Lesson: Cell membrane: Properties and Selective Permeability

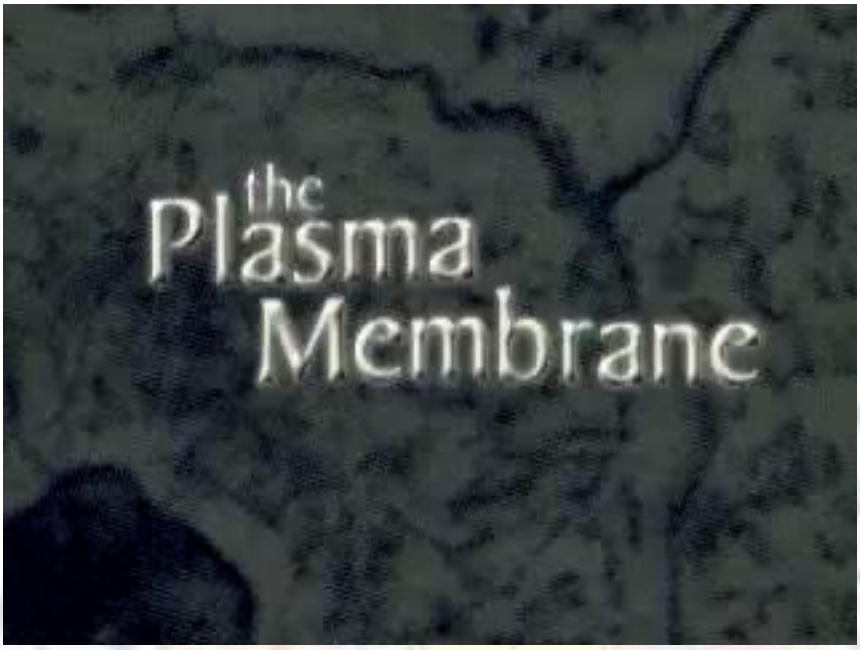
Lesson Developer: Rina Majumdar

College/Department: Maitreyi College, University of Delhi

Table of Contents

- **Introduction-Unique Properties of Biological Membranes**
  - **Fluidity of the membranes**
    - **Role of Cholesterol on Membrane Fluidity**
    - **Importance of membrane fluidity**
  - **Membrane Asymmetry**
  - **Phase Transition of the membrane**
  - **Selective Permeability of the membrane**
  - **Passive Transport**
    - **Facilitated diffusion**
    - **Probable mechanisms for FD**
  - **Active Transport**
    - **The Na^+ / K^+ exchange pump**
    - **Other important Ion Transport systems**
      - **Channel protein**
      - **Carrier protein.**
  - **Bulk Transport**
    - **Endocytosis**
      - **Pinocytosis**
      - **Receptor-mediated endocytosis**
      - **Phagocytosis**
    - **Exocytosis**
- **Summary**
- **Glossary**
- **Exercises**
- **References**

Introduction-Unique Properties of Biological Membranes



Video: A breif overview of plasma membrane

Source: http://www.youtube.com/watch?v=moPJkCbKjBs

All living organisms are characterised by a highly complex cellular system, which have to perform a wide range of biochemical processes for its existence. Cell is the ultimate unit of structure and function of all living systems. The membrane that delimits each cell plays a vital role in the cellular function. The biological living membranes of all cells share certain physical properties, which makes them adapt to different environmental conditions and perform a wide range of different functions. The cell membrane is a highly dynamic entity and the protein-lipid interactions within a membrane keep changing according to their functions. Some of the properties, which maintain the dynamism of the membrane are discussed below.

Fluidity of the membranes

Membranes are highly flexible and the various molecules within these,are not tightly packed, rather held together by hydrophobic interactions, which are much weaker than the covalent bonds. Both the lipid and the protein components of the membranes are in a constant state of dynamism. The molecular weight of the lipids is much smaller than the proteins hence the lipids can travel much faster than the proteins. A phospholipid molecule can possibly make three types of movements within a bilayer .

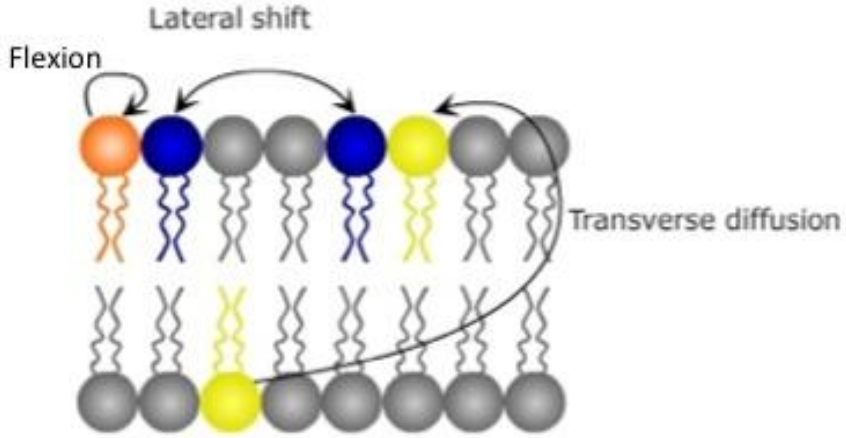


Figure: Fluidity of lipid molecules in the membrane
Source: Author

a) Phospholipids can diffuse **laterally** within the same leaflet with a considerable ease, around 10^{-9} times per second.
b) A very rare phospholipid movement is to **flip-flop** transversely across the membrane which takes place around 10^{5} times per second. The hydrophilic head group of the lipids have to cross the hydrophobic (centre) barrier of the membrane, which is thermodynamically unfavourable. Enzymes called **flippases** activate the movement of lipids from one leaflet to the other.
c) Phospholipid molecules can rotate rapidly without changing their position within a bilayer, which is termed as **flexion** motion , around 10^{-9} per second. The kink in one of the unsaturated fatty acid tail of phospholipid molecules plays a dramatic role in preventing the compact packaging of the lipids within the membrane monolayers.

The protein molecules of the membrane also do not maintain a fixed position but may slowly diffuse laterally. D. Frye and M. Edidin by **hybrid** cells (heterokaryons) experiment demonstrated the lateral diffusion of the protein molecules. They prepared hybrid cell from the fusion of human and mouse cells, using fluorescentlabelled antibody and followed the distribution of the plasma membrane protein in the hetero-karyon (two different nucleus within the hybrid cell) in different time intervals. Initially the protein on the two 'halves' of the fused cells were different , characteristic of each cell, but in less than an hour, the protein of both the cell membranes were evenly distributed through simple diffusion. No ATP (metabolic energy) was required since the metabolic inhibitor did not prevent the movement.

