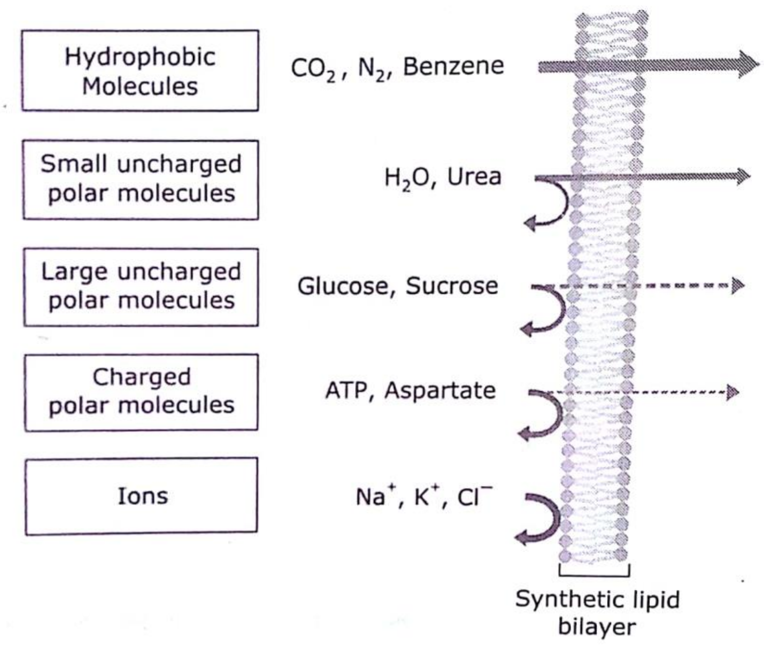
Transport Across Membrane

By : J K Nath (Asst Professor)

Introduction :

Because the contents of a cell are completely surrounded by its plasma membrane, all communication between the cell and the extracellular medium must be mediated by this structure. The plasma membrane is a barrier that retains the dissolved materials of the cell so that they do not simply leak out into the environment, yet it must allow the necessary exchange of materials into and out of the cell. The lipid bilayer of the membrane is ideally suited to prevent the loss of charged and polar solutes from a cell. Consequently, some special provision must be made to allow the movement of nutrients, ions, waste products, and other compounds in and out of the cell. There are basically two means for the movement of substances through a membrane: passively by diffusion or actively by an energy-coupled transport process. Both types of movements lead to the net flux of a particular ion or compound. The term *net flux* indicates that the movement of the substance into the cell (*influx*) and out of the cell (*efflux*) is not balanced, but that one exceeds the other.

Most biological molecules are unable to diffuse through the protein-free lipid bilayer. Small non-polar molecules , such as O_2 and CO2, readily dissolve in lipid bilayers and , therefore, diffuse rapidly across them. Small uncharged polar molecules, such as water or urea, also diffuse across a lipid bilayer. By contrast, lipid bilayers are highly impermeable for charged molecules.



