

Cell Physiology

Cell: Is The basic structural, functional, and smallest living unit of the body, and its aggregate form is tissue or organ.

Cells consist of three main parts:

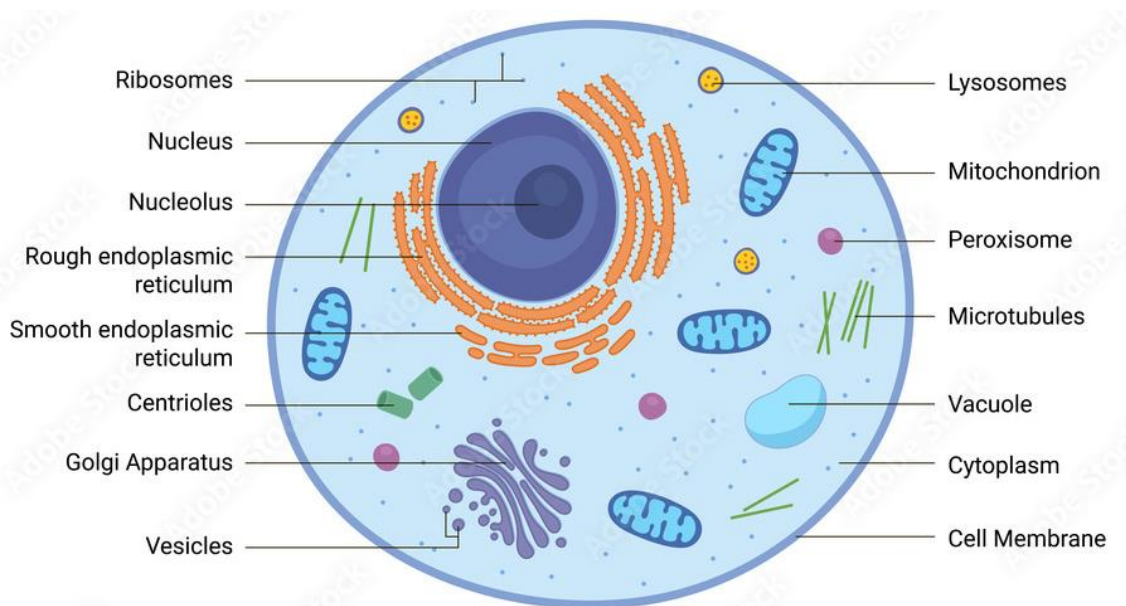
- 1- Plasma membrane or cell membrane
- 2- Cytoplasm
- 3- Nucleus

Plasma Membrane: Each cell is enclosed by a membrane called the plasma membrane, which separates intracellular fluid from extracellular fluid. It is a selectively permeable membrane that regulates the transport of substances into and out of the cell. It allows some substances to pass through it and excludes others. The permeability can be varied due to the presence of ion channels and other transport proteins.

Cytoplasm: Cytoplasm consists of all the contents of the cell between the plasma membrane and the nucleus. It is divided into the cytosol and organelles.

- Cytosol is the fluid portion of cytoplasm containing water, solutes, suspended particles etc.
- Organelles, also known as little organs, have a characteristic shape and perform specific functions, e.g., ribosome, endoplasmic reticulum, Golgi complex, lysosome, peroxisomes, mitochondria etc.

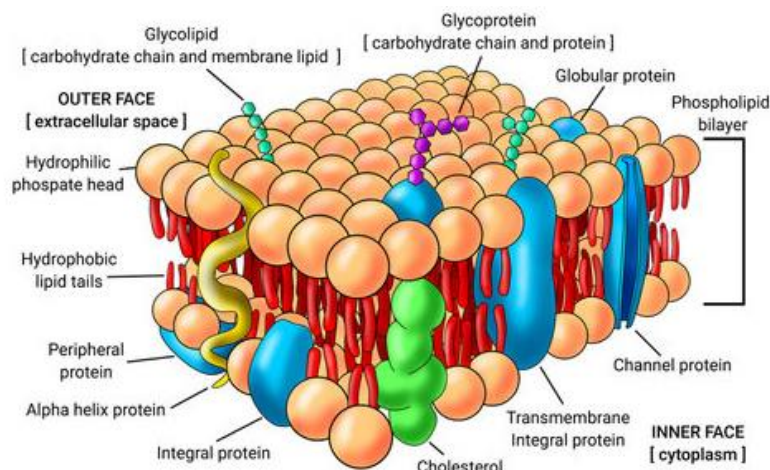
Nucleus: The Nucleus contains most of the DNA in the cell. It contains chromosomes, and each chromosome contains genes that control all the functions of the cell.