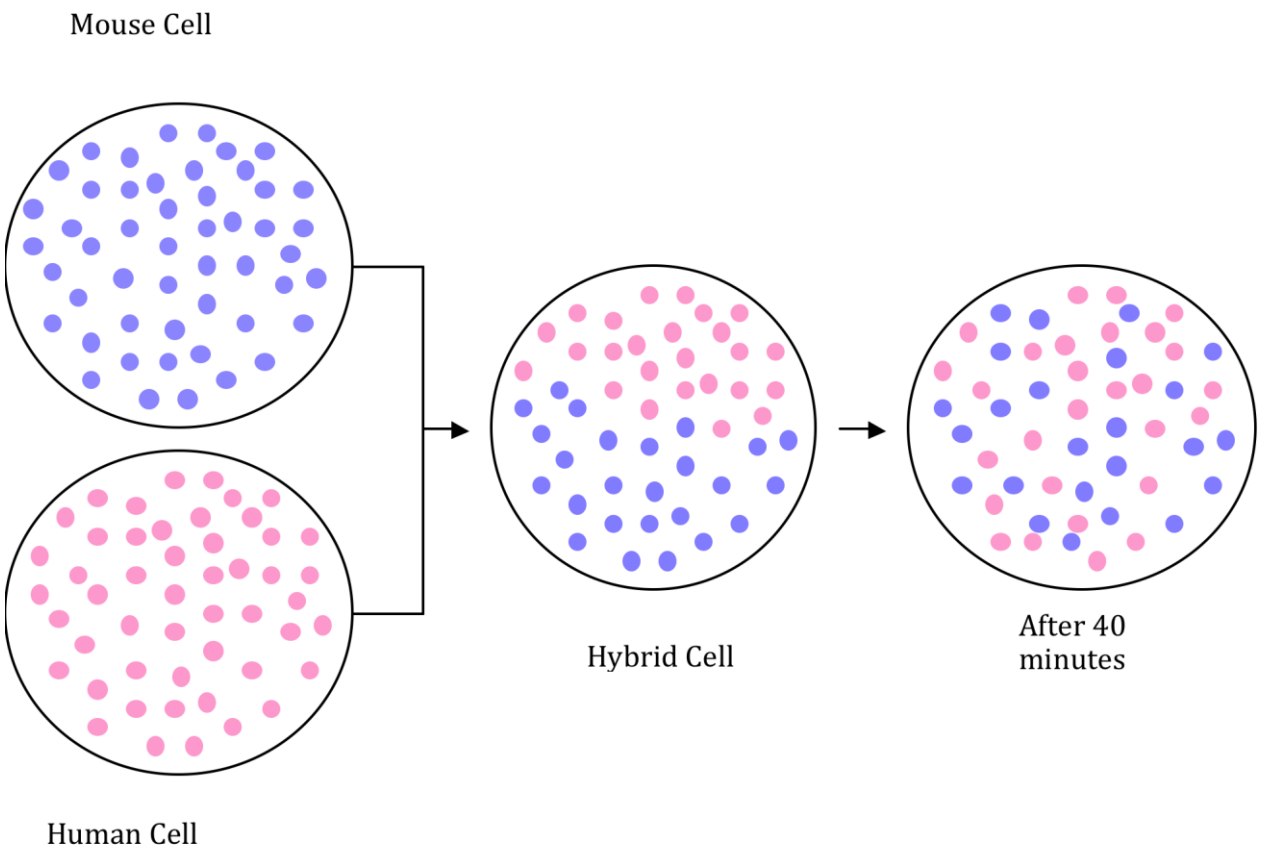


Figure : Membrane mobility demonstrated by cell fusion experiment

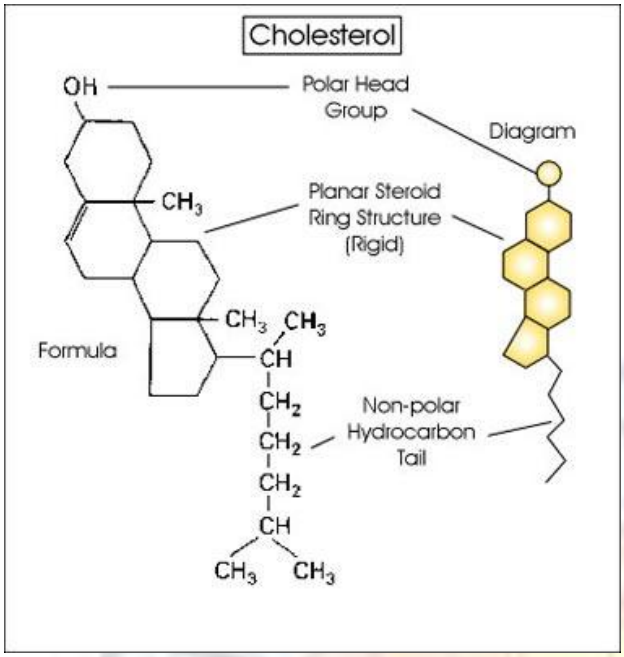
Source:

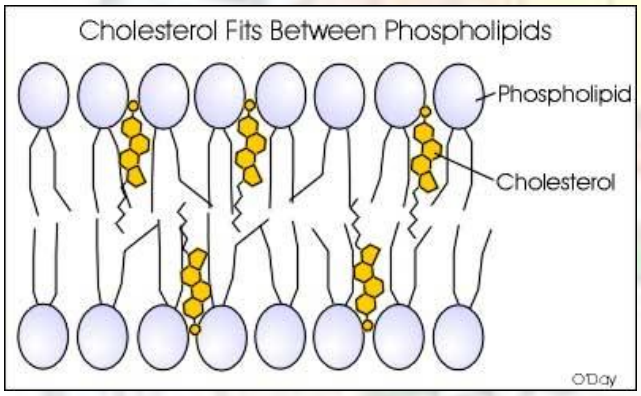
Evidence is there to show that mobility of some integral proteins is restricted through a system of cytoskeleton, that radiate through the cytoplasm.

http://bealbio.wikispaces.com/Cell+and+Cell+Membrane

Role of Cholesterol on Membrane Fluidity

In animals, cholesterol is present in both the monolayers, which constitute almost 50 per cent of the total membrane lipids on a molecular basis. One cholesterol molecule is present per 2-3 molecules of phospholipids. The small polar hydroxyl group of the highly hydrophobic cholesterol lies close to the polar head group of a neighbouring phospholipid molecule where it forms a hydrogen bond with the oxygen of the phospholipid. The highly hydrophobic rigid steroid rings and the hydrocarbon chain of the cholesterol lie close to the saturated region of the hydrocarbon tails of the fatty acid, which lies next to the polar head group of the phospholipid molecules. This prevents even the saturated hydrocarbon chains of the fatty acid to come closer, maintaining a loose arrangement.





http://www.nfsdsystems.com/w3bio315/

Figure: Role of cholesterol in maintaining fluidity of membrane

Importance of membrane fluidity

* The function of the membrane is due to its protein component, which gets oriented at particular site to perform a particular function within the frame-work of the lipid bilayer.

*The orientation and interaction of the various membrane proteins along with the lipids is feasible due to its fluidity.

*The basic cellular processes such as cell movement, cell growth, cell division, formation of intercellular junctions, secretion (endocytosis and exocytosis) etc. would not be feasible if membranes were rigid and non- fluid.

Membrane Asymmetry

The fluidity of the proteins and lipids within a membrane results in its asymmetry. Both the amount and composition of the lipids and proteins, not only vary in different types of membranes but even within each monolayer. Although the protein asymmetry is not very clearly marked, the lipid distribution has been studied extensively in the erythrocyte membrane.

	Interior Lipid Monolayer (%)	**Exterior Lipid Monolayer (%)**
Total	50	50
Sphingomyelin	6	20
Phosphatidyl choline	9	23
Phosphatidyl ethanolamine	25	6
Phosphatidyl serine	10	0
Phosphatidyl inositol	0	0

Table: The lipid composition of membrane

Source: Author

The table clearly reveals that the cholinephosphatides are primarily present in the outer monolayer and inner monolayer contains more of aminophosphatides. Rest of the phospholipids differ in different membranes. The asymmetry once established, is maintained, because 'flip-flop' movement of the lipid molecules is rare due to the hydrophobic centre of the lipid bilayer. Membrane carbohydrate also adds to the membrane asymmetry. The carbohydrate component of the membrane is prevalent only on the outer monolayer, the cytoplasmic side is devoid of any carbohydrate. This relates to the functional role of the carbohydrate . Proteins remain differentially distributed within the two monolayers of the plasma membrane, which are related to their functions.

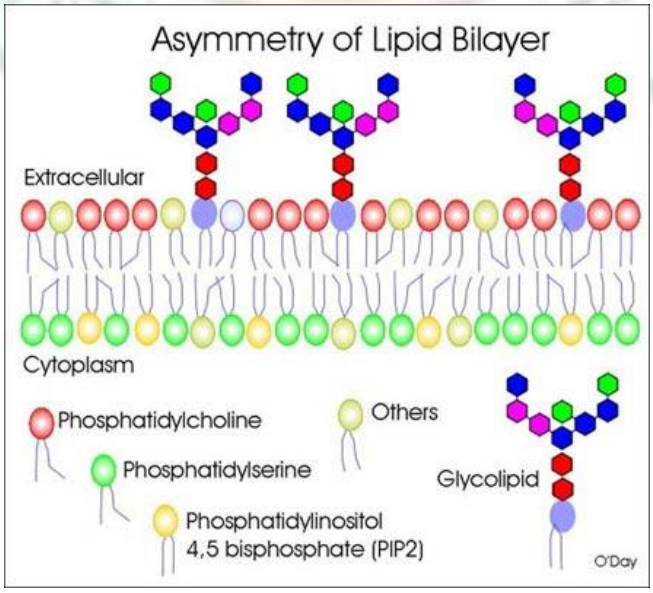


Figure : Asymmetry of lipid bilayer

Source: http://www.nfsdsystems.com/w3bio315/

Phase- Transition of the membrane

Membrane fluidity changes with the temperature as has been observed with the artificial lipid bilayer (liposome). Depending on the nature of the lipid present in the membrane, it has a characteristic **transition temperature** at which it gels ("freeze") when cooled and becomes fluid again ("melt")when temperature rises. This characteristic property of the membrane, is known as **phase transition.** The most important properties of the lipid molecules, which regulate the phase transition of cell membranes, are the length and the degree of unsaturation of the fatty acid chains of the phospholipids. Greater the number of double bonds, more is the **kink** in the fatty acid chain resulting into loose packaging of the phospholipids.

In animal cell membranes, the amount of cholesterol acts as a temperature buffer. In all biological membranes, the lipid composition is such that the phase transition is prevented to maintain the physical structure and functions of the membrane even in extreme environmental conditions. Lipid composition of the cell membrane changes as an adaptation to the changing temperature. Plants like winter Wheat can tolerate extreme cold climate, since the percentage of unsaturated phospholipids increases in autumn, preventing the membrane to solidify in winter. Similarly membrane lipids have more unsaturation in the fatty acid chains, in animals surviving in freezing temperature. The intramolecular variability of the phospholipid molecules, which usually has one saturated and the other slightly unsaturated hydrocarbon chain, (with 1-2 double bonds) keeps most membrane lipids in a semi -fluid state. The membrane architecture helps them to perform all the physiological and protective functions for the cell irrespective of its surrounding temperature.

