LS-1101-2022

Lipids and Membranes

Introduction

- **Lipids are hydrophobic, nonpolar molelcules.**
  - **They are soluble in nonpolar solvent.**
  - **They are insoluble in polar solvents, such as water**
- **They are isolated from the other biological molecules by extracting them with nonpolar solvents.**

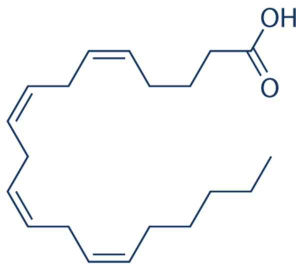
Introduction

The types of lipids

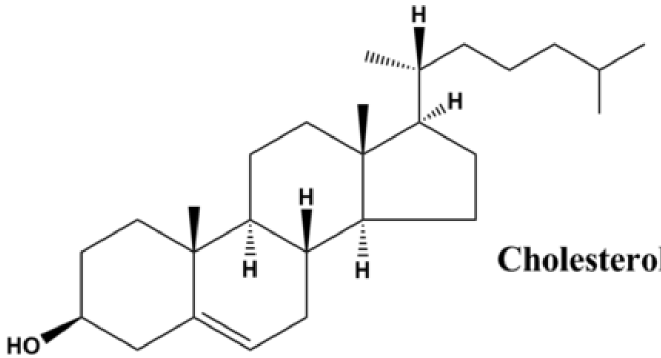
- Fatty Acids
  - In the carboxylic acid family
- Waxes
  - Fatty Acids + Alcohols
- Triglycerides
  - 3 Fatty acids + glycerol
- Phospholipids and glycolipids
  - 2 fatty acids + glycerol + phosphate + X
- Steroids
  - Derivatives of cholesterol
- Eicosanoids
  - Derivatives of the Fatty acid arachidonic acid

Membranes

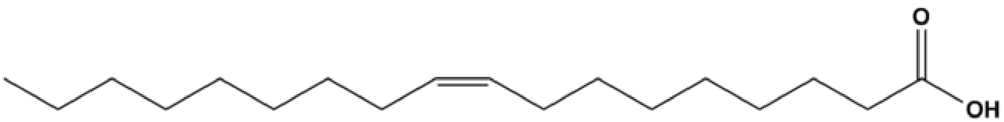
- Formed from phospholipids and glycolipids



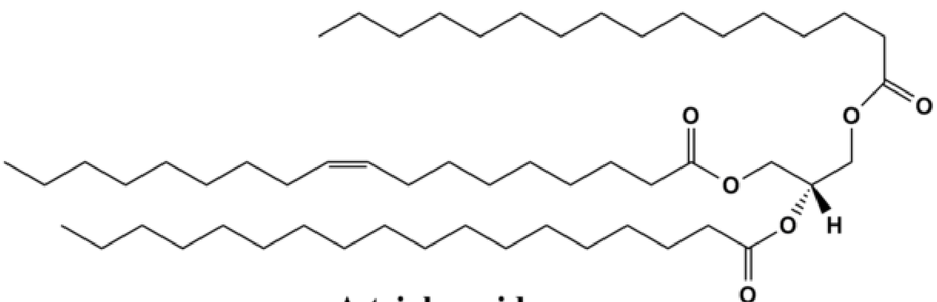
Lipids



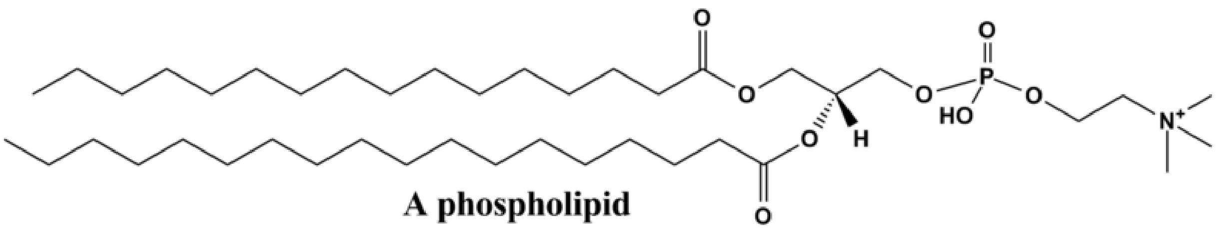
Cholesterol



A free fatty acid



A triglyceride



A phospholipid

Functions

Energy storage

Membrane structure

Membrane transport

Cell Signaling

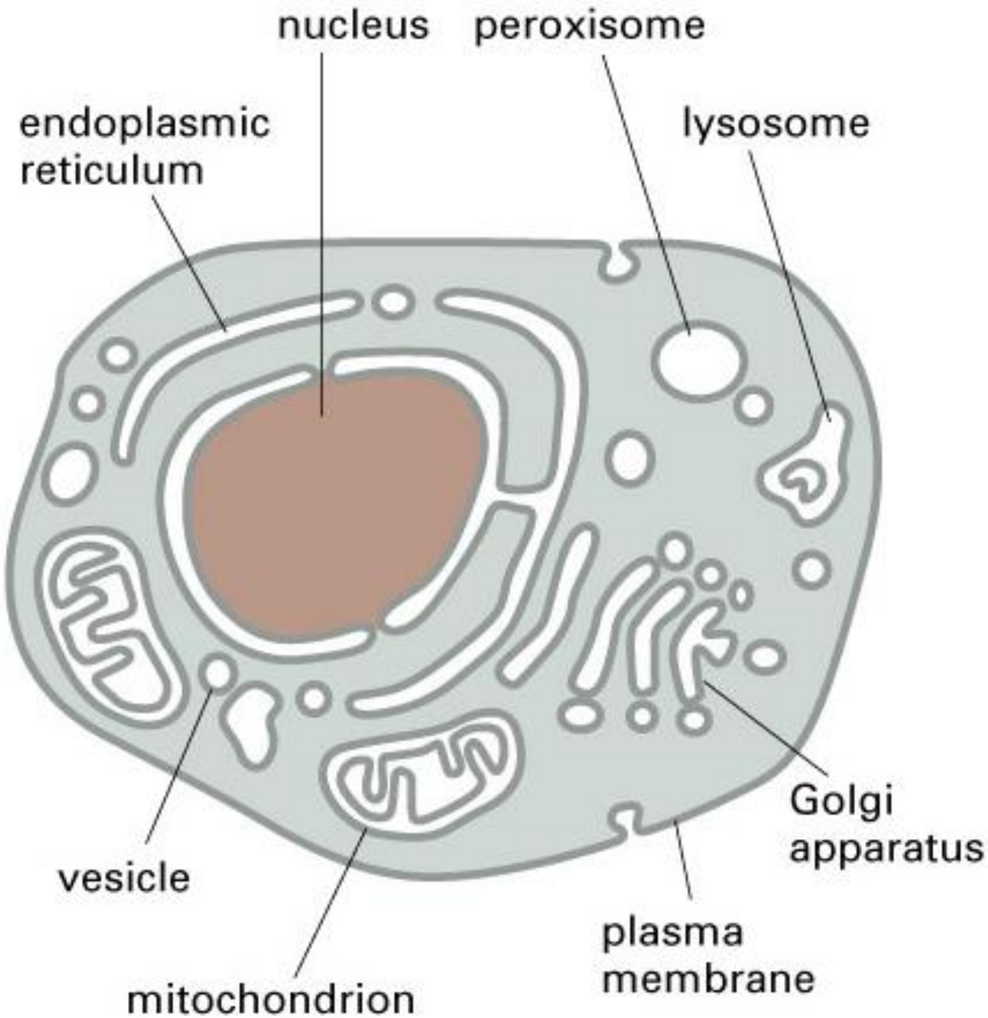
Any other function?

[Fats give more energy when broken down]()

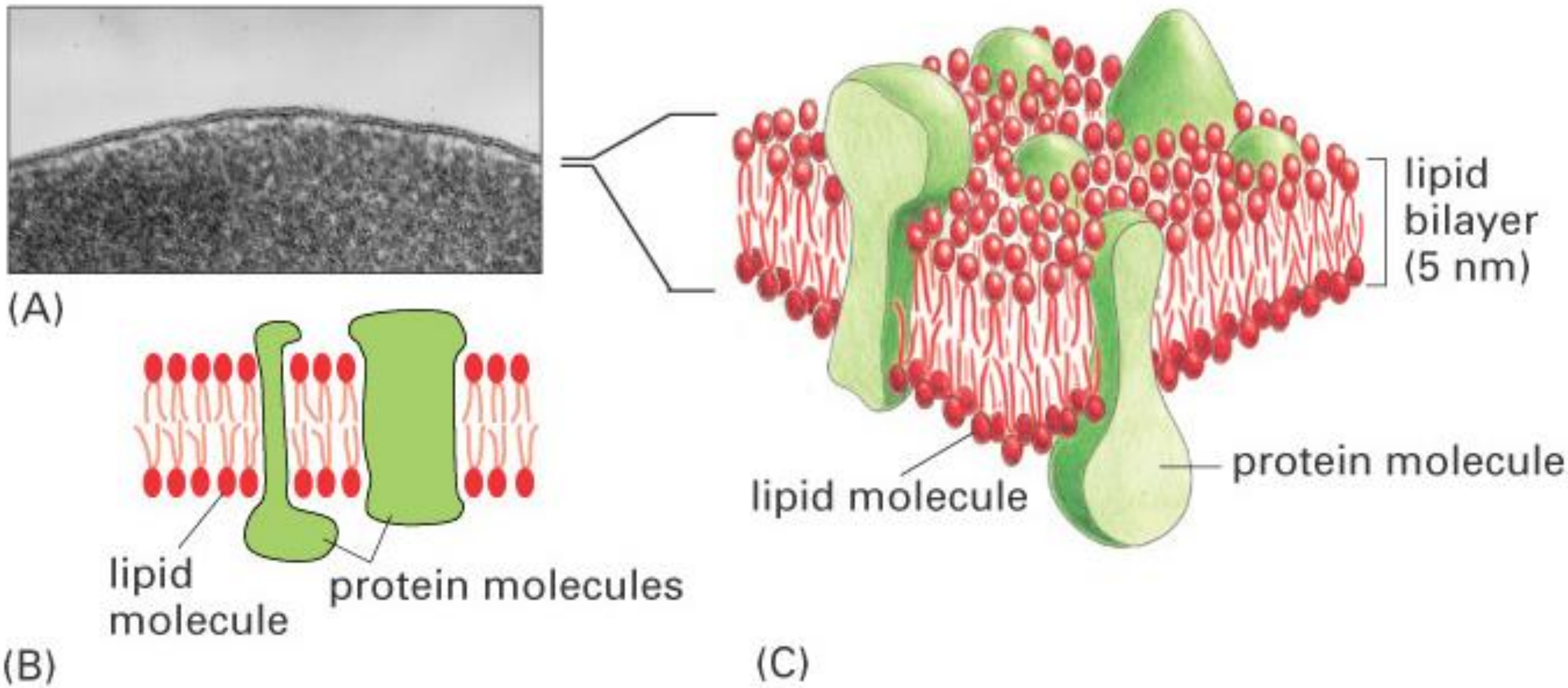
[Fats can be store in less space than glucose]()

[Fats need less water to be stored]()

Membranes form many compartments in the cell

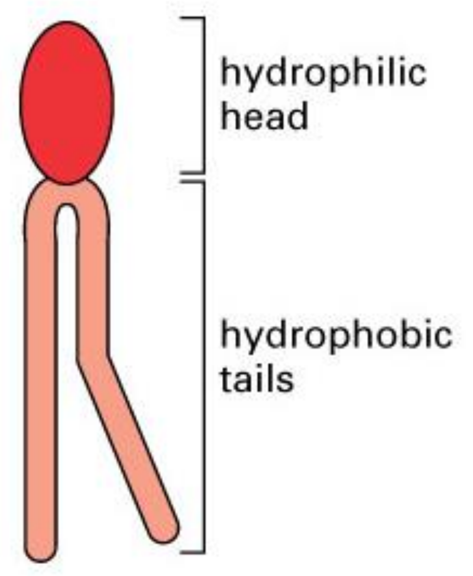


Biological membranes are composed of a lipid bilayer

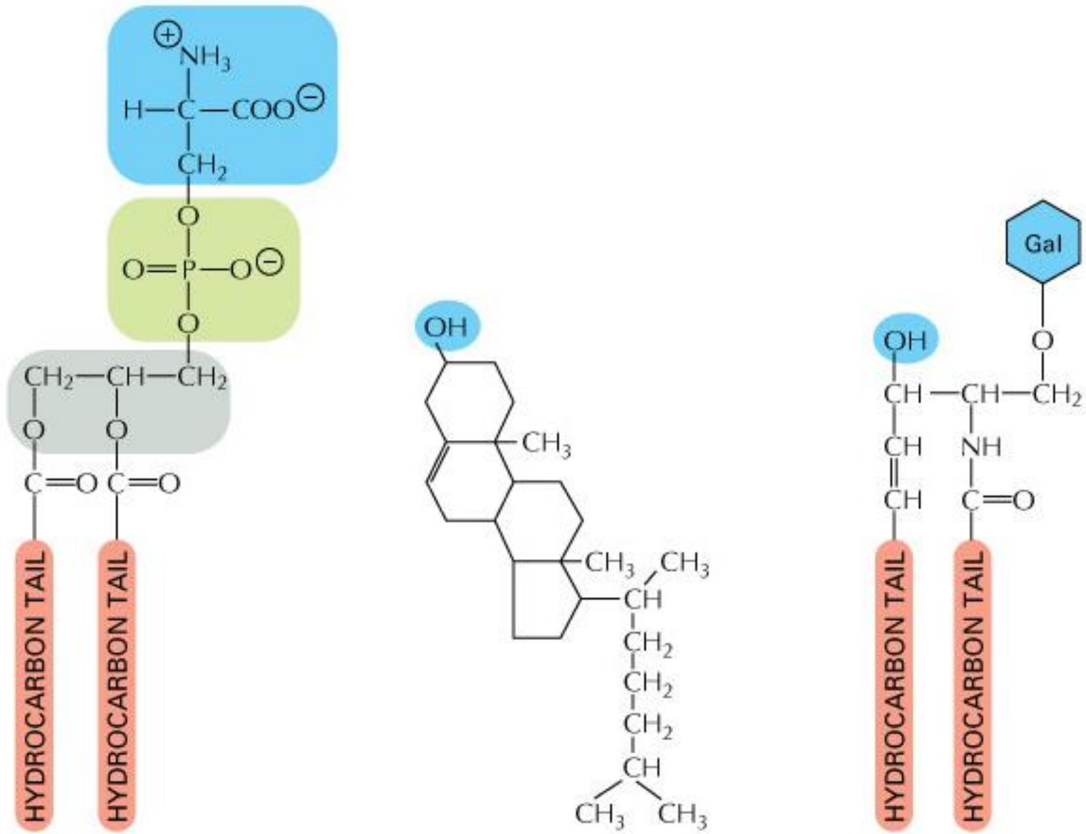


Membrane lipids are amphipathic molecules

- Membrane lipids are <u>amphipathic</u>
- Hydrophilic heads (polar) form hydrogen bonds with water
- Hydrophobic tails (non-polar) are excluded by water molecules