Structure of Cell Membrane:

Cell membrane is a three-layered structure showing an outer electron dense layer, middle electro loosened layer and inner electron dense layer. Membrane is primarily lipoprotein in nature and sometimes it may be glycoprotein.

The lipids are phospholipids, cholesterol and sphingomyelin. Phospholipids are phosphatidyl choline and phosphatidyl ethanol amine. The head end of the molecule contains a phosphate portion and is relatively soluble in water and is called polar or hydrophilic end. The tail is relatively insoluble and is called nonpolar or hydrophobic end.



The uncharged hydro- phobic end resides within the depth of the cell membrane and the charged hydrophilic end is exposed to cytoplasm.

There are different proteins embedded in the cell membrane. Periphenl proteins stud the inside and outside of the membrane. When the protein extends throughout the thickness of the membrane, it is called transmembrane protein channel.

1- Lipids:

Biological membranes are primarily composed of phospholipids, cholesterol, and glycolipids, all of which are amphipathic molecules with distinct hydrophilic head groups and hydrophobic fatty-acid tails. These lipids spontaneously organize into a continuous bilayer in which the polar heads face the intracellular and extracellular fluids, while the hydrophobic tails form the membrane's core. Despite the close apposition of the inner and outer leaflets, lipid exchange between the two layers is minimal, preserving membrane asymmetry and structural integrity.

1.1. Phospholipids: Phospholipids are the main structural lipids of cell membranes, composed of fatty acid tails and phosphate-containing head groups. Major types

include several phosphatidyl compounds and sphingomyelin, which provides structural variation and functional diversity.

- 1.2. Cholesterol: Cholesterol, the second most abundant membrane lipid, is largely hydrophobic with a single polar hydroxyl group that aligns near the bilayer surface. Its rigid four-ring steroid nucleus decreases membrane fluidity while enhancing structural strength and stability.
- 1.3. Glycolipids: located mainly in the membrane's outer leaflet, consist of a sphingosine-linked fatty acid tail and a carbohydrate head group. They form a carbohydrate-rich cell coat that supports cell recognition, intercellular communication, and antigenic properties.

2. Proteins:

The lipid bilayer acts as a barrier to most hydrophilic substances, permitting only small lipid-soluble molecules to diffuse freely. To sustain cellular functions in an aqueous environment, the plasma membrane incorporates proteins that facilitate ion and molecule transport, enable cell-cell communication, and sense external signals. These proteins are classified as peripheral, residing on the membrane surface, or integral, spanning or embedding within the bilayer.

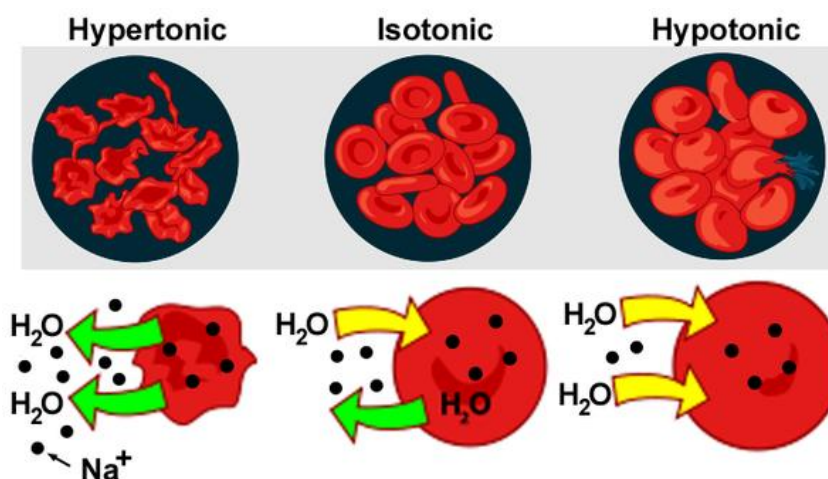
- 2.1 Peripheral proteins loosely associate with the plasma membrane's inner or outer surface and can be removed with mild treatments. Intracellular peripheral proteins include enzymes, ion channel regulators, vesicle-trafficking factors, and cytoskeletal tethers such as spectrin and actin. Extracellular counterparts encompass enzymes, antigens, and adhesion molecules, many of which are anchored via glycosylphosphatidylinositol (GPI).
- 2.2. Integral: Integral membrane proteins penetrate the lipid core. They are anchored by covalent bonds to surrounding structures and can only be removed by experimentally treating the membrane with a detergent. Some integral proteins may remain localized to one or the other of the two membrane leaflets without actually traversing its width. Others may weave across the membrane many times (transmembrane proteins) .