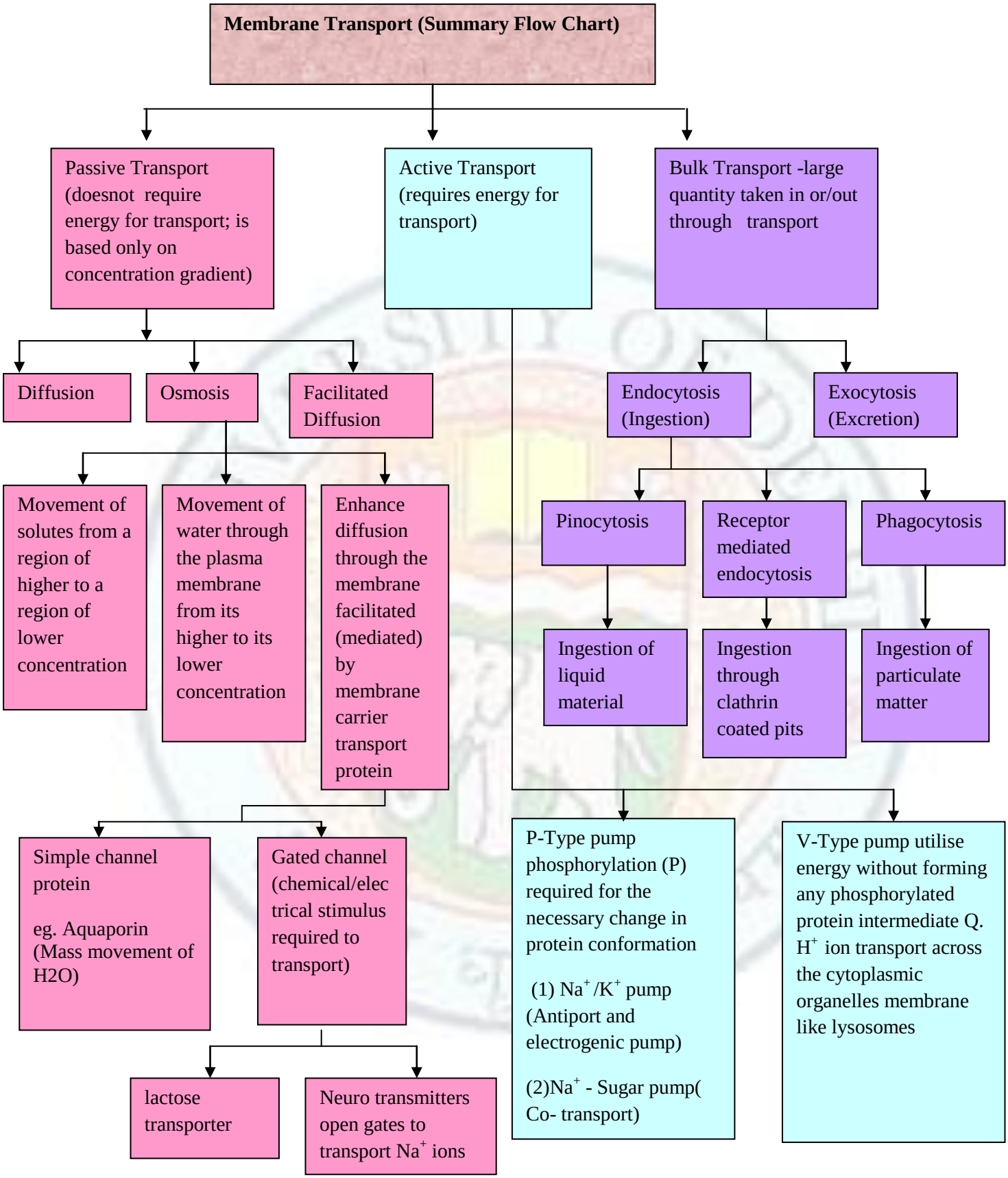
Cholesterol also plays an important role in membrane fluidity at different temperatures. At relatively higher human body temperature such as 37^0C, cholesterol makes the membrane less fluid by preventing the mobility of the phospholipids, whereas at lower temperature it prevents the phospholipid molecules to come closer and solidify. Hence, the cholesterol acts as "**temperature buffer**".

Selective Permeability of the membrane

A membrane is permeable when it allows the substance to pass through it. All plasma membrane are permeable to water. If only water can pass through the membrane it is said to be semipermeable. However, when various molecules cross the membrane differentially, that is some molecules like water pass through more readily, compared to

others like salt, sugar etc, the membrane is called **selectively permeable.** One of the most important properties of plasma membrane is to regulate the molecular traffic into and out of the cell, which is a continuous process to keep the cell physiologically active. The biochemical cycles within the cell require sugars, amino acids and other nutrients, which enter the cell, whereas the metabolic waste products leave the cell through the membrane. Gaseous exchange during respiration, also mediate through the membrane. The concentrations of the inorganic ions such as Na^+, K^+, Ca^{++} and Cl^- continuously shuttle across the membrane, to keep ionic balance of the cell. Membrane can act as a selective barrier to restrict the entry and exit of different types of molecules, depending on the metabolic state of the cell. The rate at which these molecules travel across the membrane is regulated, depending on the requirement of the cell. The lipid bilayer being the primary structural organization of the cells, nonpolar molecules , such as hydrocarbons, carbon dioxide and oxygen can easily cross the hydrophobic barrier without the help of the proteins. However, the polar molecules such as glucose and other sugars require the help of different types of **transport proteins** to cross the hydrophobic lipid core of the membrane. Extremely small polar molecules like water, charged ions etc find it difficult to penetrate the membrane.

There are three major types of membrane transport namely
(1) Passive transport (2) Active transport (3) Bulk transport


Membrane Transport (Summary Flow Chart)
Passive Transport (doesnot require energy for transport; is based only on concentration gradient)
Active Transport (requires energy for transport)
Bulk Transport -large quantity taken in or/out through transport
Diffusion
Osmosis
Facilitated Diffusion
Endocytosis (Ingestion)
Exocytosis (Excretion)
Movement of solutes from a region of higher to a region of lower concentration
Movement of water through the plasma membrane from its higher to its lower concentration
Enhance diffusion through the membrane facilitated (mediated) by membrane carrier transport protein
Pinocytosis
Receptor mediated endocytosis
Phagocytosis
Ingestion of liquid material
Ingestion through clathrin coated pits
Ingestion of particulate matter
Simple channel protein
eg. Aquaporin (Mass movement of H2O)
Gated channel (chemical/electrical stimulus required to transport)
P-Type pump phosphorylation (P) required for the necessary change in protein conformation
(1) Na+ /K+ pump (Antiport and electrogenic pump)
(2)Na+ - Sugar pump(Co- transport)
V-Type pump utilise energy without forming any phosphorylated protein intermediate Q. H+ ion transport across the cytoplasmic organelles membrane like lysosomes
lactose transporter
Neuro transmitters open gates to transport Na+ ions

Passive Transport

The characteristic feature of all molecules is to spread out evenly into the available space due to **thermal motion**, which is a type of energy that makes each molecule move randomly. The movement of molecules is directional, i.e. the solute molecules always move from a region of **higher** concentration to a region of **lower** concentration, a process called **diffusion.** Water molecules continuously move across the plasma membrane from a region of low solute concentration to a region of higher solute concentration to establish concentration equilibrium. This movement of water in response to the concentration gradient of the solute molecules is, known as **osmosis**.

Animation: Embed

http://highered.mcgraw-hill.com/sites/0072495855/student_view0/chapter2/animation__how_osmosis_works.html ; http://www.hartnell.edu/tutorials/biology/osmosis.html#2

Osmosis of small permeable molecules such as salt, sugars and amino acids can be easily demonstrated using artificial membranes such as cellophane .

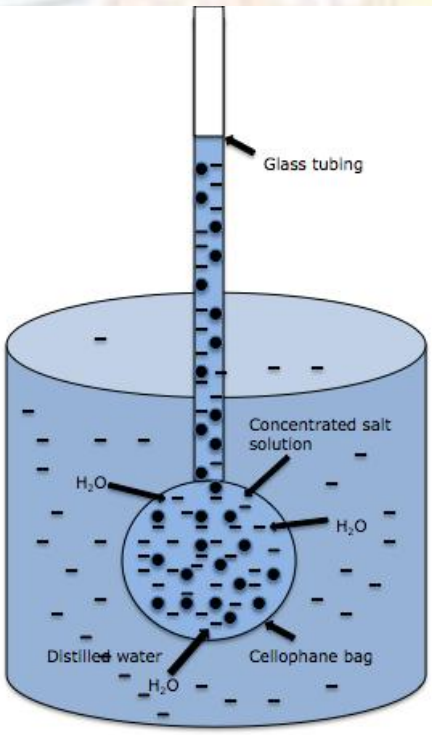


Figure: Demonstration of osmosis

Source: Author

Permeability constant: Diffusion of solutes depends on the difference of solute concentration between the two regions that is, the **concentration gradient.** In every cell, there exists a concentration difference between the internal and external environment.

