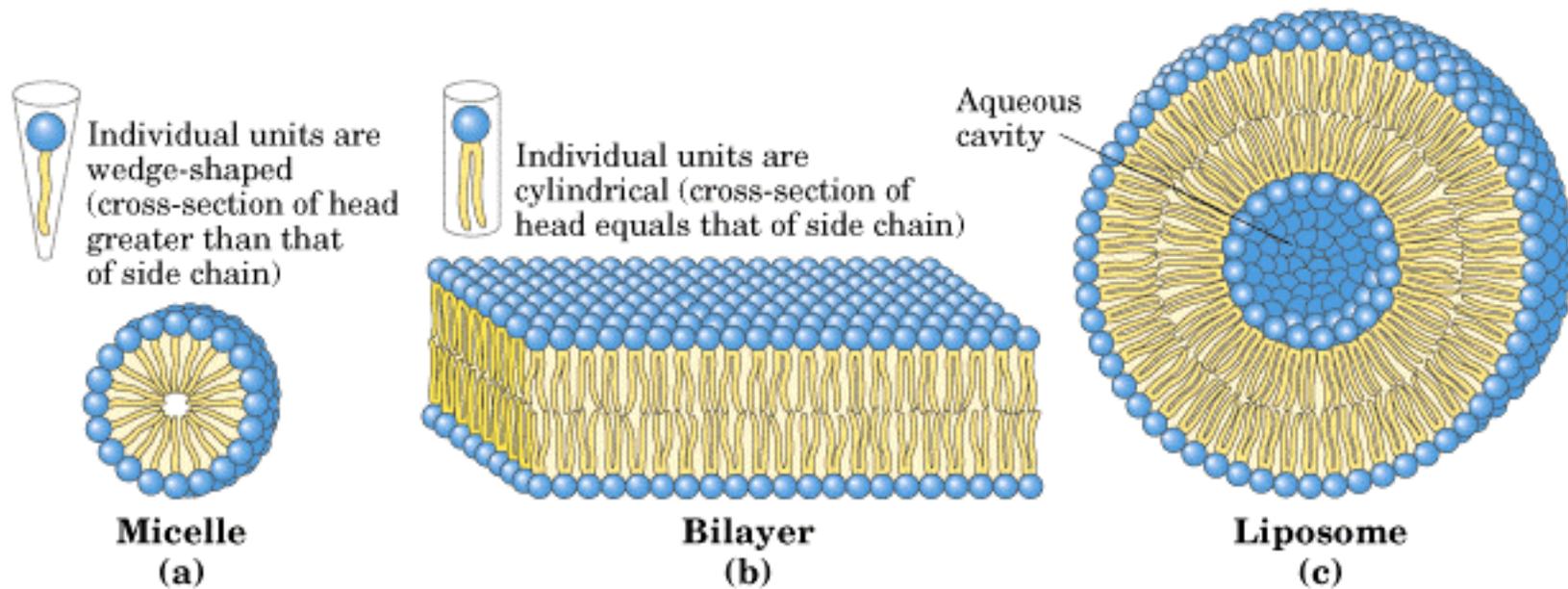


## 2. Membranas Biológicas y Transporte.

Biología D 2012

Carlos Morgan S.

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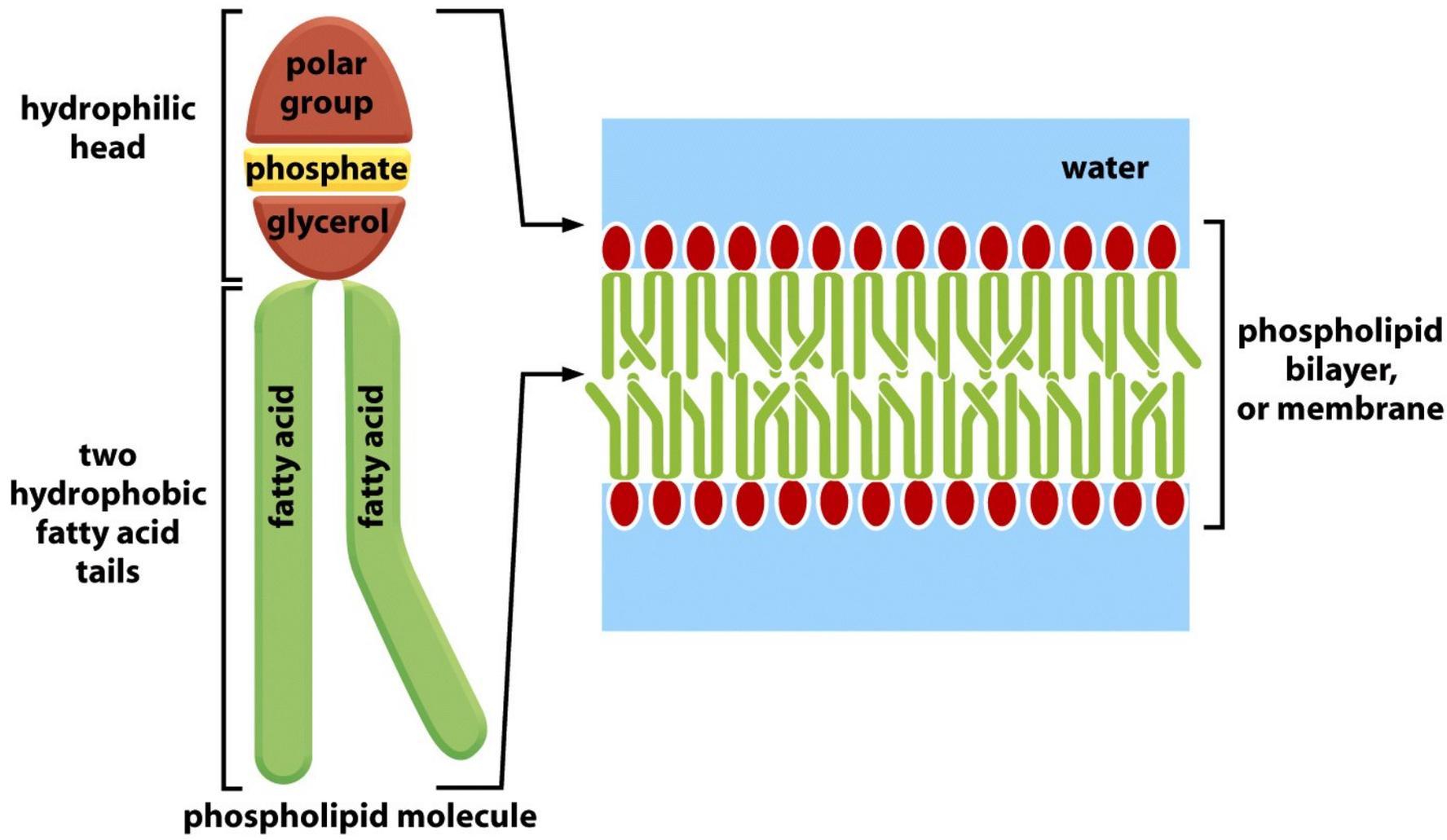
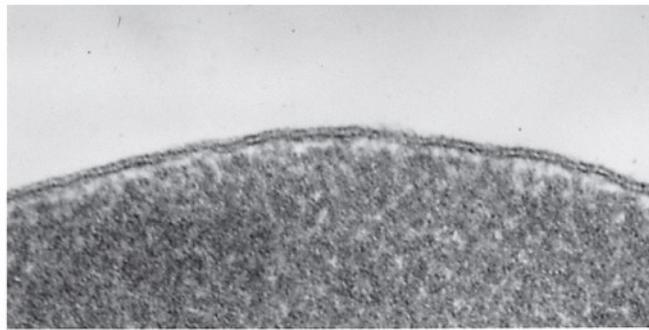
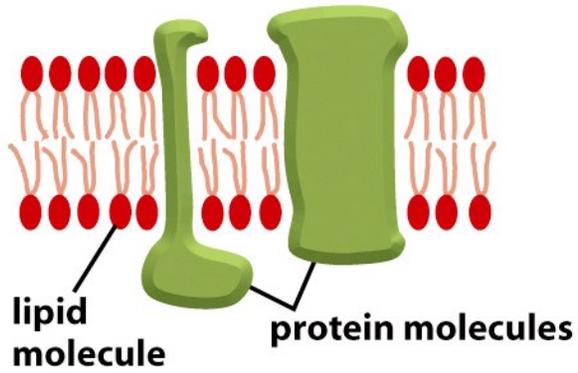


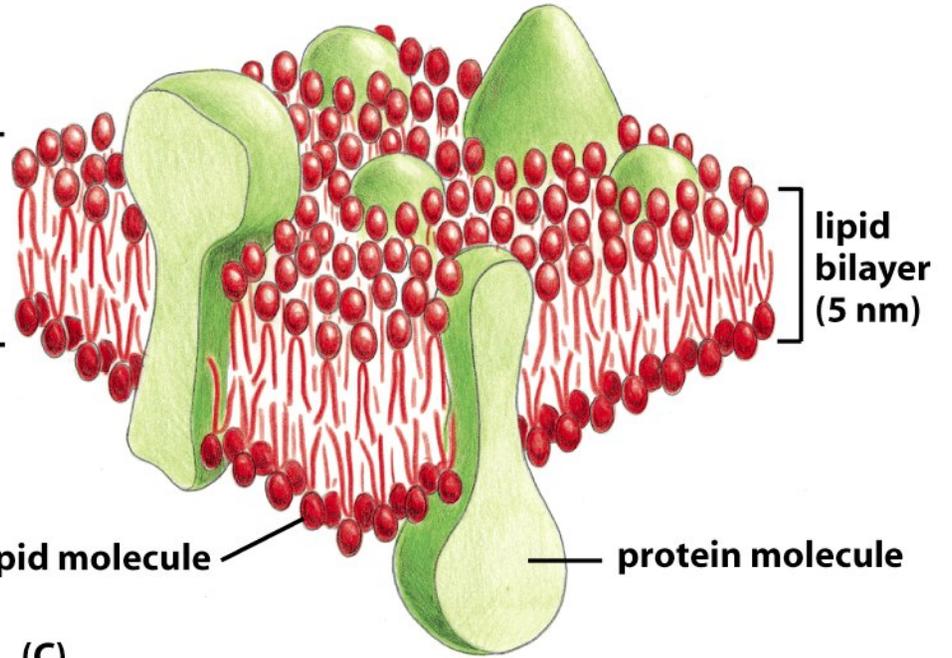
Figure 2-22 *Molecular Biology of the Cell* (© Garland Science 2008)



(A)



(B)



(C)

Figure 10-1 *Molecular Biology of the Cell* (© Garland Science 2008)

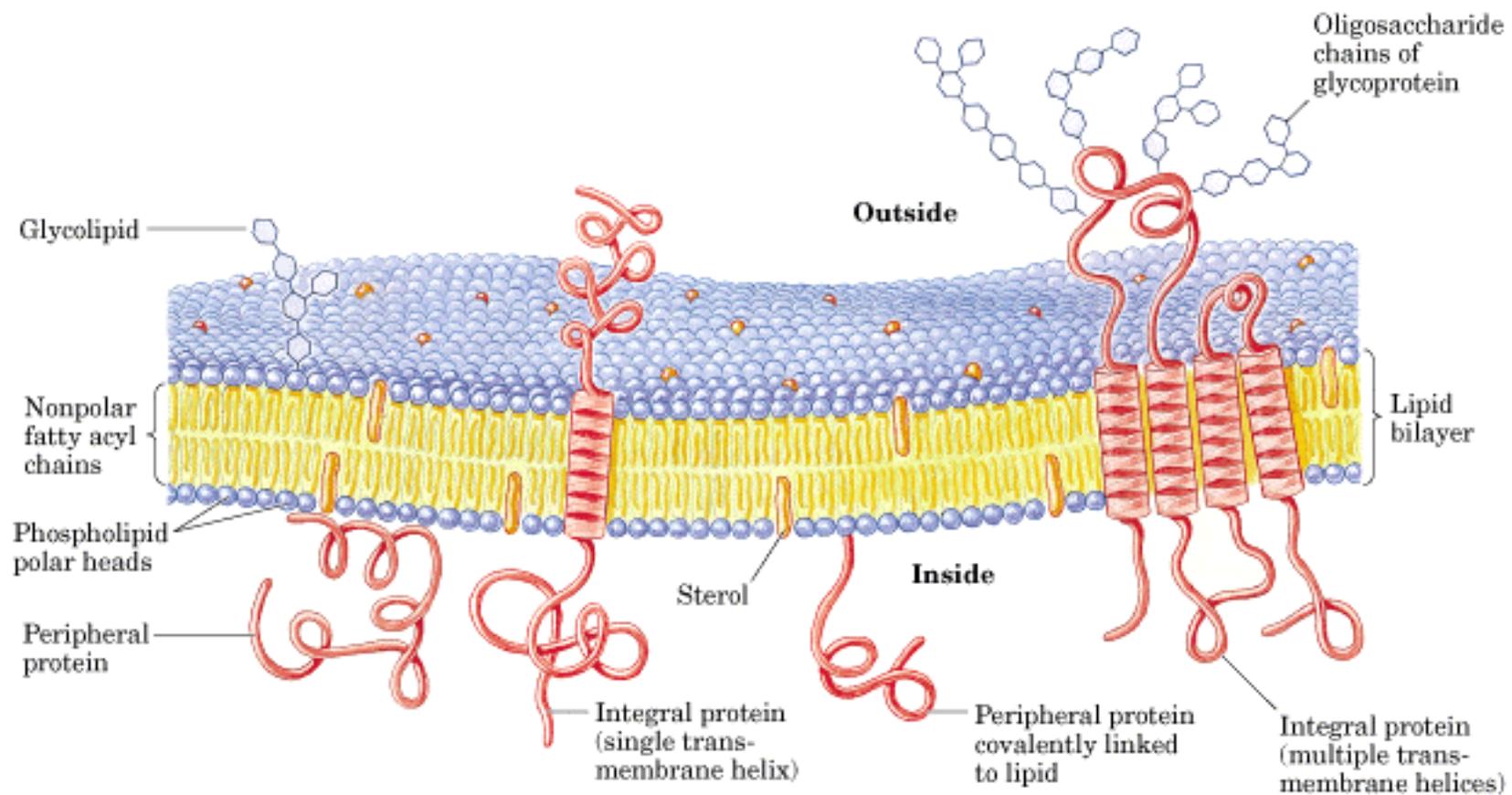
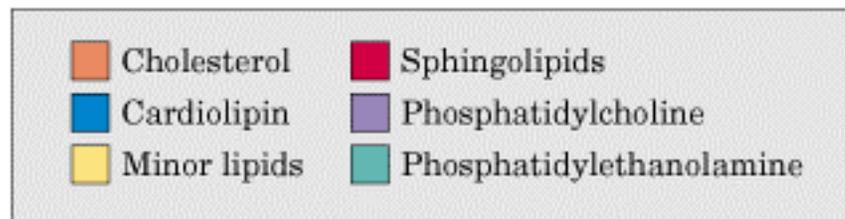
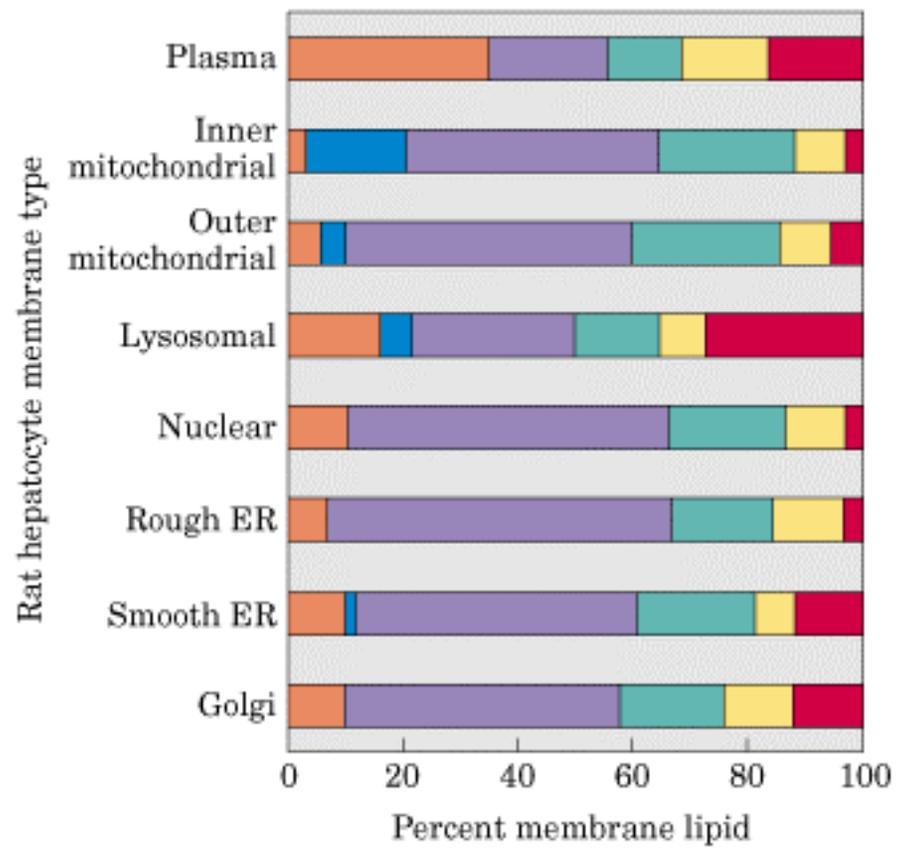


table 12-1

## Major Components of Plasma Membranes in Various Organisms

	Components (% by weight)			Sterol type	Other lipids
	Protein	Phospholipid	Sterol		
Human myelin sheath	30	30	19	Cholesterol	Galactolipids, plasmalogens
Mouse liver	45	27	25	Cholesterol	—
Maize leaf	47	26	7	Sitosterol	Galactolipids
Yeast	52	7	4	Ergosterol	Triacylglycerols, steryl esters
<i>Paramecium</i> (ciliated protist)	56	40	4	Stigmasterol	—
<i>E. coli</i>	75	25	0	—	—



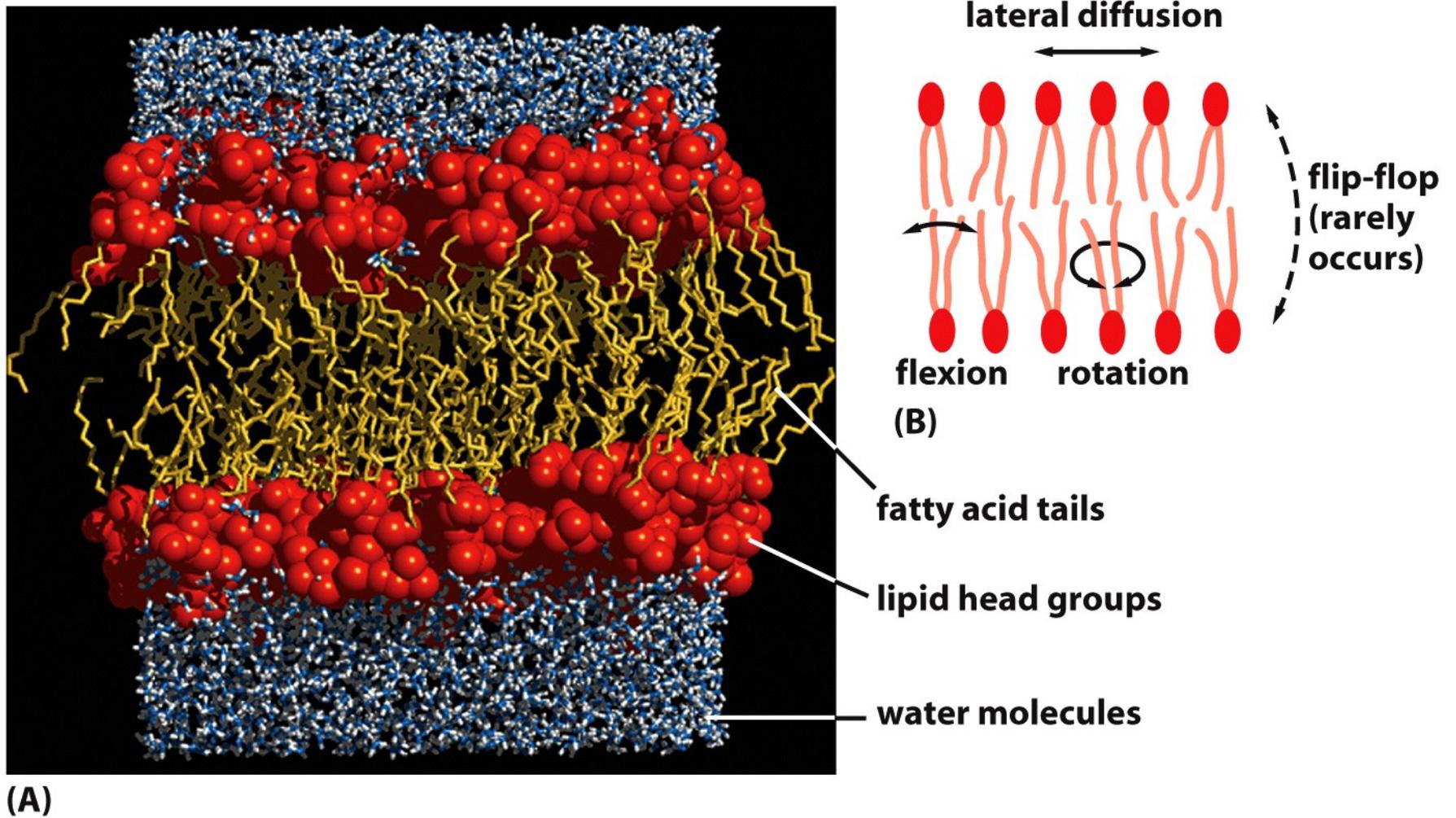


Figure 10-11 *Molecular Biology of the Cell* (© Garland Science 2008)

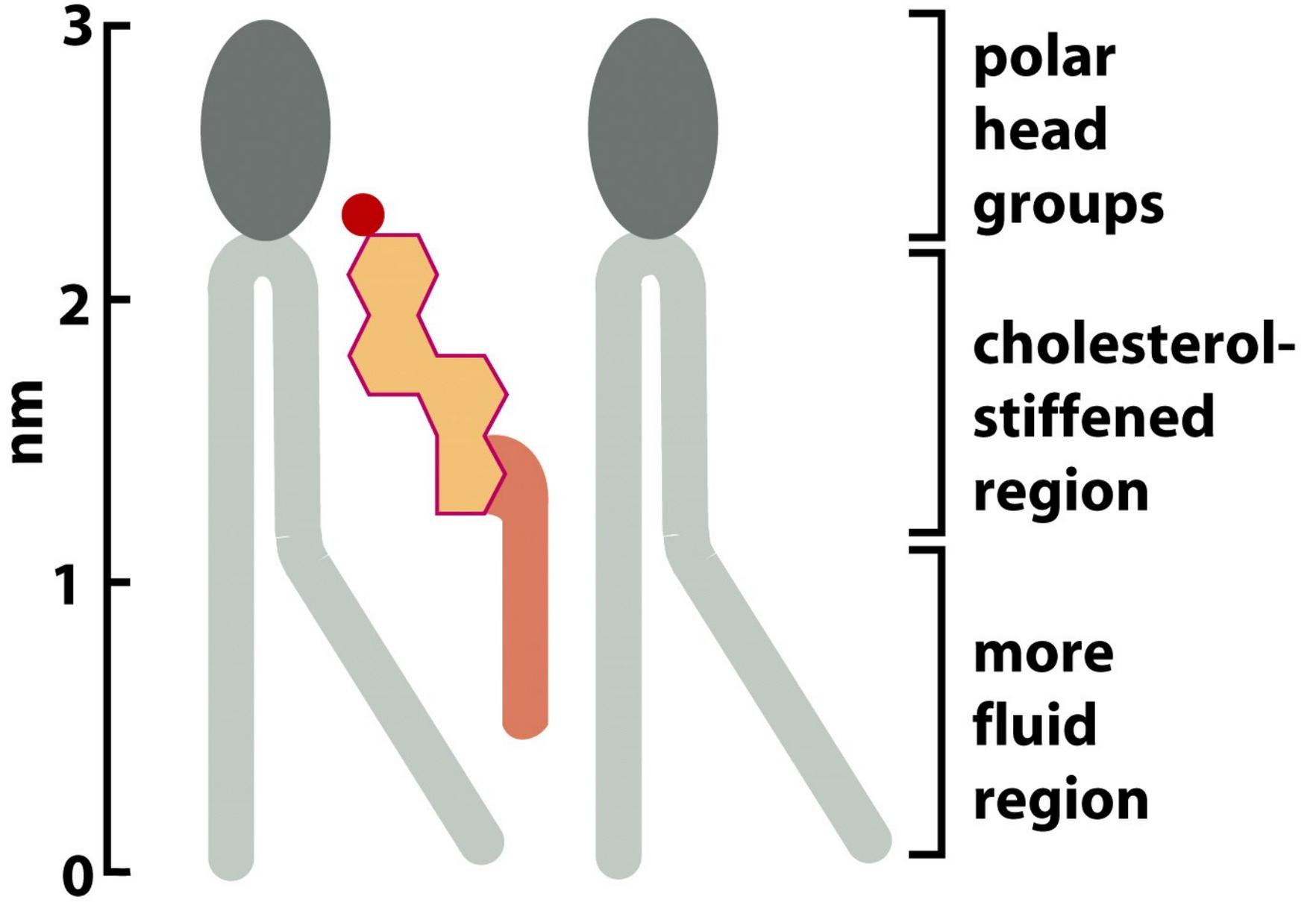


Figure 10-5 *Molecular Biology of the Cell* (© Garland Science 2008)