TRANSPORT PROCESSES ACROSS THE CELL MEMBRANE

- 1- Osmosis
- 2- Diffusion
- 3- Active transport
- 4- Endocytosis and exocytosis

1- Osmosis: is defined as the movement of water molecules (solvent) across a semi-permeable membrane from a region of lower solute concentration to an area of higher solute concentration.

During osmosis, water molecules pass through the plasma membrane in two ways: (1) by moving through the lipid bilayer because of their small size and high kinetic energy, (2) by moving through aquaporins which are membrane proteins functioning as water channels.



Hypertonic solution: is any external solution that has a high solute concentration and low water concentration compared to body fluids.

Hypotonic solution: is any external solution that has a low solute concentration and high water concentration compared to body fluids.

Isotonic solution: is any external solution that has the same solute concentration and water concentration compared to body fluids.

Osmolarity: total concentration (osmoles per liter) of all solutes (penetrating + non-penetrating).

Osmolality: osmoles per kg of solvent (more precise for physiology).

Tonicity: refers only to nonpenetrating solutes (those to which the cell membrane is impermeable). Tonicity predicts cell volume changes.

If outside solution has many penetrating solutes, they may equilibrate across the membrane and not affect tonicity.

Thus, two solutions with equal osmolarity can have different tonicity depending on solute permeability.

Application:

A. Intracellular / Extracellular Fluid Equilibrium

The distribution of solutes between intracellular fluid (ICF) and extracellular fluid (ECF) largely determines osmotic forces across the cell membrane.

Because water permeability is very high relative to solute permeability, cells rapidly equilibrate in terms of tonicity: ICF and ECF remain isotonic under normal conditions.

Electrolytes (especially sodium, potassium, chloride) are key in controlling osmotic balance because they largely do not cross membranes freely.

B. Edema & Fluid Shifts

Osmotic pressure differences can drive fluid out of capillaries (into interstitial space) or back into capillaries, influencing edema formation.

In conditions of hypoalbuminemia, the plasma colloid osmotic pressure is reduced, altering fluid balance.

C. Kidneys & Urine Concentration

The kidney uses osmotic gradients in the renal medulla (high osmolarity in interstitium) to pull water out of collecting ducts, concentrating urine.

ADH (antidiuretic hormone) regulates water permeability (via insertion of aquaporins) in the collecting duct, allowing osmosis to operate.

2- Diffusion: is a passage of ions or molecules from region of higher concentration to region of low concentration and occur either through the lipid matrix or through transmembrane protein channels.

A- Diffusion through lipid matrix: The lipid bilayer is freely permeable to water because the molecules are small and have high kinetic energy and It is also permeable to urea.

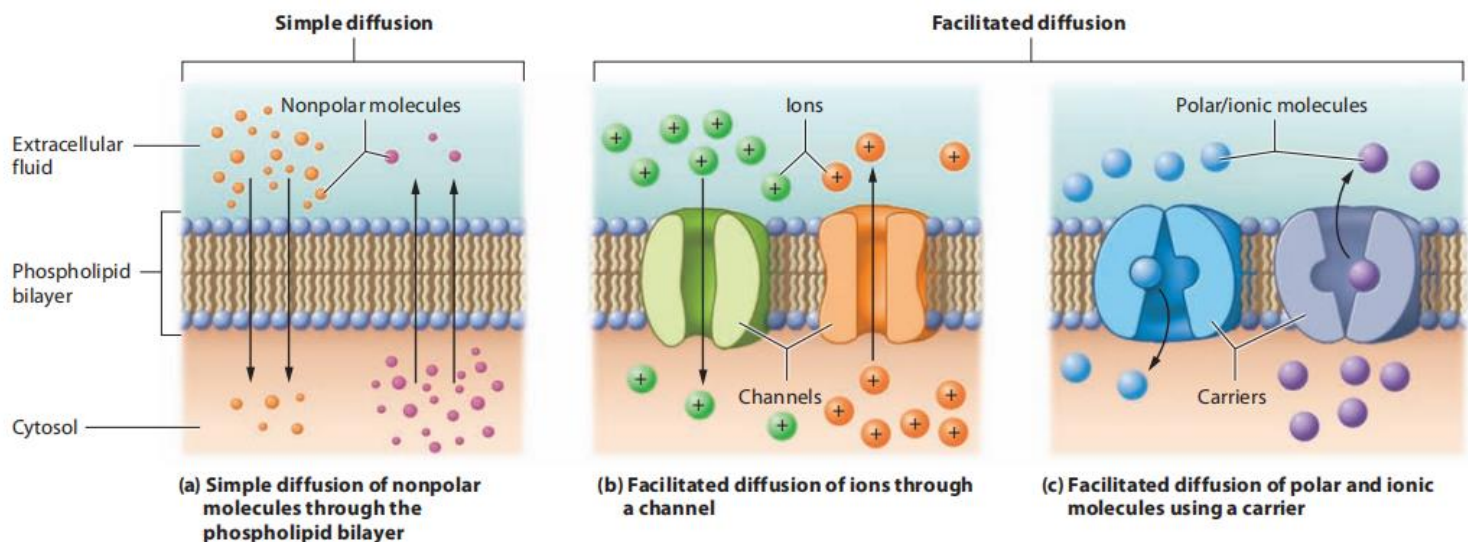
Its permeability to other substances depends on their size, lipid solubility and charge. Plasma membrane is permeable to Non-polar, uncharged, hydrophobic substances like O₂, CO₂, N₂, fatty acids, alcohol, steroid hormones etc.

