eunoia JUNIOR COLLEGE

Membrane Transport

1. Overview of Topic

Cells need to regulate the movement of substances into and out of themselves. Substances such as water, oxygen, glucose and minerals are important in the synthesis of new molecules and important cellular processes. According to the fluid mosaic model, cell membranes are selectively permeable due to the nature of the phospholipids and proteins from which they are made. The movement of different molecules depends on the nature of the substances through transport processes such as osmosis, diffusion and active transport.

Membranes allow cells to create and maintain internal environments that are different from external environments. Membranes are not just found on the most exterior ends of a cell to provide that barrier between the exterior and interior. Especially for eukaryotic cells, there are internal membrane structures that partition the cell into specialised compartments so that cellular processes can occur with optimal activity e.g. chloroplasts and mitochondria. The endomembrane system, consisting of rough and smooth endoplasmic reticulum and Golgi apparatus, is responsible for protein processing and vesicular transport within the cell.

2. Learning Outcomes

(j) explain the fluid mosaic model and the roles of the constituent biomolecules (including phospholipids, proteins, glycolipids, glycoproteins and cholesterol) in cell membranes

(k) outline the functions of membranes at the surface of cells and membranes within the cell

(l) explain how and why different substances move across membranes through simple diffusion, osmosis, facilitated diffusion, active transport, endocytosis and exocytosis

3. References

Reece, J. B., Urry, L. A., Cain, M. L., Wasserman, S. A., Minorsky, P. V. and Jackson, R. B. (2011) Campbell Biology (Ninth Edition) (Pearson Higher Education) ISBN 0321739752

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4. Types of Membranes

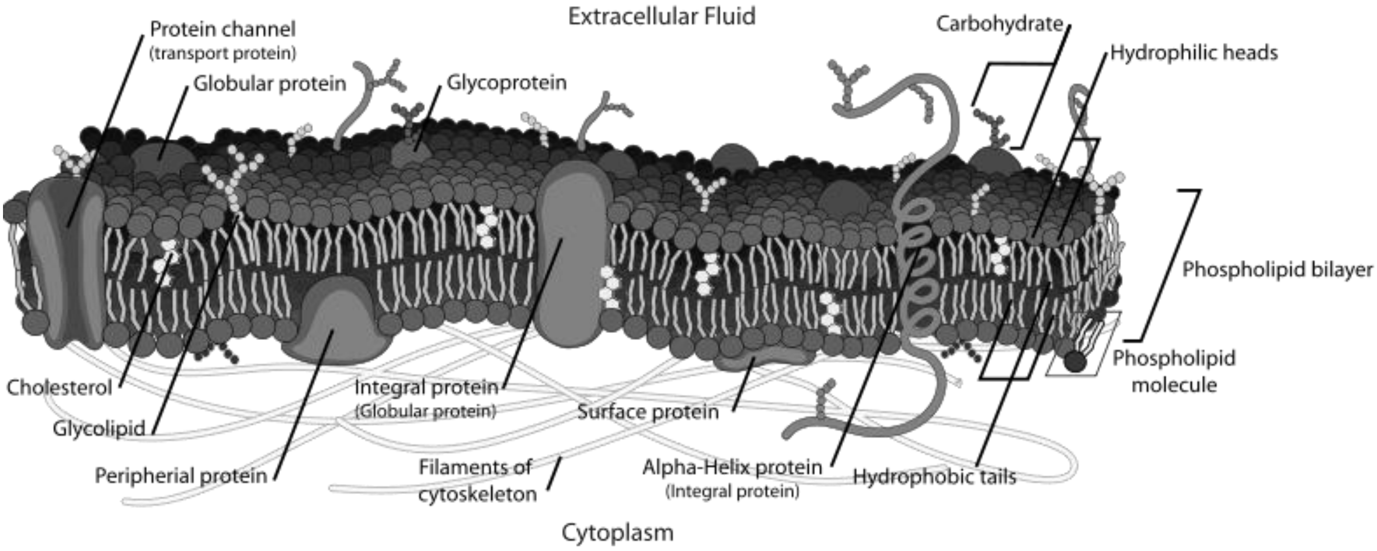
There are generally two different types of membranes:

External cell membrane that surrounds cells (known as plasmalemma or plasma membrane / cell surface membrane)

Intracellular membranes of organelles typically found within eukaryotic cells.

