.2 | The Chemical Composition of Membranes (4 of 6)

### Membrane Lipids: Cholesterol

- **Cholesterol** is smaller and less amphipathic.
- A sterol that makes up to 50% of animal membrane lipids.
- Carbon rings are flat and rigid.



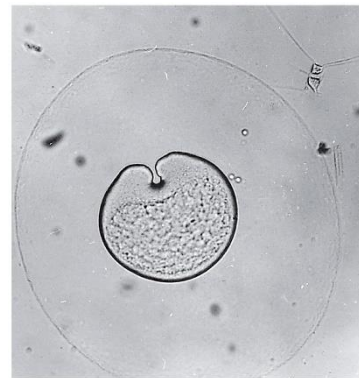
**Cholesterol molecules** (green) oriented with their small hydrophilic end facing the external surface of the bilayer

# 4.2 | The Chemical Composition of Membranes (5 of 6)

## The Nature and Importance of the Lipid Bilayer

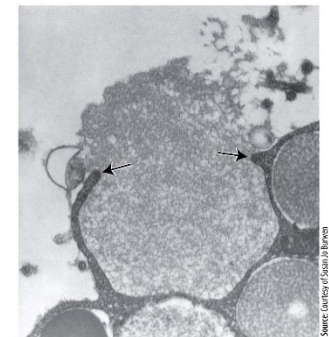
- Membranes form extensive inter-connected networks within the cell.
- Lipid bilayers are flexible.
- The lipid bilayer helps to maintain the proper internal composition of a cell.

**Movement:** ruffling of the plasma membrane of a migrating cell



**Division:** invagination of the plasma membrane during cell division

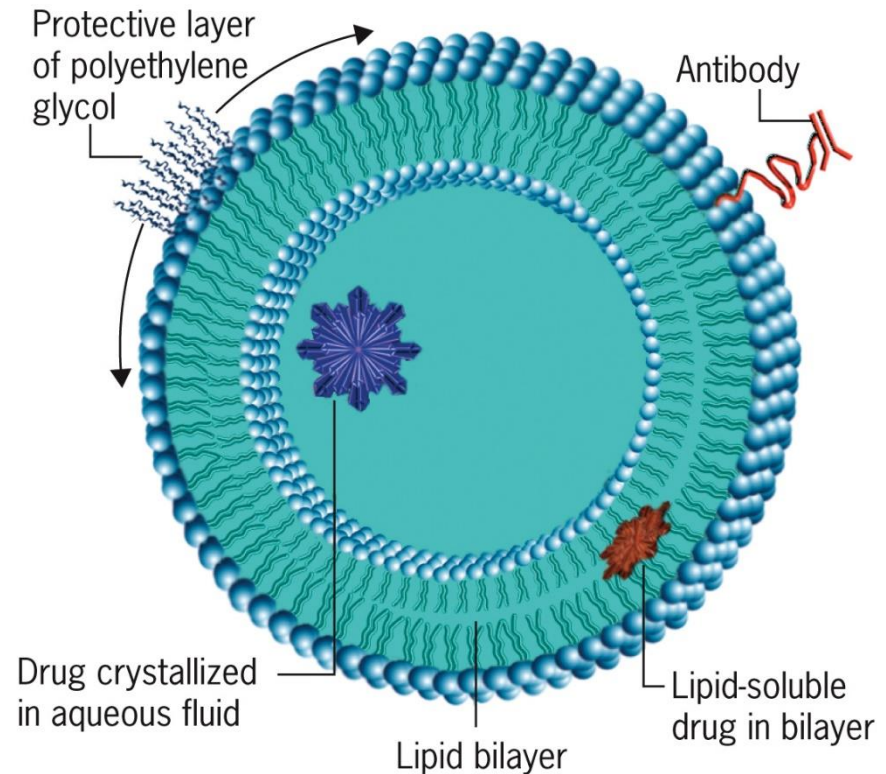
**Fusion:** plasma membranes of sperm and egg unite



# 4.2 | The Chemical Composition of Membranes (6 of 6)

## The Nature and Importance of the Lipid Bilayer

- The lipid bilayer can self-assemble
- Liposomes have proven invaluable in membrane research.
- Membrane proteins can be inserted into liposomes.
- Liposomes are vehicles to deliver drugs or DNA within the body



**Liposomes:** synthetic vesicles

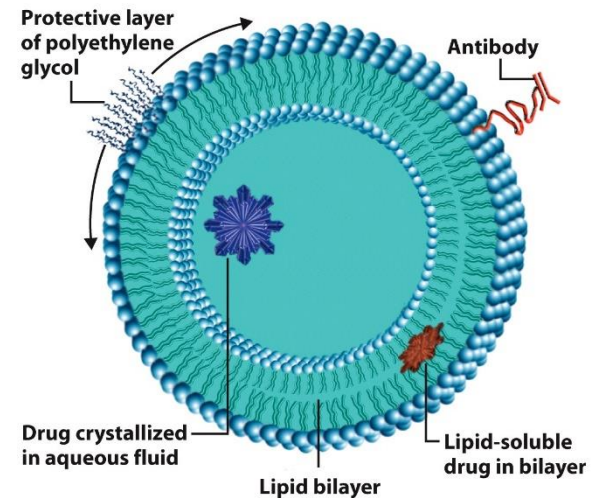
# The Nature and Importance of the Lipid Bilayer

Liposomes are vehicles to deliver drugs or DNA within the body; they can be linked to the liposome wall or contained at high concentration within its lumen.

These walls are constructed to contain specific proteins for selective binding to the surfaces of particular target cells.

Stealth liposomes contain an outer polymer coating that protects the liposomes from immune destruction.

Caelyx, a stealth liposome containing doxorubicin, is an accepted therapy for treatment of metastatic breast cancer.

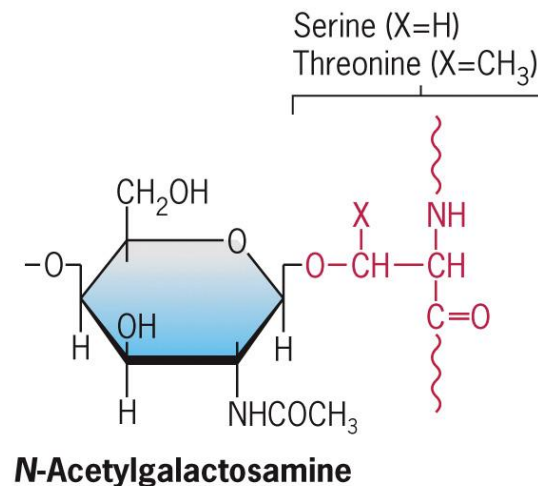
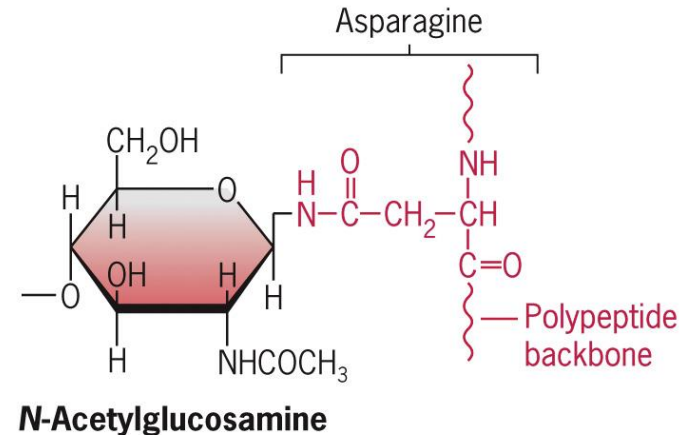


Copyright © John Wiley & Sons, Inc. All rights reserved.

**Liposomes: synthetic vesicles**

## 4.2 | Membrane Carbohydrates (1 of 2)

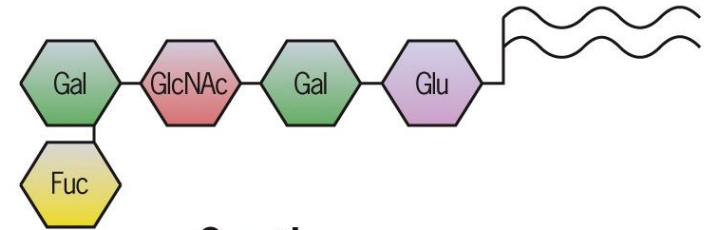
- Plasma membranes of eukaryotic cells have carbohydrate, glycoproteins and glycolipids.
- Oligosaccharides may be attached to several different amino acids by two types of linkages: *N*-linkages and *O*-linkages.
- Carbohydrate projections play an important role in mediating the interactions of a cell with its environment.



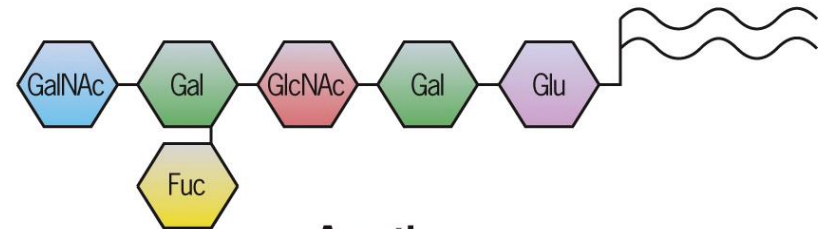
Two types of linkages that join sugars to a polypeptide chain

## 4.2 | Membrane Carbohydrates (2 of 2)

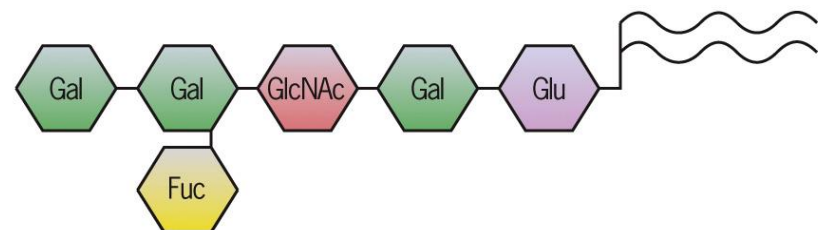
- Glycolipid carbohydrates of the red blood cell plasma membrane determine whether a person's blood type (A, B, AB, or O).
- A: Enzyme adds *N*-acetylgalactosamine to the end of the chain.
- B: Enzyme adds galactose to the chain terminus.
- AB: Both enzymes present.
- O: Lack enzymes capable of attaching either terminal sugar.



