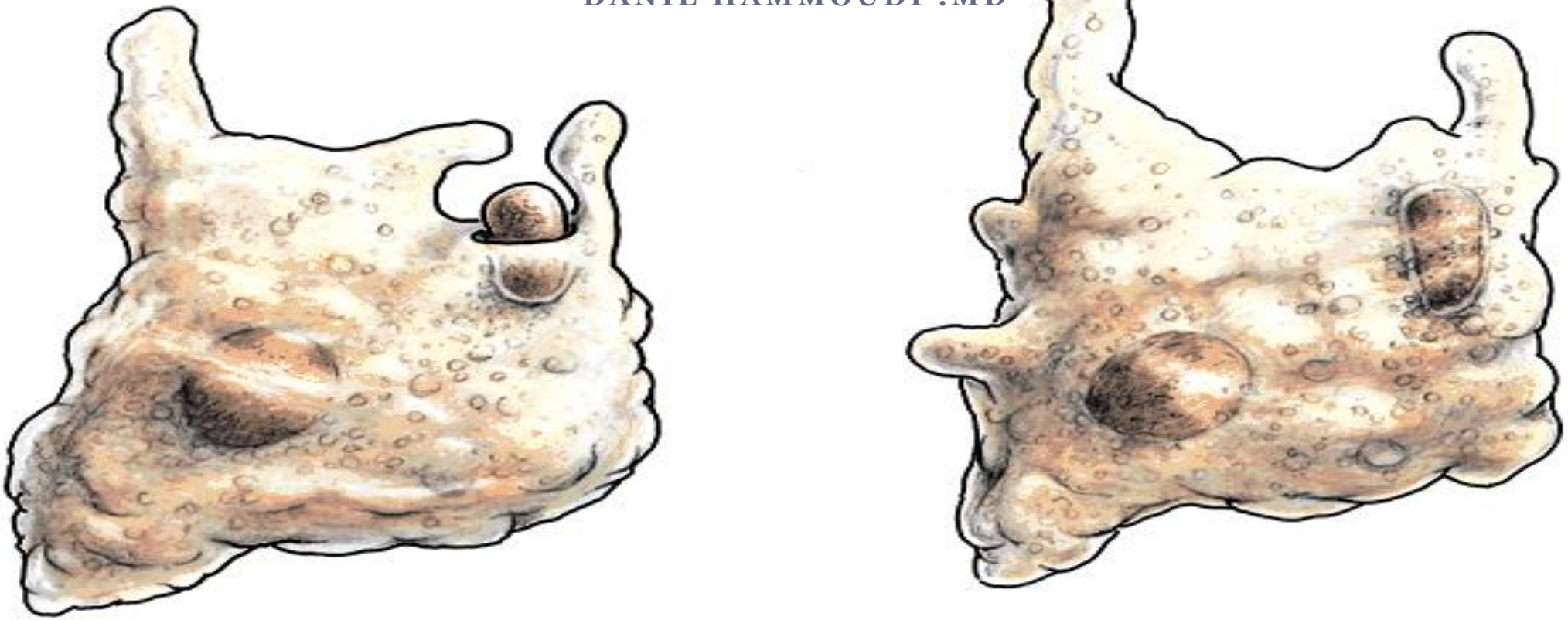
The cells

DANIL HAMMOUDI .MD



Chemical Structure of the Plasma Membrane

14. Describe the plasma membrane according to the fluid mosaic model. Include glycolipids, glycoproteins, phospholipids, cholesterol, integral proteins, and peripheral proteins.

Membrane Transport

15. Define the following terms: intracellular fluid, extracellular fluid, and interstitial fluid.

16. Define diffusion and describe how molecules diffuse across a plasma membrane. Include the following terms in your description: passive process, simple diffusion, facilitated diffusion, carriers, and channels.

17. Define and describe osmosis. Include the following terms in your description: solvent, solute, solution, hypertonic, hypotonic, and isotonic.

18. Explain what happens to a cell placed in a hypertonic, hypotonic, or isotonic solution.

19. List and explain the five factors that affect the rate of transport of substances across cell membranes. These factors are size of the material, temperature, the presence or absence of channels or other facilitating devices, particle charges, and the concentration gradient for the material being transported.

20. Define and describe active processes by which materials move across cell membranes.
Active processes include active transport and vesicular transport. Include the following terms

in your description: ATP, pumps, exocytosis, endocytosis, phagocytosis, and receptormediated endocytosis.

Cellular Structures

21. Describe the structures and functions of the following membrane junctions: tight junctions, desmosomes, and gap junctions

Cell Theory

- The cell is the basic structural and functional unit of life
- Organismal activity depends on individual and collective activity of cells
- Biochemical activities of cells are dictated by subcellular structure
- Continuity of life has a cellular basis

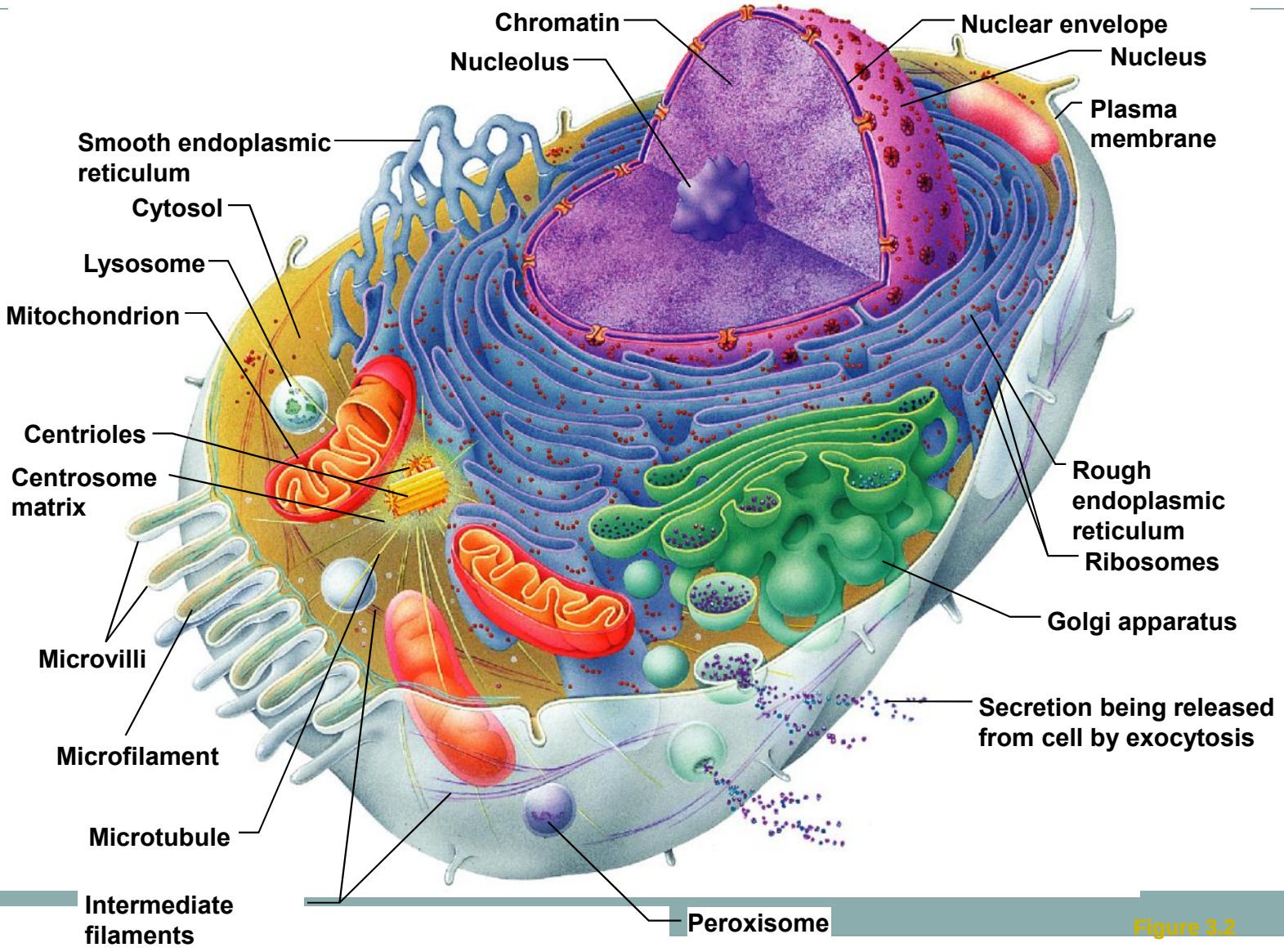
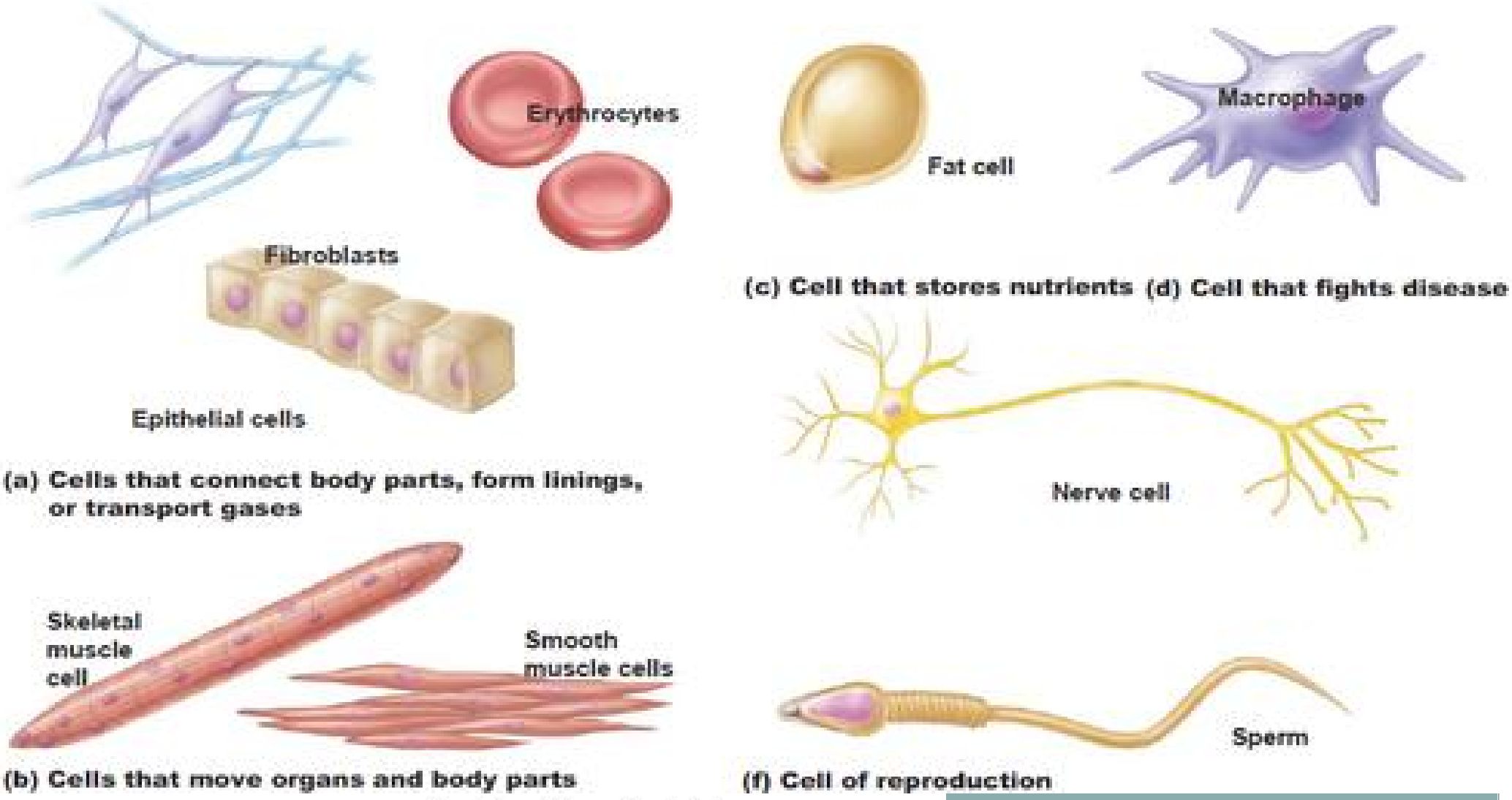

Chromatin
Nucleolus
Nuclear envelope
Nucleus
Plasma membrane
Smooth endoplasmic reticulum
Cytosol
Lysosome
Mitochondrion
Centrioles
Centrosome matrix
Rough endoplasmic reticulum
Ribosomes
Golgi apparatus
Microvilli
Secretion being released from cell by exocytosis
Microfilament
Microtubule
Intermediate filaments
Peroxisome

Figure 3.2

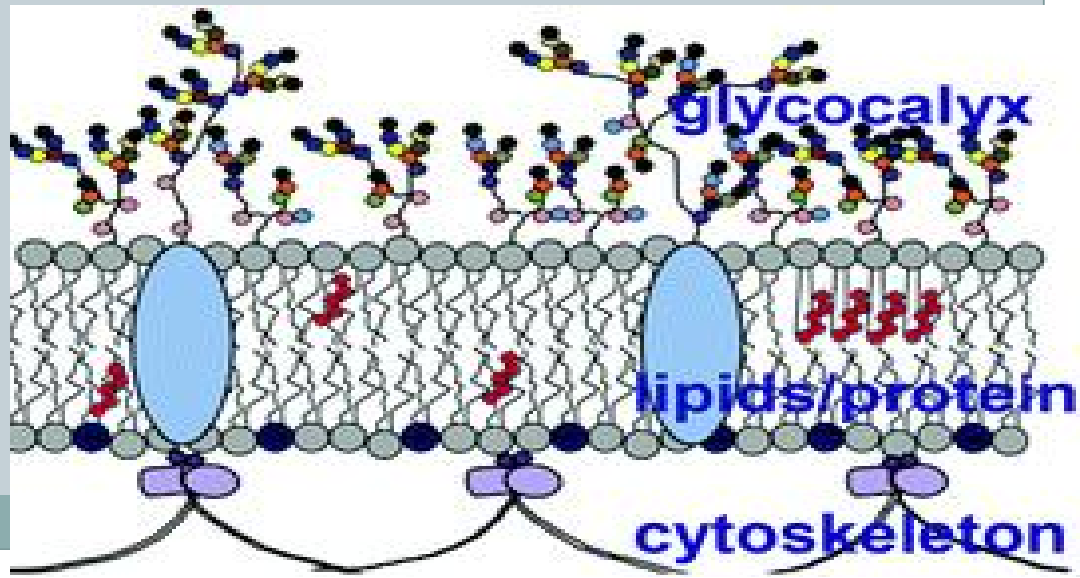


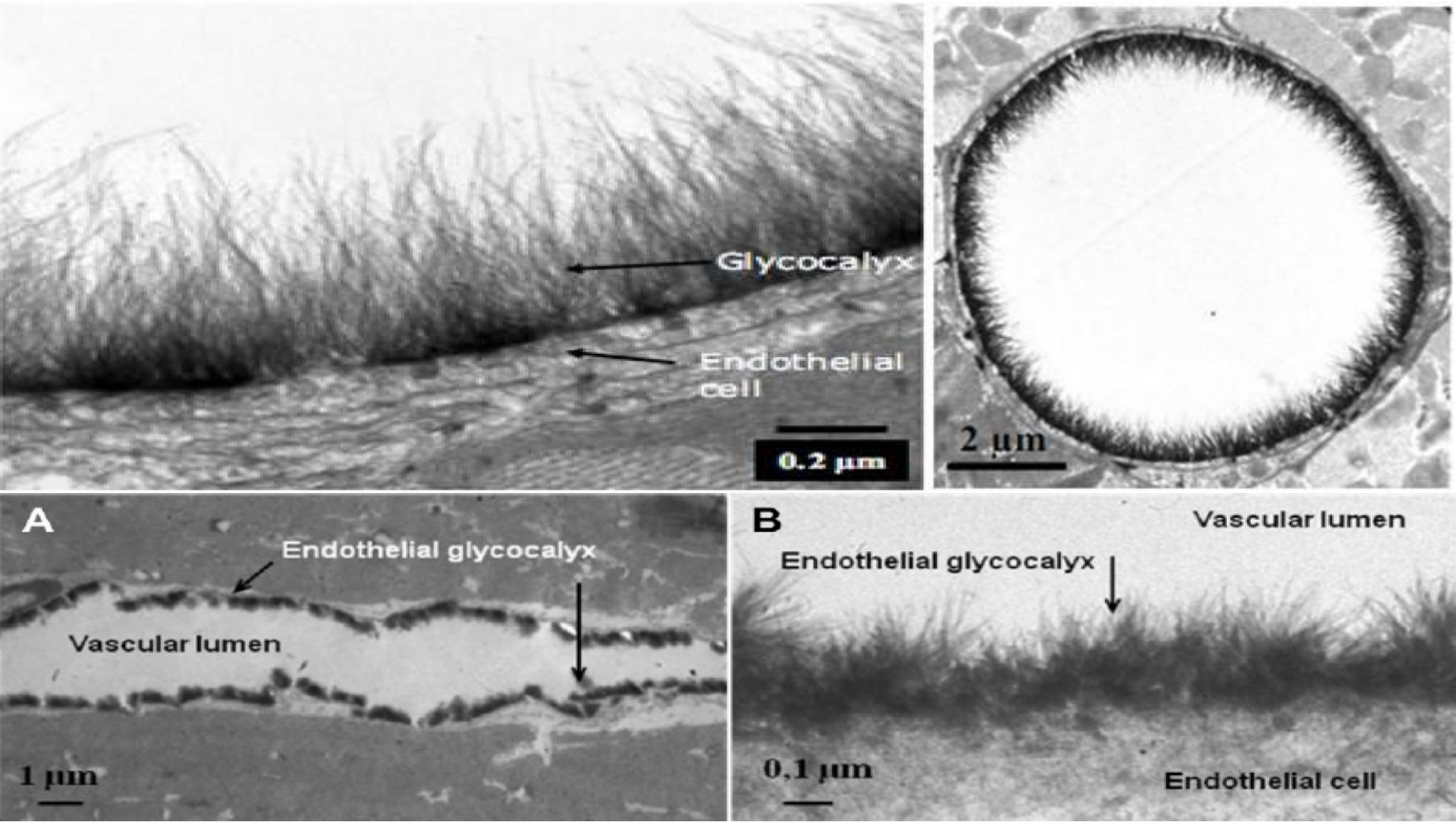
Specialised Human Body Cells

Plasma Membrane

- Separates intracellular fluids from extracellular fluids
- Plays a dynamic role in cellular activity
- ***Glycocalyx*** is a glycoprotein area abutting the cell that provides highly **specific biological markers** by which ***cells recognize one another, unique to each cells***

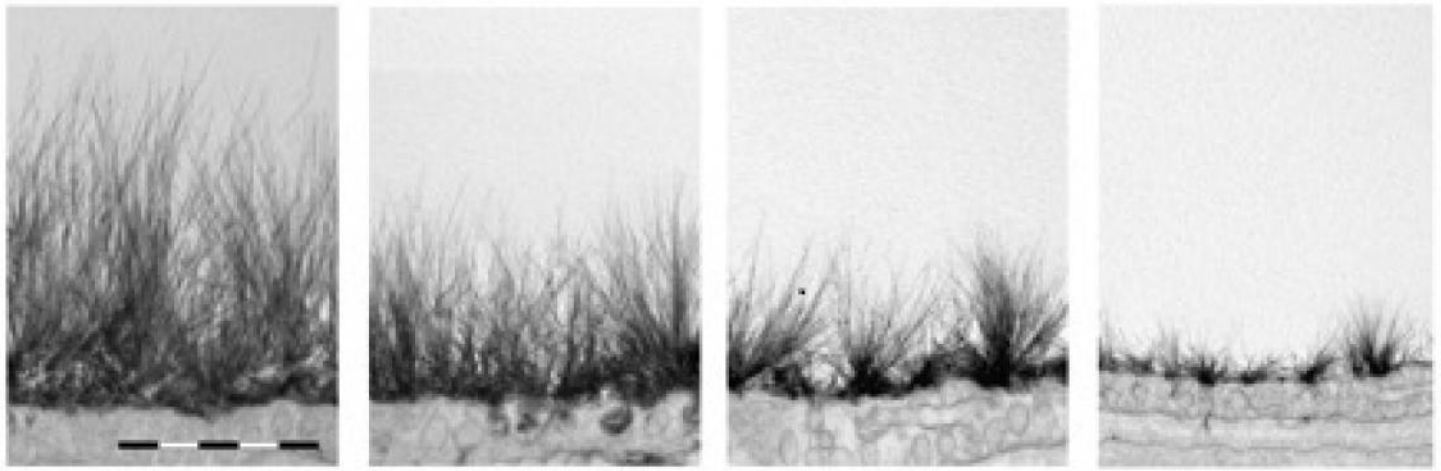
- **Act as an ID tag**
- **Block cancer signal**
- **Embryo growth**
- **Cell protection**
- **Immunity to infection**
- **Cell adhesion**
- **Fertilization**




Glycocalyx
Endothelial cell
0.2 µm
2 µm
A
Endothelial glycocalyx
Vascular lumen
1 µm
B
Vascular lumen
Endothelial glycocalyx
0.1 µm
Endothelial cell

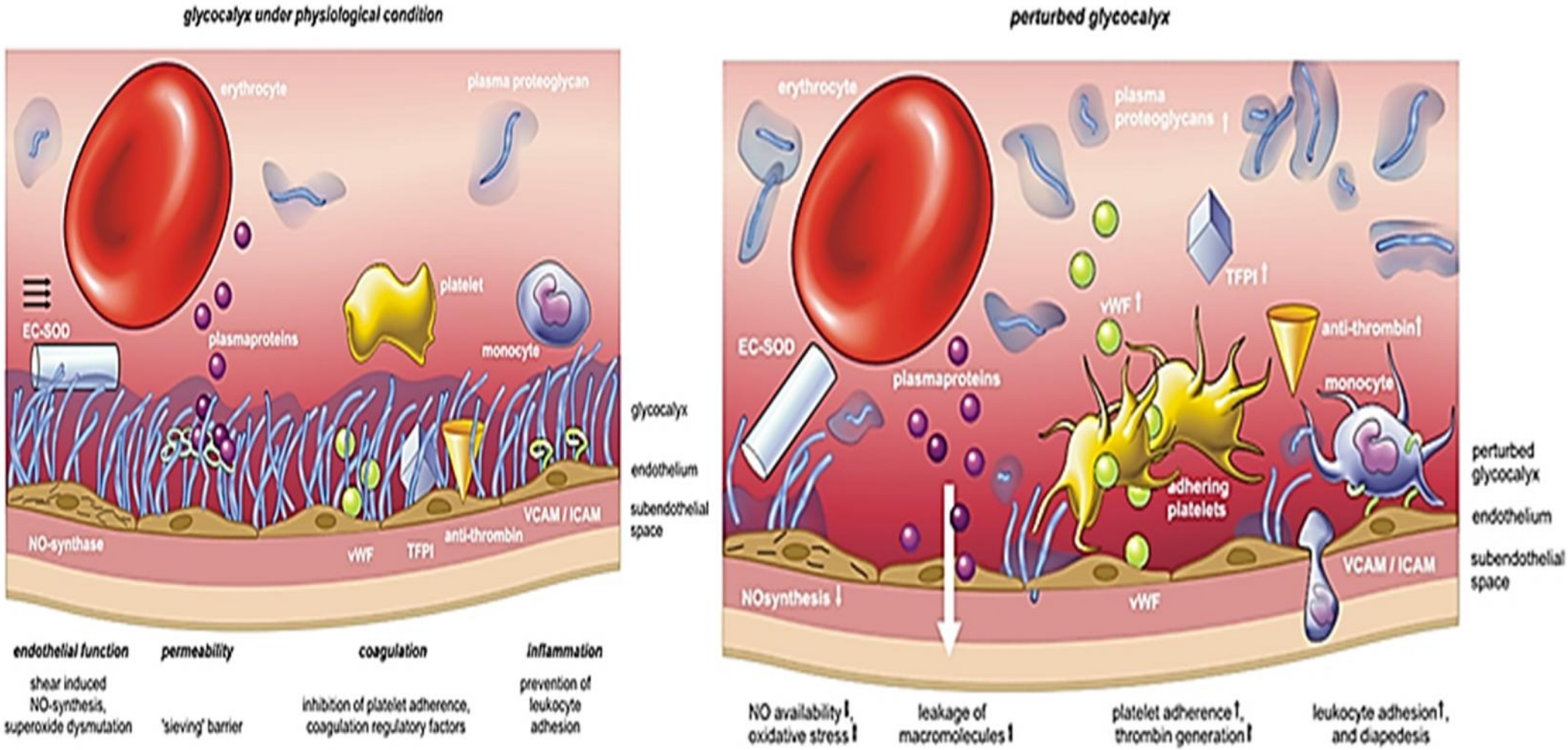
GLYCOCALYX AFFECTED BY:

Aging
Diet
Disease
Exercise
Genetics
Smoking
Stress



HEALTHY GLYCOCALYX

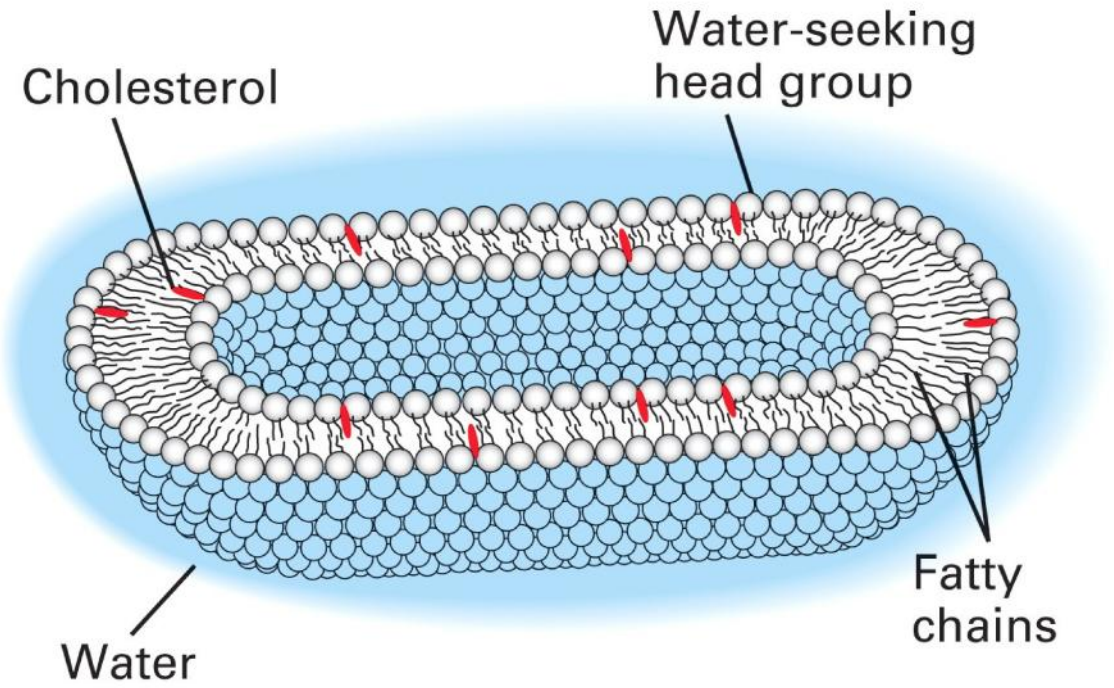
UNHEALTHY GLYCOCALYX



glycocalyx perturbation occurs when the circulation gets exposed to atherogenic stimuli such as oxidized lipoproteins, hyperlipidemia, and hyperglycemia.