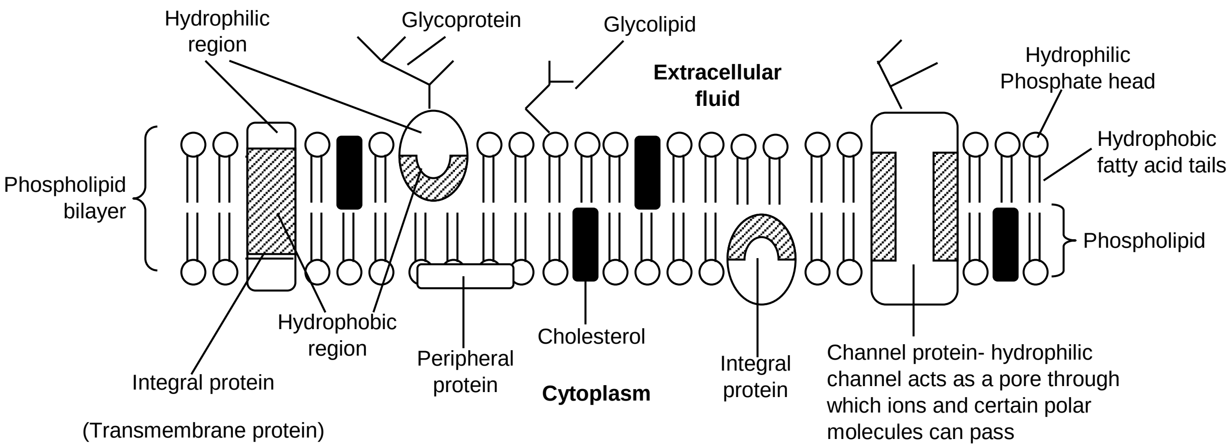
5. Membrane Structure: The Fluid Mosaic Model

The membrane is a fluid bilayer of phospholipid molecules in which proteins are dispersed and embedded like a mosaic pattern. This mosaic pattern is not static because proteins are constantly moving in a fluid sea of phospholipids. This is described by the **Fluid Mosaic Model**.

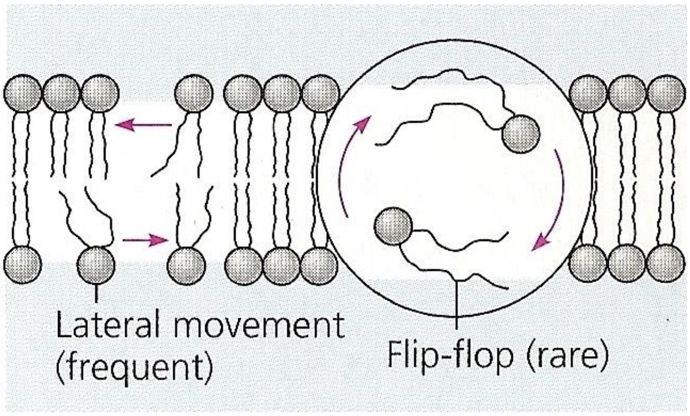


Like a **mosaic**, the cell surface membrane is a complex structure made up of the following components: Phospholipids, Cholesterol, Glycolipids, Proteins (peripheral and integral) and Glycoproteins.

The relative amounts of these components **vary** from membrane to membrane depending on the function of the membrane. Typically, the membrane is never identical on both sides and is described as asymmetrical.



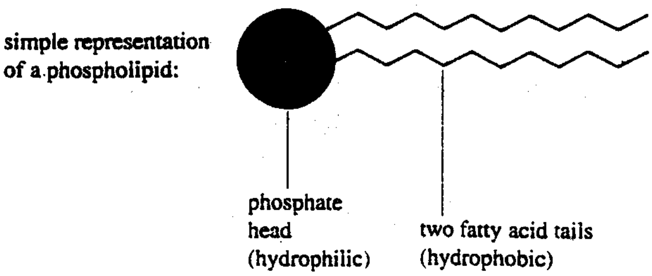
The membrane is **fluid** and in dynamic motion. Hydrophilic portions of both proteins and phospholipids are maximally exposed to water while the hydrophobic portions of proteins and phospholipids are in the non-aqueous environment in the core of the bilayer resulting in a stable membrane structure. As the hydrophobic interactions are weak, this allow most membrane lipids and proteins to drift laterally within the plane of the membrane. Flip-flopping across the membrane is rare.