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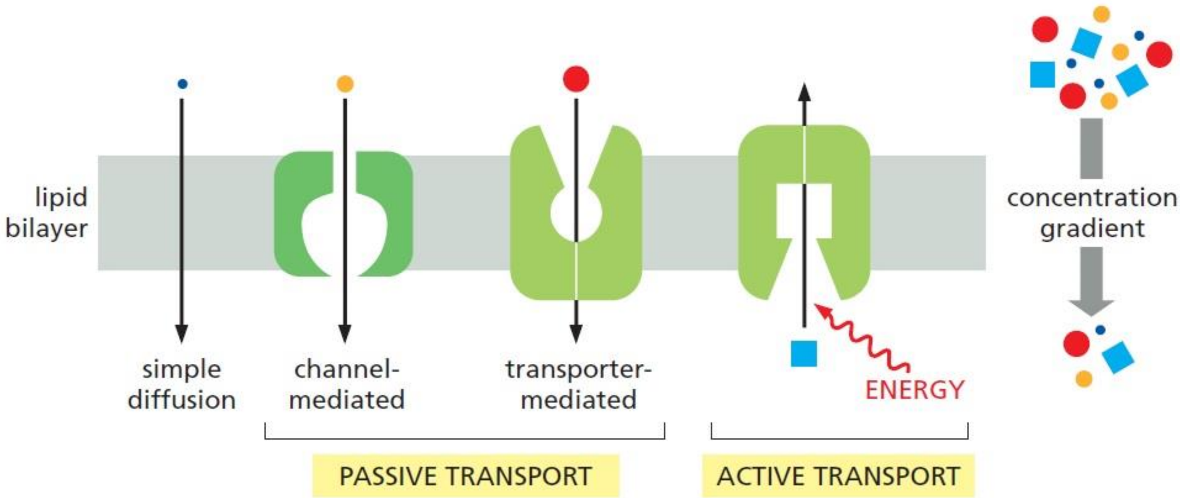
Three fundamentally different mechanisms are involved in the movement of solutes across membranes. A few types of molecules move across membranes by ***simple diffusion***—direct, unaided movement of solute molecules into and through the lipid bilayer in the direction dictated by the difference in the concentrations of the solute on the two sides of the membrane.

For most solutes, however, movement across biological membranes at a significant rate is possible only because of the presence of ***transport proteins***—integral membrane proteins that recognize substances with great specificity and speed their movement across the membrane. In some cases, transport proteins move solutes down their free energy gradient in the direction of thermodynamic equilibrium. This gradient represents the difference, on opposite sides of the membrane, in concentration, charge, or both concentration and charge. This process is known as ***facilitated diffusion*** of solutes and requires no input of energy.

In other cases, transport proteins mediate the ***active transport*** of solutes, moving them against their respective free energy gradients in an energy-requiring process. Active transport must be driven by an energy-yielding process such as the hydrolysis of ATP or the simultaneous transport of another solute, usually an ion such as H+ or Na+, down its free energy gradient.



Passive Transport :

Passive transport occurs along the gradient (downhill) and without the use of metabolic energy. If a solute is uncharged, its movement is influenced by its concentration gradient only whereas, if a transported solute carries a net charge, its movement is influenced by both its chemical gradient (the difference in solute concentration) and the electrical gradient across the membrane. The combination of these two forces, called the electrochemical gradient, determines the direction of transport of a charged molecule across a membrane. Thus, an ion diffuses not simply down its concentration gradient but, more exactly, down its electrochemical gradient. Passive transport across plasma membrane may be simple and facilitated diffusion.

Simple diffusion :

During simple diffusion, a solute simply dissolves in the lipid bilayer, diffuses across it. No membrane proteins are involved and the direction of transport is determined simply by the relative concentrations of the solute inside and outside of the cell. The relative diffusion rate of any solute across a pure lipid bilayer is proportional to its concentration gradient across the layer and to its hydrophobicity and size.

Movement of solutes by simple diffusion is always from a higher to a lower concentration, and the rate is described by Fick's law of diffusion.