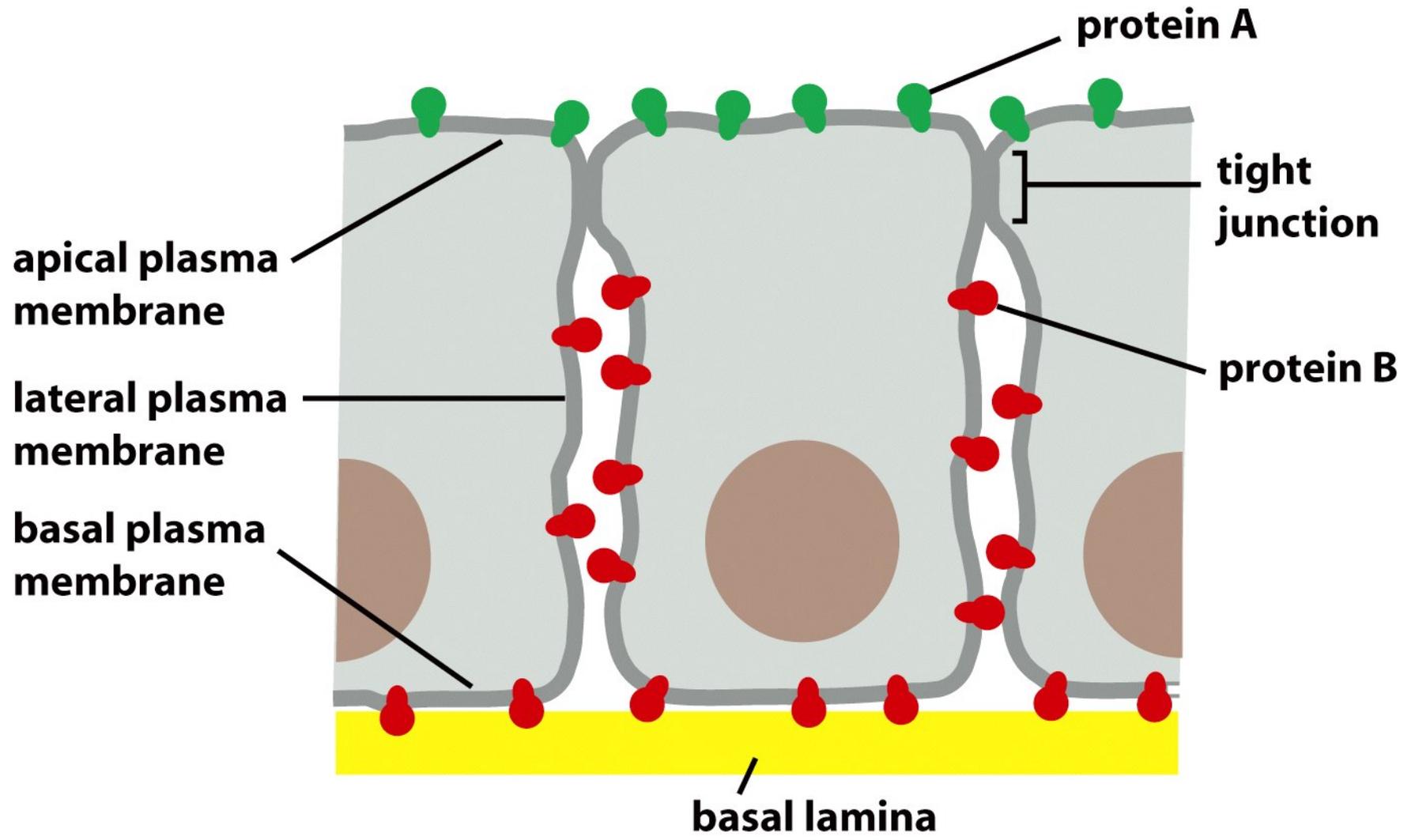


Figure 10-37 *Molecular Biology of the Cell* (© Garland Science 2008)

table 12-2

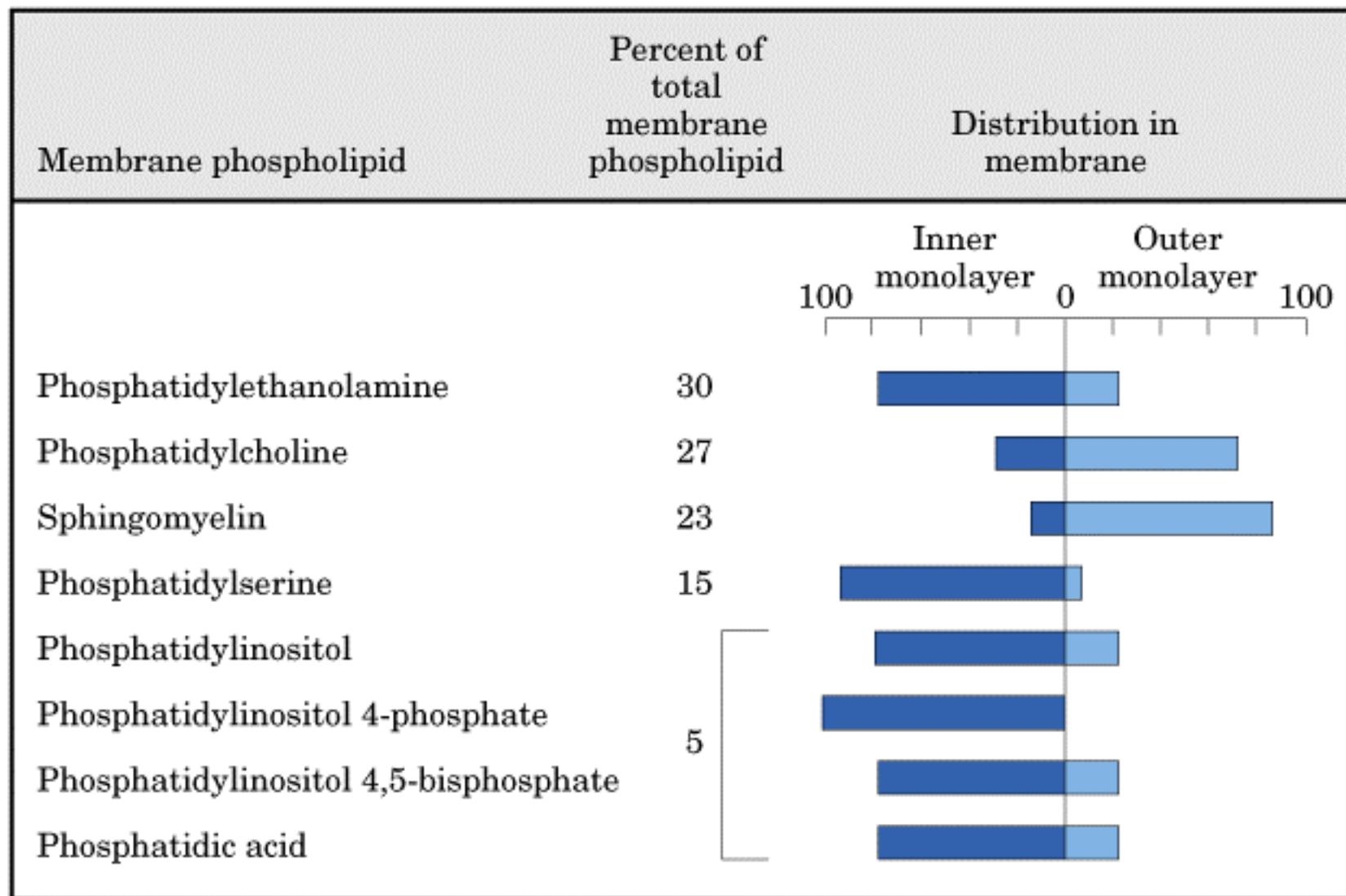
**Fatty Acid Composition of *E. coli* Cells Cultured at Different Temperatures**

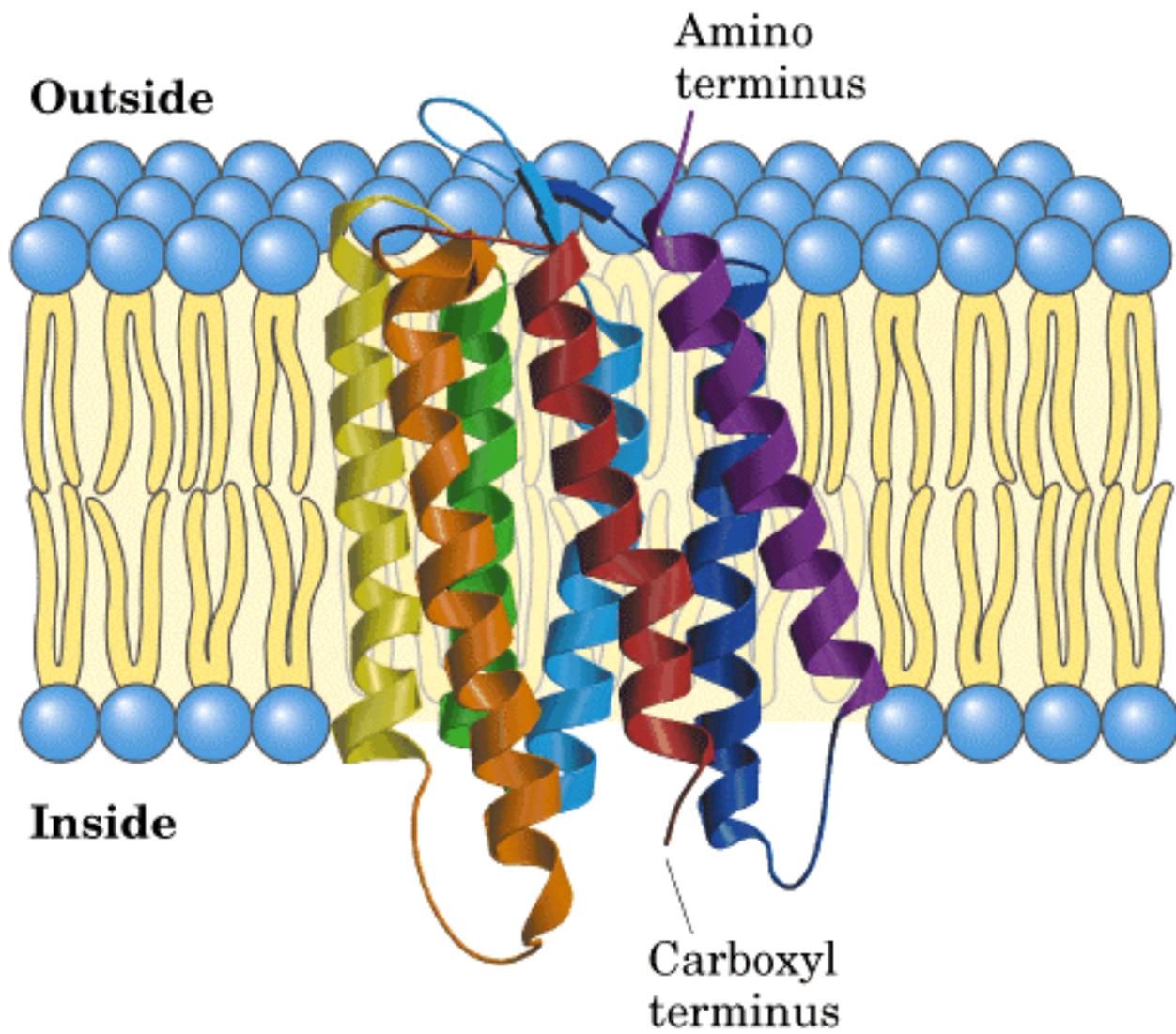
	Percentage of total fatty acids*			
	10 °C	20 °C	30 °C	40 °C
Myristic acid (14:0)	4	4	4	8
Palmitic acid (16:0)	18	25	29	48
Palmitoleic acid (16:1)	26	24	23	9
Oleic acid (18:1)	38	34	30	12
Hydroxymyristic acid	13	10	10	8
Ratio of unsaturated to saturated <sup>†</sup>	2.9	2.0	1.6	0.38

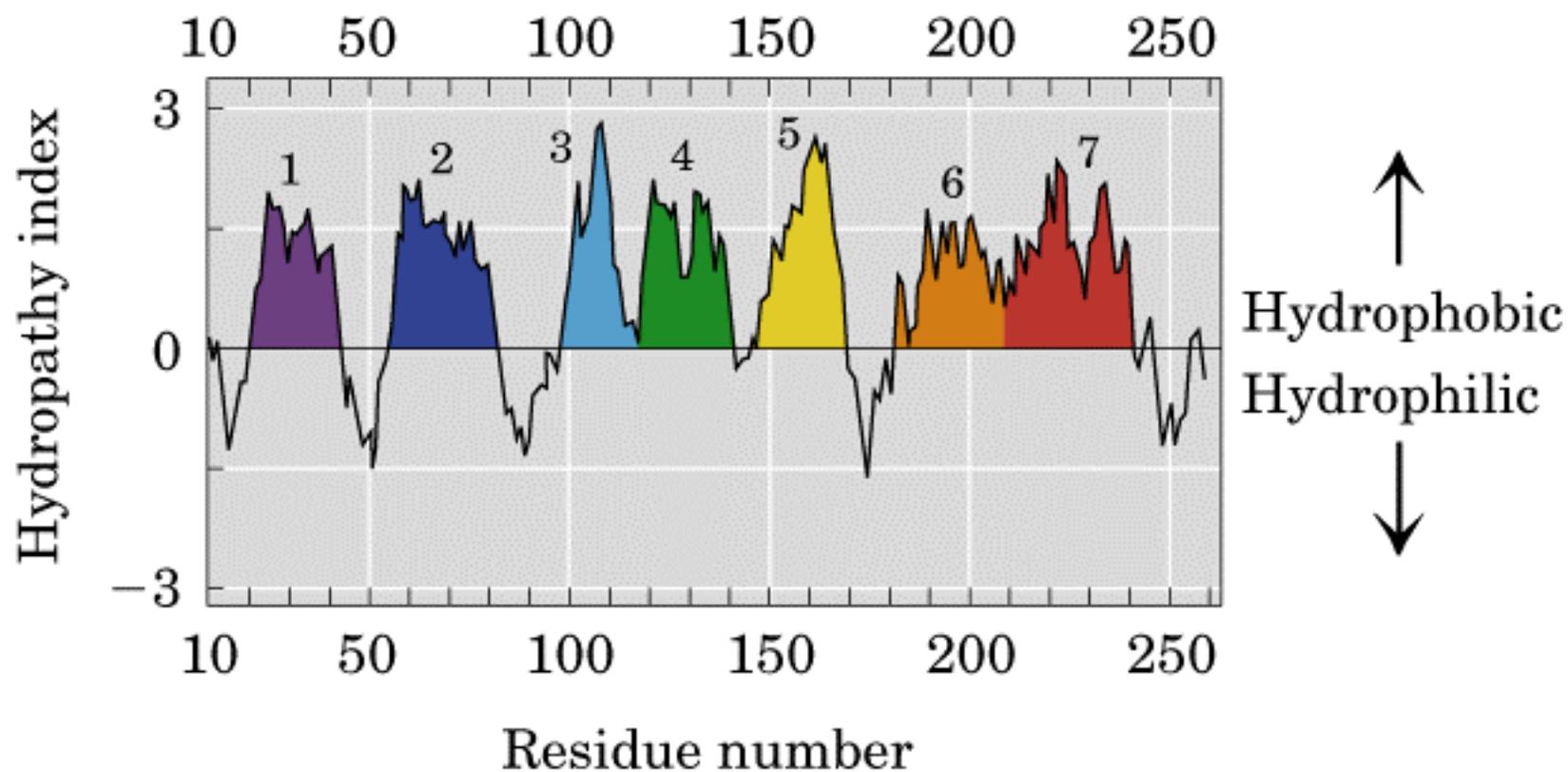
**Source:** Data from Marr, A.G. & Ingraham, J.L. (1962) Effect of temperature on the composition of fatty acids in *Escherichia coli*. *J. Bacteriol.* **84**, 1260.

\*The exact fatty acid composition depends not only on growth temperature but on growth stage and growth medium composition.

<sup>†</sup>Calculated as the total percentage of 16:1 plus 18:1 divided by the total percentage of 14:0 plus 16:0. Hydroxymyristic acid was omitted from this calculation.

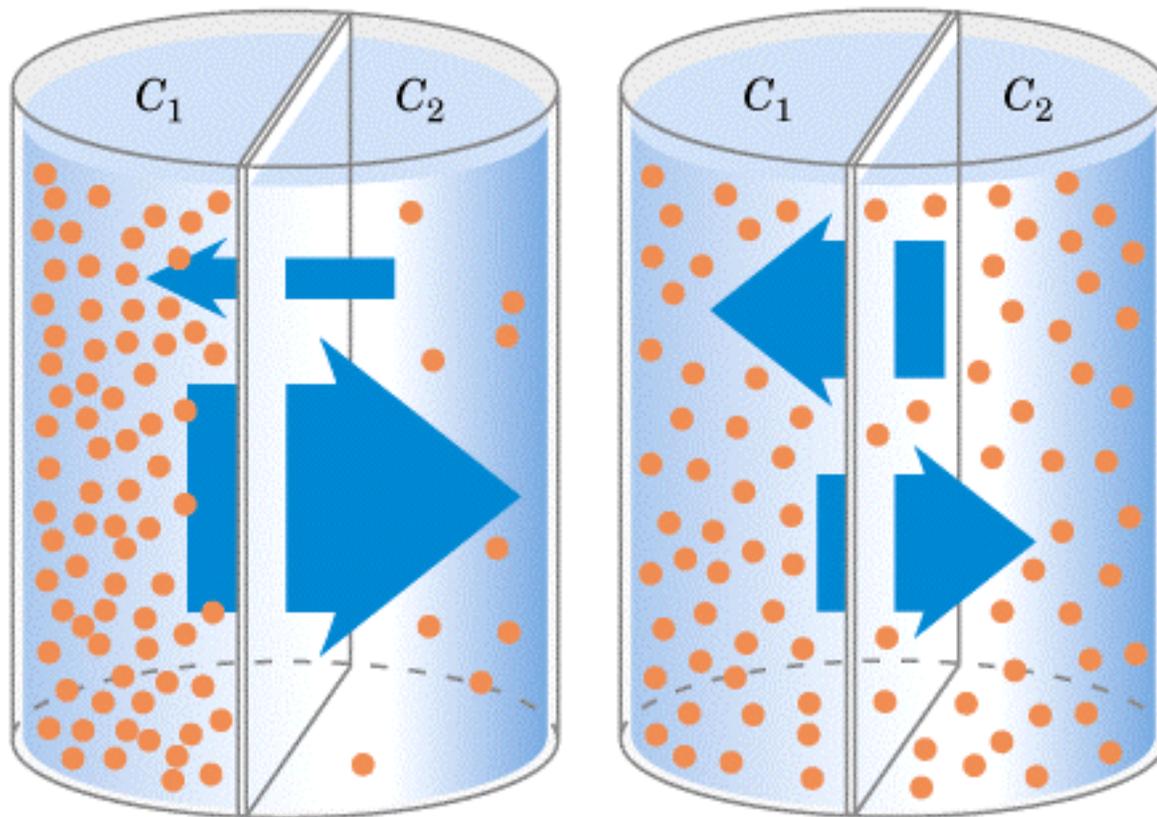






**Bacteriorhodopsin**

**(b)**



$$C_1 \gg C_2$$

Before equilibrium  
Net flux  
→

$$C_1 = C_2$$

At equilibrium  
No net flux

(a)

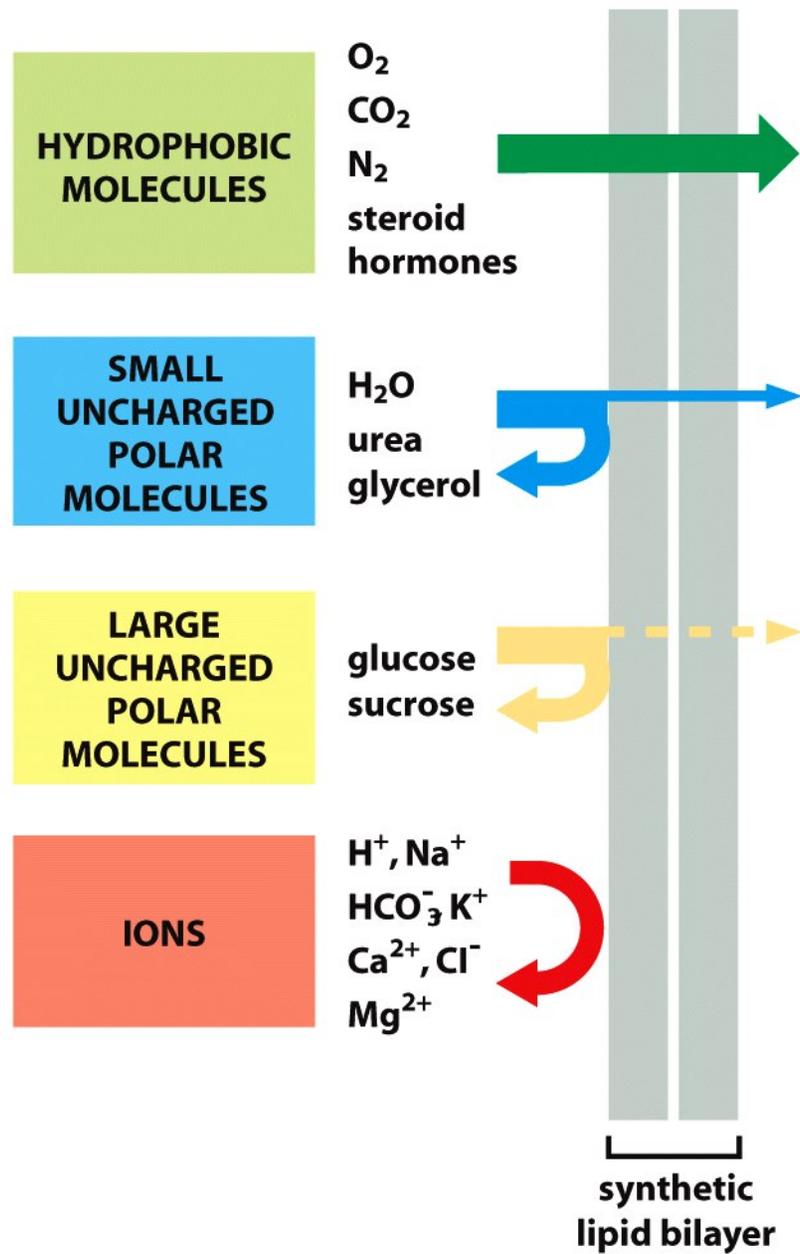


Figure 11-1 *Molecular Biology of the Cell* (© Garland Science 2008)

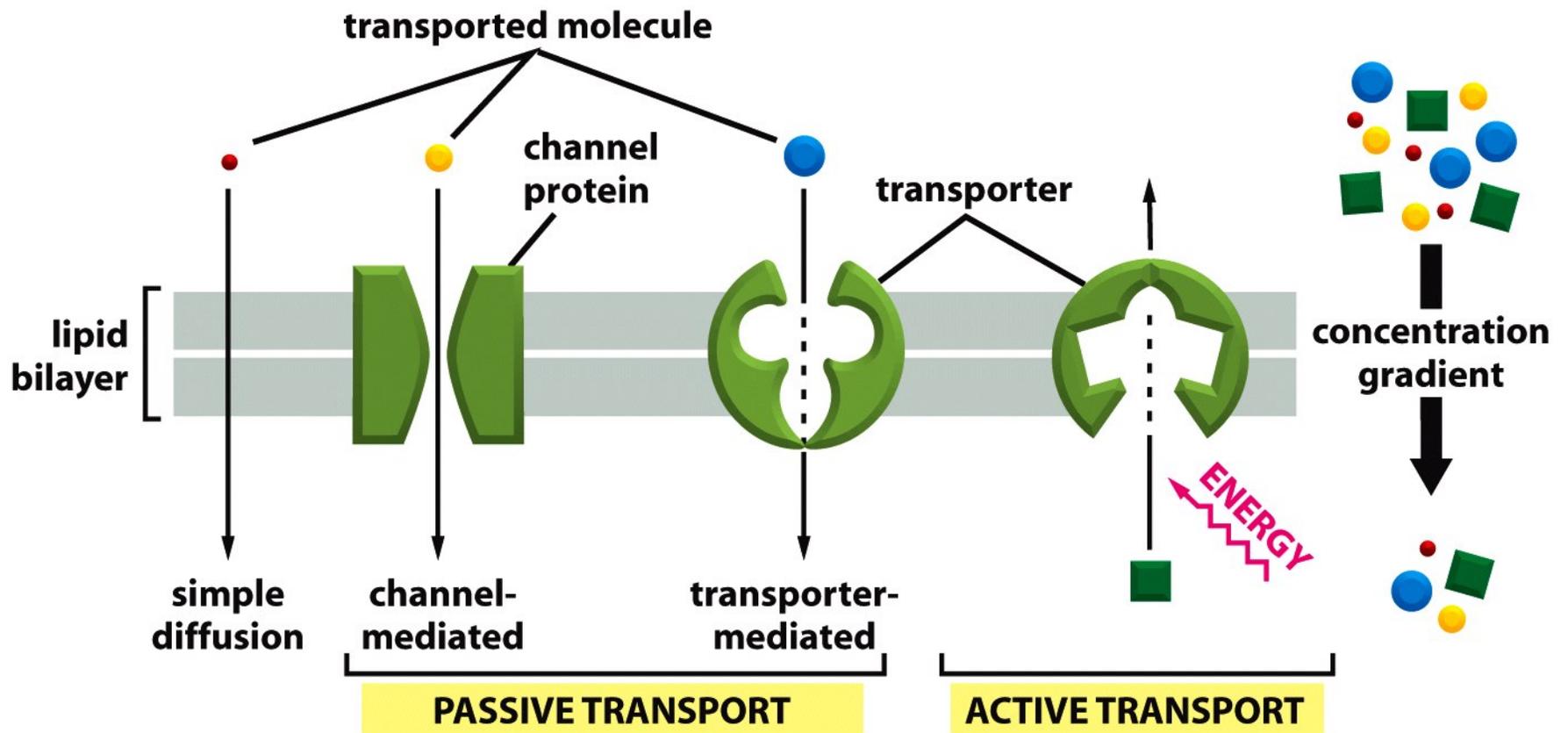


Figure 11-4a *Molecular Biology of the Cell* (© Garland Science 2008)