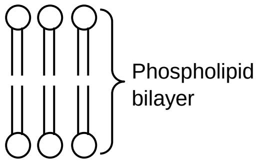


6. Components of Membrane

Phospholipid

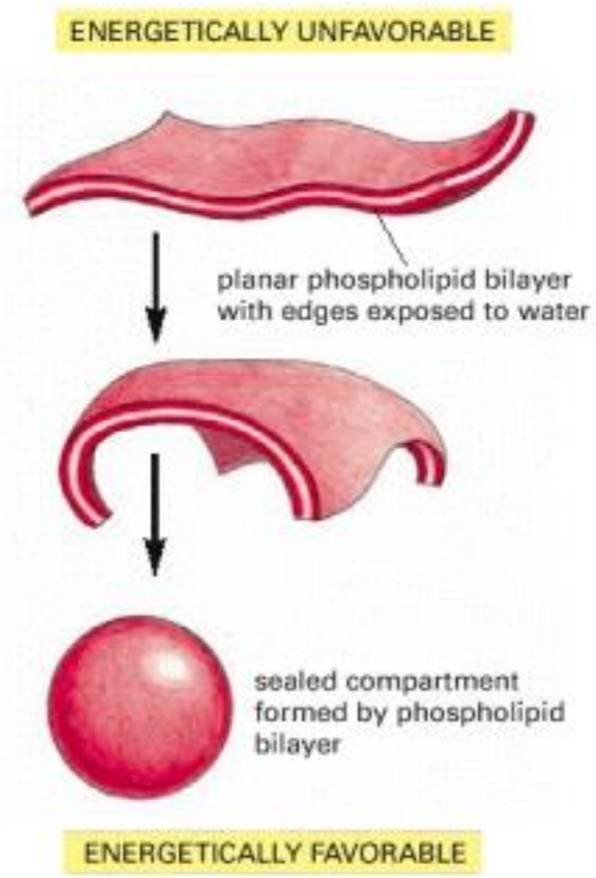
It is an **amphipathic** molecule as it has both hydrophilic and hydrophobic components within its structure. The negatively charged phosphate group can interact with water and therefore hydrophilic while the two hydrocarbon tails are hydrophobic.





In an aqueous medium, phospholipids are able to form stable bilayers spontaneously as they tend to line up with polar heads in water and hydrocarbon tails away from water. Phospholipids in the membrane are held together by weak hydrophobic interactions. The formation of bilayers prevents energetically unfavorable interactions of the fatty acid chains with the aqueous medium.

The same forces that drive phospholipids to form bilayers also provide a self-healing property. A small tear in the bilayer creates a free edge with water; because this is energetically unfavorable, the lipids spontaneously rearrange to eliminate the free edge.

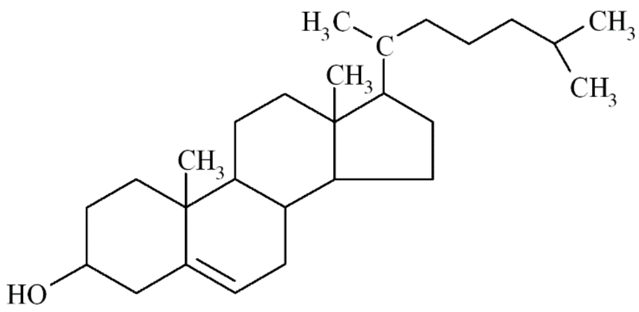


The closed structure is stable because it avoids the exposure of the hydrophobic hydrocarbon tails to water, which would be energetically unfavorable.

Cholesterol

Sterols are the most abundant group of steroids made up of a hydroxyl (-OH) group and a hydrocarbon chain. E.g.: cholesterol. Cholestrol is non-polar, therefore, generally hydrophobic. It also has a carbon skeleton consisting of 4 interconnected rings.

A sterol which help maintain fluidity of membrane by preventing close orderly packing of phospholipid molecules when the temperature is low and also has an effect in holding the phospholipids together when the temperature is high (*refer to the Section on Membrane Fluidity*).



Protein

Membrane proteins can be classified based on their positioning in the membrane.

Peripheral or extrinsic proteins are loosely attached at the polar surface of the phospholipids They are rich in amino acids with hydrophilic side chains which permit interaction with surrounding water and the polar surface of the phospholipid bilayer

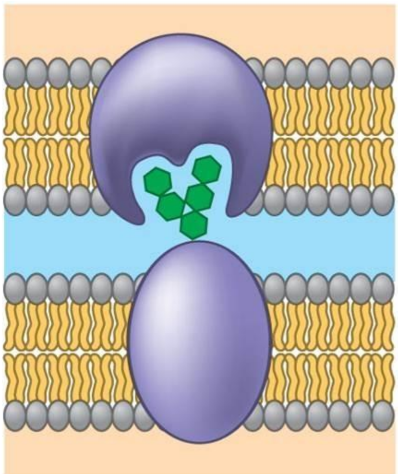
Integral or intrinsic proteins are either partially embedded in the phospholipid bilayer or span the membrane entirely (transmembrane protein)

Proteins that are embedded in lipid layers contain both hydrophilic and hydrophobic regions which interact with the polar heads of the lipid layer and the hydrocarbon tails of the phospholipids respectively.

