Membrane Structure and Membrane Transport of Small Molecules

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Introduction

- Cell membranes define compartments of different compositions.

- Membranes are composed of a large number of different **lipids** and **proteins** that exhibit dynamic organisation and behaviour.

- The lipid bilayer of biological membranes has a very low permeability for most biological molecules and ions.
  - Materials that are soluble in lipids can pass through the cell membrane easily

Homeostasis

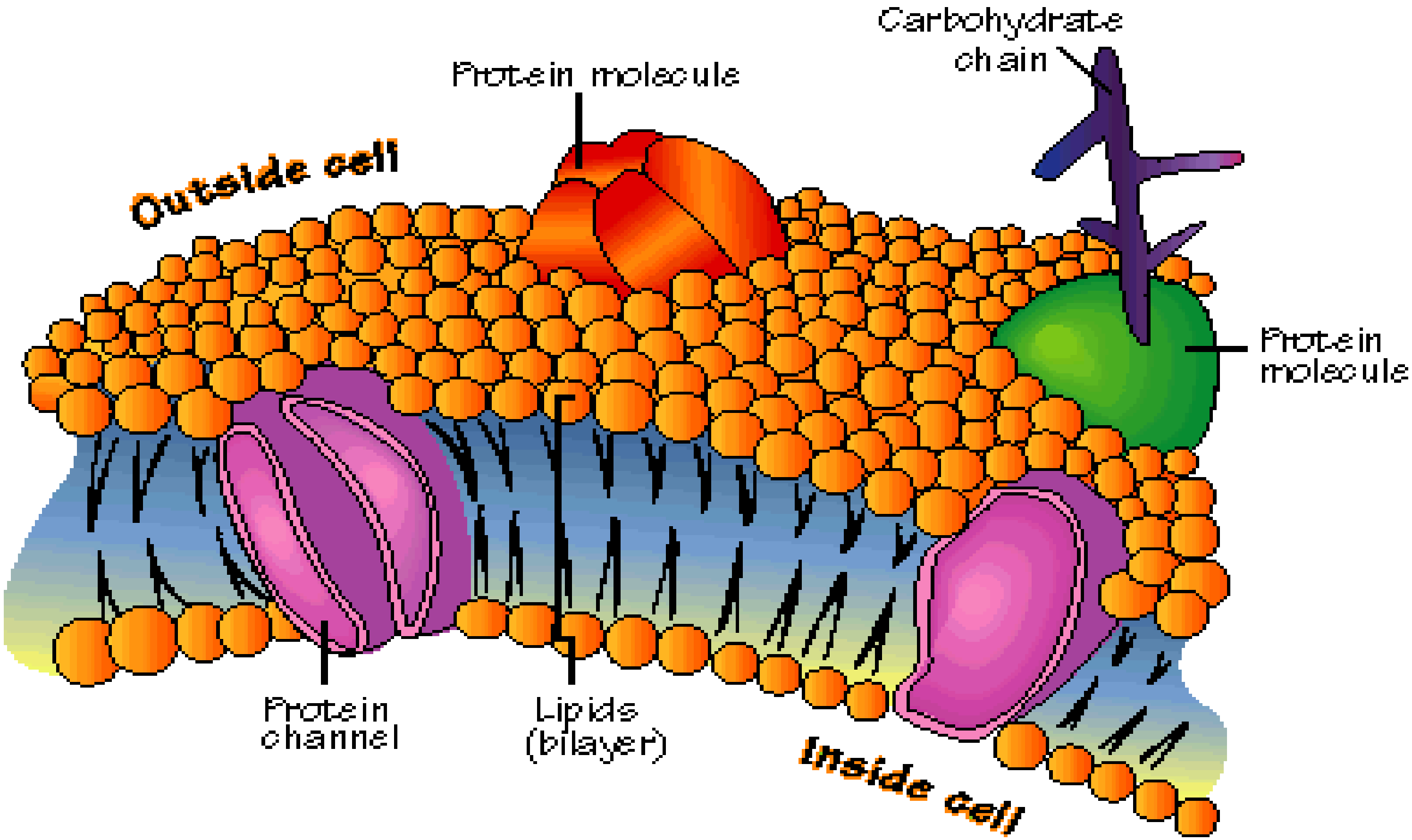
- Balanced internal condition of cells
- Also called equilibrium
- Maintained by plasma membrane controlling what enters & leaves the cell

Introduction

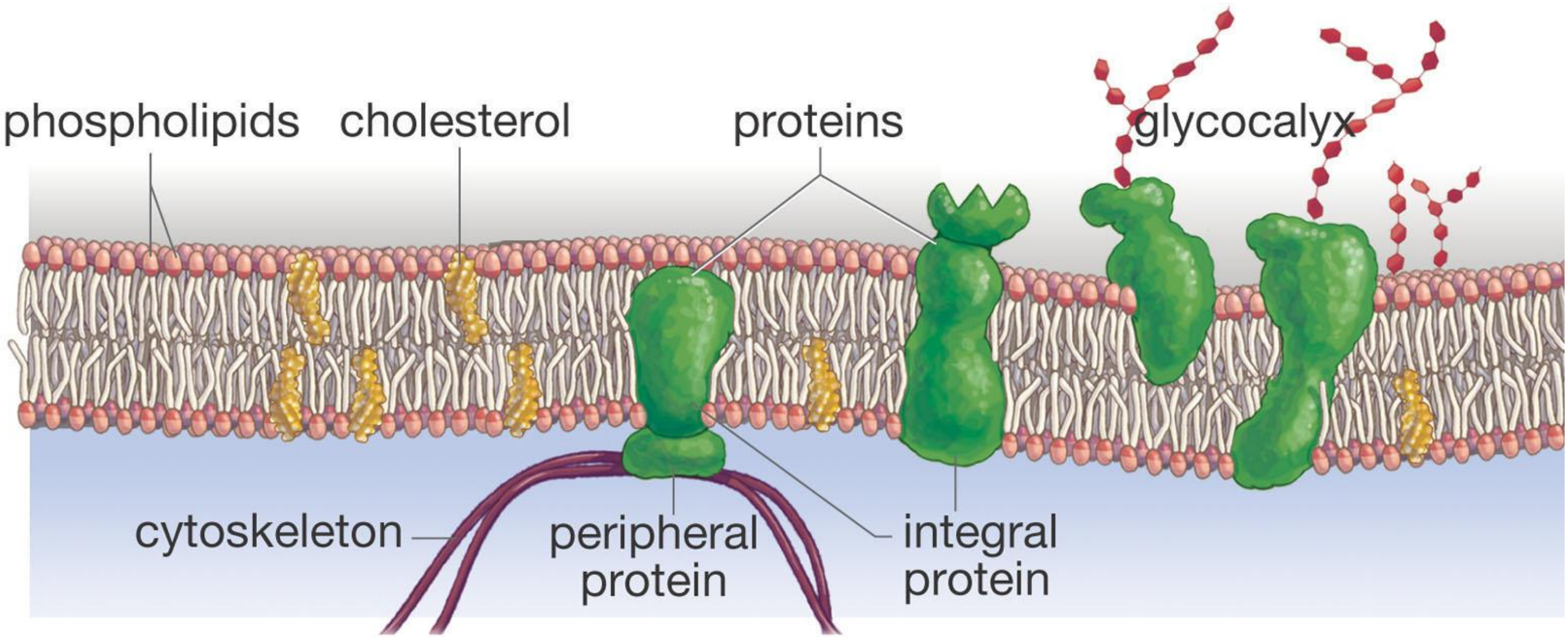
- The **plasma membrane** plays several key roles in the cell:
  - Seperates the interior of the cell from the extracellular environment
  - Regulates the materials in and out of the cell
  - Communicates with other cells

- Cell membranes also form compartments within eukaryotic cells where they participate in and serve as surfaces for the reactions necessary for life.

Structure of the Cell Membrane



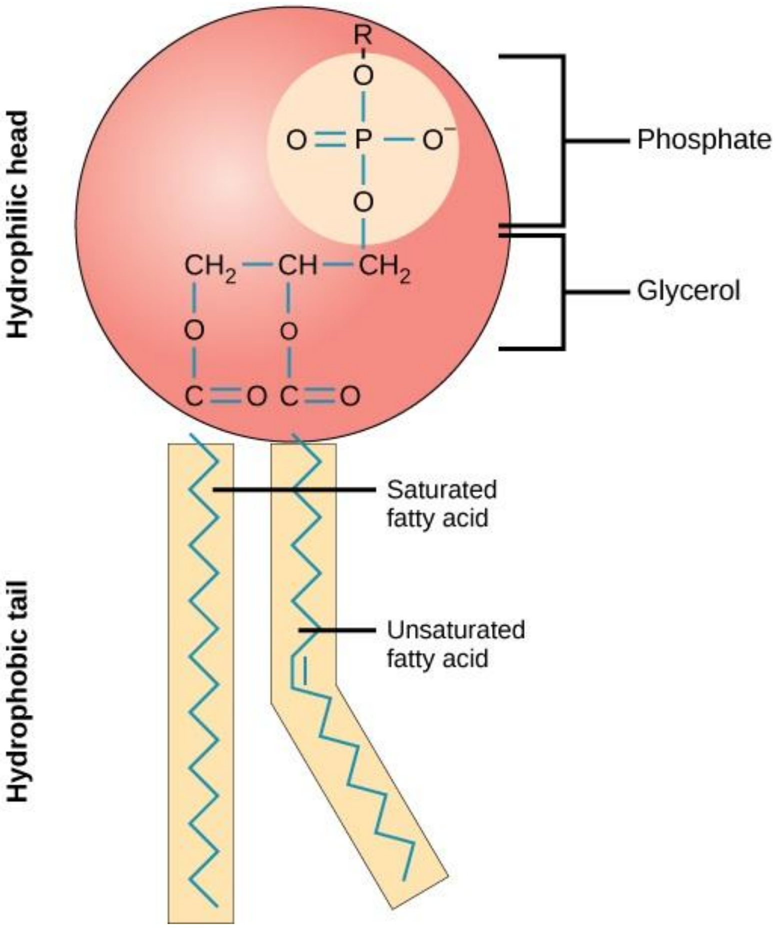
Membrane Components



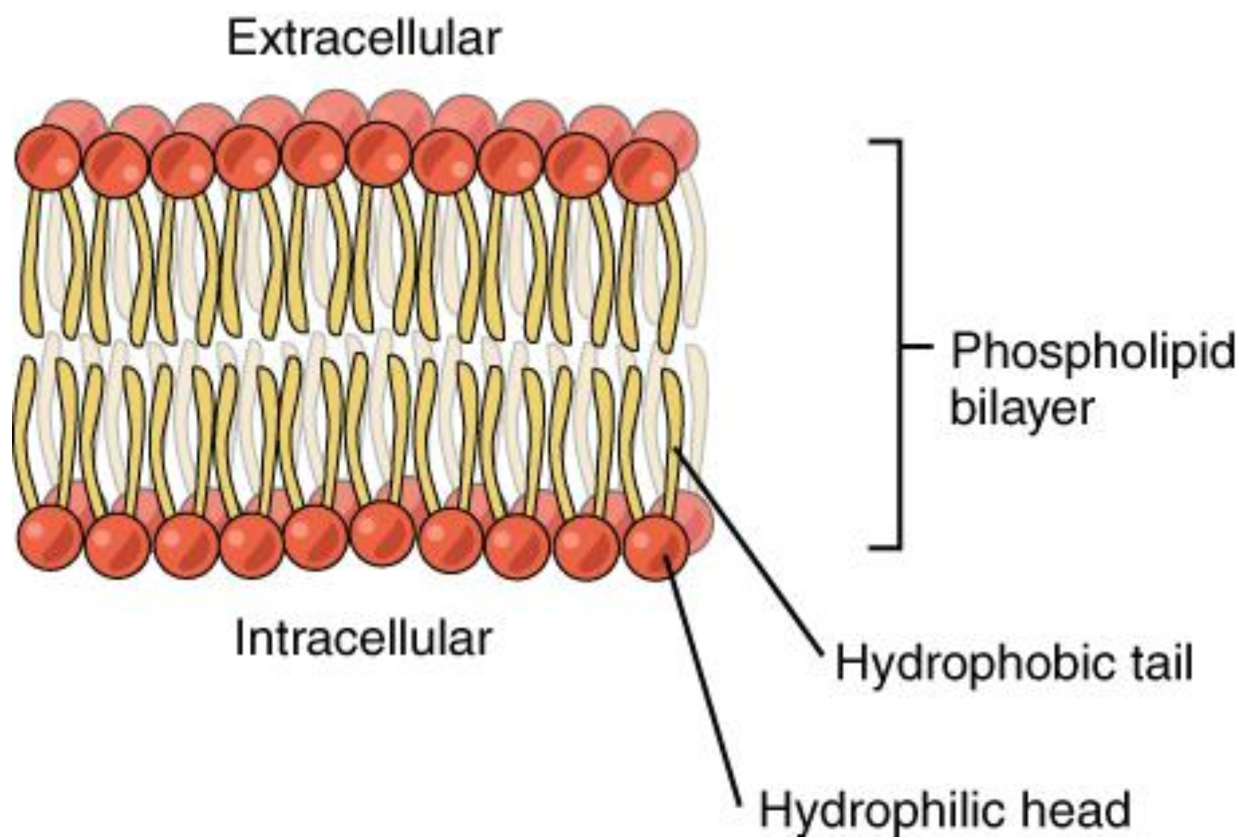
- **Phospholipid bilayer**
- **Cholesterol**
- **Proteins**
- **Glycocalyx**

Phospholipids

- **Phospholipids** make up the cell membrane.
- Phospholipids contain
  - two fatty acids (nonpolar, hydrophobic): tail
  - Head is polar containing the glycerol and phosphate group. This region is hydrophilic.



Phospholipids



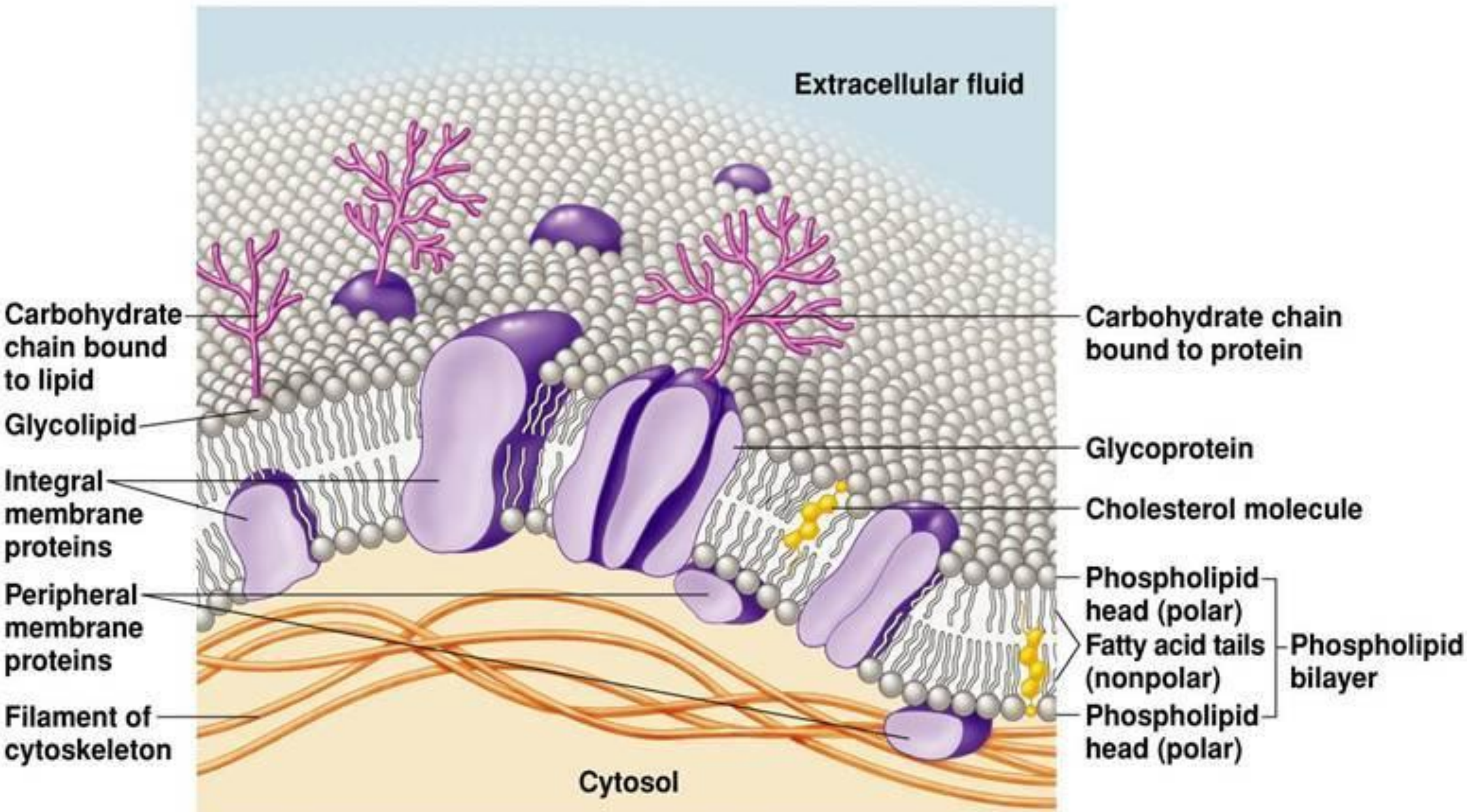
Phospholipids

- When exposed to an aqueous solution, the heads are attracted to the water phase, and the nonpolar tails are repelled from the water phase.
- This property, which is also known as **amphipathicity**, causes lipids to naturally assume single layers (**micelles**) or double layers (**bilayers**) which contribute to their biological significance in membranes.
- Lipid micelle and bilayer formation is exergonic (releases energy).