**O antigen**



**A antigen**



**B antigen**

Blood-group antigens

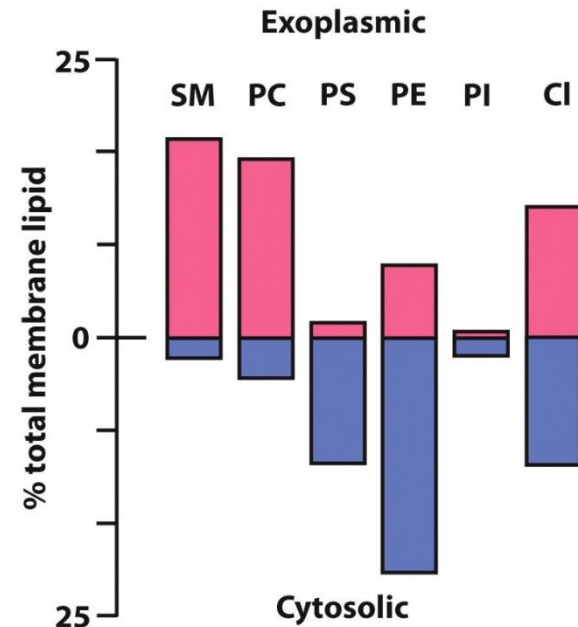
## 8.2 | The Lipid Composition of Membranes

### The Asymmetry of the Membrane Lipids

The lipid bilayer consists of two distinct leaflets that have a distinctly different lipid composition.

Compared to the inner leaflet, the outer leaflet has a relatively high concentration of PC (and sphingomyelin) and a low concentration of PE and PS.

The lipid bilayer is composed of two semi-stable, independent monolayers having different physical and chemical properties.



Copyright © John Wiley & Sons, Inc. All rights reserved.

SM: sphingomyelin  
PC: phosphatidylcholine  
PS: phosphatidylserine  
PE: phosphatidylethanolamine  
PI: phosphatidylinositol  
CI: cholesterol

## 8.2 | The Lipid Composition of Membranes

### The Asymmetry of the Membrane Lipids

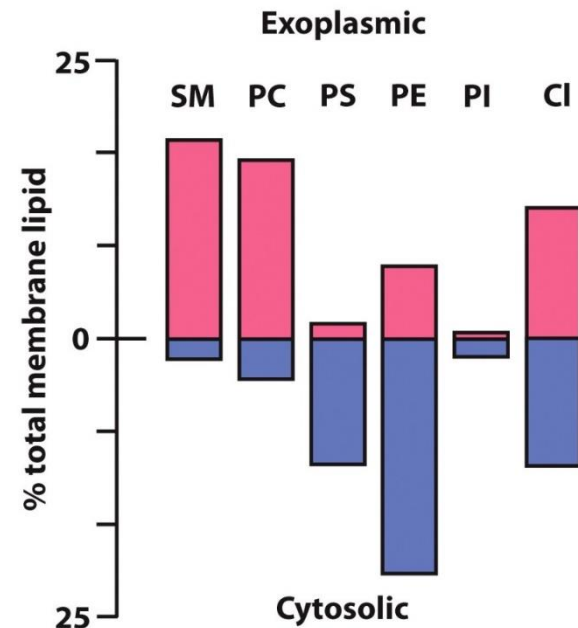
Glycolipids are in the outer leaflet where they act as receptors for ligands.

PE (inner) promotes membrane curvature for membrane budding and fusion.

PS (inner) has a negative charge to bind positively charged lysine and arginine residues on adjacent proteins.

PS (outer) on aging lymphocytes marks the cells for destruction by macrophages.

PI (inner) can be phosphorylated, which converts the lipid into a phosphoinositide for signal transduction pathways.



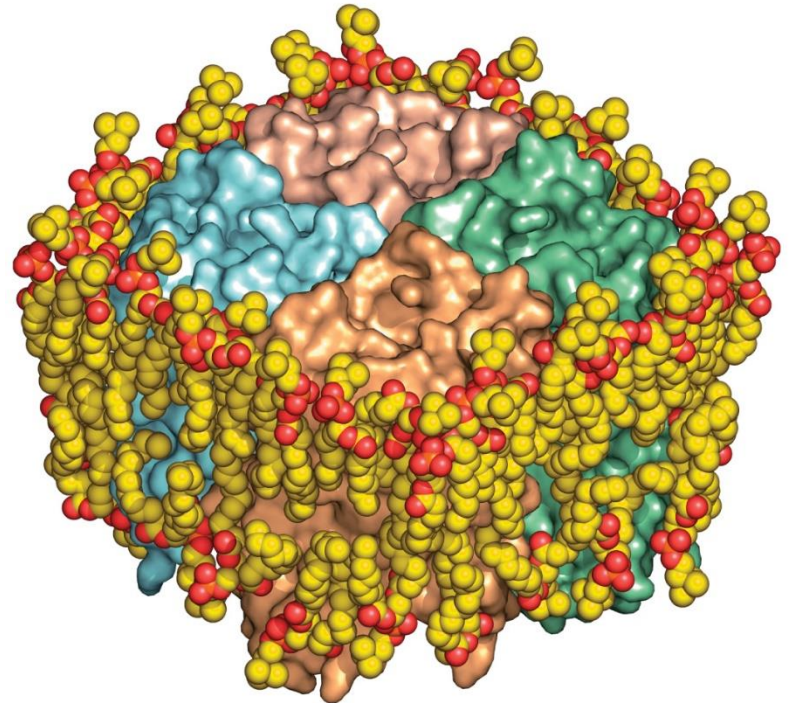
Copyright © John Wiley & Sons, Inc. All rights reserved.

SM: sphingomyelin  
PC: phosphatidylcholine  
PS: phosphatidylserine  
PE: phosphatidylethanolamine  
PI: phosphatidylinositol  
CI: cholesterol

## 4.3 | Membrane Proteins (1 of 2)

### Integral Membrane Proteins

- Integral membrane proteins function as receptors that bind ligands, channels or transporters to move ions/solutes across the membrane.
- They are amphipathic, having both hydrophilic and hydrophobic portions.
- This preserves the permeability barrier of the membrane.



Source: From Carola Hunte and Sebastian Richers, *Curr. Opin. Struct. Biol.* 18:407, ©2008, with permission from Elsevier Science.

Driven by van der Waals forces between amino acids and lipids, proteins can be surrounded by a closely applied shell of lipid molecules.

## 4.3 | Membrane Proteins (2 of 2)

### Peripheral Membrane Proteins

- Peripheral proteins associate with the membrane by weak electrostatic bonds.
- Other cytosolic peripheral proteins act as enzymes, specialized coats, or factors that transmit transmembrane signals.
- Peripheral proteins typically have a dynamic relationship with the membrane, being recruited or released as needed.

## 8.4 | Membrane Proteins

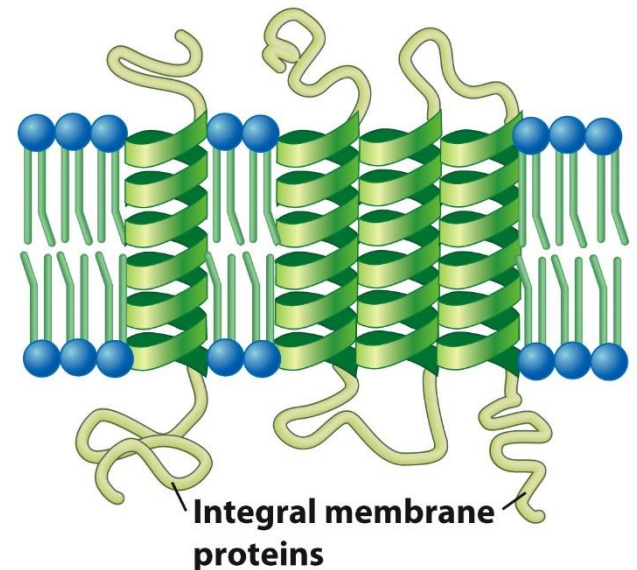
Membrane proteins attach to the bilayer **asymmetrically**, giving the membrane a distinct “**sidedness**”

Membrane proteins grouped into 3 classes:

**Integral proteins:** Penetrate and pass through lipid bilayer; make up 25 -30% of all encoded proteins and 60% of current drug targets.

Amphipathic- hydrophilic domains anchor them in the bilayer and hydrophilic regions form functional domains outside of the bilayer.

Channel proteins have hydrophilic cores that form aqueous channels in the membrane-spanning region.



Copyright © John Wiley & Sons, Inc. All rights reserved.

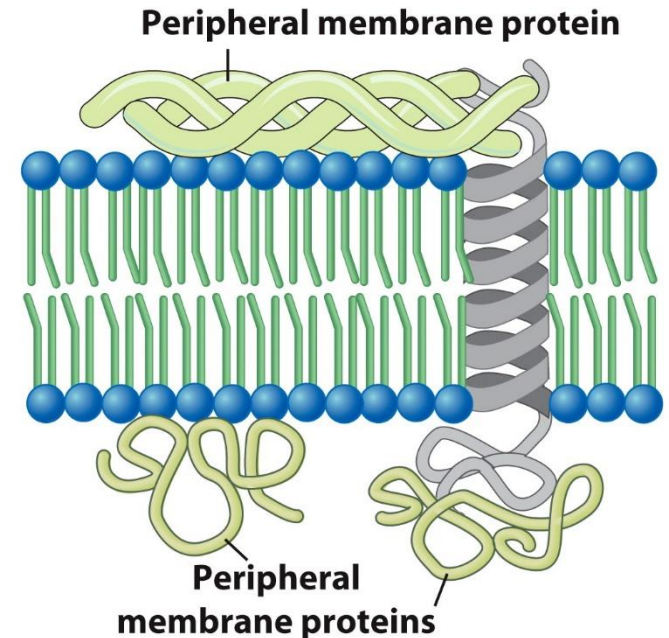
Integral proteins

## 8.4 | Membrane Proteins

Membrane proteins can be grouped into three distinct classes:

**Peripheral proteins:** Attached to the membrane by weak bonds and are easily solubilized.

Located entirely outside of bilayer on either the extracellular or cytoplasmic side; associated with membrane surface by non-covalent bonds.



Copyright © John Wiley & Sons, Inc. All rights reserved.

Peripheral proteins

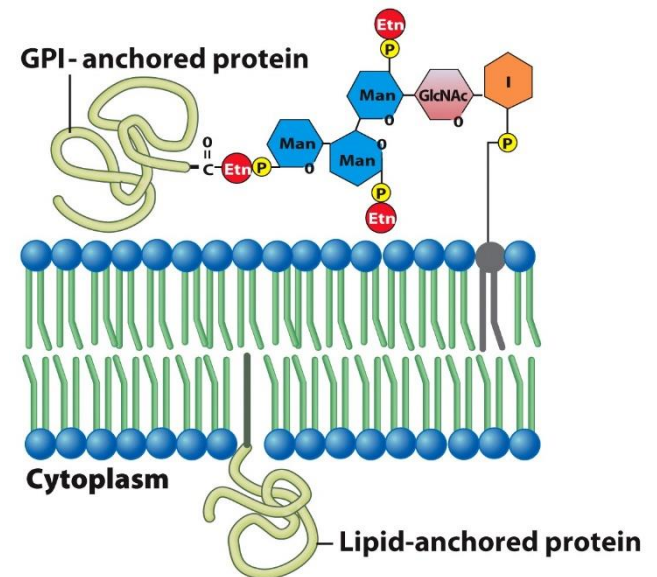
## 8.4 | Membrane Proteins

Membrane proteins can be grouped into three distinct classes:

**Lipid-anchored membrane proteins** are distinguished both by the types of lipid anchor and their orientation.

Glycophosphatidylinositol (**GPI**)-linked **proteins** found on the outer leaflet can be released by inositol-specific phospholipases.

