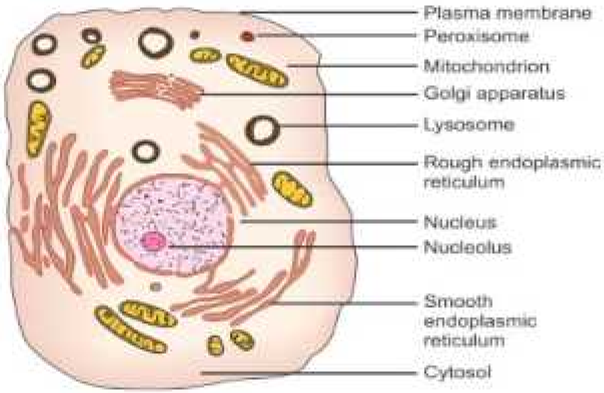
Cell membrane

A cell has three major components, Cell membrane (Plasma membrane), Cytoplasm with its organelles, Nucleus :



Typical of eukaryotic cell

Membranes are highly viscous, plastic structures. Plasma membranes form closed compartments around cellular protoplasm to separate one cell from another and thus permit cellular individuality. The plasma membrane has **selective permeabilities** and acts as abarrier, there by maintaining differences in composition between the inside and outside of the cell. The selective permeabilities are provided mainly by **channels** and **pumps** for ions and substrates. The plasma membrane also exchanges material with the extracellular environment by exocytosis and endocytosis, and there are special areas of membrane structure the gap junctions through which adjacent cells exchange material. In addition, the plasma membrane plays key roles in **cell cell interactions** and in **transmembrane signaling.**

The Body's Internal Water Is Compartmentalized

Water makes up about 60% of the lean body mass of the human body and is distributed in two large compartments.

A. intra Cellular Fluid (ICF): This compartment constitutes two-thirds of total body water and provides the environment for the cell

(1) Make, store, and utilize energy
(2) Replicate
(3) Perform special functions.

B. Extra Cellular Fluid (ECF)

This compartment contains about one-third of total body water and is distributed between the plasma and interstitial compartments. The extracellular fluid is a delivery system. It brings to the cells nutrients (eg, glucose, fatty acids, amino acids), oxygen, various ions and trace minerals, and a variety of regulatory molecules (hormones). Extracellular fluid removes CO2 and waste.

The Ionic Compositions of Intracellular& Extracellular fluid

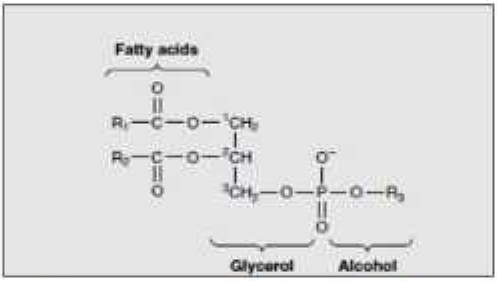
A-Internal environment is rich in K+ and Mg2+, and phosphate is its major anion.

B-Extracellular fluid is characterized by high Na+ and Ca2+ content, and Cl^- is the major anion. Note also that the concentration of glucose is higher in extracellular fluid than in the cell, whereas the opposite is true for proteins.

Membrane lipids

A-Phospholipid

Major phospholipid classes present in membranes, **phosphoglycerides** are the more common and consist of a glycerol backbone to which are attached two fatty acids in ester linkage and a phosphorylated alcohol.



The fatty acid constituents are usually even-numbered carbon molecules, most commonly containing 16 or 18 carbons. They are unbranched and can be saturated or unsaturated.

B. Glycosphingolipid

The glycosphingolipids are sugar-containing lipids built on a backbone of ceramide; they include Glucosylceramide (cerebrosides) and the Ganglioside. They are mainly located in the plasma membranes of cells.

C. Sterols

The most common sterol in membranes is **cholesterol**, which resides mainly in the plasma membranes of mammalian cells but can also be found in lesser quantities in mitochondria, Golgi complexes, and nuclear membranes. Cholesterol intercalates among the phospholipids of the membrane.