Other Membrane Lipids

- In addition to phospholipids, there are two other types of lipids in the plasma membrane.
- **Glycolipids** have a structure similar to phospholipids except that the hydrophilic head is a variety of sugars joined to form a straight or branching carbohydrate chain.
- **Cholesterol** is a lipid that is found in animal plasma membranes; related steroids are found in the plasma membrane of plants.
- Altogether, lipids account for about half the mass of cell membranes.

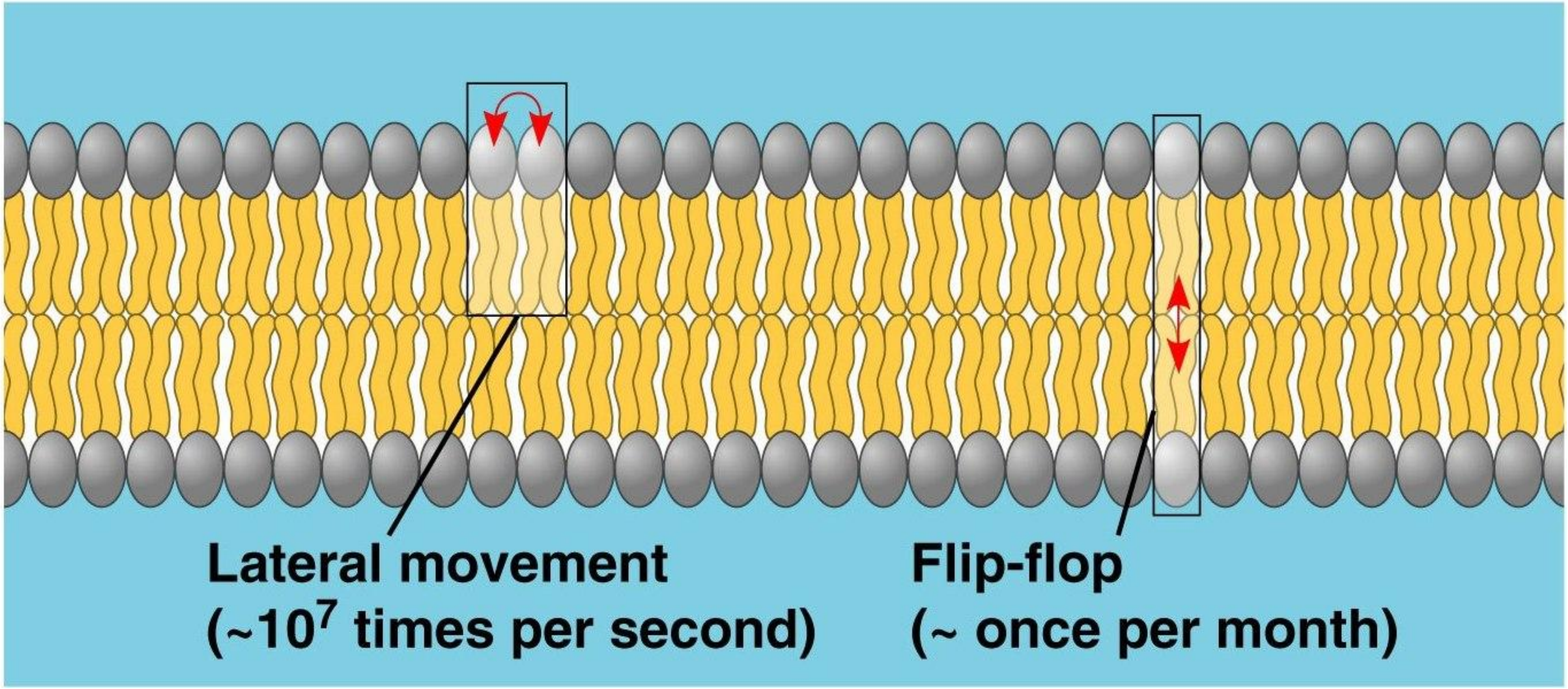
Other Membrane Lipids



Membrane Fluidity

- The fatty acids of the phospholipids make the membrane somewhat fluid.
- The fluid nature of the membrane allows individual lipid molecules to move laterally within each layer.
- Membrane fluidity is affected by several factors, two of which are particularly important: **lipid composition** and **temperature**.

Membrane Fluidity



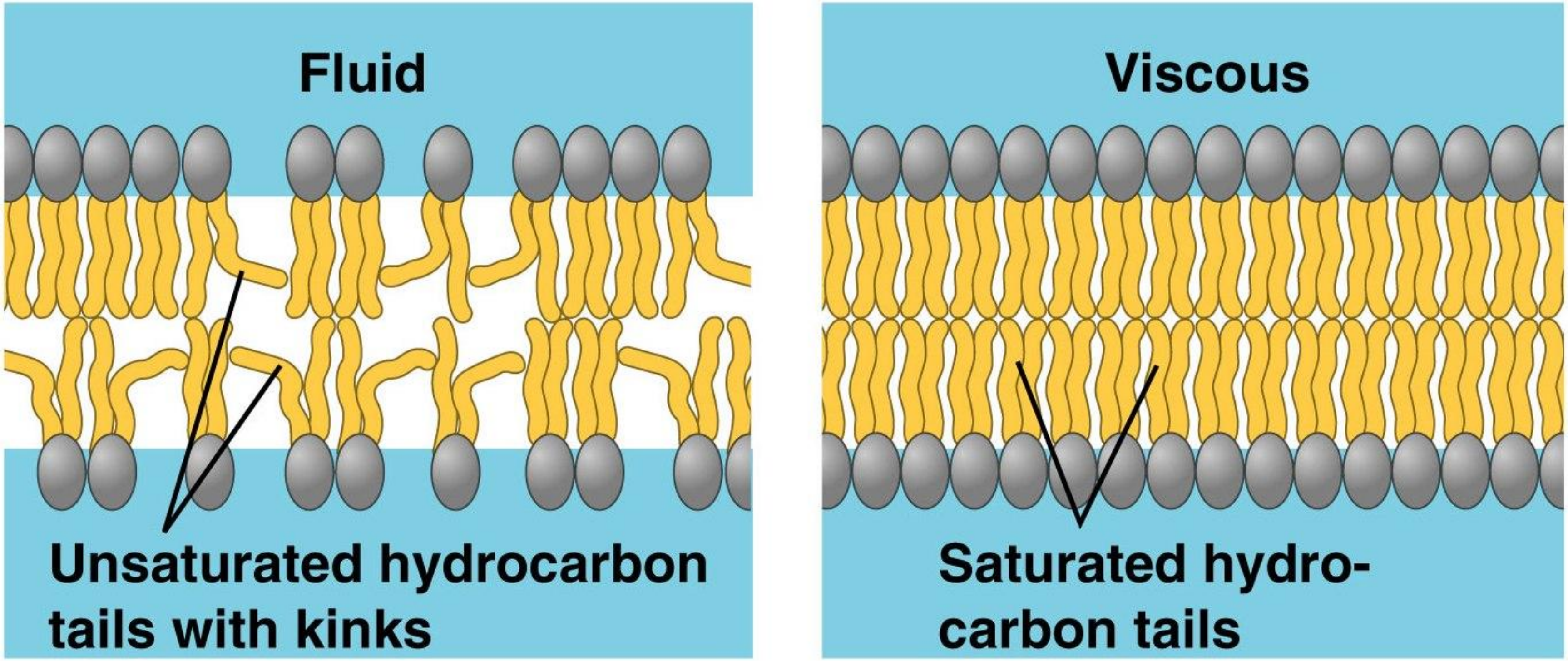
Membrane Fluidity

- **Membrane fluidity** is important for the cell because it affects membrane functions, such as
  - catalysis ,
  - signal transduction,
  - membrane transport, and
  - membrane trafficking.

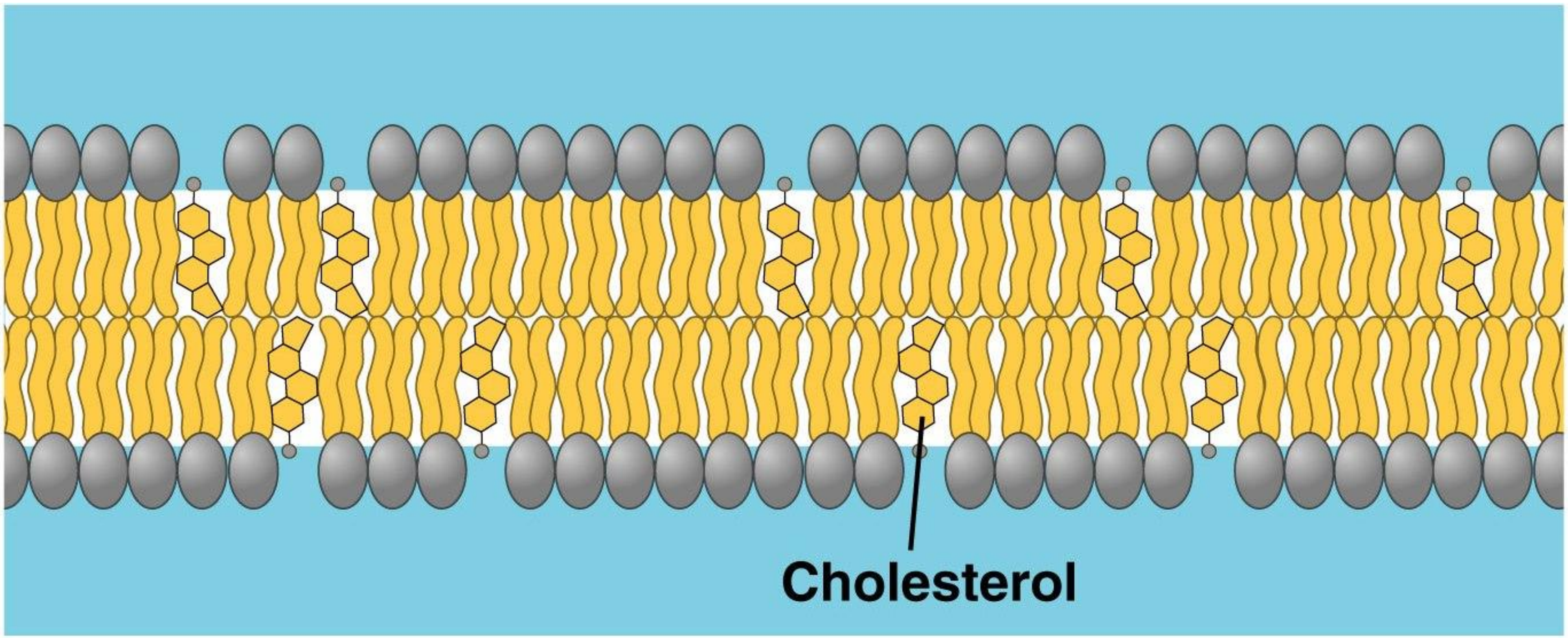
Membrane Fluidity

- Cholesterol and long-chain, saturated fatty acids pack tightly together, resulting in **less fluid** membranes.
- Unsaturated fatty acids or those with shorter chains tend to **increase** membrane fluidity.
- Membrane fluidity **decreases** under cold conditions because molecules move more slowly at lower temperatures.

Membrane Fluidity



Membrane Fluidity



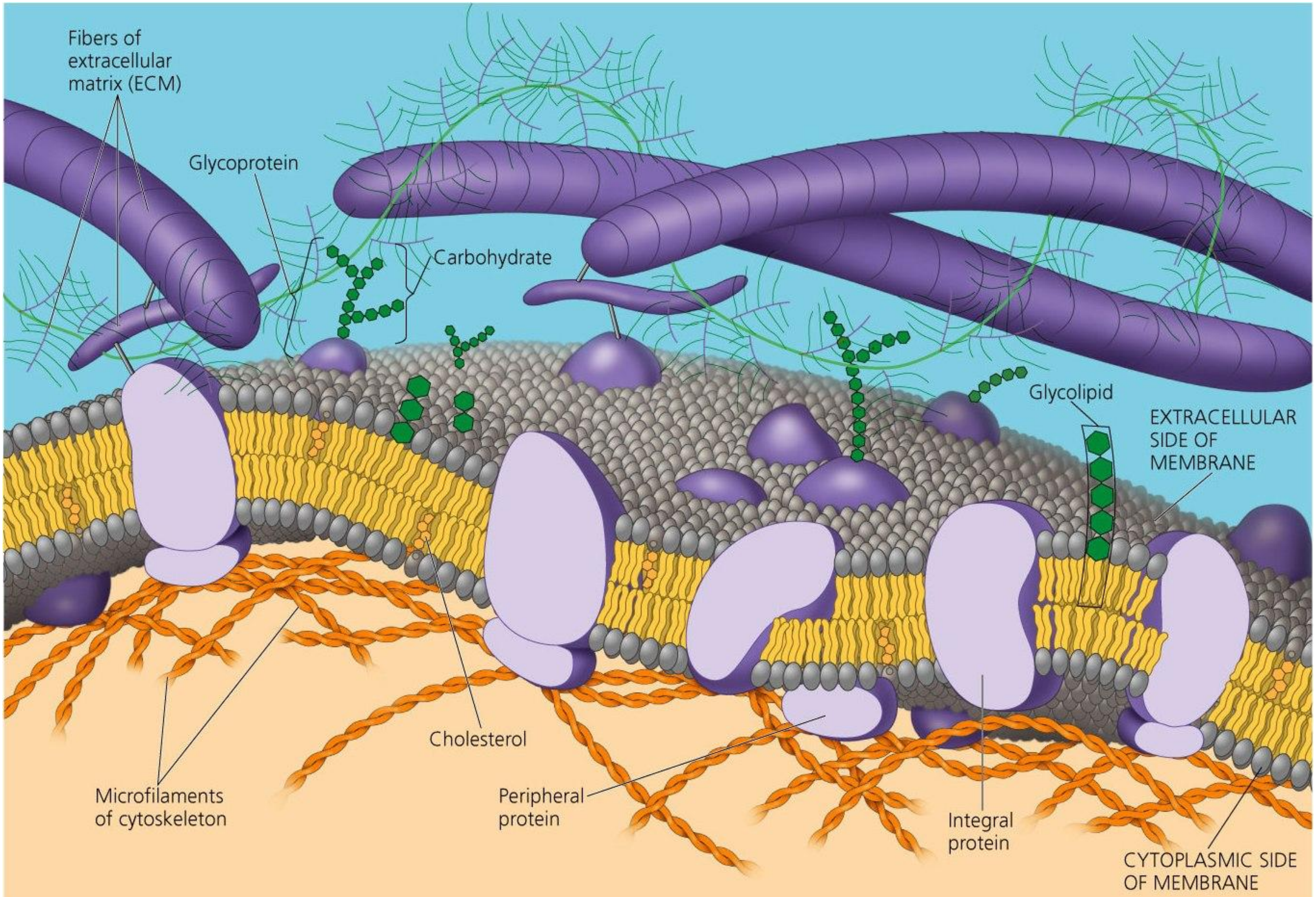
Membrane Proteins

- Phospholipids are 50 times more than the proteins in the membrane.
  - BUT the proteins are so large that they sometimes make up half the mass of a membrane.
- Like lipids, some membrane proteins move relatively freely within the phospholipid bilayer.
- The proteins in a membrane may be **peripheral proteins** or **integral proteins**.
- Peripheral proteins:
  - on outside or inside surface of the membrane
  - held in place either by covalent bonding or noncovalent interactions.