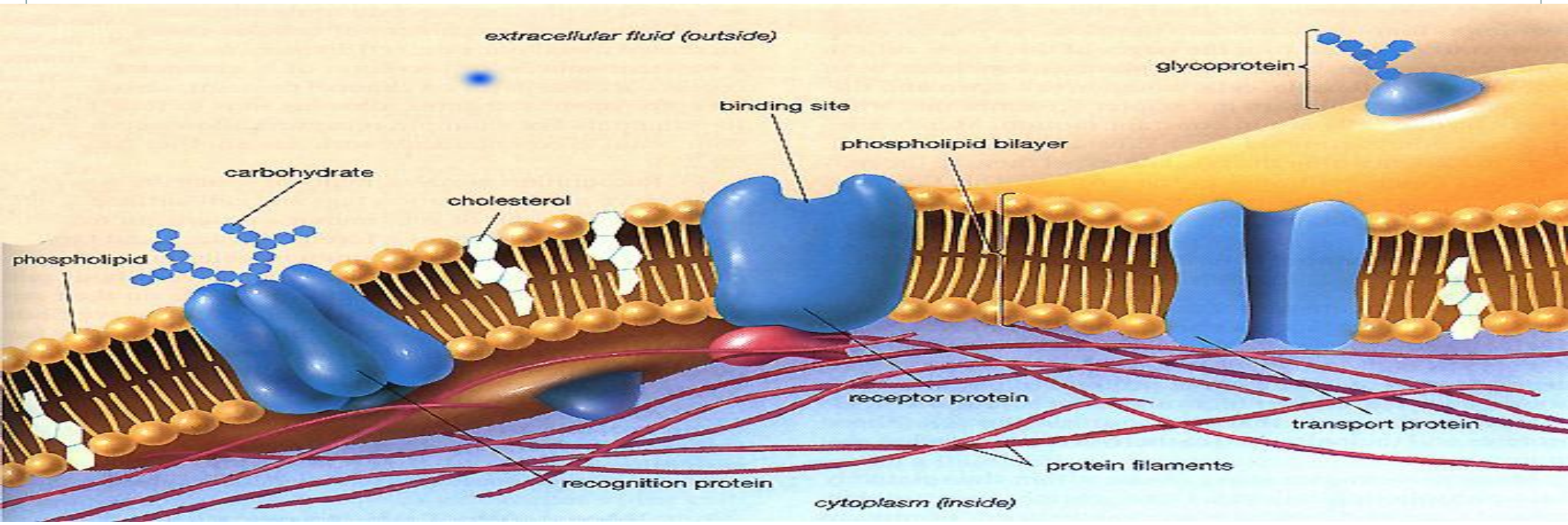
Membranes define cellular and organelle boundaries

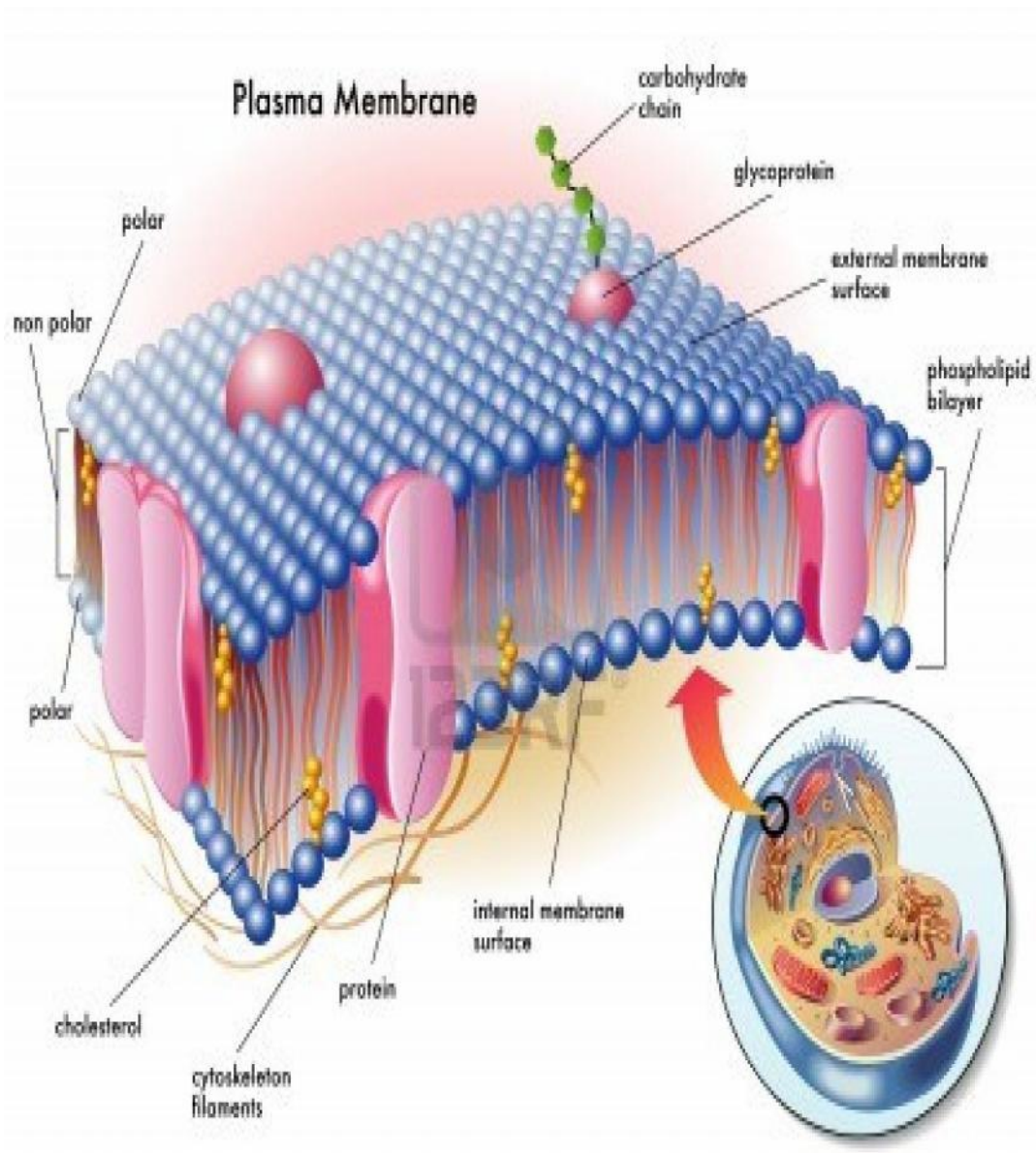
- How does chemistry dictate function?
- Why are there different lipid types?
- How does material get across membranes?

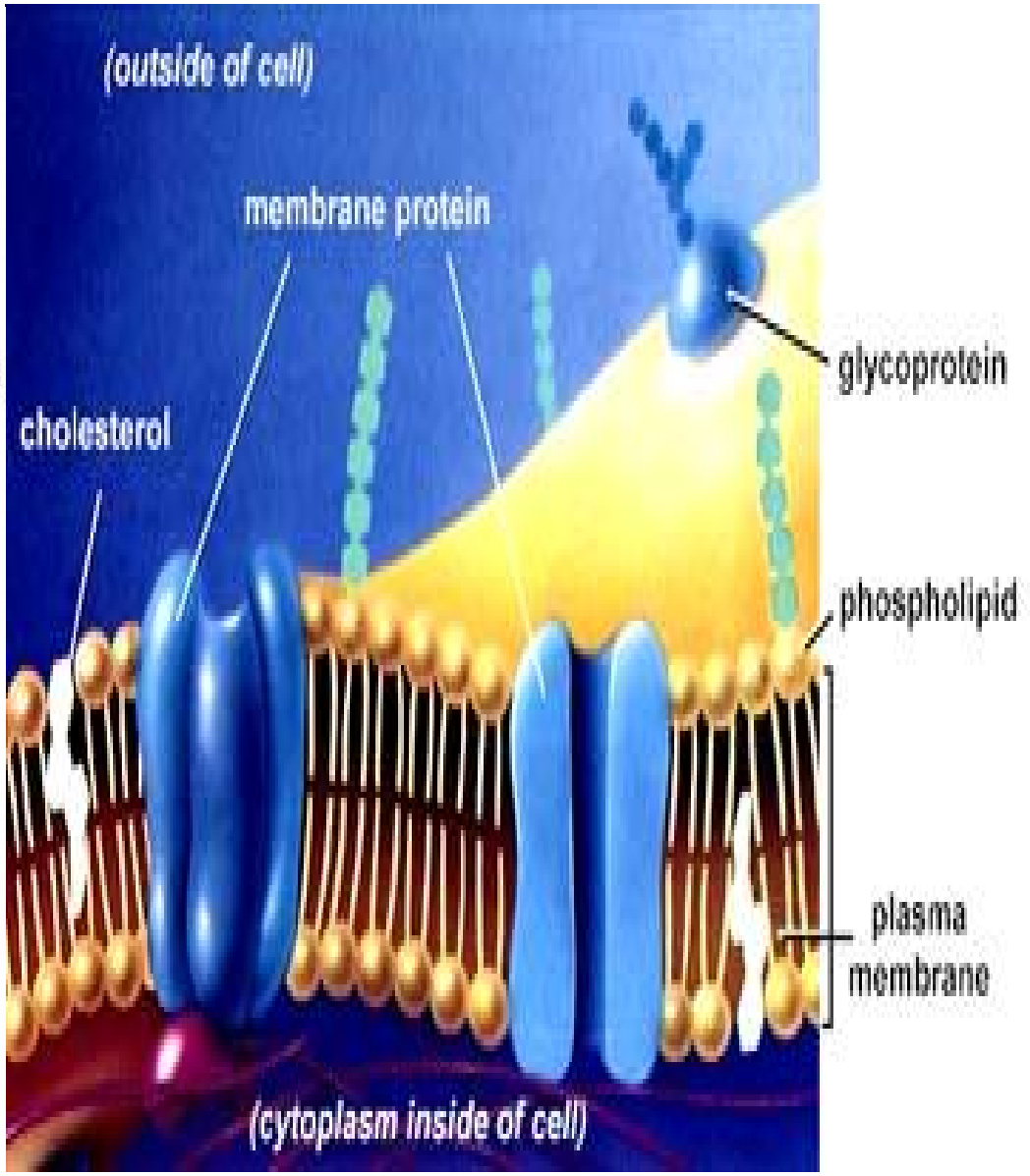


Fluid Mosaic Model

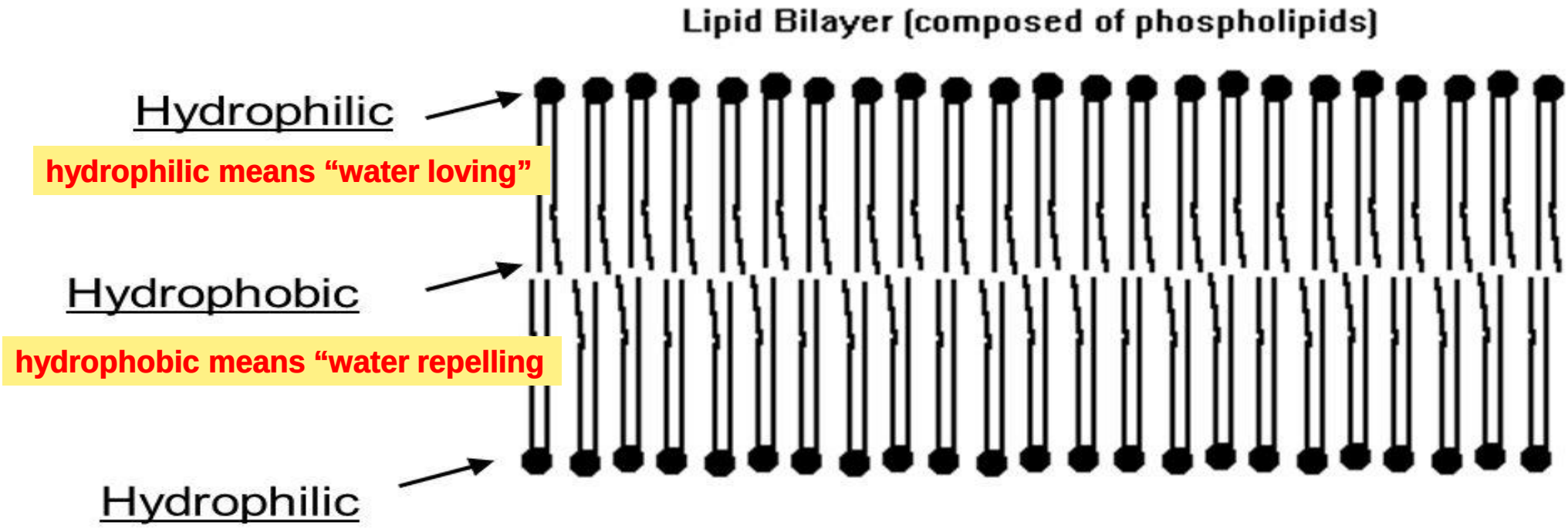
- **Double bilayer of lipids** with imbedded, dispersed **proteins**
- Bilayer consists of ***phospholipids, cholesterol, and glycolipids***
  - Glycolipids are lipids with bound carbohydrate
  - **Phospholipids have hydrophobic and hydrophilic bipoles**




Plasma Membrane
carbohydrate chain
glycoprotein
polar
external membrane surface
non polar
phospholipid bilayer
polar
internal membrane surface
protein
cholesterol
cytoskeleton filaments


(outside of cell)
membrane protein
glycoprotein
cholesterol
phospholipid
plasma membrane
(cytoplasm inside of cell)

Cell Membrane Structure



Fluid Mosaic Model

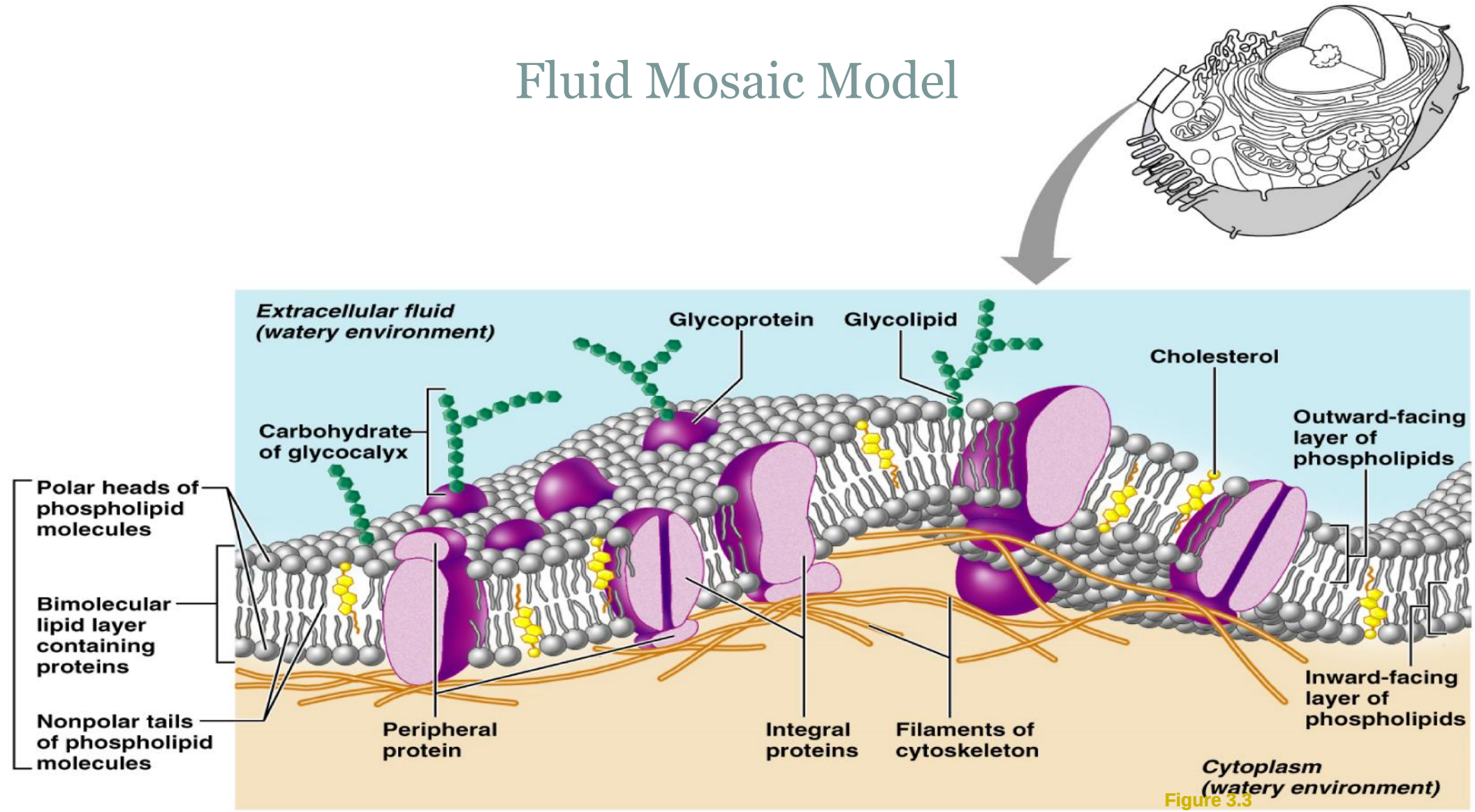
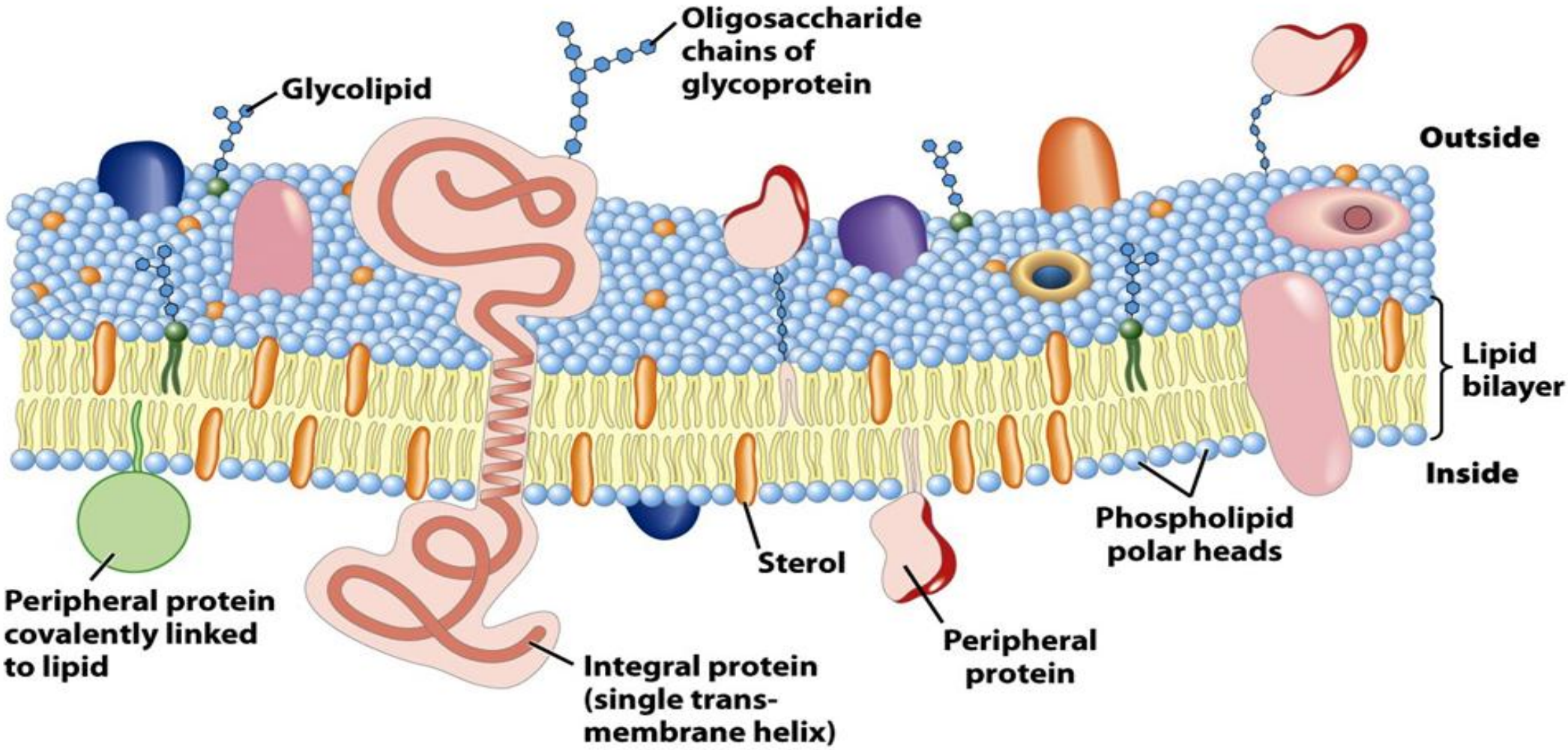
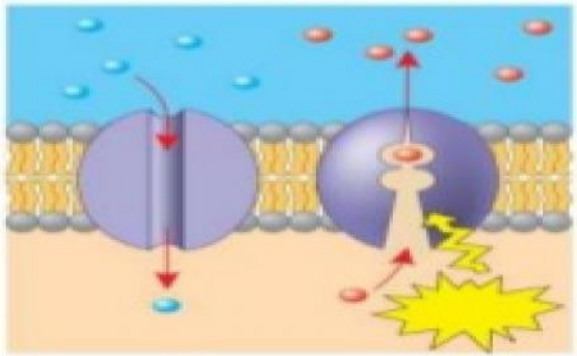