Membrane Proteins

Proteins of the membrane are classified into two major categories:

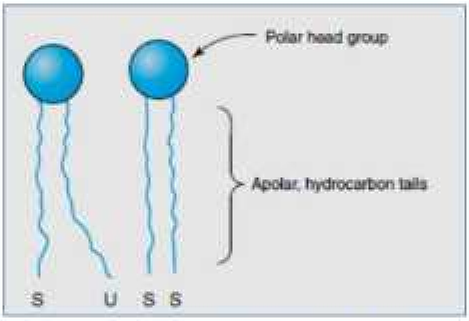
- **Integral proteins** are either partially or totally immersed in the lipid bilayer. Many integral membrane proteins span the lipid bilayer from one side to the other and are called transmembrane Protein whereas others are partly embedded in either the outer or inner leaflet of the lipid bilayers . Transmembrane proteins act as Enzymes and transport carriers for ions as well as water soluble substances, such as glucose.
- **Peripheral proteins** are attached to the surface of the lipid bilayer by electrostatic and hydrogen bonds. They bound loosely to the polar head groups of the membrane phospholipid bilayer Peripheral proteins function almost entirely as enzymes and receptors

Membrane Carbohydrates

Membrane carbohydrate is not free. It occurs in combination with proteins or lipids in the form of glycoproteins or glycolipids. Most of the integral proteins are glycoproteins and about one-tenth of the membrane lipid molecules are glycolipids. The carbohydrate portion of these molecules protrude to the outside of the cell, dangling outward from the cell surface

Membrane Lipids Are Amphipathic

All major lipids in membranes contain both hydrophobic and hydrophilic regions and are therefore termed **"amphipathic."** Membranes themselves are thus amphipathic.If the hydrophobic regions were separated from the rest of the molecule, it would be insoluble in water but soluble in oil. Conversely, if the hydrophilic region were separated from the rest of the molecule, it would be insoluble in oil but soluble in water. The amphipathic nature of a phospholipids is represented in Figure. Thus, the polar head groups of the phospholipids and the hydroxyl group of cholesterol interface with the aqueous environment .**Saturated fatty acids** have straight tails, whereas **unsaturated fatty acids,** which generally exist in the cis form in membranes, make kinked tails .

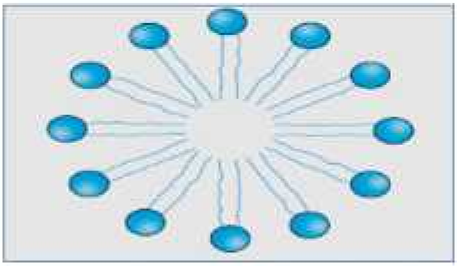


The polar head group is hydrophilic, and the hydrocarbon tails are hydrophobic or lipophilic. The fatty acids in the tails are saturated (S) or unsaturated (U).

Membrane Lipids Form Bilayers

A **micelle** is such a structure; the hydrophobic regions are shielded from water, while the hydrophilic polar groups are immersed in the aqueous environment. However, micelles are usually relatively small in size (eg, approximately 200 nm) and thus are limited in their potential to form membranes, b**imolecular layer,** or **lipid bilayer. Bilayers,** not micelles, are indeed the key structures in biologic membranes.

Lipid bilayers are formed by **self-assembly.** When lipid molecules come together in a bilayer, the entropy of the surrounding solvent molecules increases.



Diagrammatic cross-section of a micelle.

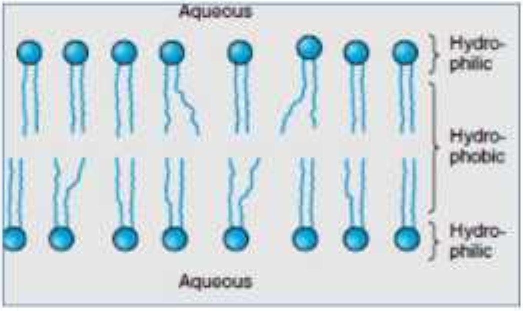


Diagram of a section of a bilayer membrane formed from phospholipid molecules.

The unsaturated fatty acid tails are kinked and lead to more spacing between the polar head groups, hence to more room for movement. This in turn results in increased membrane fluidity.

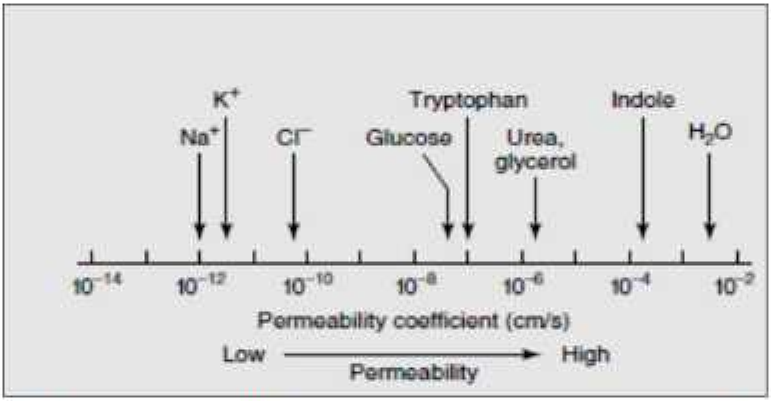


Figure: Permeability coefficients of water, some ions, and other molecules in lipid bilayer membranes.