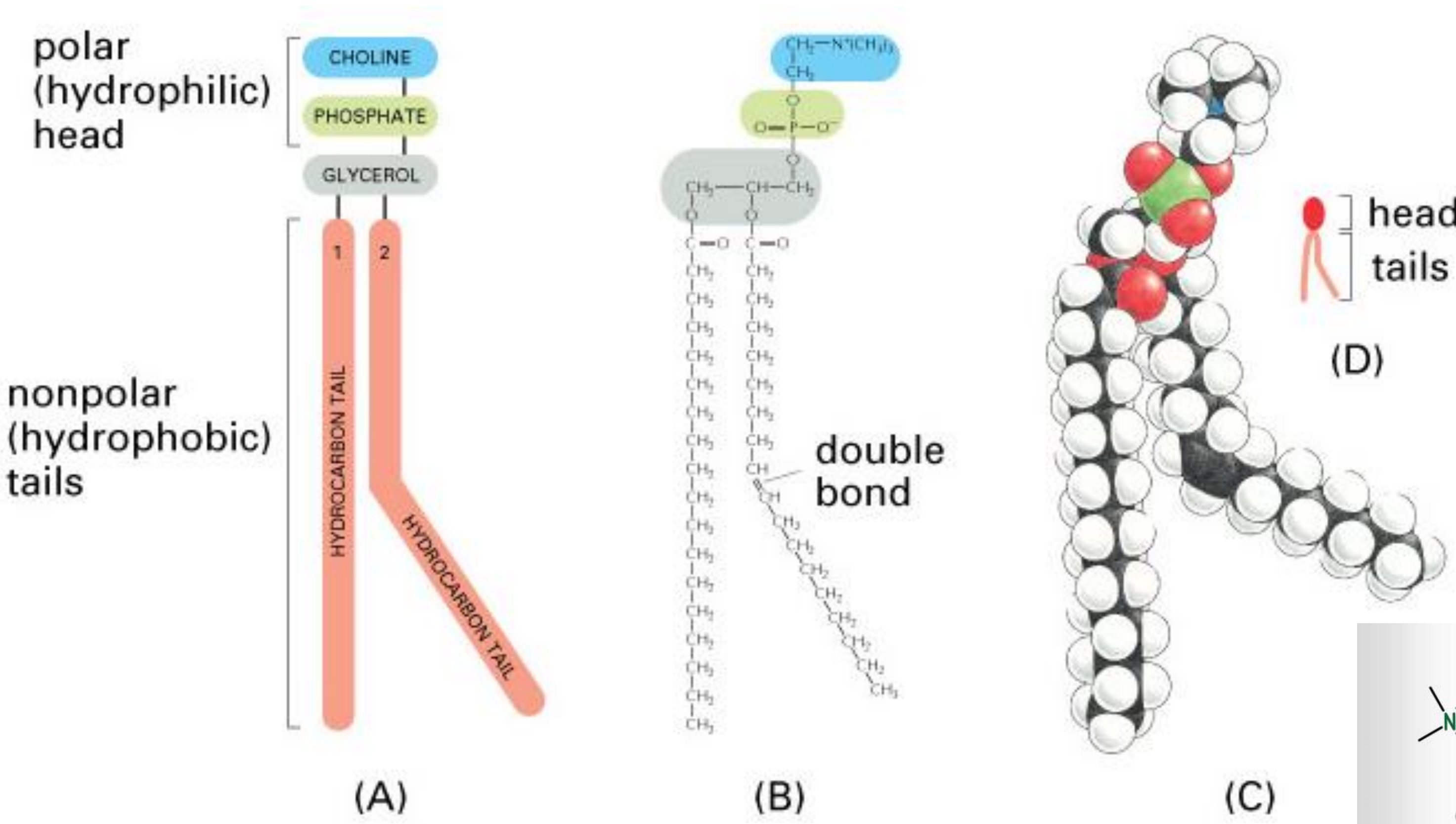


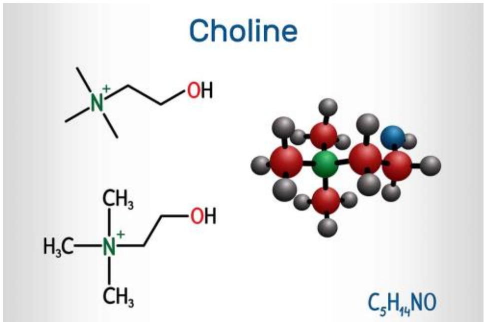
Three classes of membrane lipids



phosphatidylserine (phospholipid) | cholesterol (sterol) | galactocerebroside (glycolipid)

Membrane lipids





Phosphatidylcholine is the most abundant phospholipid in cell membranes

Packing arrangements of lipid molecules in an aqueous environment

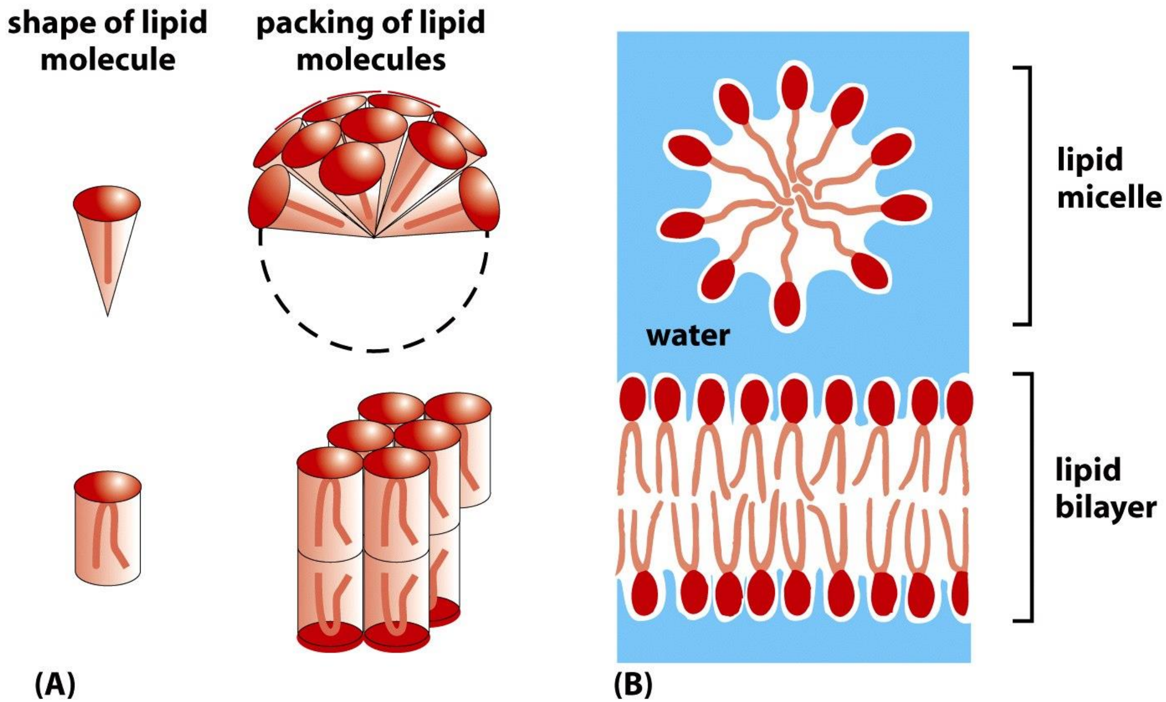


Figure 10-7 Molecular Biology of the Cell 5/e (© Garland Science 2008)

Cone-shaped lipid molecules for micelles, cylinder-shaped lipids form bilayers

Phospholipid bilayers spontaneously close to form a sealed compartment

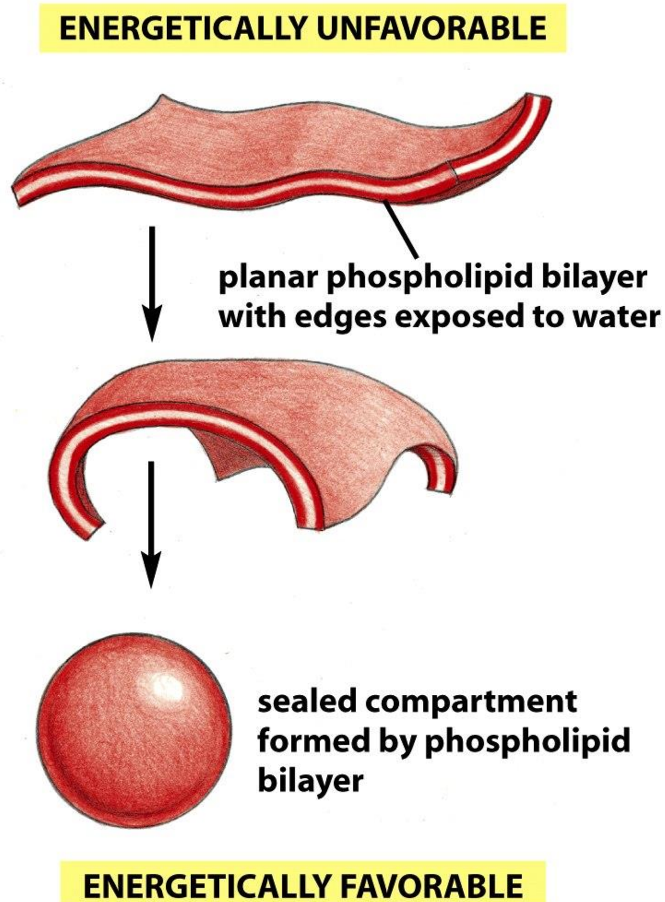
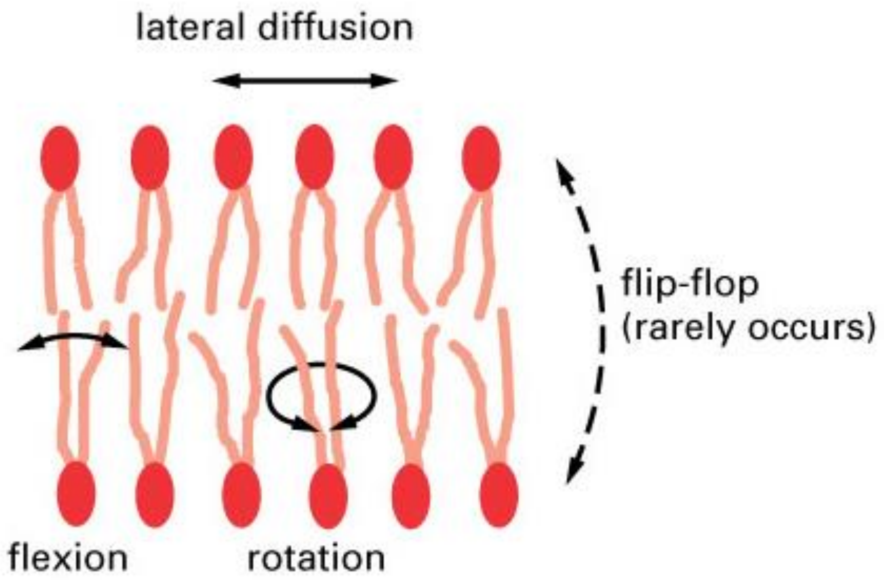


Figure 10-8 Molecular Biology of the Cell 5/e (© Garland Science 2008)

The membrane bilayer is a fluid



•Lateral diffusion occurs rapidly within the plane of the membrane

•Individual phospholipids may rotate axially

•Flip-flopping from one side to the other is very rare as it is energetically unfavorable

The membrane bilayer is a fluid

Fluorescence Recovery After Photo-bleaching (FRAP)

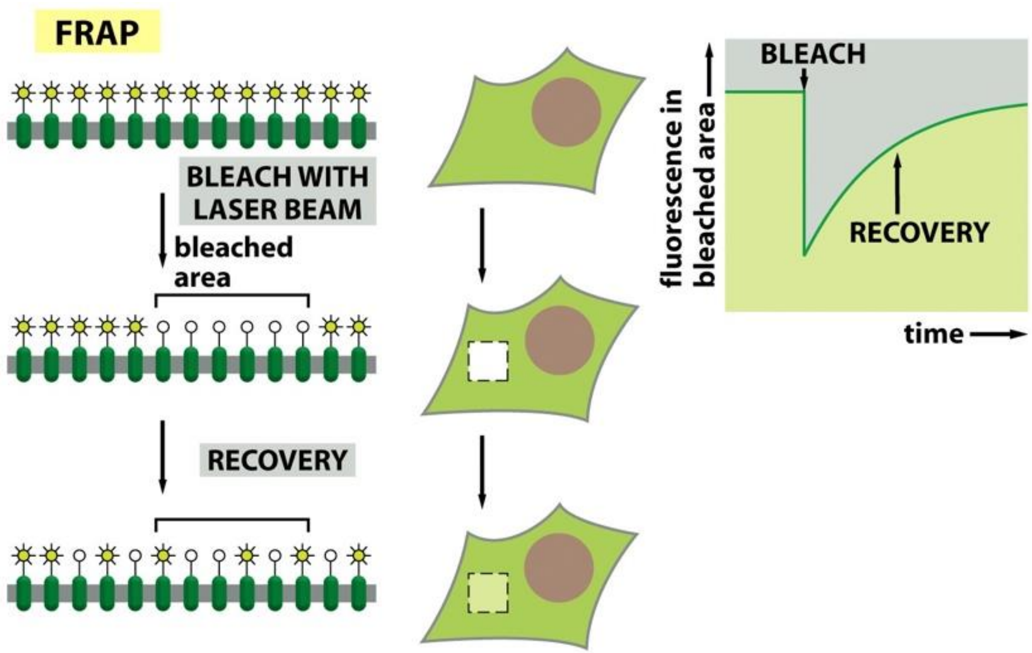
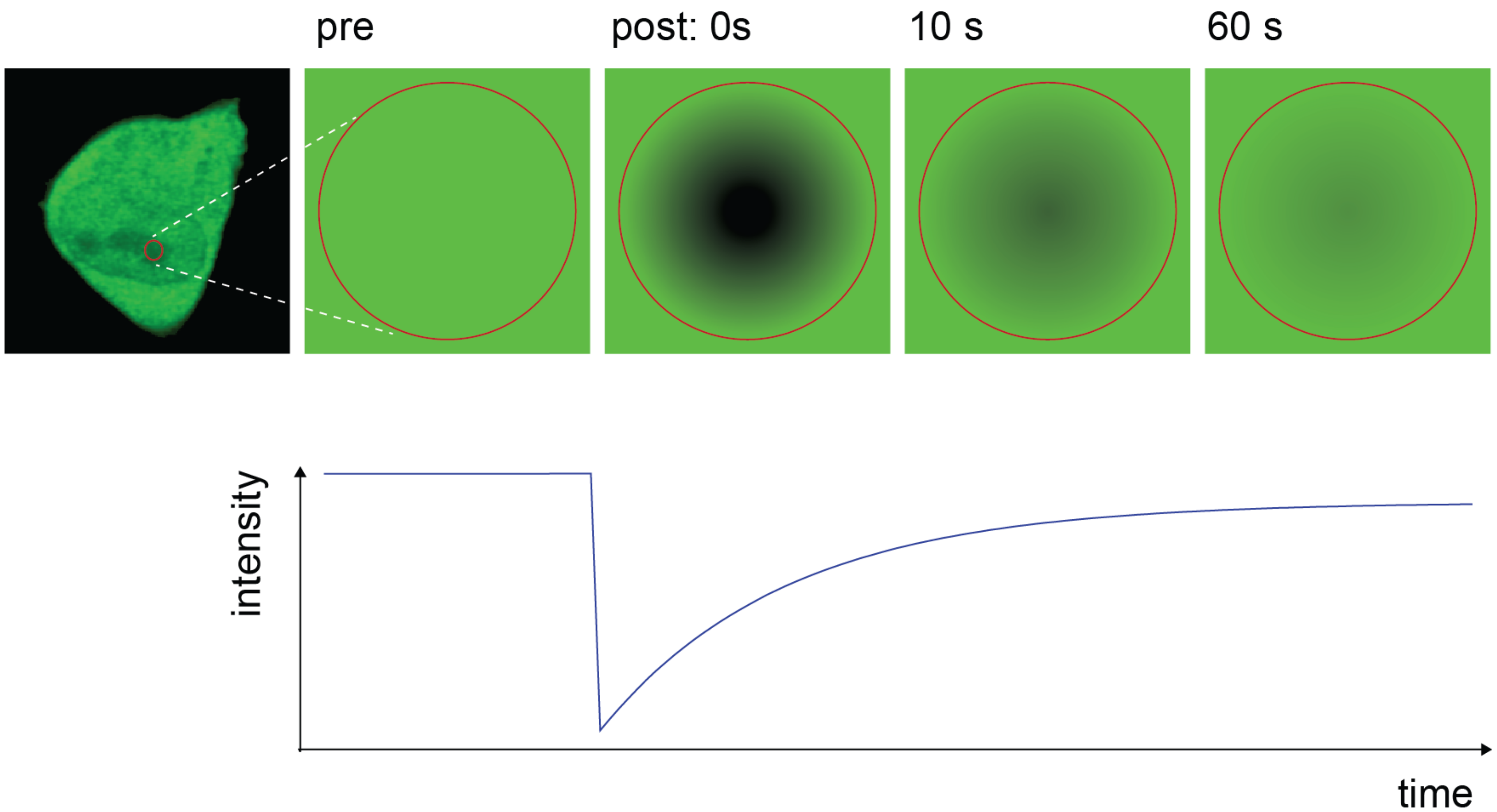