Membrane Proteins

- Integral proteins
  - within the membrane
  - have hydrophobic regions embedded within the membrane and hydrophilic regions that project from both surfaces of the bilayer (**transmembrane proteins**).
- Many integral proteins are **glycoproteins**.
- As with glycolipids, the carbohydrate chain of sugars is on the surface of the membrane → called **glycocalyx**.
- Glycocalyx helps protect and lubricate the cell surface and is involved in specific cell–cell recognition.

Membrane Proteins

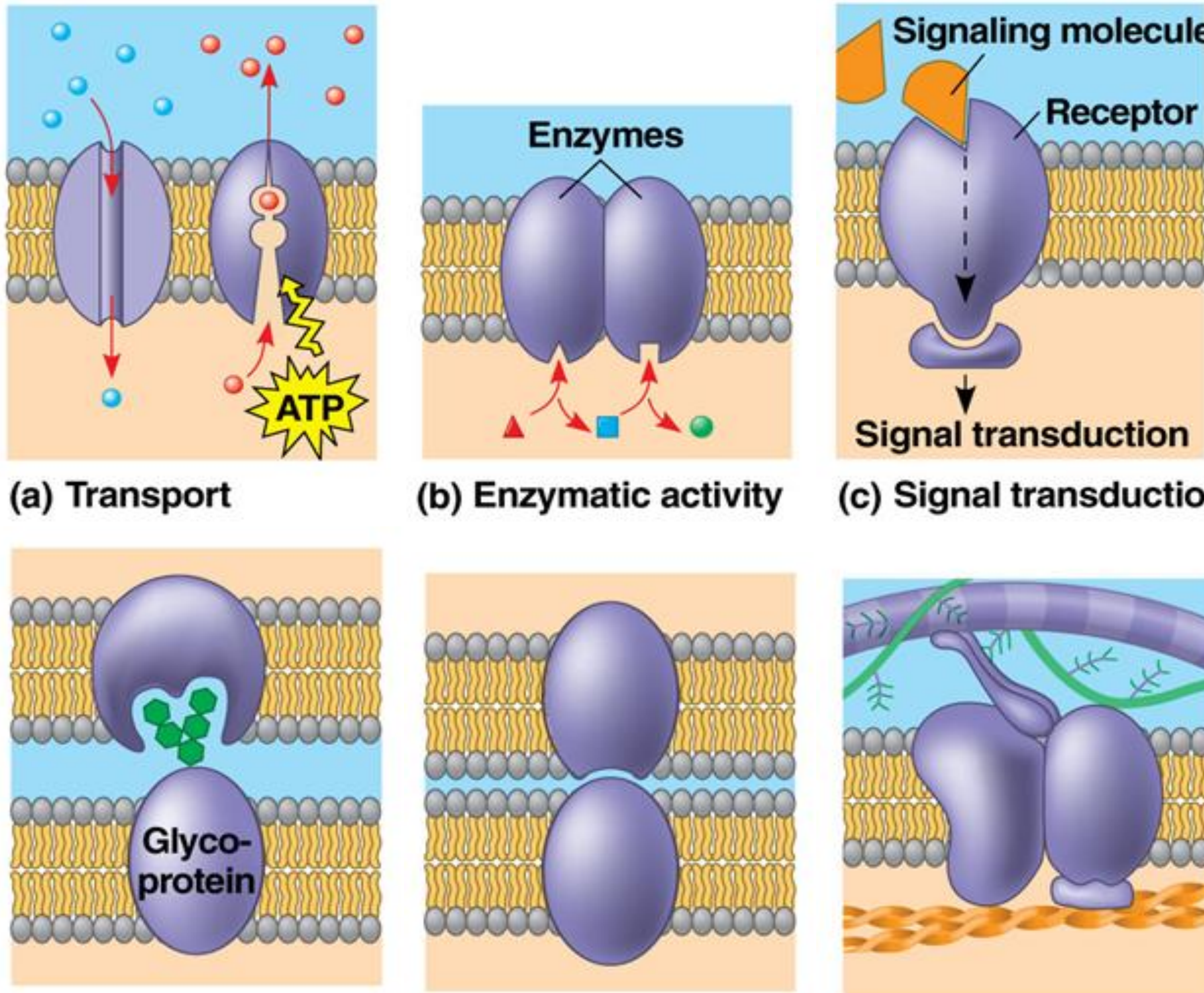


Membrane Proteins

- Function of the membrane is mainly determined by integral proteins.
- Functions of integral proteins:
  - Passing on the molecules or ions through the membrane.
  - Receptors that bring about cellular responses to signals
  - Some are enzymes that carry out metabolic reactions directly.
- Peripheral proteins often have a structural role
  - they help to stabilise and shape the plasma membrane

Membrane Proteins

Functional class	Description	Example
Carrier proteins	Combine with a substance and help it to move across the membrane	Na^+–K^+ pump
Channel proteins	Act as pores through which a substance can simply move across the membrane	K^+ leak channels
Recognition proteins	Serve as identification tags that are specifically recognised by membrane proteins of other cells	Major histocompatibility complex (MHC) glycoproteins
Anchor proteins	Are the bridges for cell–cell and cell–extracellular matrix (ECM) interactions	Integrins
Receptor proteins	Are shaped in such a way that a signalling molecule can bind to it	Growth hormone receptors
Enzymatic proteins	Catalyse a specific reaction	Adenylate cyclase



(a) Transport

(b) Enzymatic activity

(c) Signal transduction

(d) Cell-cell recognition

(e) Intercellular joining

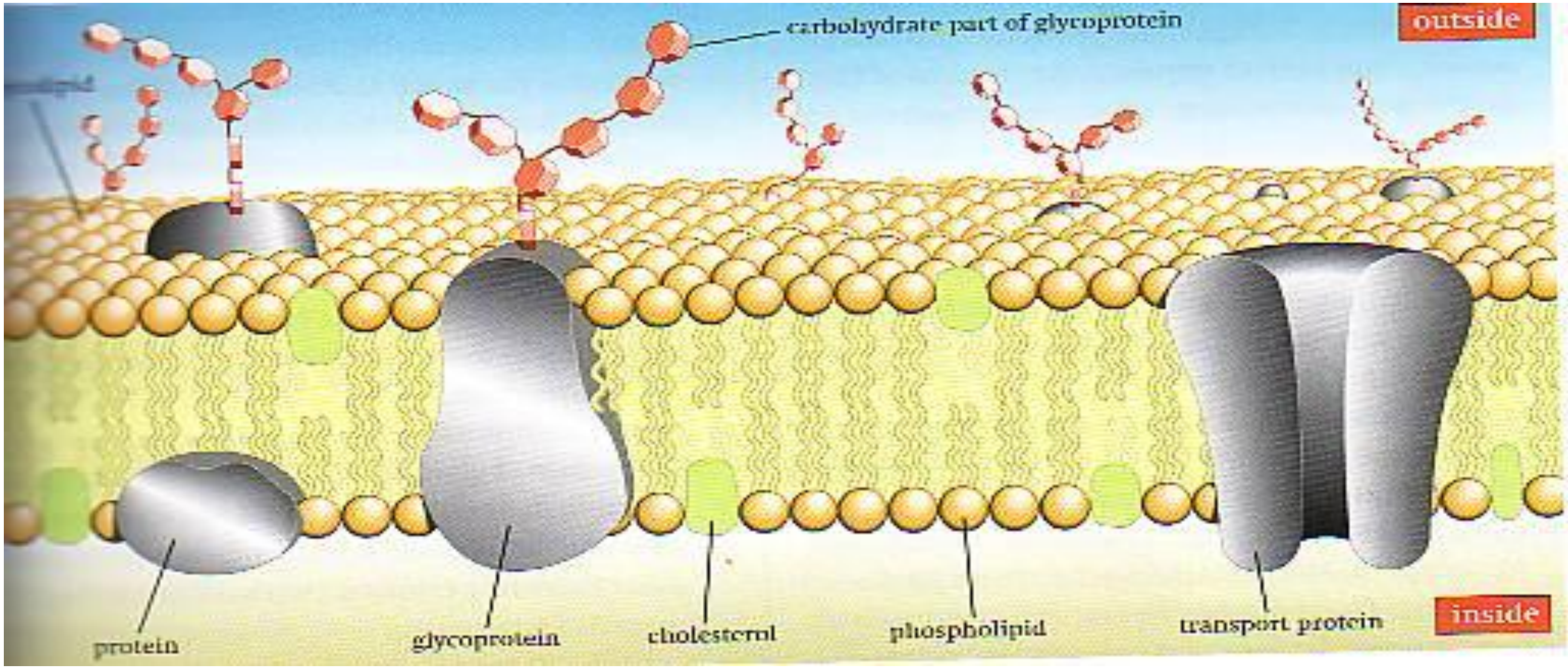
(f) Attachment to the cytoskeleton and extracellular matrix (ECM)

Membrane Structure

- Membrane structure are mosaic.
  - Proteins form different patterns

- The plasma membrane is **fluid-mosaic model** due to the fluidity and the mosaic arrangement of the protein molecules

FLUID MOSAIC MODEL



FLUID- because individual phospholipids and proteins can move side-to-side within the layer, like it's a liquid.

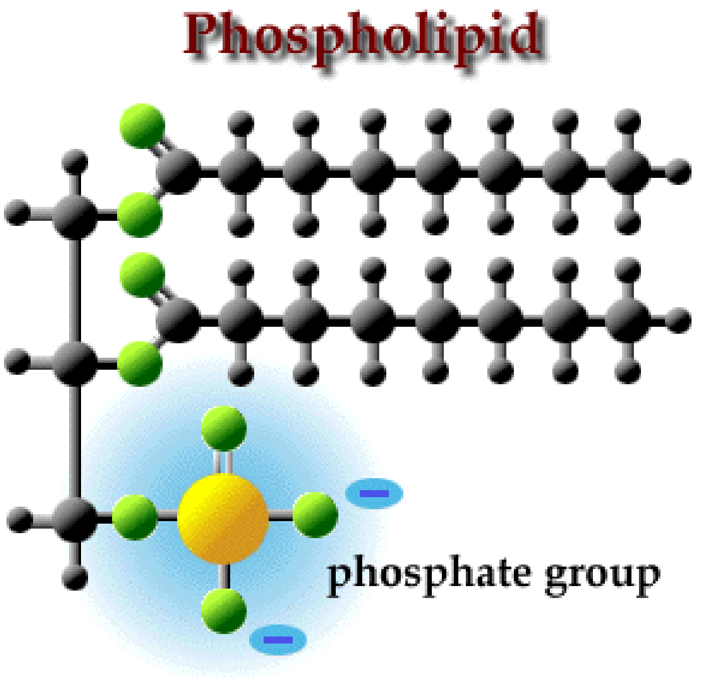
MOSAIC- because of the pattern produced by the scattered protein molecules when the membrane is viewed from above.

Membrane Structure

- The plasma membrane is **asymmetrical**
  - the two halves are not identical.
- Membrane asymmetry results from the following facts:
  - The outer and inner lipid layers have different lipids.
  - The proteins are differentially located in the outer, inner or middle parts of the membrane.
  - Glycolipids and glycoproteins are exposed only on the outer surface and cytoskeletal filaments attach to proteins only on the inner surface.

Solubility

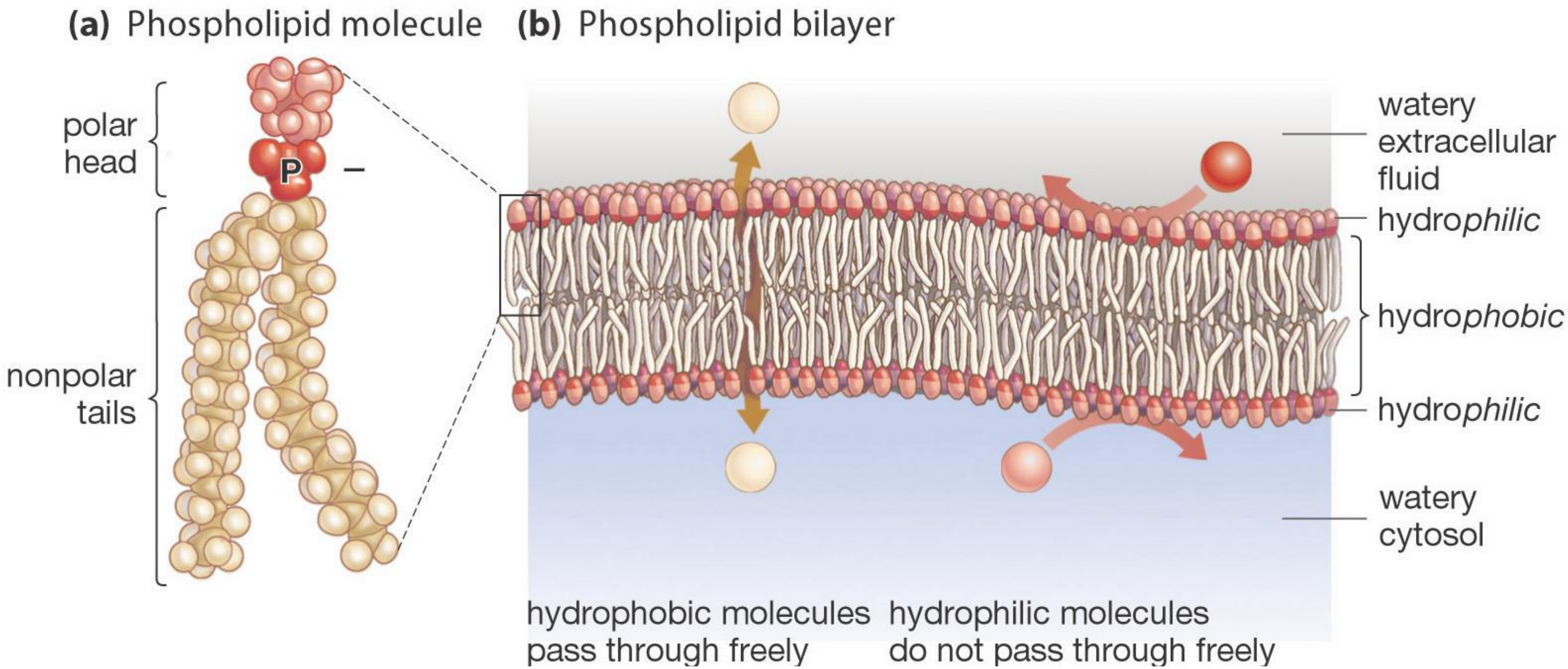
- **Materials that are soluble in lipids can pass through the cell membrane easily**



Membranes as Selective Barriers

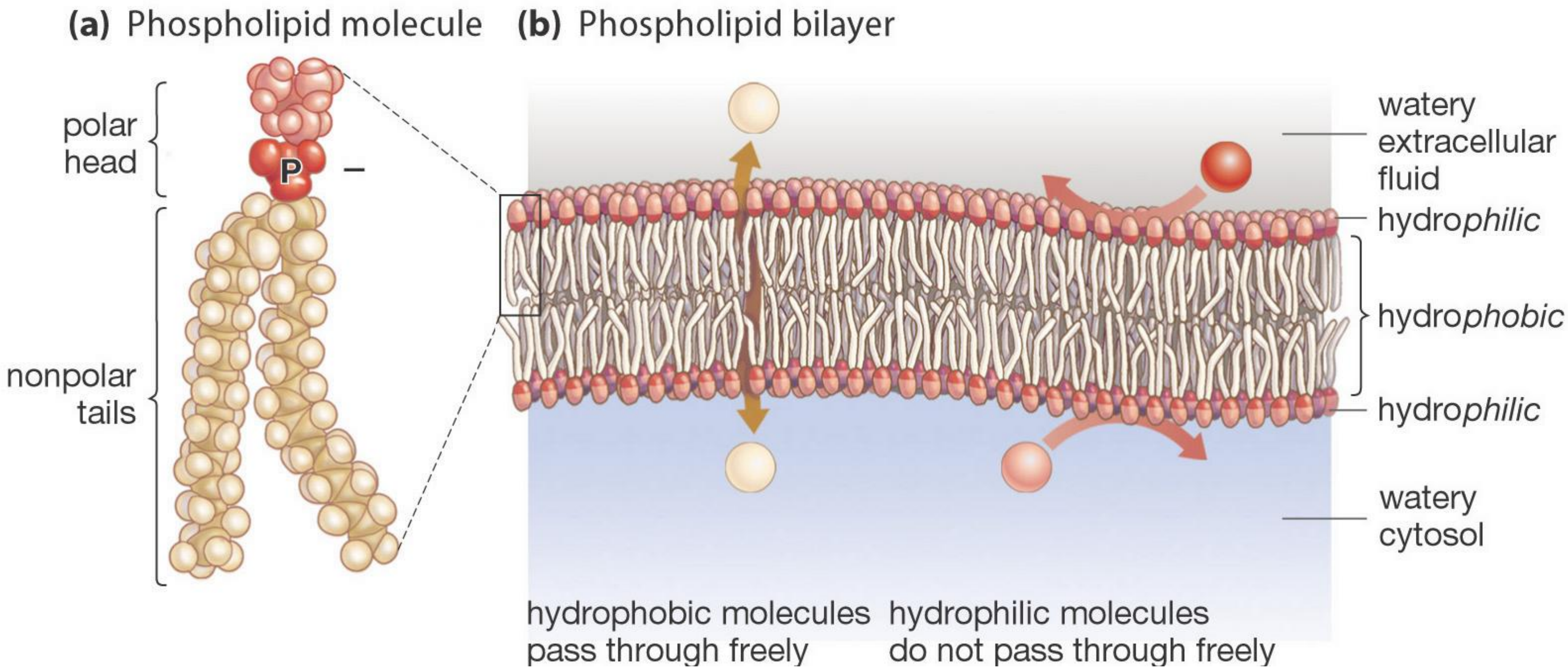
- Membrane has **selective permeability**
  - regulate which substances pass through them
- Macromolecules cannot cross the membrane because they are too large.
- Ions and charged molecules cannot cross the membrane because they are unable to enter the hydrophobic phase of the lipid bilayer.
- Small, noncharged molecules such as oxygen and alcohols are lipid-soluble and therefore can cross the membrane.

