Cell membrane functions

1. **Physical barrier:** Establishes a flexible boundary, protects cellular contents, and supports cell structure. Phospholipid bilayer separates substances inside and outside the cell.
2. **Selective permeability:** Regulates entry and exit of ions, nutrients, and waste molecules through the membrane.
3. **Electrochemical gradients:** Establishes and maintains an electrical charge difference across the plasma membrane.
4. **Communication:** Contains receptors that recognize and respond to molecular signals.

Cell membrane transport

The cell membrane is a selectively permeable membrane, also regarded as a semi-permeable membrane, because it allows some molecules to pass through it while preventing other molecules from passing.

Permeable molecules to the cell membrane include lipophilic molecules (fat-soluble) and small hydrophobic molecules like O2, CO2, N2, and benzene. And small uncharged polar molecules like water, glycerol, and ethanol.

Non-permeable molecules to the cell membrane include large, uncharged polar molecules like sugar and amino acids. And ions like H^+, Na^+, K^+, Cl^-, Ca^{++}, Mg^{++}, $HCO3^-$.

Molecules cross the plasma membrane in 2 ways:

1. **Passive ways**: no energy used. Include simple diffusion and facilitated diffusion.
2. **Active ways**: use energy. Include active transport and vesicular transport.

- **Passive ways:** the movement of substances down a concentration gradient due to the kinetic energy of the substance; no cellular energy is required; continues until equilibrium is reached.

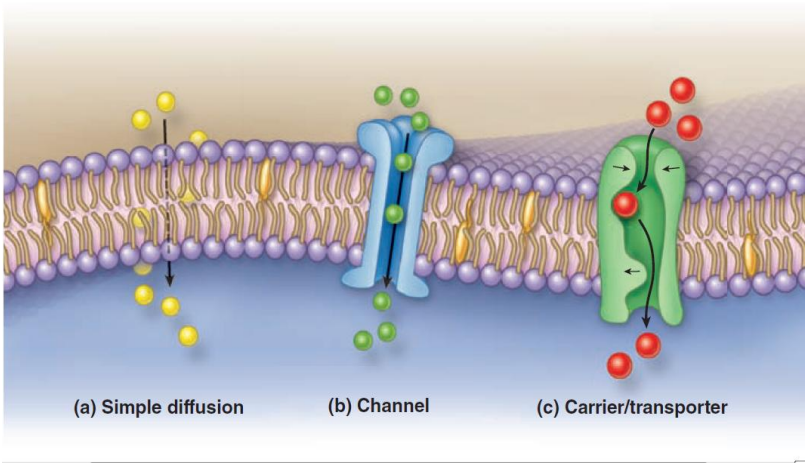


Figure shows major mechanisms by which molecules cross membranes.

1. **Simple diffusion** is the movement of small, nonpolar molecules from a higher concentration gradient to a lower concentration gradient via a selectively permeable membrane until they are distributed equally without using energy, for example.

   - Respiratory gases diffuse through the lipid bilayer; this is the mechanism by which oxygen enters cells and carbon dioxide exits cells.
   - Glycerol and ethanol diffuse simply through the plasma membrane.
   - Also, lipid-soluble molecules pass through the cell membrane without any energy or transport protein or carrier, including steroid hormones like{ estrogen, testosterone…..ect}, vitamin D, and lipid-soluble drugs.

2. **Facilitated diffusion:** this type of passive transport system also doesn't use energy; molecules diffuse across the plasma membrane with assistance from membrane proteins (transmembrane proteins), such as channels and carriers. Because these molecules are large molecules or charged or polar, they can't cross the phospholipid part of the membrane without help.
   a. **Channel proteins**: Channels are transmembrane proteins that are ion selective and are regulated on the basis of the cell's needs used for movement of small polar or charged molecules like water and ions. There are particular channel proteins for each particular molecule. Channel proteins transport solutes down their concentration gradient.

   Water molecules, for instance, cannot cross the membrane rapidly (although, due to their small size and lack of a full charge, they can cross at a slow rate). The phenomenon of water movement through semi permeable membrane called **osmosis**.

   Osmosis is the movement of water molecules through a semi-permeable membrane from a solution with a low solute concentration to a solution with a higher solute concentration until there is an equal solute concentration on both sides of the membrane.