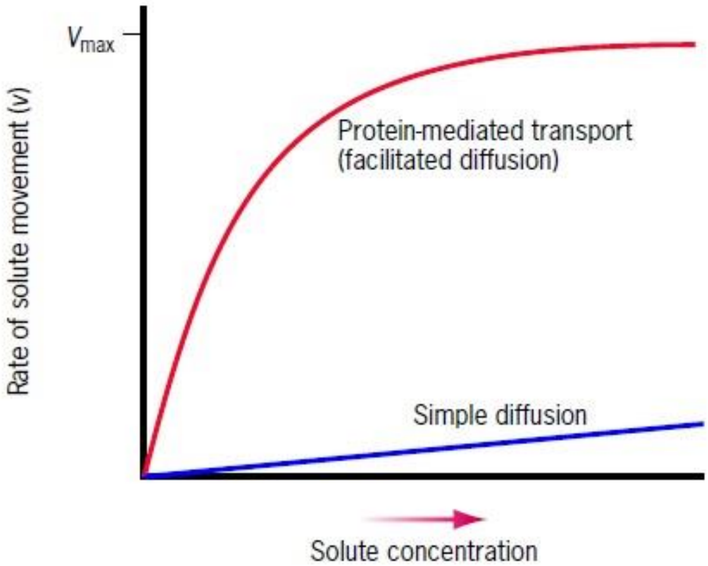
$$J = -D\,(\Delta C/\Delta X)$$

Where,
J is the flux per unit area,
D is the diffusion coefficient (usually expressed as cm^2/sec), and
ΔC is the difference in concentration between two regions separated by a distance **ΔX** (membrane thickness in case of membrane transport). The negative sign accounts for the fact that diffusion is towards the lower concentration.

Simple diffusion across lipid bilayer is a nonselective in nature by which any non-polar solute able to dissolve in the lipid bilayer is able to cross the plasma membrane and equilibrate between inside and outside of the cell. Gases (such as O_2 and CO_2), non-polar molecules (such as benzene), and small polar but uncharged molecules (such as H_2O and ethanol) are able to diffuse across the lipid bilayer of the plasma membrane.

Facilitated Diffusion :

Facilitated diffusion: Like simple diffusion, facilitated diffusion involves the movement of solutes along the concentration or electrochemical gradient. However, the passage is mediated by transport protein (carriers and channels) and is selective in nature. Facilitated diffusion may be carrier proteins or channel proteins mediated. Carrier proteins that mediate facilitated diffusion are called transporters or permeases. The rate of transport of the solute across the membrane is far greater in facilitated diffusion as compared to simple diffusion and it is more specific. Facilitated diffusion allows polar and charged molecules, such as monosaccharides, amino acids, nucleosides and ions to cross the plasma membrane.



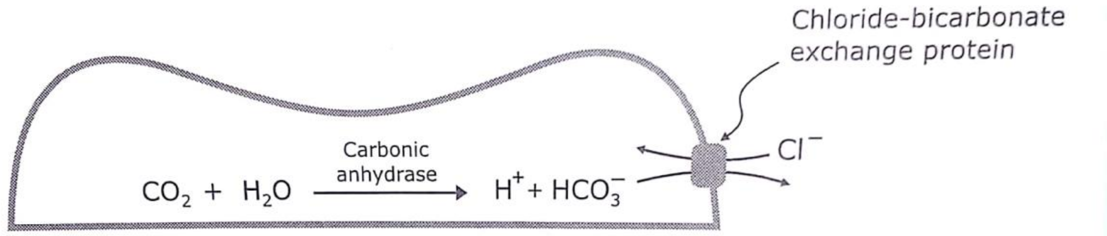
Classes of proteins that mediate facilitated diffusion

Carrier proteins mediated :
Carrier proteins or transporters, non-covalently bind specific molecules to be transported on one side of the membrane. They then undergo conformational changes that allow the molecule to pass through the membrane and be released on the other side.

Example:
Glucose transporters (GLUT) : A classic example is the movement of glucose mediated by carrier protein, glucose transporter (GLUT) . In erythrocytes , the glucose is transported using GLUT and it is rapidly phosphorylated to form glucose-6-phosphate. Once phosphorylated , the glucose no longer leaves the cell ; moreover, the

concentration of the simple glucose in the cell is lowered. As a result , theconcentration gradient of glucose across the membrane is increased , allowing the facilitated diffusion to continue to import glucose.

The Chloride-bicarbonate exchanger : It mediates the transport of two anions simultaneously. HCO_3- ion moves in one direction and Cl- moves in the opposite direction. This protein mediates the simultaneous movement of two anions: for each HCO_3- ion that moves in one direction, one CI- ion moves in the opposite direction, with no net transfer of charge i.e the exchange is electroneutral.