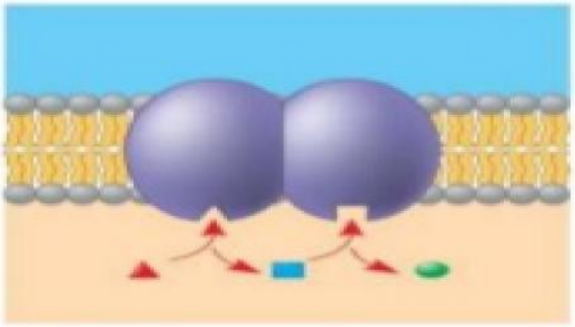
Figure 3.3


Oligosaccharide chains of glycoprotein
Glycolipid
Outside
Lipid bilayer
Inside
Phospholipid polar heads
Sterol
Peripheral protein covalently linked to lipid
Integral protein (single trans-membrane helix)
Peripheral protein

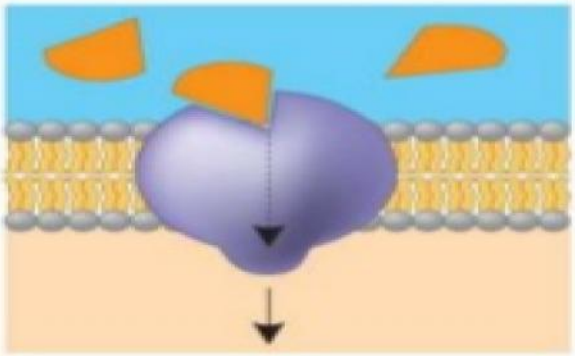
Six major functions of membrane proteins



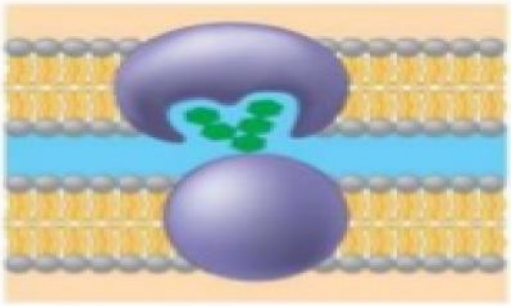
(a) Transport



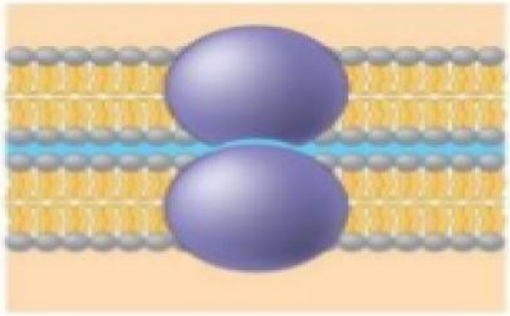
(b) Enzymatic activity



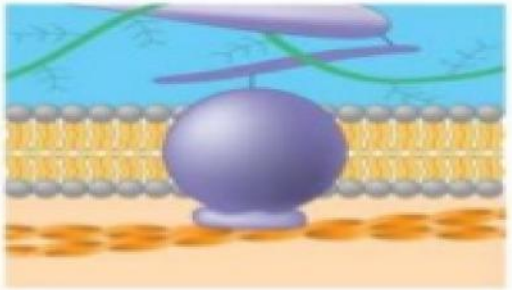
(c) Signal transduction



(d) Cell-cell recognition



(e) Intercellular joining

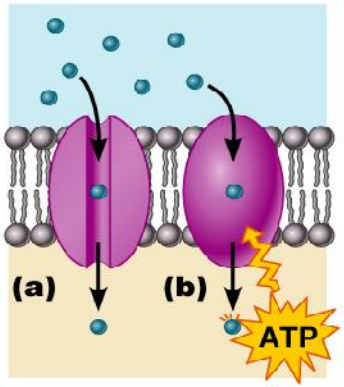


(f) Attachment to the cytoskeleton ECM

Functions of Membrane Proteins

- **Transport**

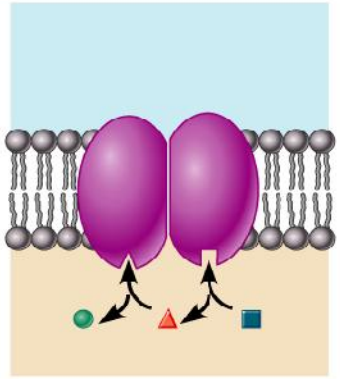
Transport Protein



Transport
(a) A protein that spans the membrane may provide a hydrophilic channel across the membrane that is selective for a particular solute. **(b)** Some transport proteins hydrolyze ATP as an energy source to actively pump substances across the membrane.

- **Enzymatic activity**

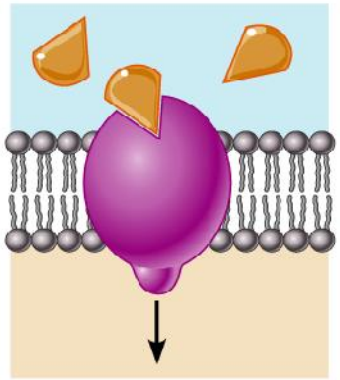
Enzymes



Enzymatic activity
A protein built into the membrane may be an enzyme with its active site exposed to substances in the adjacent solution. In some cases, several enzymes in a membrane act as a team that catalyzes sequential steps of a metabolic pathway as indicated (right to left) here.

- **Receptors for signal transduction**

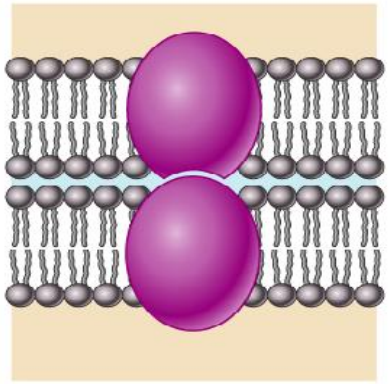
Receptor Proteins



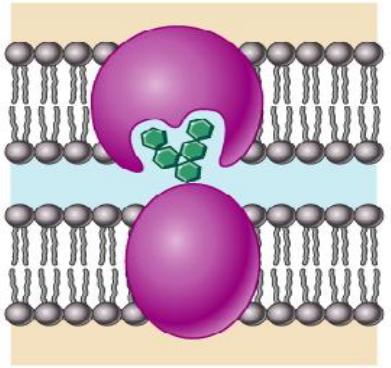
Receptors for signal transduction
A membrane protein exposed to the outside of the cell may have a binding site with a specific shape that fits the shape of a chemical messenger, such as a hormone. The external signal may cause a conformational change in the protein that initiates a chain of chemical reactions in the cell.

Functions of Membrane Proteins

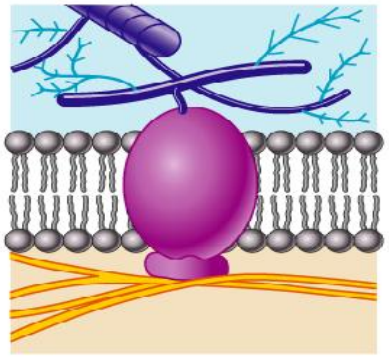
- **Intercellular adhesion**
- **Cell-cell recognition**
- **Attachment to cytoskeleton and extracellular matrix**



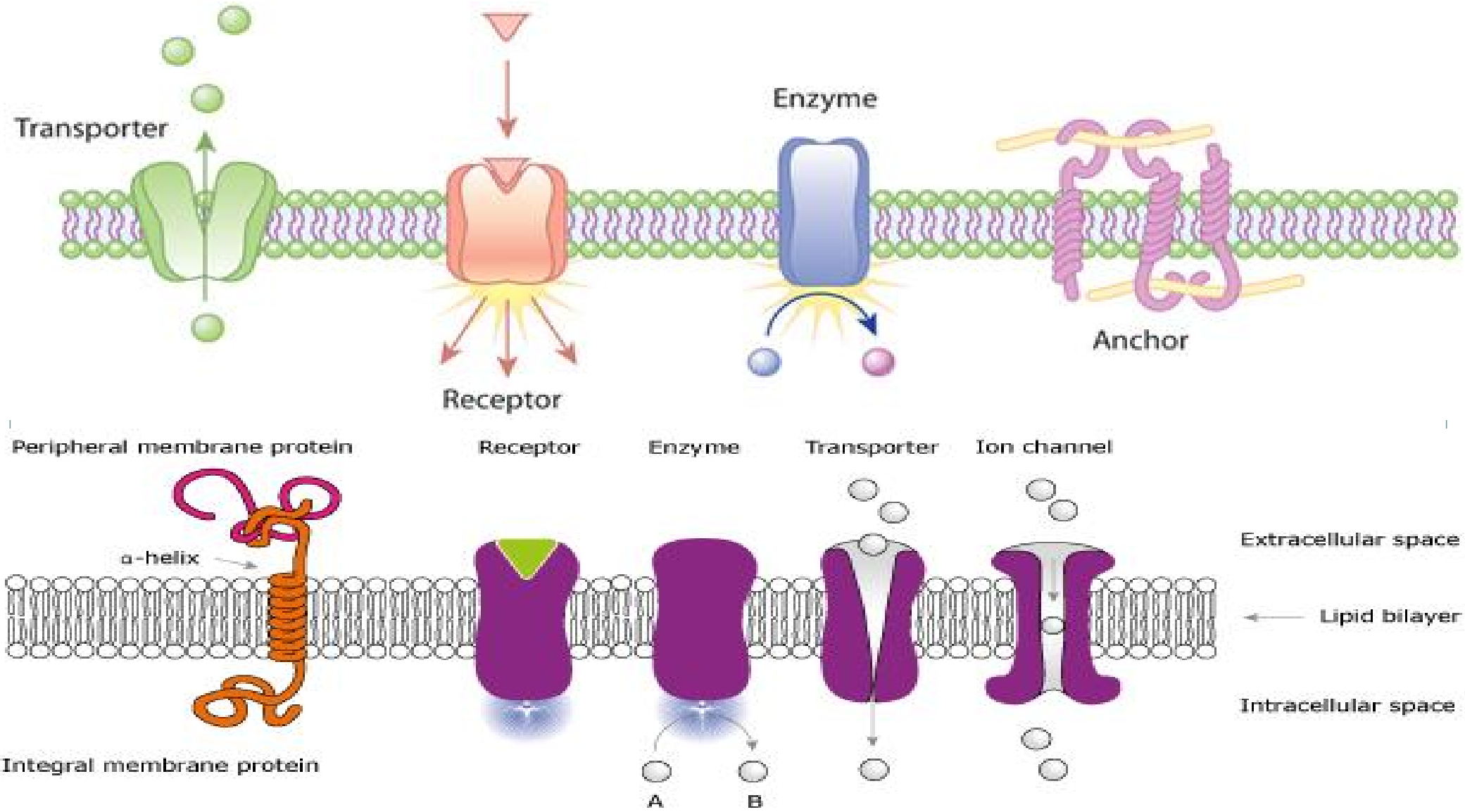
Intercellular joining
Membrane proteins of adjacent cells may be hooked together in various kinds of intercellular junctions. Some membrane proteins (CAMs) of this group provide temporary binding sites that guide cell migration and other cell-to-cell interactions.



Cell-cell recognition
Some glycoproteins (proteins bonded to short chains of sugars) serve as identification tags that are specifically recognized by other cells.

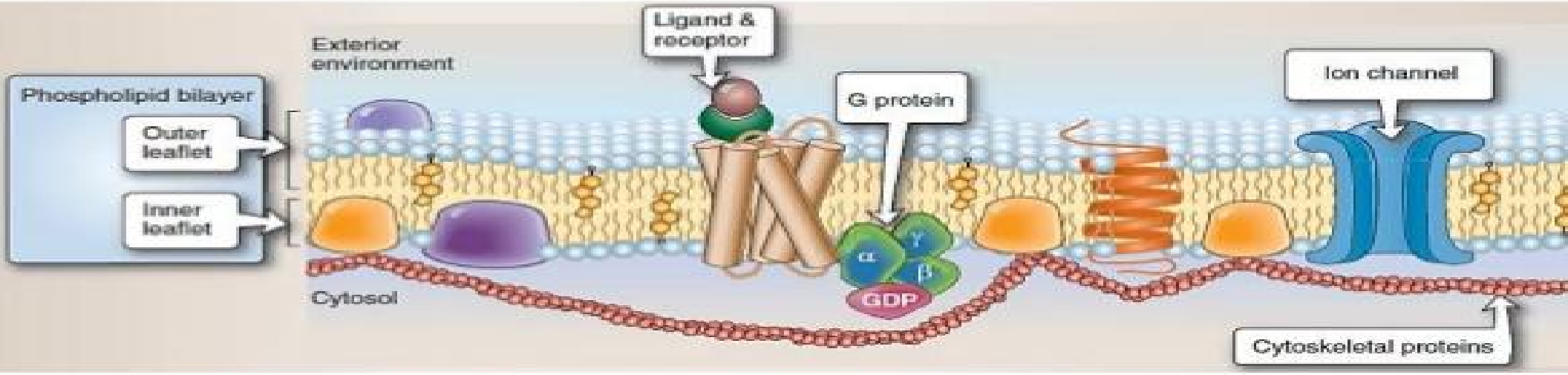


Attachment to the cytoskeleton and extracellular matrix (ECM)
Elements of the cytoskeleton (cell's internal supports) and the extracellular matrix (ECM) may be anchored to membrane proteins, which help maintain cell shape and fix the location of certain membrane proteins. Others play a role in cell movement or bind adjacent cells together.


Transporter
Receptor
Enzyme
Anchor
Peripheral membrane protein
Receptor
Enzyme
Transporter
Ion channel
α-helix
Extracellular space
Lipid bilayer
Intracellular space
Integral membrane protein
A
B

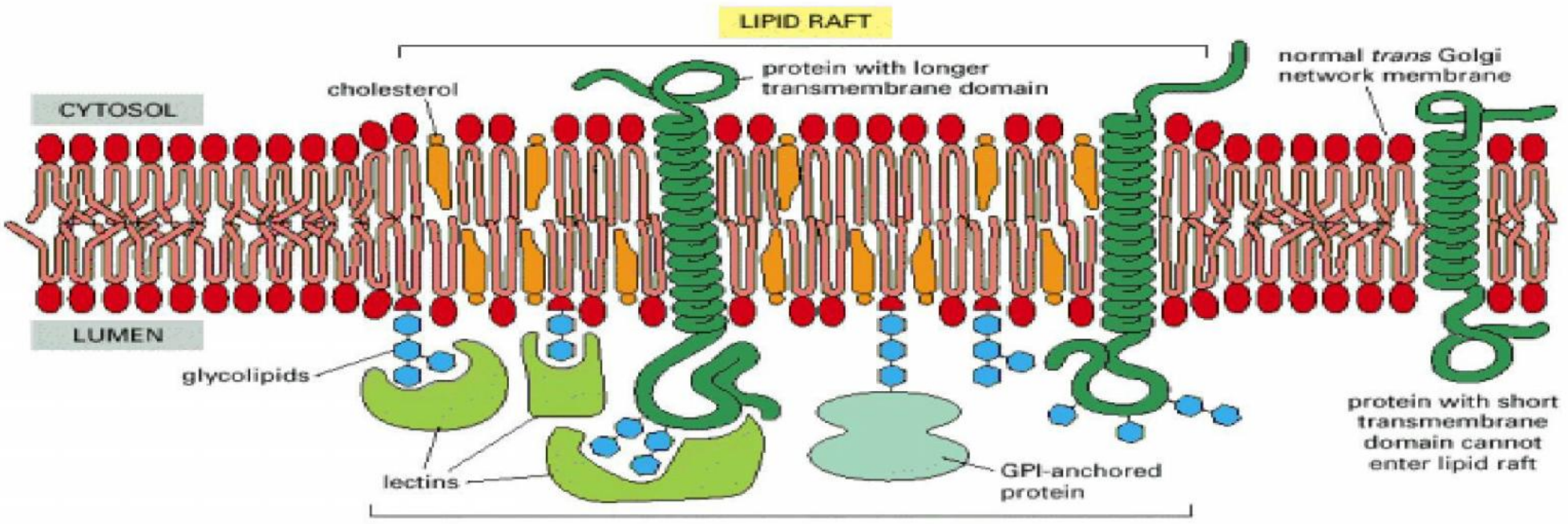
Plasma Membrane Surfaces

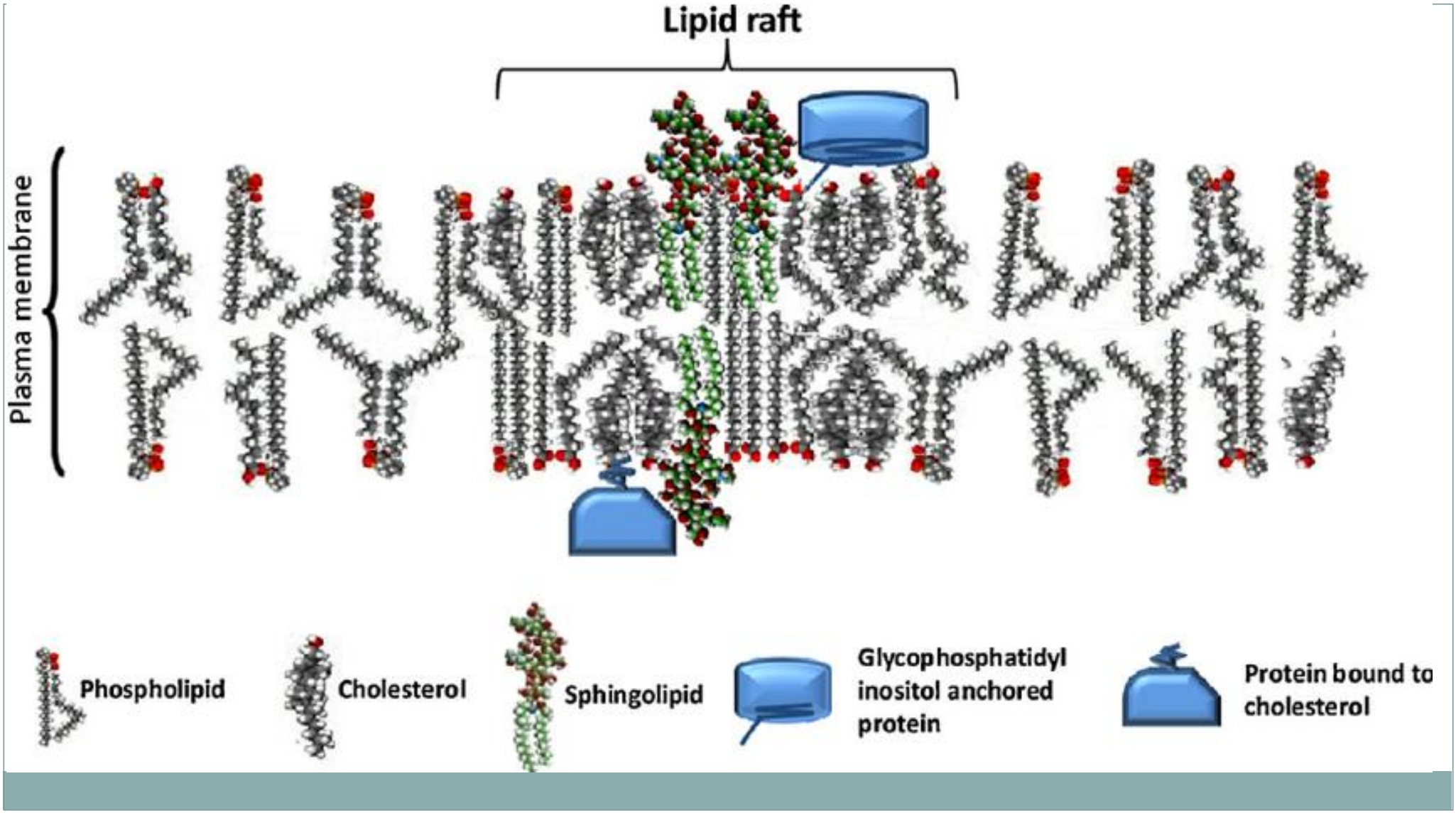
- **Differ in the kind and amount of lipids they contain**
- **Glycolipids are found only in the outer membrane surface**
- **20% of all membrane lipid is cholesterol**



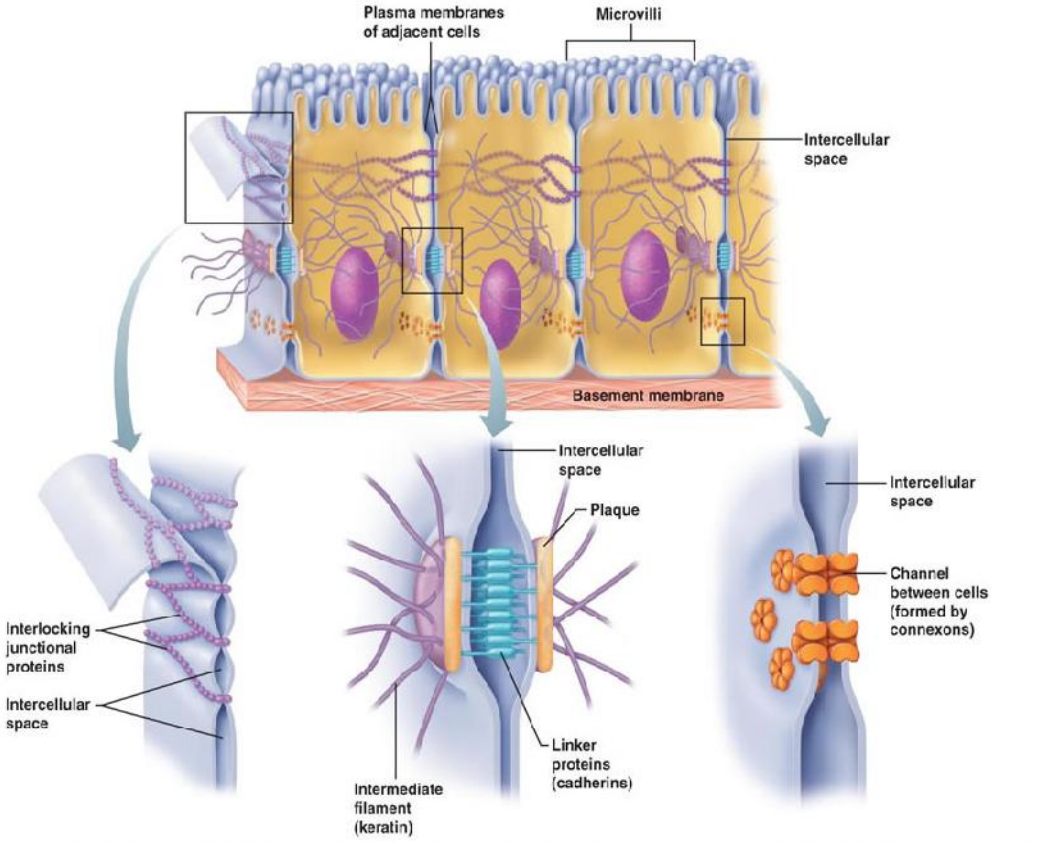
Lipid Rafts

- Make up 20% of the outer membrane surface
- **Composed of sphingolipids and cholesterol**
- **Are concentrating platforms for cell-signaling molecules**




Lipid raft
Plasma membrane
Phospholipid
Cholesterol
Sphingolipid
Glycophosphatidyl inositol anchored protein
Protein bound to cholesterol