The lipid bilayer is impermeable to ions and charged or polar molecules like glucose.

- B-** Diffusion through ion channels or transmembrane protein channels: Ions like Na, K⁺, Ca, Cl etc., can cross the cell membrane only through some channels in the cell membrane. Different types of protein channels are present, open type or those which can be closed. Open channels are also called leak channels. e.g., K⁺ channel.

Two basic types of diffusion occur through a membrane: simple and facilitated

- **Simple diffusion** mostly involves nonpolar solutes (such as hydrocarbons and lipids, and gases such as O₂ and CO₂) that pass straight through the phospholipid bilayer without assistance from a membrane protein.
- **Facilitated diffusion** involves charged or polar solutes (such as ions and glucose) that cross the phospholipid bilayer with the help of a membrane protein.

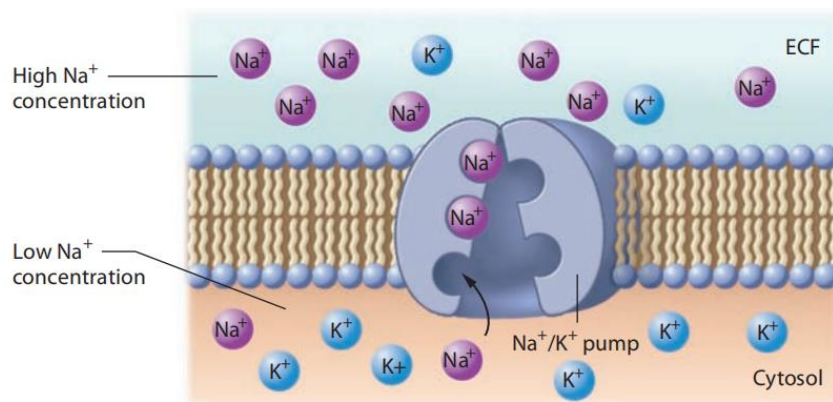


3- Active transport: The passage of substances against their electrical and chemical gradients at the expenditure of energy. The energy is provided by the hydrolysis of ATP in primary active transport. The energy stored in an ionic concentration gradient produced by primary active transport is the source of energy in secondary active transport. Both processes require a carrier protein.

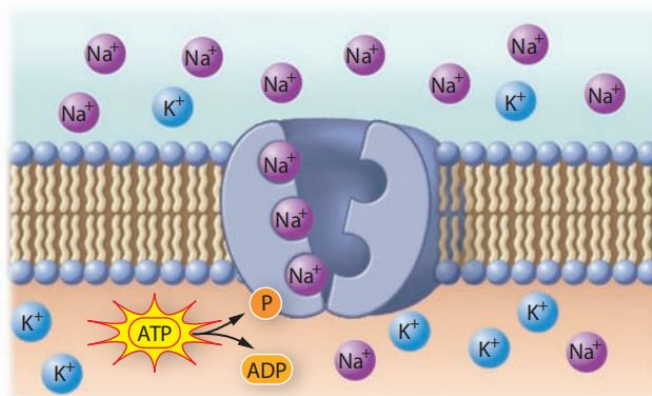
A- **Primary Active Transport:** the carrier protein involved is called pump. 40% of ATP produced in a cell is utilized for primary active transport. The enzymes which catalyze the hydrolysis of ATP is called ATPase. Different types of pumps are:

- $\text{Na}^+\text{-K}^+$ pump
- $\text{H}^+\text{-K}^+$ pump
- Ca^{2+} pump
- $\text{Na}^+\text{-H}^+$ pump

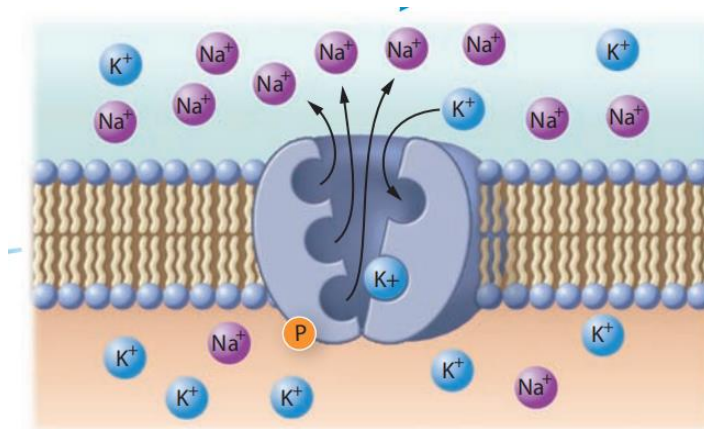
The major primary active transport pump in the body is the antiport pump known as the sodium-potassium pump. Normally the concentration of sodium ions in the ECF is about 10 times greater than that in the cytosol. The reverse is true for potassium ions—its concentration in the cytosol is about 10 times higher than its concentration in the ECF. It is absolutely critical to our homeostasis to maintain the concentration gradients of sodium and potassium ions. These gradients are required for skeletal muscles to contract, hearts to beat, nerves to send impulses, and cells to maintain their osmotic balance, among many other functions.



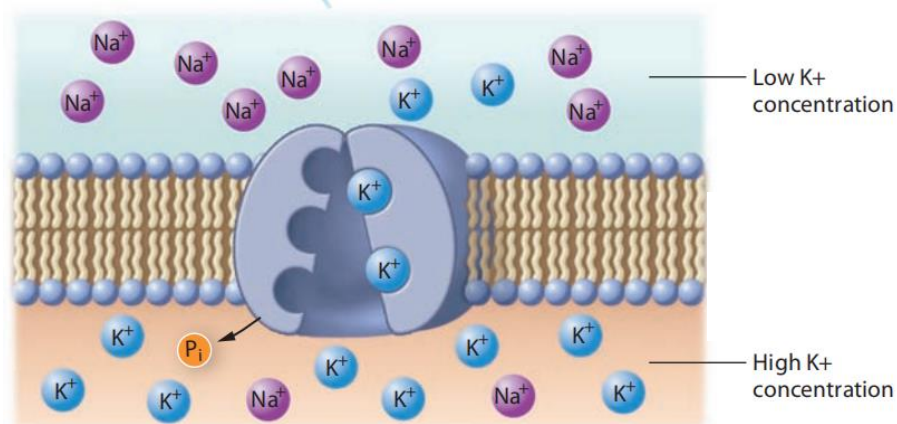
① The pump binds three Na⁺ from the cytosol.



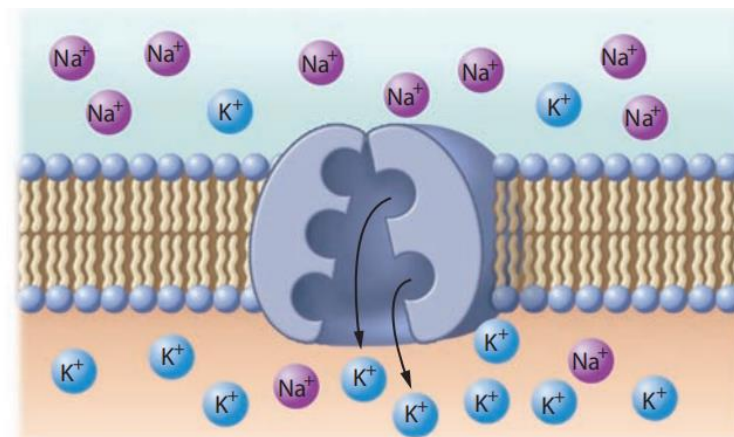
② ATP is hydrolyzed, the phosphate binds to the pump, and the pump changes shape.