The rate of diffusion for a solute is expressed as:

Ficke's equation: $dS/dt = DA(C_1-C_2/x)$ Where dS/dt = The number of moles of solute S, diffusion from region 1 to region 2 in time interval dt. D= the diffusion coefficient of the solute (moles/unit cross-sectional area/unit concentration gradient/ unit time). it depends on molecule's size and shape.

C_1 and C_2 = the concentrations of S in region 1 and 2

x = Distance between region 1 and 2

C_1-C_2/x = The concentration gradient.

In case of diffusion across the cell membrane, x is the membrane thickness.

$C_1=C_{out}$ and $C_2=C_{in}$; S is the concentration inside and outside the cell.

The term permeability constant K, describes the diffusion of a particular solute across a cell membrane.

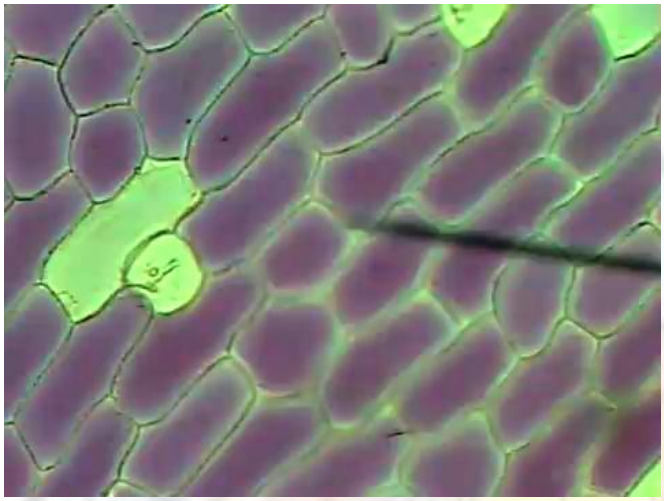
Permeability constant (K) = $dS/dt = DA (C_{in}-C_{out}/x)$

The Gibbs-Donnan effect: The R- groups of amino acids bear either positive or negative charges and determine the net ionic charge of the protein. The protein with its net charge behaves like an ion but, are generally too large to permeate the cell membrane.

The Gibbs-Donnan effect (after J.W. Gibbs and F.G. Donnan) describes the effect of proteins on the equilibrium distributions of small ions across the selectively permeable membrane. According to Gibbs-Donnan effect, when an electrolyte solution containing protein is separated by selectively permeable membrane with no protein on the other side, the concentration equilibrium on either side of the membrane may not be the same for small ions. Concentration of the ions, having the same charge as the protein, will be lower on the side containing the protein, than on the other side, which do not contain charged proteins. In this way the plant cells can accumulate small charged ions against the concentration gradient, depending on the **'fixed charge'** within the cell in passive transport. The Gibbs-Donnan effect does not influence equilibrium distribution of non-ionisable substances, such as glucose and urea.

The diffusion of substances across the biological membrane is called **passive transport**. The term passive denotes that the molecular movement across the membrane does not require chemical or metabolic energy. Concentration gradient of the solute molecule is the only factor, which regulates passive transport. Cells behave differently when kept in different solute concentration.**Tonicity** is the study,which determines the gain and loss of water by the cell when immersed in a solution. A solution is called **isotonic** (iso=same) when its solute concentration is same as the cell, pno net water movement across the membrane will happen. **Hypertonic** (hyper= high) solution has higher solute concentration than the cytoplasm of the cell, in such a situation the water from the

cytoplasm will move towards the outer solution. When plant cells are kept in a hypertonic solution they undergo plasmolysis and the water moves out from the vacoules to the space between the cell wall and cell membrane.



Animation: Plasmolysis in onion peel cells when placed in a hypertonic environment
Source: http://youtu.be/gWkcFU-hHUk

Water movement will be reversed when the cell is kept in **hypotonic** (hypo=less) solution in which the solute concentration is lower than the cell. Water always moves from its higher to its lower concentration.Animal cells, where cell wall is absent, there are chances of the cell to burst resulting into lysis, if kept in a hypotonic solution for a long time. In plants, the rigid cell wall prevents such lysis. The plant cells, are called turgid when the plasma membrane is fully stretched and forces the protoplasm (cytoplasm + cell membrane) to the margin of the cell wall.

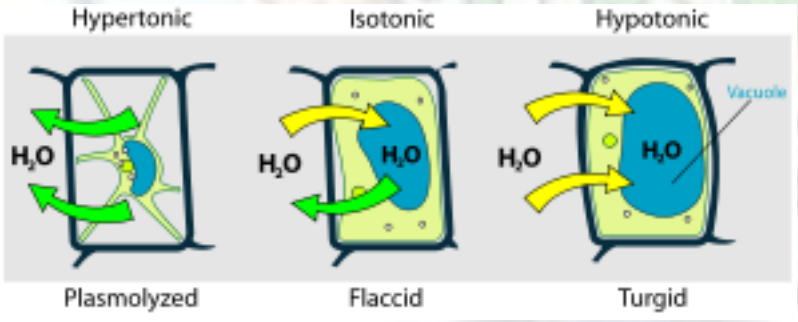


Figure: Effect of the environment on the plant cell.
Source:
http://upload.wikimedia.org/wikipedia/commons/thumb/a/ab/Turgor_pressure_on_plant_cells_diagram.svg/300px-Turgor_pressure_on_plant_cells_diagram.svg.png

Animation: Passive transport

Embed http://www.northland.cc.mn.us/biology/Biology1111/animations/passive1.html; http://bcs.whfreeman.com/thelifewire/content/chp05/0502001.html

Facilitated diffusion

It is a type of passive transport where certain water-soluble molecules cross the lipid bilayer passively with the help of **transport protein** that span the membrane. This phenomenon is known as **facilitated diffusion (FD)**.

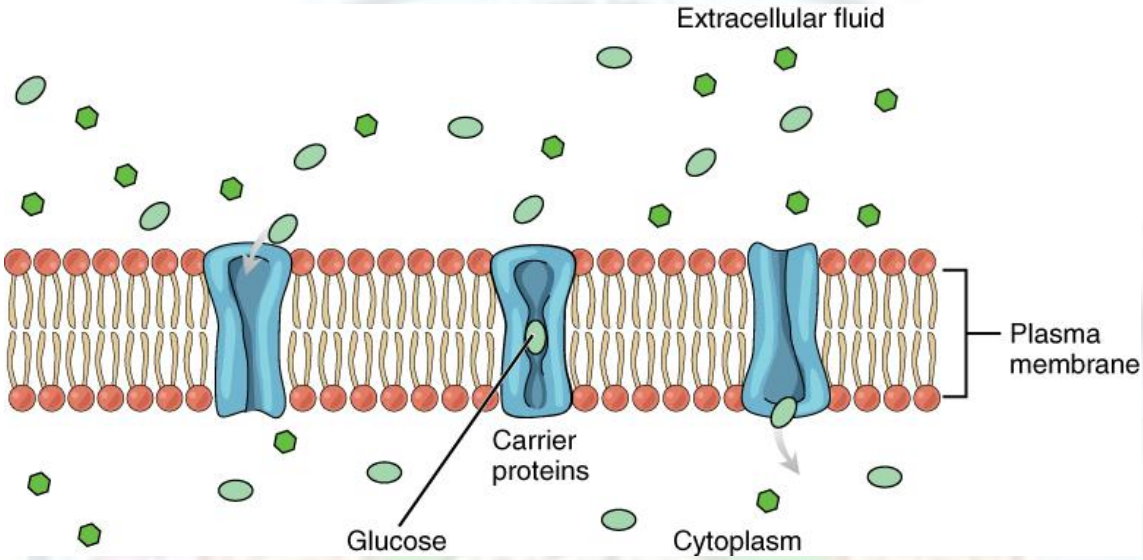


Figure: Facilitated diffusion involves the transport facilitated or mediated by specific membrane proteins

Source: http://cnx.org/content/m46411/latest/2706_Facilitated_Diffusion.jpg

Embed Animation:http://highered.mcgraw-hill.com/sites/0072495855/student_view0/chapter2/animation__how_facilitated_diffusion_works.html

FD is governed by certain characteristic features, such as:

(a) FD exhibits saturation kinetics (solute diffusion maintains the concentration gradient upto certain limit). (b) Solute transport is highly specific depending on the type of the cell for example, inward diffusion of glucose happens in erythrocytes but not fructose or lactose. (c) Structurally similar chemical molecules affect solute permeability when present together, as happens in **competitive enzyme inhibition**. (d) The chemical equilibrium attains much faster than simple diffusion. (f) Solutes cannot be transported against the concentration gradient as in passive transport. (g) Enzyme inhibitor as sulfhydryl , which affect the enzymatic protein conformation affects FD. (h) FD exhibits pH dependency like any enzymatic reaction.