Membrane Junctions

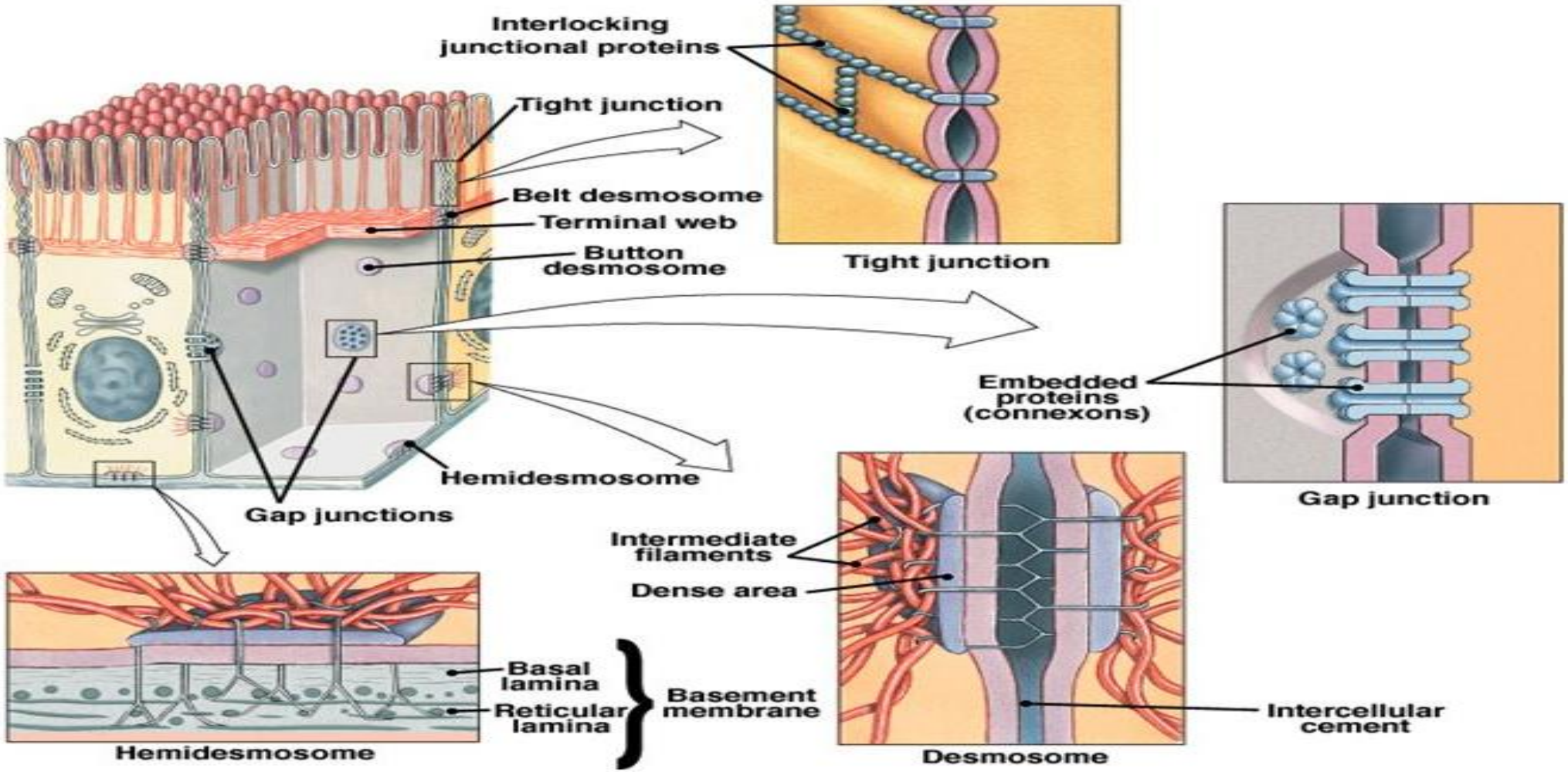


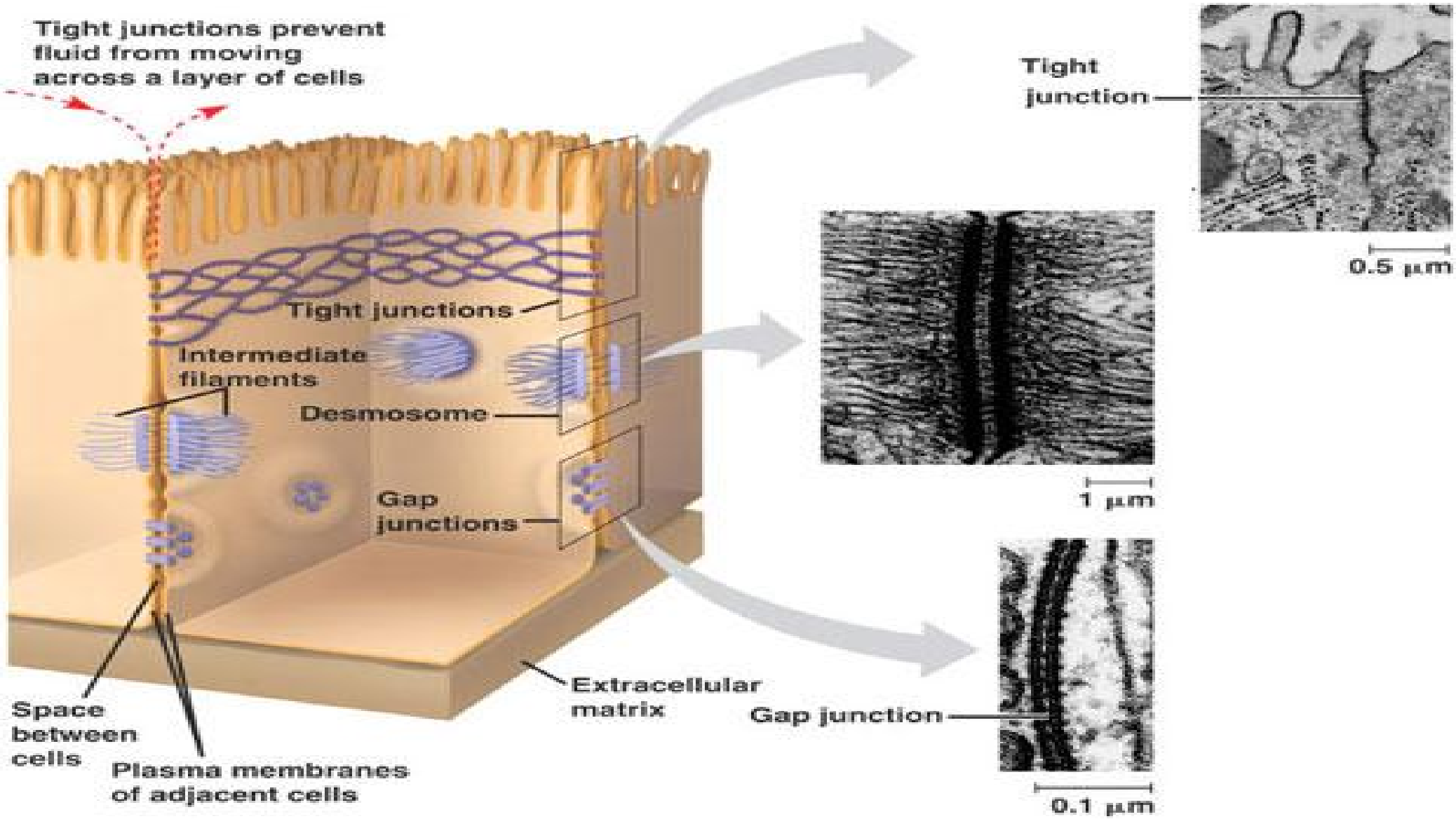
(a) Tight junctions: Impermeable junctions prevent molecules from passing through the intercellular space.

(b) Desmosomes: Anchoring junctions bind adjacent cells together like a molecular "Velcro" and help form an internal tension-reducing network of fibers.

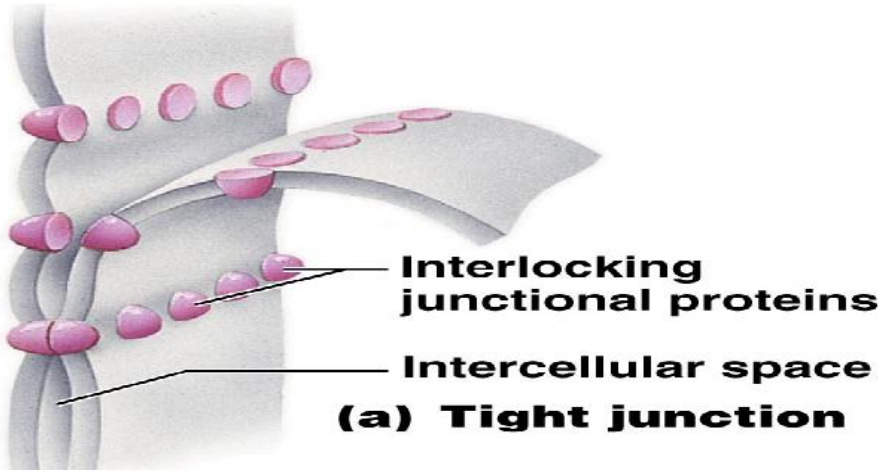
(c) Gap junctions: Communicating junctions allow ions and small molecules to pass for intercellular communication.

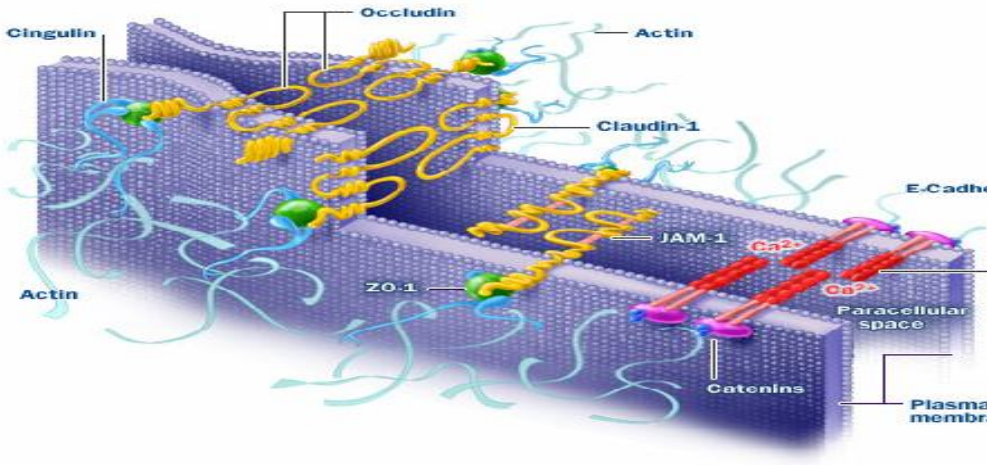
- **Tight junction – impermeable junction that encircles the cell**
- **Desmosome – anchoring junction scattered along the sides of cells**
- **Hemidesmosomes : basalmembrane to cell**
- **Gap junction – a nexus that allows chemical substances to pass between cells**

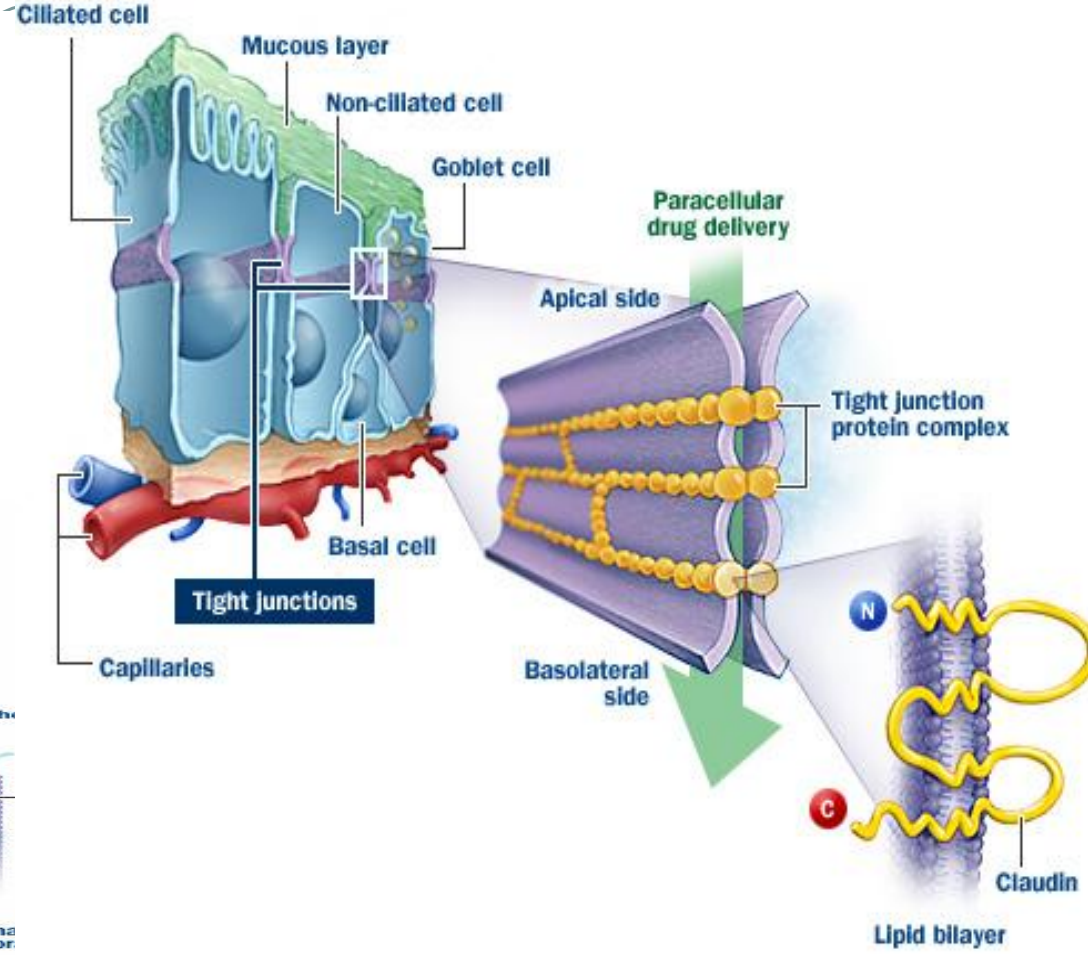

Interlocking junctional proteins
Tight junction
Belt desmosome
Terminal web
Button desmosome
Hemidesmosome
Gap junctions
Tight junction
Embedded proteins (connexons)
Gap junction
Intermediate filaments
Dense area
Intercellular cement
Desmosome
Basal lamina
Reticular lamina
Basement membrane
Hemidesmosome


Tight junctions prevent fluid from moving across a layer of cells
Tight junctions
Intermediate filaments
Desmosome
Gap junctions
Space between cells
Plasma membranes of adjacent cells
Extracellular matrix
Tight junction
0.5 µm
1 µm
Gap junction
0.1 µm

Membrane Junctions: Tight Junction





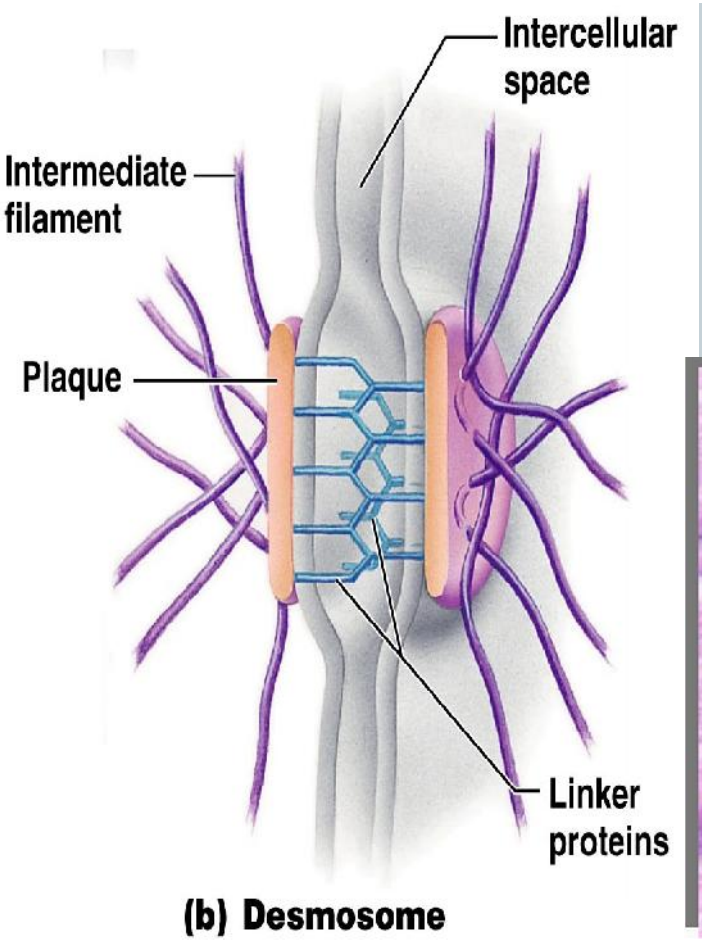


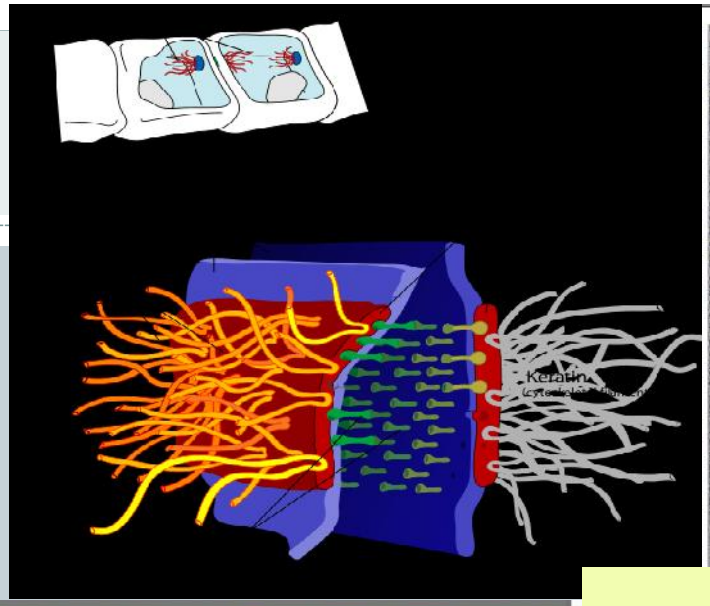
Tight junction

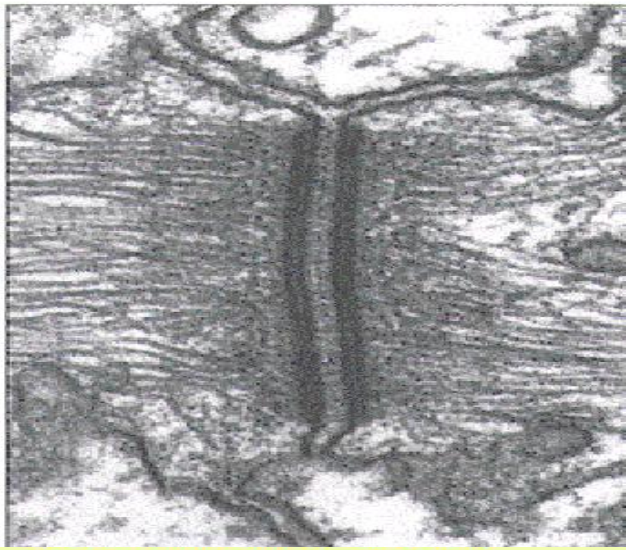
- Tight junctions are found in all tissues, but those of particular relevance to drug delivery include:
  - **Nasal tissue**
  - **Gastrointestinal tissue - where oral drugs are absorbed**
  - **Blood vessels**
  - **Blood-brain barrier**

- Tight junctions consist of proteins, for example:
  - **claudins**
  - **occludins**
  - **junctional adhesion**

Membrane Junctions: Desmosome

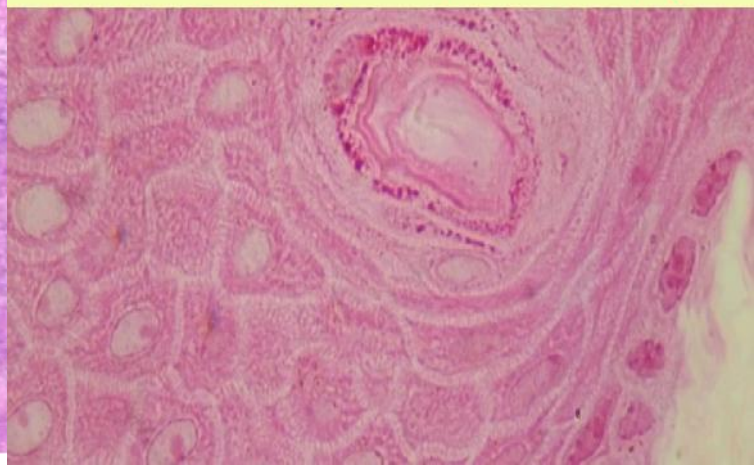




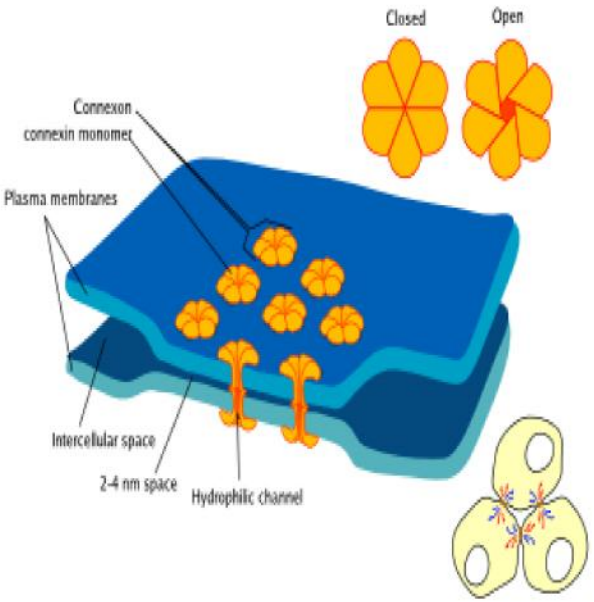


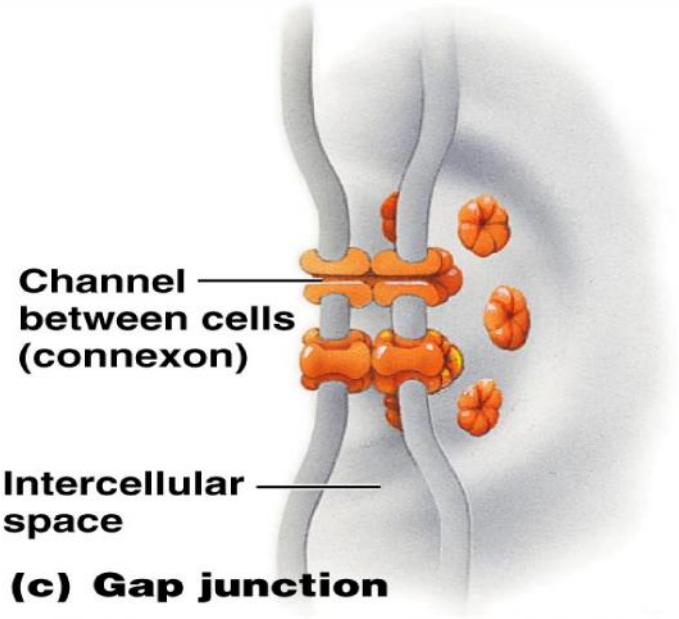
STRATUM SPINOSUM OF EPIDERMIS

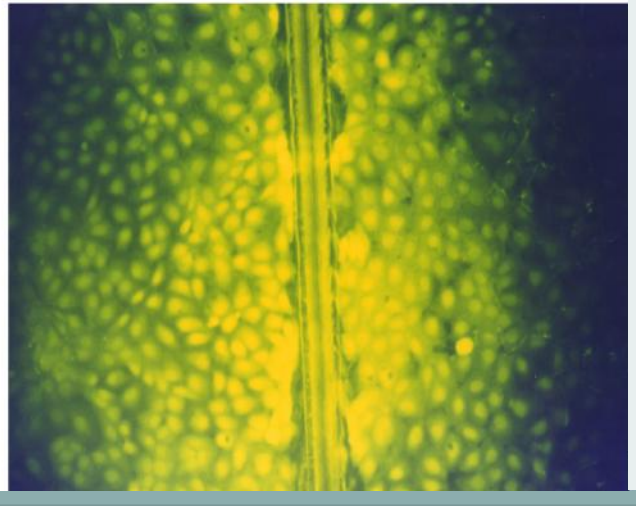
once cells shrink, intercellular junctions (desmosomes) make keratinocytes of stratum spinosum seem spiny



Membrane Junctions: Gap Junction = **nexus** or **macula communicans**







- **Protienaceous tubes that connect adjacent cells.**
- **These tubes allow material to pass from one cell to the next without having to pass through the plasma membranes of the cells.**
- **Dissolved substances such as ions or glucose can pass through the gap junctions.**
- **Large organelles such as mitochondria connot pass.**
- ***Ca++ control of gap junction opening***
- Gap junctions occur in virtually all tissues of the body, with the **exception of adult fully developed skeletal muscle and mobile cell types such as sperm or erythrocytes.**