   Transmembrane diffusion of water molecules (by osmosis) involves their passive movement through multipass transmembrane proteins called aquaporins.

   Aquaporin is an example of a channel protein that allows the rapid movement of water across the cell membrane. It facilitates the diffusion of water. Aquaporin proteins are present in the kidney, nephron, and other parts of it for absorbing the water back into the body.

   There are two types of protein channels:

   1. **Leak channels** (non-gated channels) are continuously opened. For example, an open K+ ion channel on neurons and other cells is responsible for maintaining resting potential.
   2. **Gated channels** are stimulus to open and can be regulated by membrane potentials (e.g., **voltage-gated ion channels** in neurons), neurotransmitters (e.g., **ligand-gated ion channels** such as acetylcholine receptors in muscle cells), or mechanical stress (e.g., **mechanically gated ion channels** in the internal ear).

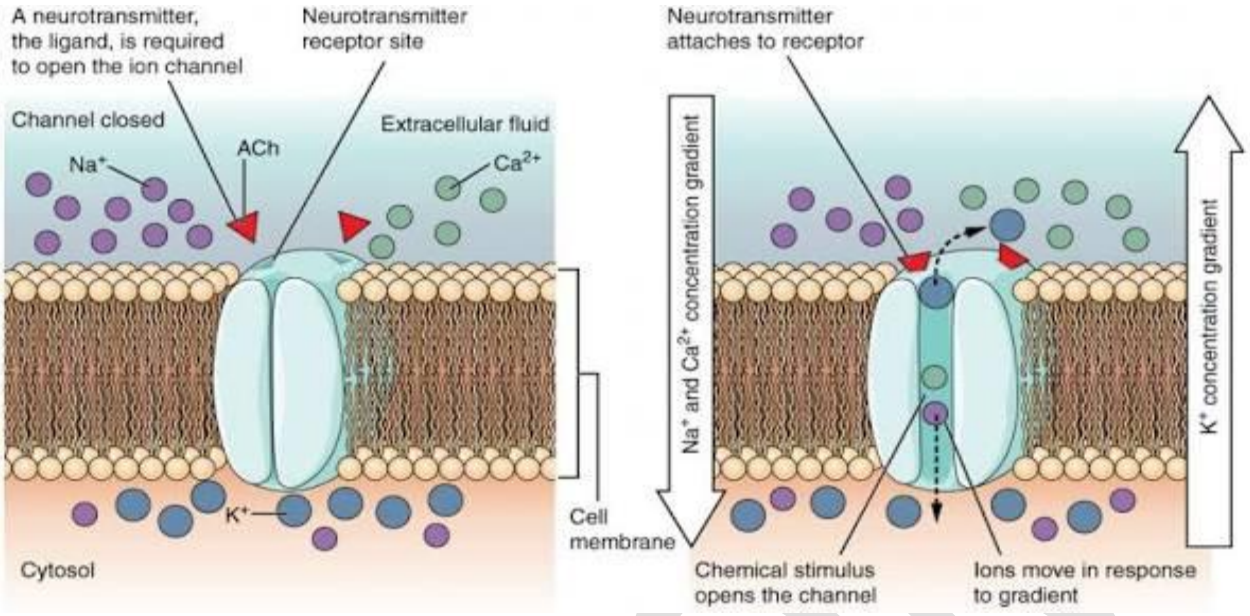


Figure shows ligand-gated ion channels

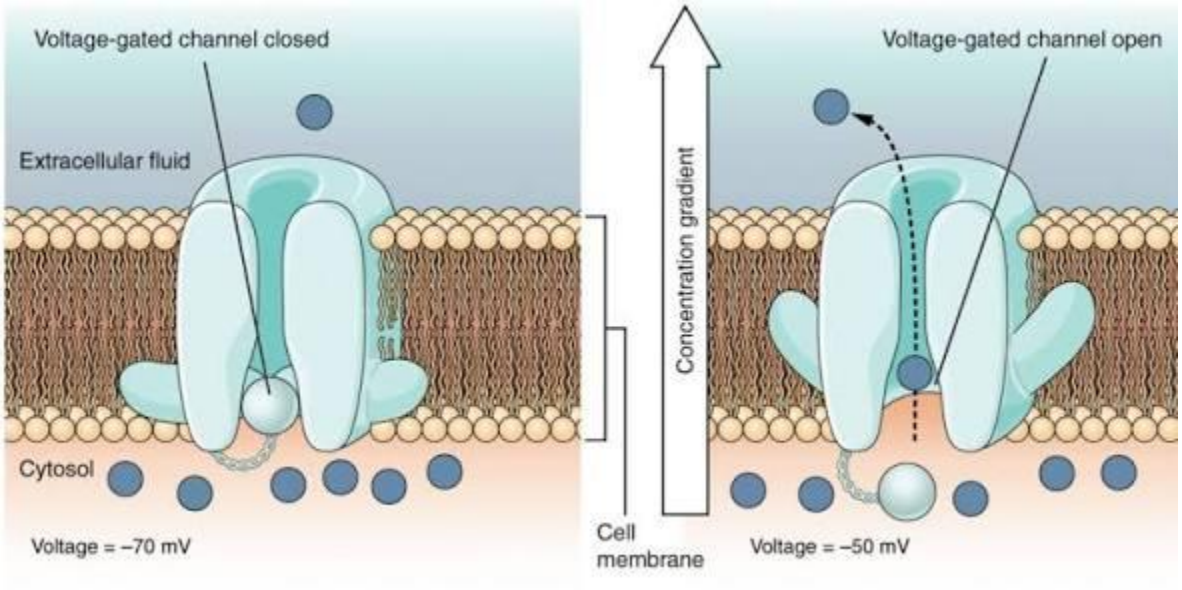


Figure shows voltage-gated ion channels

b. **Carrier-proteins**: Another class of transmembrane proteins involved in facilitated transport consists of the carrier proteins that assist in the movement of large molecules like sugar, carbohydrates, and amino acids from a high concentration gradient to a low concentration gradient. Each protein carrier, which actually changes shape during the process, sometimes called a **transporter,** binds only to a particular molecule, such as glucose transporter or amino acid transporter. Type 2 diabetes mellitus results when cells lack a sufficient number of glucose transporters.

❖ **Active ways:** movement of substances requires expenditure of cellular energy. Divided into two categories.

1. **Active transport:** directly uses a source of chemical energy (e.g., ATP) to move ions and small molecules across a membrane against their gradient.

- Small molecules and ions can be transported across the cell membrane against their concentration gradient if the appropriate transport proteins and a source of energy (ATP) are available.
- **ATP** Adenosine Triphosphate—Nucleotide with three phosphate groups.

The breakdown of ATP into ADP and one inorganic phosphate molecule by ATPase makes energy available for energy-requiring processes in cells.

- Protein transporters involved in active transport mechanisms are often called **pumps; pumps** are transmembrane proteins that use energy to move substances against their concentration gradients.
- Just as water **pump** uses energy to move water against the force of gravity.
- **Sodium-Potassium Pump,** also called Na/K ATPase, moves sodium ions (Na^+) out of and potassium ions (K^+) into cells; important in nerve and muscle cells. The sodium potassium pump causes an electrical concentration gradient (difference of charge) across the membrane, and this is known as a membrane potential. Nerve cells use this membrane potential to send electrical signals along nerves.