Figure 10-36a Molecular Biology of the Cell 5/e (© Garland Science 2008)

1. A fluorescent probe is used to label membrane proteins
2. The probe is destroyed in a small region using intense laser light
3. Fluorescence microscopy is used to observe behavior of the unbleached probe

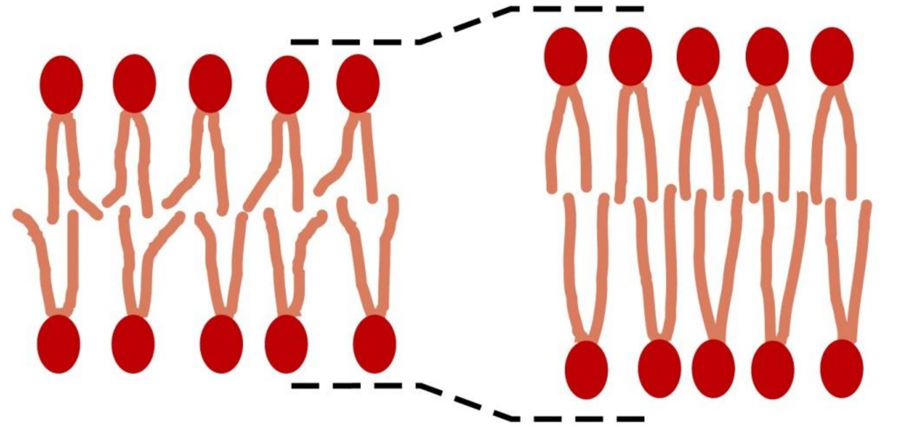


Who controls the membrane fluidity?

The composition of a membrane regulates the degree of its fluidity

- Membrane lipids with fatty acyl side chains that are saturated (no double bonds) pack tightly in the membrane and make it less fluid

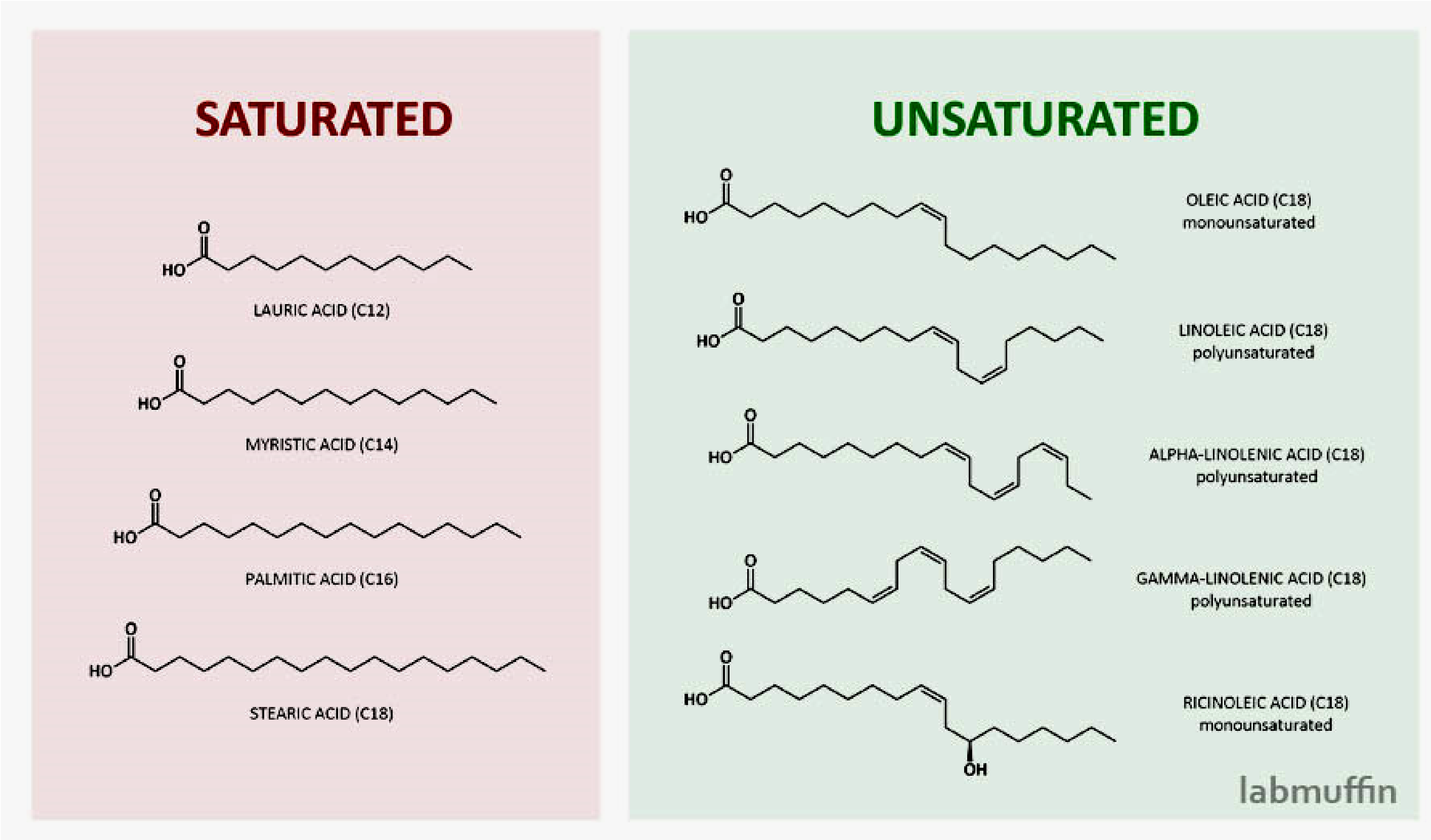
- Lipids that are unsaturated (1, 2, or 3 double bonds) pack loosely and make it more fluid

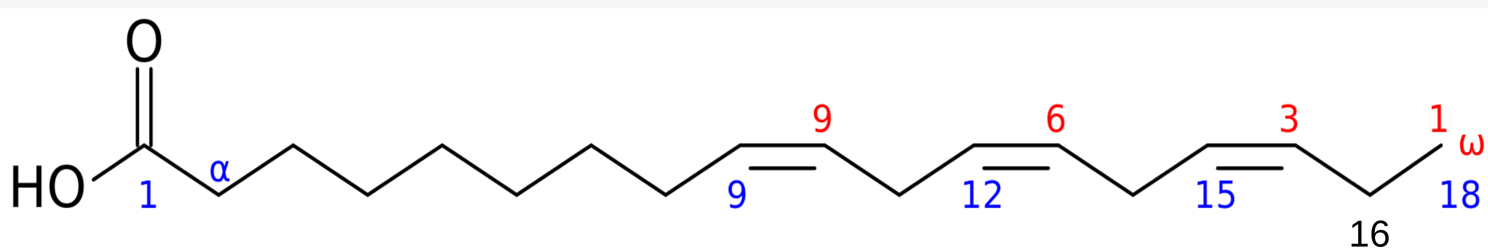


unsaturated hydrocarbon chains with *cis*-double bonds

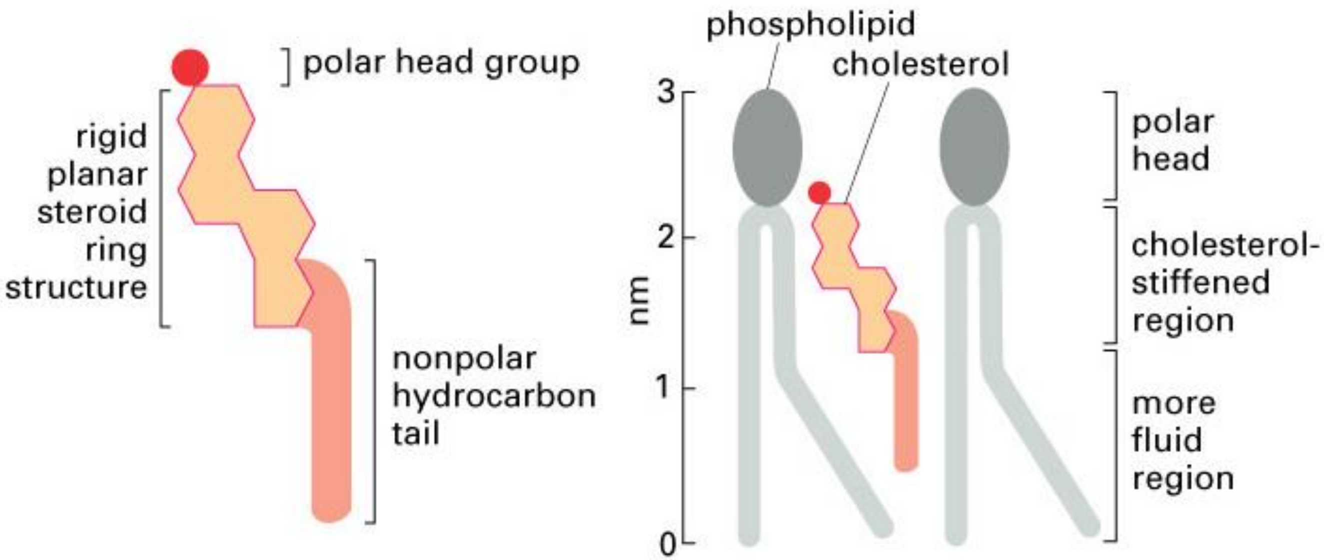
saturated hydrocarbon chains

Figure 10-12 Molecular Biology of the Cell 5/e (© Garland Science 2008)


SATURATED
LAURIC ACID (C12)
MYRISTIC ACID (C14)
PALMITIC ACID (C16)
STEARIC ACID (C18)
UNSATURATED
OLEIC ACID (C18)
monounsaturated
LINOLEIC ACID (C18)
polyunsaturated
ALPHA-LINOLENIC ACID (C18)
polyunsaturated
GAMMA-LINOLENIC ACID (C18)
polyunsaturated
RICINOLEIC ACID (C18)
monounsaturated
labmuffin