Semipermeable Membrane

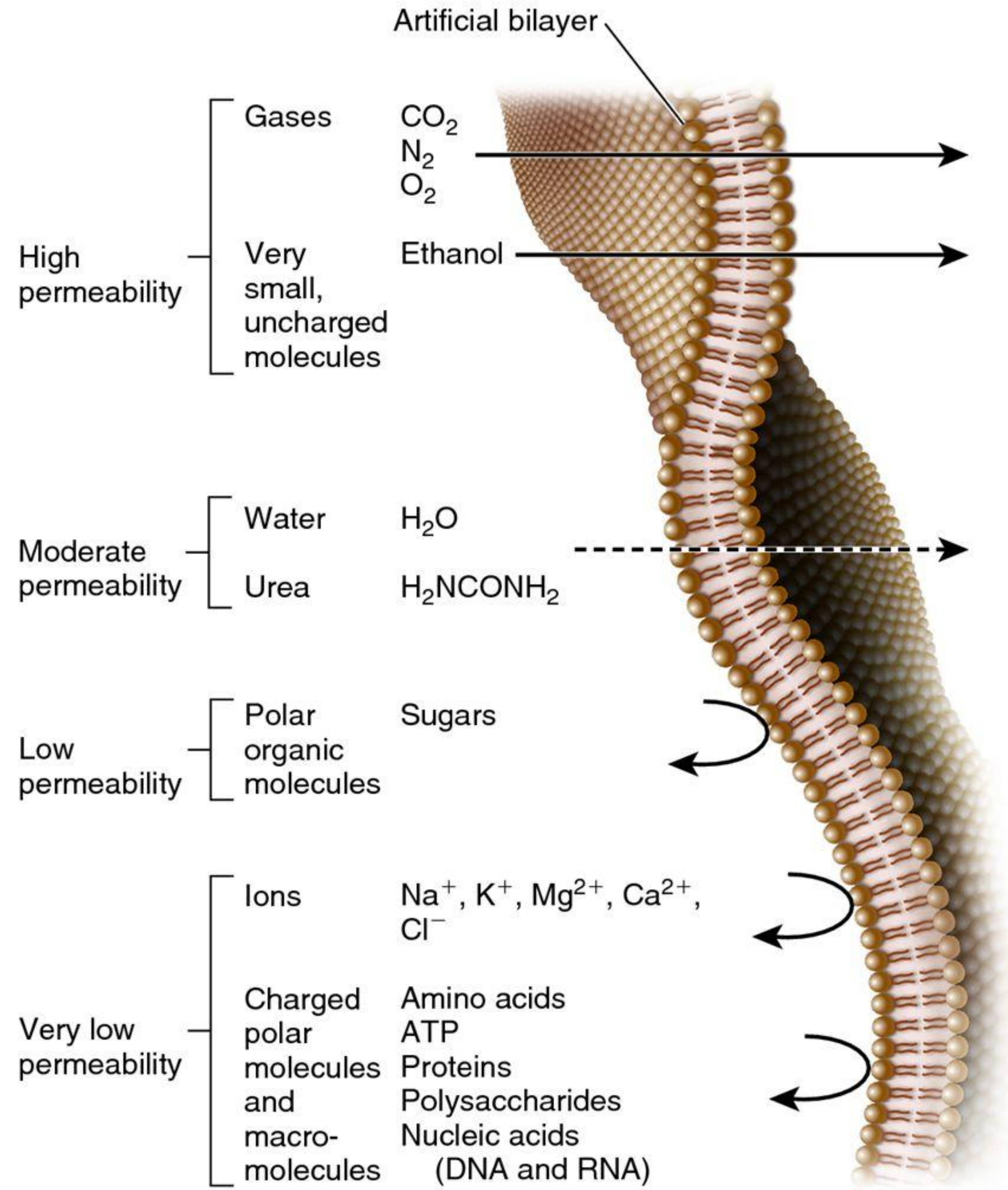


Small molecules and larger hydrophobic molecules move through easily.
e.g. O_2, CO_2, H_2O

Semipermeable Membrane



Ions, hydrophilic molecules larger than water, and large molecules such as proteins do not move through the membrane on their own.



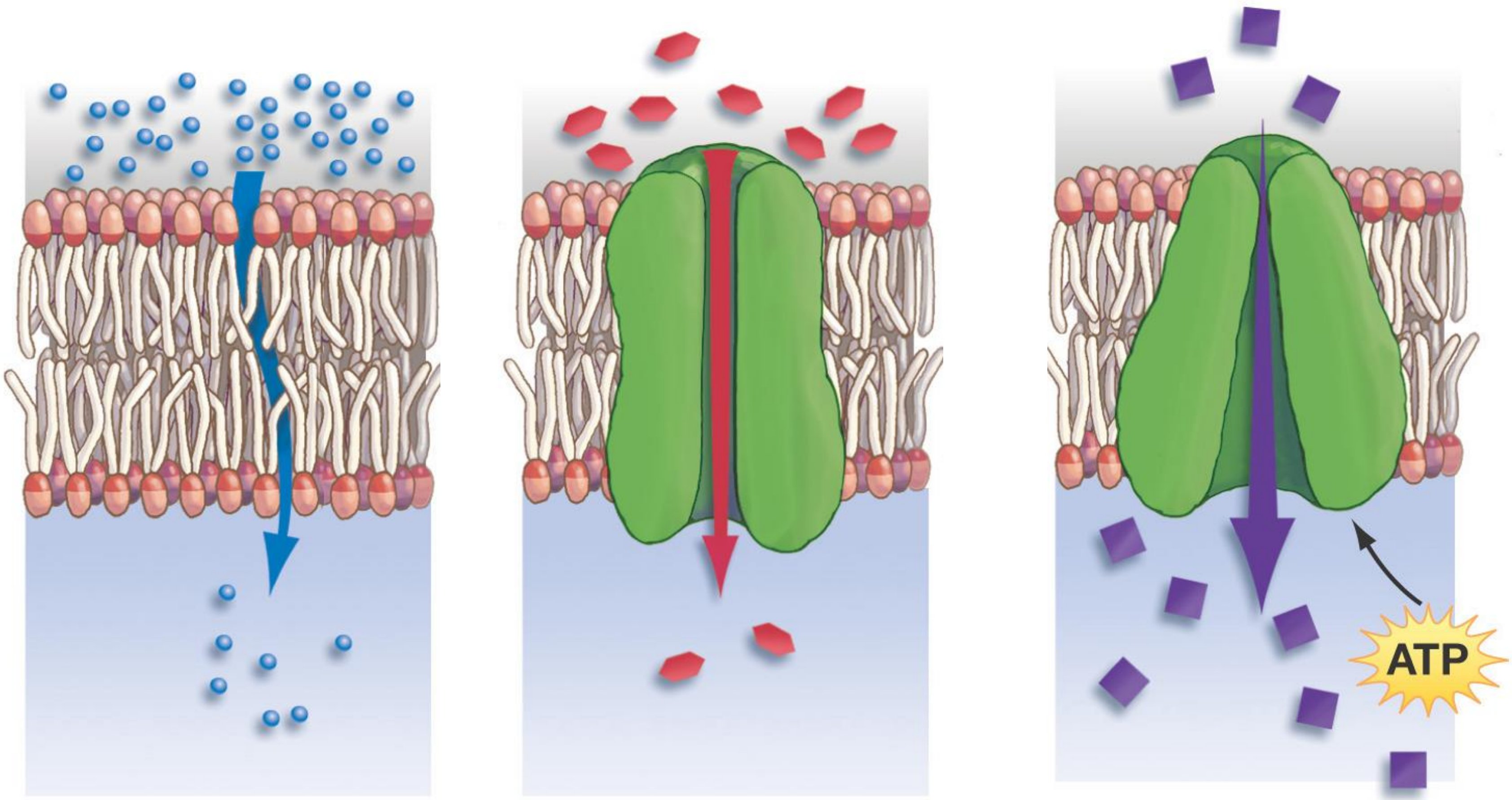
Artificial bilayer
High permeability
Gases
CO_2
N_2
O_2
Very small, uncharged molecules
Ethanol
Moderate permeability
Water
H_2O
Urea
H_2NCONH_2
Low permeability
Polar organic molecules
Sugars
Very low permeability
Ions
Na^+, K^+, Mg^{2+}, Ca^{2+}, Cl^-
Charged polar molecules and macro-molecules
Amino acids
ATP
Proteins
Polysaccharides
Nucleic acids (DNA and RNA)

Types of Transport Across Cell Membranes

Three Forms of Transport Across the Membrane

Passive transport | **Active transport**

simple diffusion | facilitated diffusion



Materials move down their concentration gradient through the phospholipid bilayer.

The passage of materials is aided both by a concentration gradient and by a transport protein.

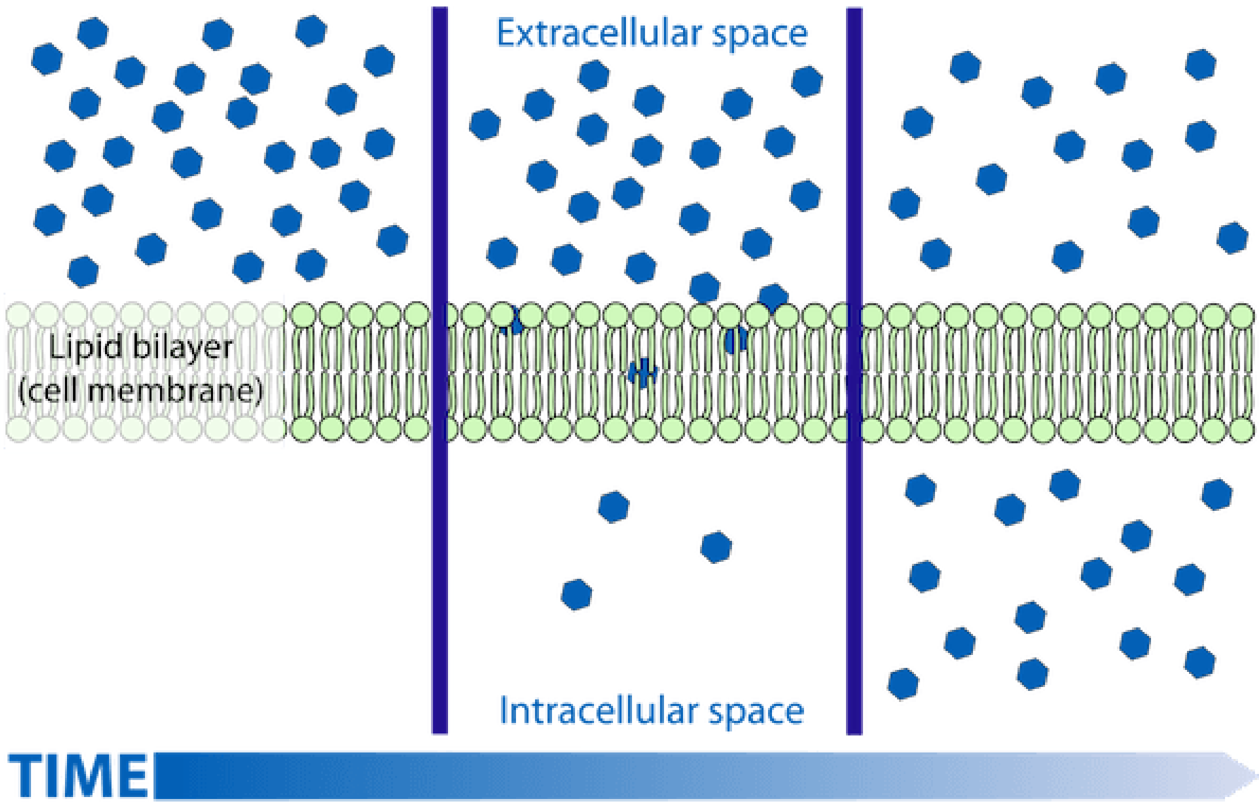
Molecules again move through a transport protein, but now energy must be expended to move them against their concentration gradient.

Membranes as Selective Barriers

- There are three methods for substances to cross membranes.
- **Passive transport:** diffusion of a substance across a membrane with no energy.
  - It involves **simple diffusion** and **facilitated diffusion**.
- **Active transport** uses energy to move solutes against their gradients.
- **Bulk transport** is the packaging of macromolecules and particles in vesicles and involves **exocytosis** and **endocytosis**.
  - require energy.

Passive Transport

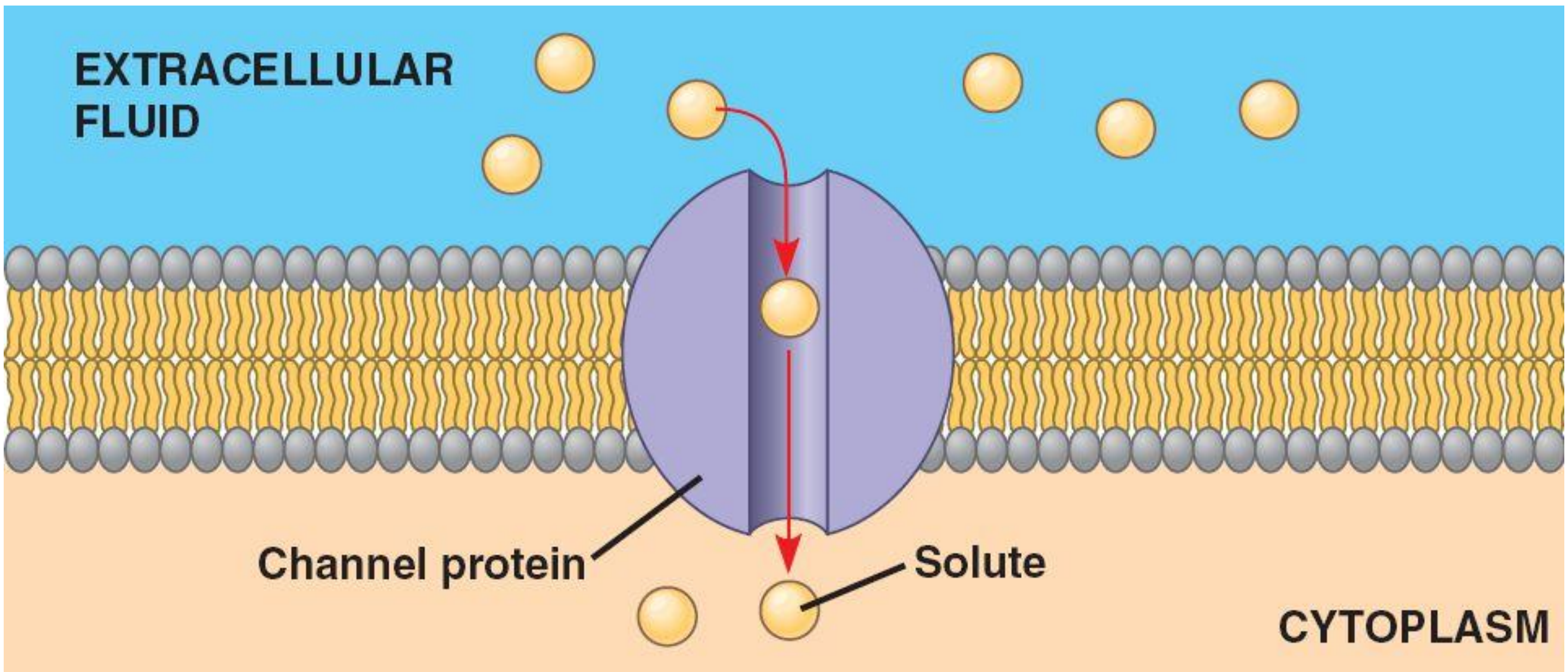
- **Simple diffusion** is the random movement of simple atoms or molecules from area of higher concentration to an area of lower concentration until they are equally distributed
- No energy required.