③ The pump releases the three Na^+ into the ECF and binds two K^+ .



④ The phosphate detaches, and the pump changes back to its original shape.



⑤ The pump releases the two K^+ into the cytosol.

B- Secondary active transport: In some tissues, the active transport of Na into the ECF by Na^+K^+ pump is coupled to the transport of other substances across the cell membrane against their concentration gradient. When Na is pumped out, the intracellular Na concentration falls and a Na gradient is produced across the cell membrane. Here the free energy stored in the Na gradient produced, is used to transport substances like amino acids, sugars, ions

etc., against their concentration gradient. The energy for the transport is not directly obtained from ATP hydrolysis. It has three types:

- **Uniport** - Here the carrier protein transports one substance in one direction, e.g., glucose transport through glucose transporters in the basal membrane of intestinal epithelial cell into the interstitial space.
- **Symport** -- Here the carrier protein transports two substances in one direction and the transport occurs only if the two substances are attached to the carrier, e.g., Na co-transport of glucose or amino acid across intestinal mucosa.
- **Antiport** -- The carrier protein transports one substance in one direction and another substance in the opposite direction. For example, Na-Ca countertransport in the cardiac muscle.

4- (A) Endocytosis: There are three types:

- a- Receptor-mediated endocytosis:
- b- Phagocytosis
- c- Pinocytosis

Receptor-mediated endocytosis: is a highly specific type of endocytosis by which cells take up specific ligands. A specific molecule that binds to a receptor is called the ligand of that receptor. The receptors for these ligands are concentrated in specific areas of the cell membrane called clathrin-coated pits.

The cell membrane fuses around the receptor-ligand complex forming a vesicle which gets pinched off into the cytoplasm called clathrin-coated vesicle.

Phagocytosis: is the process by which aged and worn-out cells, bacteria, viruses, dead tissue etc., are engulfed by phagocytes of the body, such as neutrophils and macrophages. Phagocytosis begins when the particle makes contact with the cell membrane receptor protein. This part of the plasma membrane then invaginates and the invagination is pinched off into the cell forming phagosome. Phagosome fuses with lysosome and the enzymes break down the ingested material.

Pinocytosis: is an active, energy consuming process where extracellular fluid and solutes are taken up into a cell via small vesicles.

Physiological & Clinical Relevance

- Nutrient Uptake: Iron via transferrin receptor; cholesterol via LDL receptor.
- Immune Defense: Antigen presentation after phagocytosis of pathogens.

- Synaptic Vesicle Recycling: Neurons retrieve membrane after neurotransmitter release.
- Pathogen Entry: Many viruses (influenza, SARS-CoV-2) exploit receptor-mediated endocytosis.
- Disease Example: Familial hypercholesterolemia from defective LDL receptor → impaired LDL endocytosis.

(B) Exocytosis: is the process by which intracellular vesicles fuse with the plasma membrane to release their contents to the extracellular space and/or add lipids and proteins to the cell surface.

Functional Purposes

1- Secretion of molecules:

- Hormones (e.g., insulin from pancreatic β -cells)
- Neurotransmitters (e.g., acetylcholine from presynaptic neurons)
- Digestive enzymes (e.g., pancreatic acinar cells)

2- Membrane remodeling:

- Inserting new plasma-membrane proteins (ion channels, receptors)
- Expanding surface area during cell growth or repair

Physiological and Clinical Correlates

- Neurotransmission: Synaptic vesicle exocytosis underlies communication between neurons.
- Insulin release: Defects in Ca^{2+} -dependent exocytosis contribute to certain forms of diabetes.
- Immune response: Cytotoxic T cells exocytose perforin-containing granules to kill infected cells.
- Toxins & Drugs: Botulinum and tetanus toxins cleave SNARE proteins, blocking neurotransmitter release → paralysis. Black widow spider venom causes massive neurotransmitter exocytosis → severe cramps.

Conclusion table:

Mechanism Type	Energy Requirement	Direction relative to gradients	Mediated by
Passive Transport	No energy (no ATP)	Down concentration or electrochemical gradients	Simple diffusion, facilitated diffusion (channels, carriers)
Active Transport	Requires energy (often ATP)	Against gradients	Pumps, secondary active transporters
Bulk Transport	Requires energy	Bulk movement of macromolecules or particles	Endocytosis, exocytosis