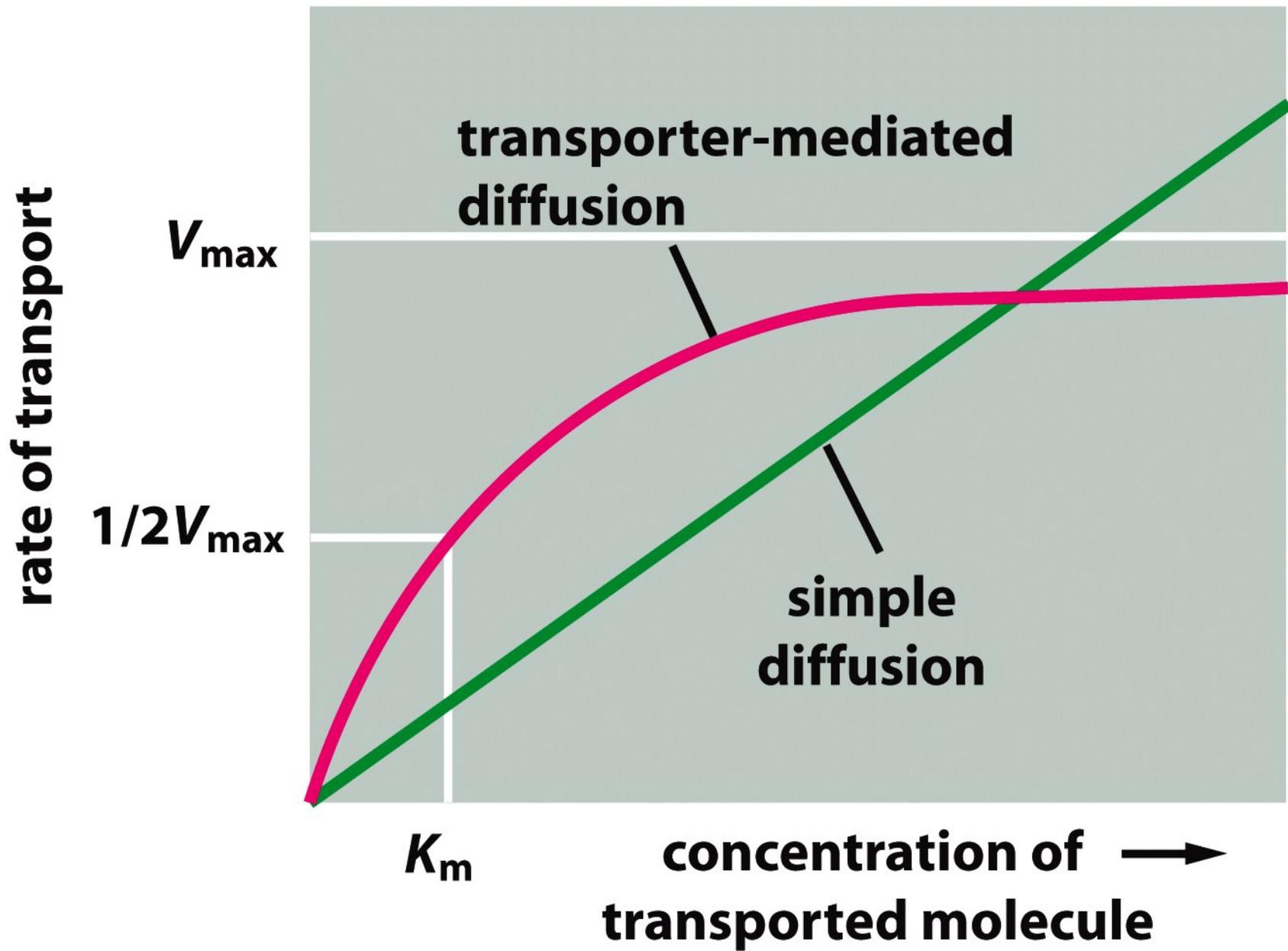
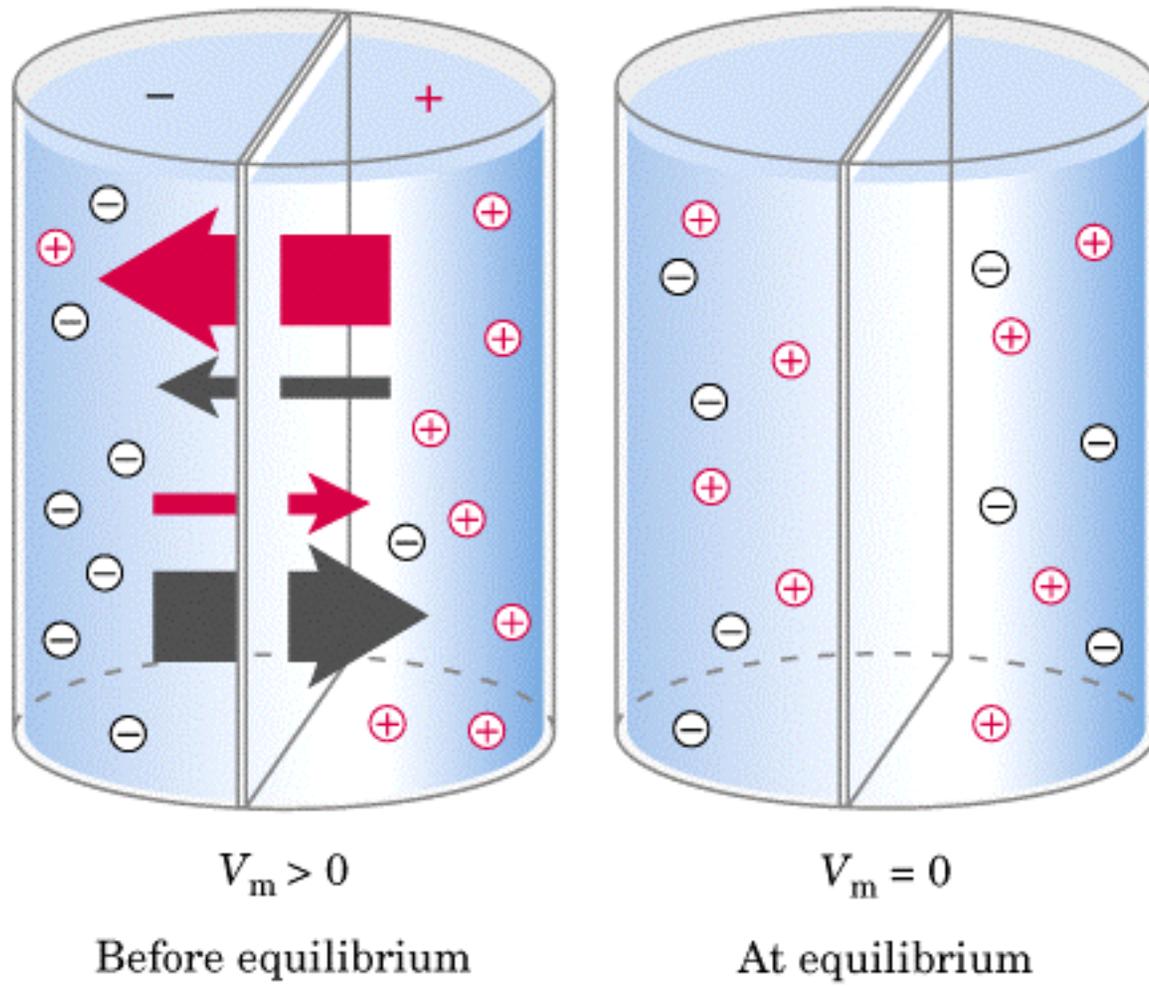


Figure 11-6 *Molecular Biology of the Cell* (© Garland Science 2008)



(b)

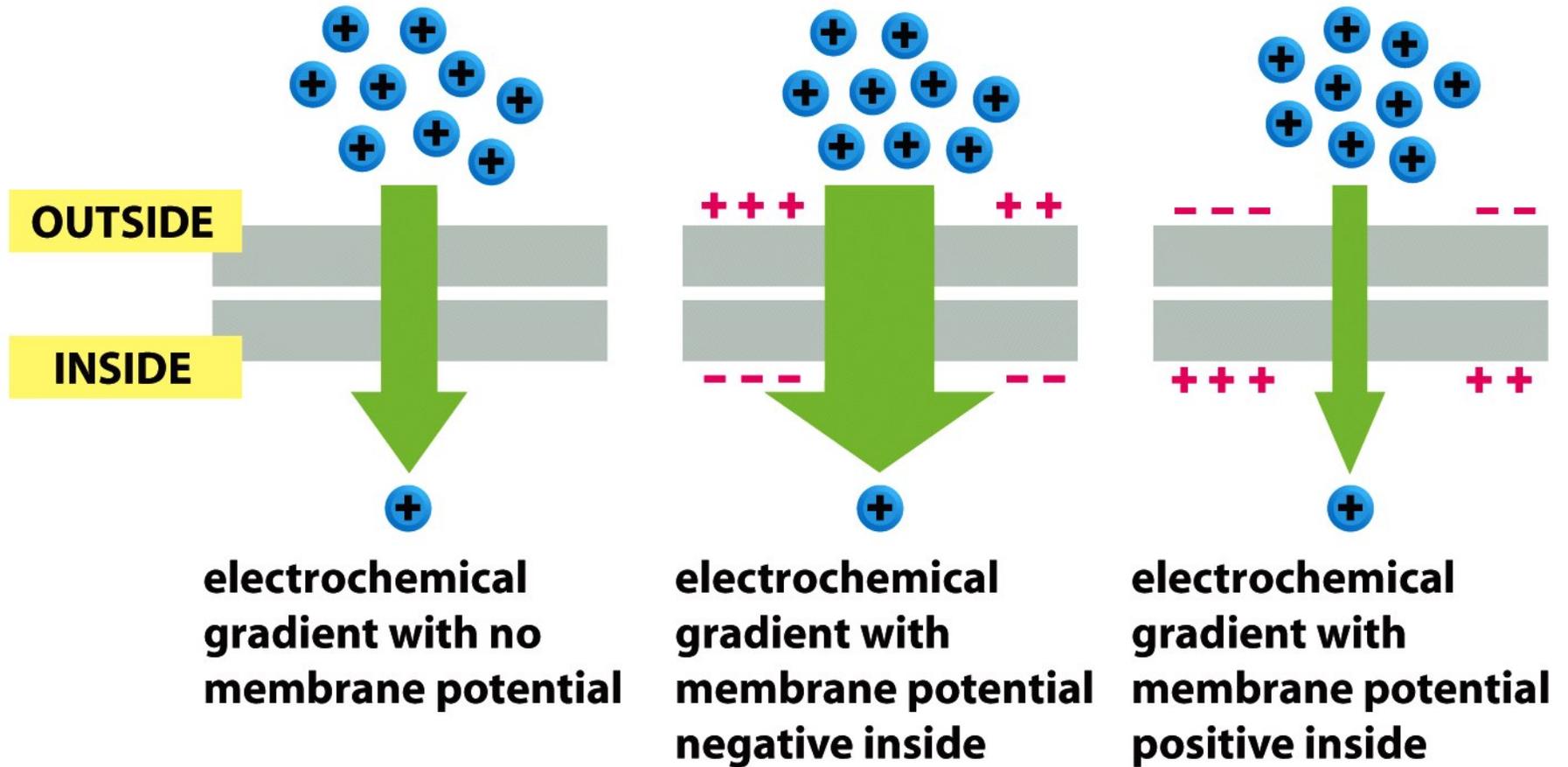


Figure 11-4b *Molecular Biology of the Cell* (© Garland Science 2008)

**Table 11–1 A Comparison of Ion Concentrations Inside and Outside a Typical Mammalian Cell**

COMPONENT	INTRACELLULAR CONCENTRATION (mM)	EXTRACELLULAR CONCENTRATION (mM)
<b>Cations</b>		
Na <sup>+</sup>	5–15	145
K <sup>+</sup>	140	5
Mg <sup>2+</sup>	0.5	1–2
Ca <sup>2+</sup>	10 <sup>-4</sup>	1–2
H <sup>+</sup>	7 × 10 <sup>-5</sup> (10 <sup>-7.2</sup> M or pH 7.2)	4 × 10 <sup>-5</sup> (10 <sup>-7.4</sup> M or pH 7.4)
<b>Anions*</b>		
Cl <sup>-</sup>	5–15	110

**\*The cell must contain equal quantities of positive and negative charges (that is, it must be electrically neutral). Thus, in addition to Cl<sup>-</sup>, the cell contains many other anions not listed in this table; in fact, most cell constituents are negatively charged (HCO<sub>3</sub><sup>-</sup>, PO<sub>4</sub><sup>3-</sup>, proteins, nucleic acids, metabolites carrying phosphate and carboxyl groups, etc.). The concentrations of Ca<sup>2+</sup> and Mg<sup>2+</sup> given are for the free ions. There is a total of about 20 mM Mg<sup>2+</sup> and 1–2 mM Ca<sup>2+</sup> in cells, but both are mostly bound to proteins and other substances and, for Ca<sup>2+</sup>, stored within various organelles.**

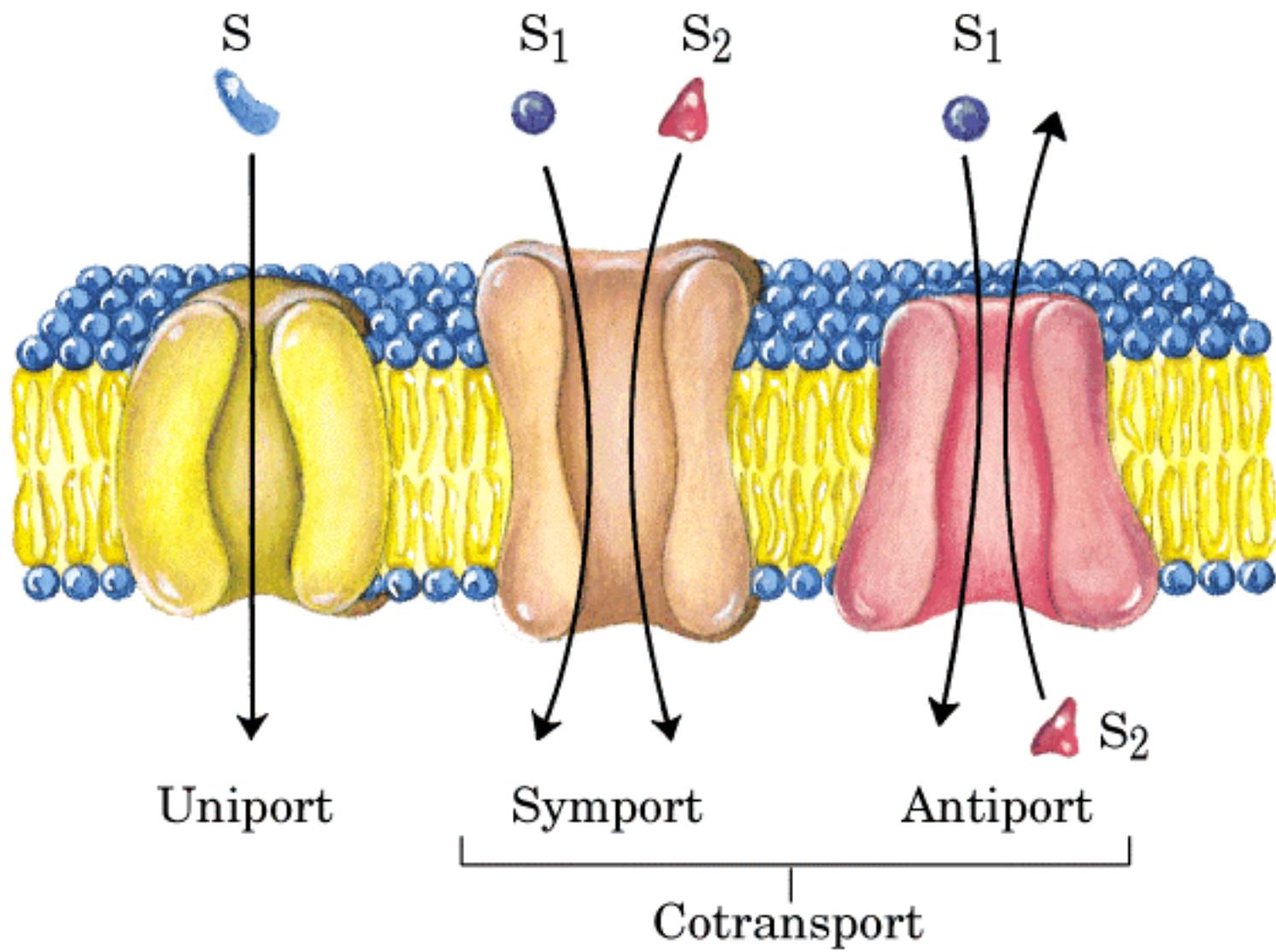
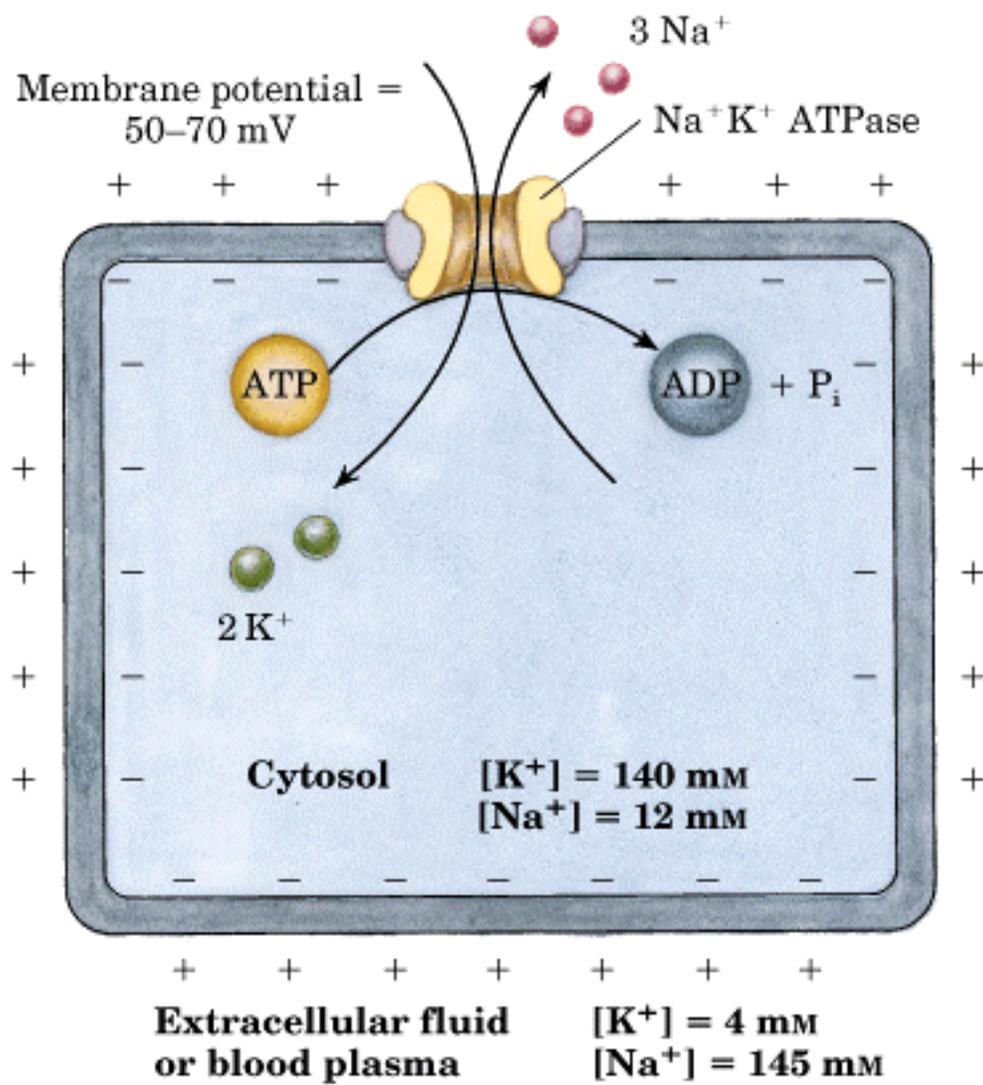


table 12–5

Cotransport Systems Driven by Gradients of Na <sup>+</sup> or H <sup>+</sup>			
Organism or tissue	Transported solute (moving against its gradient)	Cotransported solute (moving down its gradient)	Type of transport
<i>E. coli</i>	Lactose	H <sup>+</sup>	Symport
	Proline	H <sup>+</sup>	Symport
	Dicarboxylic acids	H <sup>+</sup>	Symport
Intestine, kidney of vertebrates	Glucose	Na <sup>+</sup>	Symport
	Amino acids	Na <sup>+</sup>	Symport
Vertebrate cells (many types)	Ca <sup>2+</sup>	Na <sup>+</sup>	Antiport
Higher plants	K <sup>+</sup>	H <sup>+</sup>	Antiport
Fungi ( <i>Neurospora</i> )	K <sup>+</sup>	H <sup>+</sup>	Antiport