Passive Transport

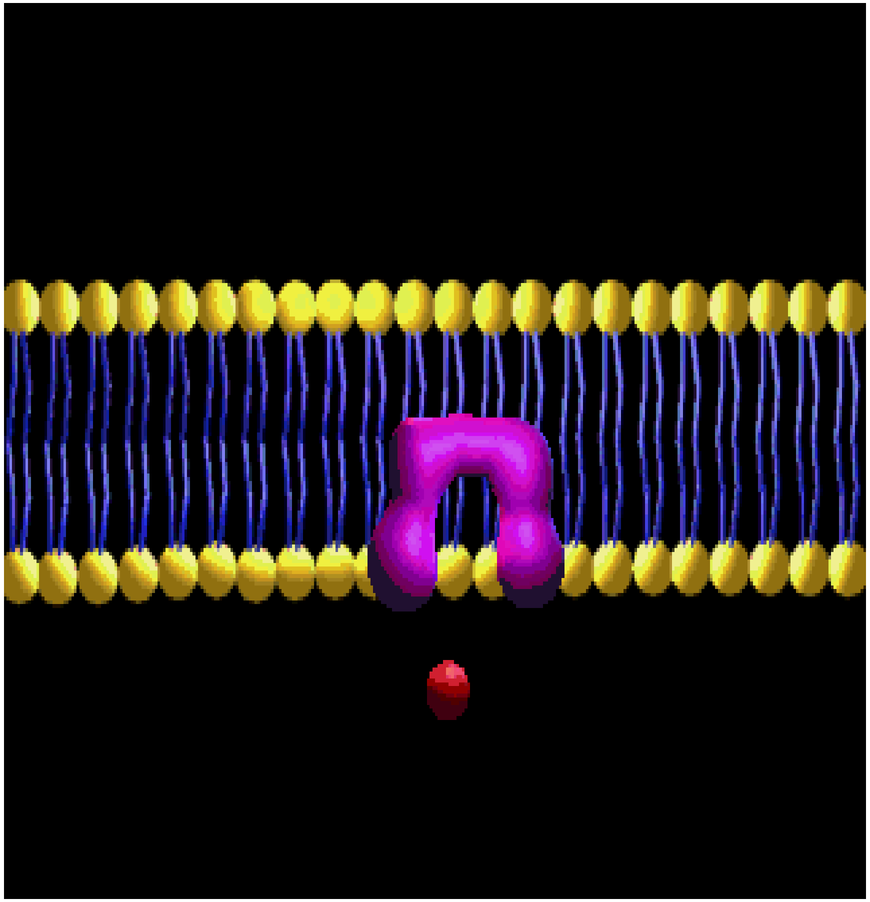
- **Facilitated diffusion:** Impermeable molecules like large, polar or charged ones diffuse passively with the help of tranport proteins that span the membrane.
- No energy required because the molecules are moving down their concentration gradient.
- The two types of transport proteins are **channel proteins** and **carrier proteins**.
- Particular channel or carrier proteins can operate in both directions.

Passive Transport



Facilitated Diffusion

- Some carrier proteins do not extend through the membrane.
- They bond and drag molecules through the lipid bilayer and release them on the opposite side.



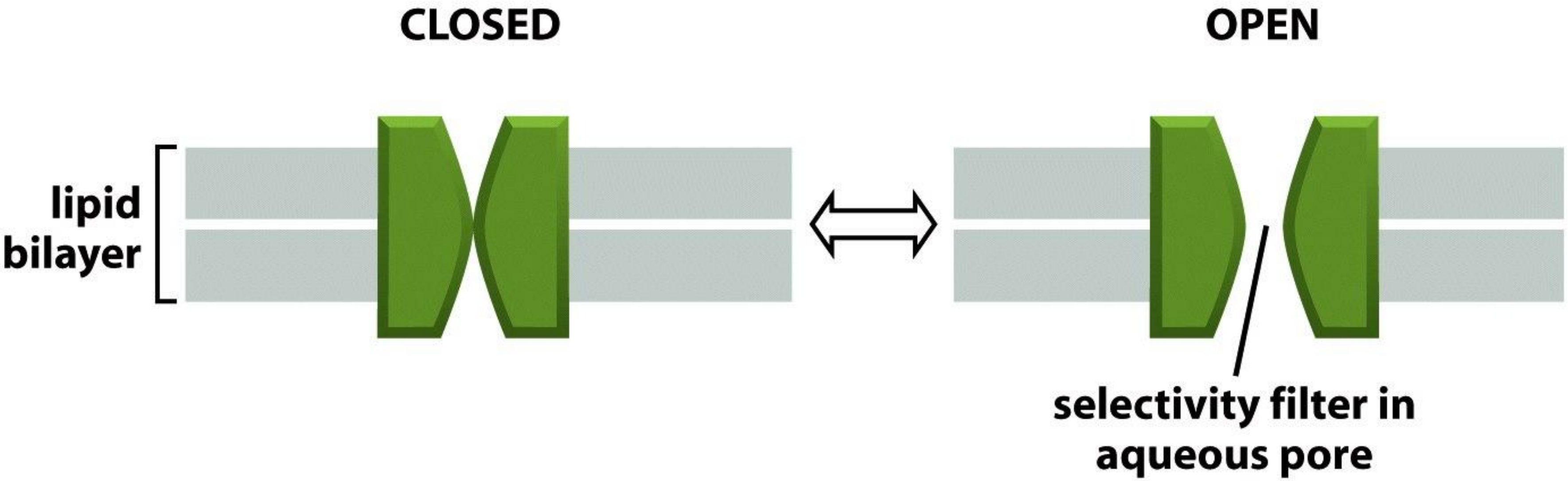
Passive Transport

- **Channel proteins** allow specific molecules or ions to cross the membrane.
- **Ion channels:** channel proteins that transport ions
- Many ion channels function as **gated channels**
  - They open or close in response to a stimulus (*e.g.*, the binding of a ligand or a change in the voltage).
- **Water channels**, or **aquaporins**: osmosis occur in plant cells and in animal cells such as red blood cells.

Passive Transport: Ion channels

- Can transport up to 100 million ions per second, a rate 10^5 times greater than that mediated by a carrier protein
- Among their many functions, ion channels:
    - control the pace of the heart
    - regulate the secretion of hormones into the bloodstream
    - generate the electrical impulses underlying information transfer in the nervous system.

Passive Transport: Ion channels

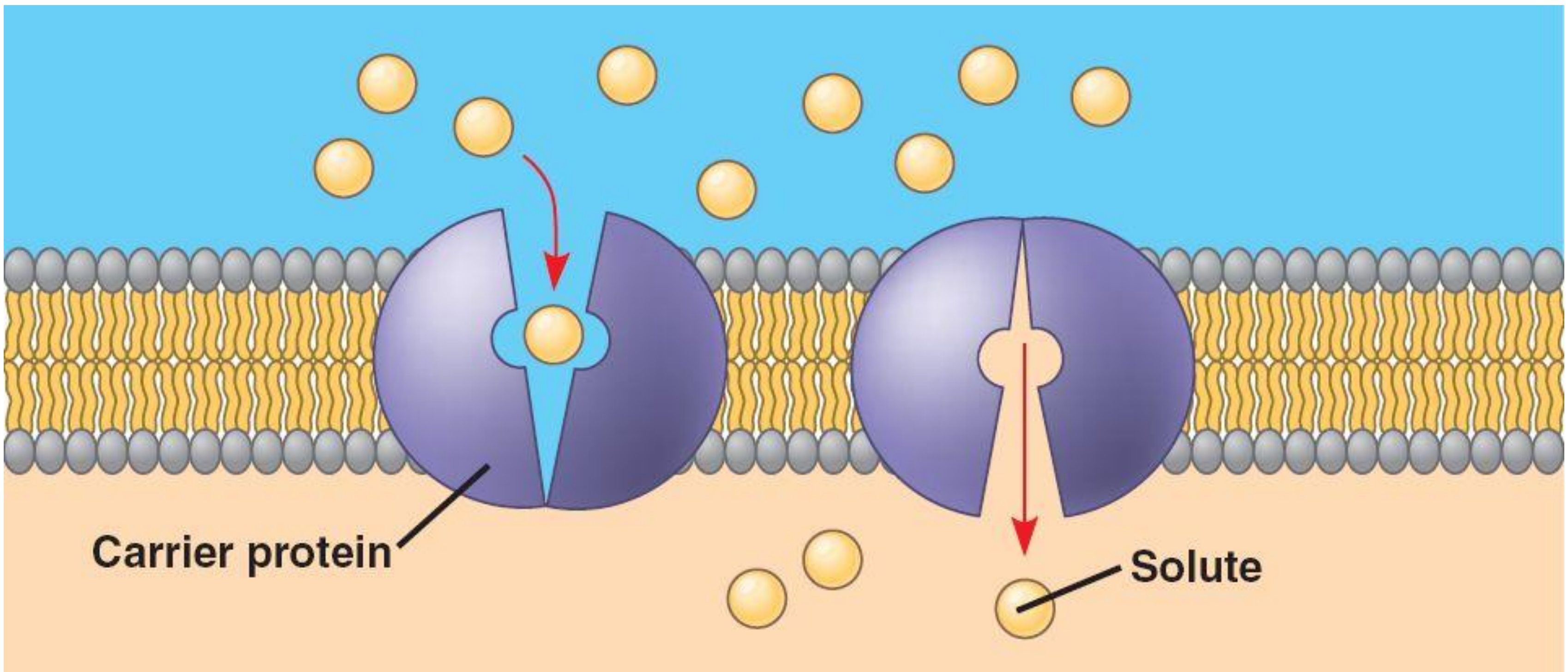


• Ion channels are ion-selective (*ion selectivity*) and fluctuate between open and closed states (*gated*)
• Ion channels, like enzymes, have their specific substrates: potassium, sodium, calcium, and chloride channels permit only their namesake ions to diffuse through their pores. The ability of channels to discriminate among ions is called ion selectivity.

Passive Transport

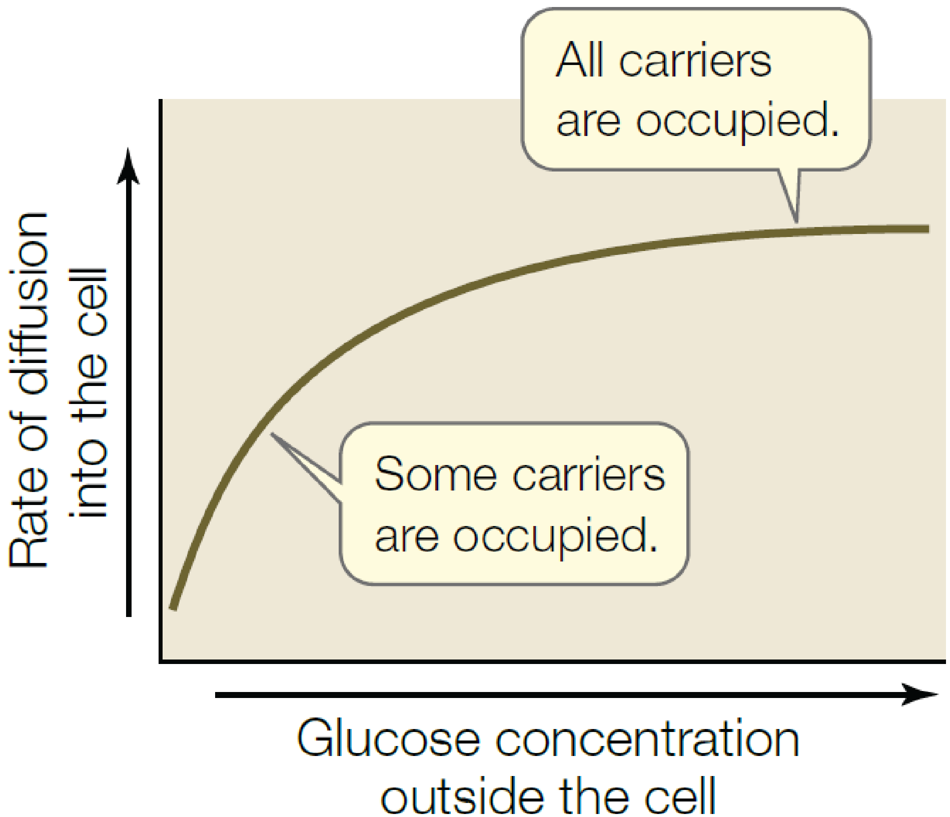
- Some substances, such as glucose and amino acids, can bind to membrane proteins →**carrier proteins**
- **Carrier proteins** speed up their diffusion through the phospholipid bilayer.

Passive Transport



Passive Transport

- There are a limited number of carrier protein molecules per unit of membrane area
    - Therefore, the rate of diffusion reaches a maximum when all the carrier molecules are fully loaded with solute molecules.
- At this point, the facilitated diffusion system is said to be **saturated**.



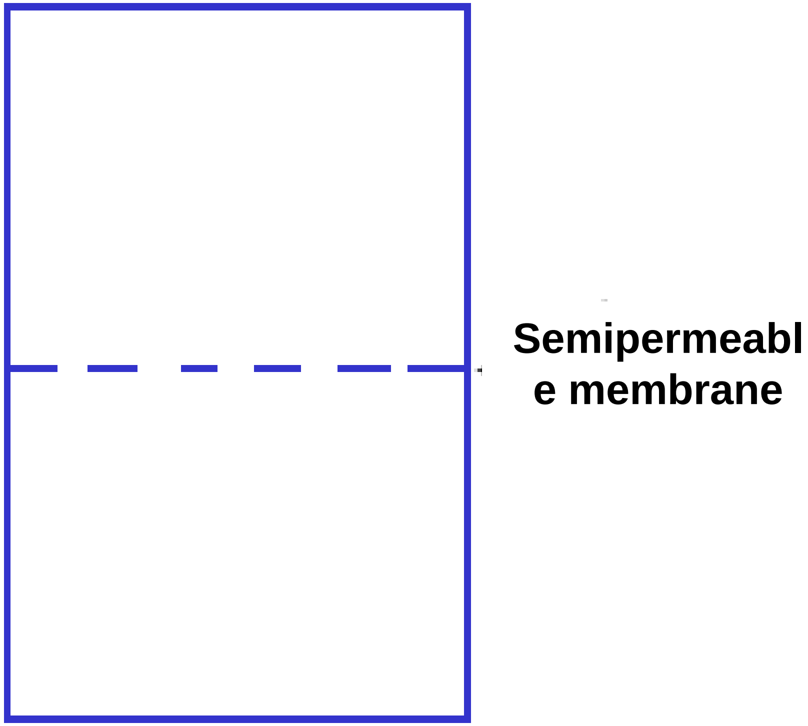
Passive Transport

- Gases (*e.g.*, O_2 and CO_2) and alcohols (*e.g.*, glycerol and ethanol) can diffuse through the lipid bilayer.
- Examples: Glucose or amino acids moving from blood into a cell.
- The diffusion of free water across a selectively permeable membrane is called **osmosis**.