Some inner-leaflet proteins are anchored to membrane lipids by long hydrocarbon chains.



Copyright © John Wiley & Sons, Inc. All rights reserved.

Lipid-anchored proteins

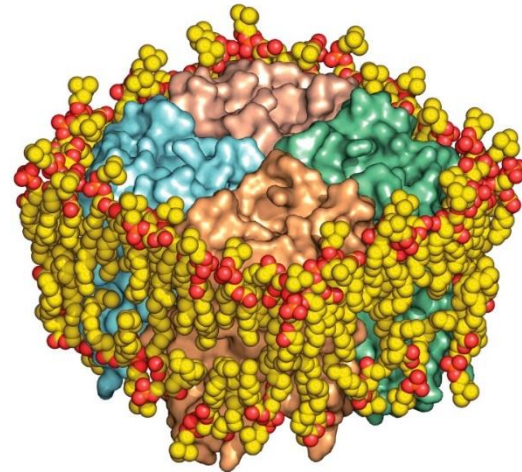
## 8.4 | Membrane Proteins

### Integral Membrane Proteins

Integral membrane proteins function as **receptors that bind ligands**, **channels or transporters to move ions/solutes across the membrane**, or **agents that transfer electrons during photosynthesis and respiration**.

They are amphipathic, having both hydrophilic and hydrophobic portions; the hydrophobic transmembrane domains form van der Waals interactions with the fatty acyl chains of the bilayer.

**This preserves the permeability barrier of the membrane, since the protein is anchored within the bilayer and has direct contact with surrounding lipid molecules.**



From Carola Hunte and Sebastian Richers, Curr. Opin. Struct. Biol. 18: 407, 2008, © 2008, with permission of Elsevier Science

Driven by van der Waals forces between amino acids and lipids, proteins can be surrounded by a closely applied shell of lipid molecules.

## 8.4 | Membrane Proteins

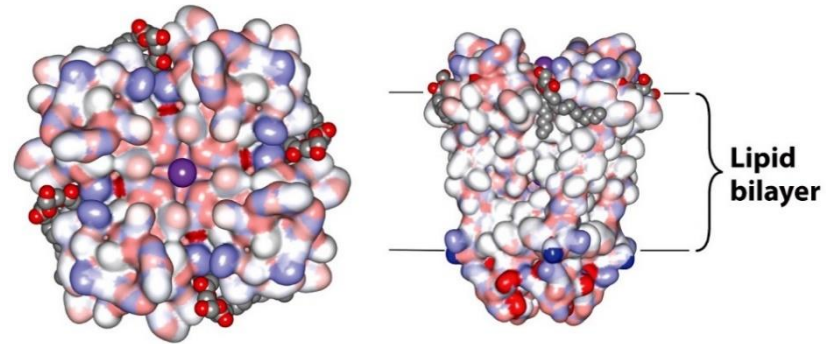
### Integral Membrane Proteins

Most lipid molecules that make contact with a transmembrane domain are rapidly exchanged with other lipid molecules in the bilayer.

Specific sites on membrane proteins can form important functional interactions with specific lipid molecules.

Anionic lipid molecules can bind at subunit interfaces of a tetrameric KcsA K<sup>+</sup> channel.

The channel does not open normally in a bilayer that lacks these specific lipid molecules.



From A.G. Lee, Trends Biochem. Sci. 36:497, 2011, © 2011; with permission from Elsevier.

Views of a tetrameric membrane protein, the bacterial K<sup>+</sup> channel

## 8.4 | Membrane Proteins

### Integral Membrane Proteins

Protein domains that project into either the cytoplasm or extracellular space tend to be like the globular proteins, with hydrophilic surfaces that interact with water-soluble substances.

Transmembrane domains can be devoid of water molecules, while others allow the water to penetrate deeply.

Large families of membrane proteins contain an interior channel with key hydrophilic residues at strategic locations that provides an aqueous passageway through the lipid bilayer.

Integral proteins need not be fixed structures but may be able to move laterally within the membrane.

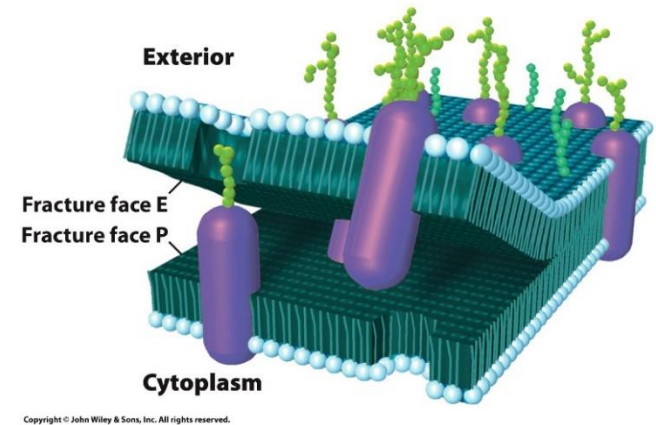
## 8.4 | Membrane Proteins

### Integral Membrane Proteins

The concept that proteins penetrate through membranes was derived primarily from the results of freeze-fracture replication.

Tissue is frozen solid and then struck with a knife blade, which often causes a fracture plane between the two leaflets of the lipid bilayer.

Deposited metals on the exposed surfaces form a shadowed *replica*, viewed by electron microscopy.



Ectoplasmic vs  
protoplasmic

## 8.4 | Membrane Proteins

### Peripheral Membrane Proteins

Peripheral proteins associate with the membrane by weak electrostatic bonds, and can usually be solubilized by extraction with **high-concentration salt solutions**.

The best studied are located on the cytosolic surface of the plasma membrane, where they form a fibrillar network that acts as a **membrane “skeleton” to provide mechanical support to the membrane and to function as an anchor for integral membrane proteins**.

Other cytosolic peripheral proteins act as **enzymes, specialized coats, or factors that transmit transmembrane signals**.

Peripheral proteins typically have a dynamic relationship with the membrane, being recruited or released as needed.

## 8.4 | Membrane Proteins

### Lipid-Anchored Membrane Proteins

Numerous peripheral membrane proteins have a glycosylphosphatidylinositol linkage that embeds them in the outer leaflet of the lipid bilayer, so are called GPI-anchored proteins.

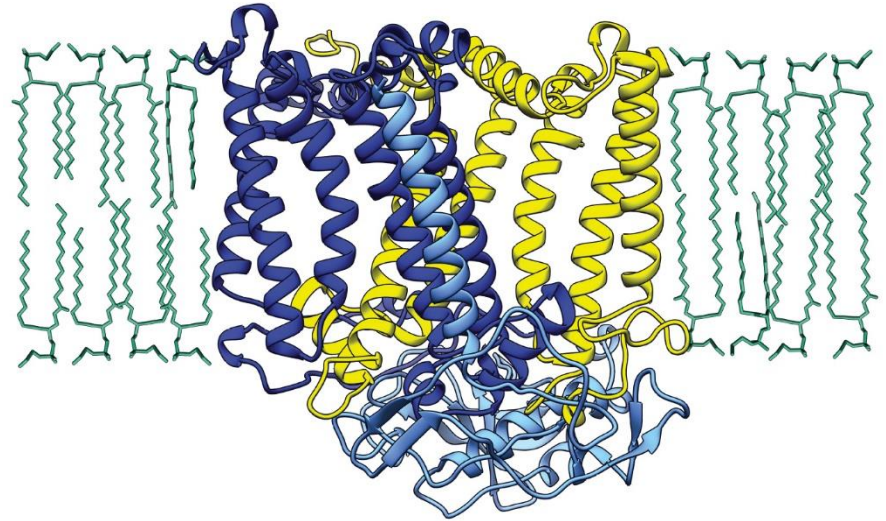
Examples include the normal cellular **scrapie protein PrP<sup>C</sup>**, as well as various **receptors, enzymes, and cell-adhesion proteins**.

Another group of proteins is anchored on the cytoplasmic side of the plasma membrane within the inner leaflet of the lipid bilayer by one or more long hydrocarbon chains.

**Two proteins associated with the plasma membrane in this way (Src and Ras) are implicated in the transformation of a normal cell to a malignant state.**

## 4.3 | Studying the Structure and Properties of Integral Membrane Proteins

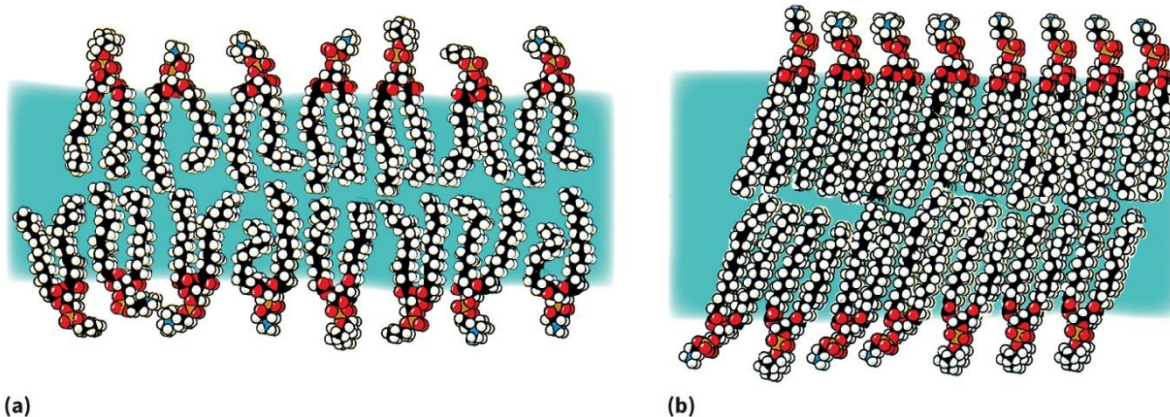
- It is very difficult to obtain crystals of integral membrane proteins for X-ray crystallography
- Most solved structures are prokaryotic versions that are smaller than eukaryotic versions.
- Homology modeling is used to learn about the structure and activity of members of a protein family.