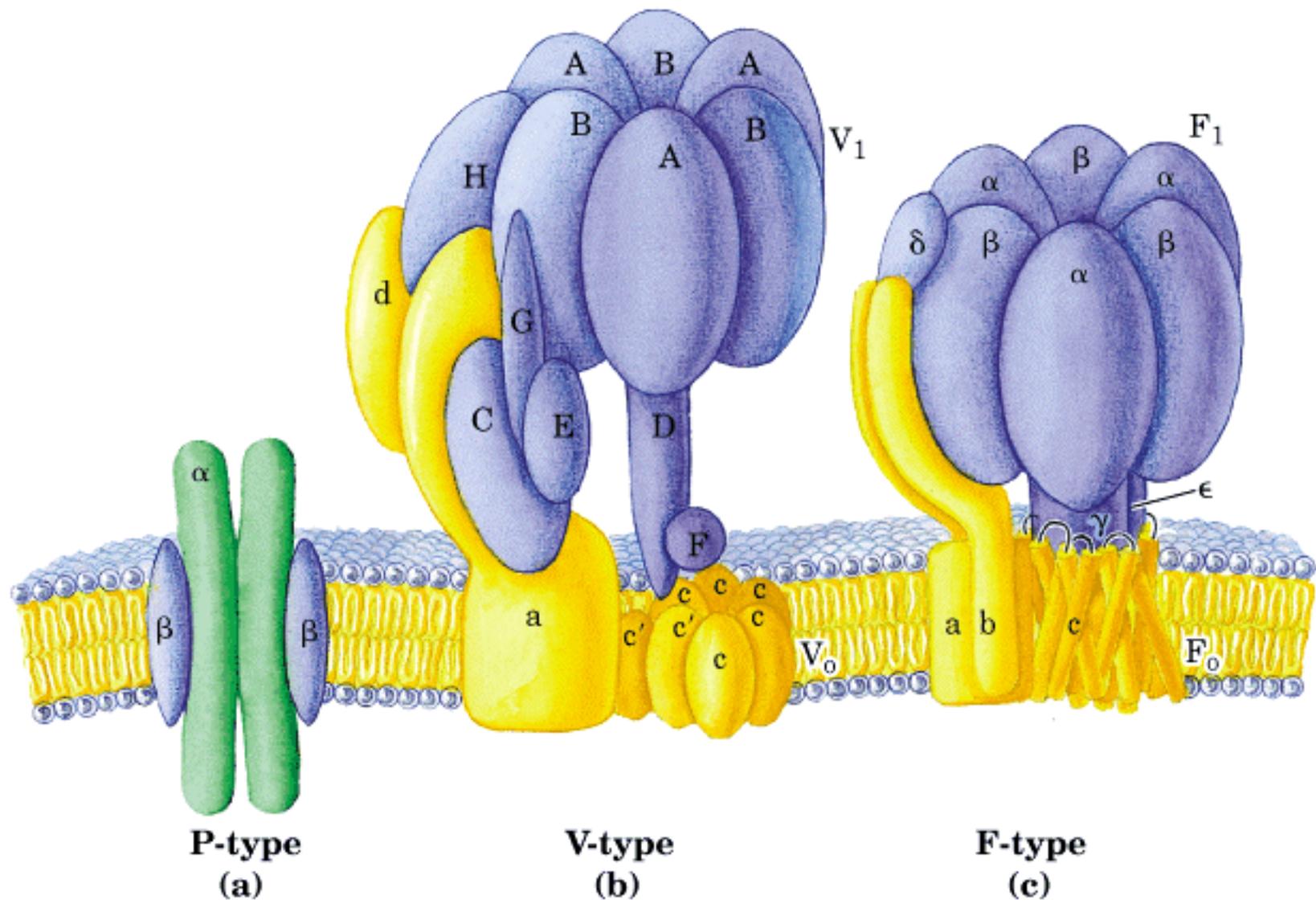
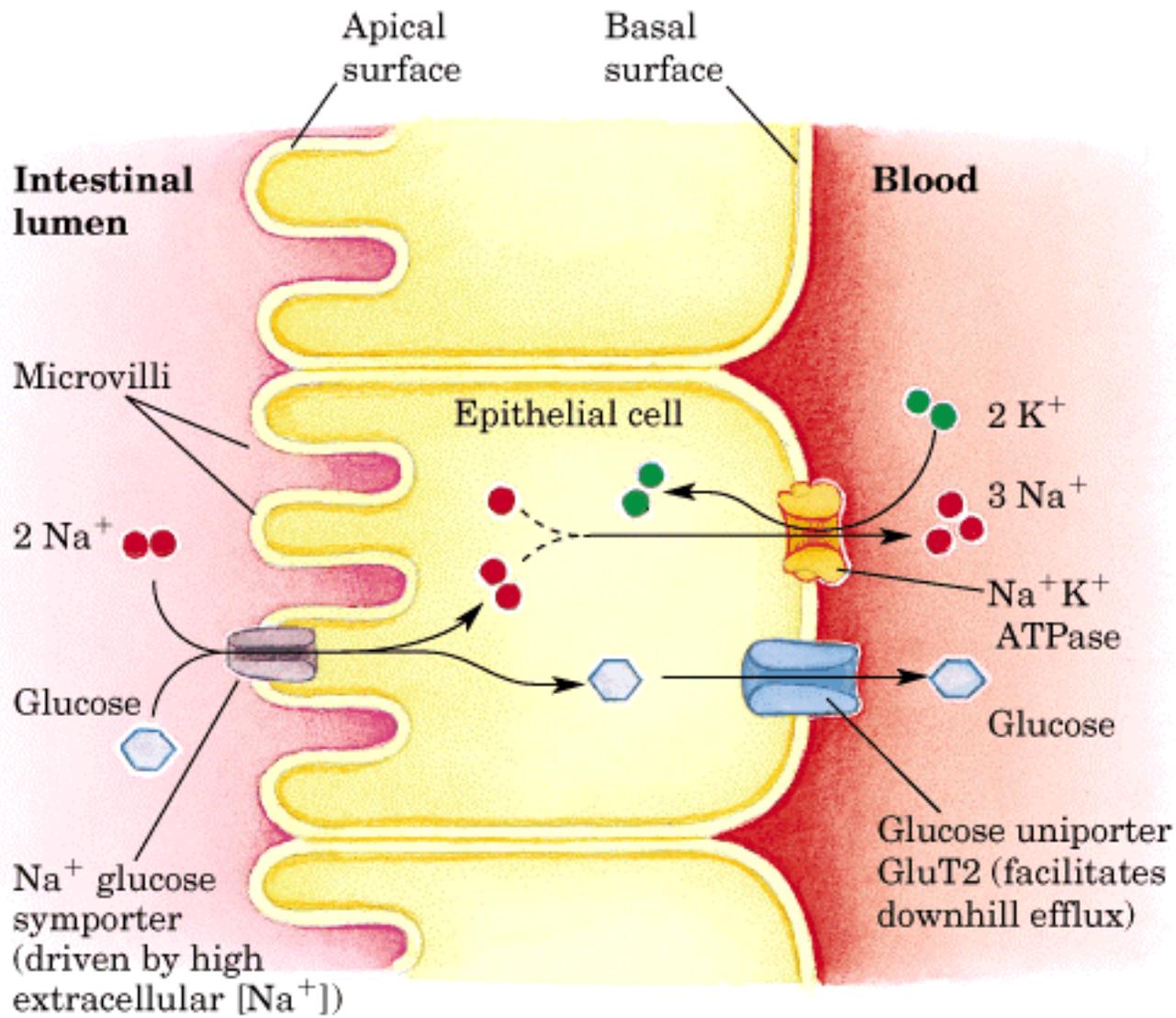
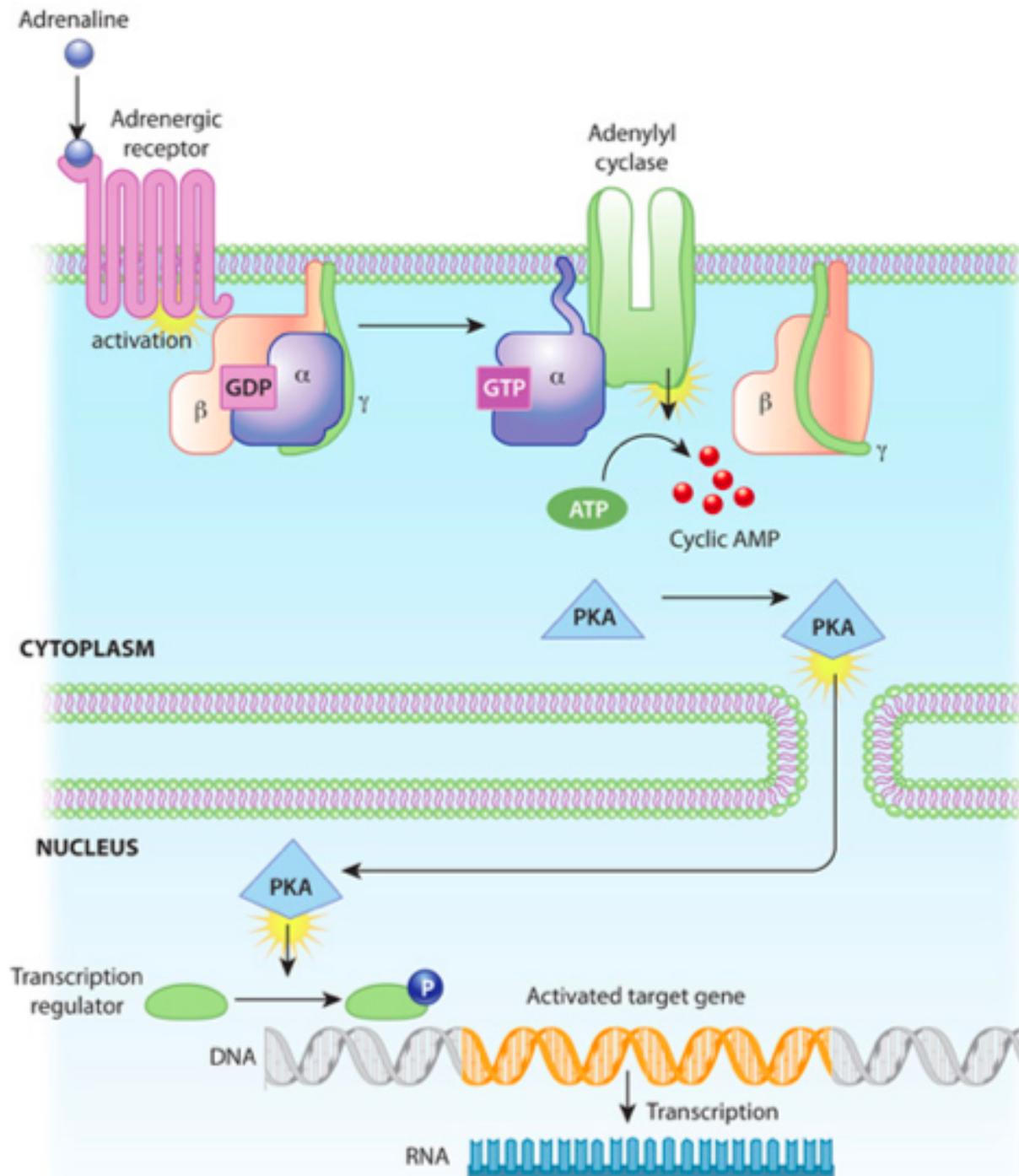
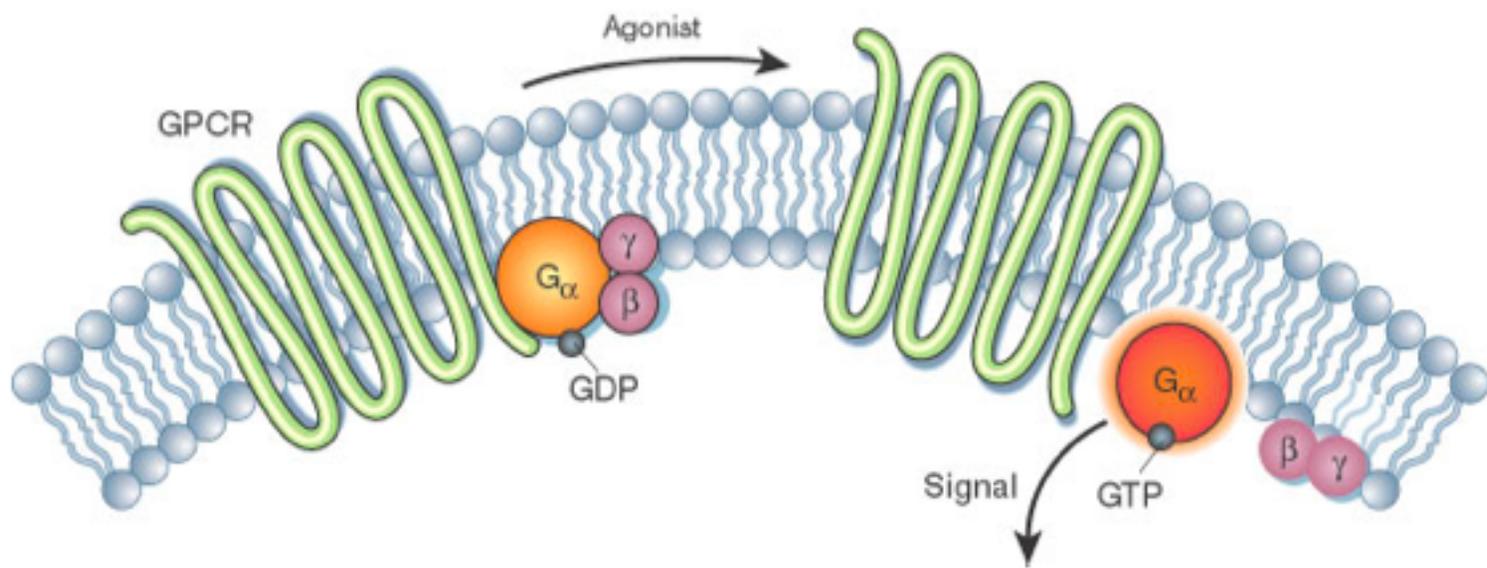


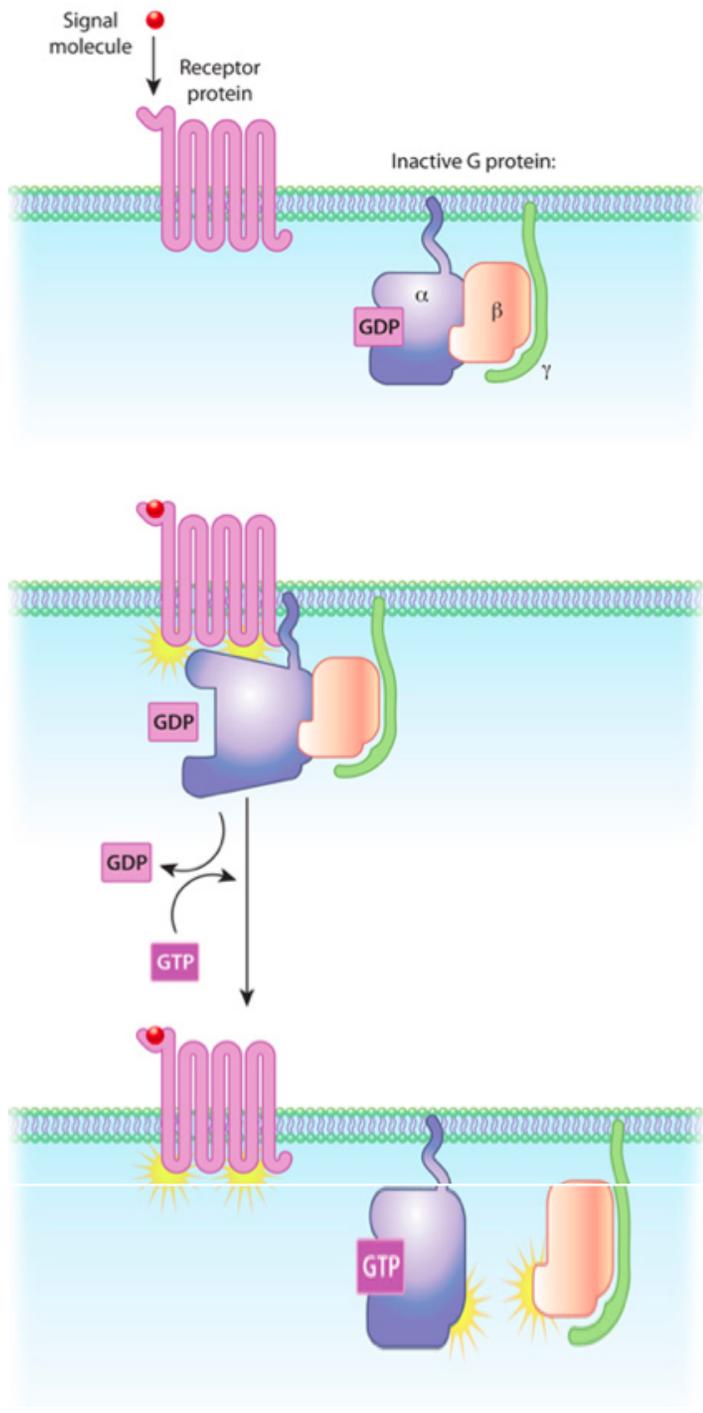
table 12-4

Four Classes of Transport ATPases			
	Organism or tissue	Type of membrane	Role of ATPase
<b>P-type ATPases</b>			
Na <sup>+</sup> K <sup>+</sup>	Animal tissues	Plasma	Maintains low [Na <sup>+</sup> ], high [K <sup>+</sup> ] inside cell; creates transmembrane electrical potential
H <sup>+</sup> K <sup>+</sup>	Acid-secreting (parietal) cells of mammals	Plasma	Acidifies contents of stomach
H <sup>+</sup>	Fungi ( <i>Neurospora</i> )	Plasma	} Create H <sup>+</sup> gradient to drive secondary transport of extracellular solutes into cell
H <sup>+</sup>	Higher plants	Plasma	
Ca <sup>2+</sup>	Animal tissues	Plasma	
Ca <sup>2+</sup>	Myocytes of animals	Sarcoplasmic reticulum (endoplasmic reticulum)	Sequesters intracellular Ca <sup>2+</sup> , keeping cytosolic [Ca <sup>2+</sup> ] low
Cd <sup>2+</sup> , Hg <sup>2+</sup> , Cu <sup>2+</sup>	Bacteria	Plasma	Pumps heavy metal ions out of cell
<b>V-type ATPases</b>			
H <sup>+</sup>	Animals	Lysosomal, endosomal, secretory vesicles	} Create low pH in compartment, activating proteases and other hydrolytic enzymes
H <sup>+</sup>	Higher plants	Vacuolar	
H <sup>+</sup>	Fungi	Vacuolar	
<b>F-type ATPases</b>			
H <sup>+</sup>	Eukaryotes	Inner mitochondrial	} Catalyze formation of ATP from ADP + P <sub>i</sub>
H <sup>+</sup>	Higher plants	Thylakoid	
H <sup>+</sup>	Prokaryotes	Plasma	
<b>Multidrug transporter</b>			
	Animal tumor cells	Plasma	Removes a wide variety of hydrophobic natural products and synthetic drugs from cytosol, including vinblastine, doxorubicin, actinomycin D, mitomycin, taxol, colchicine, and puromycin

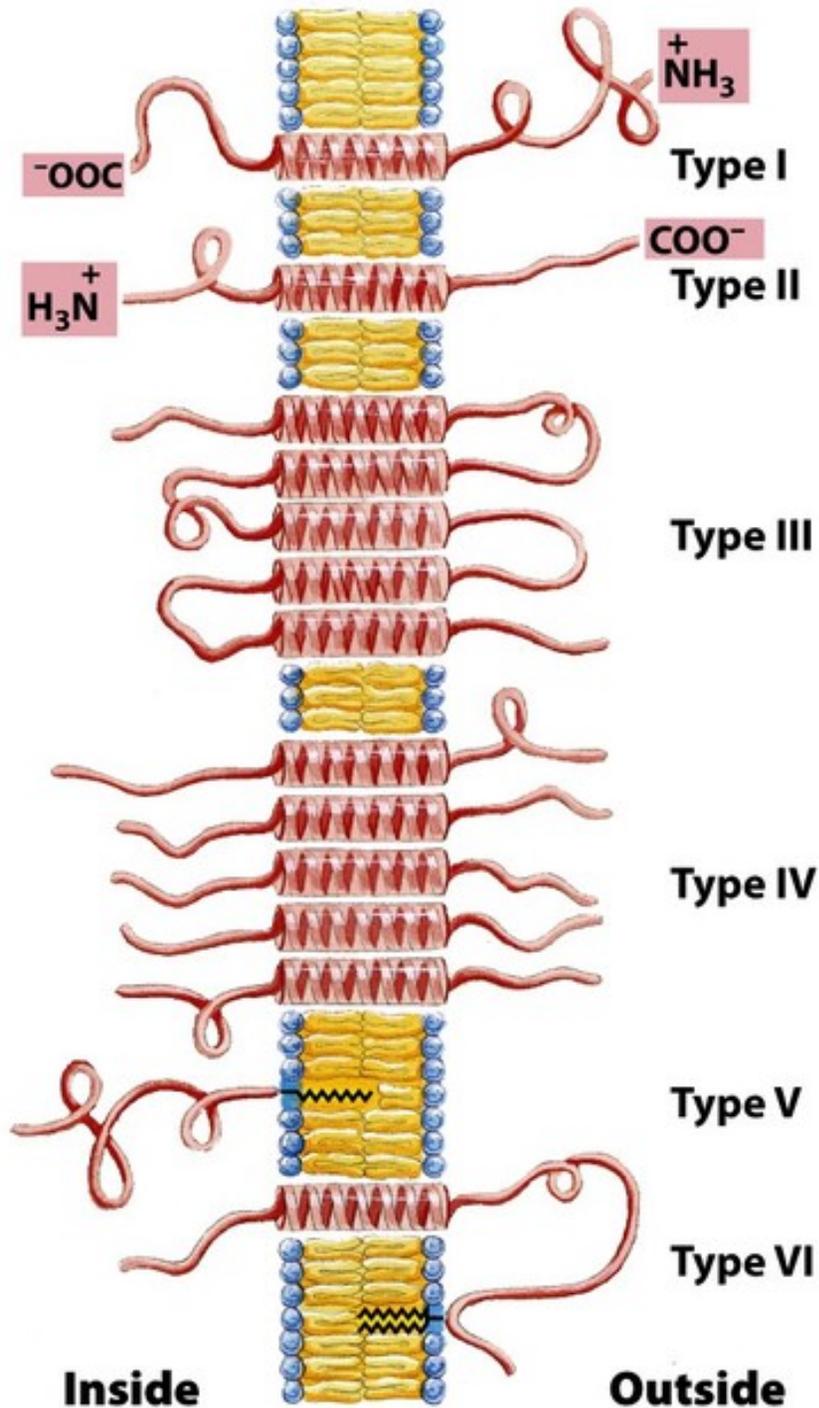




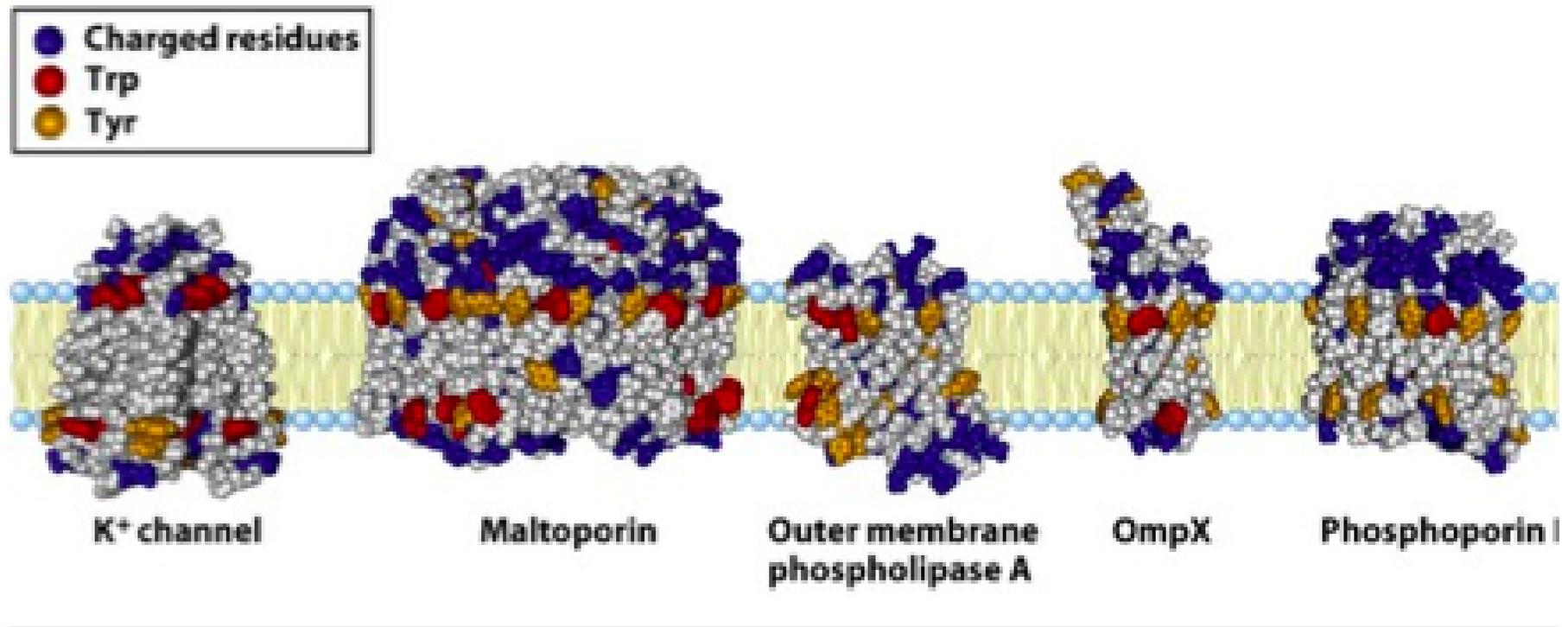








**Integral membrane proteins.** For known proteins of the plasma membrane, the spatial relationships of protein domains to the lipid bilayer fall into six categories. Types I and II have a single transmembrane helix; the amino-terminal domain is outside the cell in type I proteins and inside in type II. Type III proteins have multiple transmembrane helices in a single polypeptide. In type IV proteins, transmembrane domains of several different polypeptides assemble to form a channel through the membrane. Type V proteins are held to the bilayer primarily by covalently linked lipids (see Fig. 11-14), and type VI proteins have both transmembrane helices and lipid (GPI) anchors. In this figure, and in figures throughout the book, we represent transmembrane protein segments in their most likely conformations: as  $\alpha$  helices of six to seven turns. Sometimes these helices are shown simply as cylinders. As relatively few membrane protein structures have been deduced by x-ray crystallography, our representation of the extramembrane domains is arbitrary and not necessarily to scale.



**FIGURE 11-12 (3D Jmol representations by PDB ID: 1AF6 1QD5 1QJ9 1PHO) Tyr and Trp residues of membrane proteins clustering at the water-lipid interface.** The detailed structures of these five integral membrane proteins are known from crystallographic studies. K<sup>+</sup> channel (PDB ID 1BL8) is from the bacterium *Streptomyces lividans* (see Fig. 11-48); maltoporin (PDB ID 1AF6), outer membrane phospholipase A (PDB ID 1QD5), OmpX (PDB ID 1QJ9), and phosphoporin E (PDB ID 1PHO) are proteins of the outer membrane of *E. coli*. Residues of Tyr (orange) and Trp (red) are found predominantly where the nonpolar region (acyl chains) meets the polar head group region. Charged residues (Lys, Arg, Glu, Asp; shown blue) are found almost exclusively in the aqueous phases.

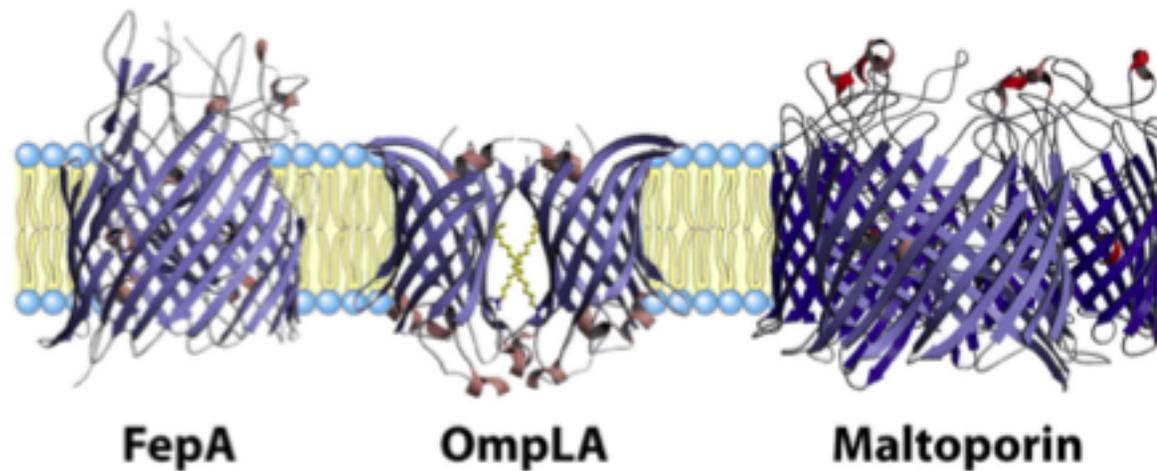
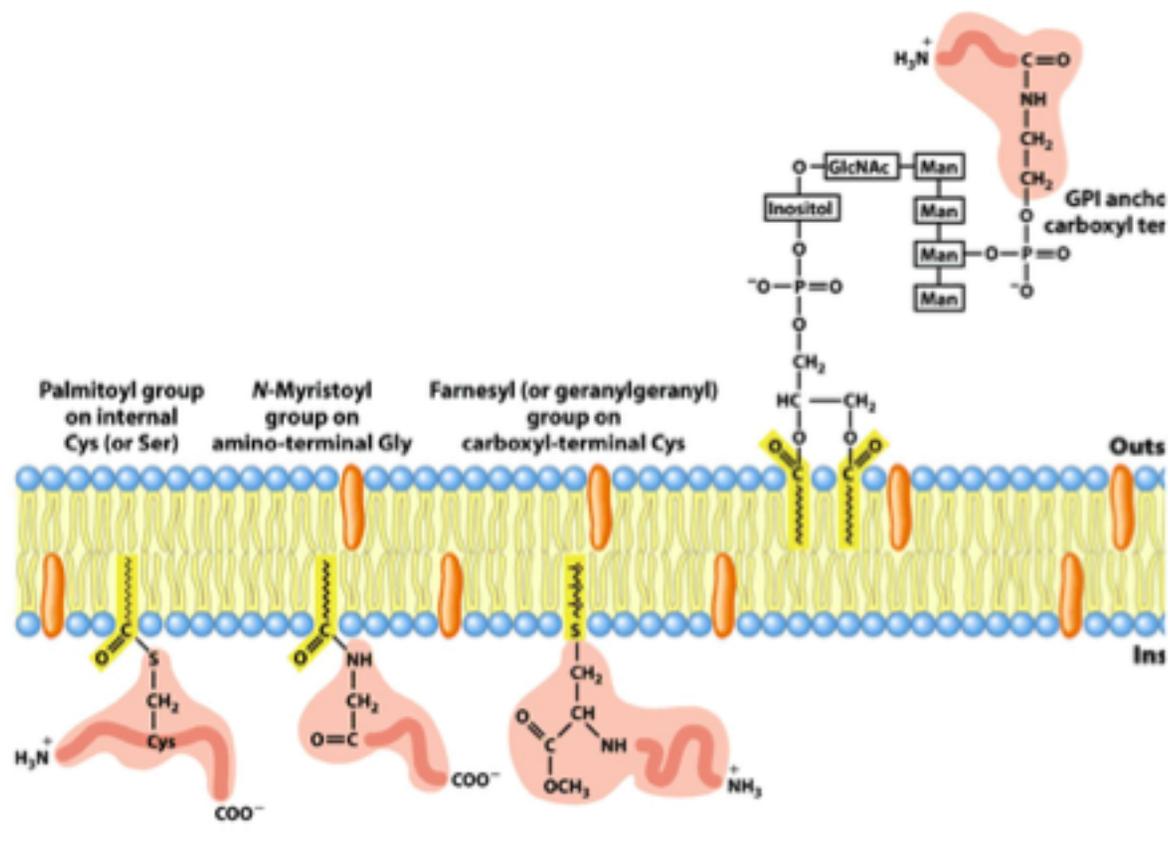
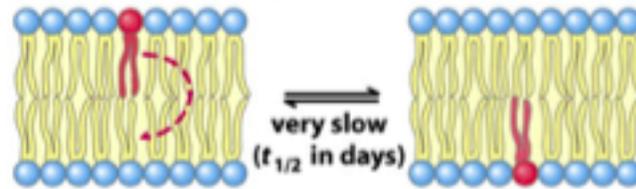


FIGURE 11-13 (3D Jmol representations by PDB ID: 1FEP 1QD5 1MAL) **Membrane prot with  $\beta$ -barrel structure.** Three proteins of the *E. coli* outer membrane are shown, viewed the plane of the membrane. FepA (PDB ID 1FEP), involved in iron uptake, has 22 membran spanning  $\beta$  strands. OmpLA (derived from PDB ID 1QD5), a phospholipase, is a 12-stranded barrel that exists as a dimer in the membrane. Maltoporin (derived from PDB ID 1MAL), a maltose transporter, is a trimer; each monomer consists of 16  $\beta$  strands.