Osmosis

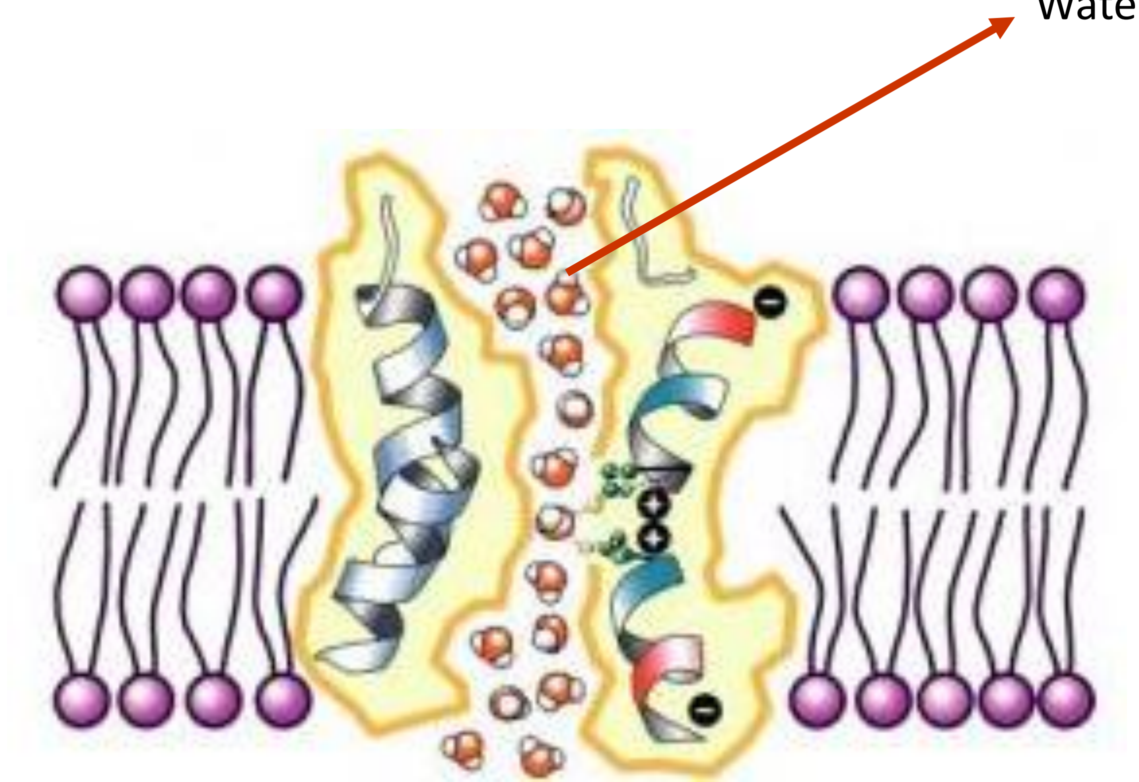
- Diffusion of water across a membrane
- Moves from HIGH water potential (low solute) to LOW water potential (high solute)

Diffusion across a membrane



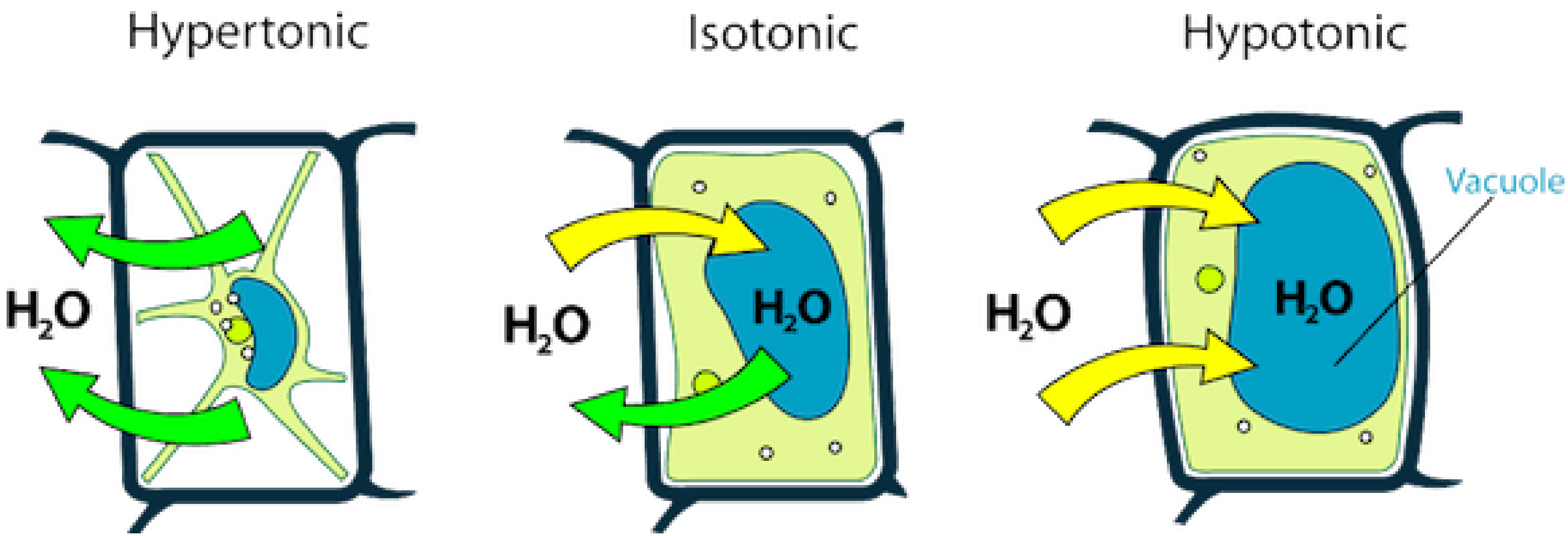
Aquaporins

- Water Channels
- Protein pores used during OSMOSIS



Passive Transport

Water moves across the membrane into the area of lower water (higher solute) content.



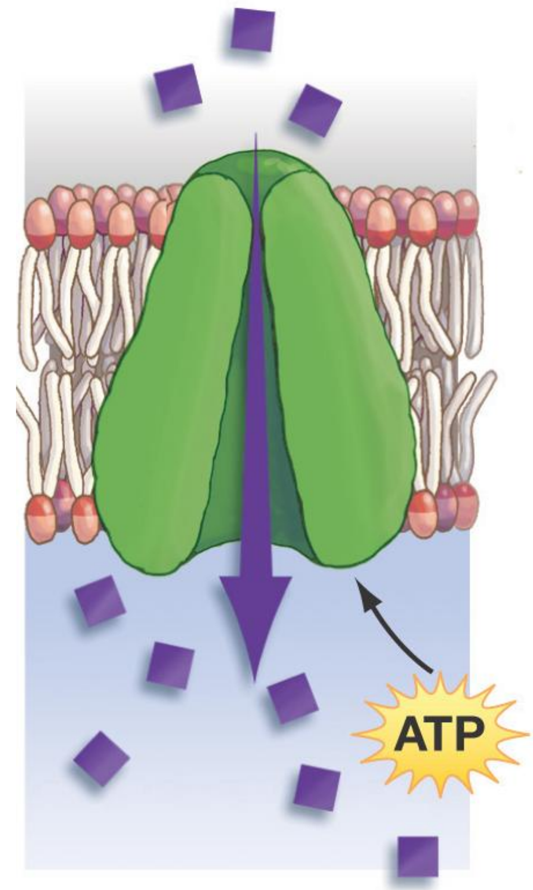
when cells are in a **hypertonic** solution, they lose water.

cells neither gain nor lose water

when cells are in a **hypotonic** solution, they gain water

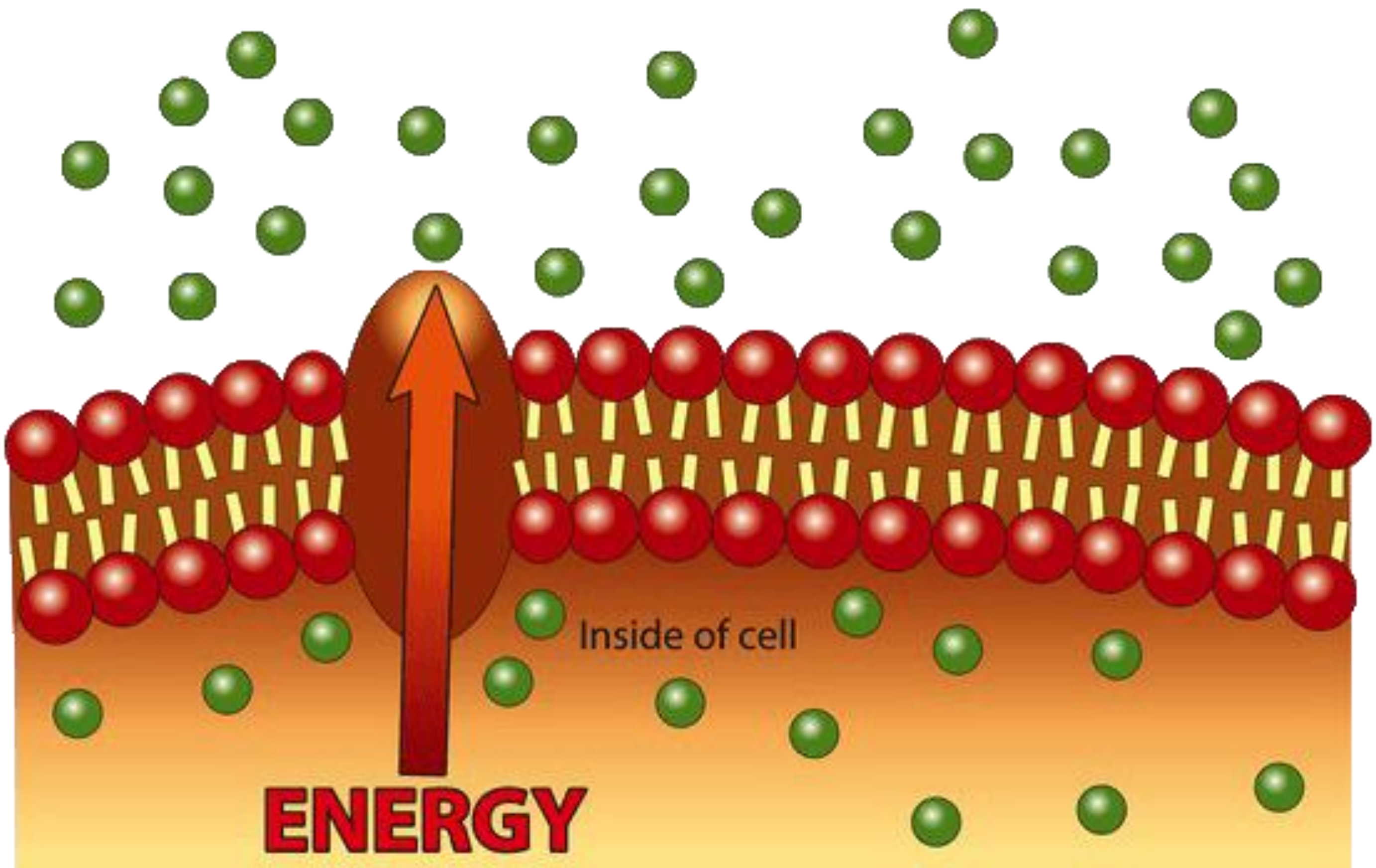
Active Transport

- **Active transport** requires the use of chemical energy to move substances across membranes against their concentration gradients.
- Moves materials from LOW to HIGH concentration
- AGAINST concentration gradient



Molecules again move through a transport protein, but now energy must be expended to move them against their concentration gradient.

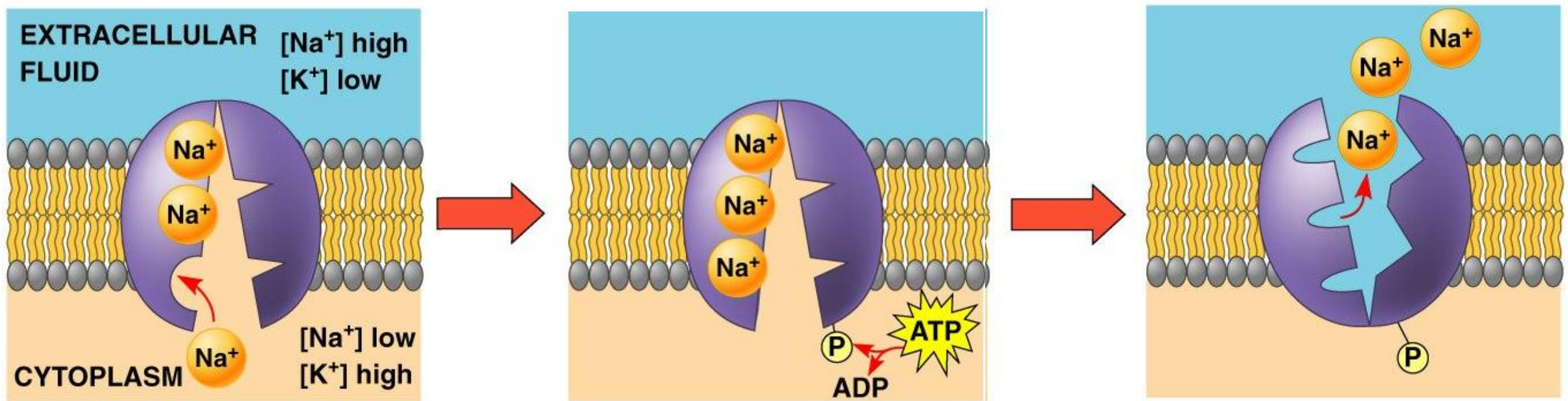
Active Transport



Active Transport

- **Sodium–potassium (Na^+–K^+) pump** uses energy released from the hydrolysis of ATP to move ions against their concentration gradients (Na^+ out, K^+ in)
- Sodium–potassium (Na^+–K^+) pump is especially associated with nerve and muscle cells.