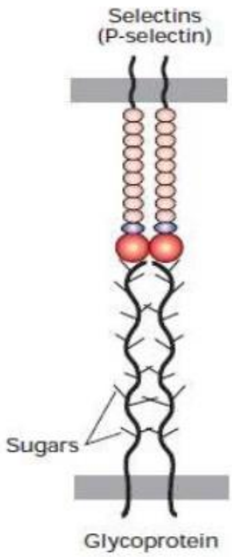
Some transmembrane proteins functions as carrier proteins and some as channel proteins *(Their roles will be covered in greater detail under Facilitated Diffusion).*

Carbohydrates

Carbohydrates in membranes tend to be covalently associated with either lipids or proteins forming glycolipids and glycoproteins respectively. Membrane carbohydrate chains are important for cell-cell recognition; adhesion of cells to neighbouring cells.



Cell-Cell recognition



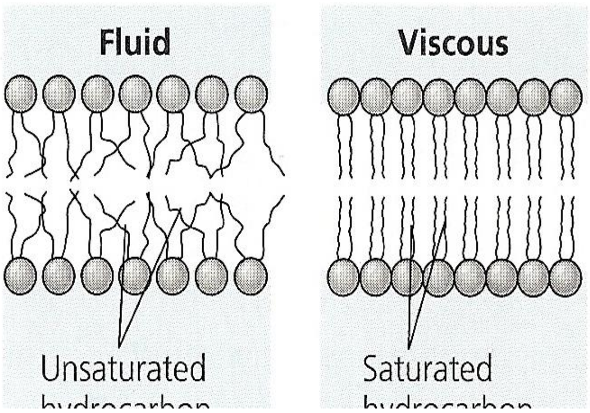
Cell-Cell adhesion

7. Membrane Fluidity

Membrane fluidity is dependent on lipid composition and the type of lipids that makes up the membrane.

The saturation of the fatty acid tails of the phospholipid affects fluidity

Saturated fatty acids chains make the membrane less fluid as the straight chains allows maximum interaction of the fatty acid tails with each other and thus exact a greater hydrophobic interaction. Unsaturated fatty acids make membranes more fluid due to the presence of C=C (carbon double bonds) which causes kinks at this points, keeping the fatty acid tails apart.

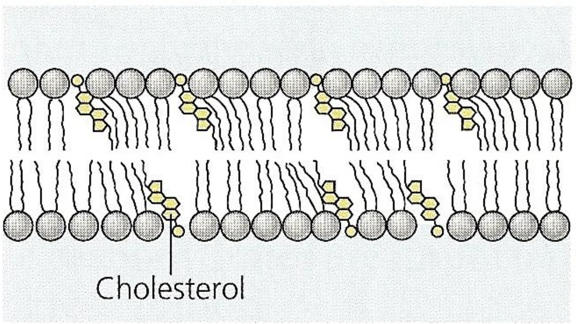


Presence of Cholesterol affects fluidity

Hydroxyl (OH) group of cholesterol forms hydrophilic interactions with phosphate head of phospholipids, steroid rings form hydrophobic interactions with fatty acid chains. Presence of cholesterol ***helps to maintain the fluidity of the membrane***.

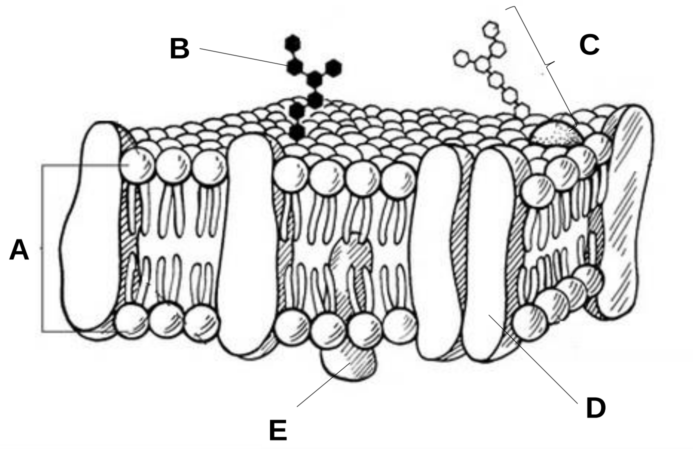
At low temperature, Phospholipid molecules have ***less kinetic energy***. The Cholesterol between them ***prevents*** them from being ***too closely packed***. Fluidity is not lost when temperature drops.