An integral protein as it resides within the plasma membrane

## 4.4 | Membrane Lipids and Membrane Fluidity (1 of 3)

- Physical state of the membrane lipid is described by its fluidity or viscosity.
- If the temperature of the bilayer is kept relatively warm (37°C), the lipid exists in a relatively fluid state.
- Molecules retain a specified orientation.



Source: R. N. Robertson, *The Lively Membranes*, Cambridge Univ. Press, 1983, reprinted with permission of Cambridge Univ. Press.

Structure of the lipid bilayer depends on the temperature: above and below the transition temperature

## 4.4 | Membrane Lipids and Membrane Fluidity (2 of 3)

### **Maintaining Membrane Fluidity**

- Internal temperatures of most organisms can fluctuate with the temperature, so cells respond by altering phospholipid composition.
- Desaturation is catalyzed by desaturases.
- The cell changes the types of phospholipids being synthesized in favor of ones containing more unsaturated fatty acids.

## 8.6 | Membrane Lipids and Membrane Fluidity

### Maintaining Membrane Fluidity

Internal temperatures of most organisms can fluctuate with the temperature, so cells respond by altering phospholipid composition. If the temperature is lowered, cells can remodel membranes to make them more cold resistant.

Remodeling is accomplished by (1) desaturating single bonds in fatty acyl chains to form double bonds, and (2) reshuffling chains between different phospholipid molecules to make ones that have two unsaturated fatty acids.

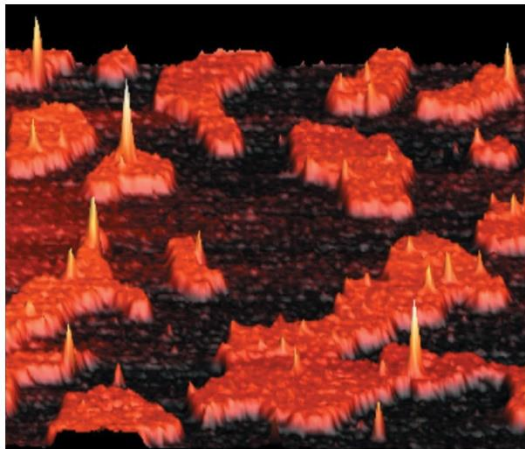
Desaturation is catalyzed by desaturases, while reshuffling is accomplished by phospholipases, which split the fatty acid from the glycerol backbone, and acyl-transferases, which transfer fatty acids between phospholipids.

In addition, the cell changes the types of phospholipids being synthesized in favor of ones containing more unsaturated fatty acids.

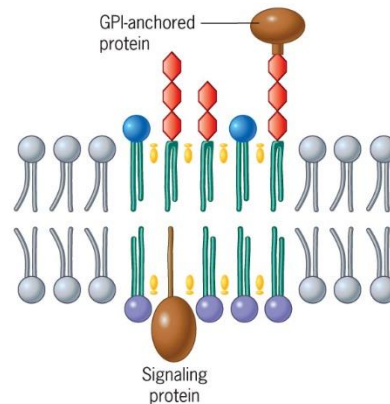
# 4.4 | Membrane Lipids and Membrane Fluidity (3 of 3)

## Lipid Rafts

- The outer leaflet of plasma membrane contains specialized regions.
- Cholesterol and sphingolipids tend to pack together to form highly ordered microdomains forming **lipids rafts**.
- They provide a favorable environment for cell-surface receptors.



(a)



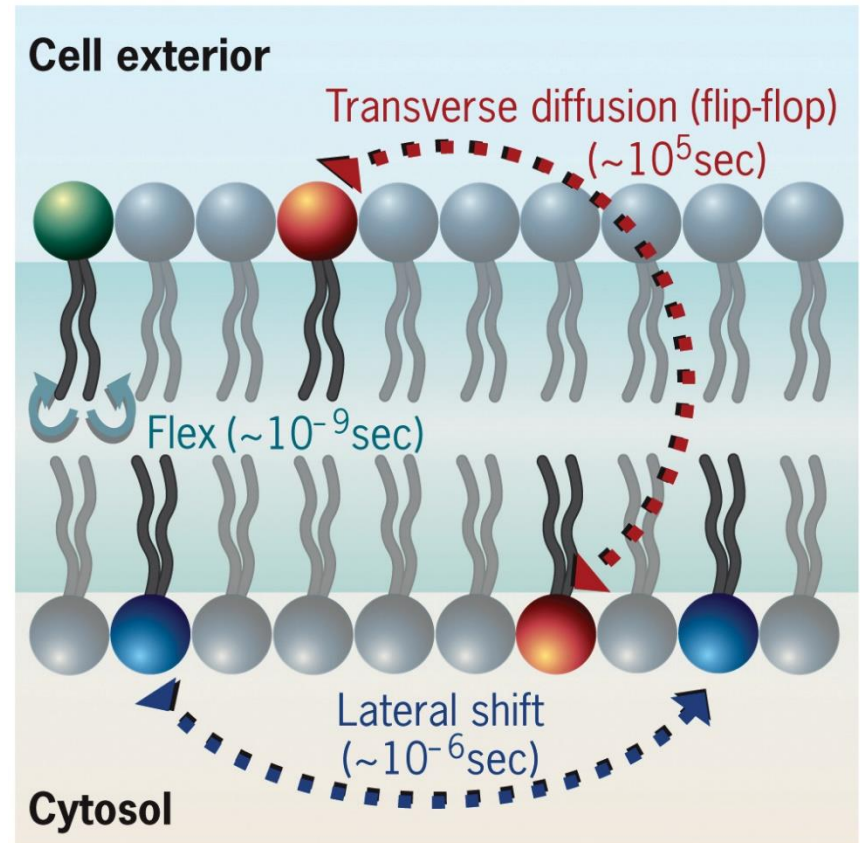
(b)

(left) Sphingomyelin organizing into orange-colored rafts; (right) Schematic model of a lipid raft

Source: (a) Republished with permission of The American Society for Biochemistry and Molecular Biology, from Placental Alkaline Phosphatase Is Efficiently Targeted to Rafts in Supported Lipid Bilayers, *The Journal of Biological Chemistry*, David E. Saslowsky et al. 277, 2002; permission conveyed through Copyright Clearance Center, Inc; (b) Adapted from the works of J. Michael Edwardson.

## 4.5 | The Dynamic Nature of the Plasma Membrane (1 of 7)

- A phospholipid can move laterally.
- A phospholipid can diffuse from one end of a bacterium to the other end in a second or two.
- Flippases are enzymes that move certain phospholipids from one leaflet to the other.

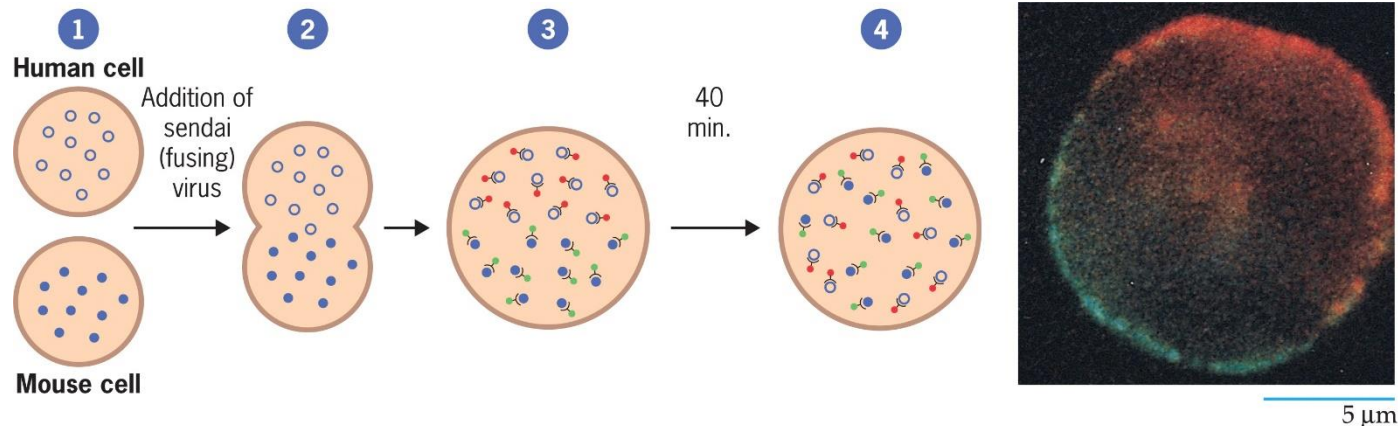


The possible movements of phospholipids in a membrane

# 4.5 | The Dynamic Nature of the Plasma Membrane (2 of 7)

## The Diffusion of Membrane Proteins after Cell Fusion

- Cell fusion is a technique whereby two different types of cells, or cells from two different species, can be fused to produce one cell.
- Labeled proteins have shown that membrane proteins can move between fused cell.



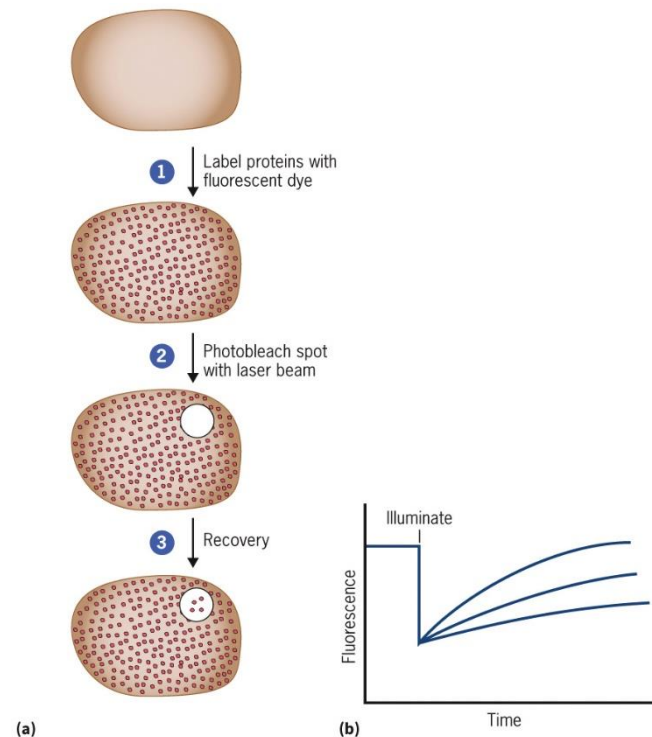
Source: Republished with permission of The Company of Biologists Ltd, from *The Rapid Intermixing of Cell Surface Antigens After Formation of Mouse-Human Heterokaryons*, L. D. Frye and Michael Edidin, 1970; permission conveyed through Copyright Clearance Center, Inc.

**Cell fusion to reveal mobility of membrane proteins: fusion of human and mouse cells**

# 4.5 | The Dynamic Nature of the Plasma Membrane (3 of 7)

## The Diffusion of Membrane Proteins after Cell Fusion

- Proteins can be labeled and tracked.
- Proteins can be immobile, mobile in a directed manner, or exhibit random movement.