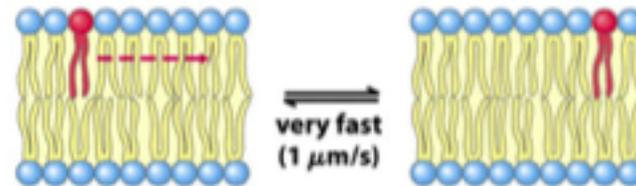


**FIGURE 11-14 Lipid-linked membrane proteins.** Covalently attached lipids anchor membrane proteins to the lipid bilayer. A palmitoyl group is shown attached by thioester link to a Cys residue; an *N*-myristoyl group is generally attached to an amino-terminal Gly; the farnesyl and geranylgeranyl groups attached to carboxyl-terminal Cys residues are isoprenoid 15 and 20 carbons, respectively. These three lipid-protein assemblies are found only on the face of the plasma membrane. Glycosyl phosphatidylinositol (GPI) anchors are derivatives of phosphatidylinositol in which the inositol bears a short oligosaccharide covalently joined to the carboxyl-terminal residue of a protein through phosphoethanolamine. GPI-linked proteins are always on the extracellular face of the plasma membrane.

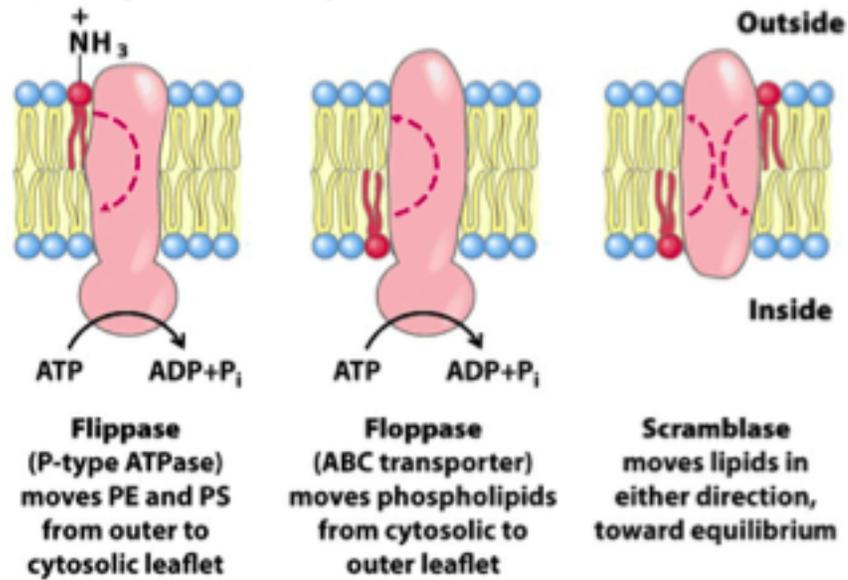
**(a) Uncatalyzed transbilayer ("flip-flop") diffusion**

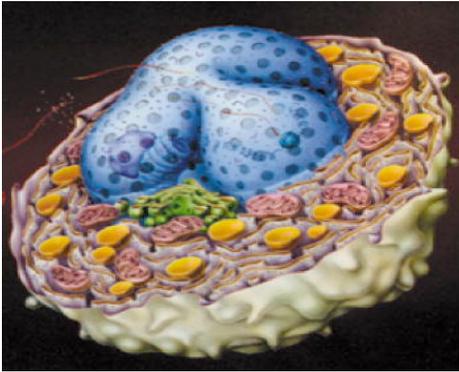


**(b) Uncatalyzed lateral diffusion**



**(c) Catalyzed transbilayer translocations**



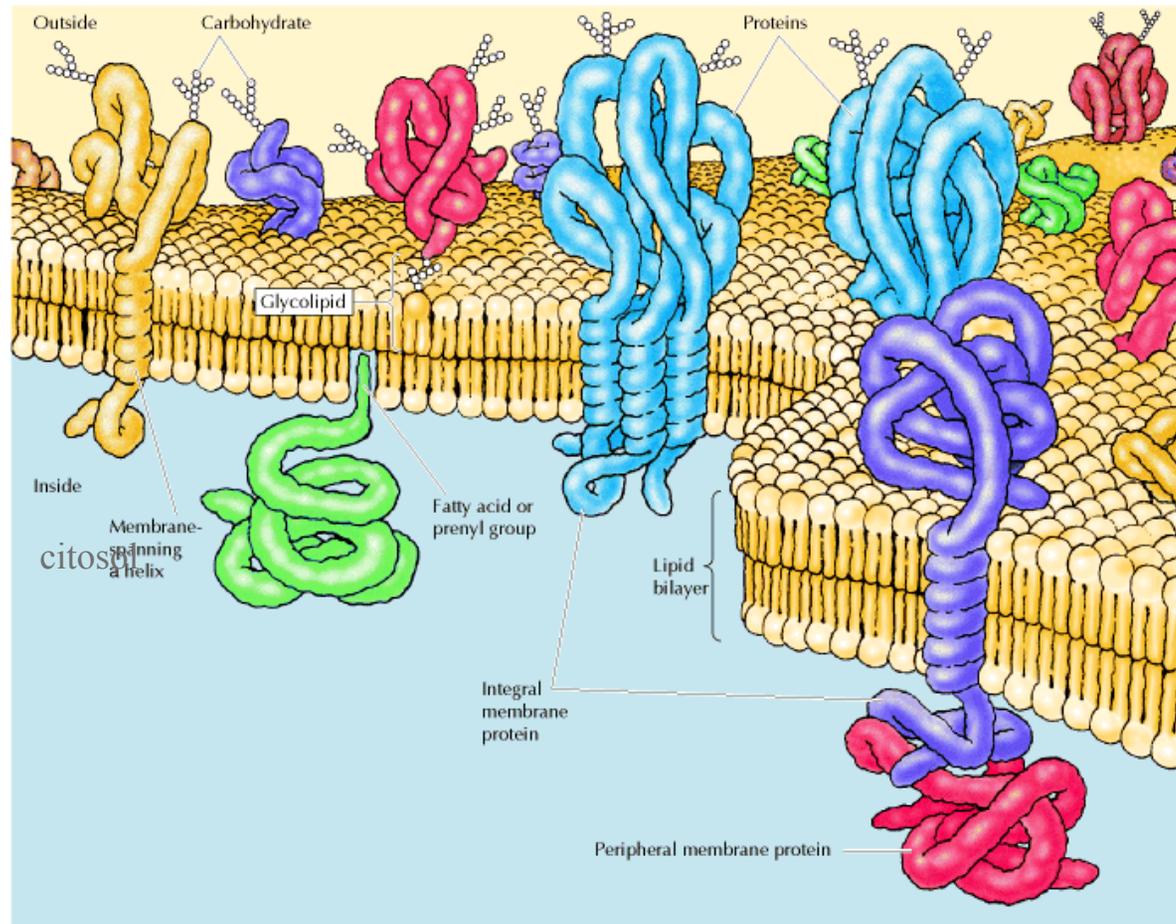


## Funciones de las Membranas Celulares

- 1.- Delimitan compartimentos controlando así su composición (barrera selectiva).
- 2.- Permiten el transporte selectivo de moléculas y iones de un compartimiento a otro.
- 3.- Participan en la transducción de señales (comunicación), participan en la producción de energía.
- 4.- Protección celular.

Modelo de Membranas-“Bicapa Lipídica” (Danielli y Davson, 1935)

Modelo del mosaico fluido de las membranas biológicas (Singer y Nicolson, 1972)

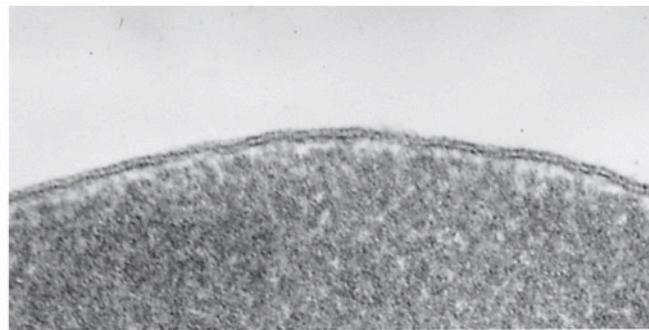


exterior

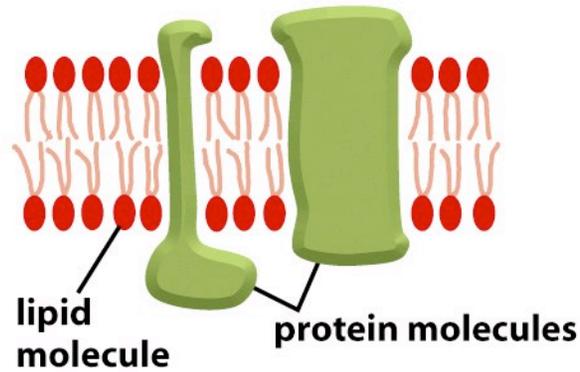
Bicapa de lípidos donde se insertan diferentes tipos de proteínas integrales a la que se asocian proteínas periféricas. -----> Fluido bidimensional, heterogéneo.

Modelo de Membranas-“Bicapa Lipídica” (Danielli y Davson, 1935)

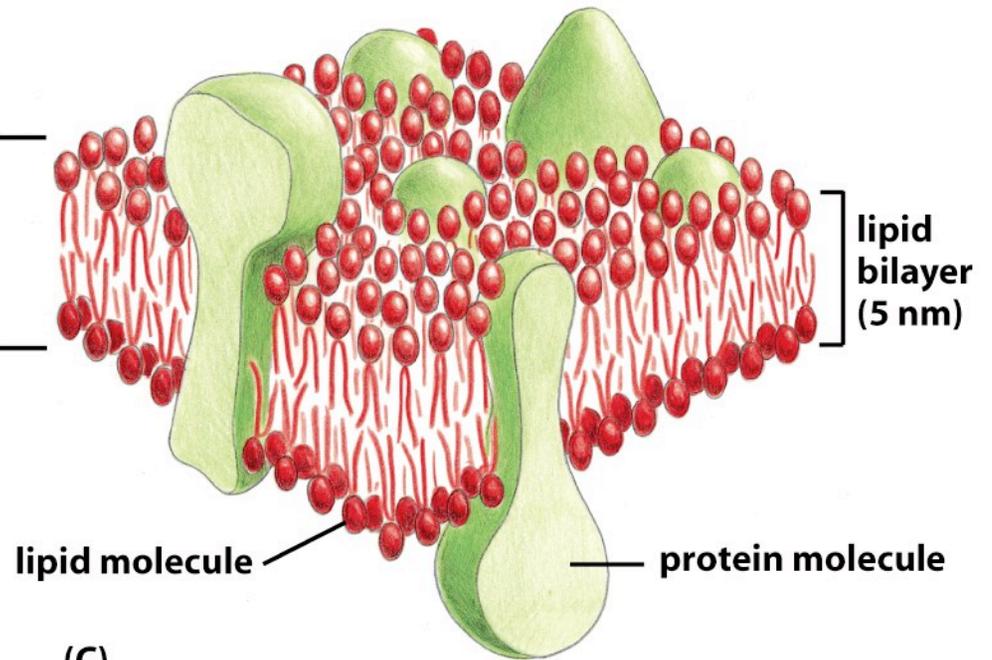
Modelo del mosaico fluido de las membranas biológicas (Singer y Nicolson, 1972)



(A)



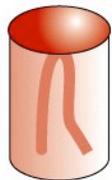
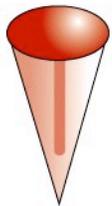
(B)



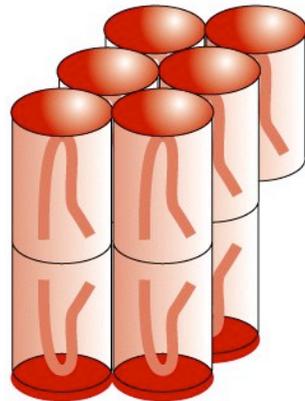
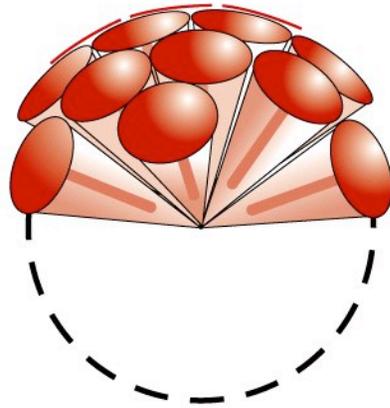
(C)

## ¿Por qué una Bicapa (Lipídica)?

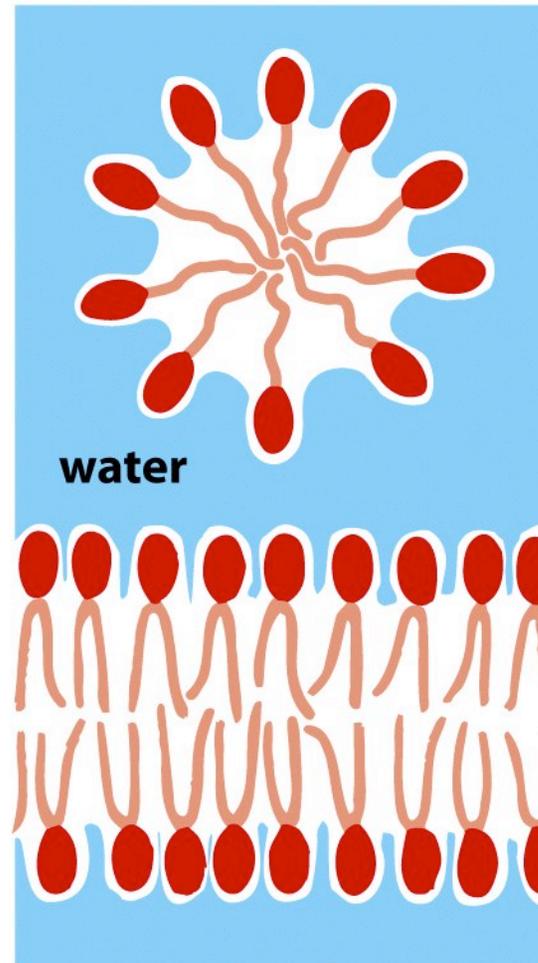
shape of lipid molecule



packing of lipid molecules



(A)



lipid micelle

lipid bilayer

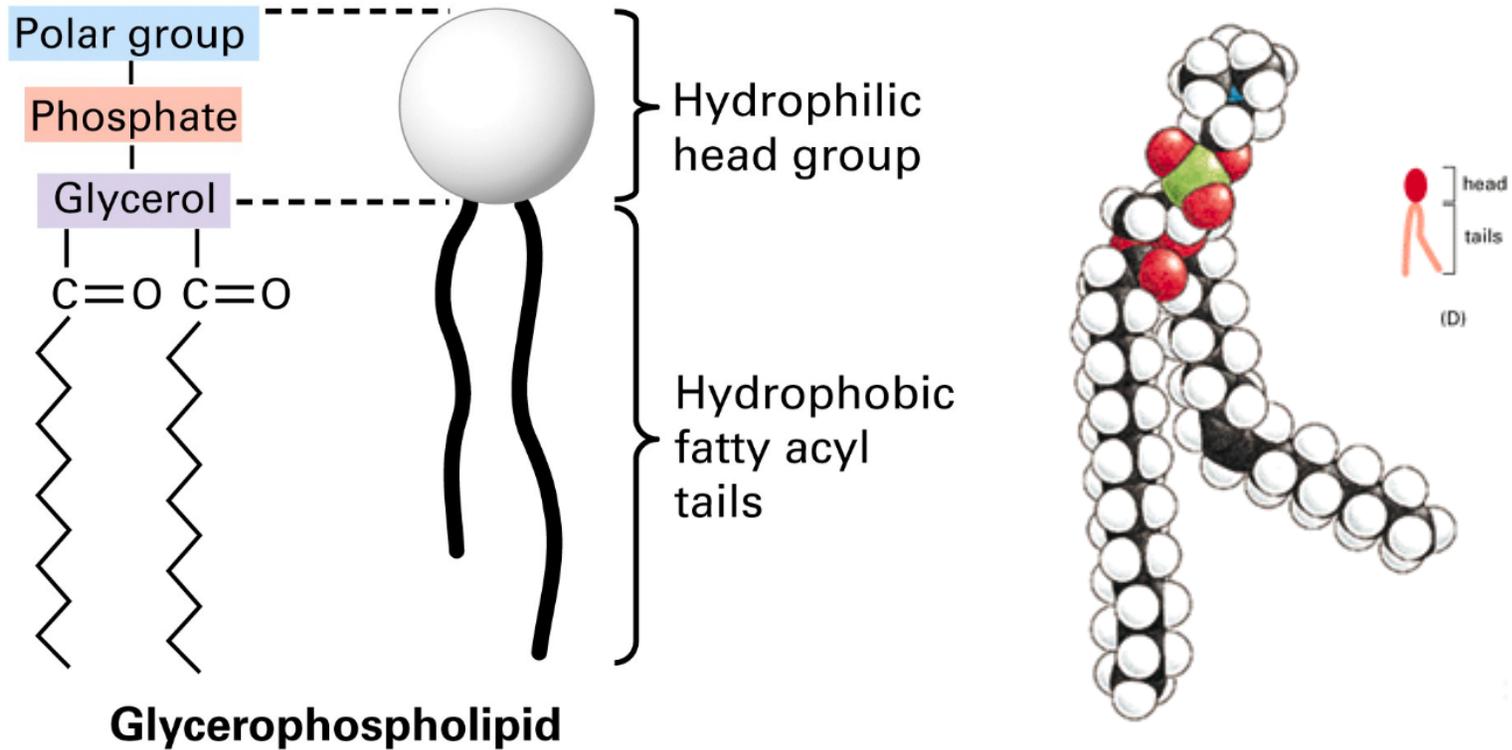
(B)

# Composición y estructura de la bicapa lipídica

## Lípidos de Membrana

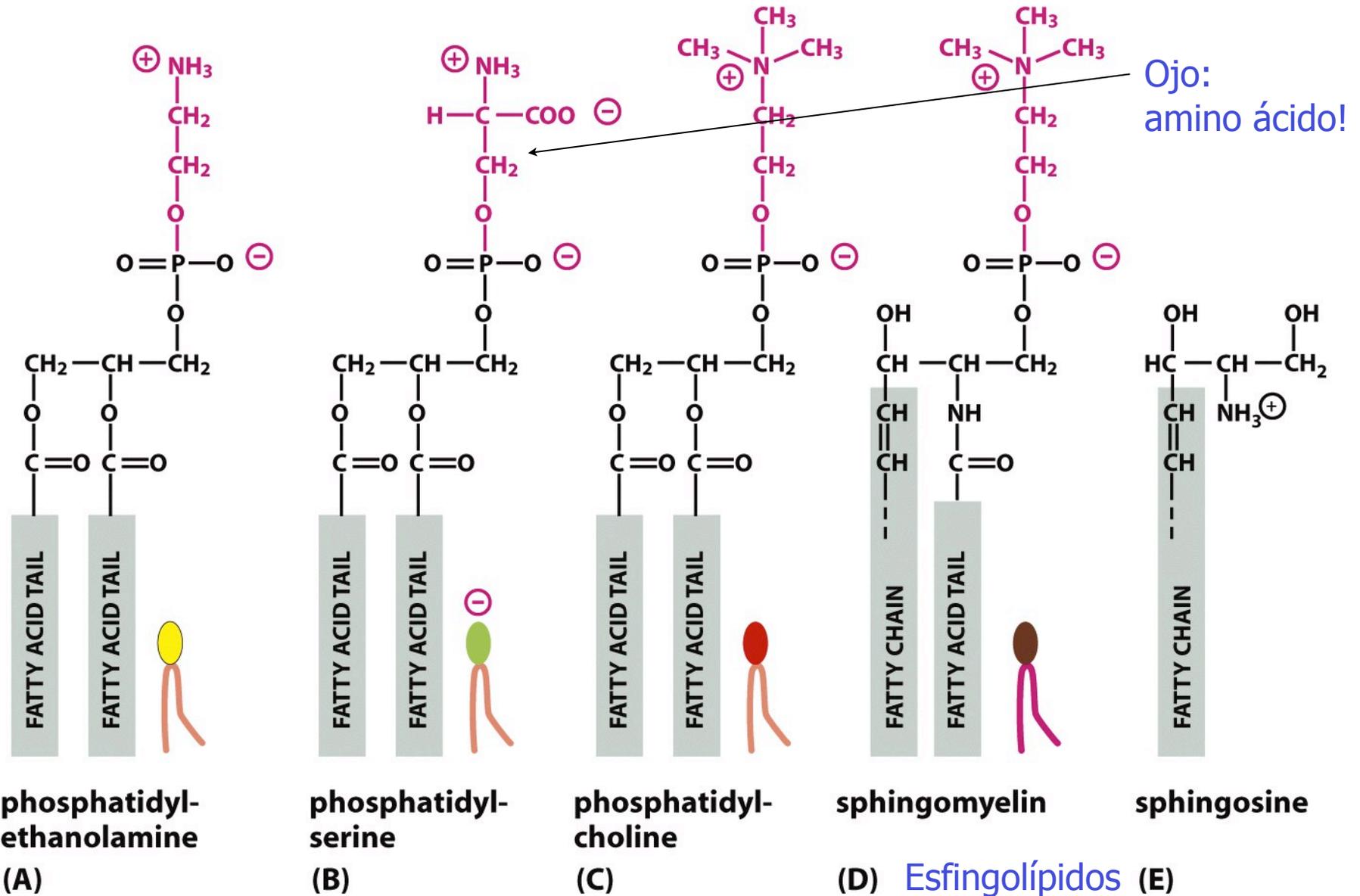
Todas las membranas celulares contienen lípidos anfipáticos (parte polar y otra hidrofóbica).

→ Fosfolípidos que están constituidos por una cabeza polar y dos cadenas o colas hidrocarbonadas.





## Composición y estructura de la bicapa lipídica



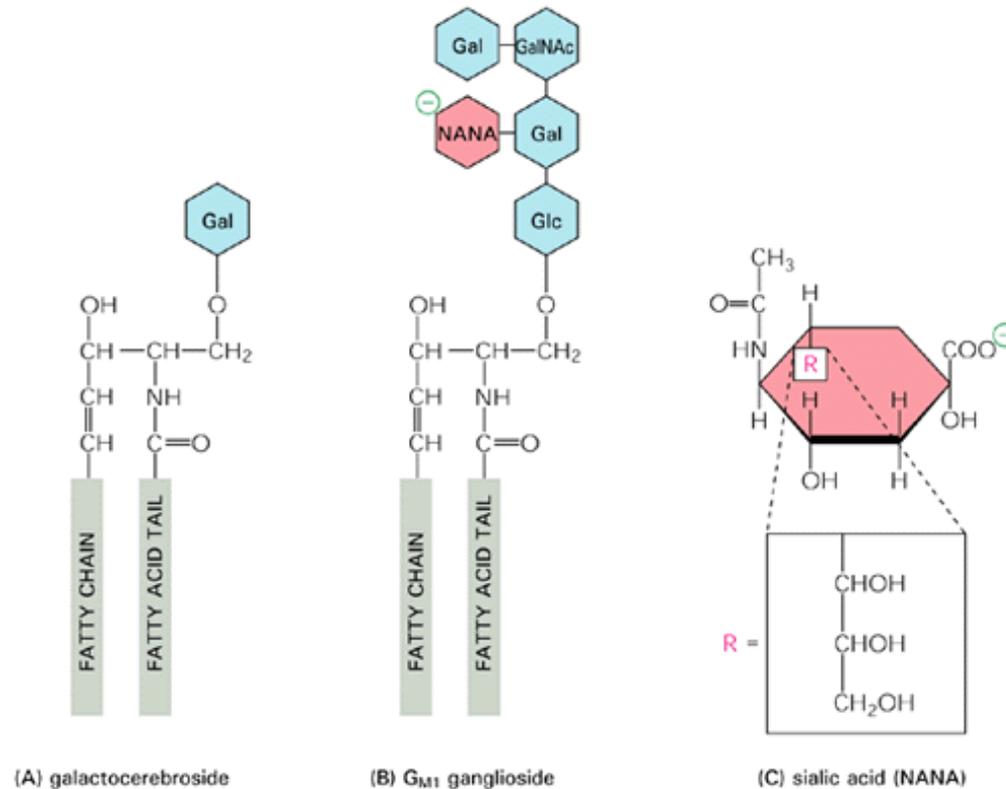
### Fosfoglicéridos

# Composición y estructura de la bicapa lipídica

## Lípidos de Membrana

**Glicolípidos:** son los que tienen uno o más residuos de azúcares.

Tienen un esqueleto de esfingosina, son esfingolípidos.