Molecules that move rapidly through a given membrane are said to have a high permeability coefficient. proteins are amphipathic molecules that can be inserted into the correspondingly amphipathic lipid bilayer. Proteins form channels for the movement of ions and small molecules and serve as transporters for larger molecules that otherwise could not pass the bilayer.

Membranes Are Dynamic Structures and Asymmetric Structures

Membranes and their components are **dynamic structures.** Different lipids have different turnover rates, and the turnover rates of individual species of membrane proteins may vary widely. The membrane itself can turn over even more rapidly than any of its constituents. This asymmetry can be partially attributed to the irregular distribution of proteins within the membranes. An **inside-outside asymmetry** is also provided by the external location of the carbohydrates attached to membrane proteins.

Artificial membranes

Artificial membrane systems can be prepared by appropriate techniques. advantages and uses of artificial membrane systems in the study of membrane function can be briefly explained:

(1) Purified membrane proteins or enzymes can be incorporated into these vesicles in order to assess what factors.

(2) The environment of these systems can be rigidly controlled and systematically varied (eg, ion concentrations).

(3) When liposomes are formed, they can be made to entrap certain compounds inside themselves, eg, drugs and isolated genes. There is interest in using liposome to distribute drugs to certain tissues, and if components(eg, antibodies to certain cell surface molecules)could be incorporated into liposomes so that they would be targeted to specific tissues or tumors, the therapeutic impact would be considerable.

Fluid mosaic model of membrane

In 1972, Singer and Nicolson postulated a theory of membrane structure called the fluid mosaic model which is now widely accepted . A mosaic is a structure made up of many different parts. Likewise, the plasma membrane is composed of different kinds of macromolecules like phospholipids, integral proteins, peripheral proteins, glycoprotein, Glycolipids and cholesterol. Fluid mosaic model allows the membrane proteins to move in two dimensions and that they are free to diffuse from place to place within the plane of the bilayers. The Singer-Nicolson model can explain many of the physical, chemical and biological properties of membranes and has been widely accepted as the most probable molecular arrangement of lipids and proteins of membranes. Also temperature at which the structure undergoes the transition from ordered to disordered (ie, melts) is called the "transition temperature" (Tm). When membrane fluidity increases, so does its permeability to water and other small hydrophilic molecules. The insulin receptor is an excellent example of altered function with changes in fluidity.

Ion Channels

Cation-conductive channels have an average diameter of about 5–8 nm and are negatively charged within the channel. The permeability of a channel depends upon the size, the extent of hydration, and the extent of charge density on the ion. There is specific channels for Na+, K+, Ca2+, and Cl. The channels are very selective, in most cases permitting the passage of only one type of ion (Na+, Ca2+, etc)

One ion can regulate the activity of the channel of another ion. For example, a decrease of Ca2+ concentration in the extracellular fluid increases membrane permeability and increases the diffusion of Na+.

Systems Transporter

Transport systems can be described in a functional sense according to the number of molecules moved and the direction of movement. A **uniport** system moves one type of molecule bidirectionally. A **symport** moves these solutes in the same direction. **Antiport** systems move two molecules in opposite directions(eg, Na+ in and Ca2+ out).

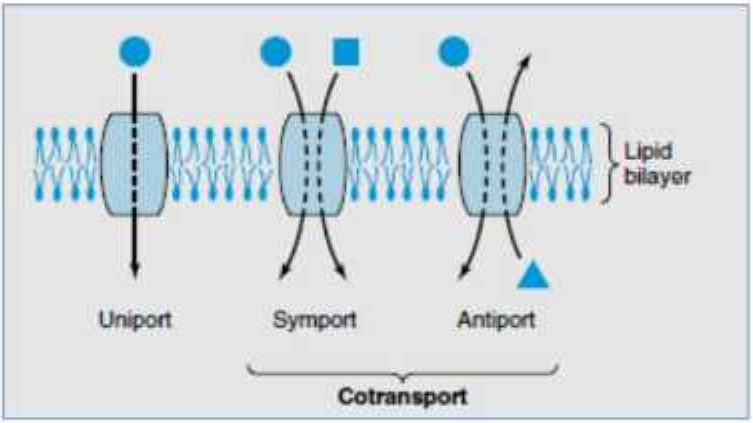


Figure: Systems Transporter

Facilitated Diffusion

Some specific solutes diffuse down electrochemical gradients across membranes more rapidly than might be expected from their size, charge, or partition coefficients.The rate at which solutes enter a cell by facilitated diffusion is determined by the following factors:

(1) The concentration gradient across the membrane.