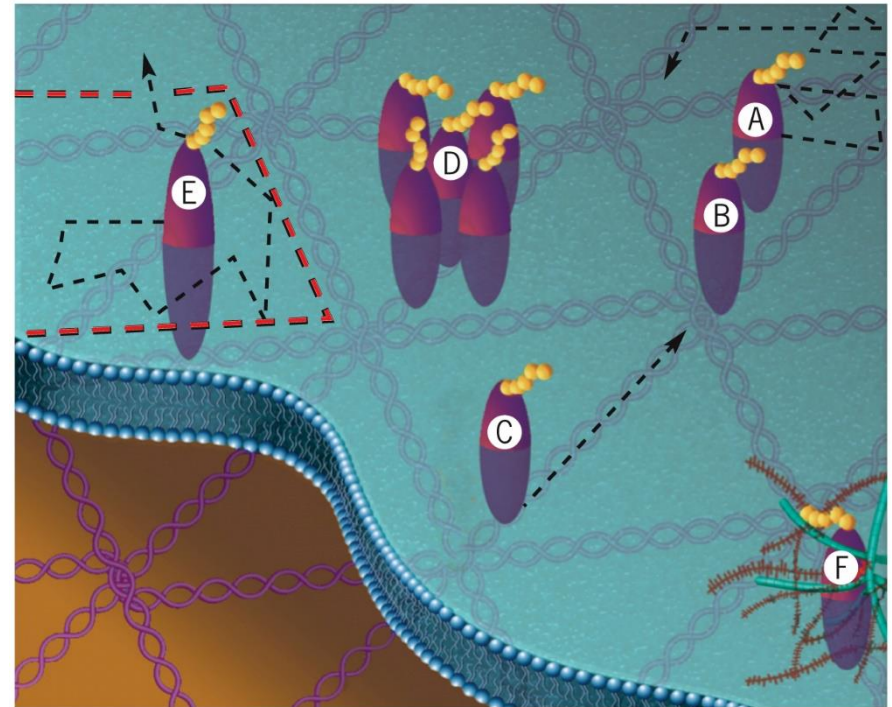


**Measuring the diffusion rates of membrane proteins by FRAP:** variable nature of fluorescence recovery is dependent upon the protein examined

# 4.5 | The Dynamic Nature of the Plasma Membrane (4 of 7)

## Control of Membrane Protein Mobility

- Protein movements are slower than predicted by protein size and membrane viscosity.
- Protein movements are limited by various interactions.
- Some proteins have barriers to lateral diffusion.



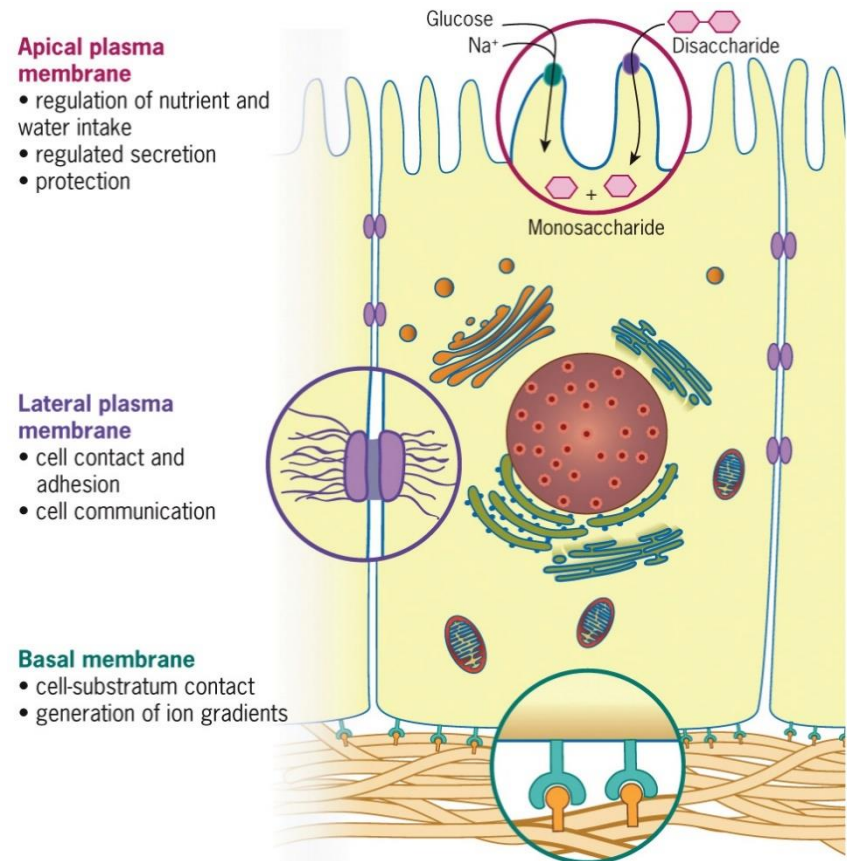
Patterns of movement of integral membrane proteins

# 4.5 | The Dynamic Nature of the Plasma Membrane (6 of 7)

## Membrane Domains and Polarity

- Most membranes vary in protein composition and mobility.
- The epithelial cells that line the intestines and kidneys have highly polarized cells.
- The apical plasma membrane absorbs substances from the lumen.

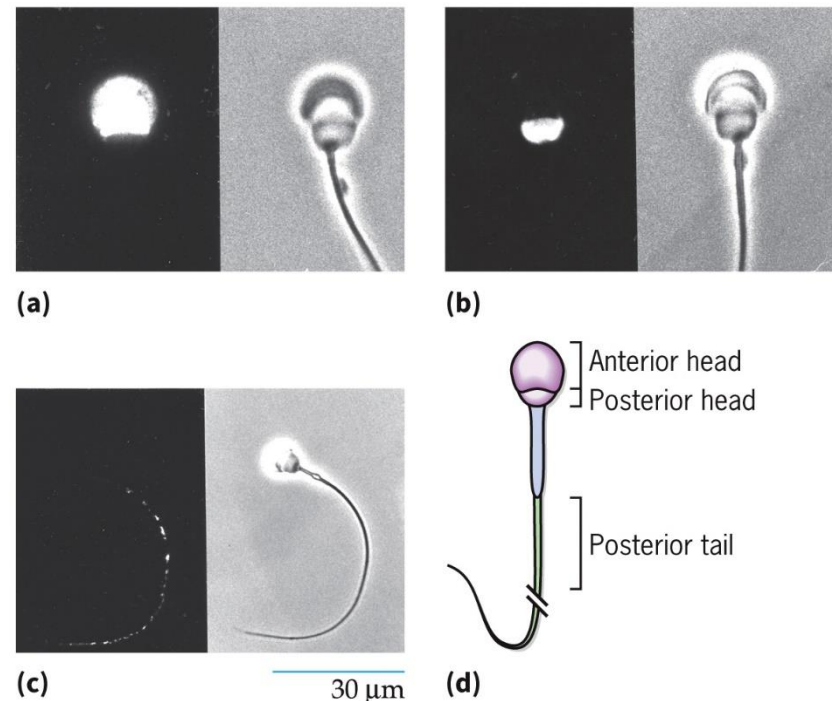
Differentiated functions of the plasma membrane of an epithelial cell



# 4.5 | The Dynamic Nature of the Plasma Membrane (7 of 7)

## Membrane Domains and Polarity

- Sperm may have the most highly differentiated structure.
- A sperm is covered by a continuous plasma membrane.
- Antibodies can detect and reflect the distribution of different proteins.

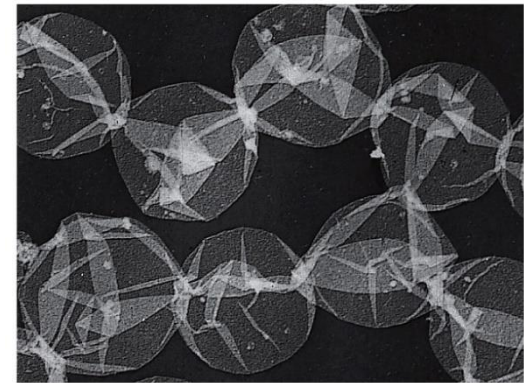
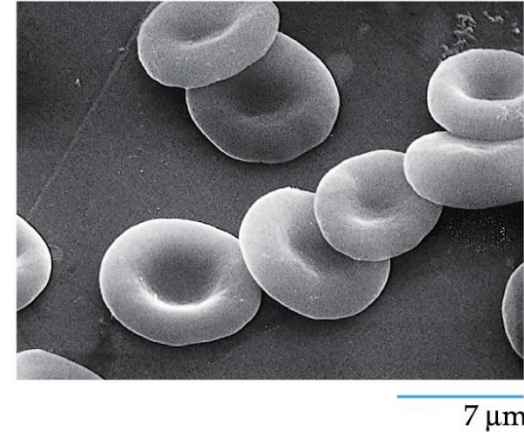


Differentiation of the mammalian sperm plasma membrane as revealed by fluorescent antibodies

Source: (a-c) From Diana Goid Myles, Paul Primakoff, and Anthony R. Bellvé, *Cell* 23:434, © 1981, with permission from Elsevier.

## 4.5 | The Red Blood Cell: An Example of Plasma Membrane Structure (1 of 2)

- The plasma membrane of the human erythrocyte is the most studied and best understood.
- Membrane proteins can be purified.

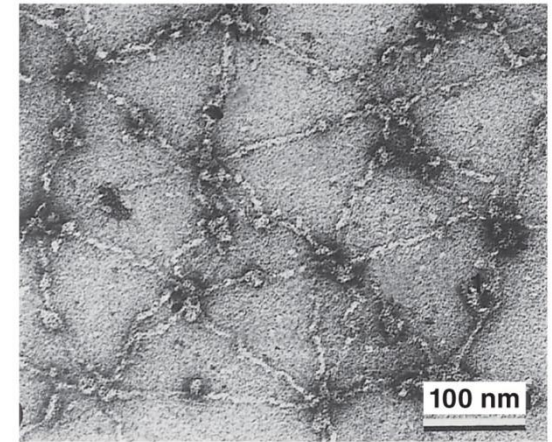
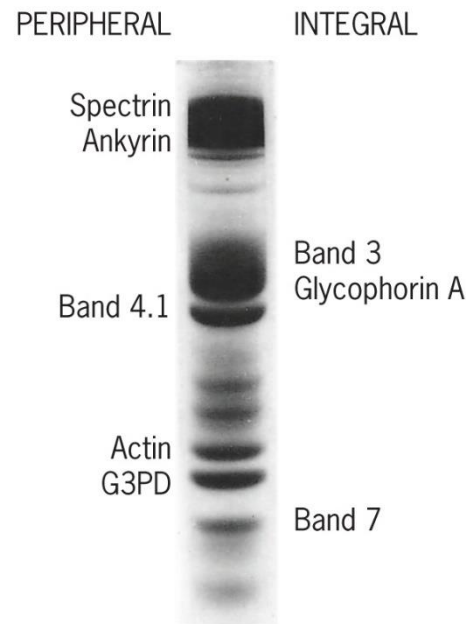


SEM of human erythrocytes and membrane ghosts

# 4.5 | The Red Blood Cell: An Example of Plasma Membrane Structure (2 of 2)

## The Erythrocyte Membrane Skeleton

- The major component of the internal membrane skeleton is **spectrin**.
- Spectrin molecules are attached to the membrane surface to **ankyrin**.
- Spectrin is linked to other cytoplasmic proteins as well.