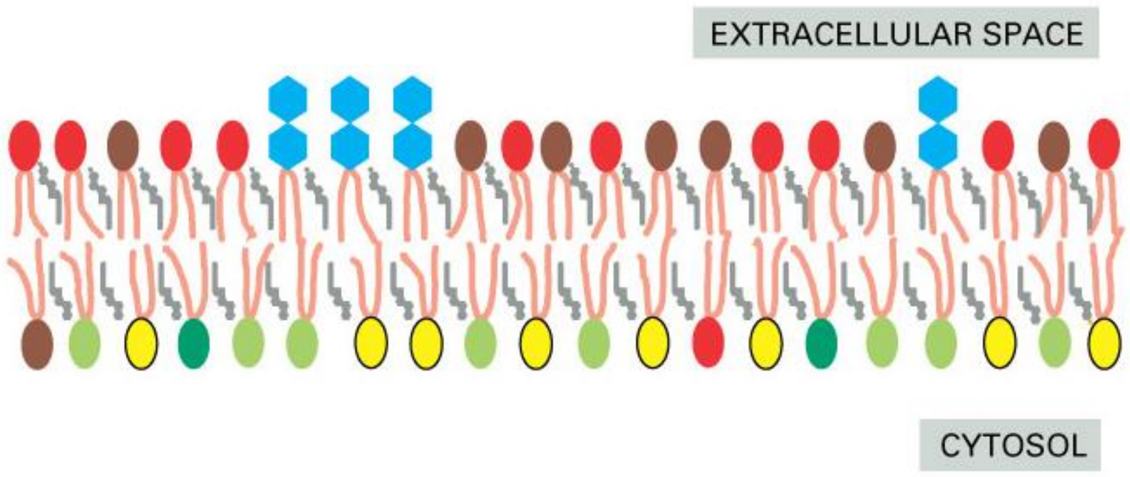

α
1
9
12
15
16
18
9
6
3
1
ω

The composition of a membrane regulates the degree of its fluidity



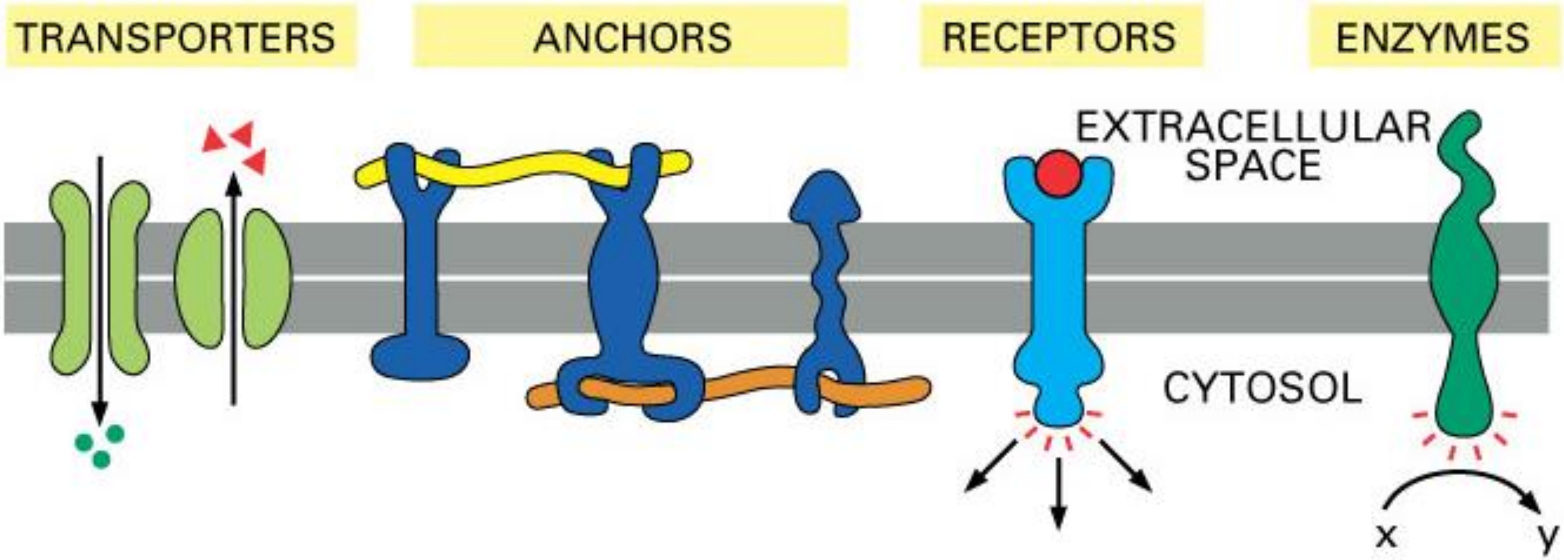
The presence of cholesterol in the membrane stiffens the bilayer making it more rigid

Cellular membranes are asymmetric



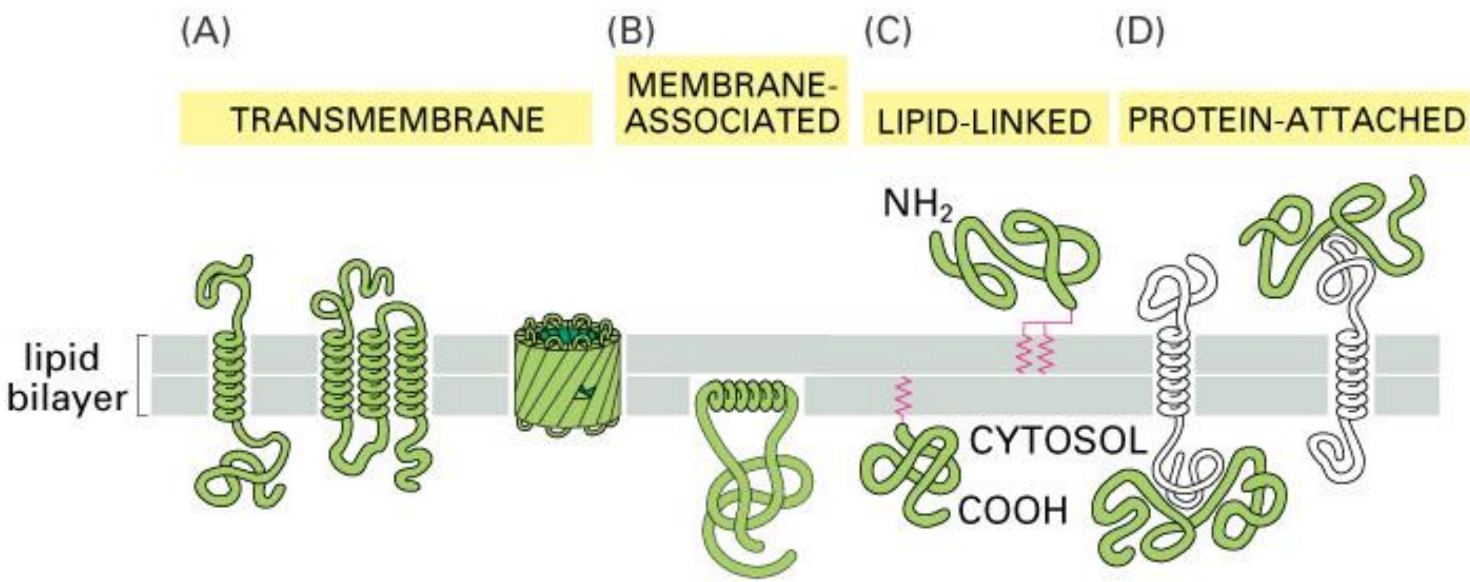
1. All lipids are synthesized on the cytosolic surface of the ER
2. Lipids in the outer leaflets are transported there by flippases
3. Continuity between organelle lumen & extracellular space

Membrane proteins



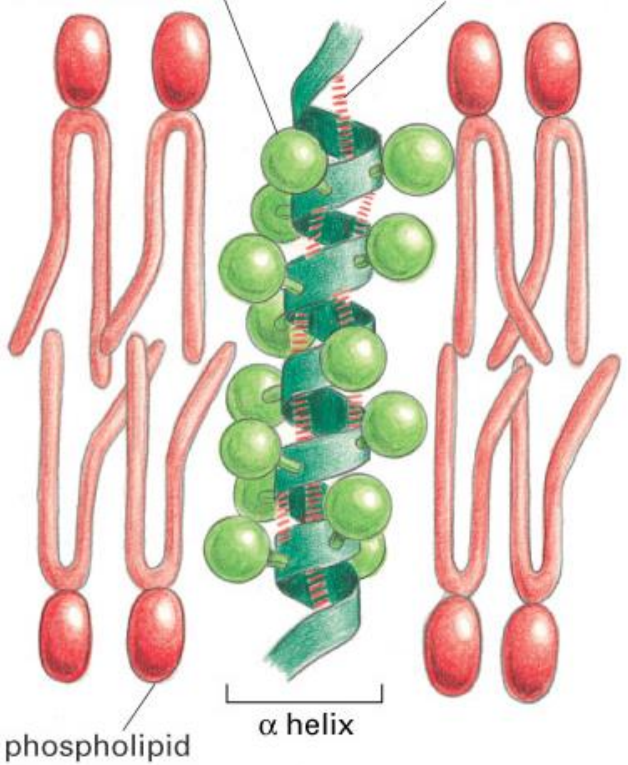
- Proteins compose ~50% of the membrane
- Membrane proteins perform many functions

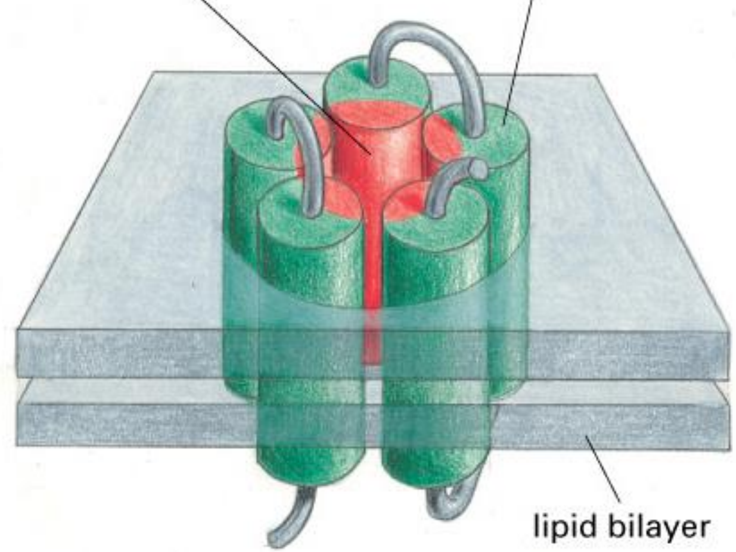
Membrane proteins associate with the bilayer in different ways



- Transmembrane proteins span the bilayer
- Peripheral membrane proteins associate with one side

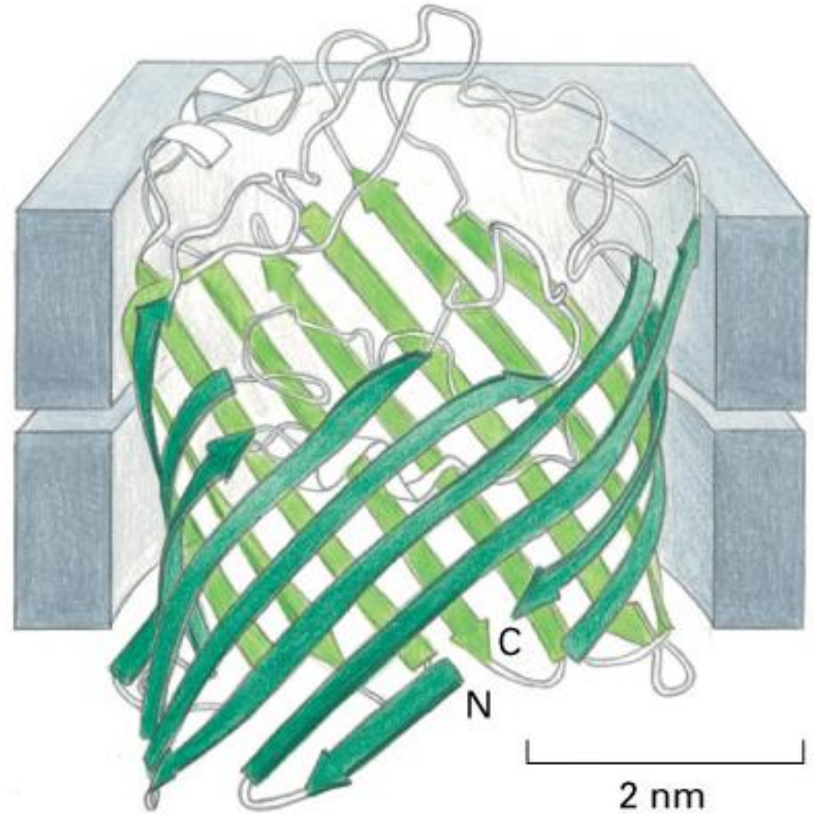
Transmembrane proteins usually span the bilayer using alpha-helices