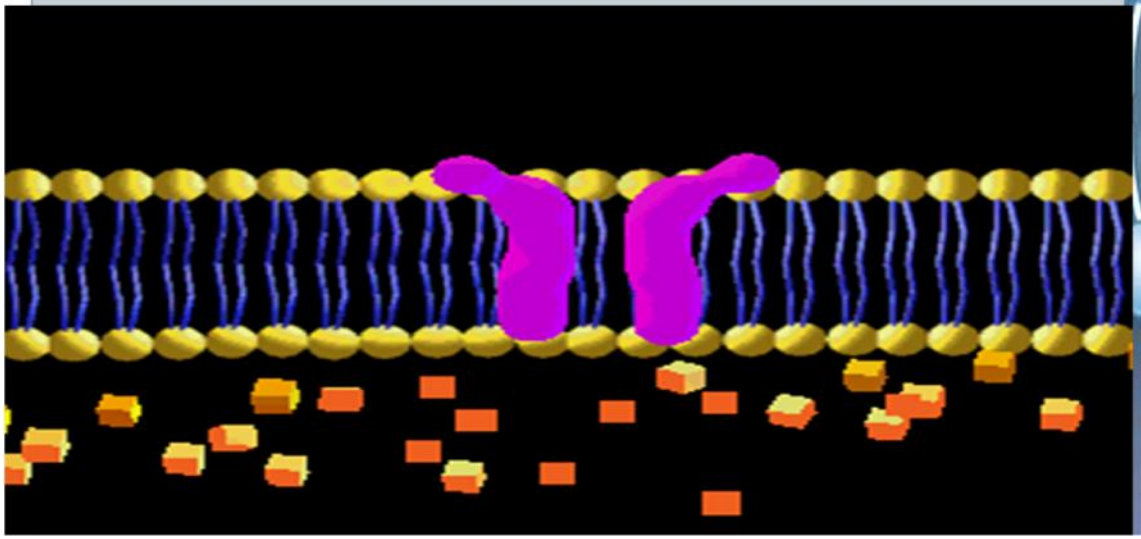
Passive Membrane Transport: Diffusion

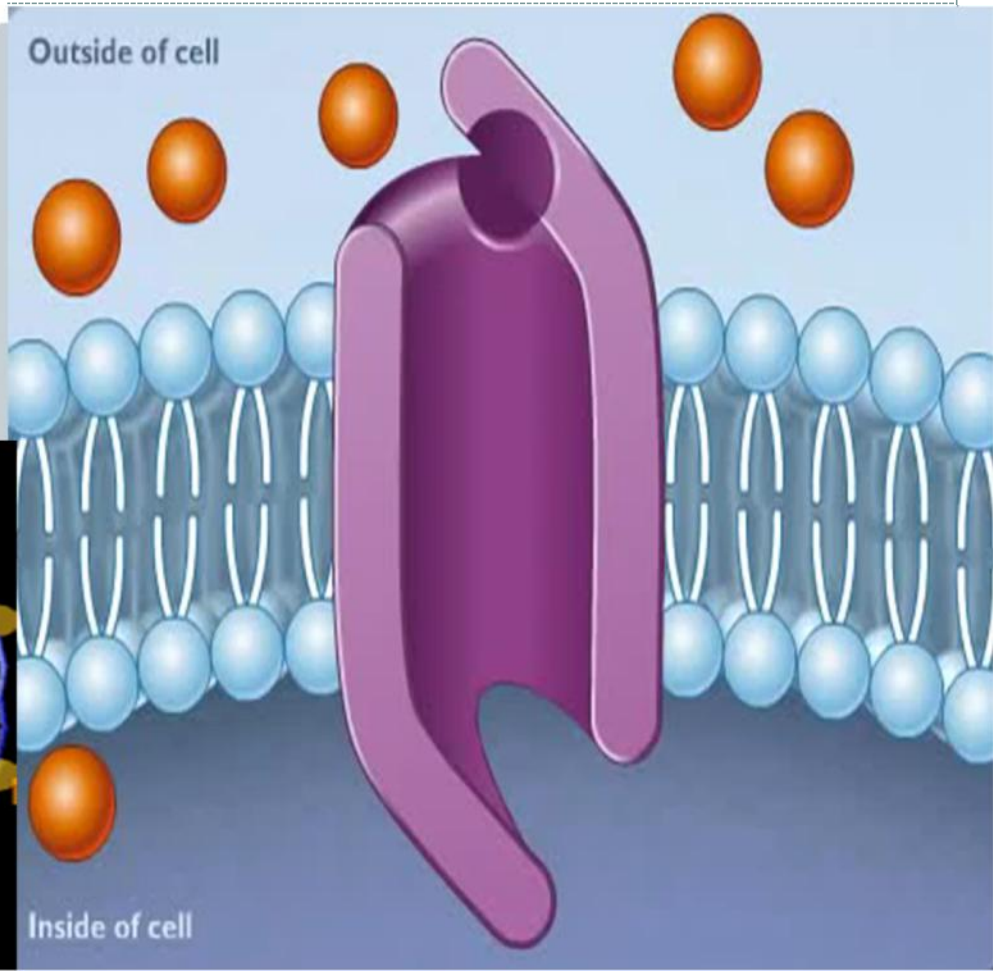
I/ Simple diffusion

II/ Facilitated diffusion

Passive Membrane Transport: Diffusion

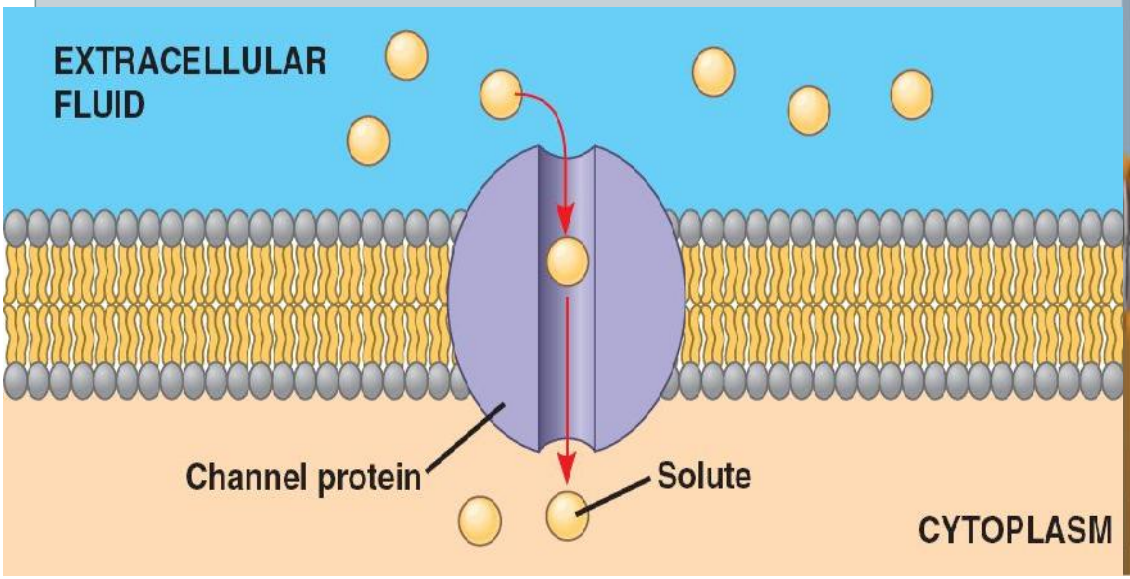
- **Simple diffusion** – nonpolar and lipid-soluble substances
  - **Diffuse directly through the lipid bilayer**
  - **Diffuse through channel proteins**

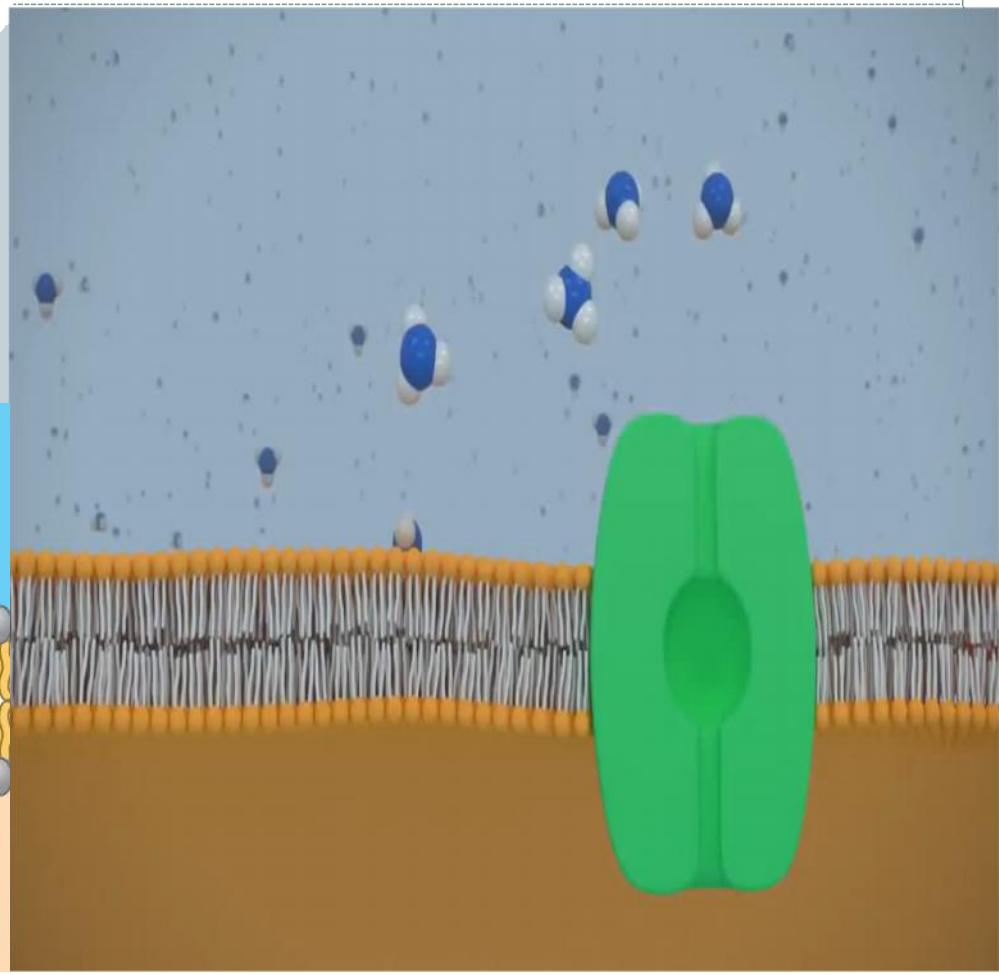




Passive Membrane Transport: Diffusion

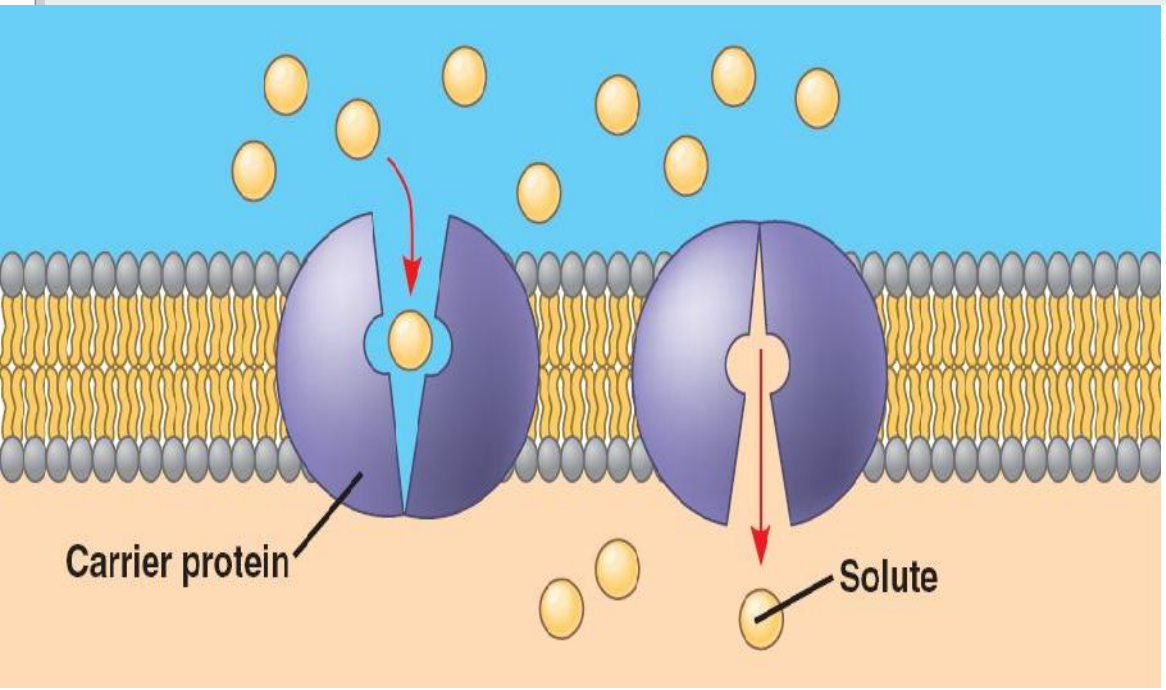
- **Facilitated diffusion**
  - Transport of glucose, amino acids, and ions
  - Transported **substances bind carrier proteins or pass through protein channels**

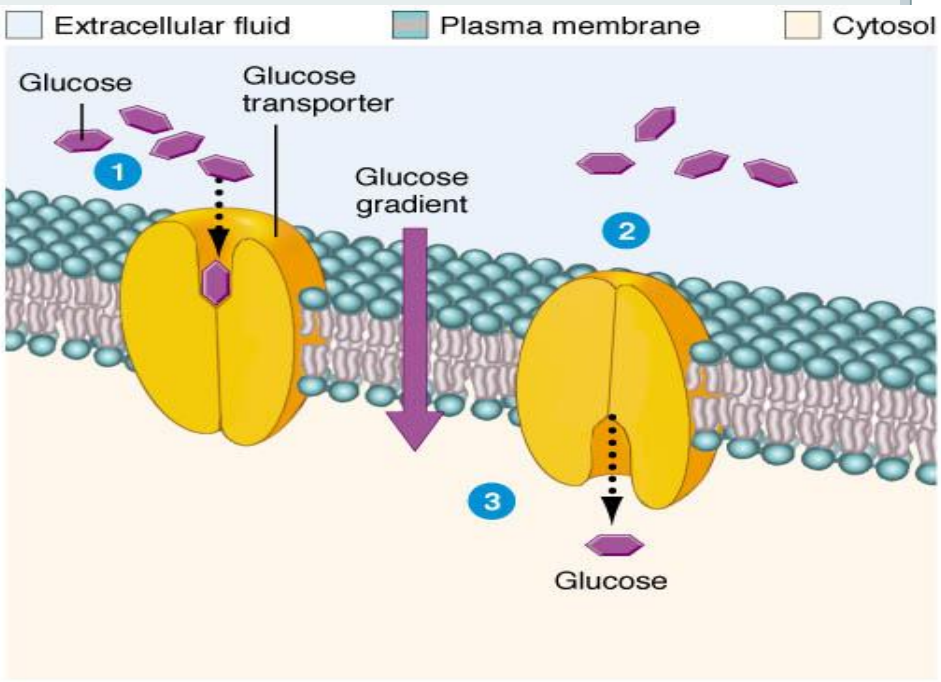




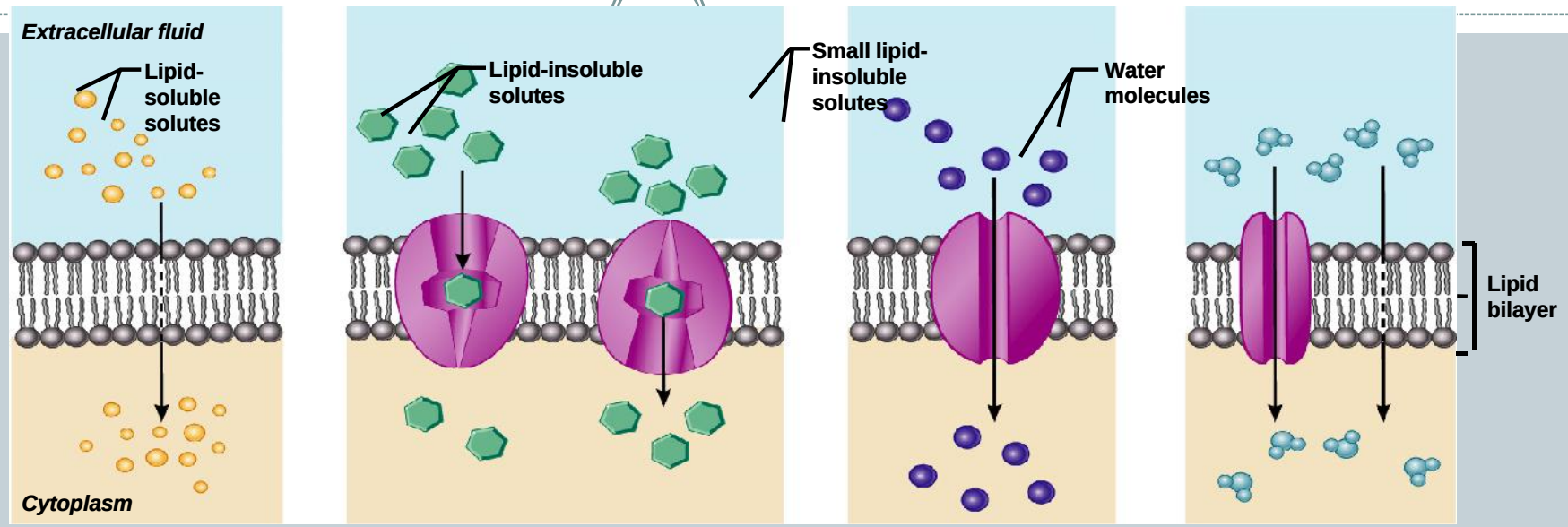
Carrier Proteins

- Are integral transmembrane proteins
- Show specificity for certain polar molecules including sugars and amino acids





Diffusion Through the Plasma Membrane



(a) Simple diffusion directly through the phospholipid bilayer

(b) Carrier-mediated facilitated diffusion via protein carrier specific for one chemical; binding of substrate causes shape change in transport protein

(c) Channel-mediated facilitated diffusion through a channel protein; mostly ions selected on basis of size and charge

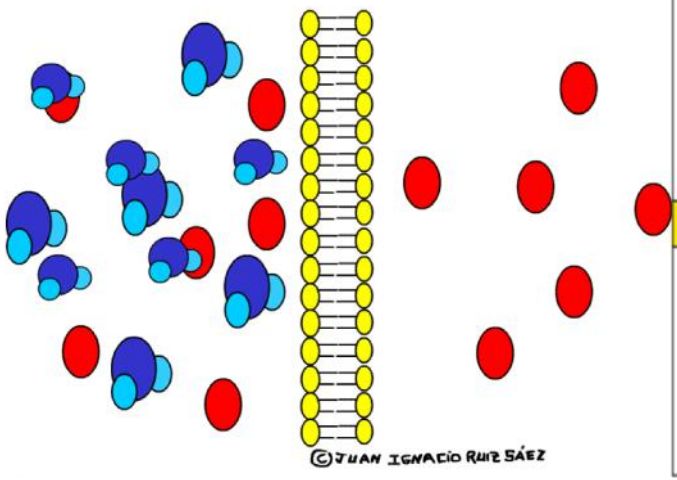
(d) Osmosis, diffusion through a specific channel protein (aquaporin) or through the lipid bilayer

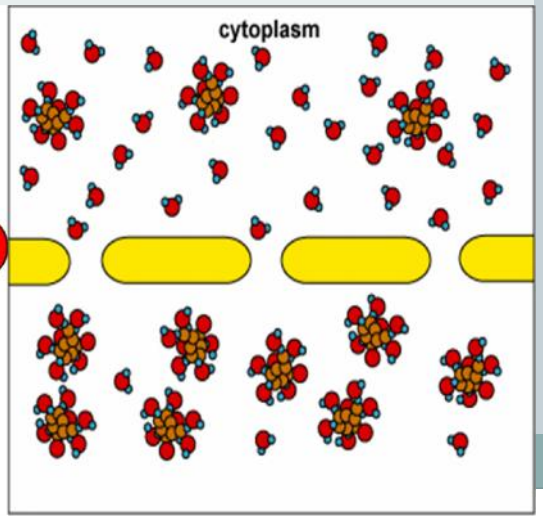
Effects of Solutions of Varying Tonicity

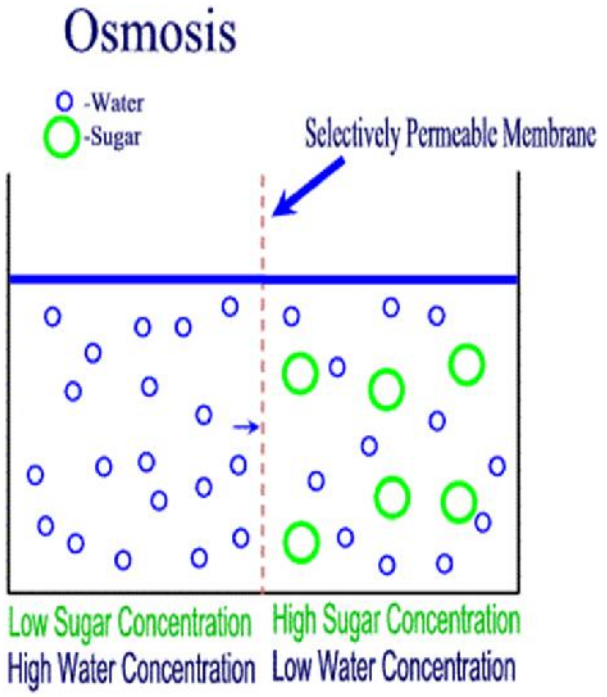
- **Isotonic** – solutions with the same solute concentration as that of the cytosol
- **Hypertonic** – solutions having greater solute concentration than that of the cytosol
- **Hypotonic** – solutions having lesser solute concentration than that of the cytosol

Passive Membrane Transport: **Osmosis**

- **Osmosis is the diffusion of water** through a cell membrane from a solution *of* ***low*** **solute concentration to a solution with high solute** concentration, up a solute concentration gradient.
- It is a **physical process** in which a **solvent moves, without input of energy**, across a **semi permeable membrane (permeable to the solvent, but not the solute)** separating two solutions of different concentrations.
- **Osmosis releases energy, and can be made to do work, as when a growing tree-root splits a stone**.