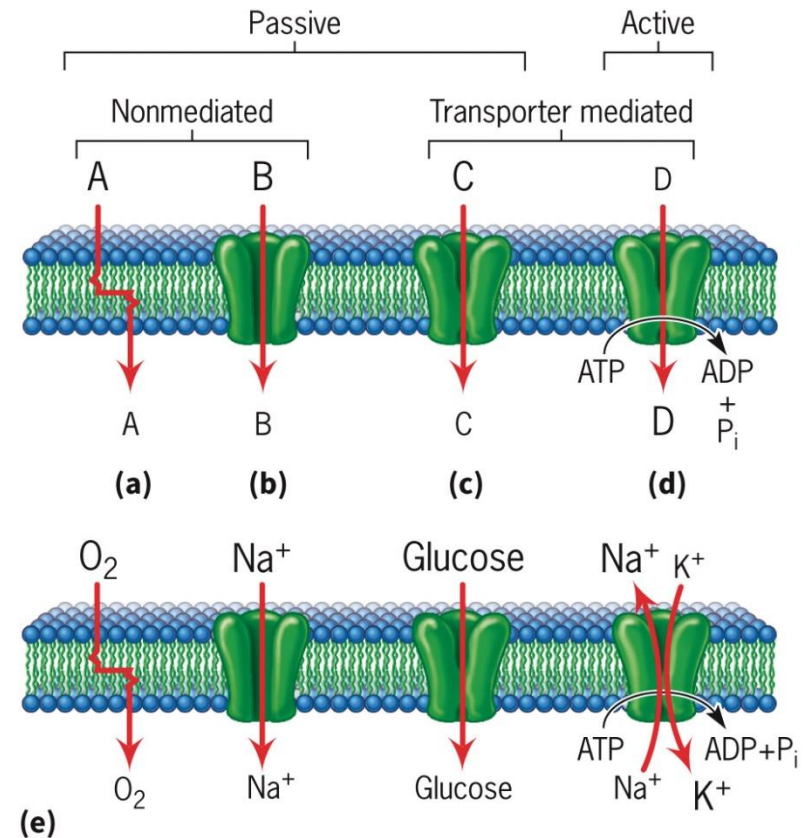


**Source:** (left) From V. T. Marchesi, H. Furthmayr, and M. Tomita, *Annu. Rev. Biochem.* vol. 45; ©1976 by Annual Reviews Inc.; (right) ©1987 Shih-Chun Liu et al. Originally published in *The Journal of Cell Biology*. <http://doi.org/10.1083/jcb.104.3.527>

**EM:** inner membrane skeleton proteins

# 4.6 | Movement Of Substances Across Cell Membranes

- Selective permeability allows for separation and exchange of materials across the plasma membrane
- **Net flux** is the difference between **influx** and **efflux** of materials.
- Substances move across membranes by diffusion and active transport.



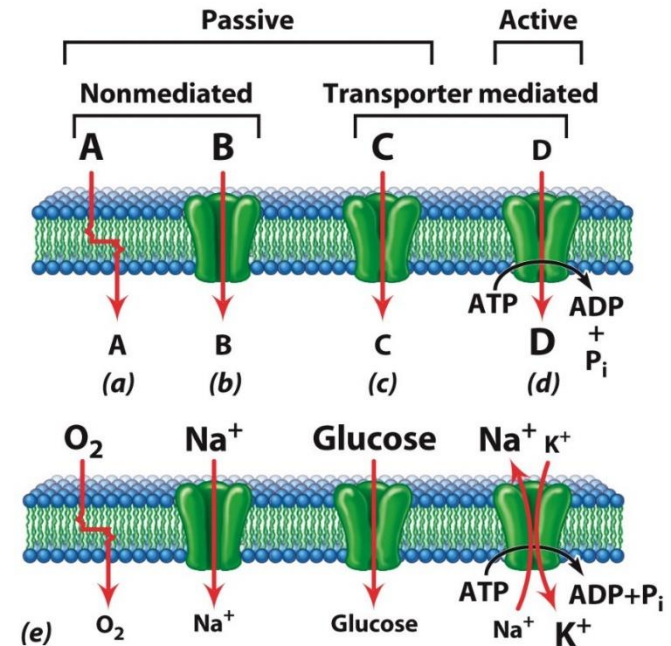
Four basic mechanisms by which solute molecules move across membranes

# Solute Movement Across Cell Membranes

Selective permeability allows for separation and exchange of materials across the plasma membrane

Substances move across membranes by:

- 1) simple diffusion through the lipid bilayer;
- 2) simple diffusion through an aqueous, protein-lined channel;
- 3) diffusion facilitated by a protein transporter;
- 4) active transport, requires an energy-driven protein “pump” to move substances against a concentration gradient



Copyright © John Wiley & Sons, Inc. All rights reserved.

Four basic mechanisms by which solute molecules move across membranes

# Diffusion Through the Lipid Bilayer

## Diffusion of Substance Through Membranes

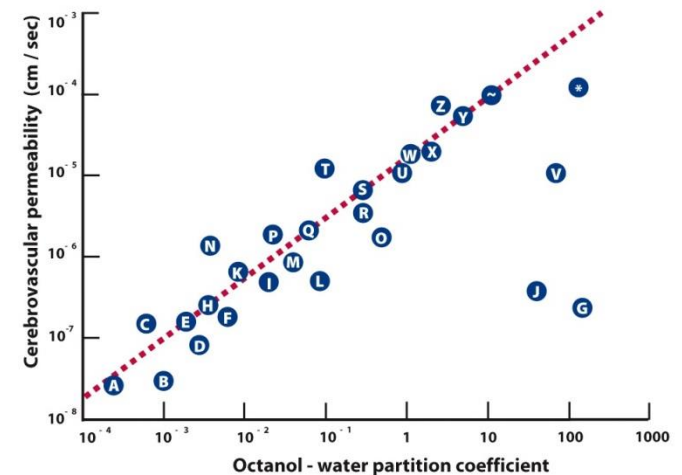
Diffusion requires both a concentration gradient and membrane permeability.

Lipid permeability is determined by the molecular size, polarity, and **partition coefficient**, the ratio of solubility in a nonpolar solvent to that in water.

Small molecules penetrate the lipid bilayer more rapidly than larger ones.

Polar molecules, like sugars and amino acids, have poor membrane penetration.

The greater the lipid solubility, the faster the penetration.



A. Sucrose	J. Vinblastine	S. Misonidazole
B. Epipodophyllotoxin	K. Curare	T. Propylene glycol
C. Mannitol	L. Thiourea	U. Metronidazole
D. Arabinose	M. Dianhydrogalacticol	V. Spirohydantoin mustard
E. <i>N</i> -methyl nicotinamide	N. Glycerol	W. Procarbazine
F. Methotrexate	O. 5-FU	X. PCNU
G. Vincristine	P. Ethylene glycol	Y. Antipyrine
H. Urea	Q. Acetamide	Z. Caffeine
I. Formamide	R. Ftorafur	~, BCNU
		*, CCNU

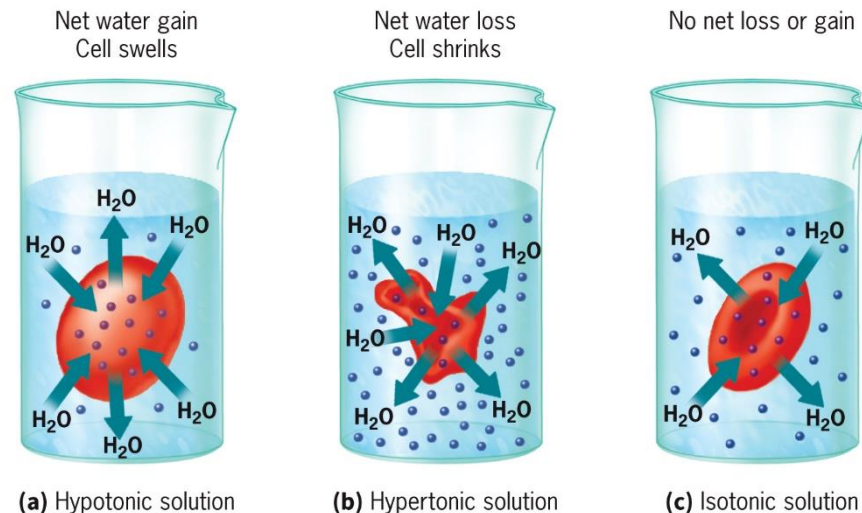
Copyright © John Wiley & Sons, Inc. All rights reserved.

The relationship between partition coefficient and membrane permeability.

# 4.6 | Diffusion Through the Lipid Bilayer (1 of 2)

## The Diffusion of Water Through Membranes

- Diffusion of water through a semipermeable membrane is called **osmosis**.
- Cells swell in **hypotonic** solution, shrink in **hypertonic** solutions, and remain unchanged in **isotonic** solutions.

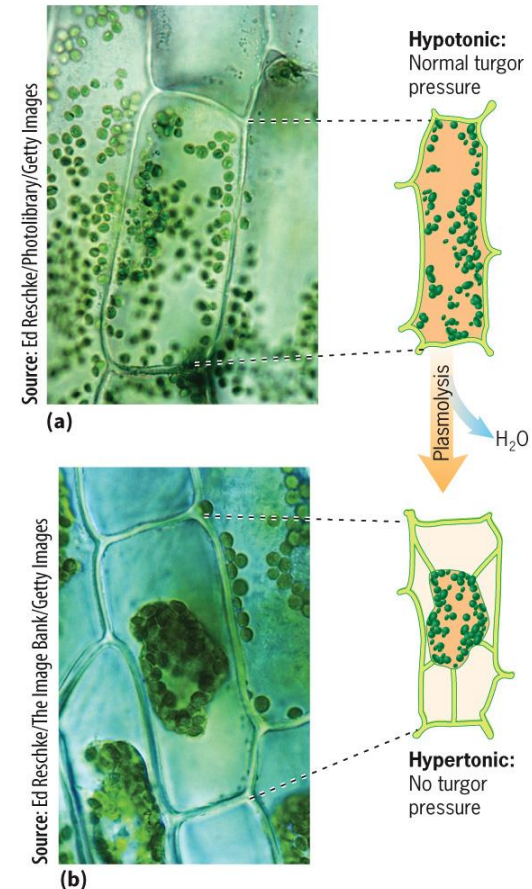


The effects of differences in the concentration of solutes on opposite sides of the plasma membrane

# 4.6 | Diffusion Through the Lipid Bilayer (2 of 2)

## The Diffusion of Water Through Membranes

- Plants utilize osmosis in different ways as they are usually hypertonic compared to their fluid environment.
- There is a tendency for water to enter the cell.
- In hypertonic solutions the plant cell undergoes **plasmolysis**.