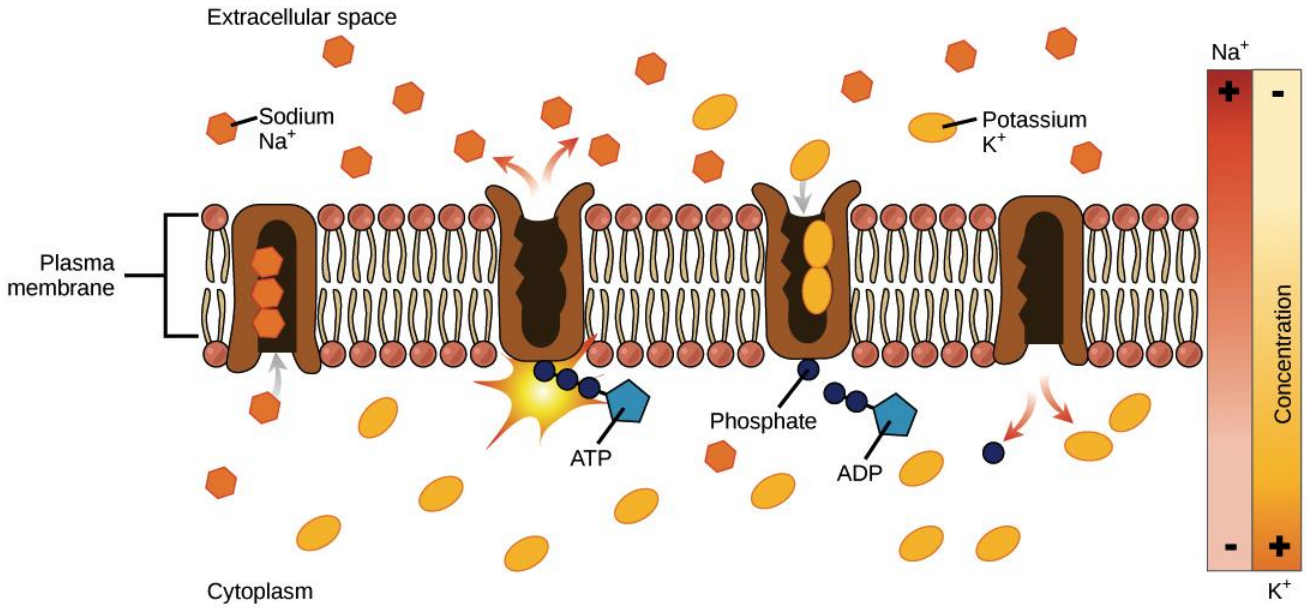


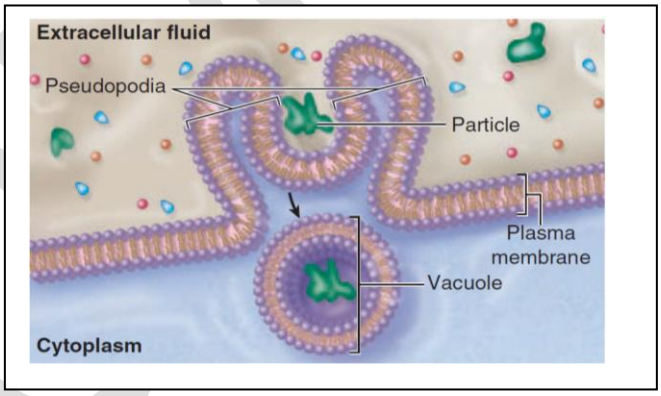
Figure shows the sodium-potassium pump cycle

One of the important clinical applications of active transport is cystic fibrosis (CF). CF is a genetic disorder that occurs when there are defects in a gene on chromosome 7, called CFTR (cystic fibrosis

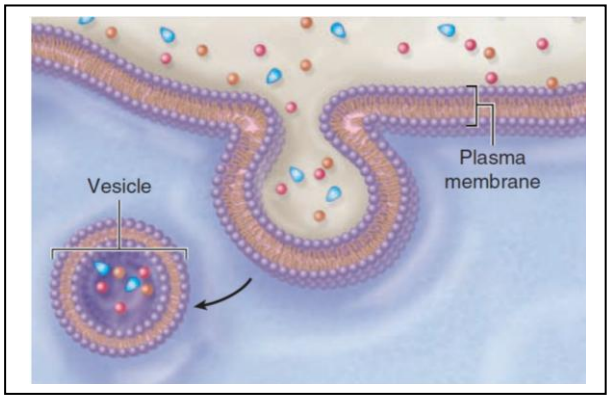
transmembrane conductance regulator), codes for the CFTR protein, which is a channel protein that controls the flow of H2O and Cl-ions in and out of cells inside the lungs. When the CFTR protein is working correctly, ions freely flow in and out of the cells. However, when the CFTR protein is malfunctioning, these ions cannot flow out of the cell due to a blocked channel. This causes cystic fibrosis, characterized by the buildup of thick mucus in the lungs.

2. **Vesicular transport**: is the transport of large substance across the plasma membrane by vesicle , which is a membrane bounded sac filled with materials include endocyosis and exocytosis.
Endocytosis: is uptake process of molecules and transport it across cell membrane into the cell interior by vesicle formation, a portion of the plasma membrane invaginates to envelop the substance, and then the membrane pinches off to form an intracellular vesicle.
There are three methods of endocytosis:

A. **Phagocytosis**: means "**cell eating**", nonselective process involves the extension from the cell of large folds called pseudopodia that engulf particles, for example bacteria, and then internalize this material into a cytoplasmic vacuole or phagosome. Best example on phagocytic cell is white blood cells (WBC) can engulf bacteria and worn- out red blood cells by phagocytosis**.** Digestion occurs when the resulting vacuole (phagocytic vacuole) fuses with a lysosome.