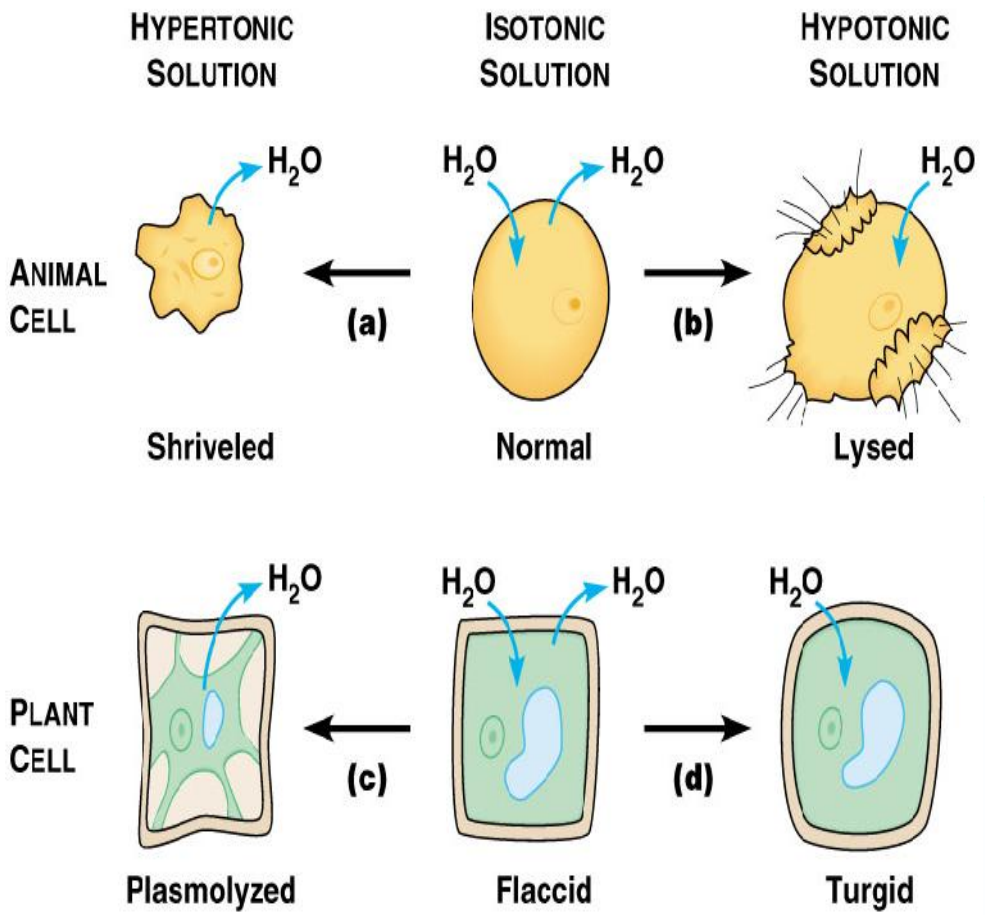
Passive Membrane Transport: **Osmosis**

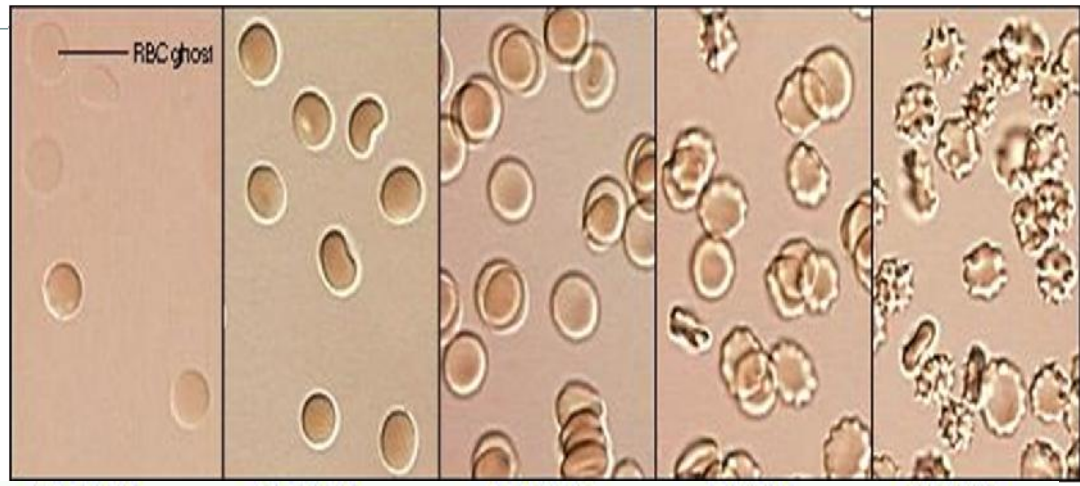
- **Occurs when the concentration of a solvent is different on opposite sides of a membrane**
- **Diffusion of water across a semipermeable membrane**

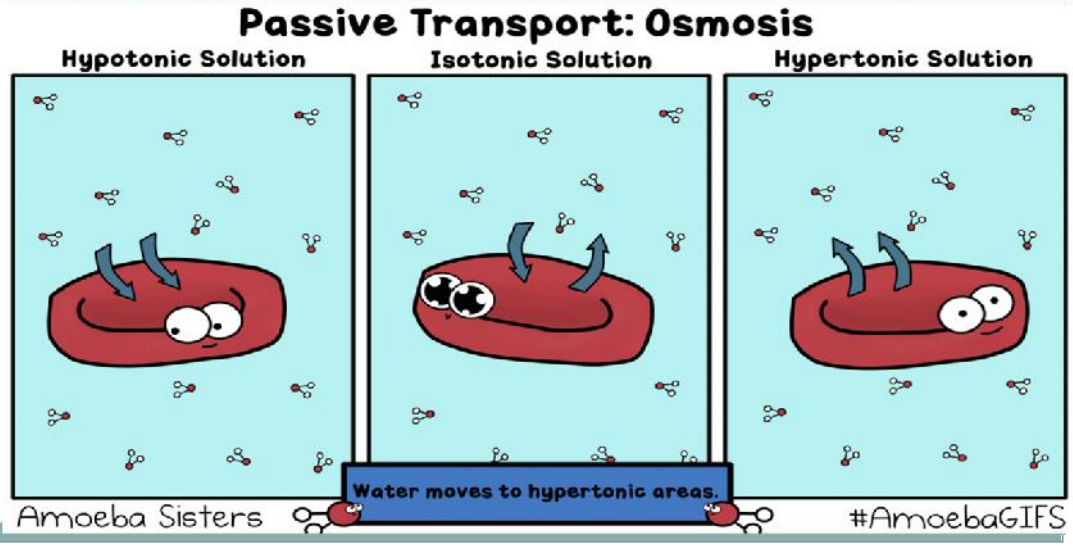
- **Osmolarity – total concentration of solute particles in a solution**
- **Tonicity – how a solution affects cell volume**

It has been estimated that an amount of water equivalent to roughly 250 times the volume of the cell diffuses across the red blood cell membrane *every second*; the cell doesn't lose or gain water because equal amounts go in and out.

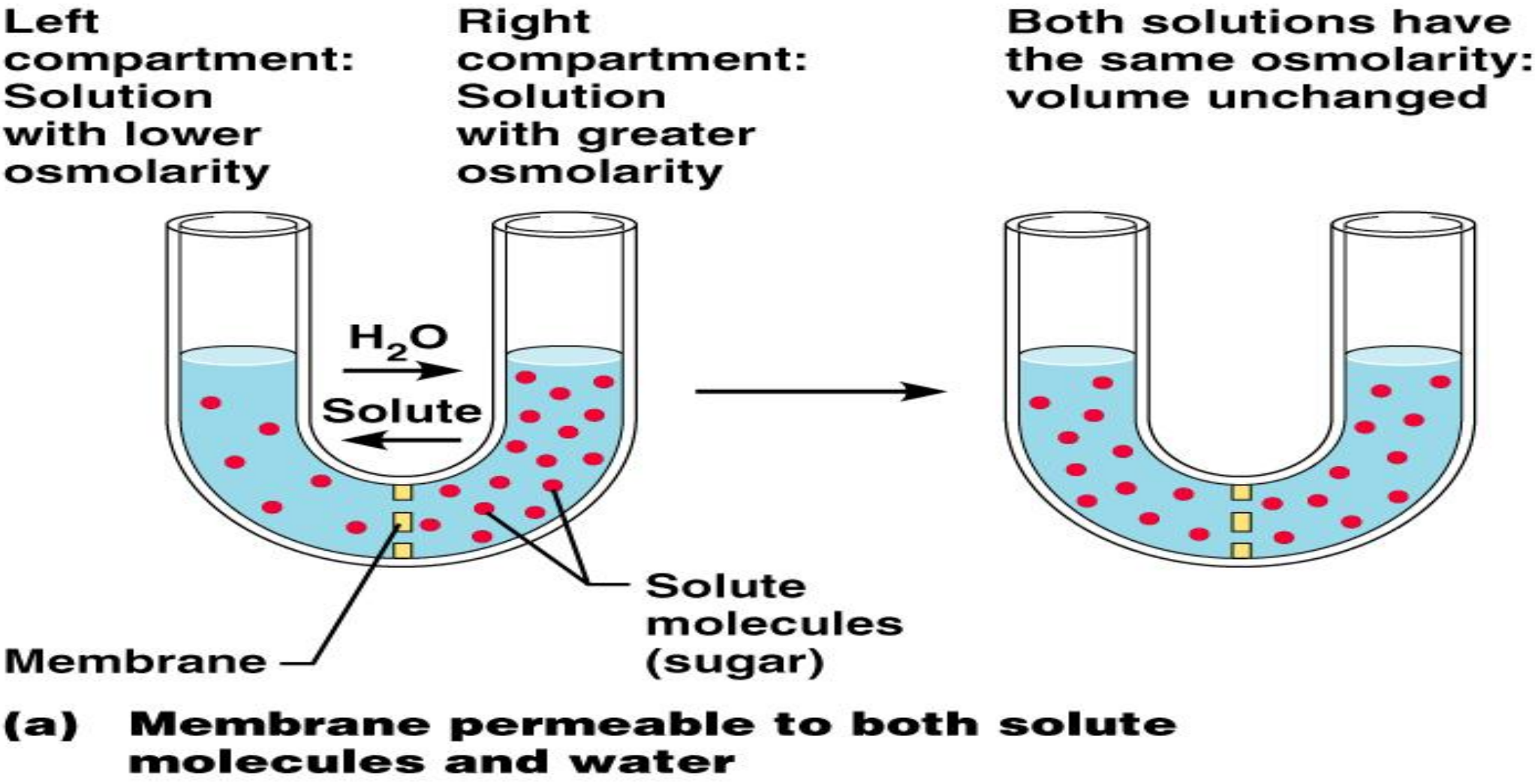
Osmotic pressure affects cell shape and life





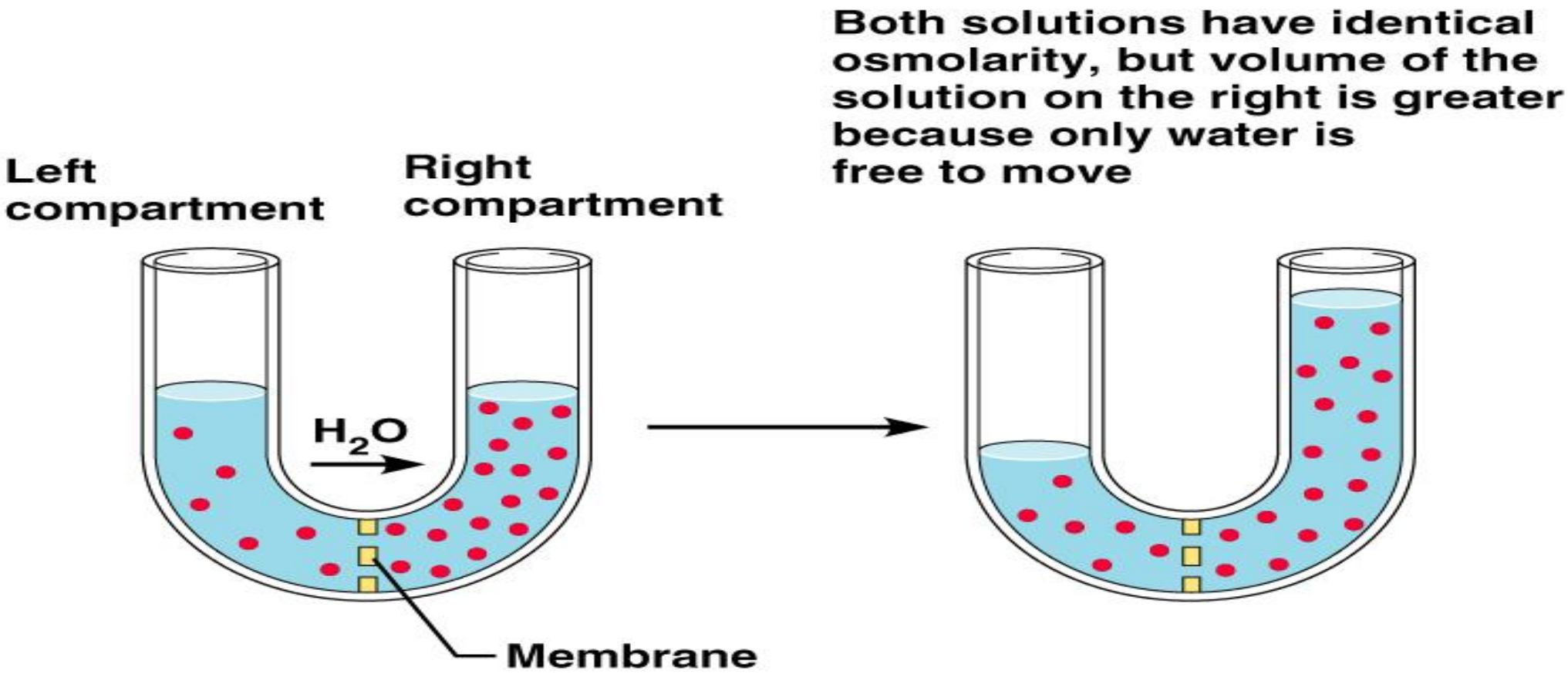


Effect of Membrane Permeability on Diffusion and Osmosis



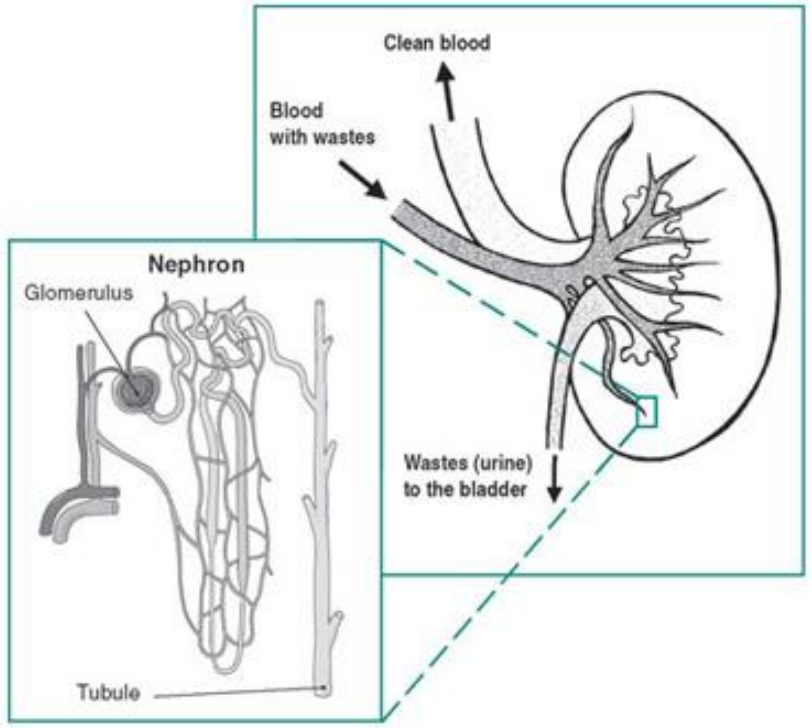
(a) Membrane permeable to both solute molecules and water

Effect of Membrane Permeability on Diffusion and Osmosis



(b) Membrane impermeable to solute molecules, permeable to water

Why this is important biologically



Kidney function is dependent upon ion and water transport

Passive Membrane Transport: Filtration

- The passage of water and solutes through a membrane by hydrostatic pressure
- Pressure gradient pushes solute-containing fluid from a higher-pressure area to a lower-pressure area

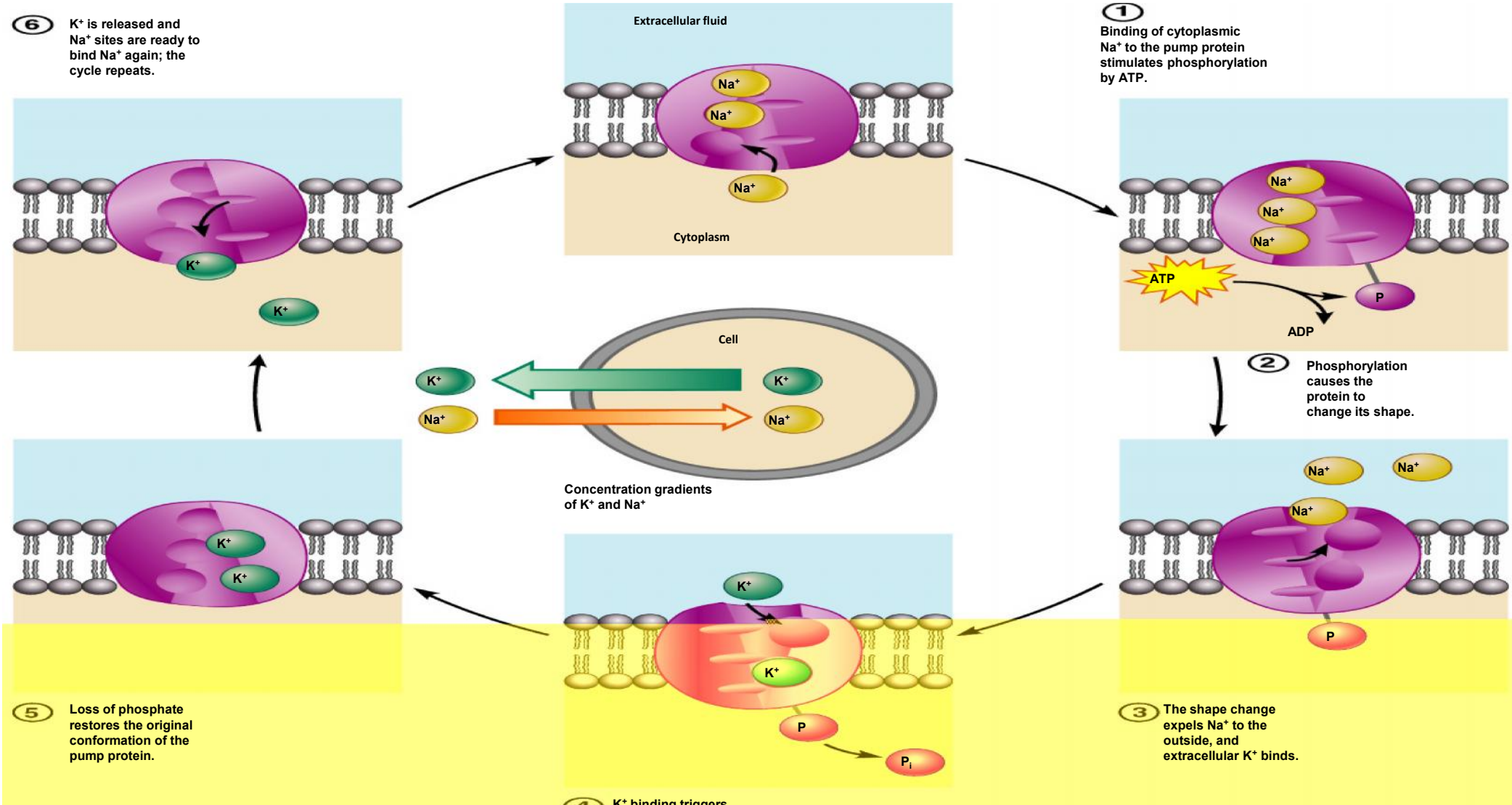

6
K+ is released and Na+ sites are ready to bind Na+ again; the cycle repeats.
Extracellular fluid
Na+
Na+
Na+
Cytoplasm
1
Binding of cytoplasmic Na+ to the pump protein stimulates phosphorylation by ATP.
Na+
Na+
Na+
ATP
P
ADP
K+
K+
Cell
K+
K+
Na+
Na+
2
Phosphorylation causes the protein to change its shape.
Concentration gradients of K+ and Na+
K+
K+
Na+
Na+
Na+
Na+
P
K+
K+
K+
P
Pi
5
Loss of phosphate restores the original conformation of the pump protein.
4
K+ binding triggers release of the phosphate group.
3
The shape change expels Na+ to the outside, and extracellular K+ binds.

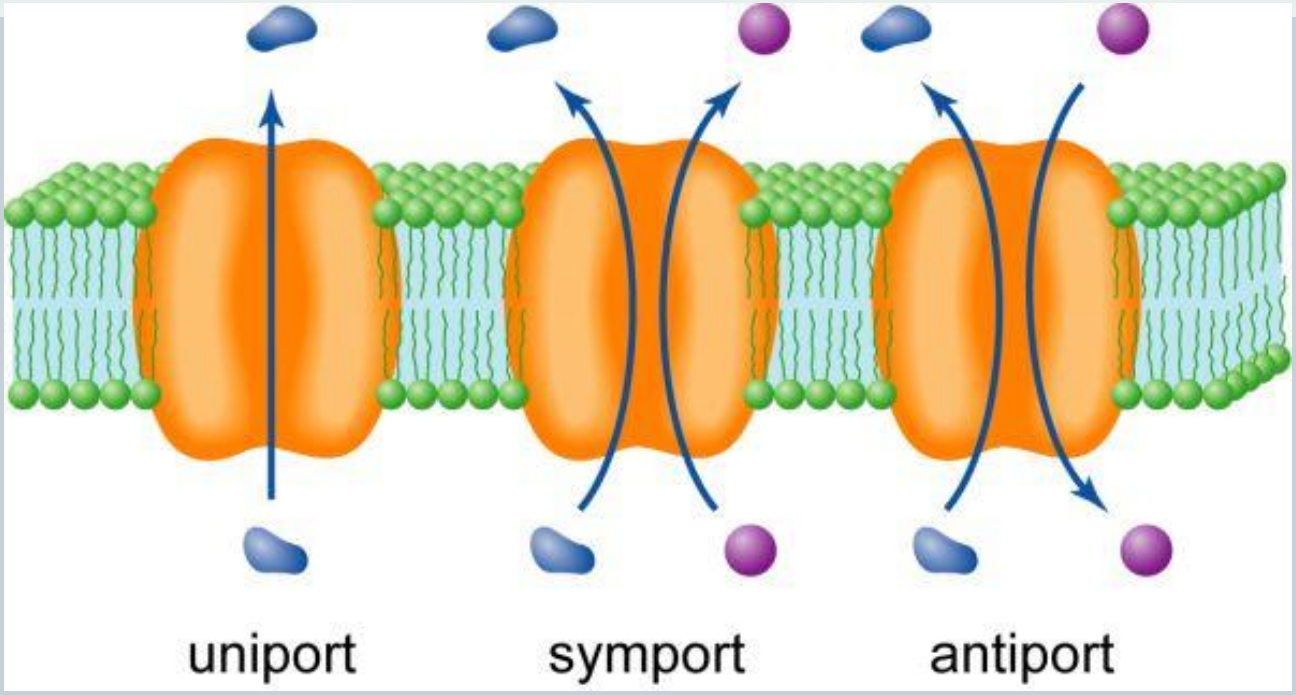
Figure 3.10

Active Transport

- **Uses ATP** to move solutes across a membrane
- **Requires carrier proteins**

Types of Active Transport

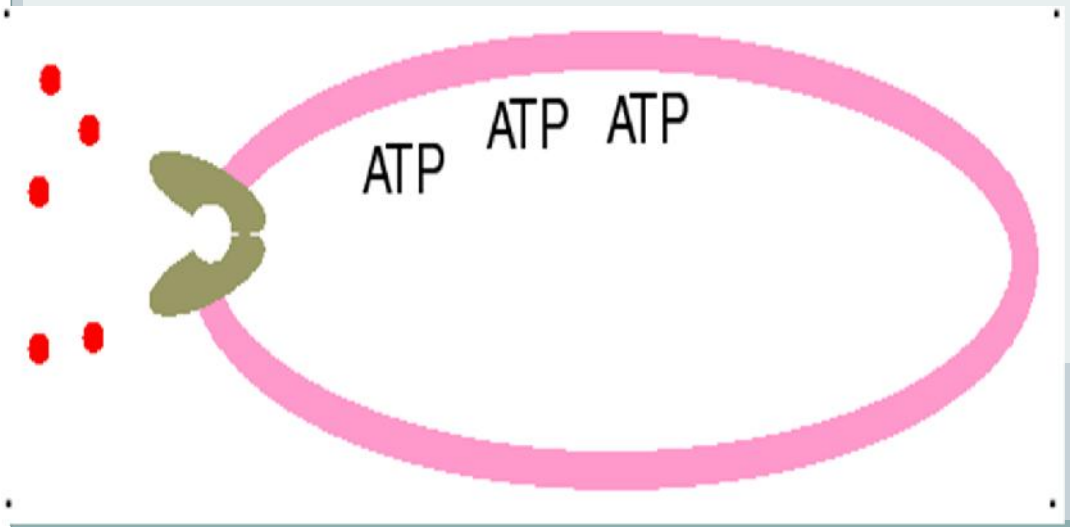
- **Symport system** – two substances are moved across a membrane in the ***same direction***
- **Antiport system** – two substances are moved across a membrane in ***opposite directions***

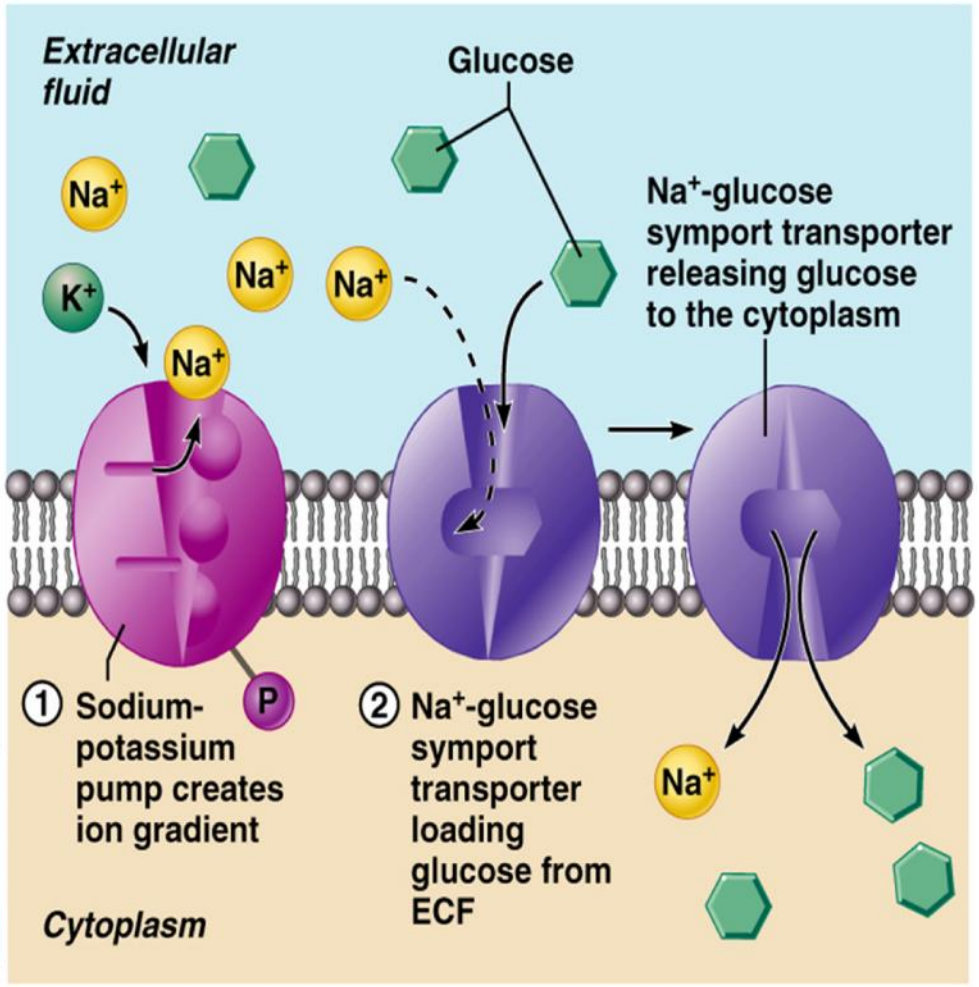


Types of Active Transport

- **Primary active transport** – **hydrolysis of ATP** phosphorylates the transport protein causing conformational change