The effects of osmosis on a plant cell

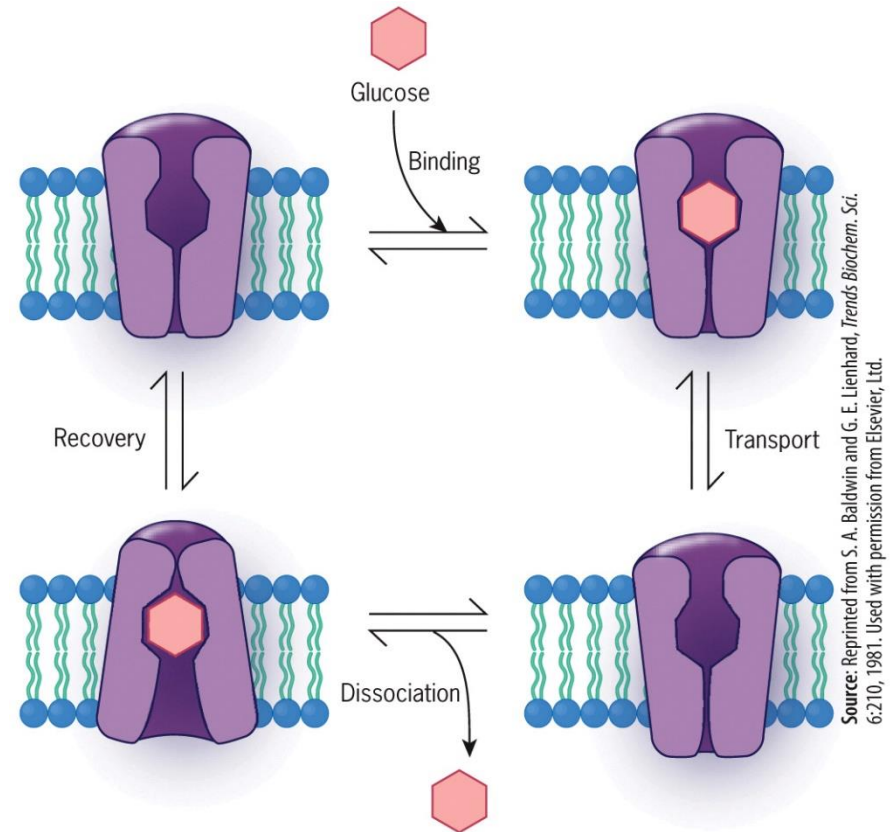
## 4.6 | The Diffusion of Ions through Membranes (1 of 2)

Most ion channels can exist in either an open or a closed conformation, and are called gated. The three major categories of gated channels are:

- 1. Voltage-gated channels:** Conformational state depends on the difference in ionic charge on the two sides of the membrane.
- 2. Ligand-gated channels:** Conformational state depends on the binding of a specific molecule (ligand).
- 3. Mechano-gated channels:** Conformational state depends on mechanical forces that are applied to the membrane.

## 4.6 | Facilitated Diffusion (1 of 2)

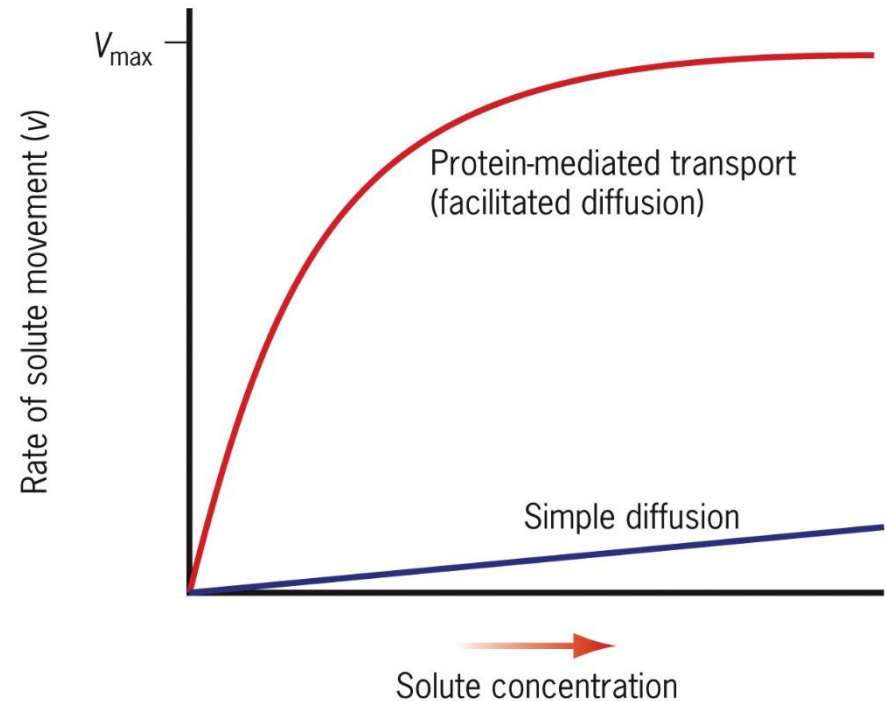
- In many cases, the diffusing substance binds selectively to a membrane-spanning protein, called a facilitative transporter.
- Facilitated transporters can mediate the movement of solutes in both directions.
- **Facilitated diffusion** is similar to an enzyme-catalyzed reaction.



Schematic model of facilitated diffusion

## 4.6 | Facilitated Diffusion (2 of 2)

- Insulin plays a key role in maintaining proper blood sugar levels.
- An increase in blood glucose levels triggers the secretion of insulin, which stimulates the uptake of glucose.
- Rising insulin levels stimulates the movement of transporters to the cell surface.



Kinetics of facilitated diffusion compared to simple diffusion

## 4.6 | Active Transport (1 of 5)

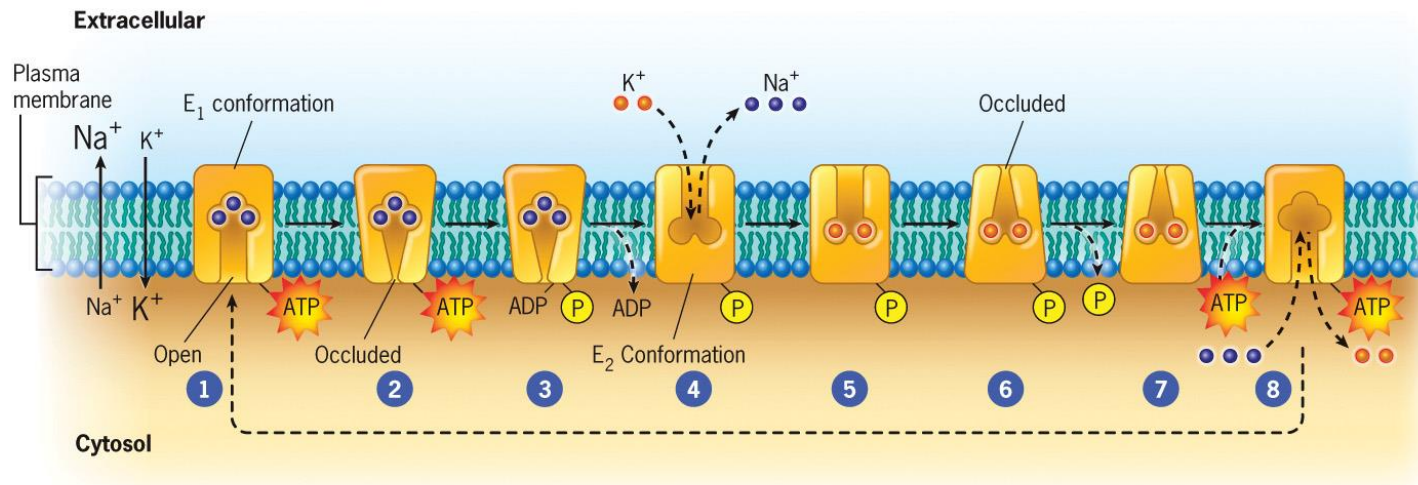
- Cells maintain an imbalance of ions across the plasma membrane, which cannot occur by either simple or facilitated diffusion.
- Gradients are generated by active transport.
- Coupled energy input is needed like ATP hydrolysis, absorbance of light, electron transport, or the flow of other substances down their gradients.

	Extracellular concentration	Intracellular concentration	Ionic gradient
Na <sup>+</sup>	150 mM	10 mM	15x
K <sup>+</sup>	5 mM	140 mM	28x
Cl <sup>-</sup>	120 mM	10 mM	12x
Ca <sup>2+</sup>	10 <sup>-3</sup> M	10 <sup>-7</sup> M	10,000x
H <sup>+</sup>	10 <sup>-7.4</sup>	10 <sup>-7.2</sup>	Nearly 2x
	(pH of 7.4)	(pH of 7.2)	

Ion Concentrations Inside and Outside a Typical Mammalian Cell

## 4.6 | Active Transport (2 of 5)

### Primary Active Transport: Coupling Transport to ATP Hydrolysis

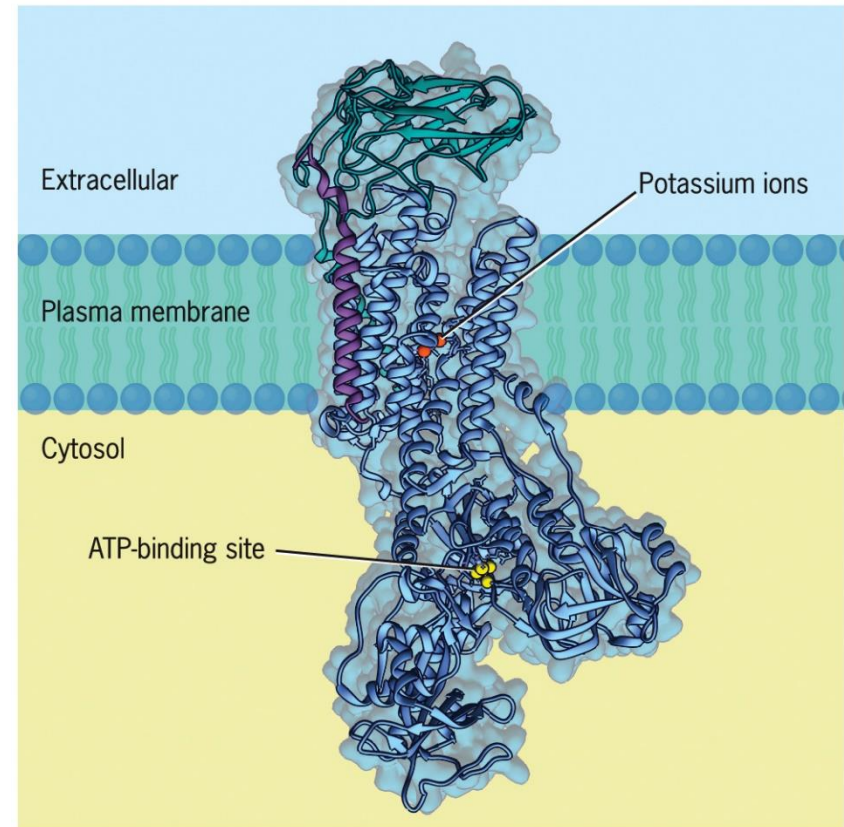


- The Na<sup>+</sup>/K<sup>+</sup> ATPase (sodium-potassium pump) requires K<sup>+</sup> outside, Na<sup>+</sup> inside, and is inhibited by ouabain.
- The ratio of Na<sup>+</sup>:K<sup>+</sup> pumped is 3:2.
- The ATPase is a P-type pump, in which phosphorylation causes changes in conformation and ion affinity that allow transport against gradients.