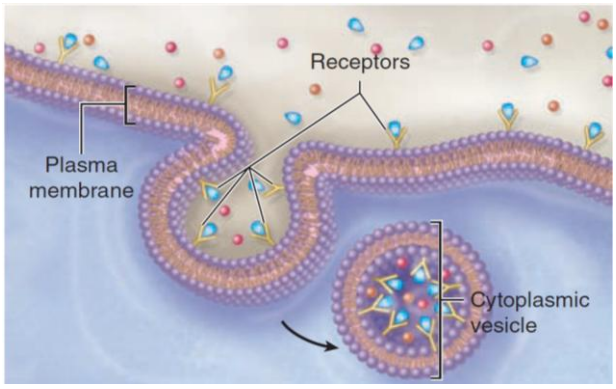
B. **Pinocytosis (**Fluid-phase endocytosis**)**: means "**cell drinking**" smaller invaginations of the cell membrane form and entrap extracellular fluid and its dissolved contents. Pinocytotic vesicles (~80 nm in diameter) then pinch off inwardly from the cell surface. In most cells such vesicles usually fuse with lysosomes. In many very thin cells, however, pinocytotic vesicles may move to the opposite cell surface where they fuse with the membrane and release their contents outside the cell. Pinocytosis takes place in almost all cells, including the secretory cells and epithelial cells of the blood vessels also cells that line the kidney tubules or intestinal wall.



C. **Receptor- mediated endocytosis**: A special form of endocytosis uses a **receptor**, a special form of membrane protein on the surface of the cell to concentrate specific molecules of interest for endocytosis, more selective form of pinocytosis or phagocytosis. In this process, specific molecules in the extracellular fluid (ligand) bind to receptors on the cell membrane and are then taken into the cell cytoplasm. When many such receptors are bound by their ligands, they aggregate in one membrane region, which then invaginates and pinches off to create a vesicle or endosome containing both the receptors and the bound ligands.

Ligands may have different fates within the endosomal compartment:

1. Receptors and ligands may be carried to late endosomes and then to lysosomes for degradation.
2. Ligands may be released internally and the receptors recycled to the cell surface.
3. Vesicles may move to and fuse with another cell surface, where the ligands are released again outside the cell



Examples of receptor-mediated endocytosis include uptake of low-density lipoproteins and insulin from the blood also many diseases are caused by defective receptors. Also, pseudohypoparathyroidism and one type of dwarfism are caused by nonfunctioning parathyroid and growth hormone receptors, respectively. In these two conditions the glands produce the respective hormones, but the target cells cannot respond because they lack normal receptors. Also an inherited form of cardiovascular disease (familial hypercholesterolemia) occurs when cells fail to take up a combined lipoprotein and cholesterol molecule from the blood.

- **Exocytosis**: is the process by which a vesicle moves from the cytoplasm to the plasma membrane, where it discharges its contents to the extracellular space. During exocytosis vesicles often formed by Golgi apparatus and carrying a specific molecule fused with plasma membrane and secretion occurs. The small (<120 nm diameter) vesicles released allow transfer of membrane proteins and other materials to nearby cells called exosomes.

e.g. release of insulin molecules from beta cells or releasing of neurotransmitter molecules into the synaptic cleft by the process of exocytosis.

Protein secretion involving exocytosis may follow two pathways:

1. Constitutive secretion is used for products that are released from cells continuously, as soon as synthesis is complete, such as procollagen for the ECM.
2. Regulated secretion occurs in response to signals coming to the cells, such as the release of digestive enzymes from pancreatic cells in response to specific stimuli.

- **This accomplishes bulk transfer of material across the cell in a process termed transcytosis.**

- **Portions of the cell membrane become part of the endocytotic vesicles or vacuoles during endocytosis; during exocytosis, membrane is returned to the cell surface. This process of membrane movement and recycling is called membrane trafficking.**

FIGURE **2–7** **Receptor-mediated endocytosis involves regulated membrane trafficking.**