At high temperature, the phospholipid molecules have ***more kinetic energy.*** *The* Cholesterol between them ***prevents*** them from ***moving too far apart***. Cholesterol stabilises the structure. Fluidity not lost when temperature rises.



Try This !

Identify the parts labelled A to E.



A: ______________________

B: ______________________

C: ______________________

D: ______________________

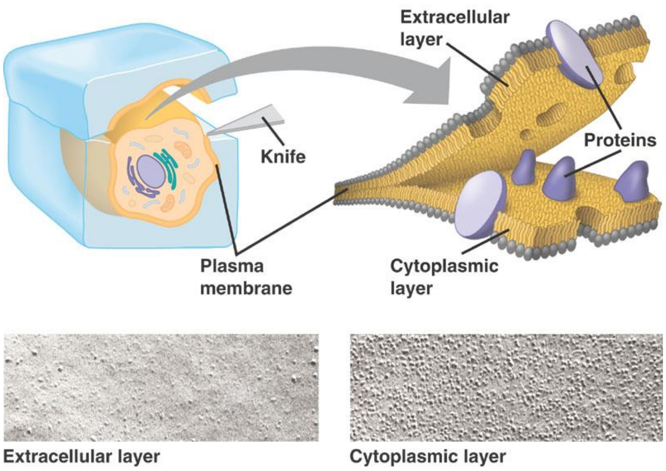
E: ______________________

BROYO

How was the molecular structure of the membrane determined?

In 1972, Singer and Nicolson proposed the Fluid Mosaic Model (through the freeze fracture technique), which accounted for the amphipathic character of proteins.

Freeze Fracturing Technique



An electron microscope technique which shows the existence of ***proteins among the phospholipid bilayer*** is the ***freeze fracture technique***.

When the membrane is cooled in liquid nitrogen and is then split into two layers (down the middle of the phospholipids bilayer), it was observed that some proteins are embedded in only one of the membrane layers (***extrinsic/ peripheral proteins***), whilst others lie in both membrane layers (***intrinsic/ integral/ transmembrane proteins***).

8. Functions of Membrane

Compartmentalisation

Membranes compartmentalize cells to allow separate compartments to be formed within cells, thus maintaining a constant internal environment within each compartments. These different internal environments provide optimal conditions for the working of enzymes in catalyzing different metabolic processes and biochemical pathways within these organelles.

For example, the enzymes in mitochondria to produce ATP and DNA replicative enzymes in the nucleus. The pH within the lysosome or mitochondrion can be maintained at a value, which would otherwise be detrimental to the processes going on in other parts of cell (*Some of these ideas will be covered at greater depth in the topics of Cell Structure and Respiration*).

Selectively permeable barrier

Membranes act as selective barriers for regulating the passage of substances in and out of cells this is due to the:

High composition of lipids which allow non-polar molecules to pass through while preventing larger polar molecules (e.g. glucose and amino acids) and charged particles/ions (e.g. Na+, H+) from getting across.

Presence of specific integral transport proteins to allow hydrophilic substances to avoid the hydrophobic core of the bilayer by passing through the hydrophilic tunnel of the transport proteins e.g. channel proteins.

Site of chemical reactions

Membranes are also sites of chemical reactions due to the presence of enzymes and proteins that are bound and organized on it for the specific biochemical reaction to take place. For example: Light reactions of photosynthesis take place on thylakoid membranes found in chloroplasts; Oxidative phosphorylation via electron transport chain of cellular respiration in inner mitochondrial membrane.

Communication with surroundings

The membrane also serves as a point of communication between one cell with another cell and even with its surrounding environment.

- Proteins at the membrane act as receptor sites for recognising external stimuli such as hormones.
- Increases surface area for exchange of substances, e.g. microvilli in cells lining small intestine for absorption of food substances.
- Cell recognition: Membranes contain certain protein molecules, which identify the cells. Presence of foreign proteins on membrane will trigger off the production of antibodies for the removal of such cells.
- Attachment or adhesion of cells to one another; e.g. tight junctions, desmosomes, gap junctions.