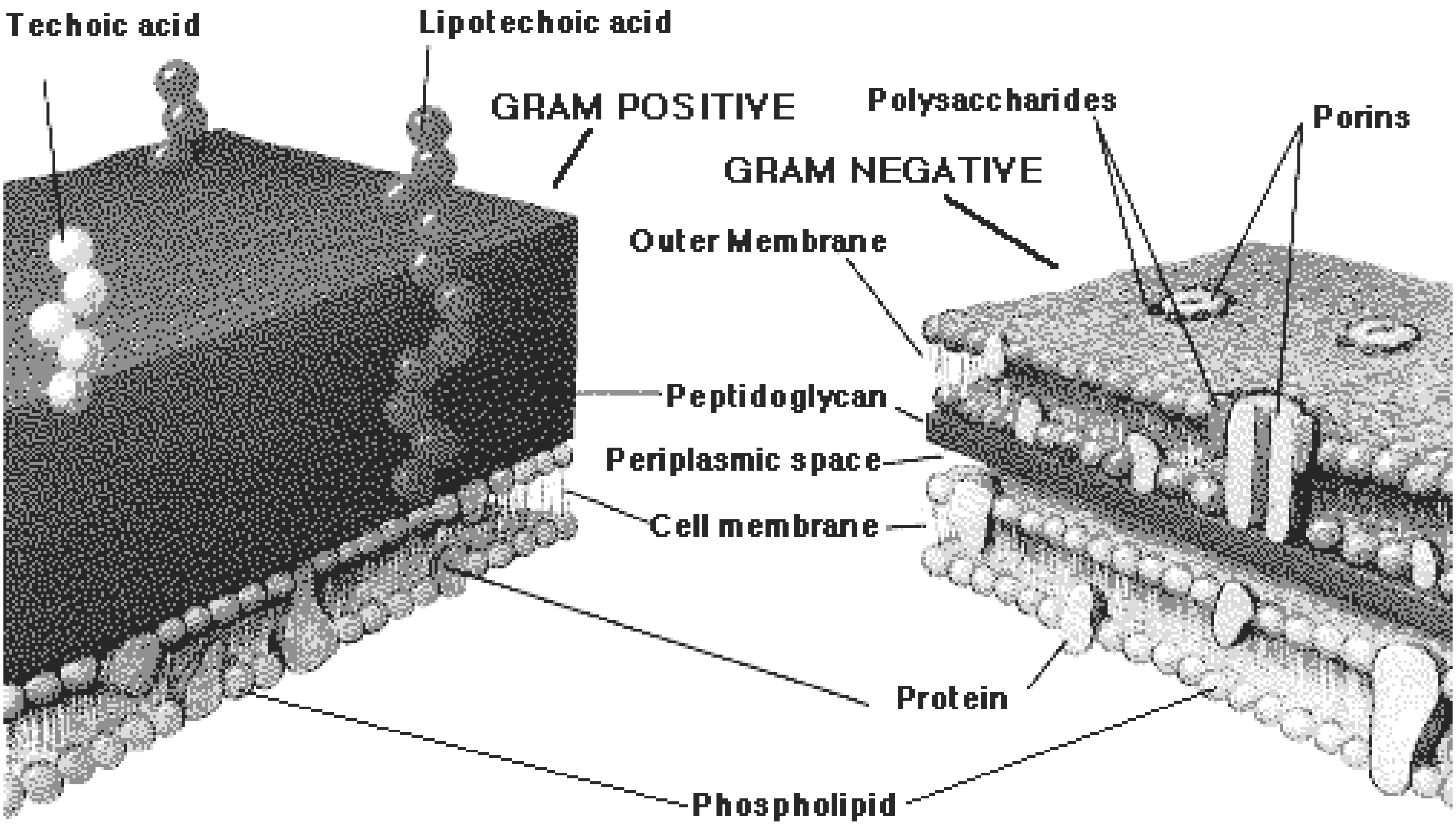




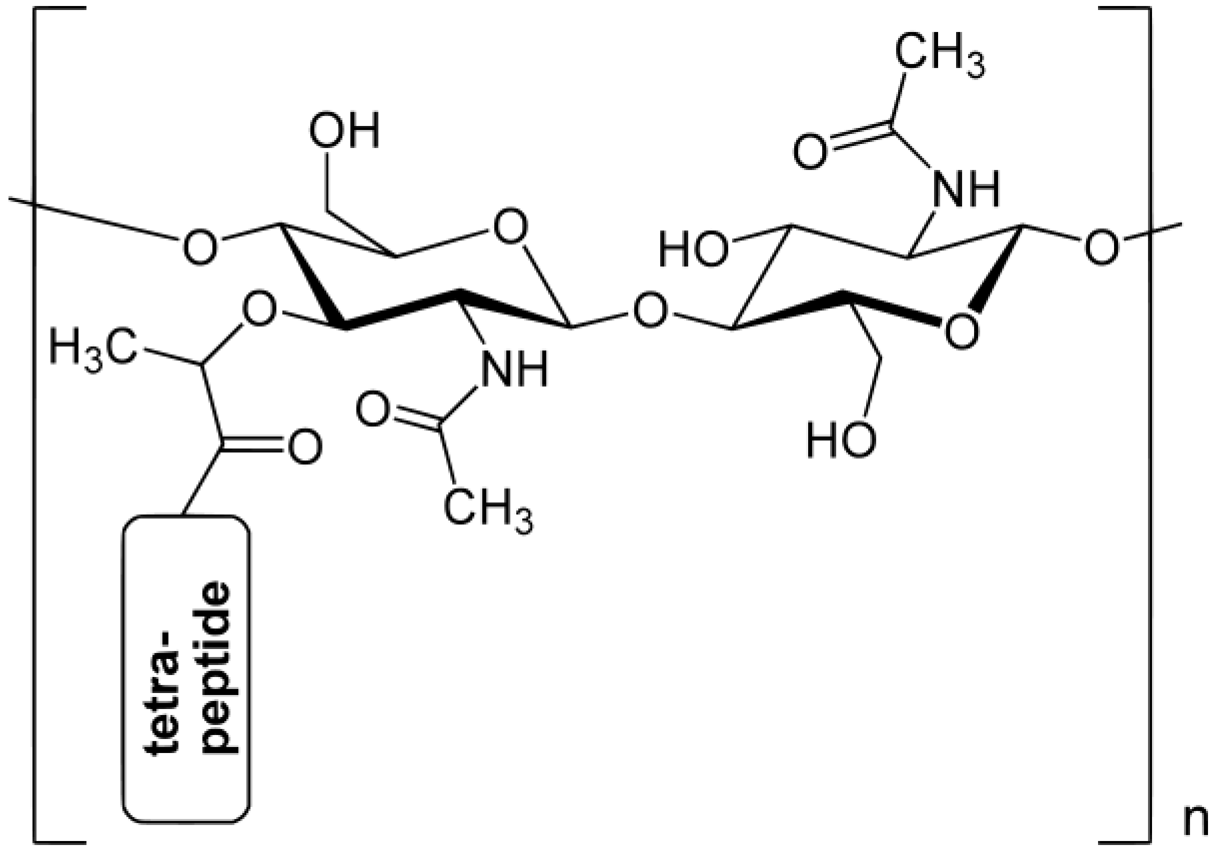
Some membrane proteins use beta-sheets to cross the bilayer

- Beta-sheets arranged in this cylindrical conformation are known as a “beta-barell”
- Hydrophilic amino acid residues face towards the pore, hydrophobics face the bilayer





Bacterial cell surface

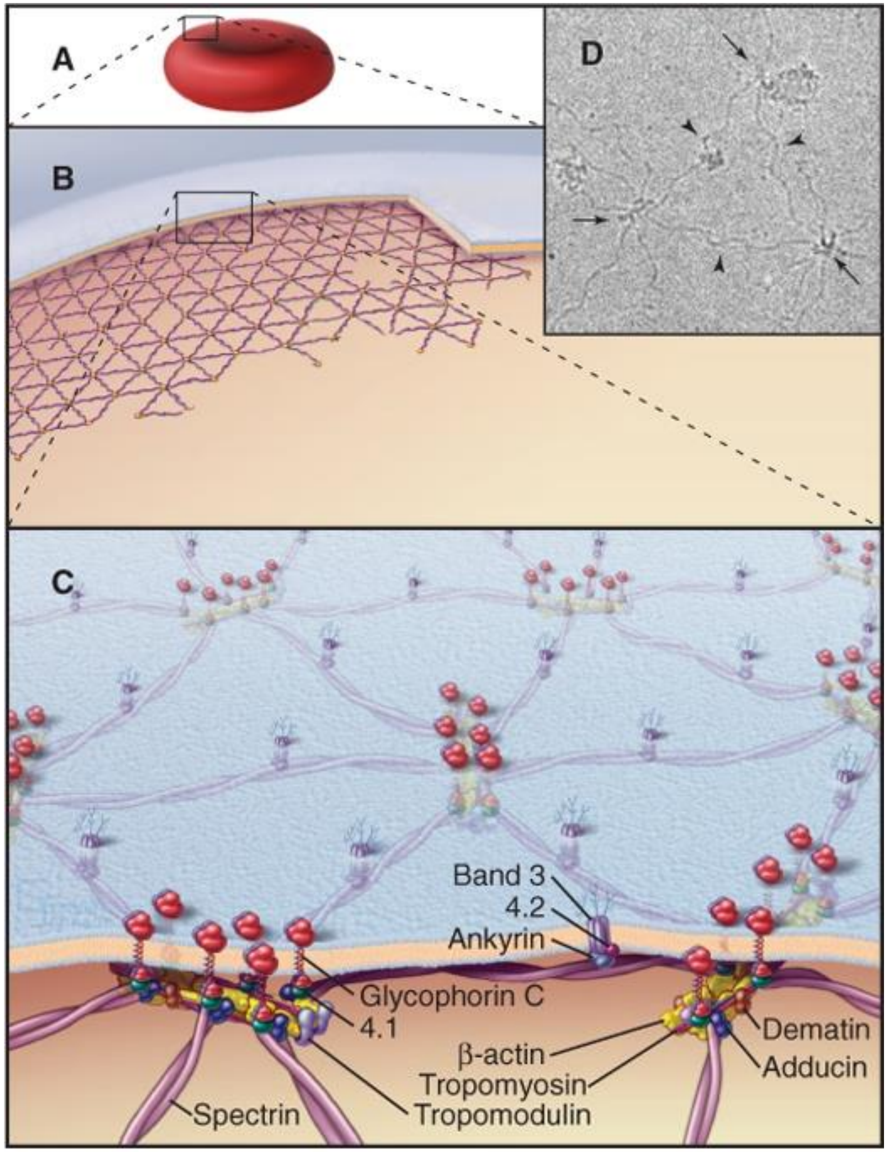


Peptidoglycan

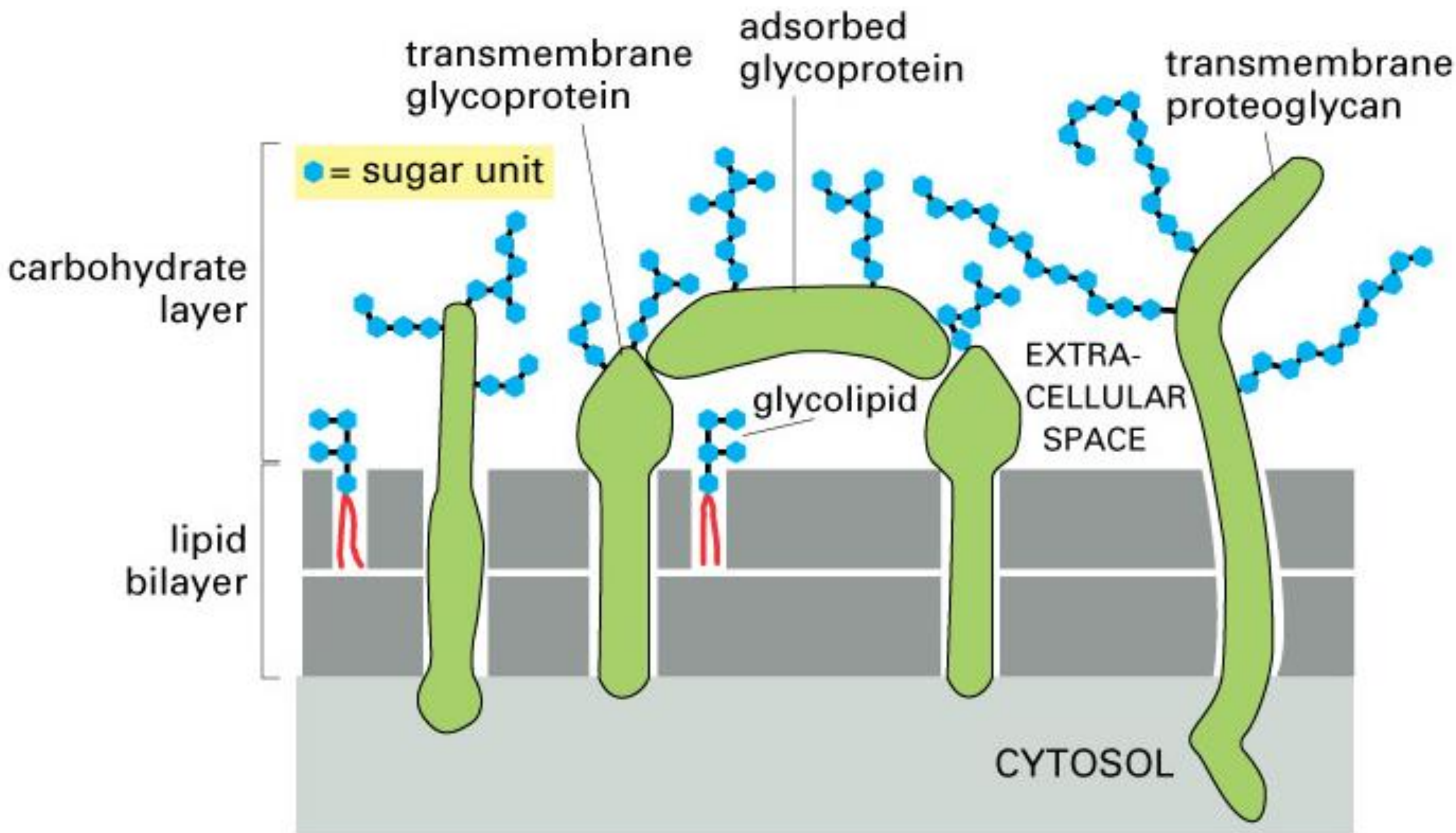
The cytoplasmic side of the membrane is called the cell cortex

- Meshwork of transmembrane proteins and filaments (spectrin)

- Mechanical support for the membrane and cell shape



The extracellular surface of the membrane is coated with carbohydrate



Extracellular glycoproteins perform numerous functions

- Carbohydrate layer protects cells from chemical and mechanical damage
- Different cell types present different combinations of glycoproteins and proteoglycan on their surface - molecular signature
- Information in the carbohydrate layer aids in cell-cell recognition and communication

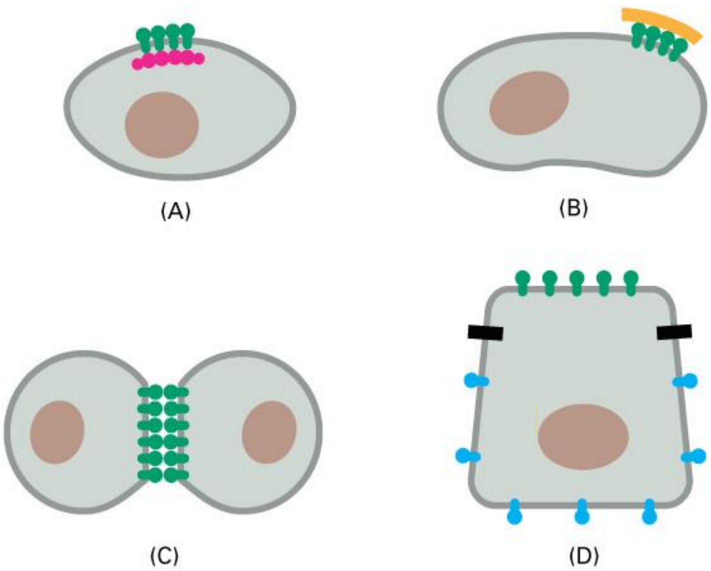
Cells use different mechanisms to restrict membrane protein movements

A. By tethering to elements inside of the cell (cortex)

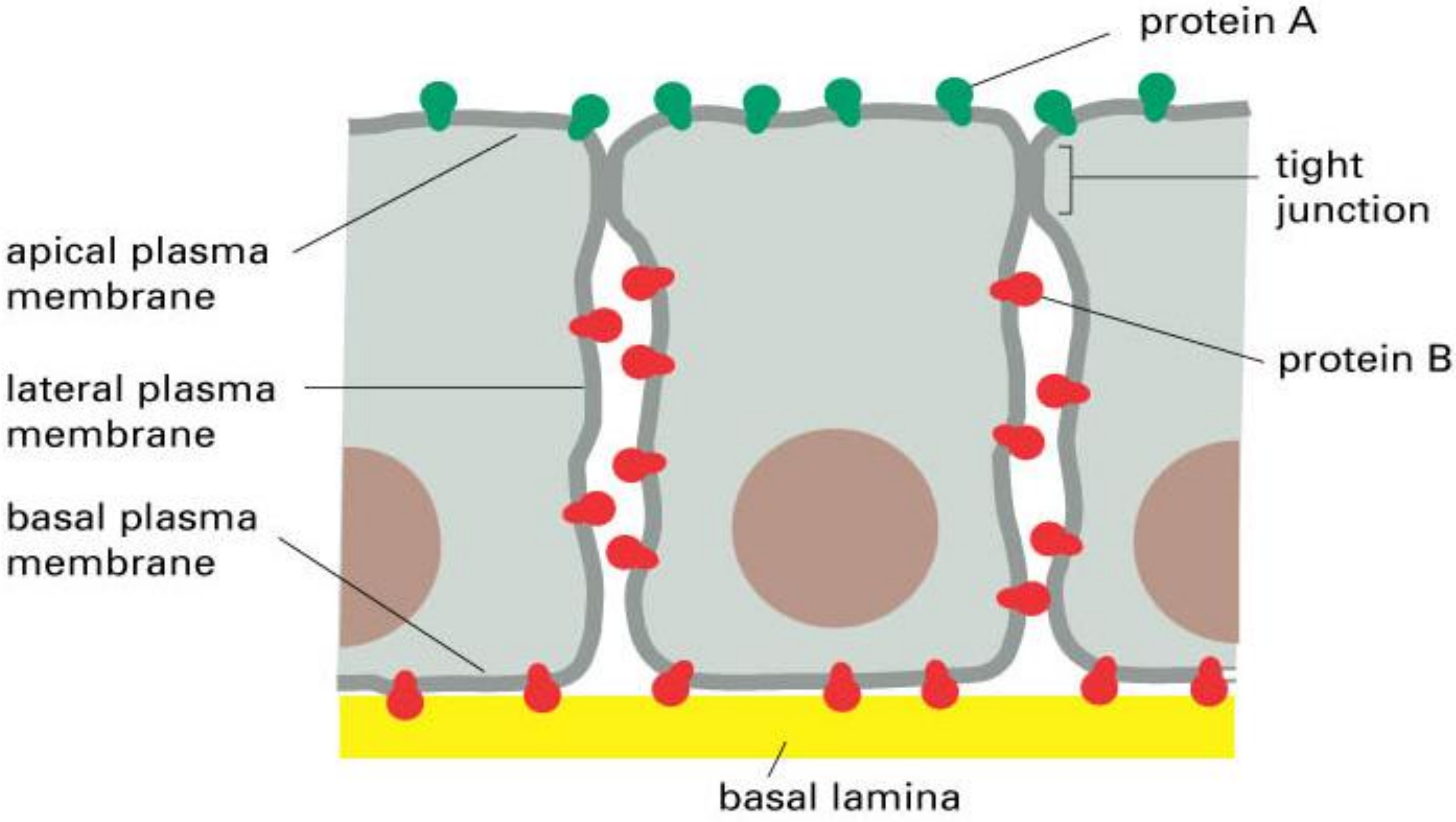
B. By tethering to elements outside of the cell