Alberts *et al.* 2002

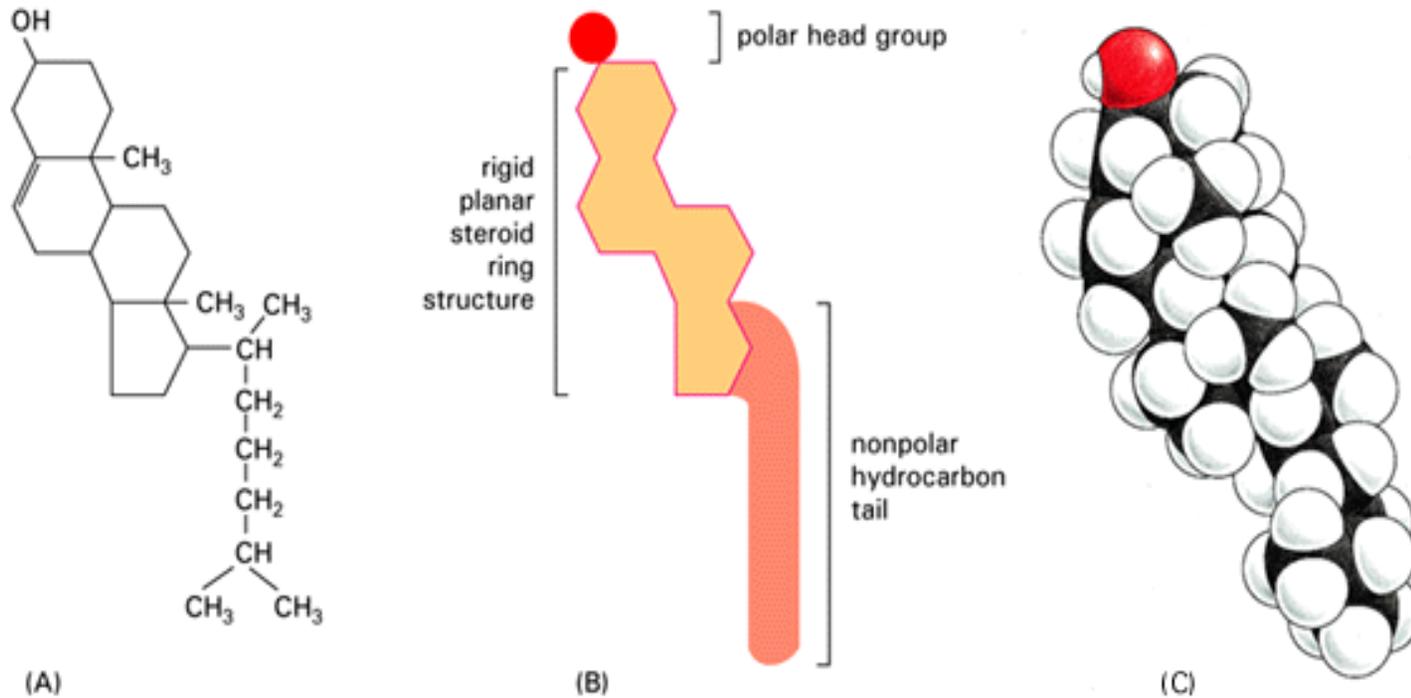
Otros lípidos como los inositol fosfolípidos, de gran importancia en procesos de transducción de señales.

# Composición y estructura de la bicapa lipídica

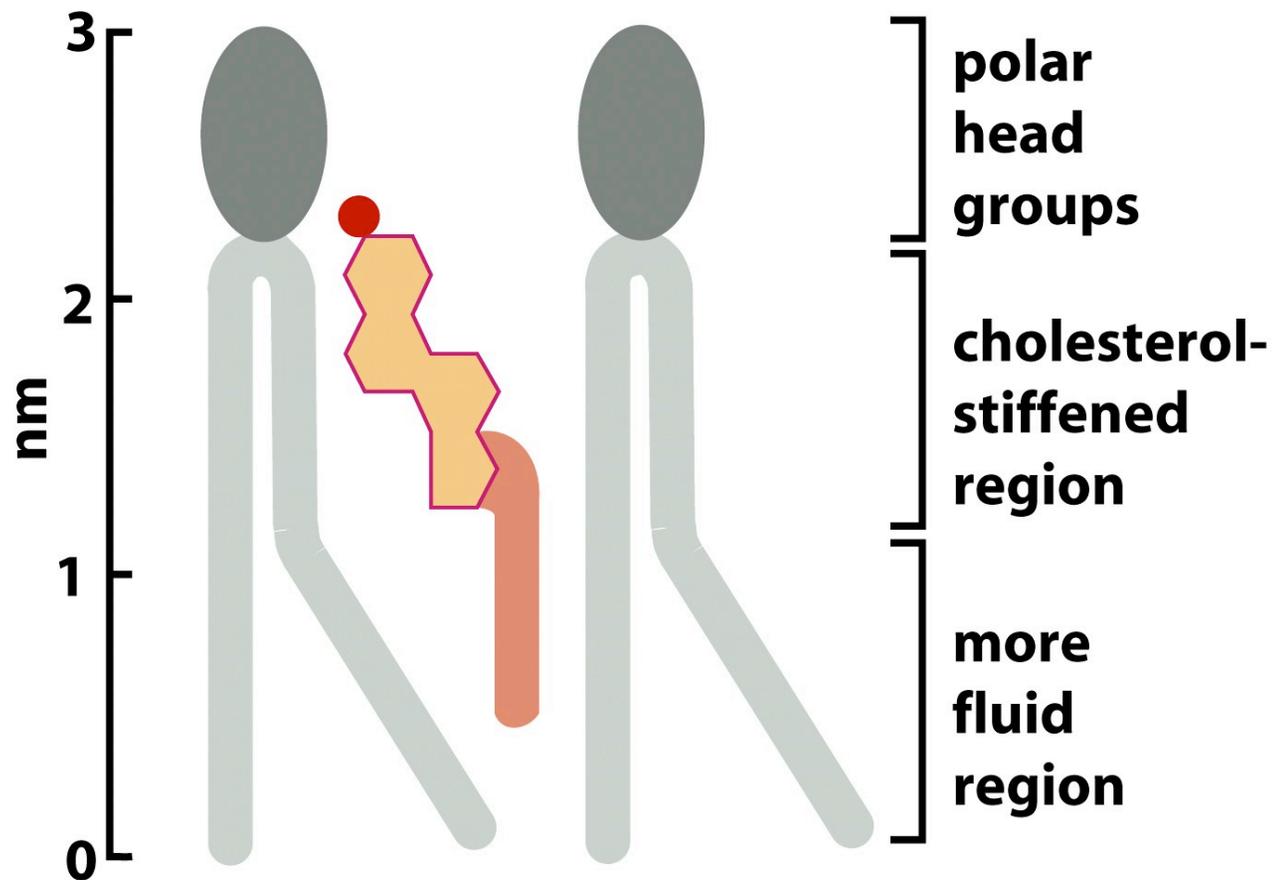
## Lípidos de Membrana

### Estructura del colesterol

Las membranas de las células eucarióticas contienen colesterol, un esteroide determinante en la fluidez de la bicapa.



Alberts *et al.* 2002



### Colesterol y Fluidez de la Membrana

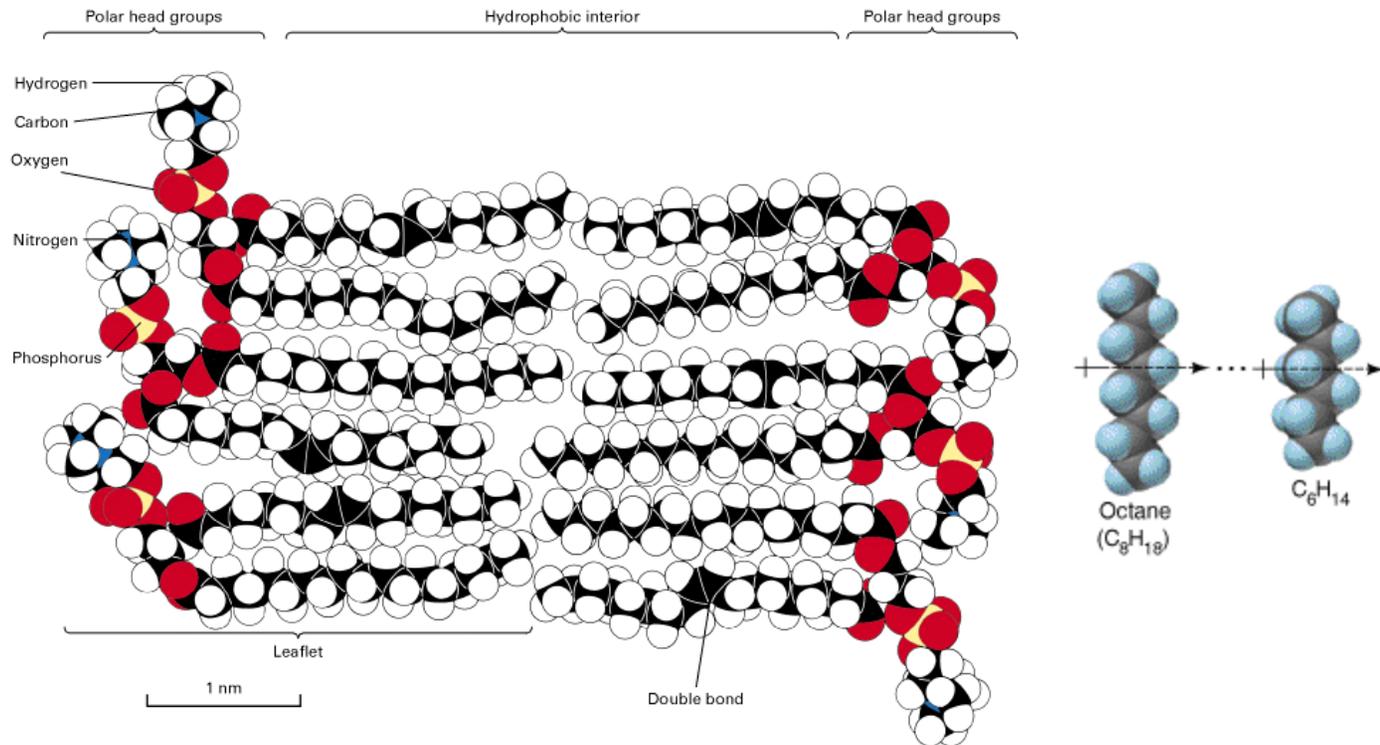
A altas temperaturas: disminuye la fluidez (interfiere con el mov. de FL en las zonas cercanas a los grupos polares)

A bajas temperaturas: mantiene la fluidez de la membrana (es lo que hace en las células eucariotas).

## Composición lipídica de diferentes membranas

Lipid	Percentage of Total Lipid by Weight						Hojas cebada
	Liver Plasma Membrane	Erythrocyte Plasma Membrane	Myelin	Mitochondrion (inner and outer membranes)	Endoplasmic Reticulum	<i>E. coli</i>	
Cholesterol	17	23	22	3	6	0	<b>35</b> (esteroles)
Phosphatidyl- ethanolamine	7	18	15	35	17	70	<b>44</b> (FLs)
Phosphatidylserine	4	7	9	2	5	trace	
Phosphatidyl- choline	24	17	10	39	40	0	
Sphingomyelin	19	18	8	0	5	0	
Glycolipids	7	3	28	trace	trace	0	
Others	22	13	8	21	27	30	<b>16</b> (cerebrósidos)

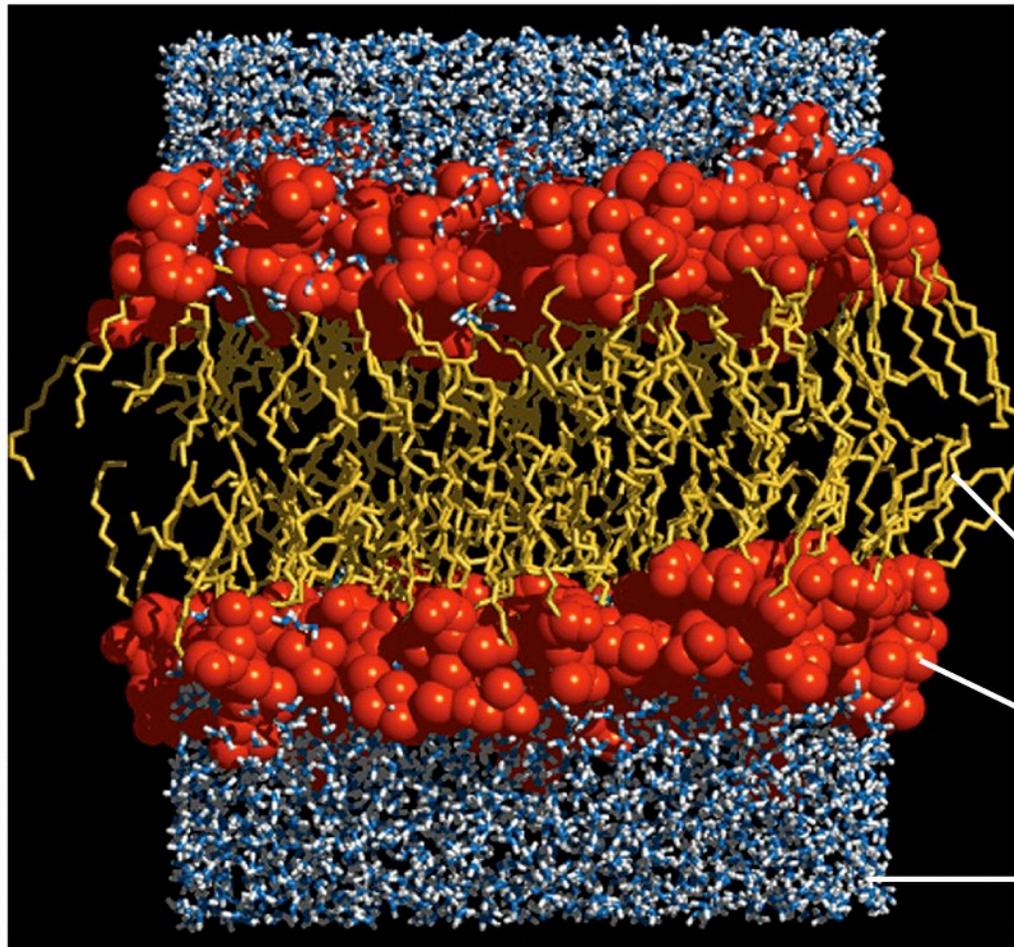
## Factores de estabilidad de la bicapa



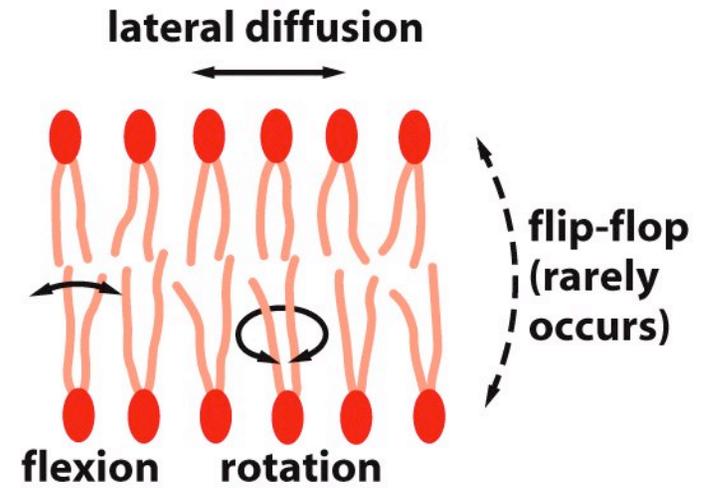
Lodish *et al.* 2004

Depende de las interacciones hidrofóbicas, las interacciones de van der Waals entre las cadenas hidrocarbonadas que favorecen el empaquetamiento de las colas.

También contribuyen los enlaces de hidrógeno e interacciones electrostáticas entre las cabeza polares y el agua.



(A)



(B)

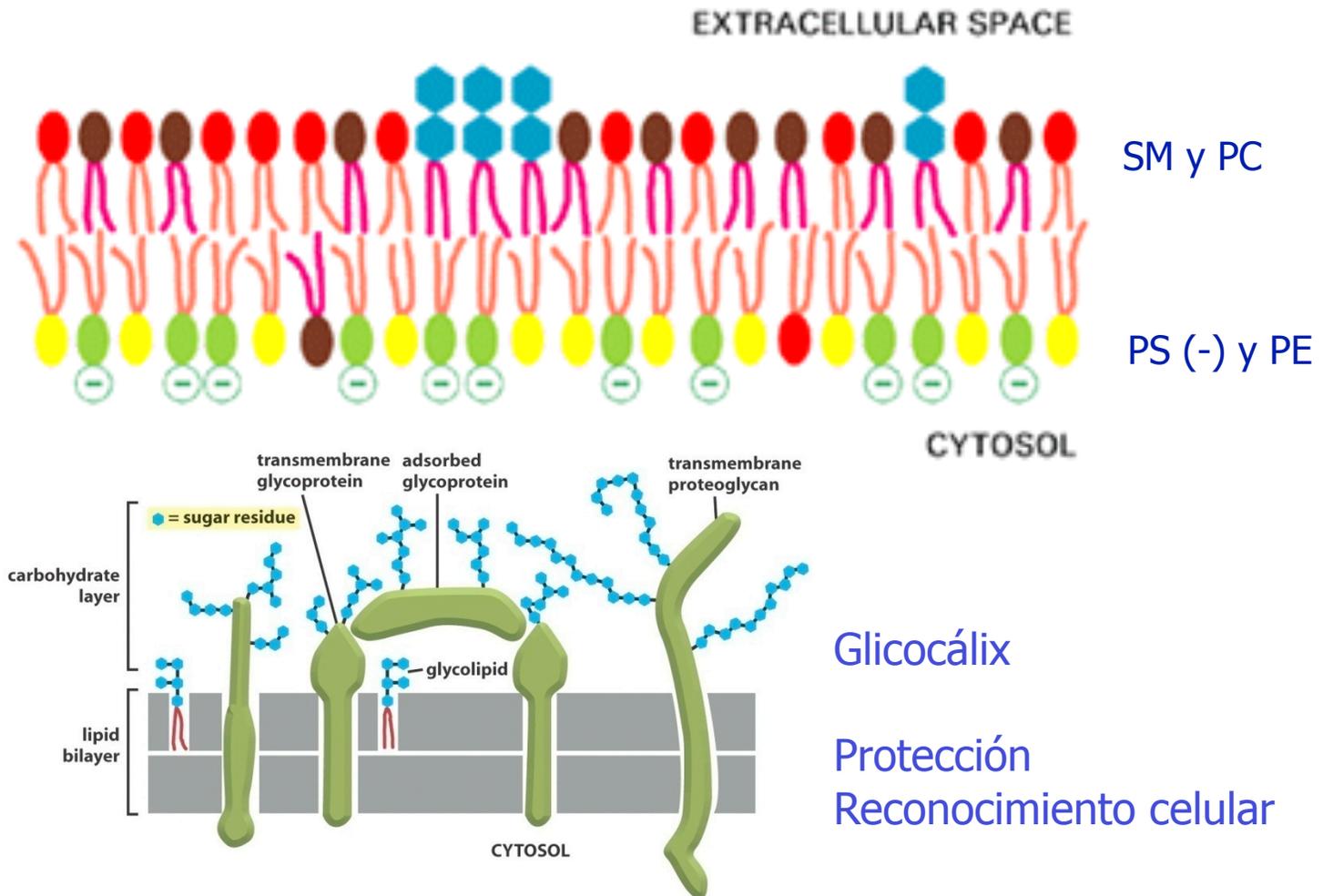
fatty acid tails  
lipid head groups  
water molecules

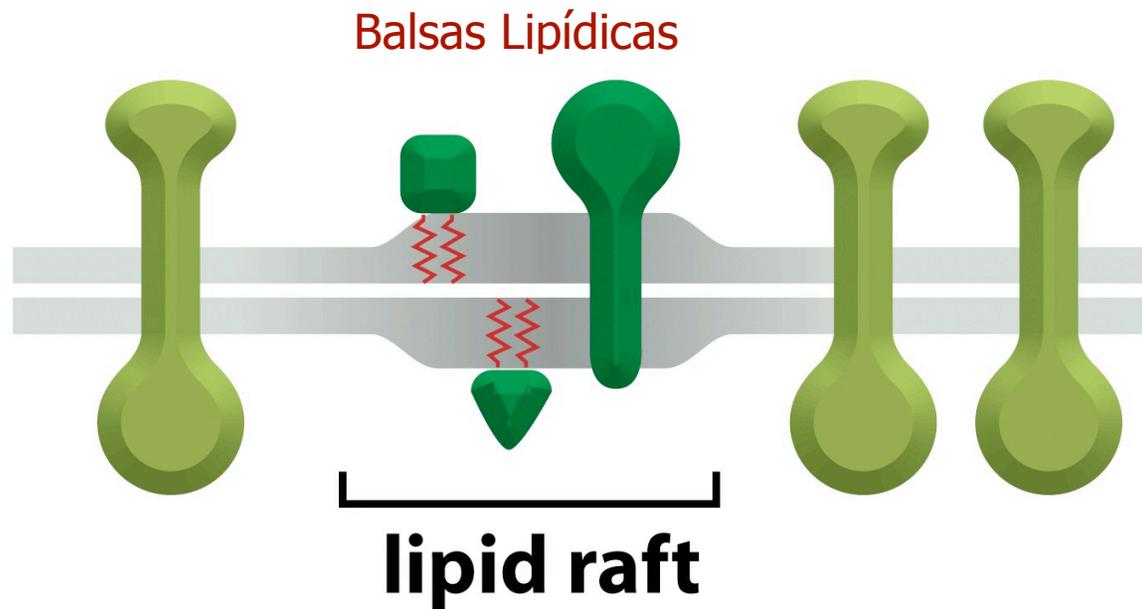
En las bicapas de fosfolípidos puros éstos no migran (flip-flop) de una monocapa a otra (flipasas).

Las moléculas de lípidos en cada monocapa están en continuo movimiento difundiéndose.

En las membranas plasmáticas los fosfolípidos se distribuyen asimétricamente en las dos monocapas.

En eritrocitos: los fosfolípidos que poseen un grupo colina (SM y PC) se encuentran predominantemente en la monocapa externa y los lípidos con grupos amino (PS y PE) se encuentran en la cara citosólica.





La membranas poseen regiones de mosaico fluido y zonas con microdominios transitorios o balsas lipídicas (lipid rafts).

Contienen esfingolípidos, colesterol y algunas proteínas de membrana que se organizan en fases líquidas ordenadas.

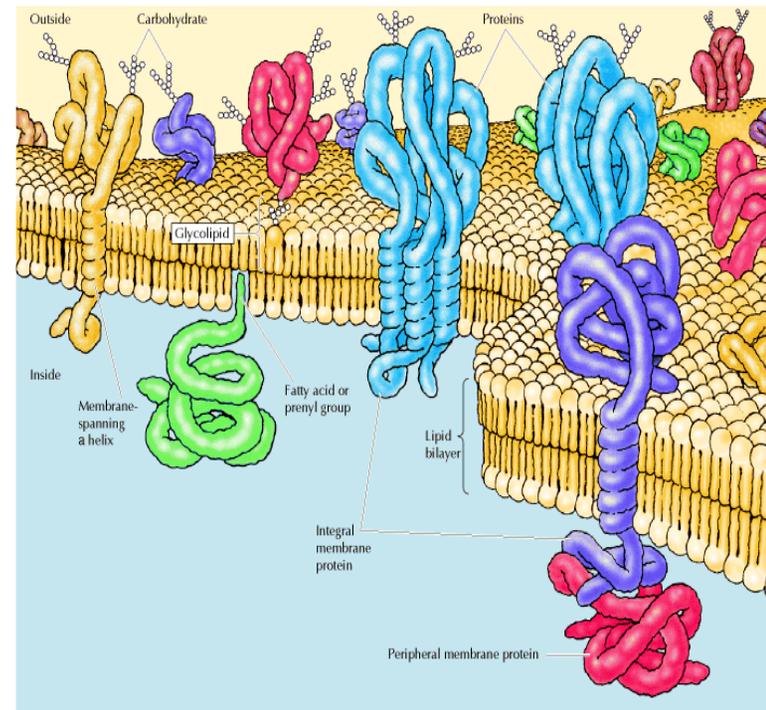
## Proteínas de Membrana

-> Función de la Membrana.

Todas las membranas biológicas contienen proteínas.

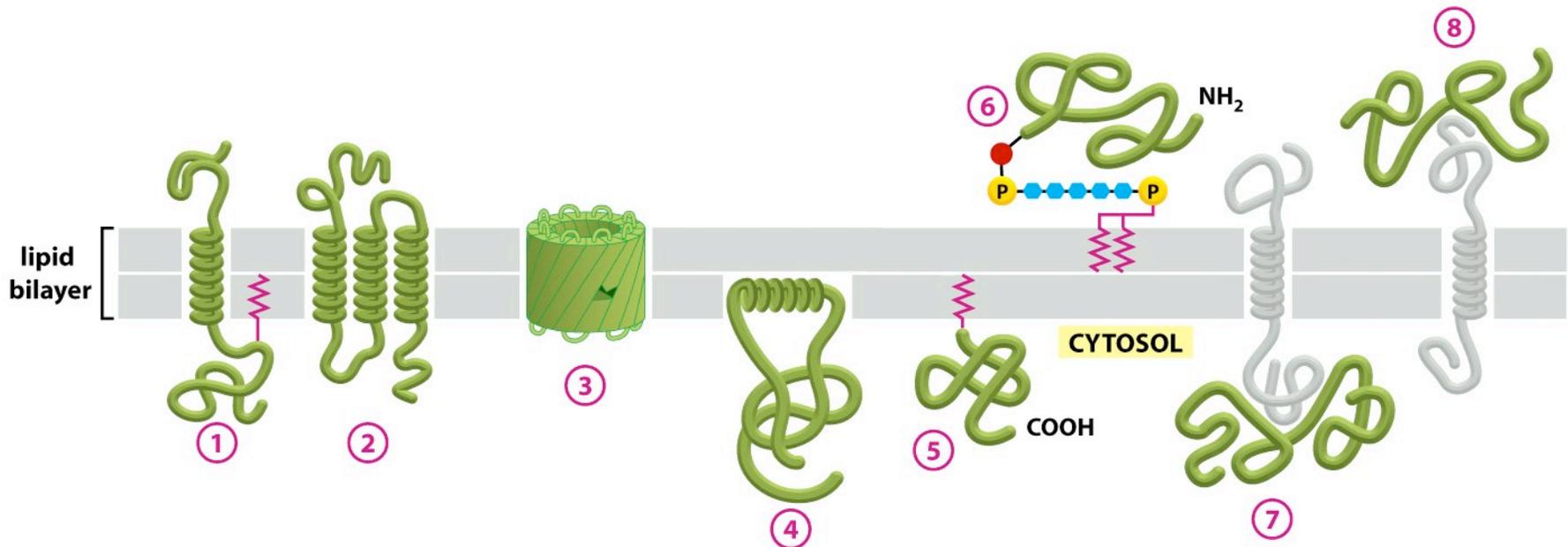
Varía la proporción:

Membrana interna mitocondrial contiene 70% de proteínas y la mielina sólo 18%.



## Proteínas de Membrana

Clases 1, 2 y 3: **proteínas de transmembrana**, con dominios hidrofílicos expuestos a los medios externo y/o interno conectados por dominios peptídicos hidrofóbicos que atraviesan la bicapa.