9. Transport across membrane

There are two broad categories of movements which can occur within a cellular environment and across a membrane; Passive and Active movement. Active movement requires the expenditure of energy, typically through the hydrolysis of ATP.

PASSIVE	ACTIVE
*Substances **move down a concentration gradient** from an area of higher to lower concentration. Cells **do not expend energy**.* **1. Simple Diffusion** **2. Facilitated Diffusion** **3. Osmosis**	*Substances move **against a concentration gradient** from an area of lower to higher concentration by an **interaction with integral proteins** in the membrane; the process requires **energy expenditure in the form of ATP*** **1. Active Transport** **2. Bulk transport – endocytosis, exocytosis**

There are a variety of factors that affect the permeability of molecules across a membrane. **Size** of the molecules: The larger the molecule, the more impermeable. **Solubility** of the molecule in lipids: Higher solubility of molecules, the more permeable. **Charge** on ions: Charged ions are not permeable as it is unable to pass the hydrophobic phospholipid bilayer core. Presence of **carrier molecules**: Presence of Protein carriers and Protein Channels allows charged ions and polar molecules to be permeable to a membrane.

Table: Permeability of the Phospholipid bilayer to different substances

Type of molecule	Example	Permeability
Hydrophobic	N_2, O_2, hydrocarbons	Freely permeable
Small polar	H_2O, CO_2, glycerol, urea	Freely permeable
Large polar	Glucose, other uncharged monosaccharides, disaccharides	Not permeable
Ions	Amino acids, H^+, HCO_3^-, Na^+, K^+, Ca^{2+}, Cl^-, Mg^{2+}	Not permeable

Diffusion

Diffusion is the movement of molecules or ions from a region of high concentration to a region of low concentration, down a diffusion gradient. It is a passive process which does not require energy in the form of ATP.

Diffusion of particles will continue but once the particles are evenly distributed, there is no longer net movement of particles in any direction. (Dynamic Equilibrium).

Relevant in:

- Nervous Control – Synaptic Transmission, diffusion of acetylcholine across the synaptic cleft.
- Photosynthesis and Respiration – diffusion of H^+ down a concentration gradient through the ATP synthase for the formation of ATP from ADP (*More will be elaborated during Photosynthesis and Respiration*)

<u>Factors affecting rate of diffusion</u>

Molecular Size	The smaller the particle, the faster it will diffuse.
Surface area of membrane	The larger the surface area, the faster the rate of diffusion e.g. microvilli increase the surface area of animal cells for absorption purposes
Concentration Gradient	The steeper the concentration gradient, the faster the rate of diffusion
Charge of ions And molecules	Charged ions attract more water molecules, resulting in the **formation of hydration shells**. Results in increasing effective size of ion Ions or molecules with a charge cannot pass through the lipid bilayer by diffusion. Other mechanisms involving integral transport proteins and ATP energy are required. Active transport: sodium/potassium ion pump is an example of this type of transport.
Lipid Solubility	Lipid soluble molecules can move through the lipid bilayer. Examples are steroid hormones such as testosterone.
Presence of pores	Pores enhance diffusion rate.
Distance	The shorter the distance over which diffusion occurs, the faster the rate
Temperature	Increase in temperature, molecules move faster.

Facilitated Diffusion

Facilitated diffusion is the movement of a substance by transport proteins from a region of high concentration to a region of low concentration with no use of energy in the form of ATP.