Probable mechanisms for FD

The solute molecule is believed to interact with specific membrane molecules, presumably proteins, thereby forming **carrier**-**solute complex**. This complex then undergoes positional change within the membrane in a way to face the other side of the membrane surface. Once the positional change occurs, the solute is released from the carrier molecule, which can recirculate .

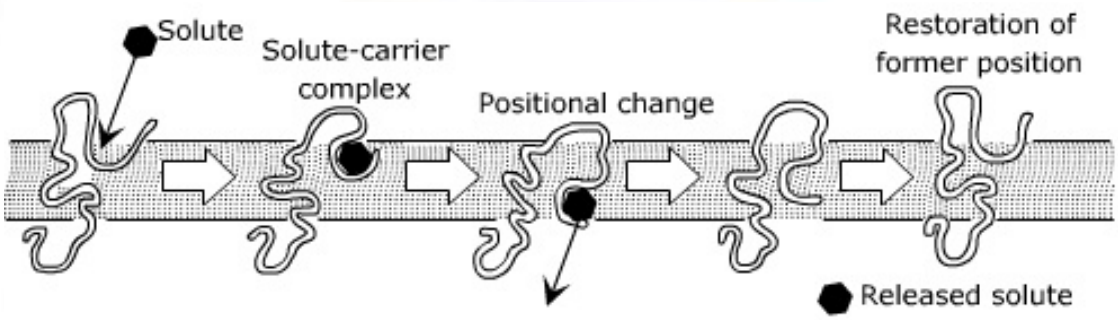


Figure: Probable mechanism of facilitated difusion

Source: Author

Another suggestion is that the carrier may be a small molecule with the solute-carrier complex formed by enzyme- catalysed reaction within a membrane. Once formed, the complex diffuses, to the other side of the membrane, where the solute is released in a second reaction. A well-defined example of facilitated diffusion can be seen in the bacterium *Escherichia coli*. In *E. coli* cells lactose neither readily permeates the cells nor gets hydrolysed by the cytoplasmic extracts of the cell grown in the absence of lactose. However, when *E. coli* cells are grown in lactose containing medium, an inducible enzyme (enzyme is formed in the presence of the substrate) called β-galactosidase appears in the medium. Galactosidase enzyme, hydrolyzes lactose to glucose and galactose. Specific transport protein appears in the membrane, which facilitates the transport of lactose within the cell. Mutant cells of *E. coli* behave differently, for example certain mutants can induce galactosidase but cannot transport lactose (transport protein absent), while other mutant cells are permeable to lactose but cannot hydrolyse lactose (enzyme absent). Hence in the wild-type cells, presence of lactose in the growth medium induces both the enzyme, as well as a carrier system called **permease** or **translocase**.

Different transport proteins are responsible for different solute molecules, the reason why FD is highly solute specific.There are two types of transport proteins namely (a) channel protein (b) carrier protein.

(a) Channel proteins, as the name suggests, provide channels within the membrane that allow small molecules to cross the membrane. Water molecules though small, but require the hydrophilic channel to cross the phospholipid bilayer. Aquaporins are water channel proteins that facilitate the massive diffusion of water in both plants and animal cells. Kidney cells have large number of aquaporins. Channel proteins can be gated-channels that is, these channels open or close in response to certain stimulus (electrical or chemical) for example, ion channels. In the nerve cells, neurotransmitter molecules stimulate the opening of the gated channel, that allows sodium ions into the cell.

(b) Carrier proteins: the lactose transporter in *E. coli* as described above is an example of carrier protein. Carrier proteins undergo subtle change in their conformation within the membrane,which facilitate the transport of the solute across the membrane. Certain inherited diseases are due to the presence of defective transport proteins. Cystinuria is one such disorder, characterised by the absence of carrier protein for cysteine and some other amino acids in kidney cells. The defective individual develops painful stones from amino acid accumulation and crystallization in the kidney(in normal individuals the amino acids get reabsorbed and return to the blood by the cysteine carrier protein in the kidney cells).

Active Transport

In both passive transport and FD, equilibrium is achieved on either side of the plasma membrane either by simple concentration gradient or through Gibbs-Donnan effect. In both types, the soluble solute inside and outside the cell plays an important role in attaining the equilibrium on either side of the membrane. Even in passive diffusion, cells can accumulate solutes by two mechanisms (1) the solute is made insoluble once it has entered the cell, insoluble materials do not contribute to the concentration gradient. (2) Solute may enter a metabolic pathway and allows additional solute permeation. In both cases, the solute transport through the membrane ultimately depends on the concentration gradient of the solute across the membrane.

Active transport is an important transport mechanism by which the substrate can move through the plasma membrane into and out of the cell **against a concentration gradient**. Only metabolically active cells can perform active transport since it is a energy governed process. Active transport can be inhibited when the cells are (a) treated with metabolic poisons such as cyanide (2) kept in very low (2-4 ^{0}C) temperature (3) deprived of the source of energy.

The best understood examples of active transport are those that involve the movement of sodium and potassium ions across the plasma membrane of erythrocytes, nerve cells and *Nitella* cells that, results in ion gradient across the membrane.

Animation: Active transport-

Embed http://bcs.whfreeman.com/thelifewire/content/chp05/0502002.html

The Na+ / K+ exchange pump

In animal cells, internal concentration of small solutes differs greatly from their surroundings. For example, erythrocytes contain 0.150 M K+, whereas the surrounding blood plasma contains only 0.005 M K+. In contrast, the blood plasma contains 0.144 M Na+ and the erythrocytes contain only 0.030 M Na+. In spite of these differences , the Na+ and K+ ions concentration gradient across the membrane is maintained. These ions can diffuse against their concentration gradient by using metabolic energy of active transport. The active transport of Na+ and K+ across the membrane requires ATP (cannot be replaced by GTP, UTP, ITP), which is correlated to ADP during active transport by a membrane bound Na+ and K+ stimulated ATPase. This enzyme may be the same that transports Na+ and K+. Two K+ ions and three Na+ ions are transported through the membrane for each ATP hydrolysis (ATP-------ADP). Three sodium ions and one molecule of ATP inside the cell are bound to specific sites on the carrier enzyme, while two potassium ions are bound to the specific site of the same enzyme, facing exterior of the cell. The binding of the substrates (Na+ and K+) with the carrier protein results in its conformational change (change in the tertiary structure resulting in the change in the active site). In the changed conformation, the ions are 'translocated' across the membrane and the ATP is hydrolysed to ADP, since the conformational change requires energy.In the changed conformation, sodium ions are released outside and the potassium ions are released inside the cell. Once the ions get detached from the carrier protein, it goes back to its initial conformation to continue the process of ion exchange across the membrane. This exchange transport system is called Sodium-Potassium Pump, which acts as an antiport (exchange of ions in opposite direction of the membrane surface).

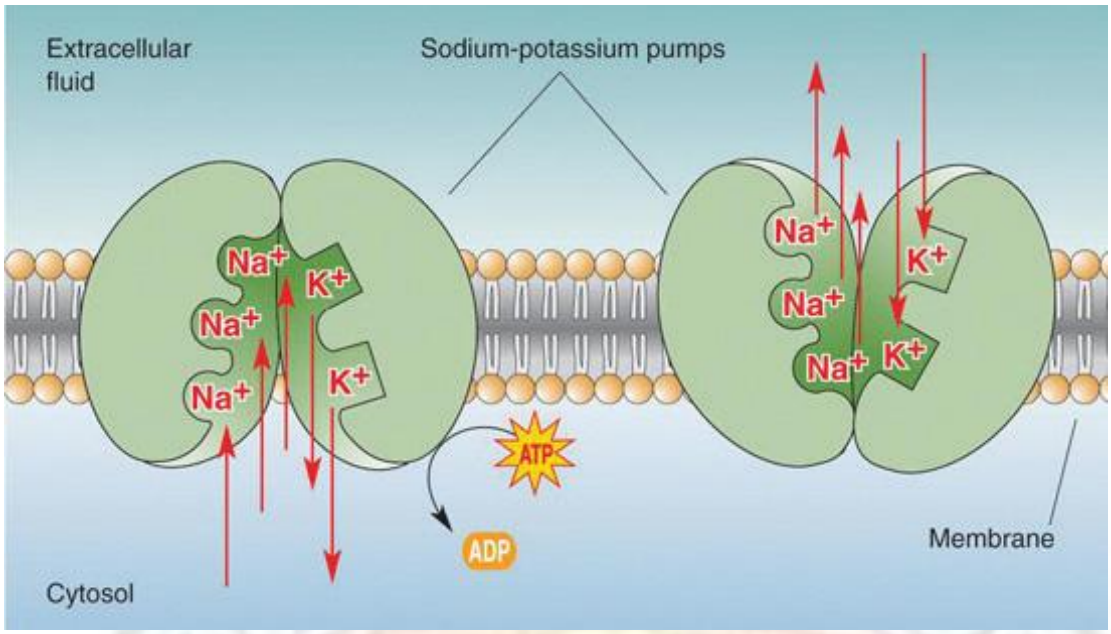


Figure: The Na^+/k^+ pump

Source: http://biologyquestions.org/sodium-potassium-ion-pump.jpg

Animation:

Embed http://highered.mcgraw-hill.com/sites/0072495855/student_view0/chapter2/animation__how_the_sodium_potassium_pump_works.html

The Sodium –Potassium pump is an example of a P-type ion pump, where "P" stands for phosphorylation, indicating the hydrolysis of ATP during the pumping cycle. Due to the transport of three sodium ions outside the cell in place of two potassium ions inside, the cytoplasm becomes slightly more electro negativ compared to the extracellular fluid. The voltage difference across the membrane is called membrane potential (can range from -50 to -200 mV). Hence this type of diffusion across the membrane is driven by two types of forces (1) chemical force (ion gradient) and (2) an electrical force due to membrane potential. These combined forces acting on the ion, is called the electrochemical gradient. For this reason, Na-K ATPase exchange pump is called an electrogenic pump in animal cell.