C. By interacting with proteins on the surface of another cell

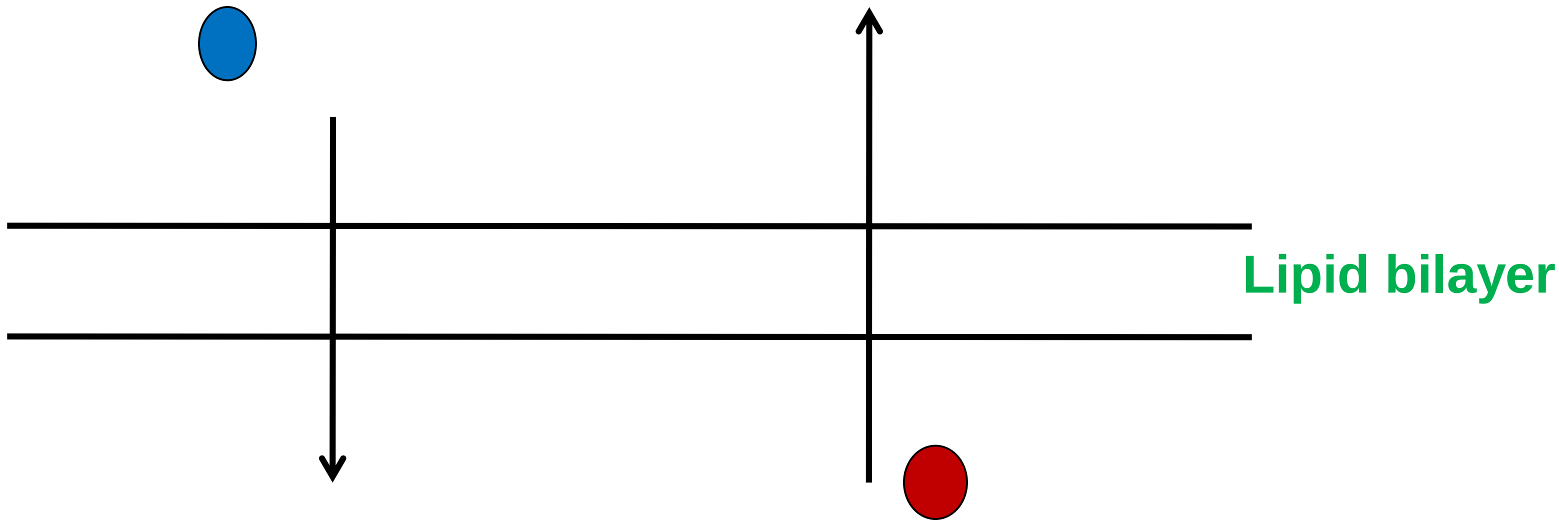
D. By diffusion barriers established within polarized cells



Epithelial cell polarity



Transport across the cell membrane



How Molecules Cross the Membrane

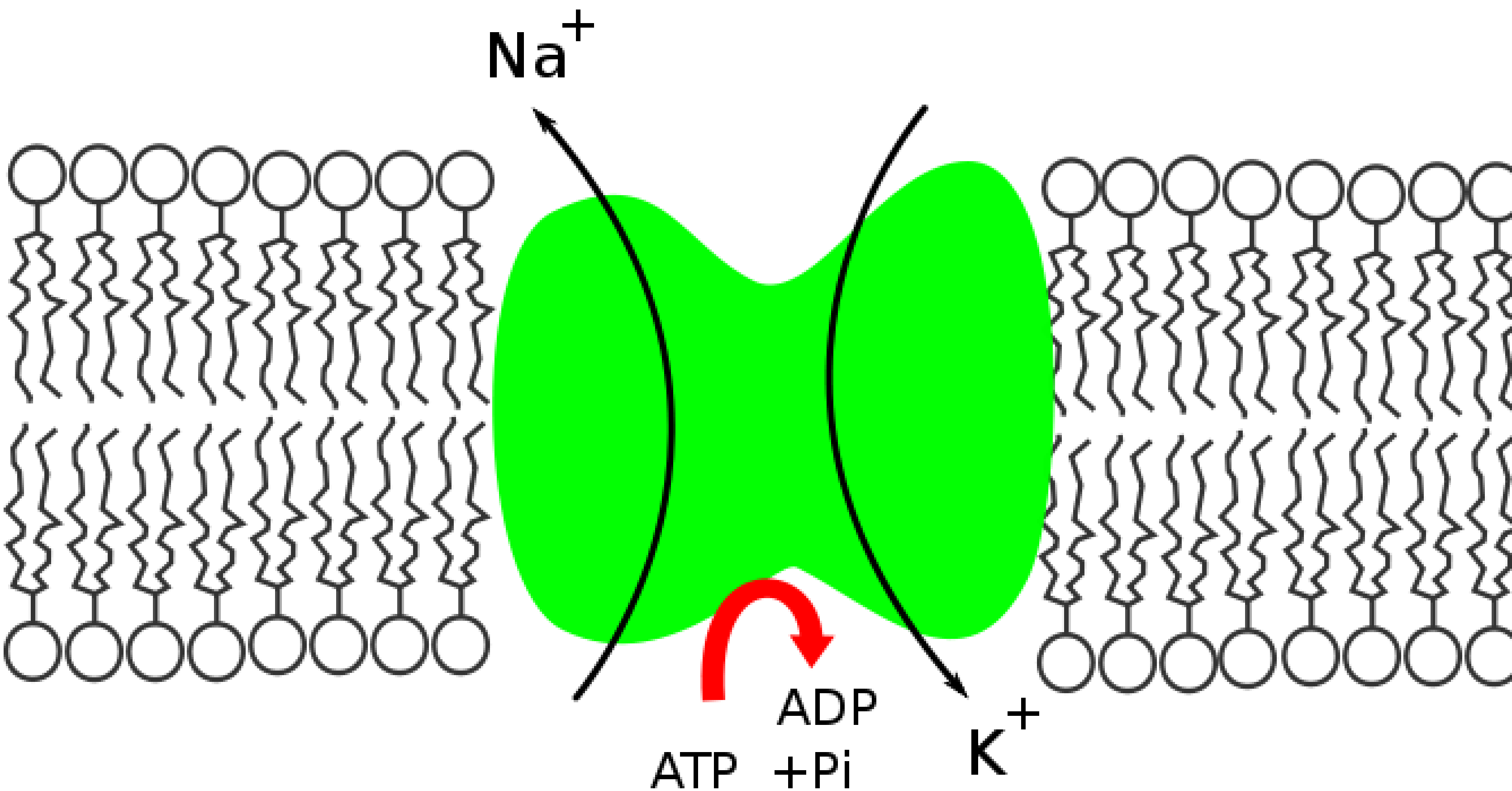
	Active/ Passive	Molecules that Move	Direction	Energy Needed?	Protein Needed?
Diffusion	Passive	small, hydrophobic	down gradient (toward low conc.)	no	no
Osmosis	Passive	water	toward high conc. of solutes	no	no
Facilitated Diffusion	Passive	any (specific transporter)	down gradient (toward low cons.)	no	yes
Active Transport	Active	any (specific transporter)	specific: in or out, dep. on transporter	yes	yes

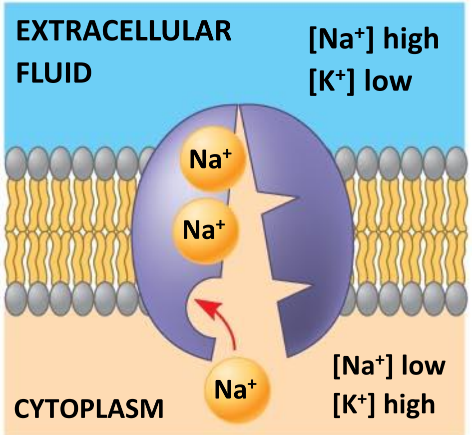
TABLE 2.1 Extracellular and Intracellular Ion Concentrations

	CONCENTRATION (mM)	
ION	INTRACELLULAR	EXTRACELLULAR
Squid neuron		
Potassium (K^+)	400	20
Sodium (Na^+)	50	440
Chloride (Cl^-)	40–150	560
Calcium (Ca^{2+})	0.0001	10
Mammalian neuron		
Potassium (K^+)	140	5
Sodium (Na^+)	5–15	145
Chloride (Cl^-)	4–30	110
Calcium (Ca^{2+})	0.0001	1–2

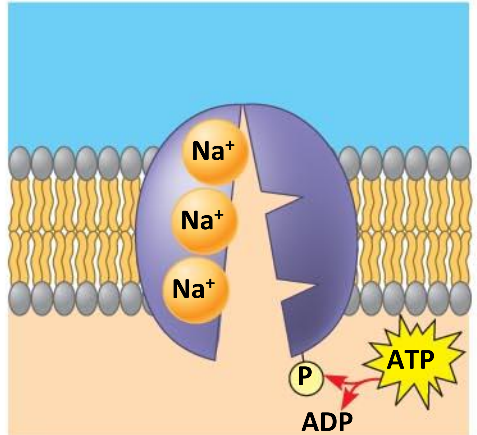
NEUROSCIENCE 5e, **Table 2.1**

Co-transport: Na^+- K^+ Pump

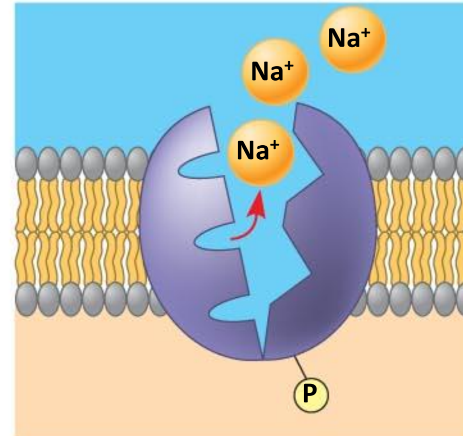




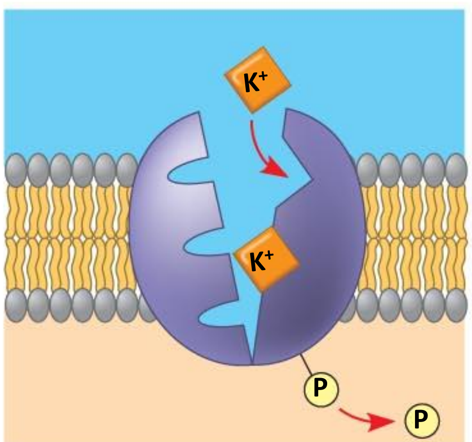
1 Cytoplasmic Na^+ bonds to the sodium-potassium pump



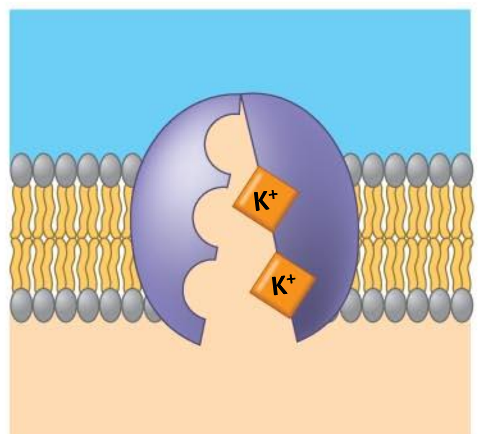
2 Na^+ binding stimulates phosphorylation by ATP.



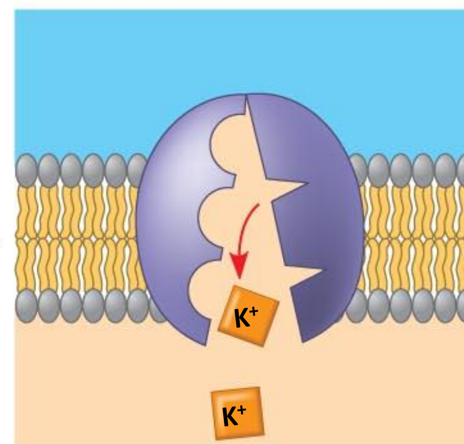
3 Phosphorylation causes the protein to change its conformation, expelling Na^+ to the outside.



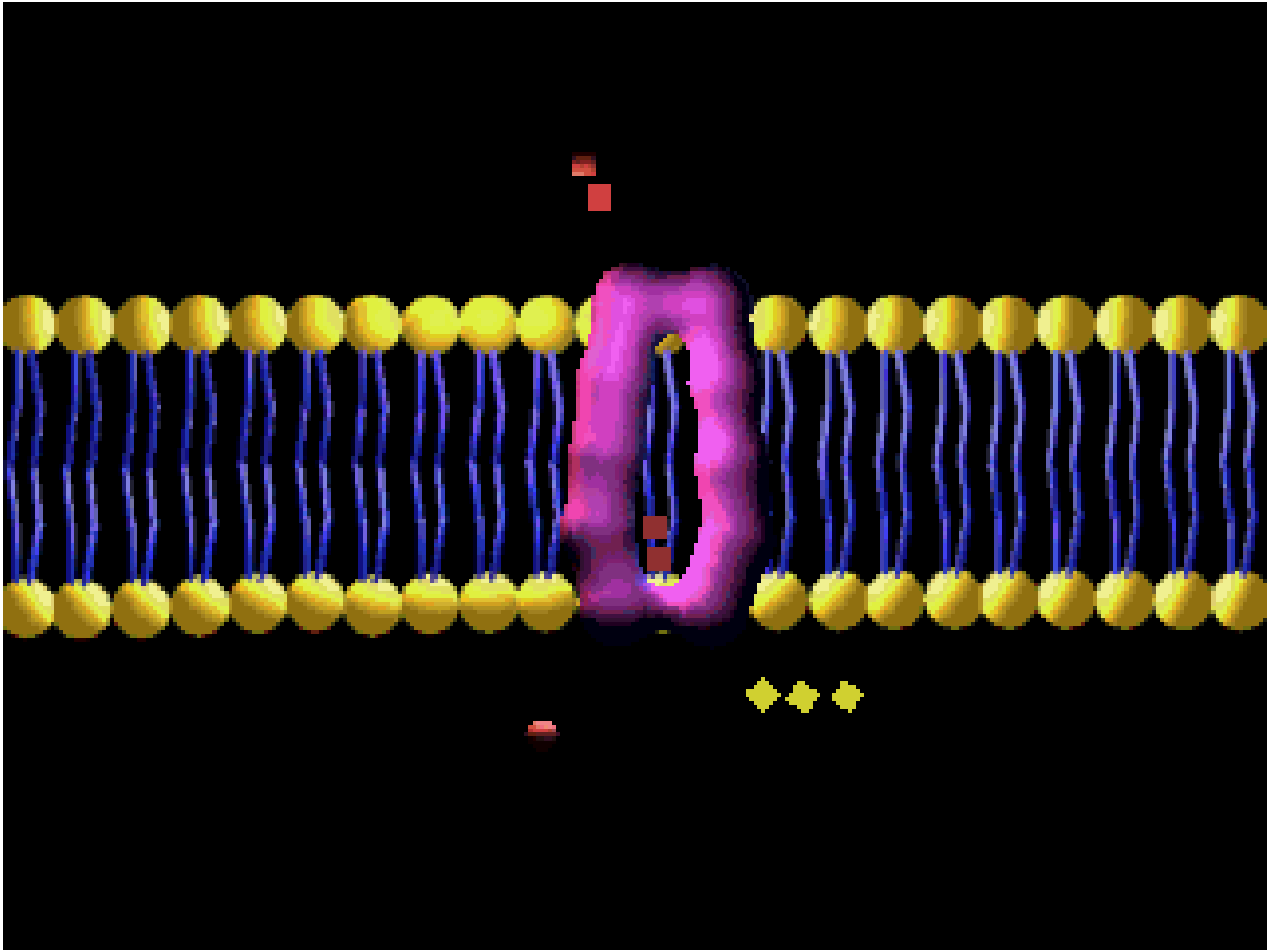
4 Extracellular K^+ binds to the protein, triggering release of the phosphate group.