Channel proteins mediated :

Channel proteins form pores through the membrane, allowing the diffusion of specific solute of the appropriate size and charge. The rate of diffusion mediated by channel protein is higher than those mediated by carriers. Channels typically show less specificity than carriers and are usually non-saturable. Channel proteins responsible for transport of inorganic ions are called **ion channels**. Ion channels are generally highly selective. Most of the ion channels are not permanently open. Some channels (called **voltage-gated channels**) open in response to change in membrane potential; others (called **ligand-gated channels**) open response to the binding of ligands.

Example :

Aquaporins : Many animal and plant cells contain specialized water channel in their plasma membrane to facilitate the water flow called **aquaporins**. These are a family of transport proteins that allow water and a few other small uncharged molecules, such as glycerol, ammonia to cross membrane.

Active Transport :

Active transport occurs against the concentration or electrochemical gradient (uphill) and is mediated by carrier proteins. Energy is required to move solutes against the gradient. The energy may come directly from **ATP hydrolysis** called as **primary active transport** or may be supplied in the form of one solute moving down its electrochemical gradient, which provides energy to drive another solute against its gradient called as **secondary active transport**. Active transport results in the accumulation of solute on one side of membrane. Active transport is different from carrier-mediated facilitated diffusion.

Examples :

Na+-K+ Pump :

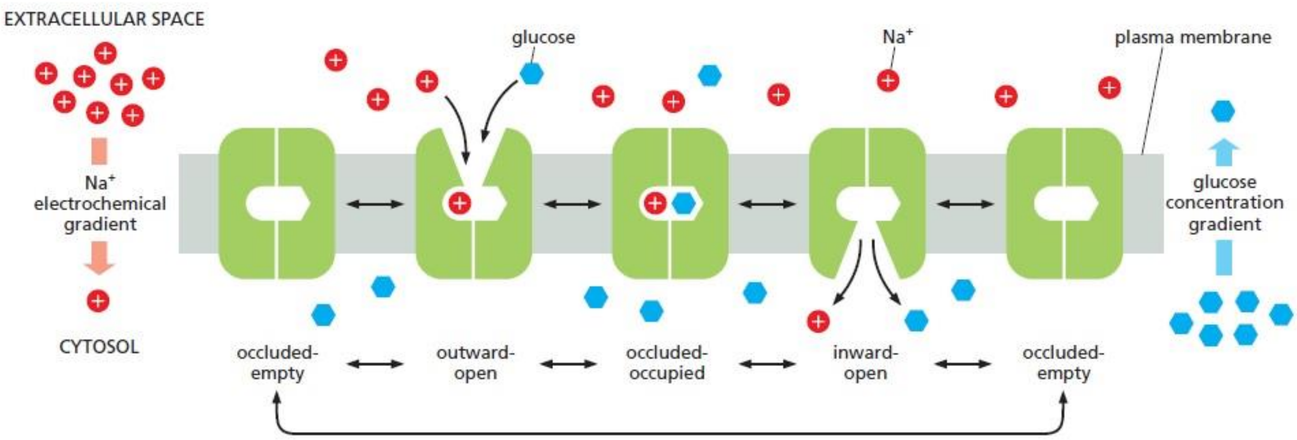
Transport of Na+ and K+ by carrier protein, Na+-K+ ATPase (or Na-K+ pump), is the most common example of primary active transport. Virtually every animal cell maintains lower Na+ concentration and high K+ concentration in cytosol than they are found in its This imbalance is established and maintained by an active transport system in the plasma membrane, involves the carrier protein Na+-K+ ATPase coupled with breakdown of ATP.

Proton pump or H+ pump :

The lysosomal membrane contains the ATP dependent proton pump that transport protons from the cytosol into the lumen of the organelle , keeping the interior of lysosome very acidic .