Other important Ion Transport systems

In plants, fungi and bacteria, the principal electrogenic pump which actively transfers H^+ ions from the cytoplasm to extracellular solution,thus controlling the pH of the cytoplasm is called a **proton pump.**

Ca^{2+-} ATPase is another well studied, P-type electrogenic pump. It is present both in plasma membrane and in the membrane of the endoplasmic reticulum (ER). Calcium pump actively transports calcium ions out of the cytosol into the extracellular space or in the lumen of the ER. In animal cells , a special type of ER called, sarcoplasmic reticulum present in the muscle cells helps in the muscle contraction and extension using Ca^{2+-} ATPase pump.

An important P-type pump, the H^+/K^+ ATPase pump is present in the cytoplasmic membrane of the parietal cells of the stomach lining. The pump helps in the secretion of concentrated acid (upto 0.16N HCl), within the stomach, to help in the digestion process.

V-Type pump: This type of pump actively transports H^+ ions across the membrane of cytoplasm, organelles and vacuoles (hence the name V-type), using energy of ATP. Membranes of secretory granules, lysosomes, plant vacuoles, animal kidney tubules contain such type of pumps, to maintain the pH or acid/base balance. It differs from P-type pump, by not forming any phosphorylated protein intermediate.

Co-transport: Several solutes can indirectly get transported by a single ATP-powered pump that transports specific solutes in a mechanism called **co-transport**. Amino acids, sugars and other nutrients are transported actively through the plasma membrane coupled to movement of Na^+ ions. Sodium- Potassium exchange pump creates a steep concentration gradient of sodium (3 sodium ions out for every 2 potassium taken in) across the plasma membrane, which is followed by active extrusion of sodium ions back through the membrane along with the co-transport of specific metabolites. The knowledge of Glucose- Sodium co-transport helps in the effective treatment of dehydration, when the patients are given solution of high concentration of glucose and common salt (NaCl). H^+-sucrose co-transport is used by plants to load photosynthetic sucrose into cells of leaf veins, which later get distributed to the non-photosynthetic parts of the plant.

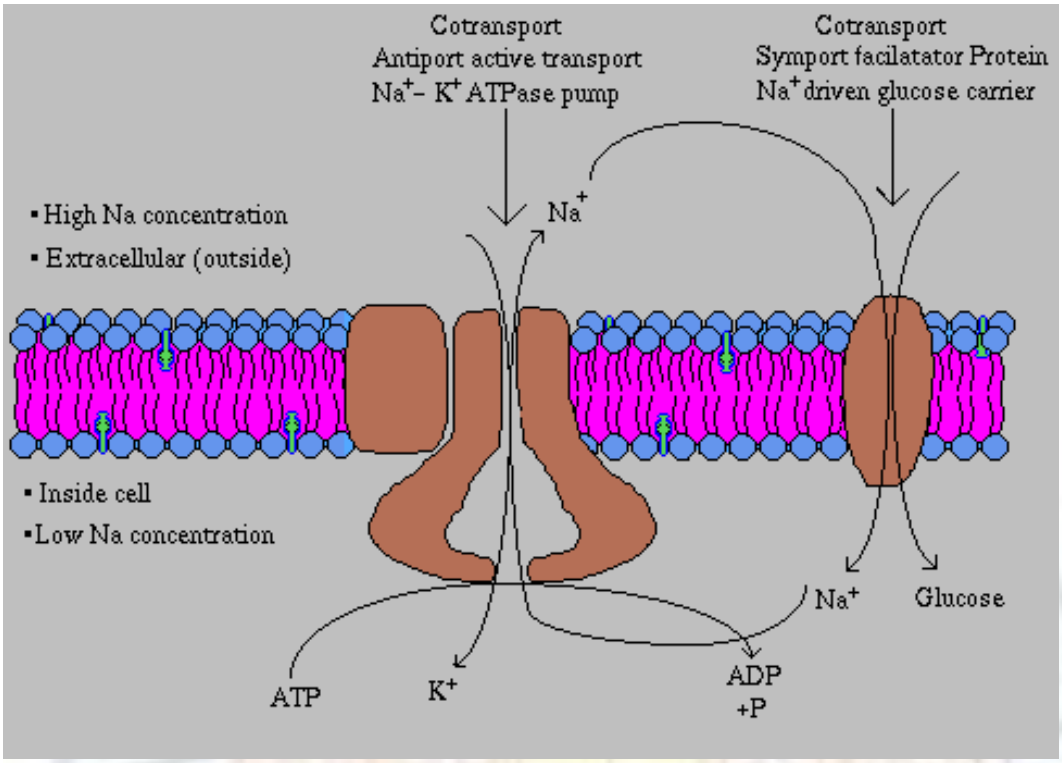


Figure: The coupled transport of Na+ ions and glucose

Source:http://upload.wikimedia.org/wikipedia/commons/9/9c/Protein_transport.png

Animation:

Embed http://highered.mcgraw-hill.com/sites/9834092339/student_view0/chapter38/cotransport__symport_and_antiport_.html

Bulk transport

Small solutes, ions, water etc enter and leave the cell by diffusing across the lipid bilayer of the plasma membrane, either by passive or active transport. However, large molecules, such as proteins, polysaccharides or large particulate materials generally cross the membrane in bulk by a mechanism that involves **vesicular transport**.As the name suggests, it involves the packaging of the macromolecules within vesicles, these vesicles then either enter or exit from the cell as the case may be. A transport system in cell that takes, in or out large quantity of material, packed within vesicles is called **bulk transport**. Like the active transport, bulk transport also requires energy, hence can be carried out only in metabolically active cells. Depending on the direction of the transport, bulk transport can be **exocytosis or endocytosis.**

Endocytosis

Endocytosis is a process through which, biological molecules and particulate matter is taken inside the cell from its immediate surrounding. During endocytosis, a small portion of the plasma membrane sinks inward to form a pocket , where the material to be ingested gets accumulated. As this invagination deepens, it pinches off, forming a vesicle containing the material from outside. The formation of the cytoplasmic vesicles from the plasma membrane and the consequent entrapment of the substance from the surrounding is called endocytosis. A small portion of the membrane gets removed during endocytosis, which gets added during exocytosis (a reverse process), maintaining the surface area of the membrane.

There are three types of endocytoisis : (1) Pinocytosis ("cellular drinking"; pinos in Greek means I drink) (2) Receptor-mediated endocytosis and (3) Phagocytosis ("cellular eating").

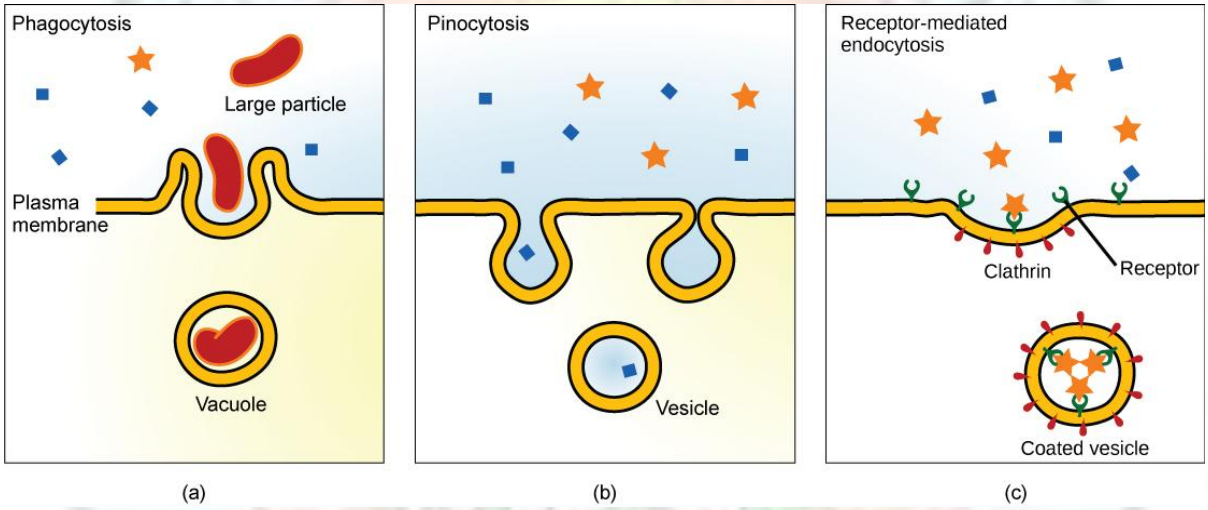


Figure: Mechanisms of endocytosis – (a) Phagocytosis (b) Pinocytosis (c) Receptor mediated endocytosis

Source: http://cnx.org/content/m45435/1.2/Figure_03_06_03abc.jpg

Pinocytosis

W.H. Lewis (1931) described the curious phenomenon in tissue culture cells where, small amount of cultural medium, was taken within the invaginated plasma membrane and pinched off as cytoplasmic vesicles. Lewis termed the process as pinocytosis, since it appeared like some form of cellular drinking. Later, S.O. Mast and W.L. Doyle (1934) observed similar process in Amoeba cells under light microscope. During 1950s, pinocytosis was demonstrated in different types of cells and tissues, using electron microscope.