## Proteínas de Membrana

Clases ancla de alfa hélice

Clase 5, ancla a cadena de ácido graso.

Clase 6, ancla de GPI (glicofosfatidilinositol)

Clase 7 y 8, ancladas a otras proteínas (enlaces no covalentes)

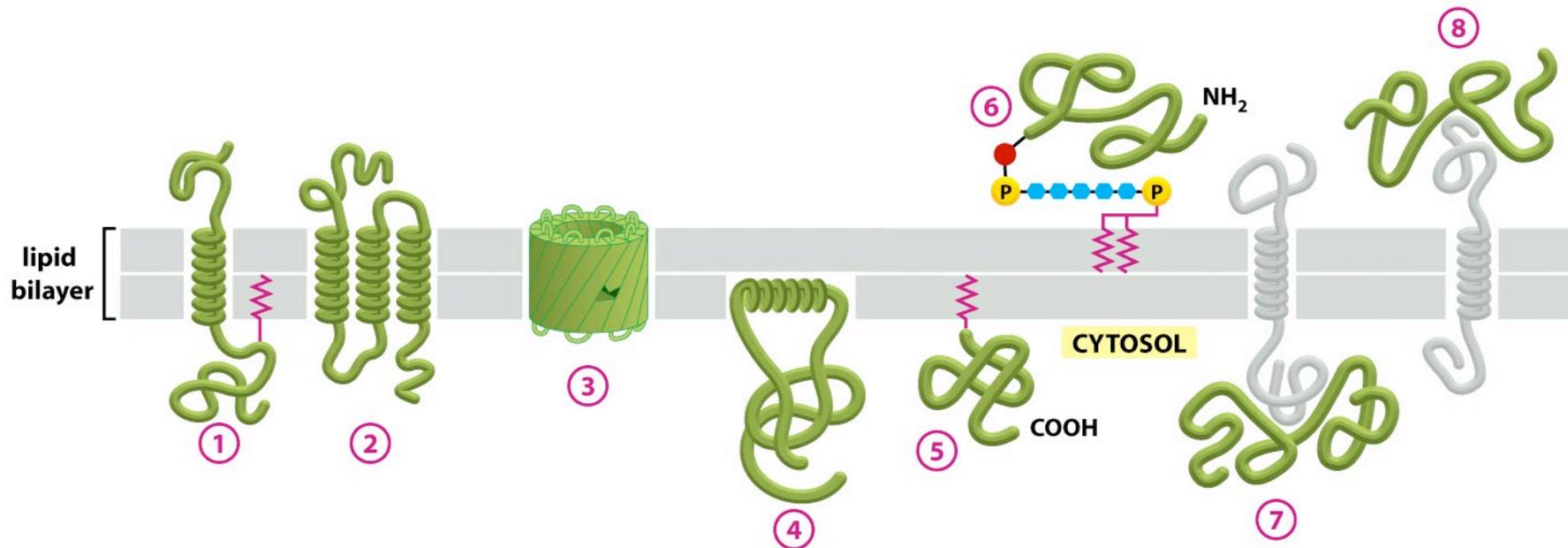
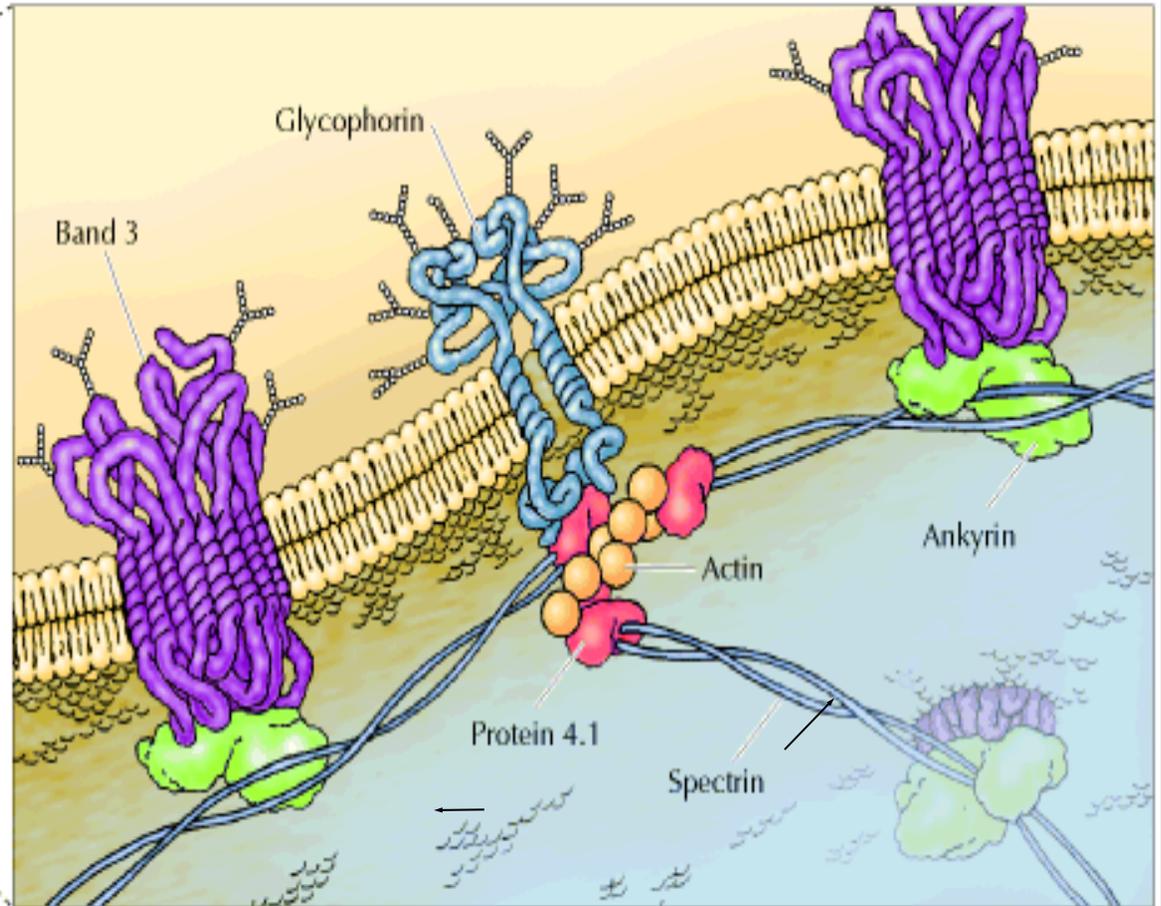
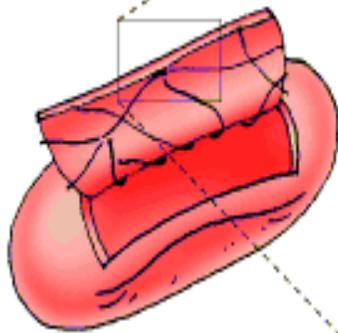


Figure 10-19 *Molecular Biology of the Cell* (© Garland Science 2008)

La membrana celular actual:



Las proteínas integrales pueden difundir lateralmente aunque ~~presentan~~ restricciones.

1.- Algunas proteínas de membrana interactúan con componentes del citoesqueleto como actina o filamentos intermedios.

2.- En algunas células las proteínas están restringidas a dominios de membrana.

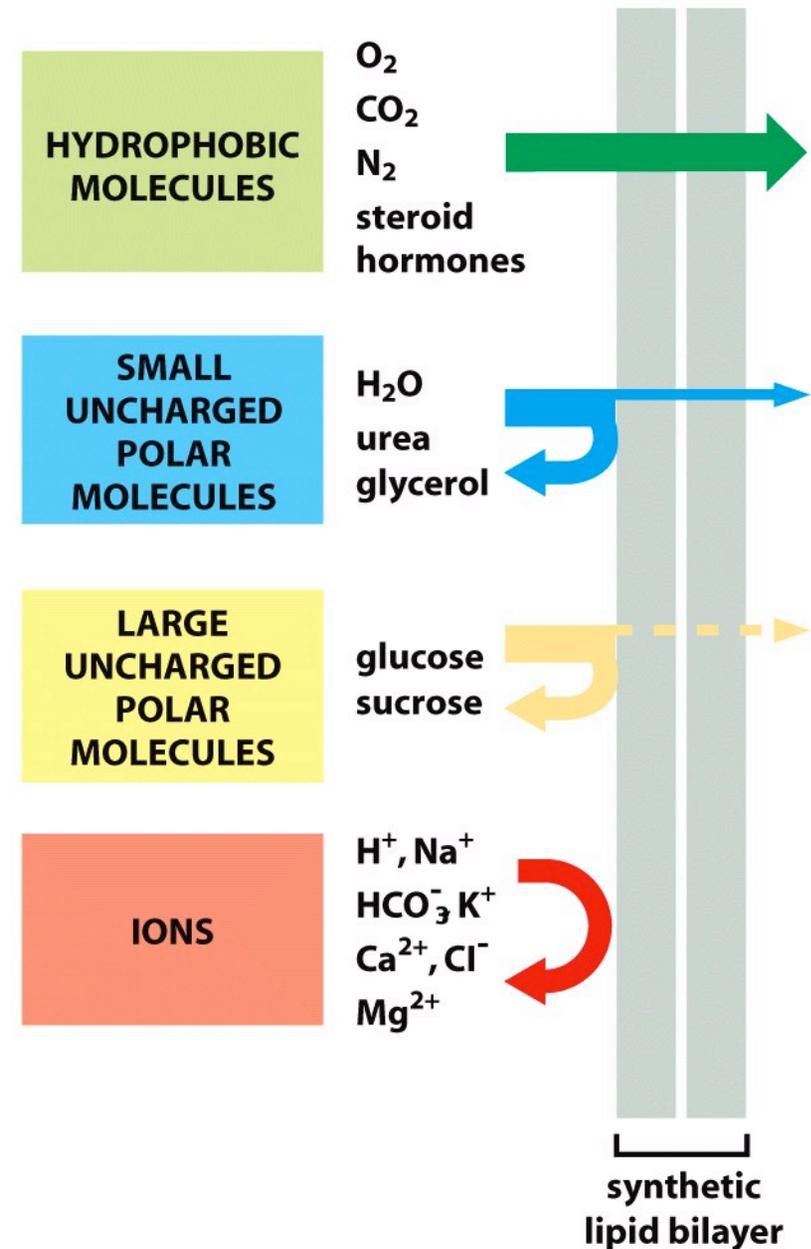
# TRANSPORTE A TRAVÉS DE MEMBRANAS BIOLÓGICAS

Difusión: desplazamiento o transporte neto de materia desde una región de mayor concentración a otra de menor concentración.

## Canales de agua o acuaporinas

En las células el agua se transporta a través de proteínas de membrana específicas llamadas canales de agua o acuaporinas.

## Difusión Simple



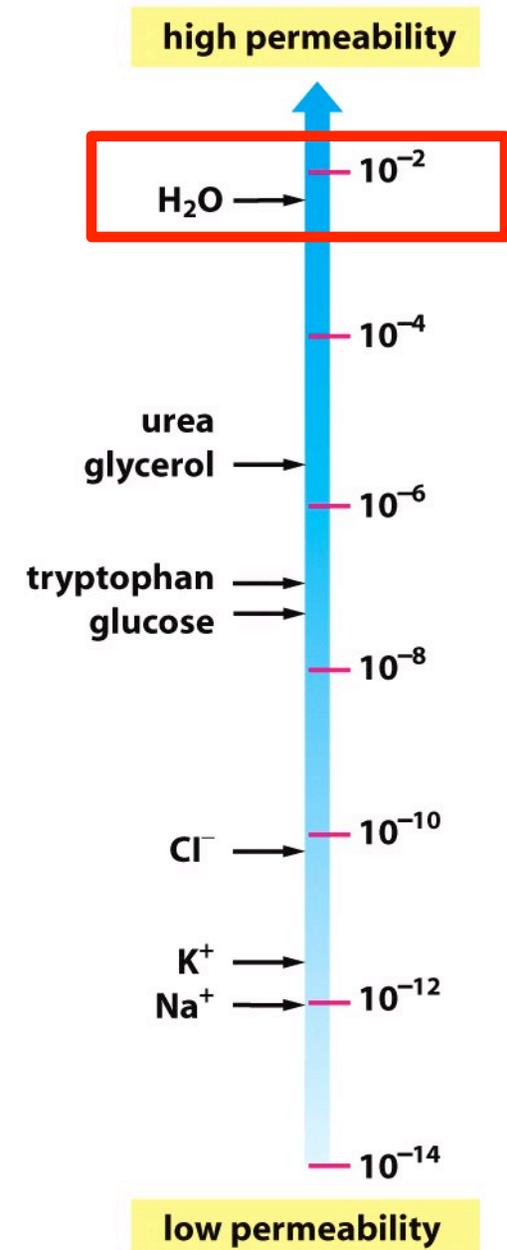
**Table 11–1 A Comparison of Ion Concentrations Inside and Outside a Typical Mammalian Cell**

COMPONENT	INTRACELLULAR CONCENTRATION (mM)	EXTRACELLULAR CONCENTRATION (mM)
<b>Cations</b>		
Na <sup>+</sup>	5–15	145
K <sup>+</sup>	140	5
Mg <sup>2+</sup>	0.5	1–2
Ca <sup>2+</sup>	10 <sup>-4</sup>	1–2
H <sup>+</sup>	7 × 10 <sup>-5</sup> (10 <sup>-7.2</sup> M or pH 7.2)	4 × 10 <sup>-5</sup> (10 <sup>-7.4</sup> M or pH 7.4)
<b>Anions*</b>		
Cl <sup>-</sup>	5–15	110

\*The cell must contain equal quantities of positive and negative charges (that is, it must be electrically neutral). Thus, in addition to Cl<sup>-</sup>, the cell contains many other anions not listed in this table; in fact, most cell constituents are negatively charged (HCO<sub>3</sub><sup>-</sup>, PO<sub>4</sub><sup>3-</sup>, proteins, nucleic acids, metabolites carrying phosphate and carboxyl groups, etc.). The concentrations of Ca<sup>2+</sup> and Mg<sup>2+</sup> given are for the free ions. There is a total of about 20 mM Mg<sup>2+</sup> and 1–2 mM Ca<sup>2+</sup> in cells, but both are mostly bound to proteins and other substances and, for Ca<sup>2+</sup>, stored within various organelles.

La velocidad con que una molécula puede pasar a través de una bicapa lipídica es proporcional a la diferencia de la concentración entre ambos lados (en mol/cm<sup>3</sup>) multiplicado por el coeficiente de permeabilidad (cm/seg). Es decir: (mol/seg\* cm<sup>2</sup>).

Coeficiente de permeabilidad= directamente proporcional a su partición en lípidos/agua

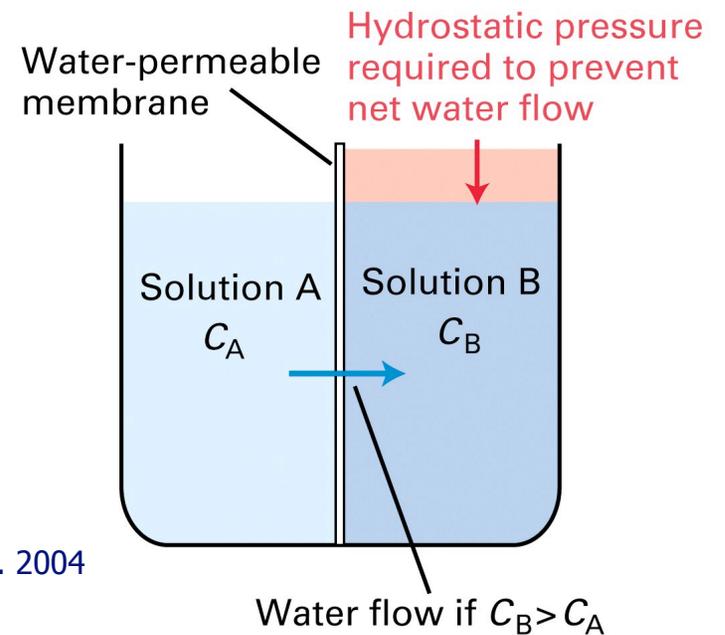
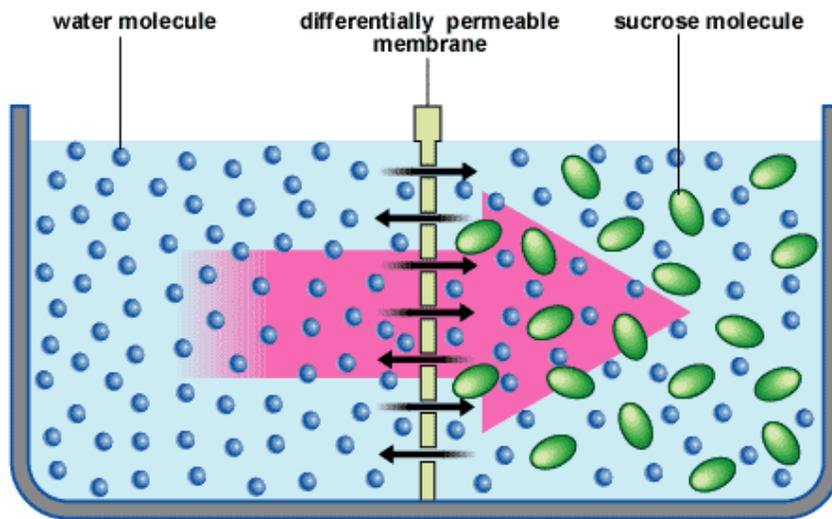


# Primero: ¿Cómo fluye el agua?

## Osmosis

Es el flujo de volumen del solvente (agua) a través de una membrana semipermeable que separa dos soluciones de diferente concentración.

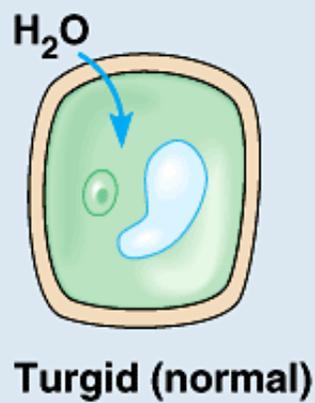
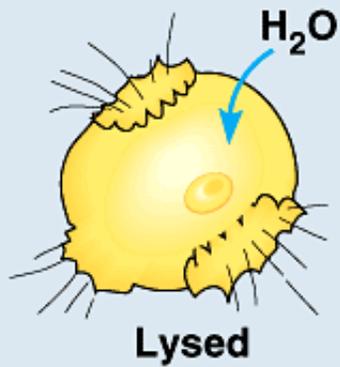
El agua fluye, no los solutos.



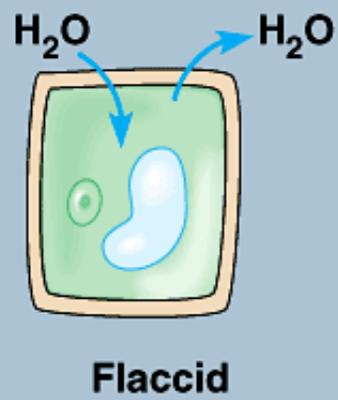
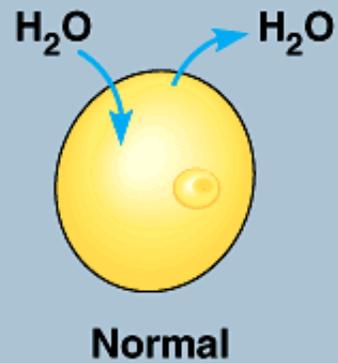
Lodish et al. 2004

## Respuestas de células animales y vegetales a cambios en la osmolaridad del medio

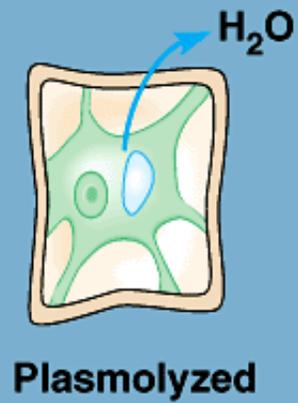
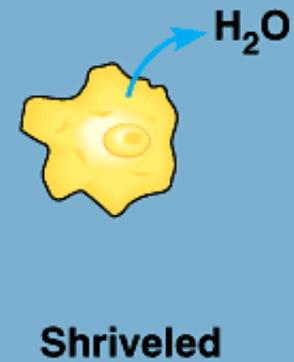
**Hypotonic solution**



**Isotonic solution**



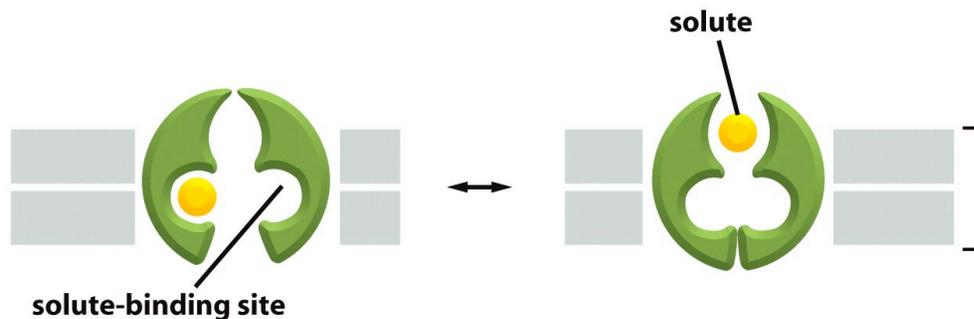
**Hypertonic solution**



**Ok, pero no siempre necesitamos que sea el agua la que atraviesa la membrana.**

### Transporte y Gradientes:

Transporte mediado por Proteínas Transportadoras (Carriers, Permesas)

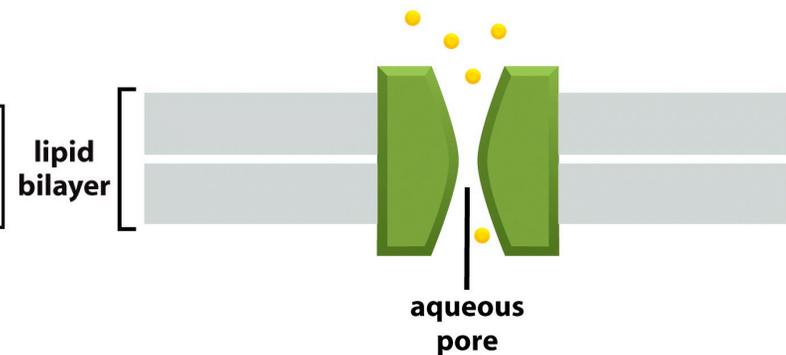


**TRANSPORTER**

Ejemplo: GLUT1, proteína que transporta Glucosa.

Sufre un cambio conformacional al transportar.