- **Secondary active transport** – use of an **exchange pump (such as the Na^+-K^+ pump)** indirectly to drive the transport of other solutes[ATP-ASE]

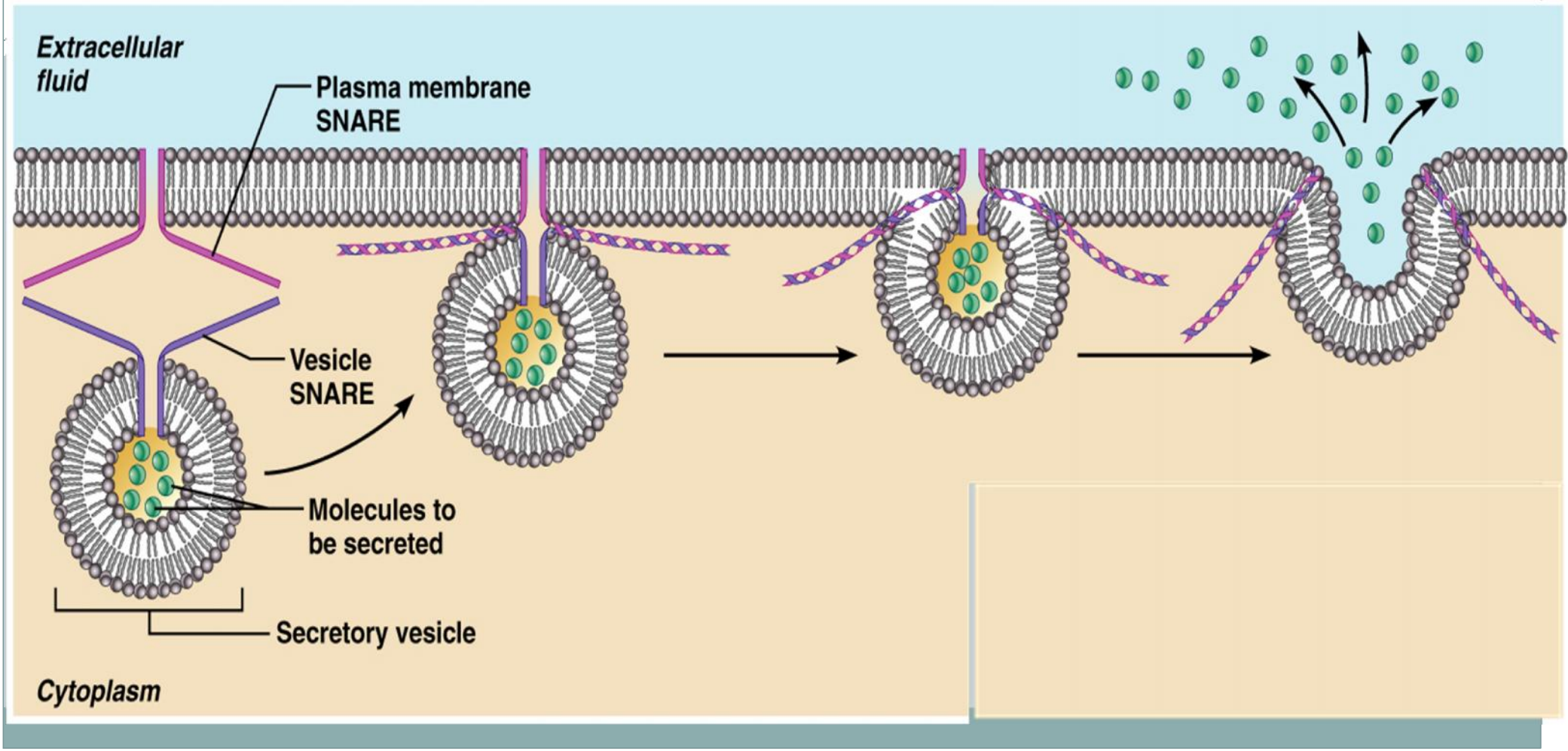




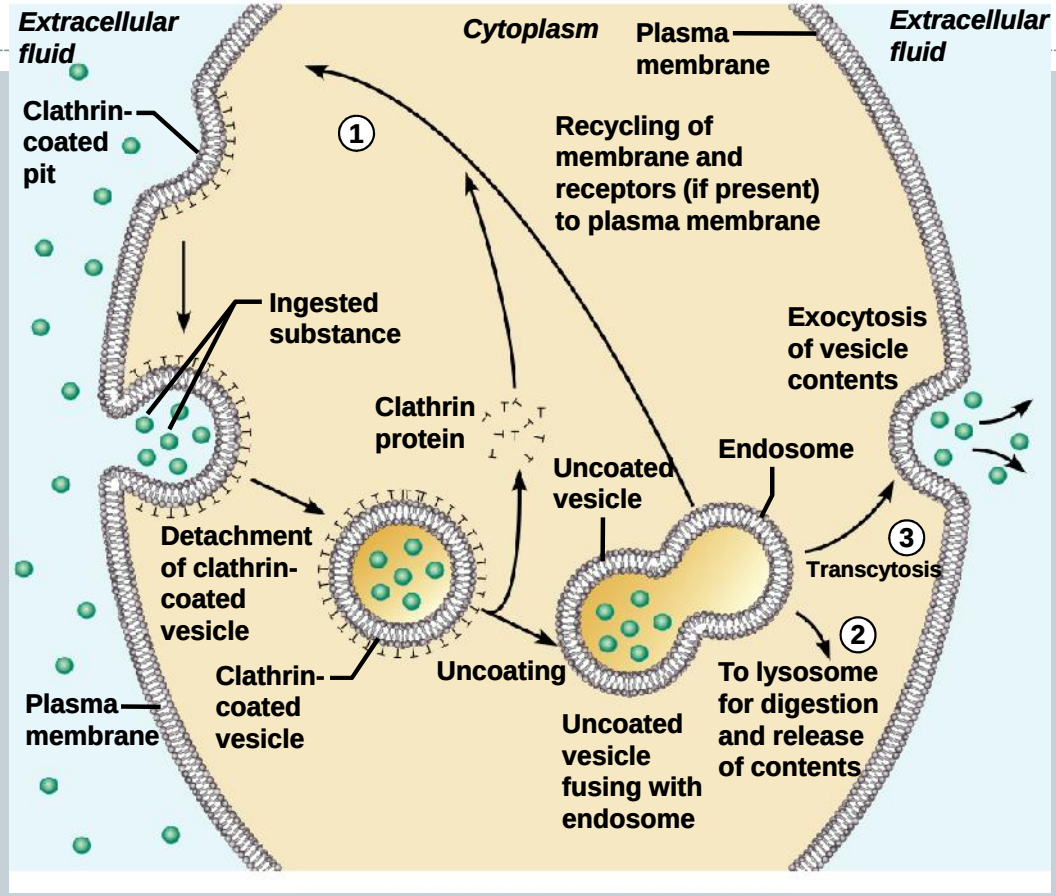
Vesicular Transport

- **Transport of large particles and macromolecules across plasma membranes**
  - **Exocytosis** – moves substance from the cell interior to the extracellular space
  - **Endocytosis** – enables large particles and macromolecules to enter the cell
  - **Transcytosis** – moving substances into, across, and then out of a cell
  - **Vesicular trafficking** – moving substances from one area in the cell to another
  - **Phagocytosis** – pseudopods engulf solids and bring them into the cell's interior
- **Fluid-phase endocytosis** – the plasma membrane infolds, bringing extracellular fluid and solutes into the interior of the cell
- **Receptor-mediated endocytosis** – clathrin-coated pits provide the main route for endocytosis and transcytosis
- **Non-clathrin-coated vesicles** – caveolae that are platforms for a variety of signaling molecules

Exocytosis


Extracellular fluid
Plasma membrane SNARE
Vesicle SNARE
Molecules to be secreted
Secretory vesicle
Cytoplasm

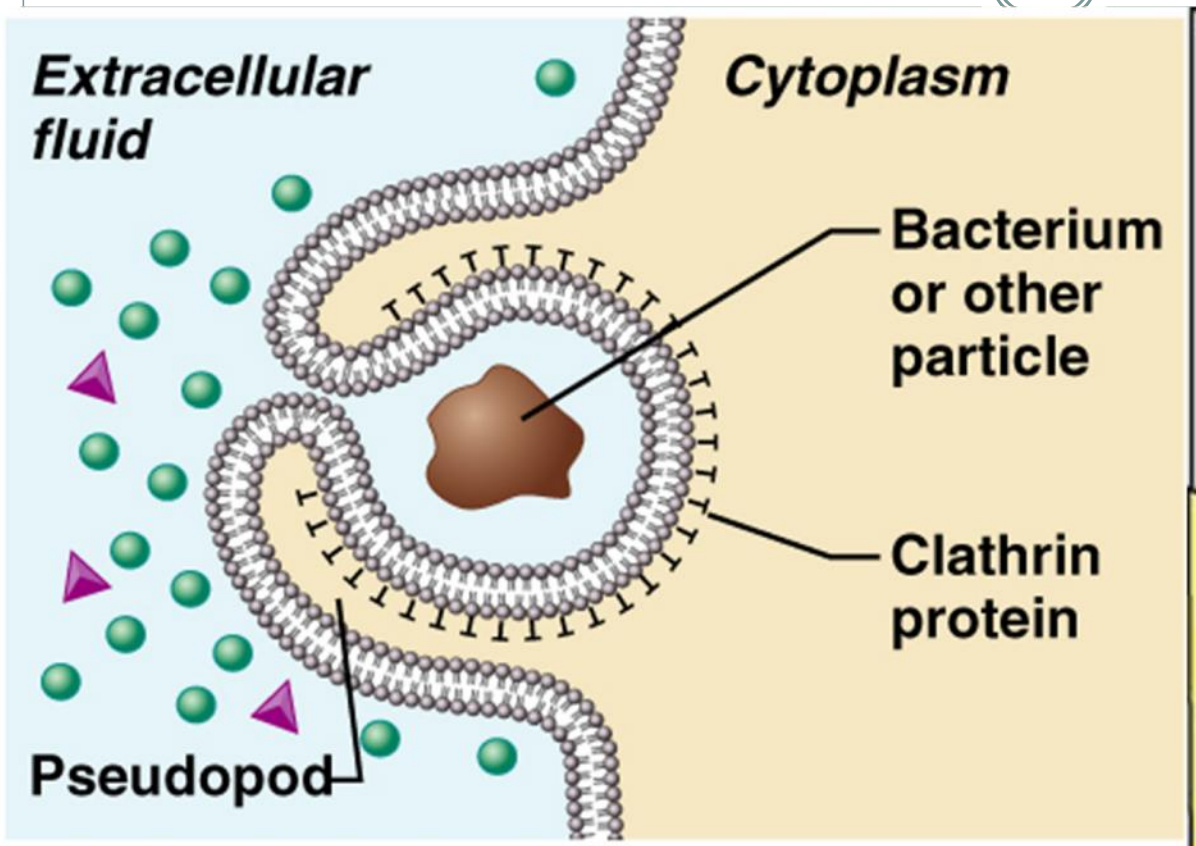
Clathrin-Mediated Endocytosis



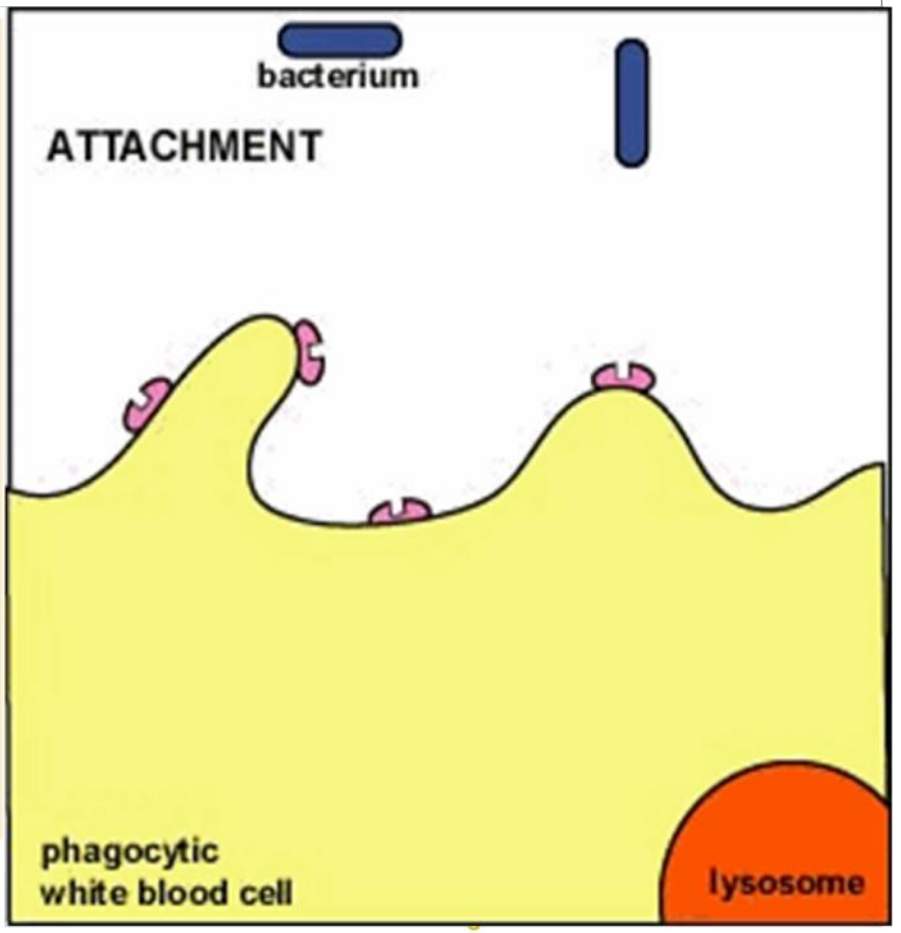
(a) Clathrin-mediated endocytosis

Figure 3.13a

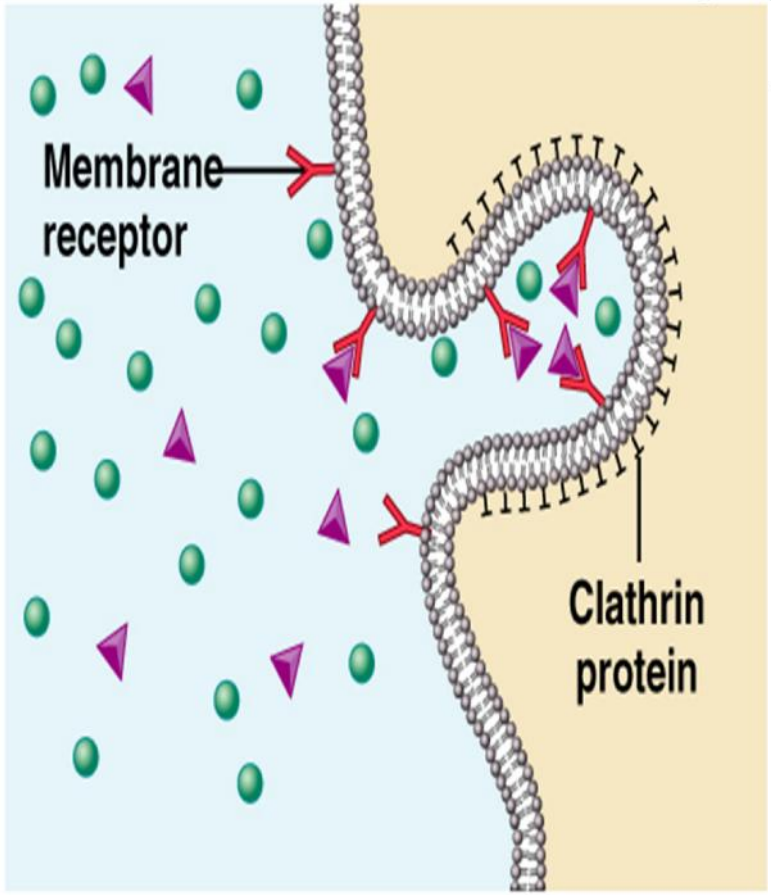
Phagocytosis



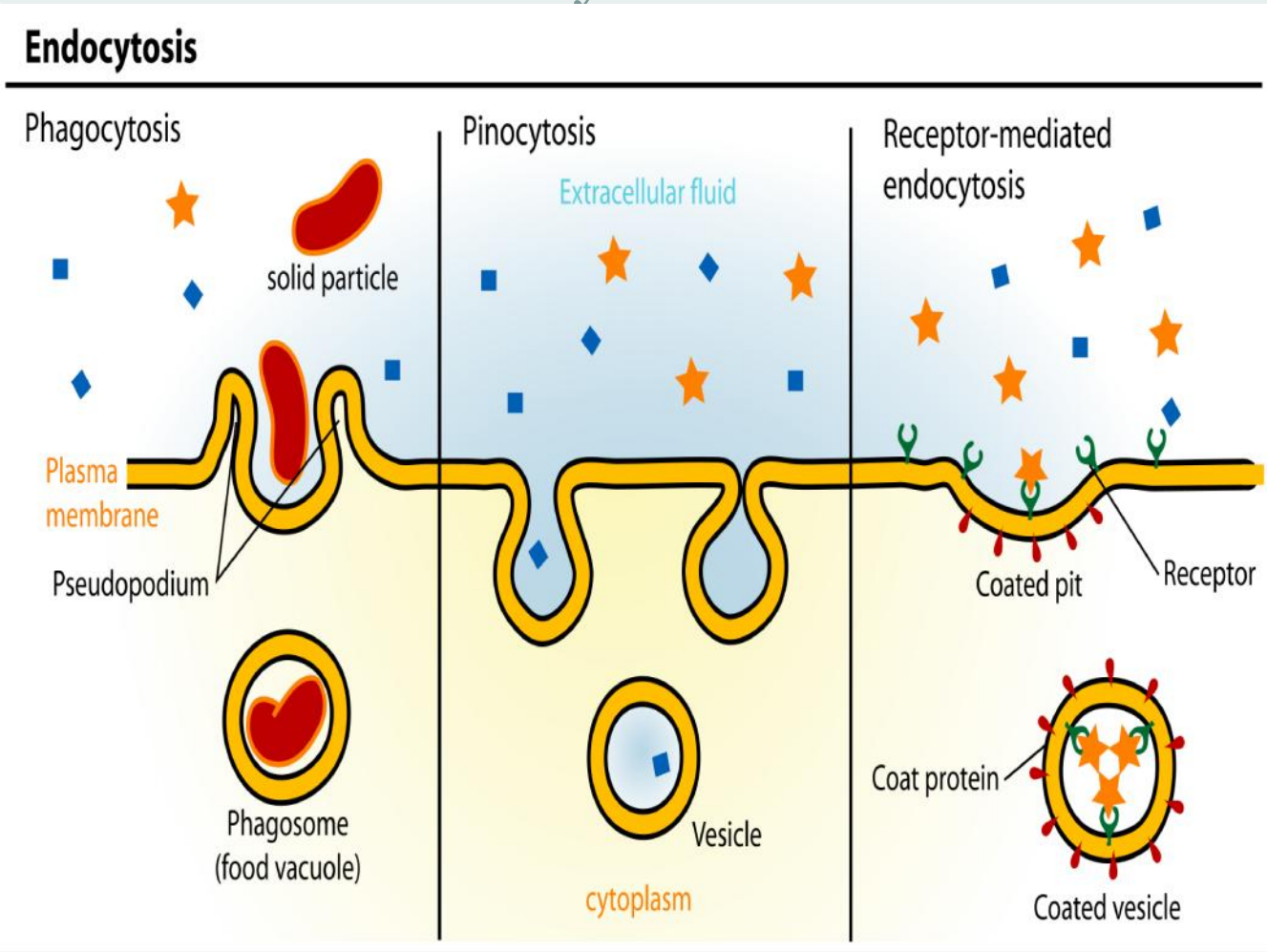
(b) Phagocytosis



Receptor Mediated Endocytosis



(c) Receptor-mediated endocytosis



Passive (Physical) Processes

- Require no cellular energy and include:
  - Simple diffusion
  - Facilitated diffusion
  - Osmosis
  - Filtration

Active (Physiological) Processes

- Require cellular energy and include:
  - Active transport
  - Endocytosis
  - Exocytosis
  - Transcytosis

Passive Membrane Transport – Review

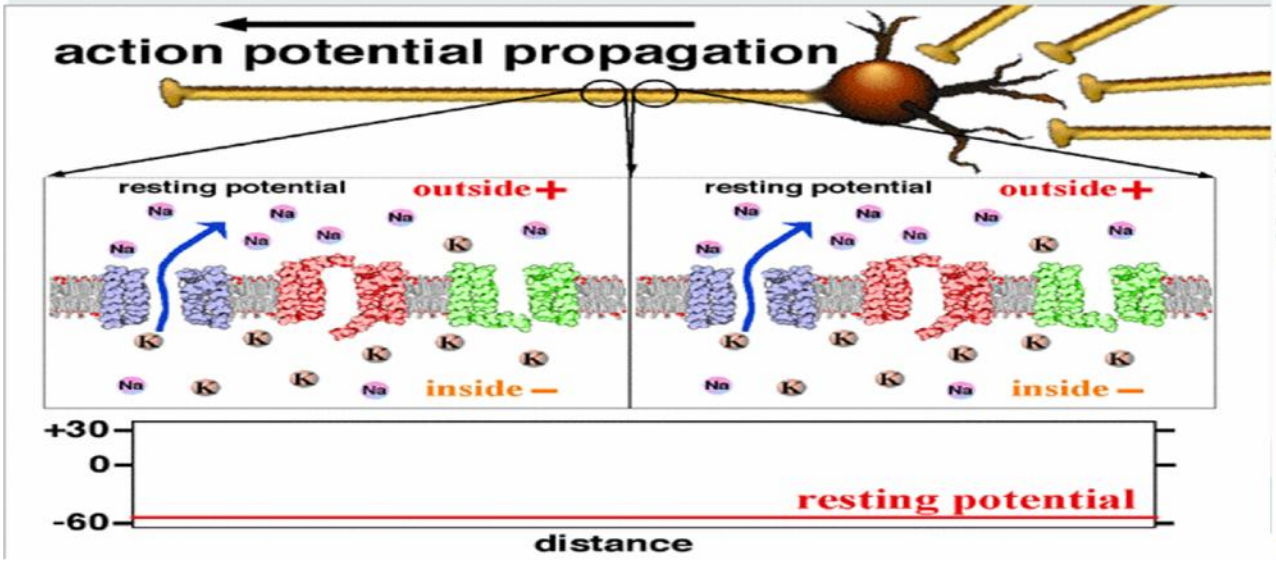
Process	Energy Source	Example
Simple diffusion	Kinetic energy	Movement of O_2 through membrane
Facilitated diffusion	Kinetic energy	Movement of glucose into cells
Osmosis	Kinetic energy	Movement of H_2O in & out of cells
Filtration	Hydrostatic pressure	Formation of kidney filtrate