Steps involved during the process of pinocytosis:

(a) **Appropriate concentration** of materials, like proteins, amino acids, certain ions etc, in the surrounding medium induce the process.

(b) The process begins by binding of the inducer substance to specific receptor in the plasma membrane.

(c) The binding of the inducer- receptor is followed by invagination of the membrane to form **either pinocytic vesicle or narrow channel.** The formation of such vesicles requires metabolic energy.

(d) Actin filaments (a type of cytoskeleton) are associated along the margins of the pinocytic vesicles, pointing towards their role in the formation of such vesicles

(e) The vesicles get detached from the plasma membrane and migrate towards the cell interior.

(f) Smaller vesicles coalesce to form larger vesicles within the cell and soon become in distinguishable from other vesicles in the cell.

(g) Depending on the size, the pinocytic vesicles vare named, micro- pinocytic vesicles (0.1 micrometer in diameter) and macro -pinocytic vesicles (1-2 micrometer in diameter).

Receptor-mediated endocytosis

Receptor-mediated endocytosis occurs in specialized cells and only specific types of substances can be taken in by this process.

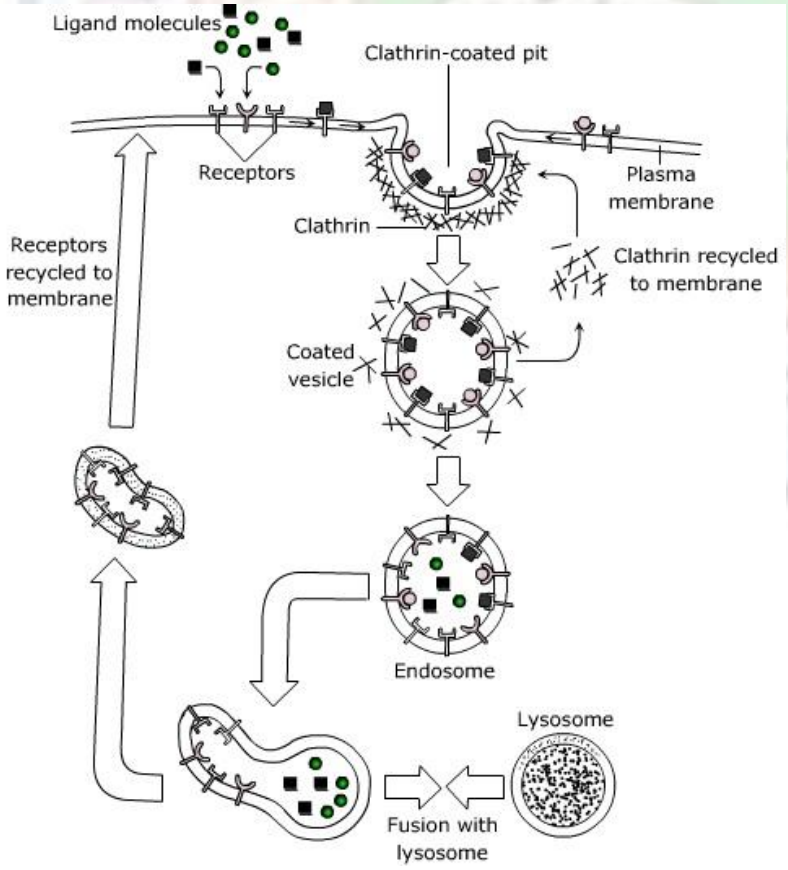


Figure: Receptor mediated endocytosis. The ligand molecules bind to the receptors on the plasma membrane. These are then coated with clathrin to form coated vesicles. The clathrin coat is lost as the vesicles move inwards and the vesicle matures into an endosome. The ligand molecules are released and the endosome fuses with the lysosome and the membrane receptors recycled back.

Source: Author

The various steps involved in this process are described below:

(a) Specific types of receptor molecules are present in the plasma membrane, which can bind with specific molecules such as, hormones, antibodies and other proteins during specific time of cellular development.

(b) The transmembrane proteins usually act as the receptor molecules for the substances,which are called **ligands**.

(c) The ligands are 'plucked' from the extracellular space, even when present in very low concentration along with other related molecules.

(d) Coated pits are present in almost all animal cells membrane and account for 20% of total membrane surface. The ligand-receptor complex gets quickly concentrated in such coated-vesicles.

(e) The 'çoat' of the pits consists primarily of **Clathrin** (a protein having three armed trimer called **triskelion**, having a mol. wt of 180,000, a cage like structure is formed by intermolecular interactions), which are tightly appressed to the cytosol-facing surface of the pit.

(f) Coated-vesicles eventually get detached from the plasma membrane and move deep into the cytoplasm. Once inside, the vesicles shed their Clathrin coats and fuse with with one another to form a larger smooth-surfaced vesicles called the **endosome/receptosomes**.

(g) The detached Clathrin get recycled to the membrane to form new coatedpits.

(h) There is a progressive release of ligands from their receptors into the lumen of endosomes.

(i) The endosomes at this stage develop a tubular portion in, which the membrane-bound but ligand free receptors are concentrated.

(j) The vesicular portion of the endosome contains free ligands. The endosome at this stage is sometimes referred as CURL (Compartment of uncoupling of Receptor and Ligand).

(k) The tubular portion later gets detached to recycle the ligand molecules, whereas the receptor molecules move deeper into the cytosol and fuse with the lysosomes, to get digested by the hydrolysing enzymes.

Animation: Receptor mediated endocytosis

Embed http://bcs.whfreeman.com/thelifewire/content/chp05/0502003.html; http://www.sumanasinc.com/webcontent/animations/content/endocytosis.html

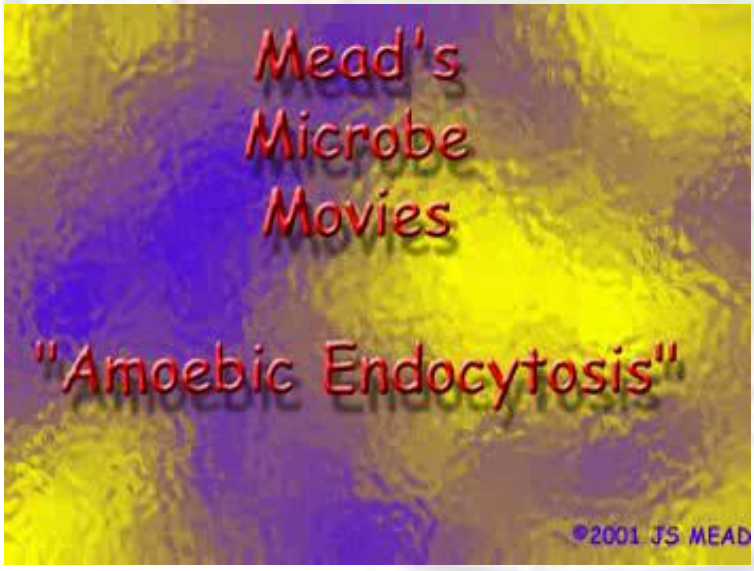
Phagocytosis

Phagocytosis involves the endocytosis of much larger quantities of particulate materials. The process of phagocytosis was first described by E.Metchnikoff in late nineteenth century. The various steps involved in phagocytosis are:

(a) Small microscopic organisms, like the entire ciliates, rotifers etc, can be phagocytosed by an Amoeba. The food particles get enclosed within one or more **food vacuoles or food cups** (Fig)

(b) The 'prey' may be, temporarily immobilized by the secretion from the phagocytic cells.

(c) Phagocytosis is characterized by the formation of foot-like projections called **pseudopodia**, which are formed by the projected membrane by flowing cytoplasm, as seen in Amoeba cells (hence phagocytosis is sometime referred to as Amoeba way of eating).