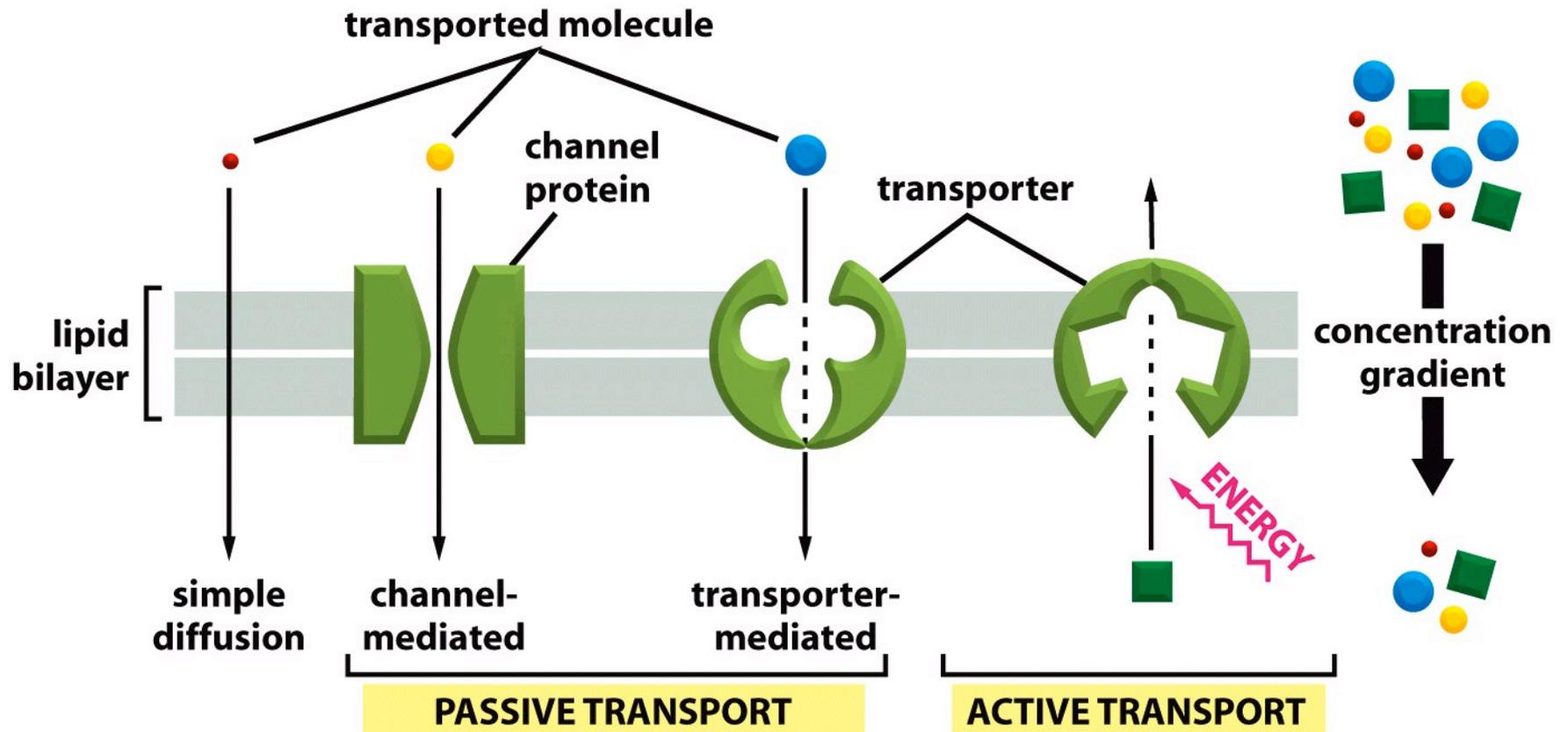
Transporte mediado por Proteínas que forman un Canal



**CHANNEL PROTEIN**

Transporte de iones, ejemplo de K<sup>+</sup>

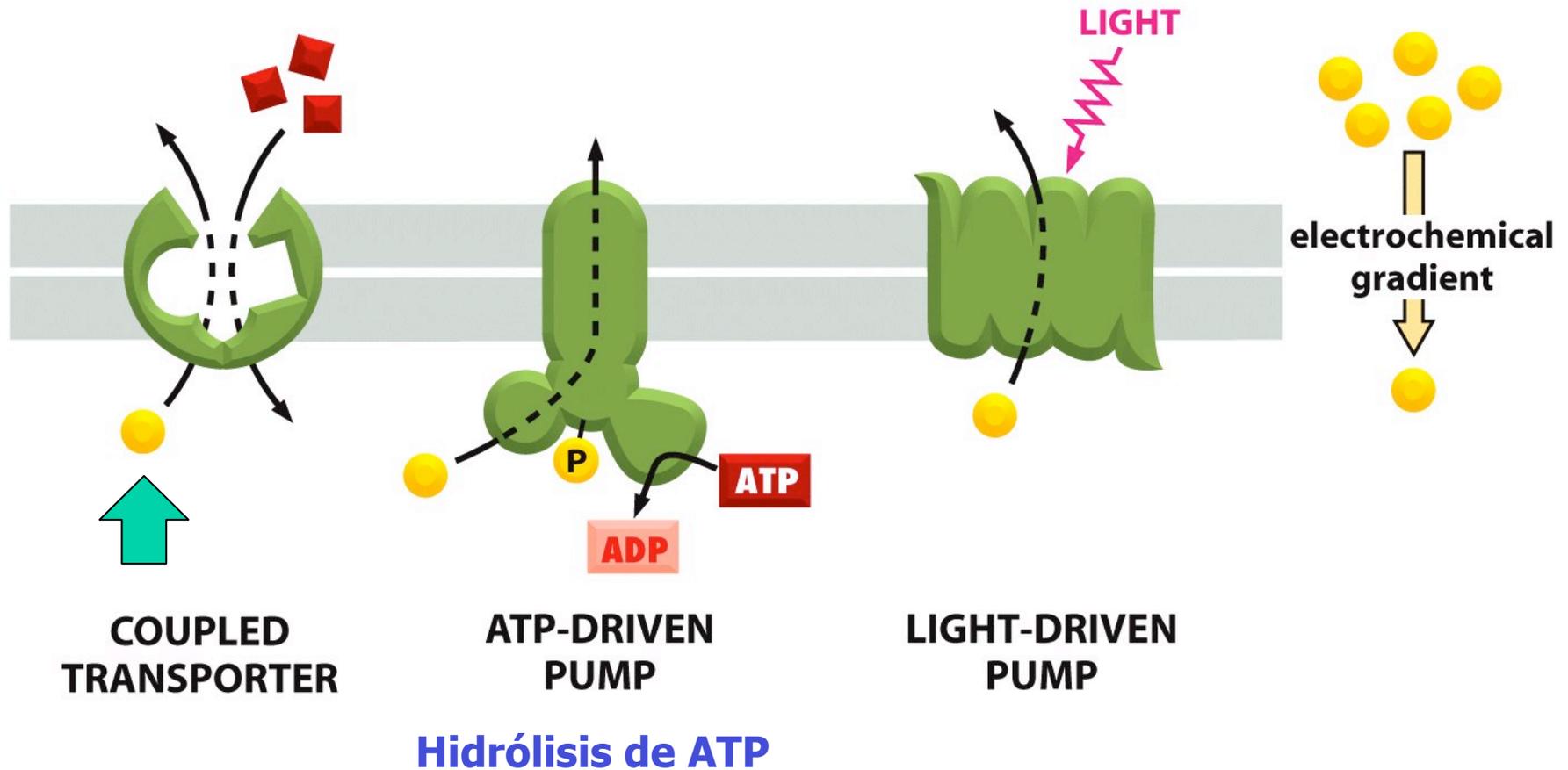
## Transporte Activo y Pasivo (o difusión facilitada)



A favor del gradiente de concentración o electroquímico

-Acoplado a una fuente energética  
-Bombas o Transportadores  
**- Puede ir en contra de la gradiente**

## Fuentes de Energía para Transporte Activo



# Tipos de Transporte

transported molecule

co-transported ion

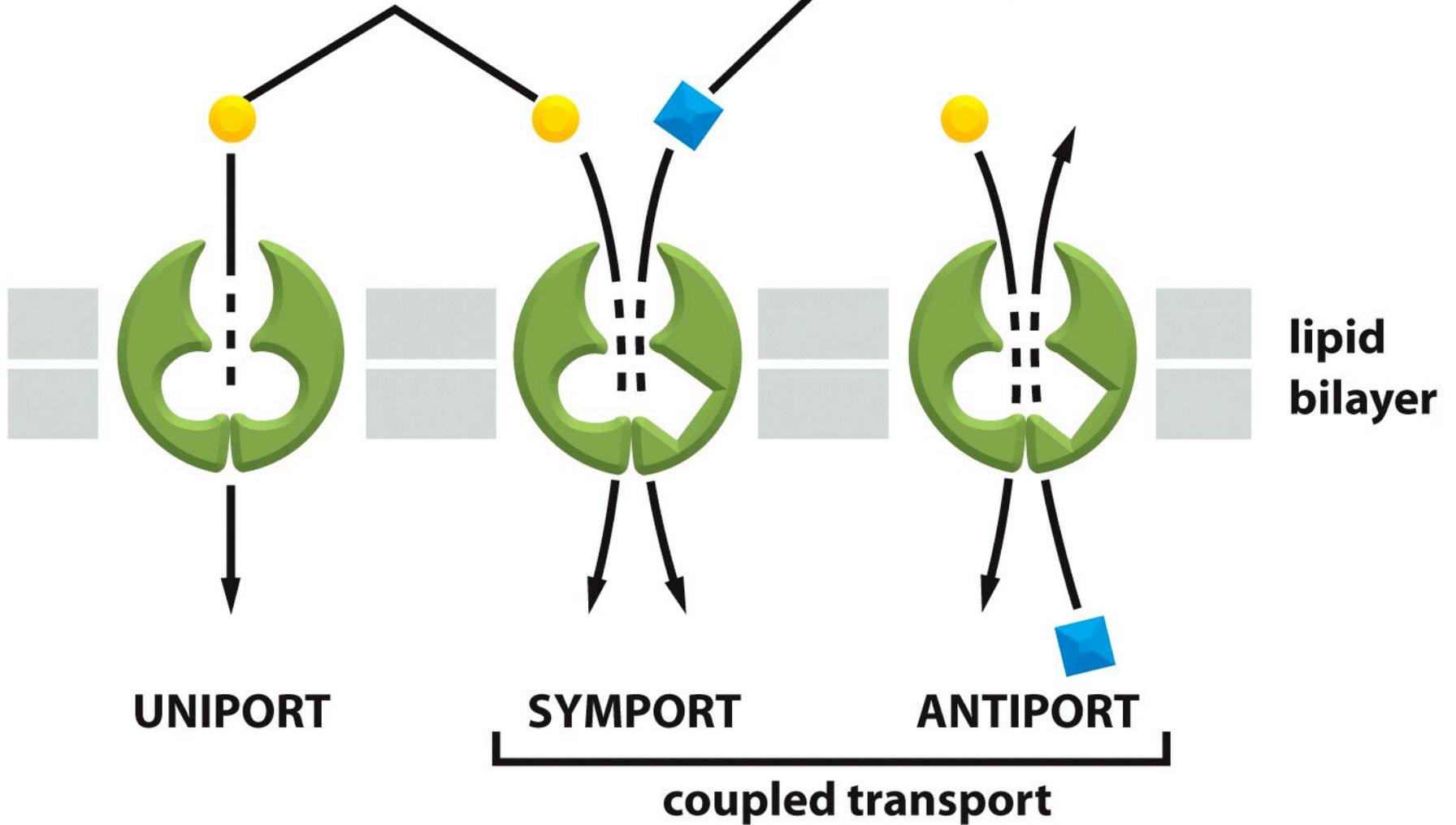
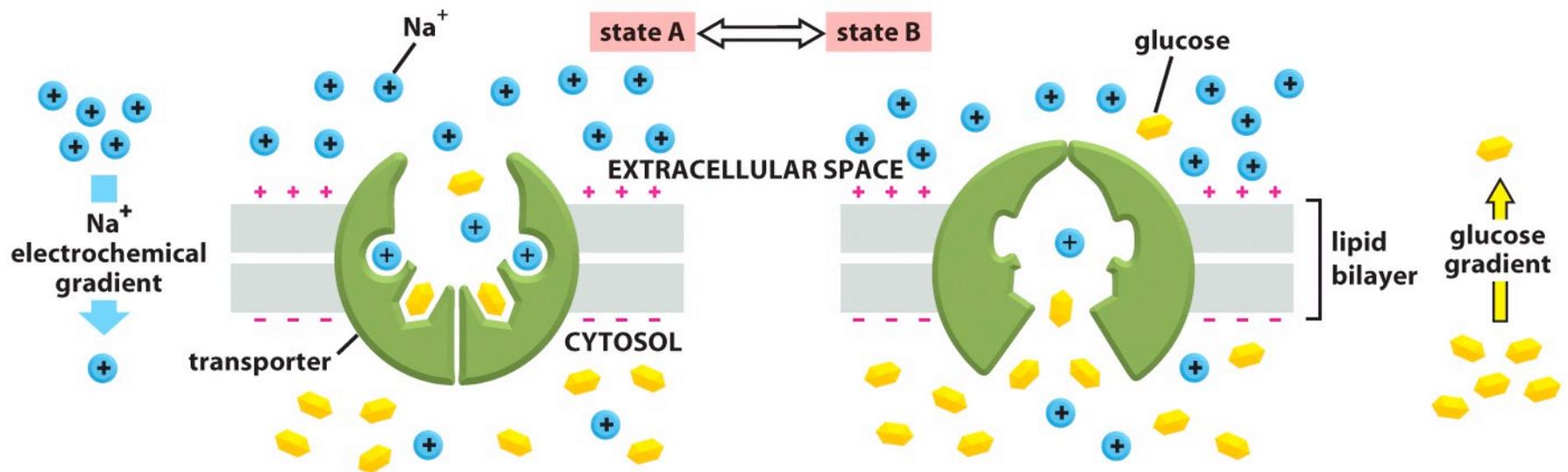


Figure 11-8 *Molecular Biology of the Cell* (© Garland Science 2008)



Glucosa viaja en contra de su gradiente de concentración gracias a la existencia de un gradiente de Na<sup>+</sup>

Es un: simporte (transporte acoplado)

# Transporte Transcelular

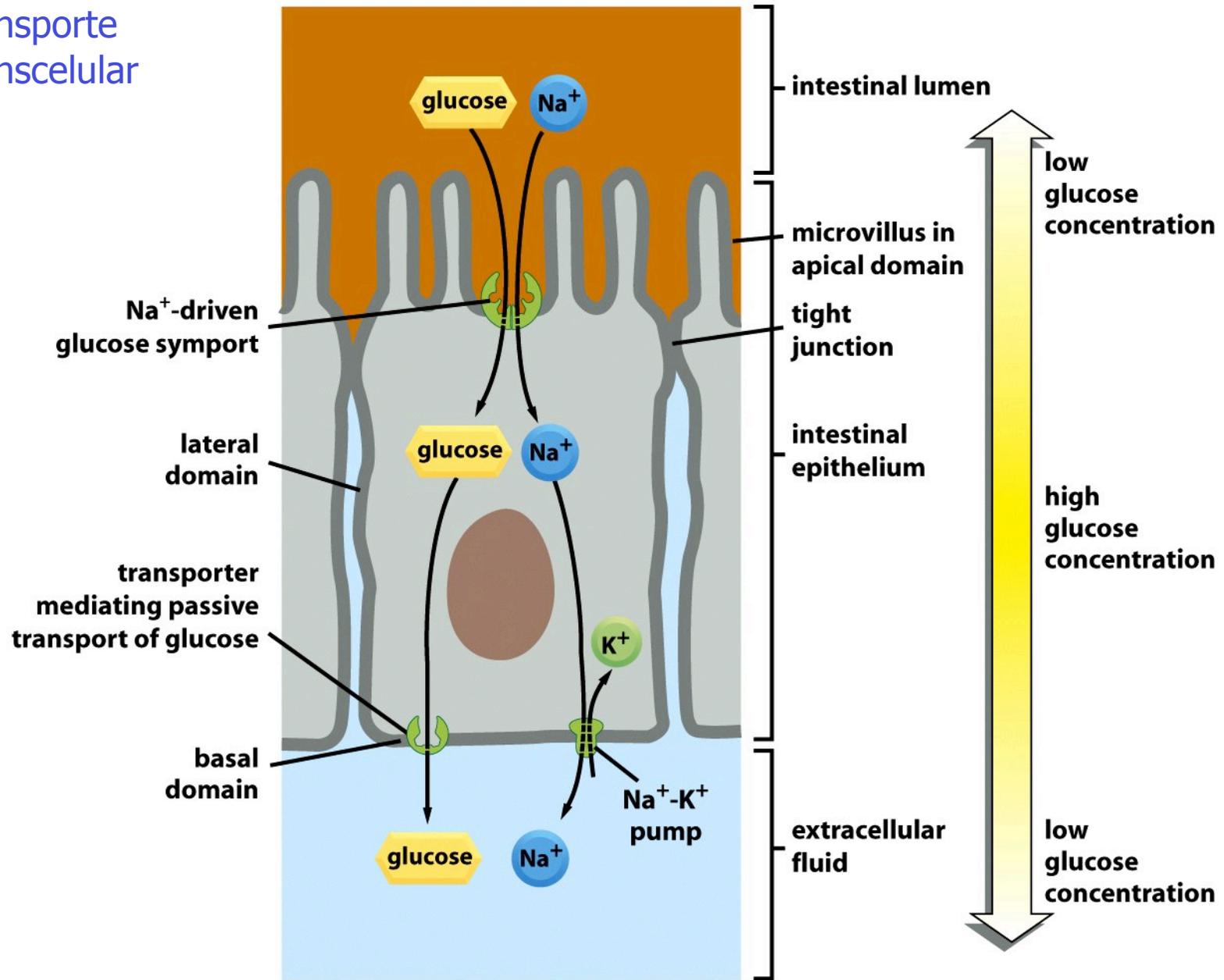
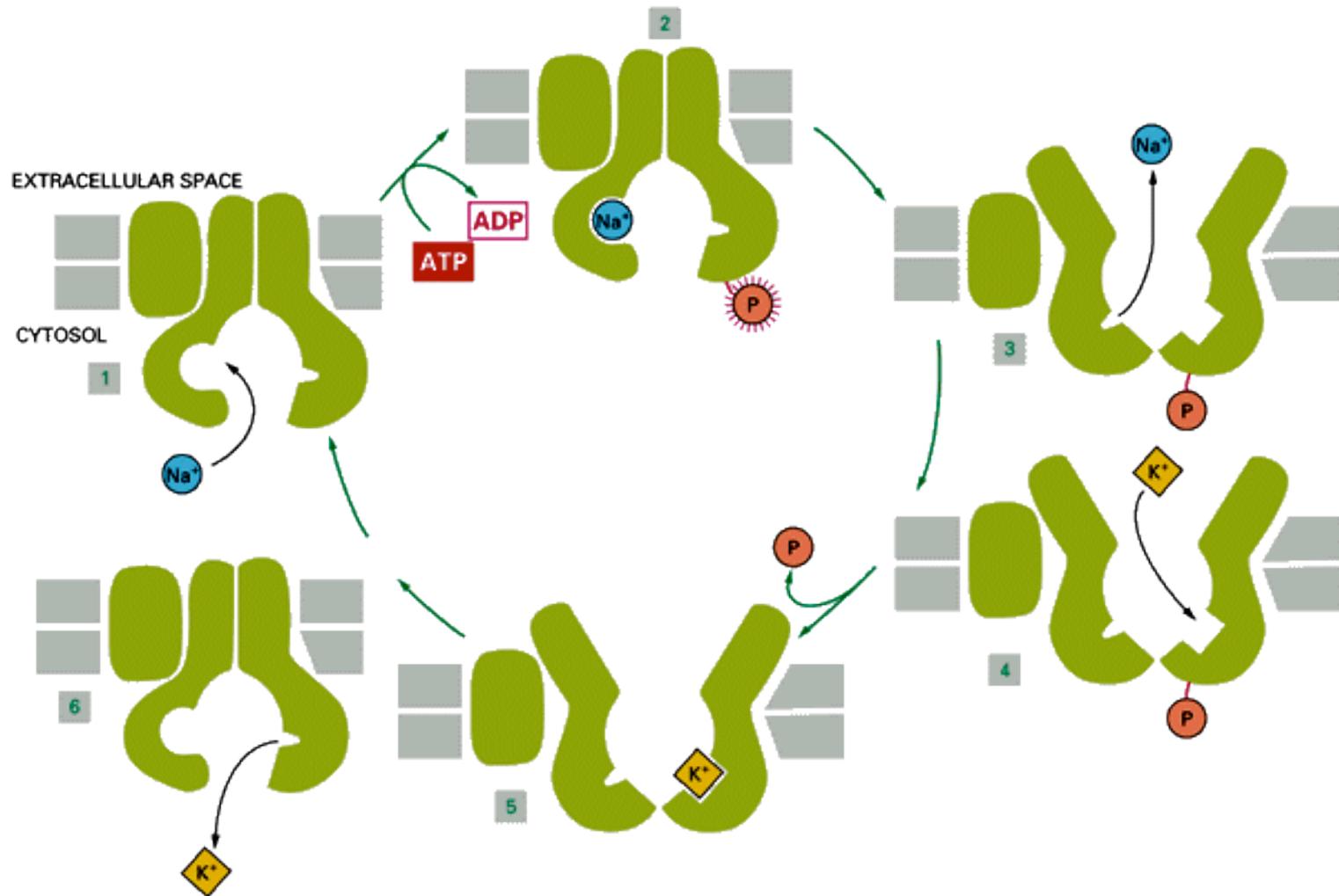


Figure 11-11 *Molecular Biology of the Cell* (© Garland Science 2008)

Transporte Activo: Bomba Sodio – Potasio ATPasa (presente en casi todas las células animales)  
Antiporter (tres Na<sup>+</sup> al exterior celular, dos K<sup>+</sup> al interior celular)



Hay más potasio en el interior celular  
Hay más sodio en el exterior celular

Canal Iónico: Fluctúa entre los estados abiertos y cerrados.

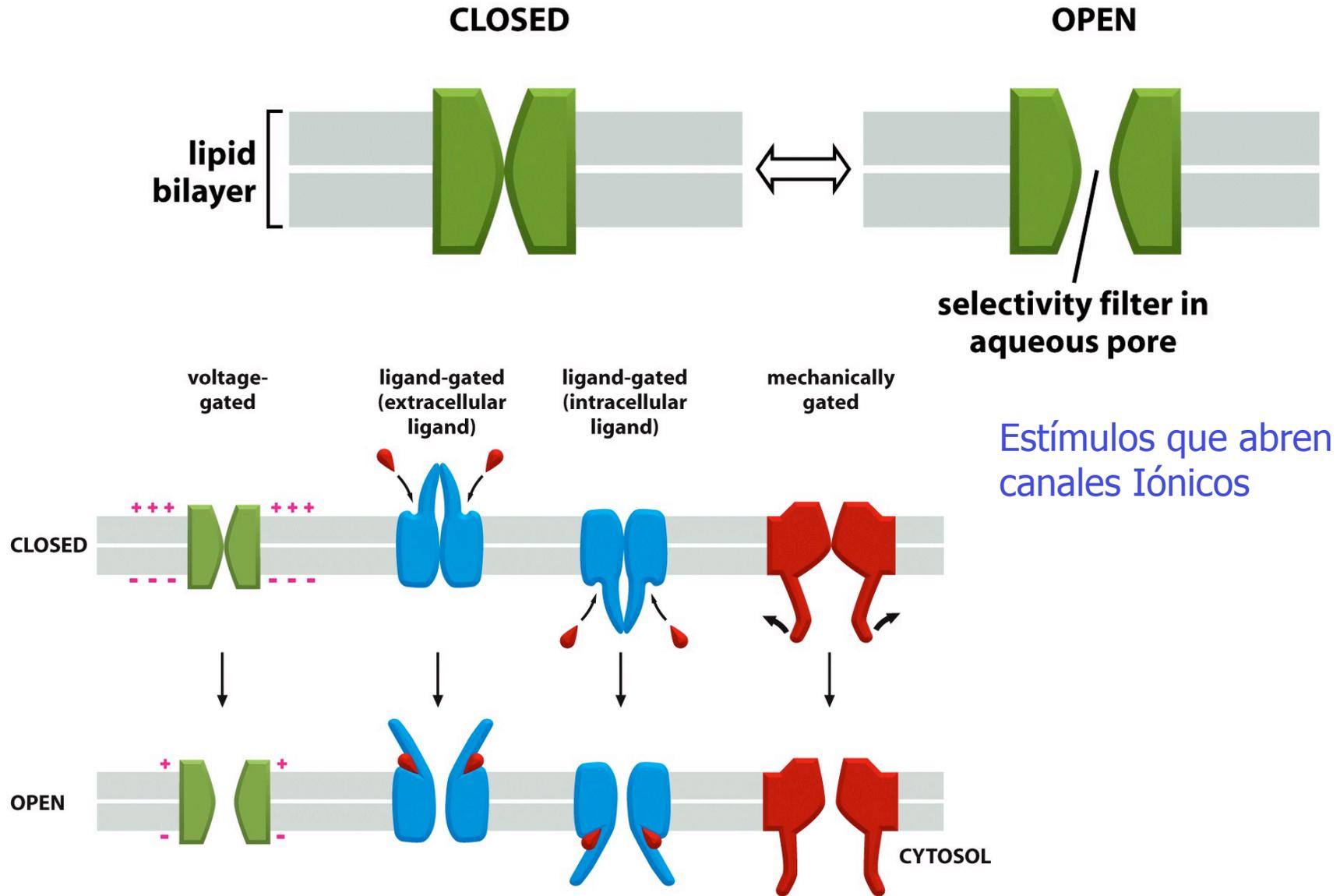


Figure 11-20 *Molecular Biology of the Cell* (© Garland Science 2008)

# Transmisión del Impulso Nervioso mediado por Canales Iónicos

## Neuronas

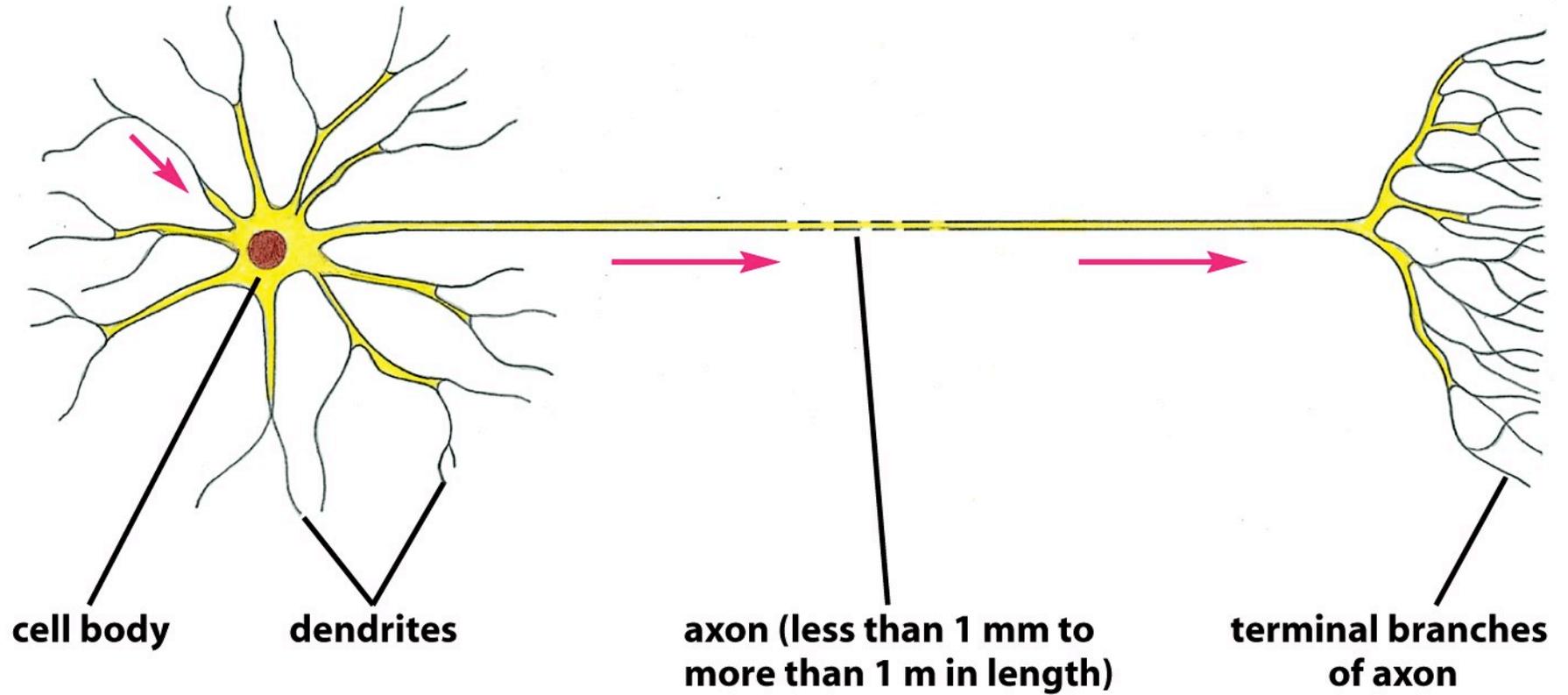


Figure 11-28 *Molecular Biology of the Cell* (© Garland Science 2008)

## INSTRUCCIONES.

-Repase la clase

-Investigue y explique los siguientes conceptos: Modelo del mosaico fluido; hidropatía; osmosis; difusión simple; diferencia de potencial eléctrico (voltaje); tallo de GPI (glicosil-fosfatidil-inositol).

-Haga un esquema y explique:

a) el funcionamiento de la bomba  $\text{Na}^+/\text{K}^+-\text{ATPasa}$ ;

b) el paso de glucosa desde el lumen intestinal a la sangre

-Lea el artículo: [http://en.wikipedia.org/wiki/Lipid\\_bilayer](http://en.wikipedia.org/wiki/Lipid_bilayer)

-Disfrute y aprenda