## 4.6 | Active Transport (3 of 5)

### Primary Active Transport: Coupling Transport to ATP Hydrolysis

- $E_1$  conformation: Ion binding sites are accessible to the inside of the cell.
- $E_2$  conformation: Ion binding sites are accessible to the outside of the cell.
- The sodium–potassium pump is found only in animal cells.



The  $\text{Na}^+/\text{K}^+$ -ATPase pump: A model of the  $E_2$  conformation

## 4.6 | Active Transport (4 of 5)

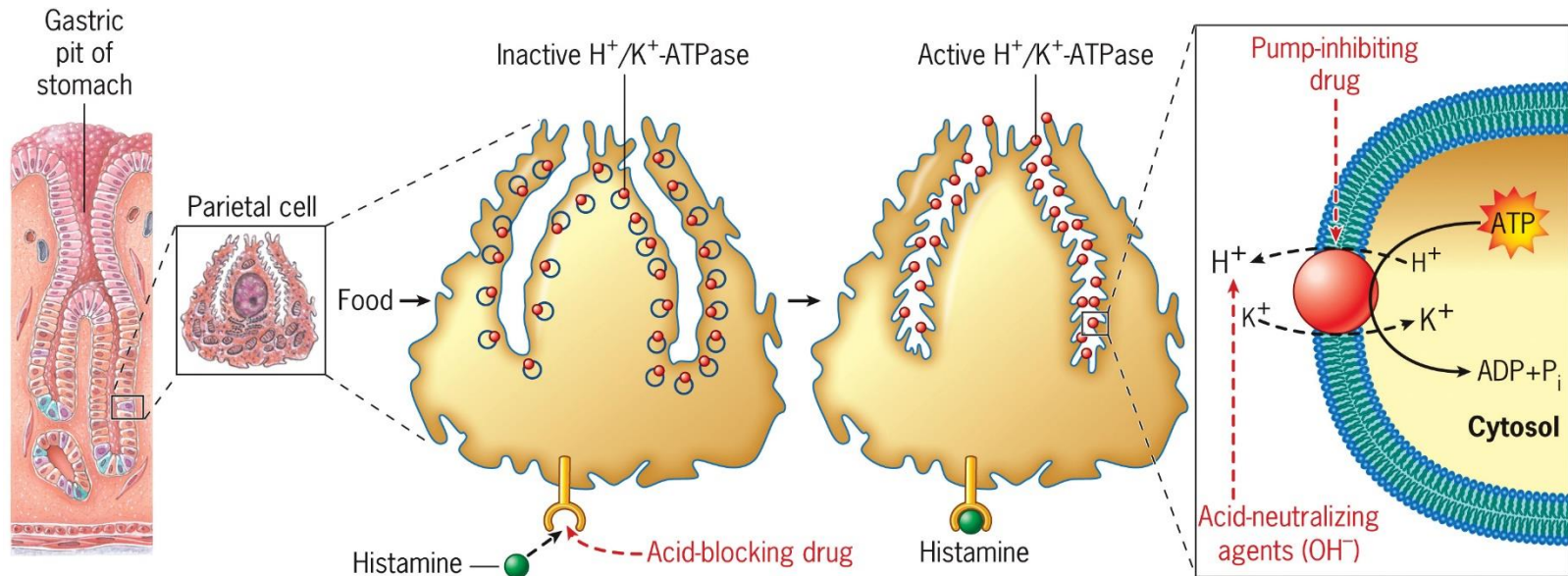
### Other Primary Ion Transport Systems

- The best studied P-type pump is the  $\text{Ca}^{2+}$ -ATPase, present in the ER to actively transport  $\text{Ca}^{2+}$  out of the cytosol into the lumen of this organelle.
- V-type pumps actively transport  $\text{H}^+$  across the walls of cytoplasmic organelles.
- A V-type pump in the plasma membranes of kidney tubules helps maintain the body's acid–base balance by secreting protons into the forming urine.

## 4.6 | Active Transport (5 of 5)

### Other Primary Ion Transport Systems

- The stomach contains the P-type pump.
- The stomach also has H/K-ATPase, which secretes a solution of concentrated acid.

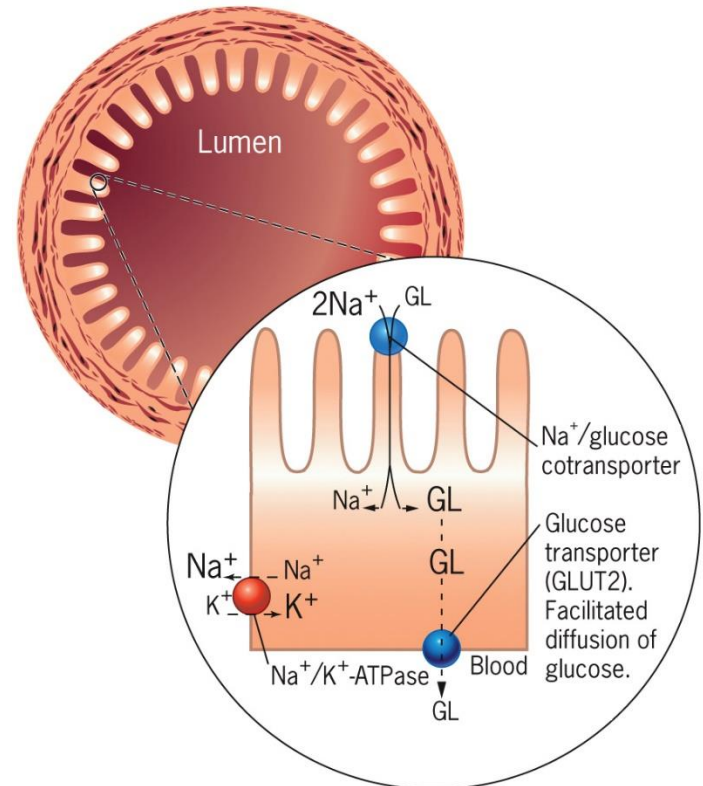


Control of acid secretion in the stomach

## 4.14 | Active Transport (1 of 2)

### Co-Transport: Coupling Transport to Existing Ion Gradients

- Potential energy stored in ionic gradients is utilized to perform work,.
- $\text{Na}^+$  concentration is kept low by a  $\text{Na}^+/\text{K}^+$ -ATPase pump.
- Diffusion of sodium ions down a concentration gradient drives the cotransport of glucose.

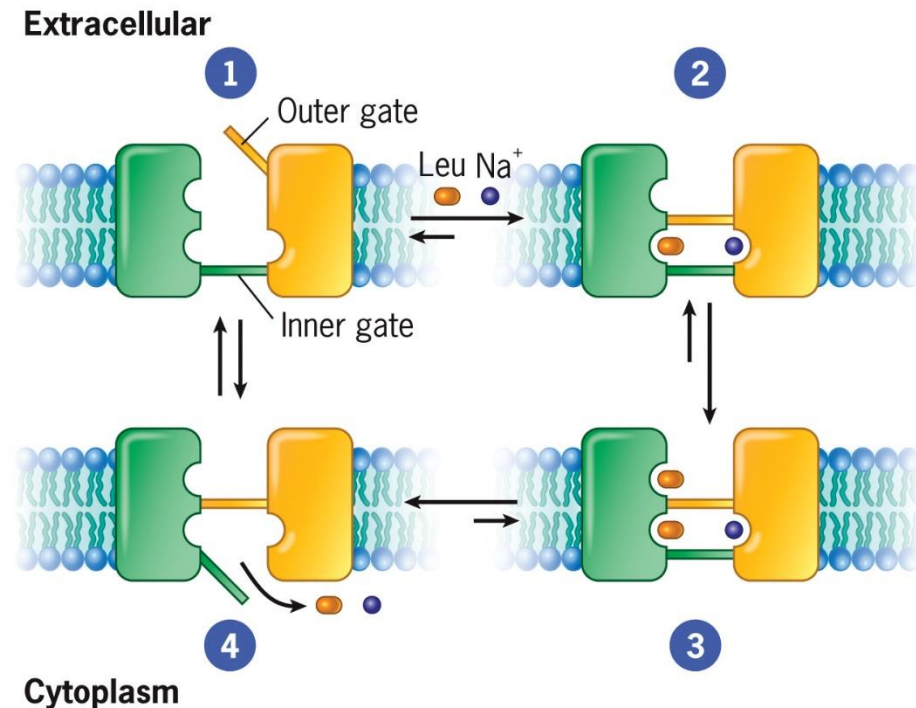


Secondary transporter: the  $\text{Na}^+$  gradient helps to transport glucose by a  $\text{Na}^+/\text{glucose}$  co-transporter

## 4.14 | Active Transport (2 of 2)

### Co-Transport: Coupling Transport to Existing Ion Gradients

- Secondary active transport of glucose is an example of symport.
- Antiporters or exchangers move two transported species in opposite directions.
- During the transport cycle, the protein's binding sites gain alternating access to the cytoplasm.



**Secondary transporter:** the Na<sup>+</sup> gradient helps to transport leucine into bacteria

Source: Reprinted by permission from Macmillan Publishers Ltd: *Nature*, 465: 171, 2010 by N. K. Karpovich and Da-Neng Wang (NYU School of Medicine).