Video: Amoeba cells showing phagocytosis

Source:

http://www.youtube.com/watch?v=W6rnhiMxtKU&feature=player_embedded

(d) The pseudopodia gradually extend, and fully encircle the food particle.

(e) The encapsulated particle, now called the phagosome, fuses with the primary lysosomes in the cell.

(f) Hydrolytic enzymes present in the lysosome help in the digestion of the engulfed material.

(g) The hydrolysed materials may be then, transported across the vacuolar membrane into the cytosol.

(h) Phagocytic process help in destroying old cells in animals.

Exocytosis

Exocytosis is reverse of endocytosis through which, large quantities of material enclosed within cell vacuoles are secreted outside the cell into its surrounding environment. During exocytosis ,the vacuole containing excretory substances move from the cellular interior towards the plasma membrane, releasing the enclosed material outside the cell. As the vesicles touch the membrane, the two membranes fuse to form a common bimolecular leaflet. The extra added membrane (vesicle membrane) gets removed during endocytosis (portion of membrane gets pinched off), there by maintaining constant surface area of the cell membrane.

Intracellular structure actively involved in the processing of cytoplasmic vesicles for exocytosis is the Golgi Apparatus. Secretory cells in animals use the process of exocytosis, to secrete various hormones, neurotransmitter etc. For example, insulin from the pancreas secreted into the extracellular fluid; neurons release neurotransmitters to other neurons and muscle cells. Plant cell wall material such as carbohydrate, proteins etc, are delivered through exocytosis from the Golgi cisternae membrane.

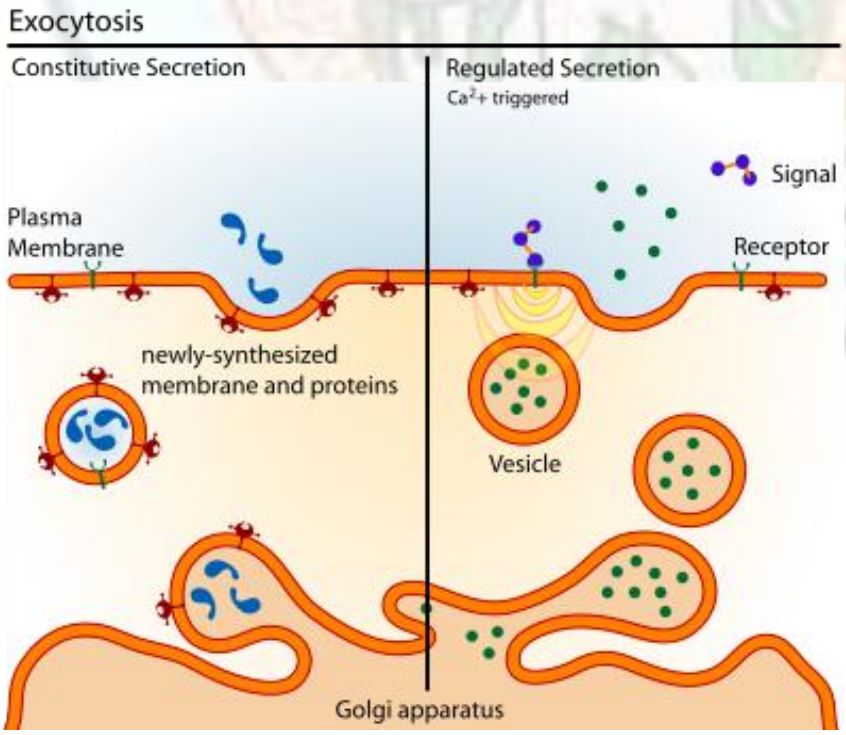


Figure: Exocytosis can be constitutive or regulated (in response to a signal for e.g. Ca^{+2})

Source:

http://upload.wikimedia.org/wikipedia/commons/thumb/1/16/Exocytosis_types.svg/399px-Exocytosis_types.svg.png

Summary

Cell membrane posseses certain unique properties, which help living organisms to survive in different environmental conditions and carry out different metabolic activities. The uniqueness of biological membrane is due to its chemical composition. The amphipathic nature of membrane lipids maintains a constant bimolecular lipid leaflet and the presence of one or two cis-double bonds in one of the fatty acid chain in phospholipid maintains the loose fittings of the lipids within each monolayer thus helping in the fluidity of the membrane.The cholesterol molecules, in animal membrane, are positioned in a way to help maintain the membrane fluidity as well as help in the phase-transition of the membrane and act as a temperature buffer. Protein component of the membrane play an important role in the selective permeability of the membrane.Transport of solutes across the membrane is one of the important function on which the different cellular processes depends. The transport of materials across the membrane can be a passive or an active phenomenon. The latter requires energy and can accumulate solutes against the concentration gradient. Large quantities of materials can be taken into the cell or can move out of the cell by endocytosis or exocytosis respectively.

Glossary

Active transport: Energy requiring transport across the membrane, against the concentration gradient.

Bulk transport: Vesicular movement of large quantity of materials across the membrane

Co transport: Type of active transport, where simultaneous coupled transport of two different types of molecules across the membrane takes place

Diffusion: Movement of molecules in the direction of its lower concentration

Endocytosis: Bulk transport of material from the cell's immediate surrounding to cell's interior

Exocytosis: Reverse of endocytosis

Fixed charge: Ionic charge within the cell due to Gibbs-Donnan effect

Facilitated diffusion: Increased rate of diffusion through specific transport protein in the presence of a concentration gradient

Flippase: The enzyme responsible for the flip-flop movement of the lipid molecules within the lipid bilayer

Hypotonic: A situation when solute concentration in one compartment is lower than the surrounding

Hypertonic: A reverse situation than hypotonic

Isotonic: When solute concentration is equal in the two adjacent compartments

Plasmolysis: The shrinking of the protoplast, when a cell is, immersed in any hypertonic solution, due to the loss of water from cell's interior

Tonicity: Study that determines the direction of water movement, when cells are immersed in any solution

Transition temperature: The temperature at which, the movement of membrane lipid molecules is greatly reduced and the membrane changes from a fluid to a crystalline state

Osmosis: Water movement through a semipermeable membrane from a region of higher concentration to a region of lower concentration

Passive transport: Transport across the membrane, based on concentration gradient without any energy expenditure

Exercises

(1) What is phase transition? Explain how do biological membranes resist phase transition.

(2) Why cell membranes of Polar bear or Penguin do not freeze?

(3) Describe the role of cholesterol molecules in maintaining the fluidity of the membrane.

(4) How do membrane cholesterol molecules function as temperature buffer?

(5) Cell membranes show asymmetry: justify the statement.

(6) Differentiate between the following giving appropriate examples: (a) Passive transport and Active transport (b) P-type pump and V-type pump (c) Simple diffusion and Facilitated diffusion (d) Endocytosis and Exocytosis (e) Pinocytosis and Phagocytosis

(7) Explain the following terms: (a) Aquaporin (b) Permease (c) Carrier protein (d) Gated- transport (e) Co-transport (f) Electrogenic pump (g) Endosome (h) CURL (i) Flip-flop movement

(8) With the help of well- labelled diagram, explain the various steps of Sodium-Potassium pump.

(9) Explain the steps involved during the process of pinocytosis and phagocytosis.

(10) What is bulk transport? Describe the various types of bulk transport.

References

1.Karp, G. 2010. Cell and Molecular Biology: Concepts and Experiments. 6 Edition. John Wiley & Sons. Inc.

2. De Robertis, E.D.P. and De Robertis, E.M.F. 2006. Cell and Molecular Biology. 8th edition. Lippincott Williams and Wilkins, Philadelphia.

3. Cooper, G.M. and Hausman, R.E. 2009. The Cell: A Molecular Approach. 5th edition. ASM Press & Sunderland, Washington, D.C.; Sinauer Associates, MA.

4. Becker, W.M., Kleinsmith, L.J., Hardin. J. and Bertoni, G. P. 2009. The World of the Cell. 7th edition. Pearson Benjamin Cummings Publishing, San Francisco.

5. Raven, P.H et al (2006) Biology. 7th edition. Tata Mc Graw-Hill Publications, New Delhi

Suggested Readings

Frye, L.D. and M. Edidin. 1970. The rapid intermixing of cell surface antigens after formation of mouse-human heterokaryons. Journal of Cell Science. 7:319-335.

Nicolson, G.L., R. Hyman, and S.J. Singer. 1971. The two-dimensional topographic distribution of H-2 histocompatibility alloantigens on mouse red blood cell membranes. The Journal of Cell Biology. 50:905-910.

Nicolson, G.L., S.P. Masouredis, and S.J. Singer. 1971. Quantitative two-dimensional ultrastructural distribution of Rho(D) antigenic sites on human erthryocyte membranes. Proceedings of the National Academy of Sciences. 68:1416-1420.

Singer, S.J. and G. L. Nicolson. 1972. The fluid mosaic model of the structure of cell membranes. Science. 175: 720-731.