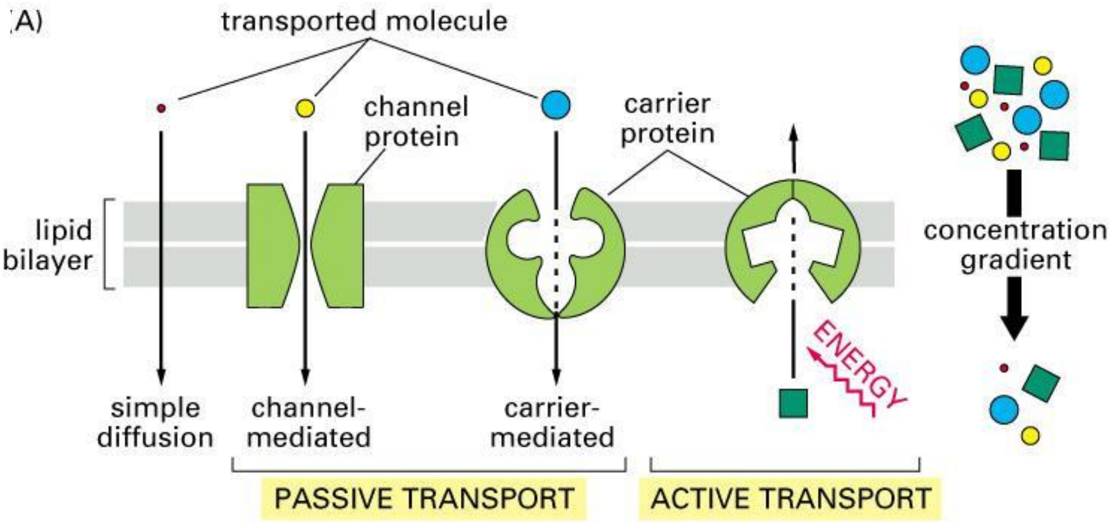
Role of transport protein is to facilitate diffusion of substances that are insoluble in phospholipids by providing hydrophilic channels via **transmembrane channel proteins** or transportation of substances via conformational change of **carrier proteins**. Diffusion can occur through the channel in either direction depending on the relative concentrations of the substrate across the membrane.

Transport proteins are highly specific. The 2 types are:

Channel proteins
Channel proteins are transmembrane proteins which a fixed conformation to provide a hydrophilic tunnel across the membrane that is selective for a particular solute. Some channels can open and close like gates. Such gated channels open only when they receive an appropriate signal e.g. voltage change across membrane, binding of another molecule/ion with the protein.

Carrier proteins
Carrier proteins are transmembrane proteins which undergoes rapid changes in conformation when the molecule is being transport binds to the binding site of the carrier protein. It exists in two alternate conformations; thus, moving a solute across the membrane as the shape of the protein changes.

Some carrier proteins transport solutes with the change in conformation triggered by hydrolysis of ATP. In such cases, the solute is moved against a concentration gradient and the carrier protein is referred to as a pump. Such a process is called Active Transport (*elaborated later*).



Factors affecting rate of facilitated diffusion

Chance collision	The higher the chance collision between transport proteins and substrates, the faster the rate of facilitated diffusion
Number of Transport Proteins	The higher the number of carrier or channel proteins, the faster the rate of facilitated diffusion
Number of Substrate Binding sites on the carrier protein	The higher the number of substrate binding sites, the faster the rate of facilitated diffusion

Osmosis

Osmosis is the movement of water molecules from a region of higher water potential to a region of lower water potential through a selectively/partially permeable membrane.

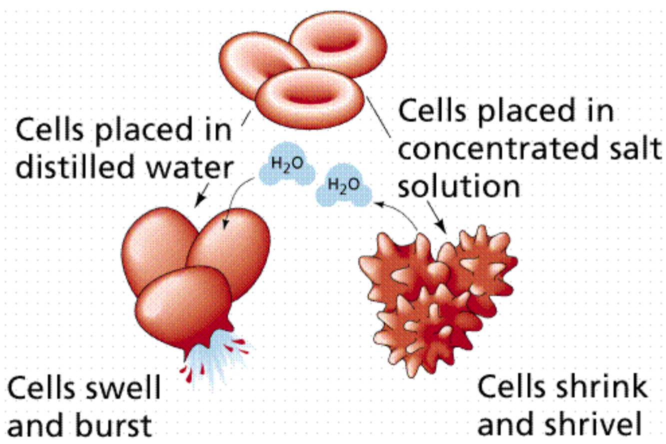
The water molecules pass through temporary gaps between the dynamic phospholipids tails. No transmembrane protein needed. Osmosis continues until a dynamic equilibrium is achieved between the two regions.

Osmosis in Animal Cells

Animal cells do not have cell walls and the cell surface membrane is too delicate to prevent the cell from expanding and bursting in a solution of higher water potential. Water potential of the cytoplasm is affected only be the amount of dissolved solutes in it.