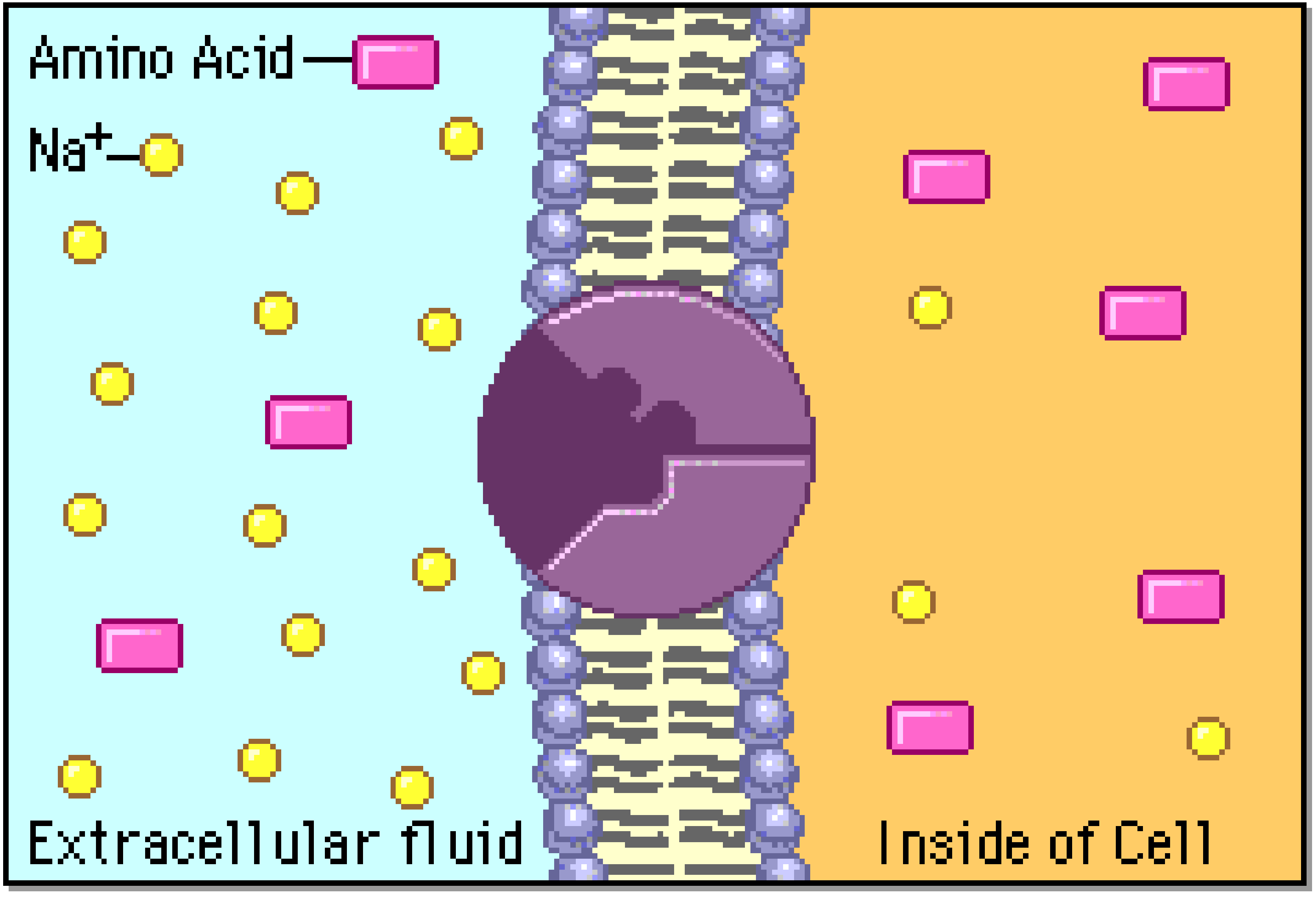


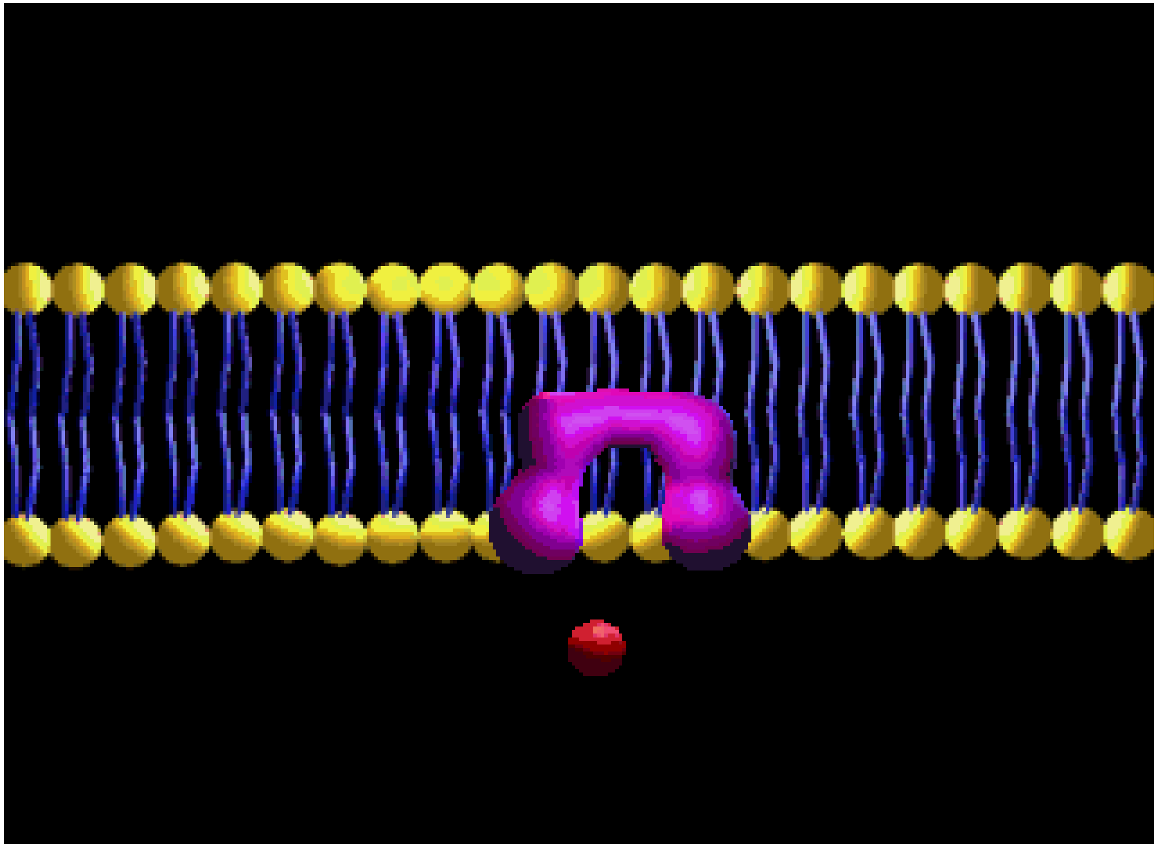
5 Loss of the phosphate restores the protein's original conformation.



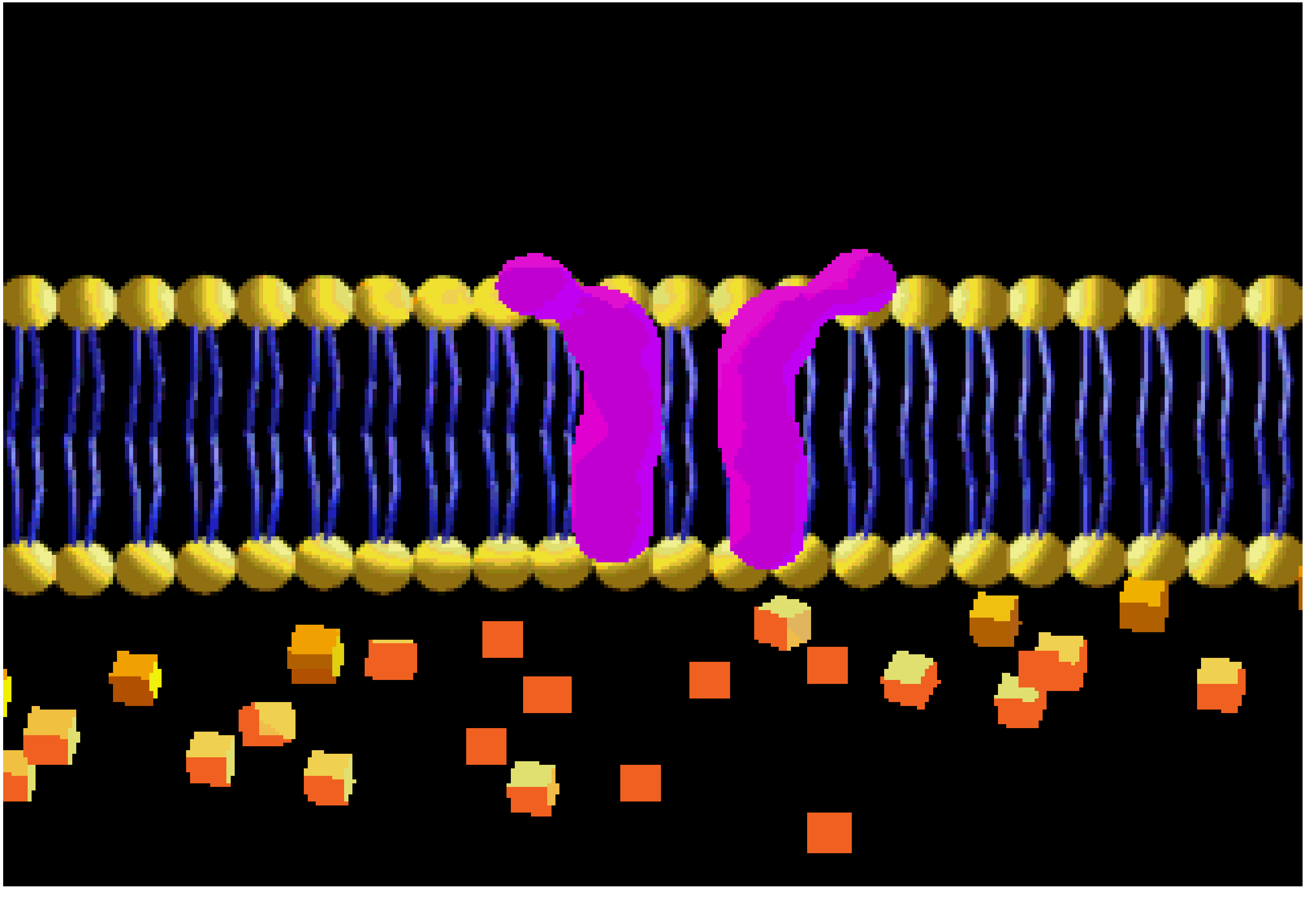
6 K^+ is released and Na^+ sites are receptive again; the cycle repeats.