Sodium –Glucose Transporter :

The transmembrane protein Na+-glucose transporter is an example of secondary active transport which allows Na+ and glucose to enter the cell together . Na+-glucose symporters are a family of glucose transporters present on the apical surface of the epithelium cell of the small intestine and actively transport glucose molecules into the cell from the gut. The Na+ flows down their concentration gradient while the glucose molecules are transported against their concentration gradient in to the cell.



Differences between Active and Passive Transport :

Active Transport	Passive Transport
Requires energy (usually ATP) for moving molecules against gradients.	Does not require energy; molecules move along gradients.
Moves molecules against their concentration gradient.	Moves molecules along their concentration gradient.
Highly specific; can transport specific molecules.	Less specific; transports molecules based on size and charge and polarity
Utilizes protein pumps or carriers to move molecules.	Uses protein channels or pores for movement.
Examples :Sodium-potassium pump, proton pump.	Examples :Simple diffusion, facilitated diffusion, osmosis.

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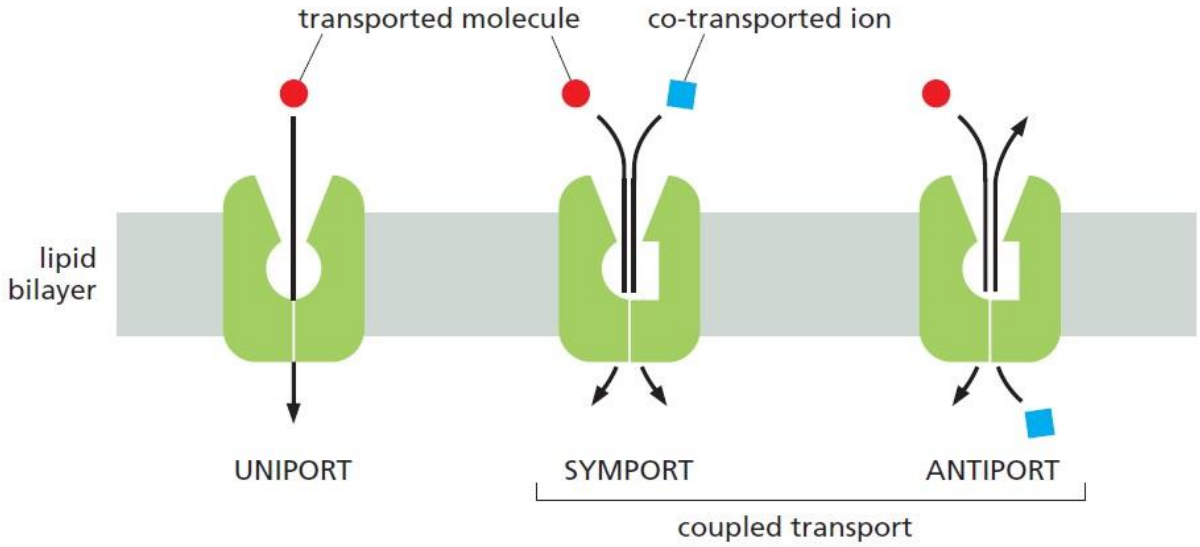
Uniport, symport and antiport :

Those carrier proteins which simply transport a single solute from one side of the membrane to the other; are called **uniports**. Others function as **coupled transporters**, in which the transfer of one solute depends on the simultaneous transfer of a second solute, either in the same direction (**symport**) or in the opposite direction (**antiport**). Both symport and antiport collectively form the cotransport. Most animal cells, for example, must take up glucose from the extracellular fluid, where the concentration of the sugar is relatively high, by passive transport through the glucose transporters (such as D-hexose permease) that operate as the uniports. By contrast, intestinal and kidney cells must take up glucose from the lumen of the intestine and kidney tubules, respectively, where the concentration of the sugar is low. These cells actively transport glucose by symport with Na+ ions whose extracellular concentration is very high.



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