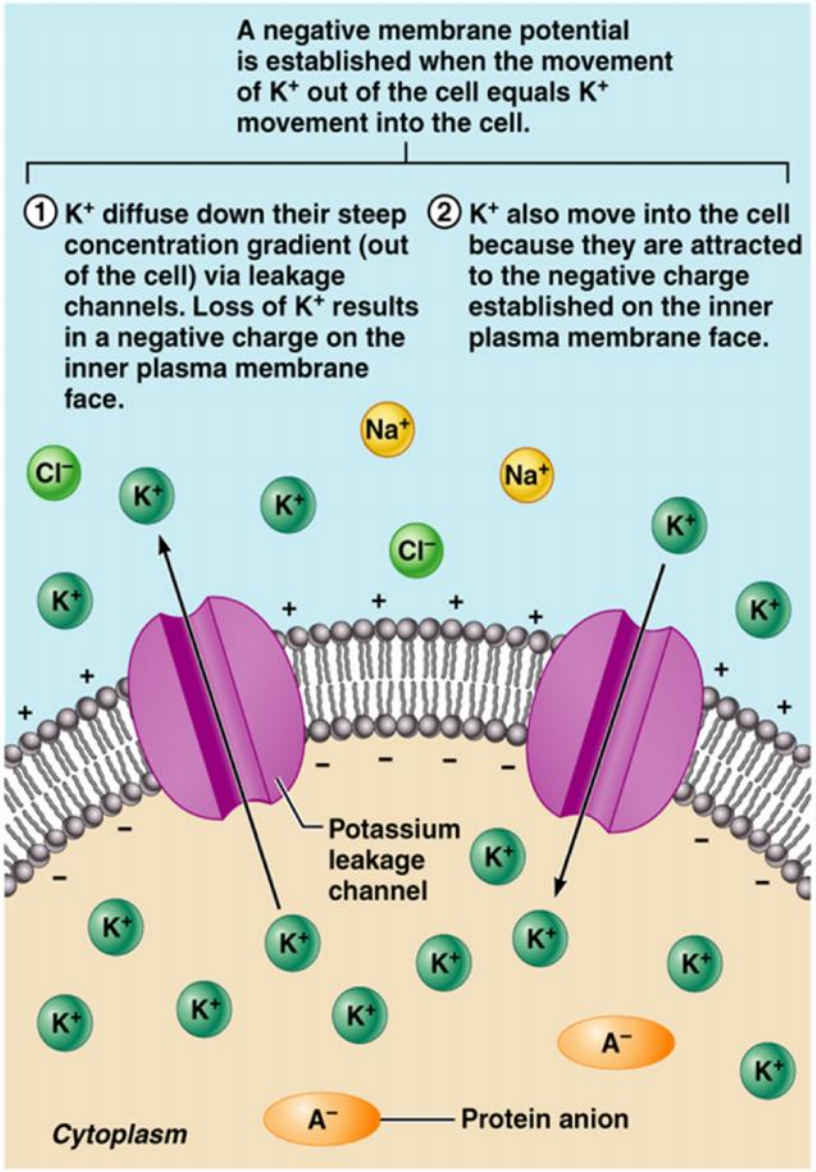
Active Membrane Transport – Review

Process	Energy Source	Example
Active transport of solutes	ATP	Movement of ions across membranes
Exocytosis	ATP	Neurotransmitter secretion
Endocytosis	ATP	White blood cell phagocytosis
Fluid-phase endocytosis	ATP	Absorption by intestinal cells
Receptor-mediated endocytosis	ATP	Hormone and cholesterol uptake
Endocytosis via caveoli	ATP	Cholesterol regulation
Endocytosis via coatomer vesicles	ATP	Intracellular trafficking of molecules

Membrane Potential

- Voltage across a membrane
- Resting membrane potential – the point where K^+ potential is balanced by the membrane potential
  - Ranges from –20 to –200 mV
  - Results from Na^+ and K^+ concentration gradients across the membrane
  - Differential permeability of the plasma membrane to Na^+ and K^+
- Steady state – potential maintained by active transport of ions

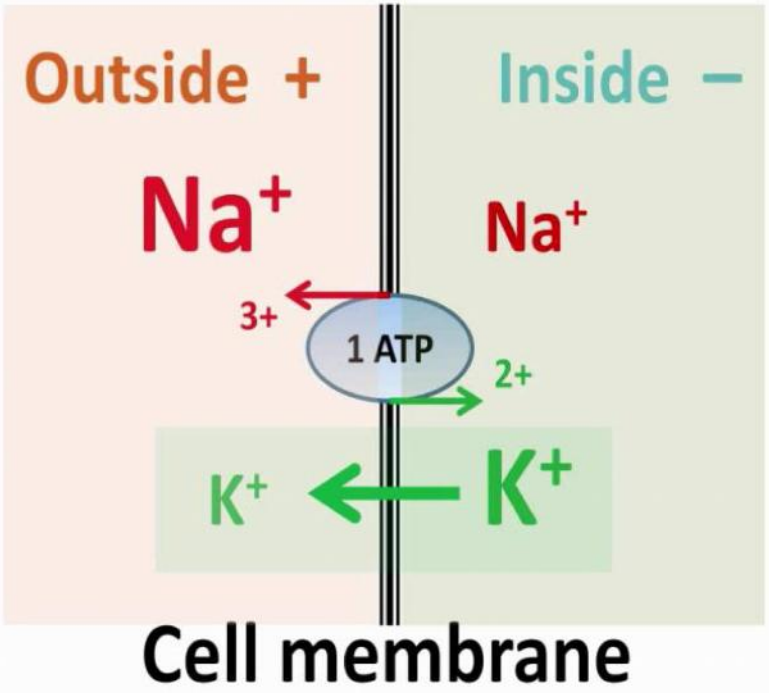


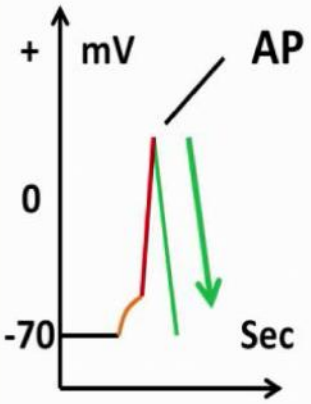


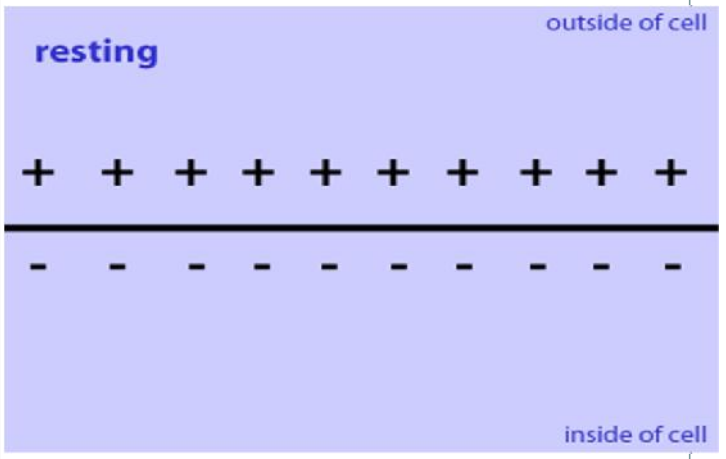
Action Potential (AP): Repolarization

Na^+ channels close, K^+ channels open; K^+ diffusion

TP: +30 mV back to -70 mV



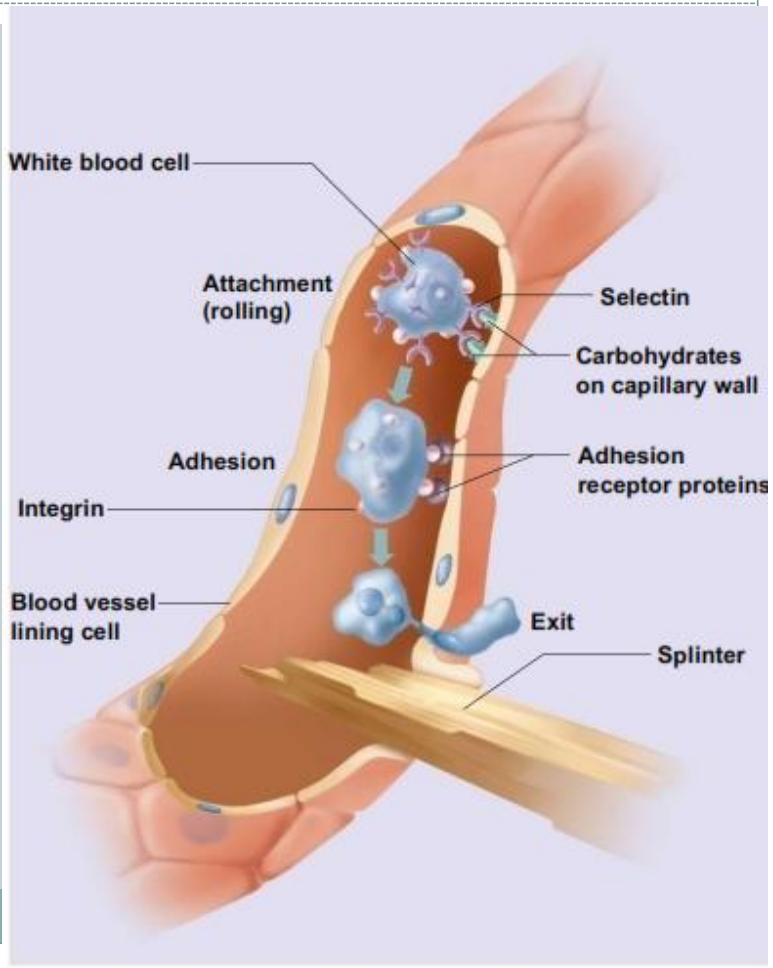




Faulty Ion Channels Cause Disease

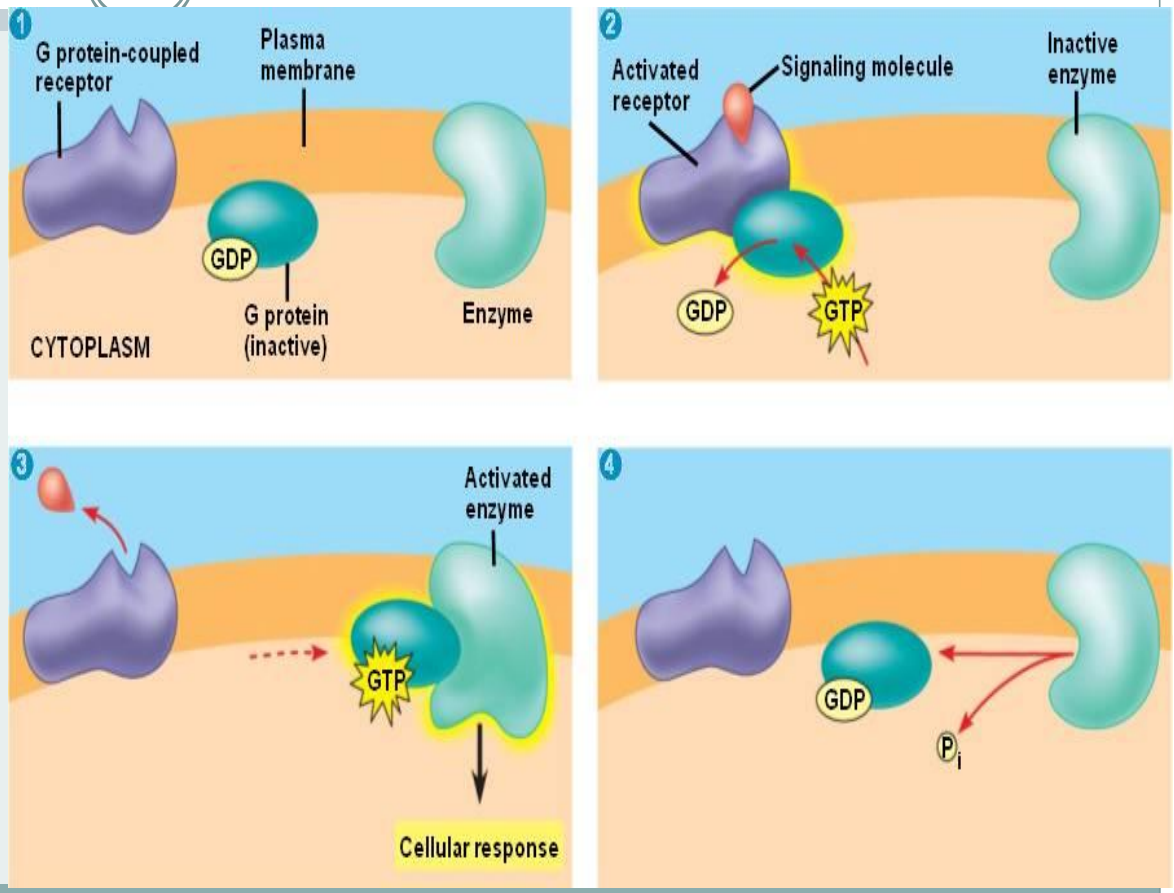
Cell Adhesion Molecules (CAMs)

- Anchor cells to the extracellular matrix
- Assist in movement of cells past one another
- Rally protective white blood cells to injured or infected areas
- Guide cells on the move
- Selectin – allows white blood cells to “anchor”
- Integrin – guides white blood cells through capillary walls
- Important for growth of embryonic tissue
- Important for growth of nerve cells



Roles of Membrane Receptors

- **Contact signaling** – important in normal development and immunity
- **Electrical signaling** – voltage-regulated "ion gates" in nerve and muscle tissue
- **Chemical signaling** – **neurotransmitters** bind to chemically gated channel-linked receptors in nerve and muscle tissue
- **G protein-linked receptors** – ligands bind to a receptor which activates a G protein, causing the release of a second messenger, such as cyclic AMP



Operation of a G Protein

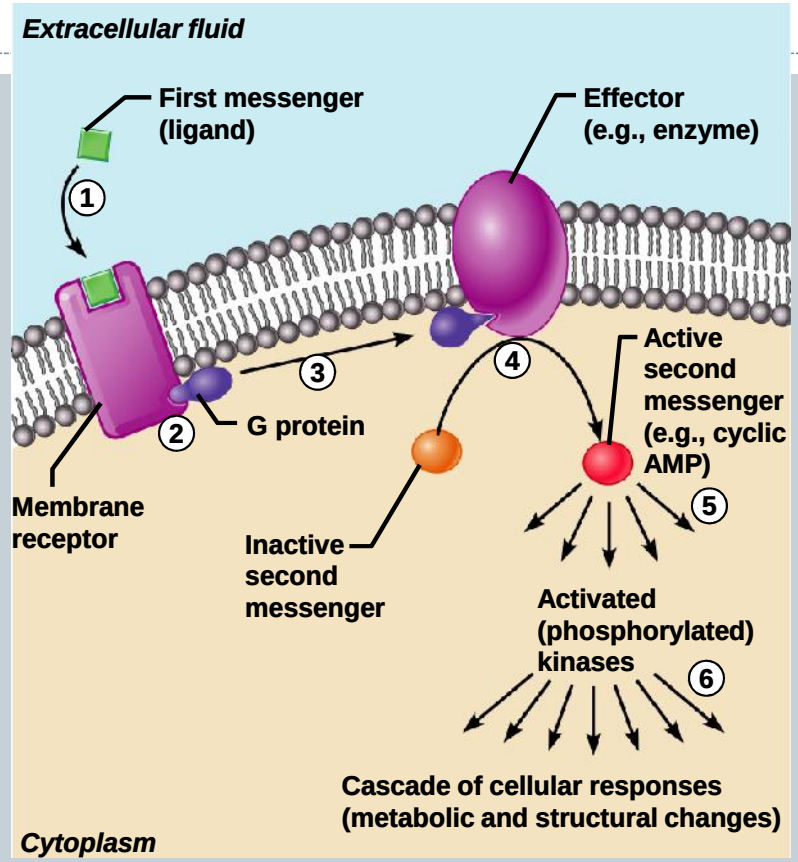


Figure 3.16

Cytoplasm

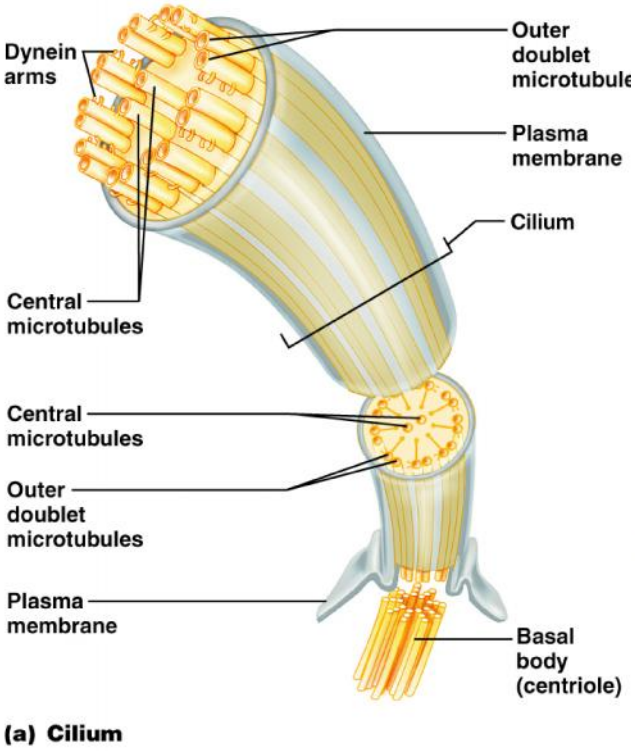
- **Cytoplasm – material between plasma membrane and the nucleus**
- **Cytosol – largely water with dissolved protein, salts, sugars, and other solutes**
- **The cytosol (cf. *cytoplasm*, which also includes the organelles) is the internal fluid of the cell, and where a portion of cell metabolism occurs.**
  - **Proteins within the cytosol play an important role in signal transduction pathways and glycolysis.**
  - **They also act as intracellular receptors and form part of the ribosomes, enabling protein synthesis.**

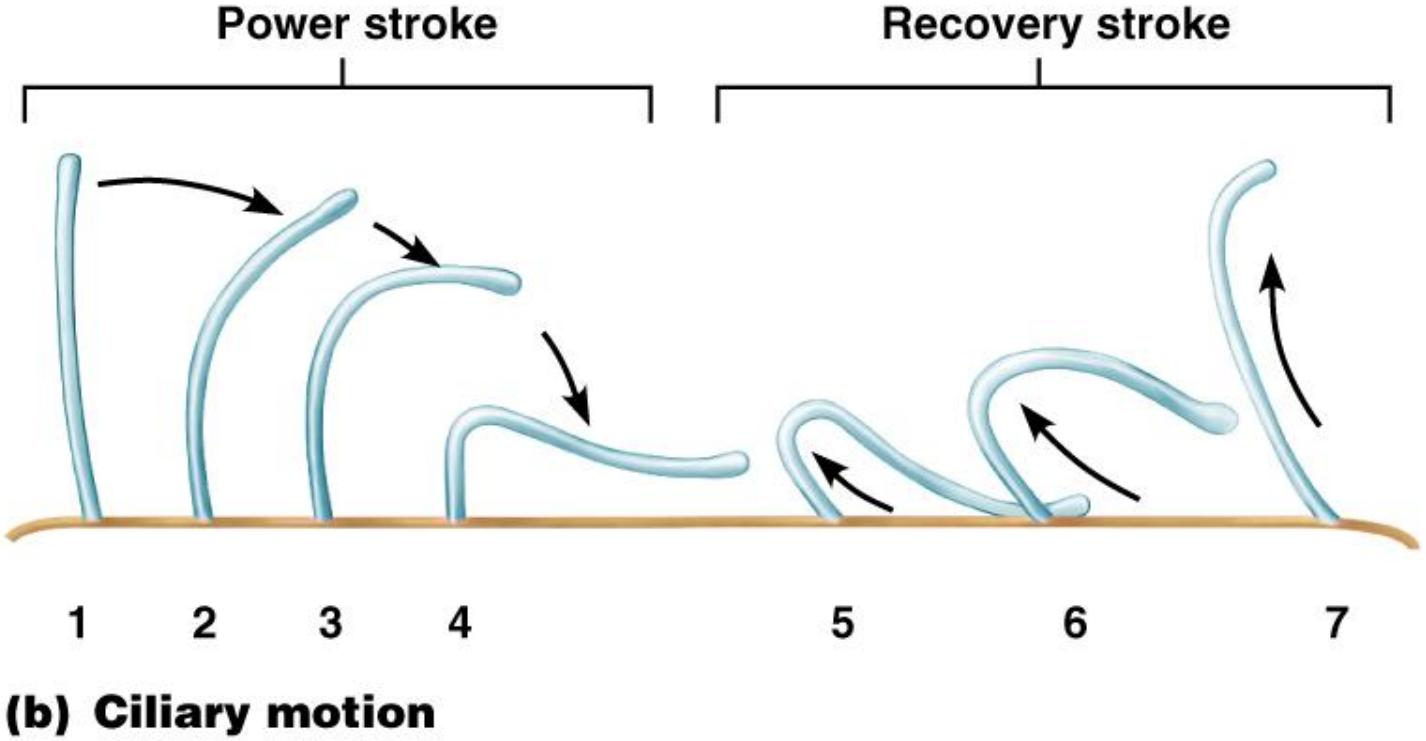
- **Cytoplasmic organelles – metabolic machinery of the cell**
- **Inclusions – chemical substances such as glycosomes, glycogen granules, and pigment**

- Cytosol = water
- Organelles = solids

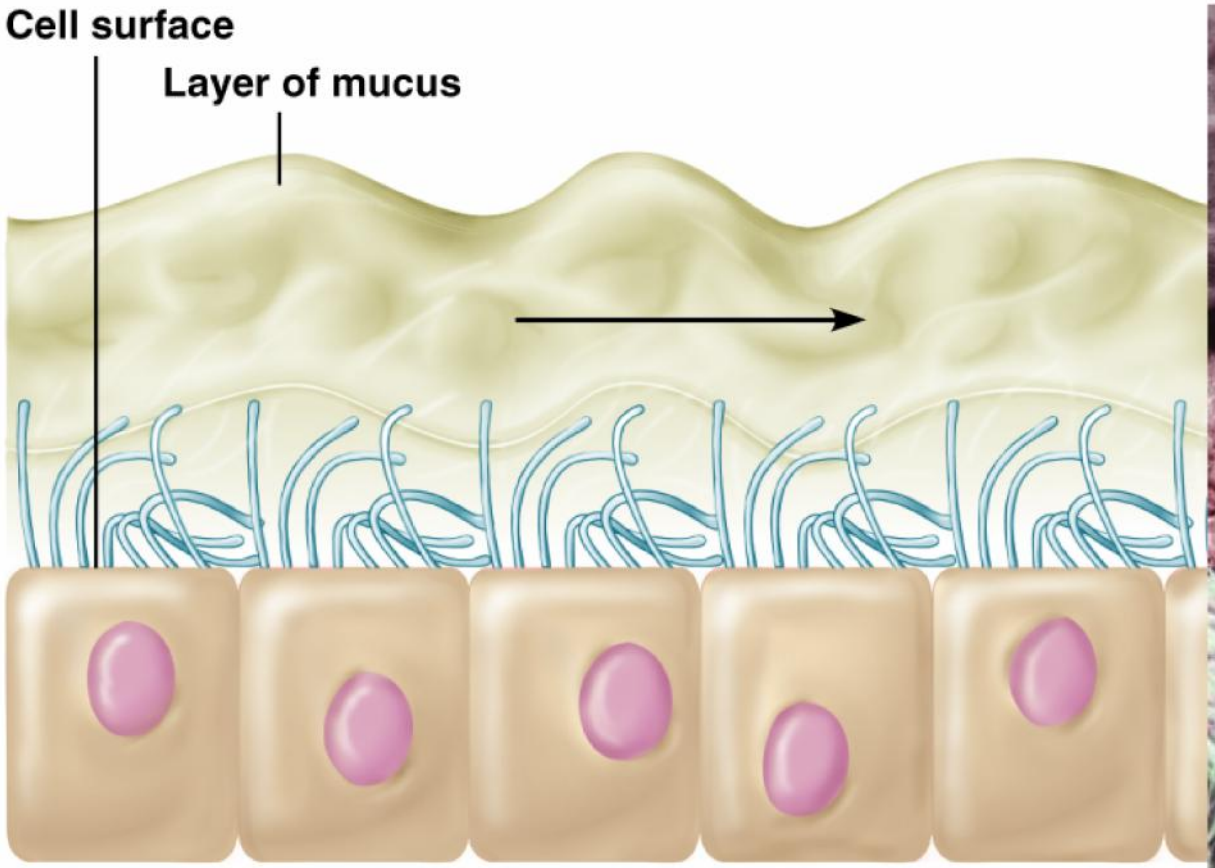
Cilia

- Whip-like, motile cellular extensions on exposed surfaces of certain cells
- Move substances in one direction across cell surfaces





Cilia



(c) Movement of mucus across cell surfaces