(2) The amount of carrier available.

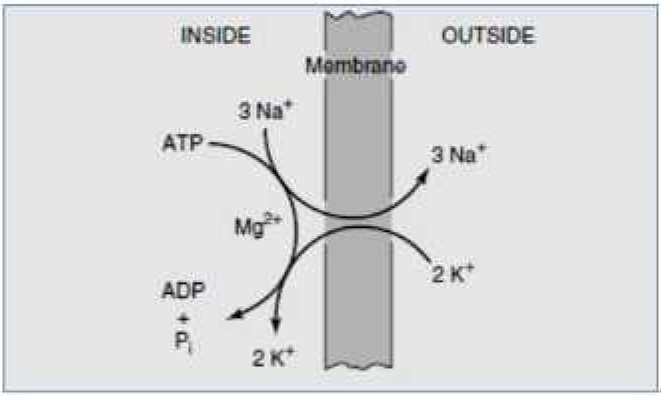
(3) The rapidity of the solute-carrier interaction.

(4) The rapidity of the conformational change for both the loaded and the unloaded carrier.

Hormones regulate facilitated diffusion by changing the number of transporters available. **Insulin** increases glucose transport in fat and muscle by recruiting transporters from an intracellular reservoir. Insulin also enhances amino acid transport in liver and other tissues.

Active Transport

The process of active transport differs from diffusion in that molecules are transported away from thermodynamic equilibrium; hence, **energy is required.** The maintenance of electrochemical gradients in biologic systems is so important that it consumes perhaps 30–40% of the total energy expenditure in a cell. In general, active transport needed to maintain a low intracellular Na+ concentration and a high intracellular K+ concentration), along with a net negative electrical potential inside the cell. The pump that maintains these gradientsis an **ATPase** that is activated by Na+ and K+ (Na+-K+ATPase) as shown in Figure:



Major differences between Facilitated diffusion and active transport:

(1) Facilitated diffusion can operate bidirectional, whereas active transport is usually unidirectional.

(2) Active transport always occurs against an electrical or chemical gradient, and so it requires energy.

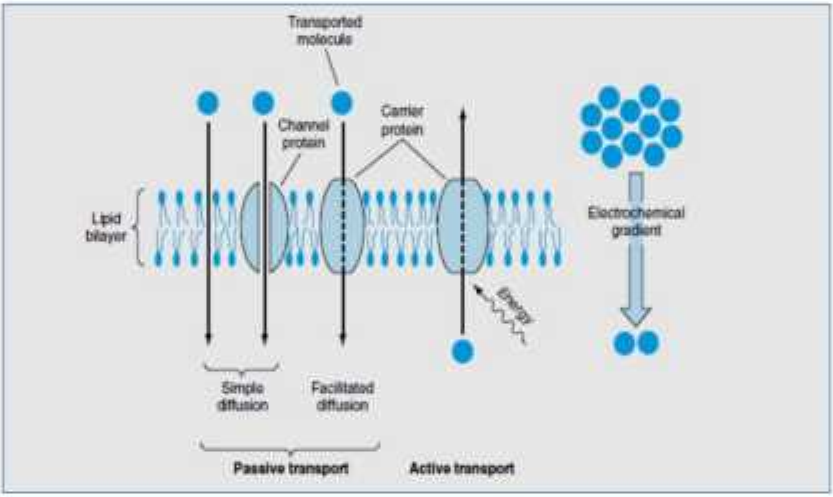


Figure: Facilitated Diffusion and Active transport

Membrane selectivity: listed in Table:

Cross-membrane movement of small molecules
- Diffusion (passive and facilitated)
- Active transport

Cross-membrane movement of large molecules
- Endocytosis
- Exocytosis

Signal transmission across membranes
- Cell surface receptors
  1. Signal transduction (eg, glucagon → cAMP)
  2. Signal internalization (coupled with endocytosis, eg, the LDL receptor)