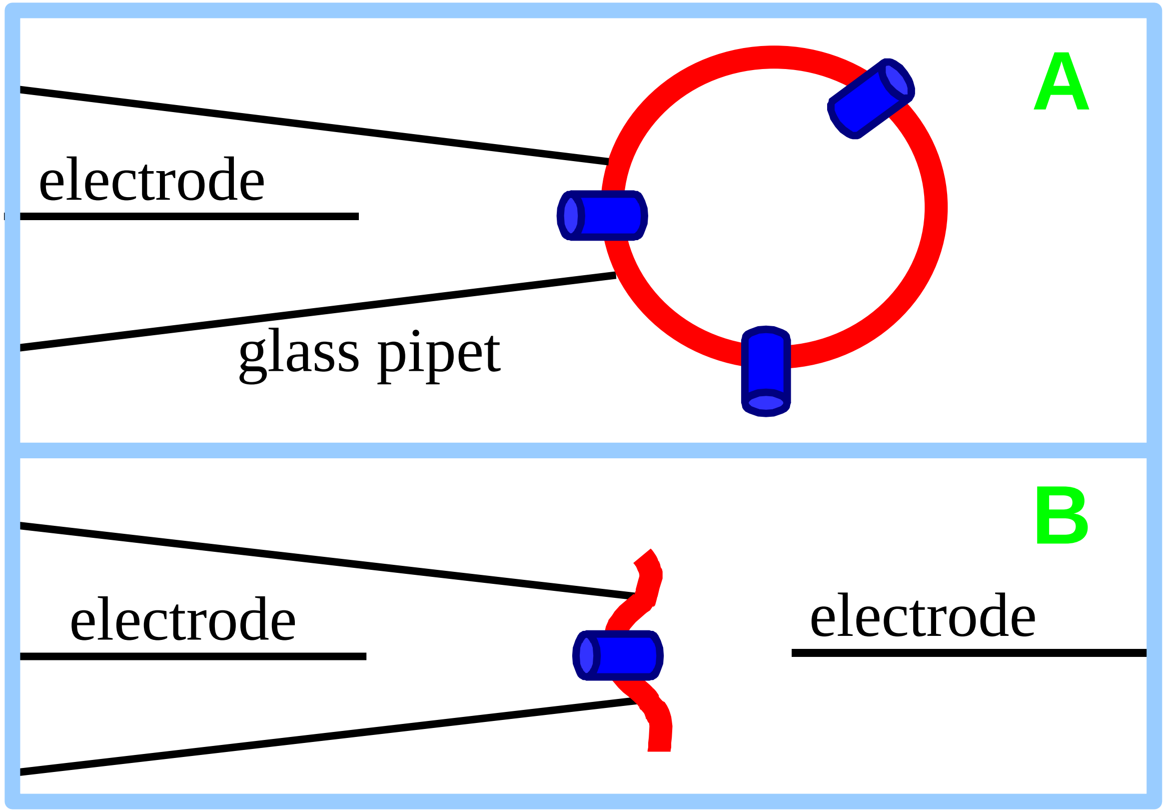

Amino Acid
Na^+
Extracellular fluid
Inside of Cell



Channel mediated transport



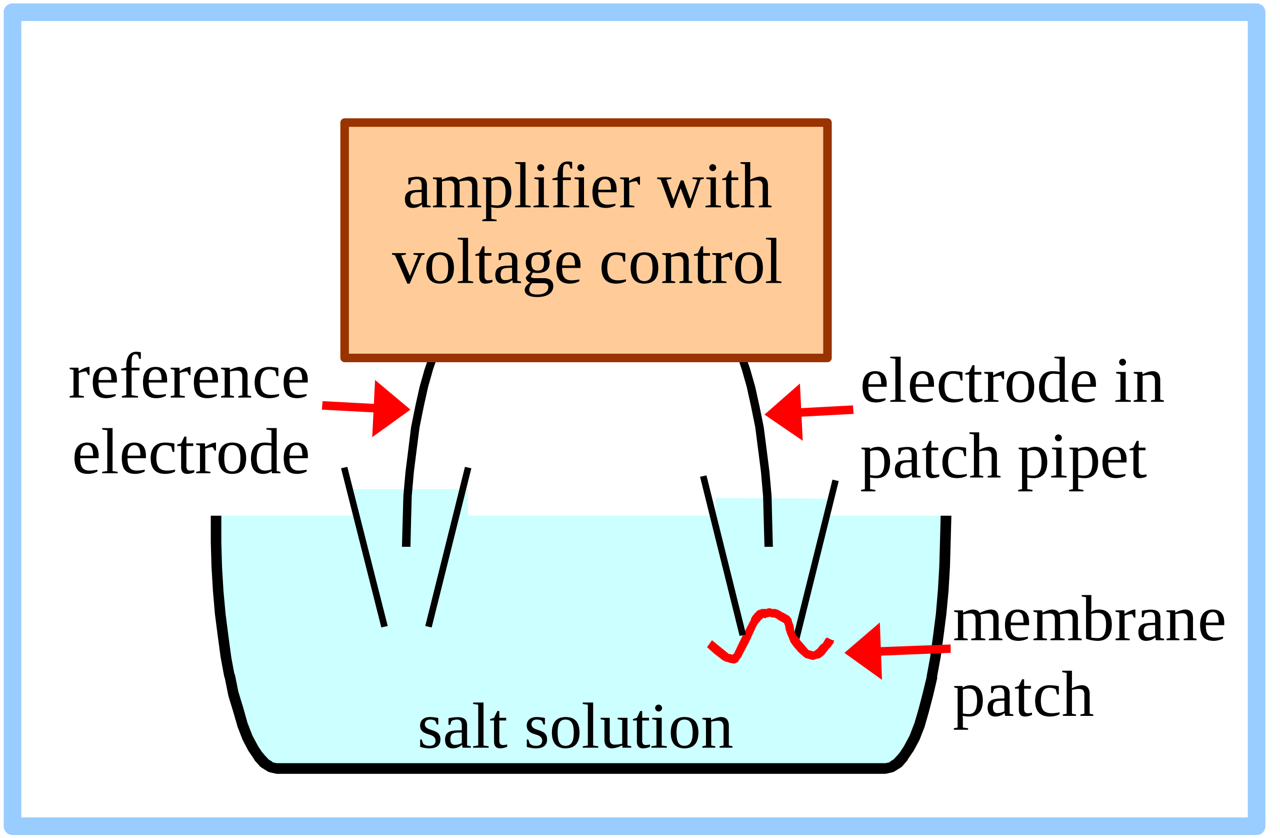
Patch Clamping



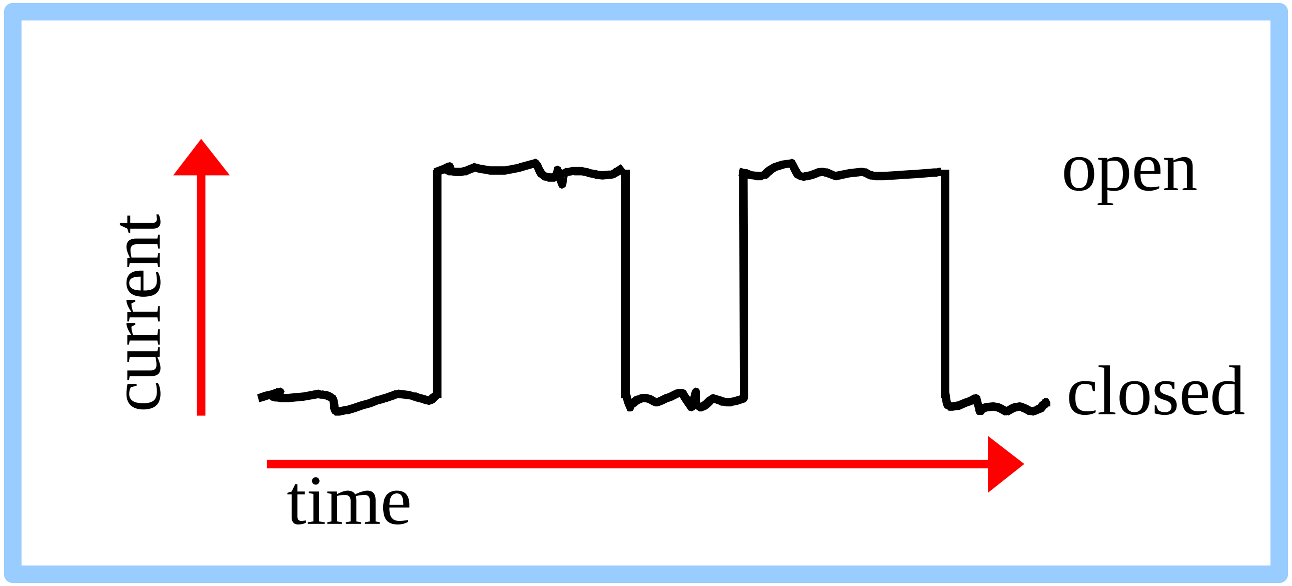
The technique of **patch clamping** is used to study ion channel activity.

A narrow bore micropipet may be pushed up against a cell or vesicle, and then pulled back, capturing a fragment of membrane across the pipet tip.

Patch Clamping



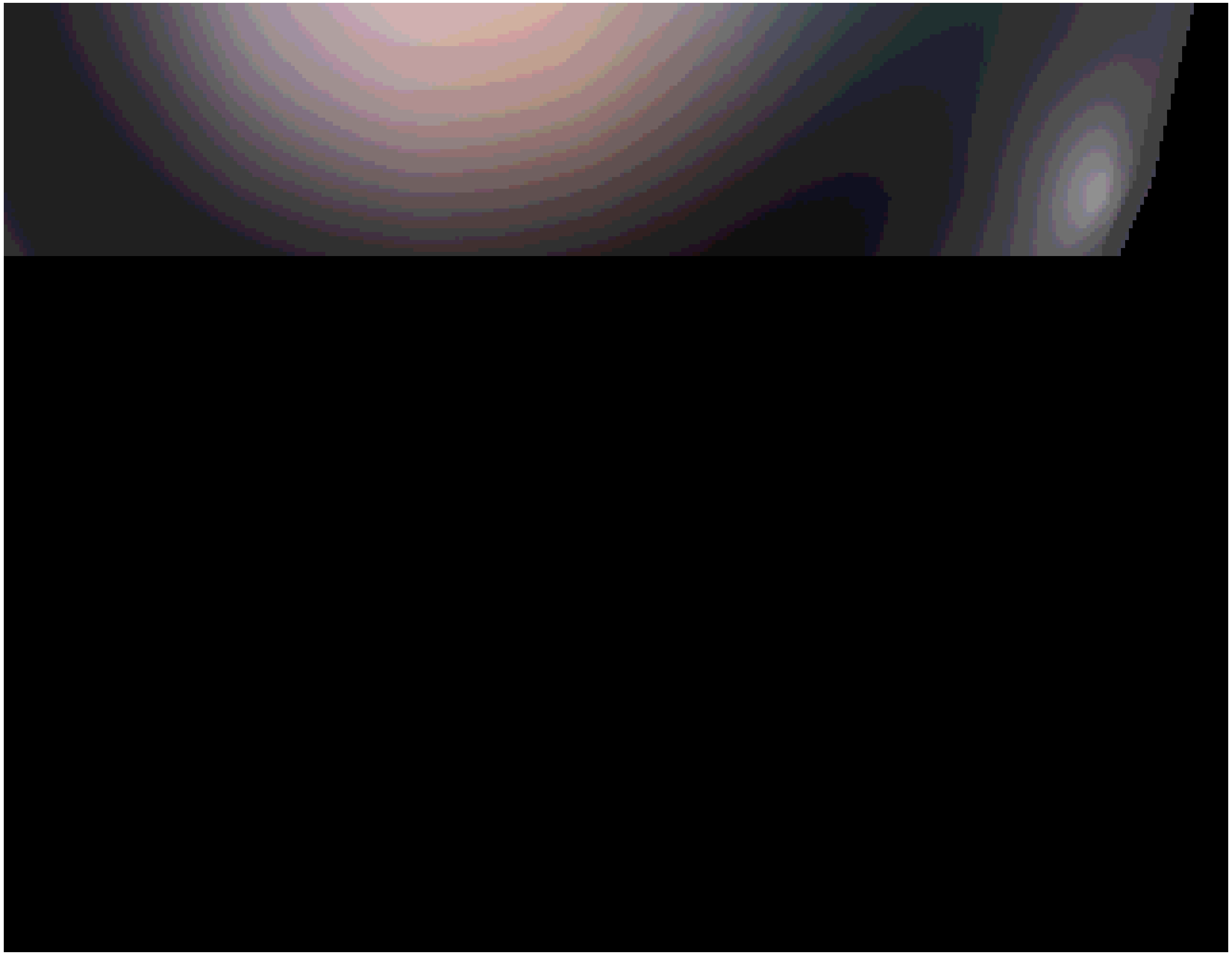
A **voltage** is imposed between an electrode inside the patch pipet and a reference electrode in contact with surrounding solution. **Current** is carried by ions flowing through the membrane.

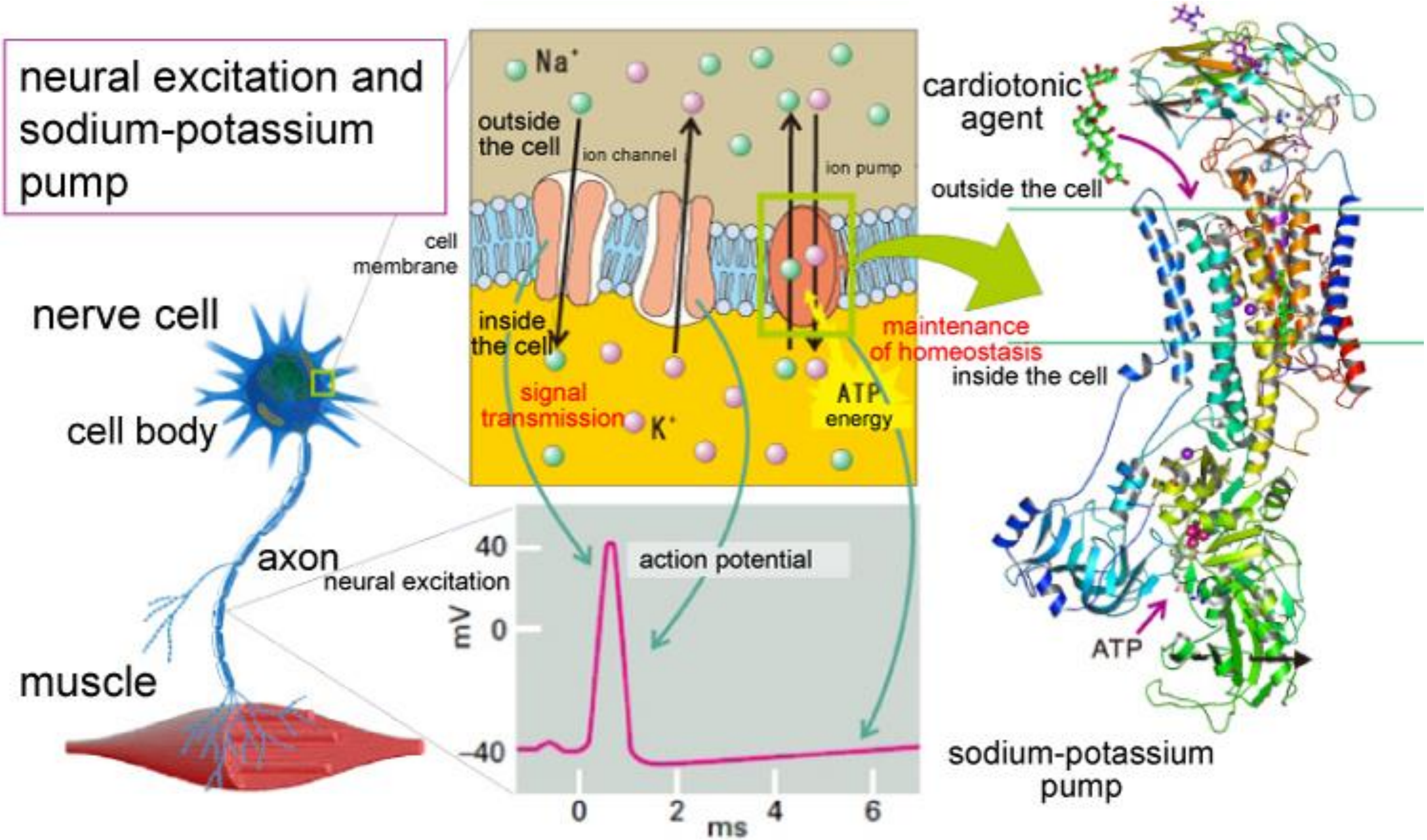


If a membrane patch contains a **single channel** with 2 conformational states, the current will fluctuate between 2 levels as the channel opens and closes.

The **increment in current** between open & closed states reflects the **rate of ion flux** through one channel.

Vesicle mediated transport





neural excitation and sodium-potassium pump
nerve cell
cell body
axon
muscle
cell membrane
Na+
outside the cell
ion channel
ion pump
inside the cell
signal transmission
K+
ATP energy
maintenance of homeostasis
neural excitation
action potential
40
0
-40
mV
0
2
4
6
ms
cardiotonic agent
outside the cell
inside the cell
ATP
sodium-potassium pump