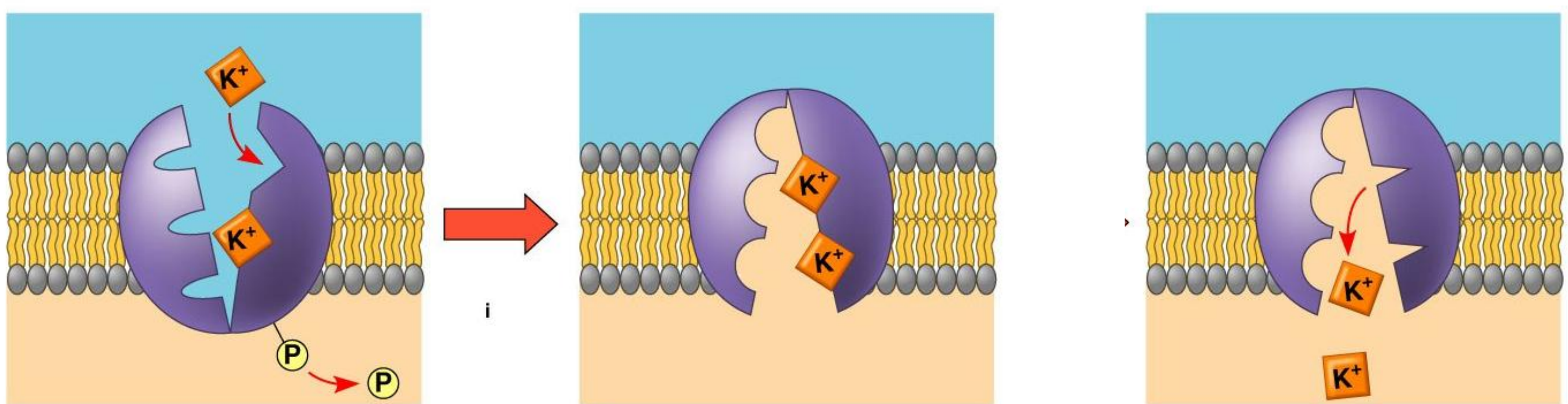
Active Transport



1 Cytoplasmic Na$^+$ binds 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.

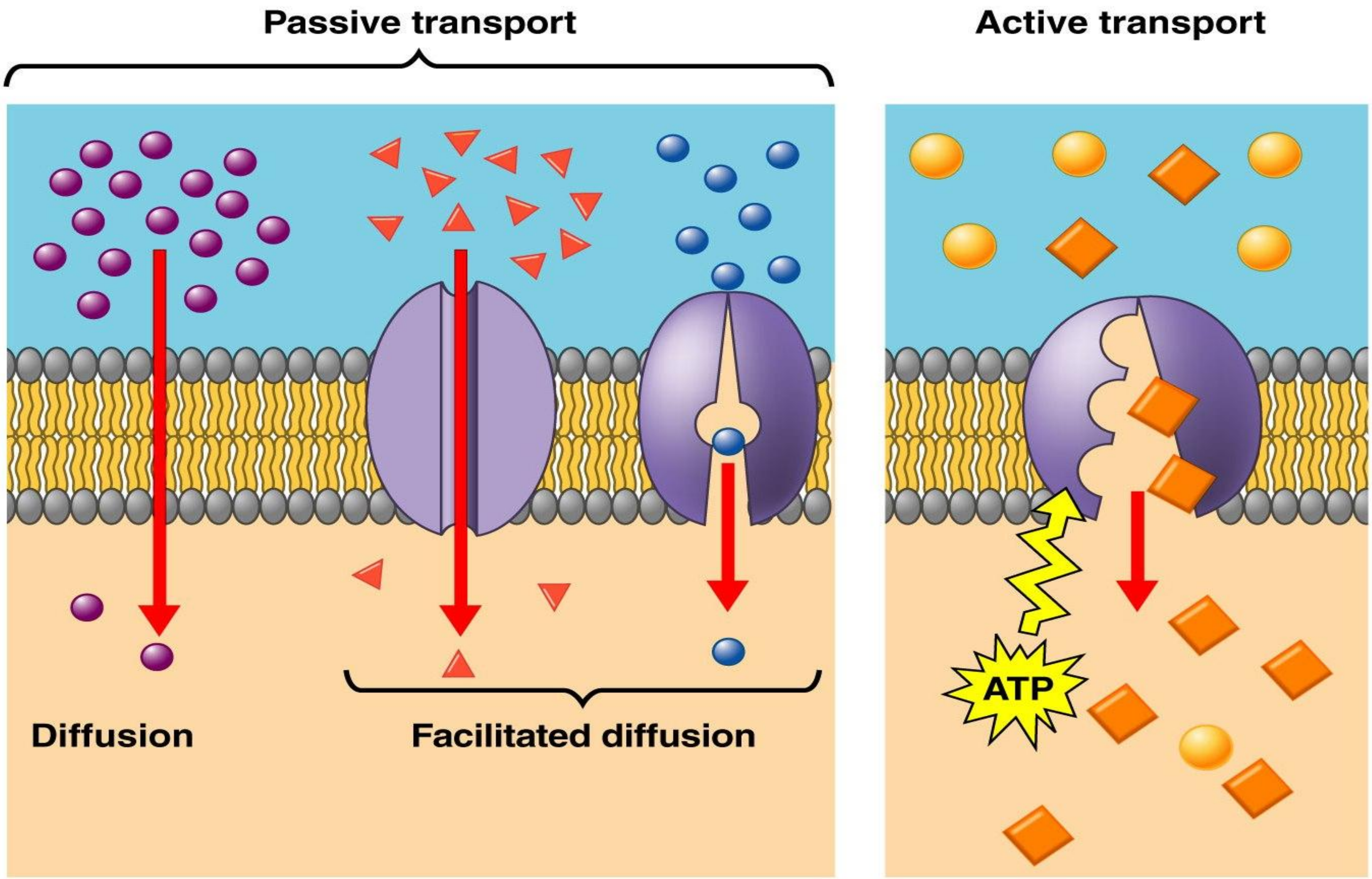


4 Extracellular K$^+$ binds to the protein, triggering release of the phosphate group.

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

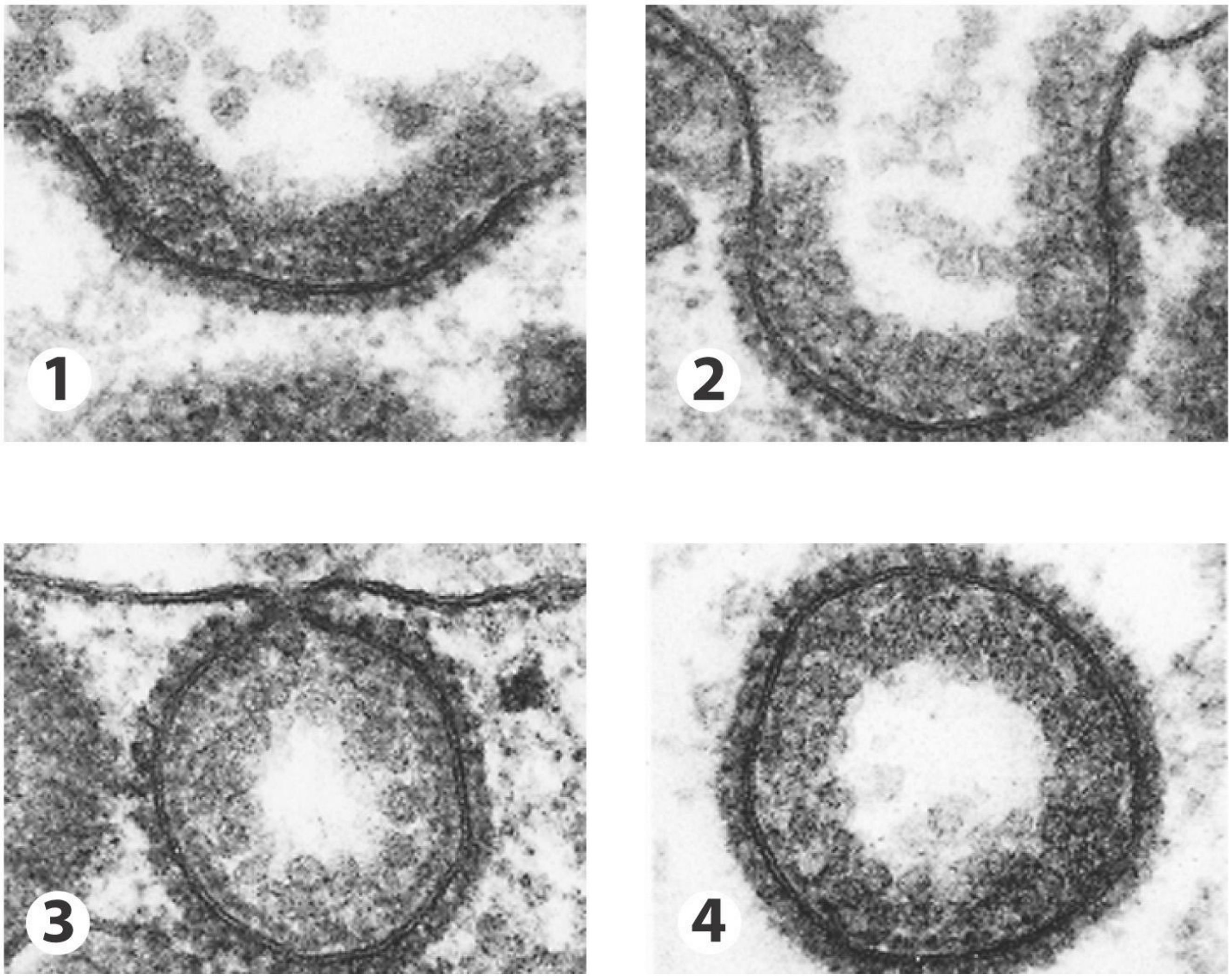
6 K$^+$ is released and Na$^+$ sites are receptive again; the cycle repeats.

Active Transport

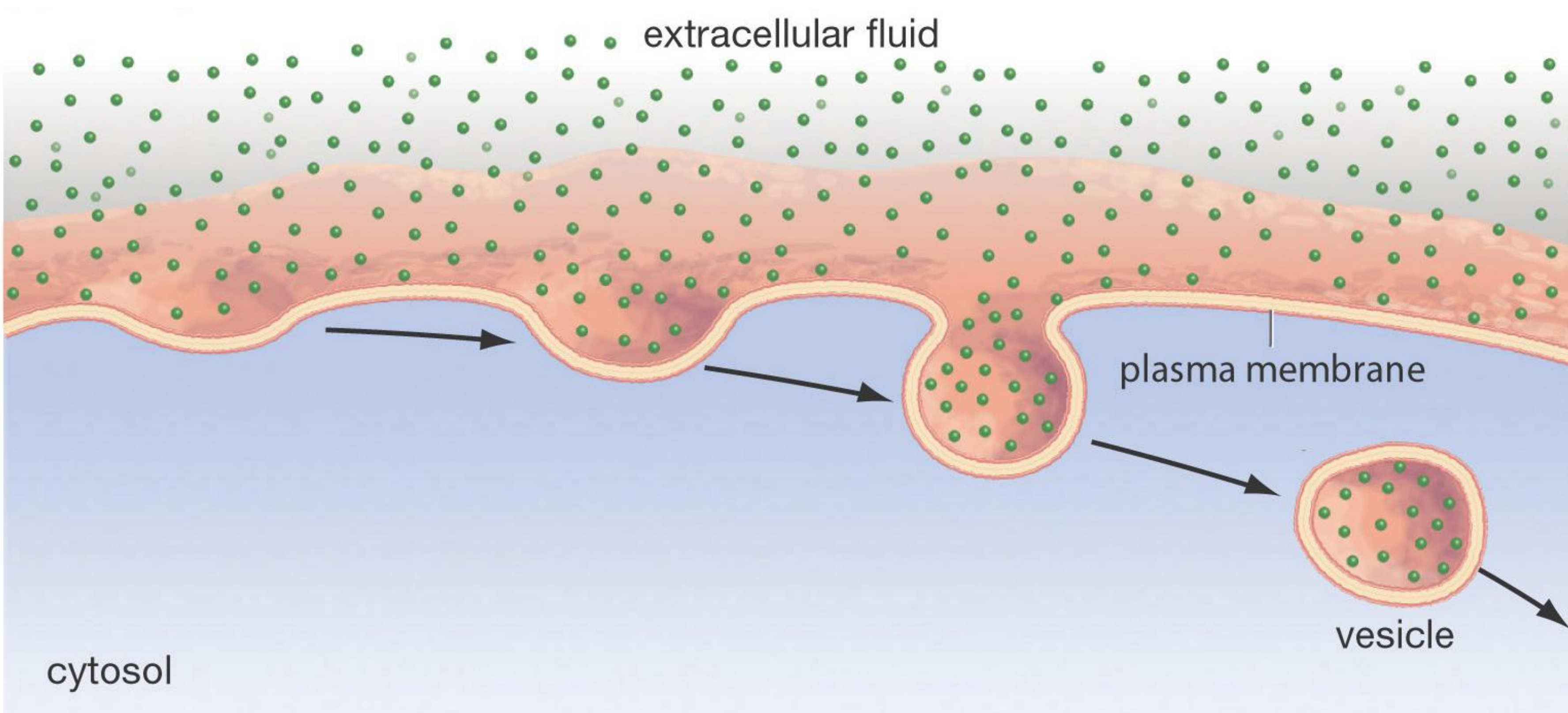


Moving the "Big Stuff"

Large molecules move materials into the cell by one of three forms of endocytosis.



Pinocytosis



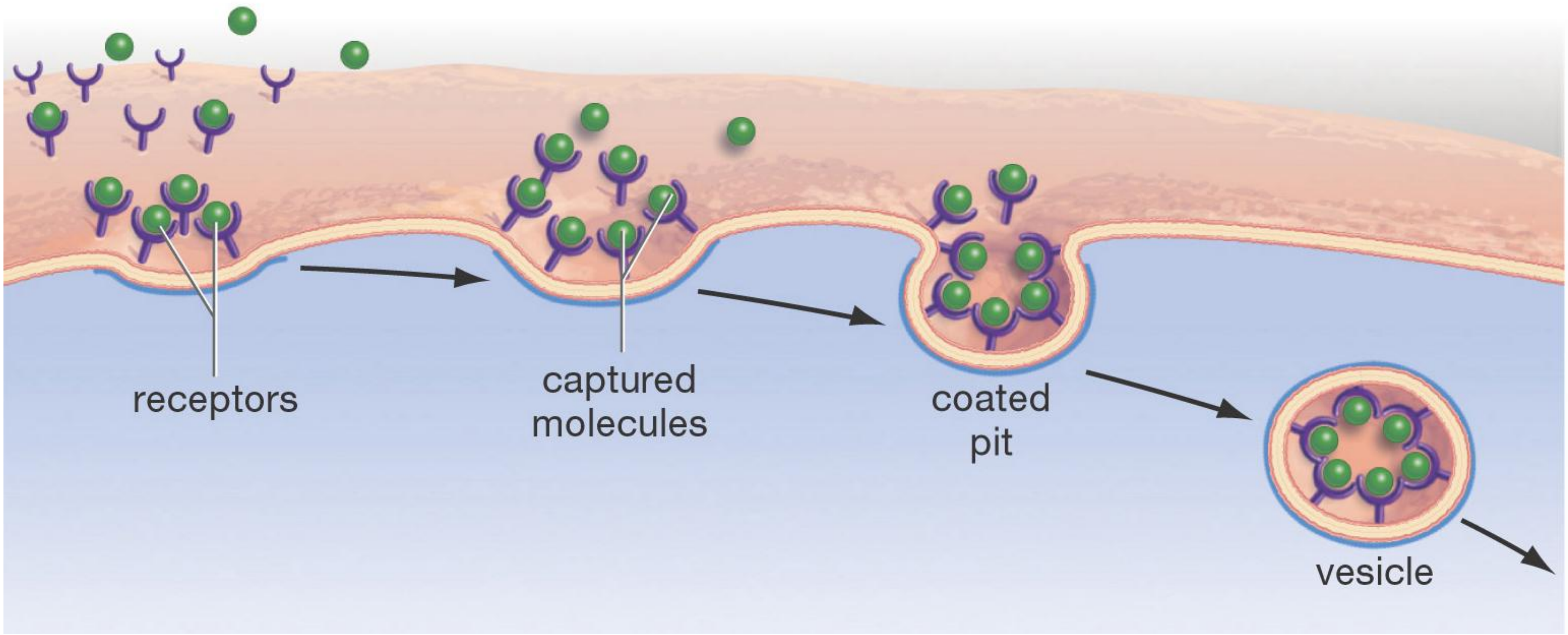
Most common form of endocytosis.

Takes in dissolved molecules as a vesicle.

Pinocytosis

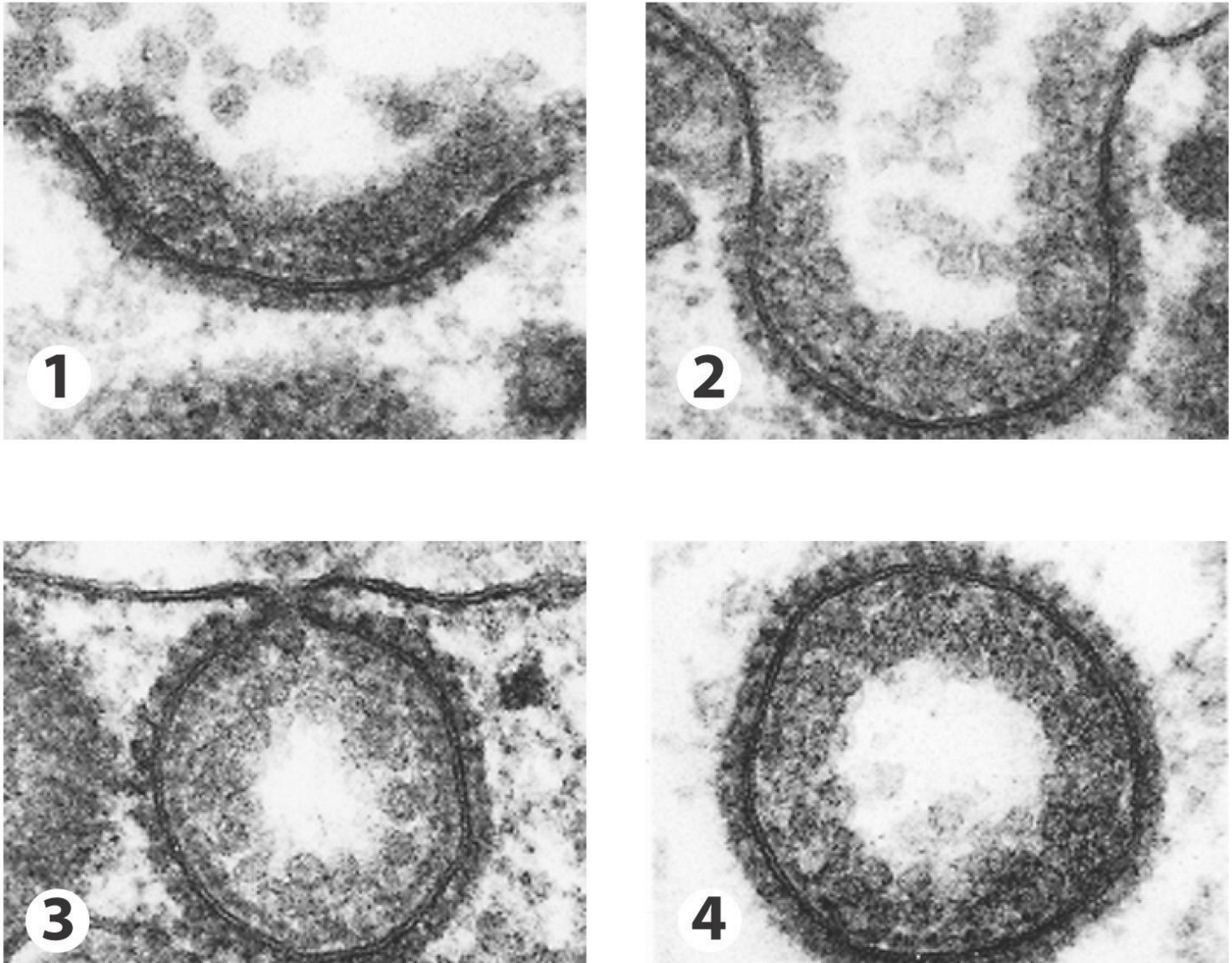
- Cell forms an invagination
- Materials dissolve in water to be brought into cell
- Called "Cell Drinking"

Receptor-Mediated Endocytosis

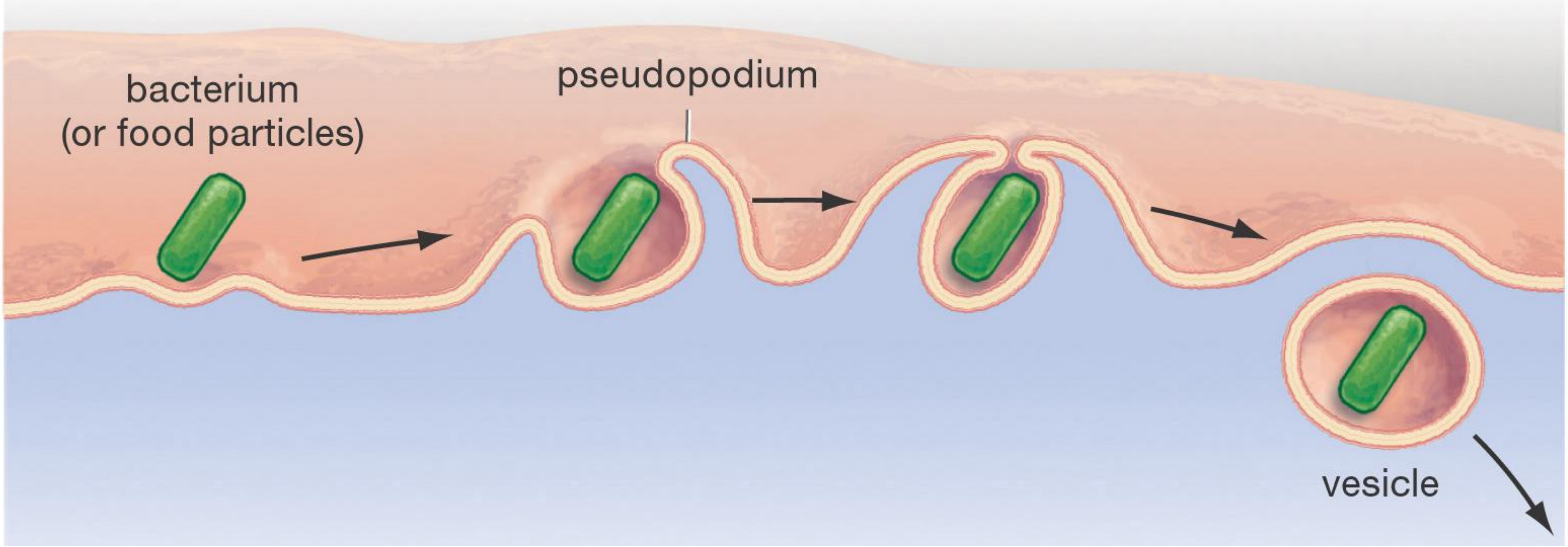


Some integral proteins have receptors on their surface to recognize and take in hormones, cholesterol, etc.

Receptor-Mediated Endocytosis



Endocytosis – Phagocytosis



Used to engulf large particles such as food, bacteria, etc. into vesicles

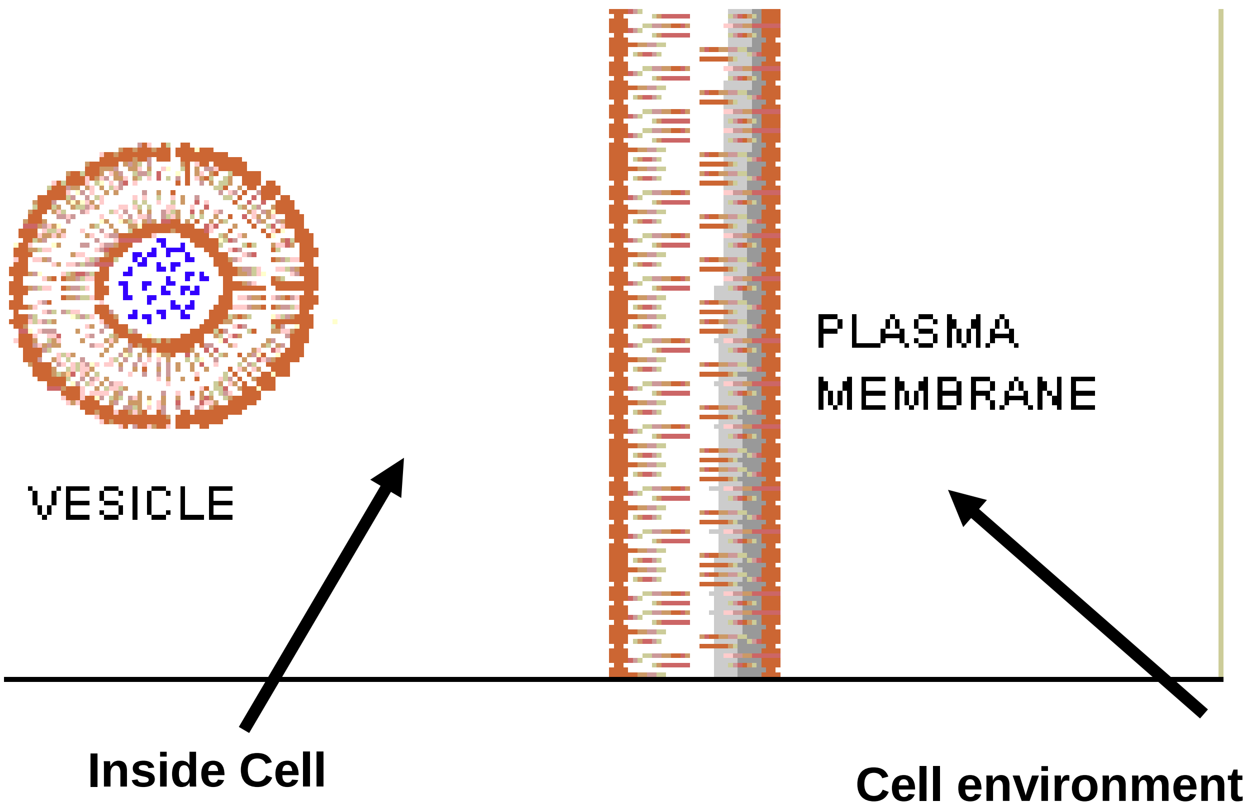
Called "Cell Eating"

Phagocytosis

- Capture of a yeast cell (yellow) by membrane extensions of an Immune System Cell (blue)

Exocytosis

- The opposite of endocytosis
- **Large molecules** that are manufactured in the cell are **released** through the cell membrane.



Summary

- ✓ Both membrane phospholipids and membrane proteins have hydrophilic and hydrophobic regions, giving them dual solubility properties. Hydrophobic regions of these membrane components are oriented inward and hydrophilic regions oriented outward.
- ✓ Biological membranes are based on a fluid phospholipid bilayer in which phospholipids can diffuse laterally. Membrane fluidity is dependent on the lipid composition of the membrane and on temperature.
- ✓ Integral membrane proteins are embedded in the phospholipid bilayer; peripheral proteins are attached to the membrane surface. Different patterns of membrane proteins give the membrane the look of a mosaic.
- ✓ Membrane proteins play essential roles in many biological processes, such as molecular transport, signalling, biocatalysis, interaction and fusion between cells.

Summary

- Membranes also contain glycoproteins and glycolipids, oligosaccharide groups of which form a viscous layer called glycocalyx on the surface of the cell. Many of the molecular recognition events take place in this layer of the cell membrane.

- Diffusion is the kinetic movement of molecules or ions from an area of high concentration to an area of low concentration (that is, down their concentration gradients).

- Osmosis is the diffusion of water. As all cells are composed of mostly water, maintaining osmotic balance is essential to life.

Summary

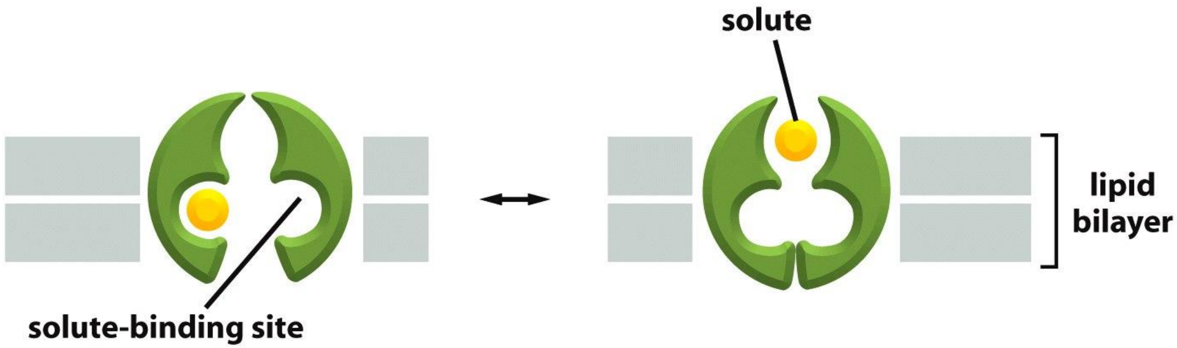
- ✓ Ions and large polar molecules cannot cross the phospholipid bilayer. This is due to the selectively permeable nature of the cell membrane. Diffusion can still occur with the help of proteins, hence this process is referred to as facilitated diffusion.

- ✓ Transport proteins can be either channels or carriers.

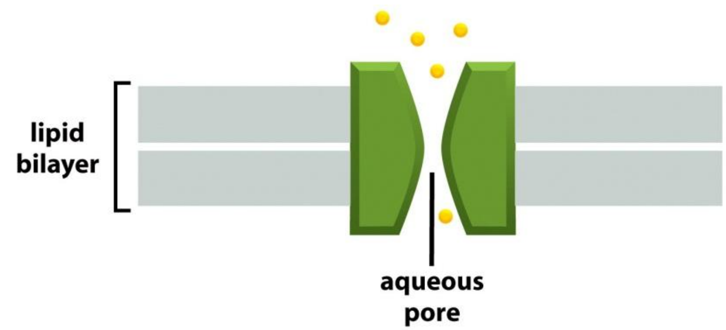
- ✓ Ion channels (most gated) form aqueous pores in the membrane and allow the diffusion of specific ions; carriers bind to the molecules they transport so the rate of transport is limited by the number of carriers in the membrane.

- ✓ Cells employ active transport to move substances across the plasma membrane against their concentration gradients, either accumulating them within the cell or extruding them from the cell. Active transport uses specialised carrier proteins (pumps) that require energy from ATP.

Two main classes of membrane transport proteins: Transporters and Channels



TRANSPORTER



CHANNEL PROTEIN

<u>All these proteins are multi-pass transmembrane proteins</u>

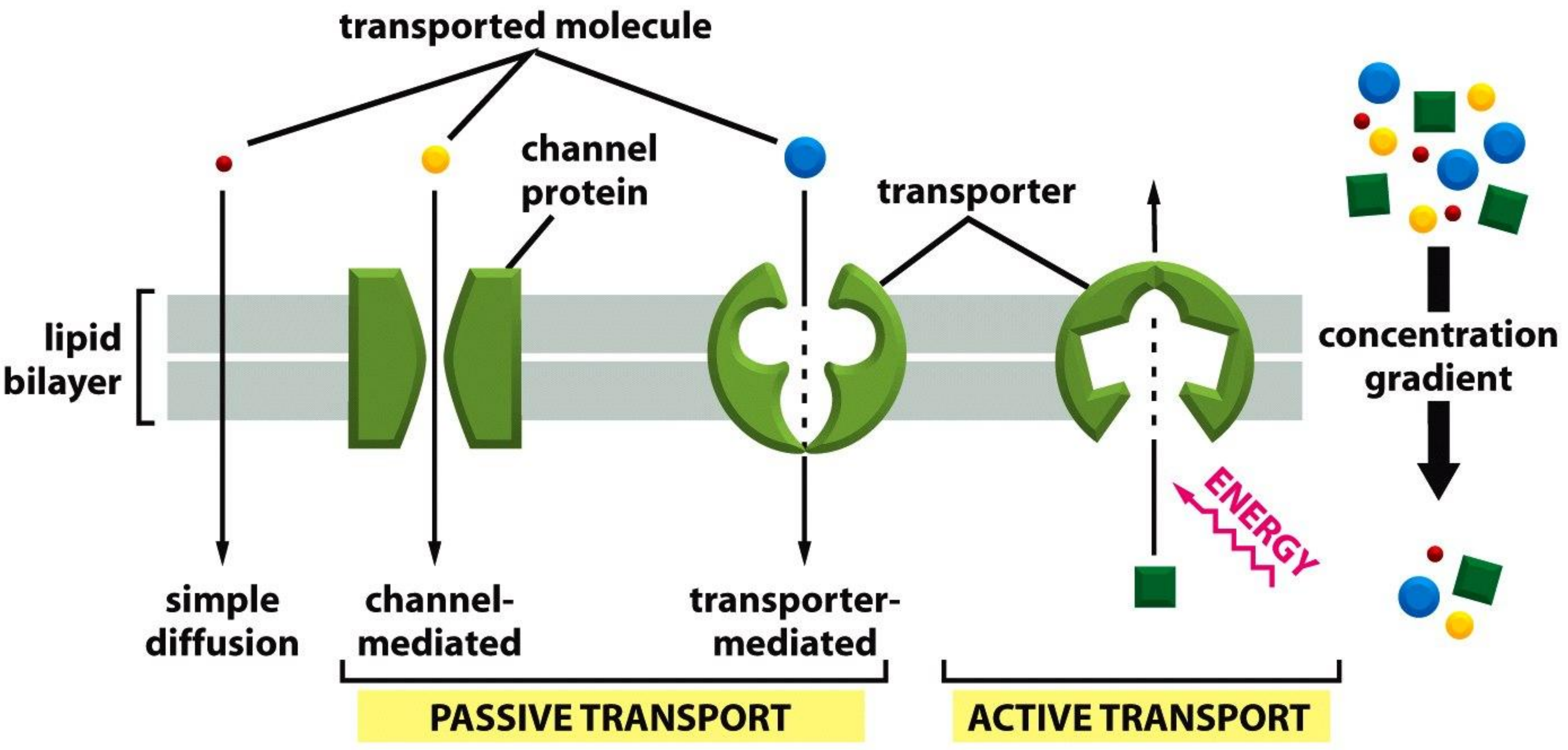
1. Transporters bind to a specific solute and undergo a series of conformational changes.

2. Channel proteins interact with the solute much more weakly; form aqueous pores; transport at a much faster rate.

Summary

	SIMPLE DIFFUSION	FACILITATED DIFFUSION	ACTIVE TRANSPORT
Driving force	Concentration gradient	Concentration gradient	ATP hydrolysis
Direction of transport	With gradient of transported substance	With gradient of transported substance	Against gradient of transported substance
Metabolic energy required?	No	No	Yes
Membrane protein required?	No	Yes	Yes
Saturation at high concentrations of transported molecules	No	Yes	Yes

Solutes cross membranes by passive or active transport



Reading:

pp. 617–650 (Chapter 10)

pp. 651–694 (Chapter 11)

*Figures are mainly obtained from the Molecular Biology of the Cell, 5th Ed.