$$\text{Water Potential } (\Psi_W) = \text{Solute potential } (\Psi_s)$$

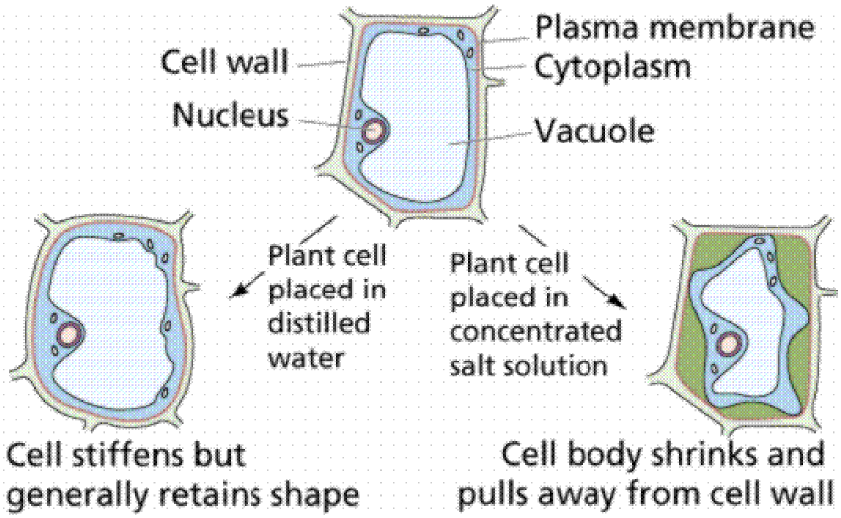
Solute potential is a measure of the change in water potential of a solution caused by dissolved solutes. The more solutes are dissolved in water, the lower is the $\mathbf{\Psi_S}$ of the solution ie. more negative.



Osmosis In Plant Cells
Plant cells have cellulose cell wall. Water potential of a plant cell is affected by Solute Potential and Pressure Potential.

Water Potential (Ψ_W) = Solute potential (Ψ_s) + Pressure potential (Ψ_p)

Solute Potential of cell sap is a measure of its solute concentration which tends to lower its water potential so that water molecules tend to move into the cell. Pressure Potential is a measure of the pressure exerted by the cell wall on the cell contents. It tends to force water out of the cell.



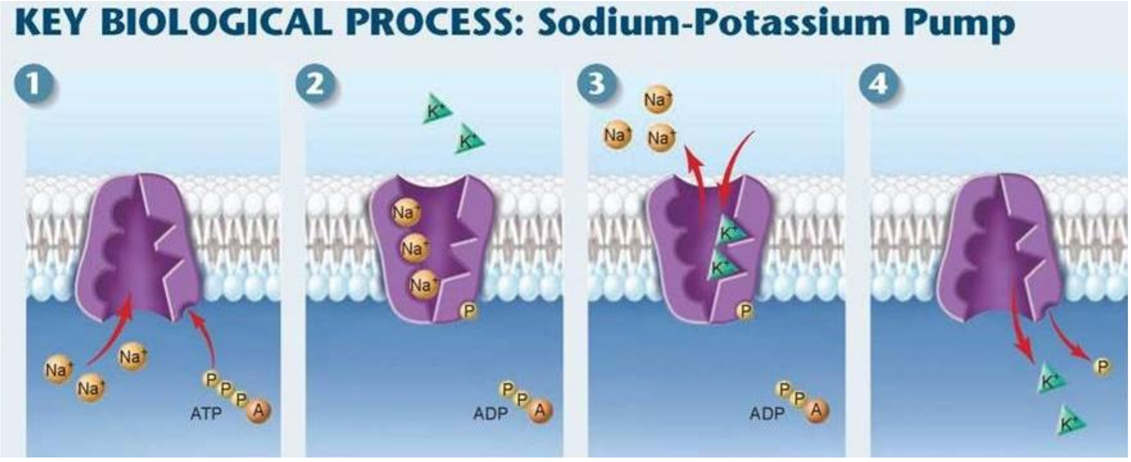
Active transport

Active transport is the energy (ATP) consuming transport of molecules or ions across a membrane against a concentration gradient achieved by carrier proteins called 'pumps' situated in the cell membrane. A supply of energy (ATP) is needed to trigger the conformational change of the protein to move the molecules against its natural tendency to diffuse in the opposite direction. Movement is usually in one direction only (unlike diffusion which is reversible).

Active transport is a major factor in the ability of a cell to maintain internal concentrations of small molecules that differ from concentrations in its environment.

Relevant in:

- Nervous Control – sodium/potassium pump (Na^+/K^+ pump) of neurons which actively transports $3Na^+$ out of the cell and $2K^+$ into the cell and so as to maintain an ionic gradient of high K^+ and low Na^+ in the cell relative to the outside. This is important for nerve transmission.



Bulk transport

Bulk transport is the movement of macromolecules (e.g. proteins or polysaccharides) in or out of the cell. There are two types of bulk transport, exocytosis and endocytosis, and both require the expenditure of energy (ATP)

Relevant in:

- Genetics of viruses and bacteria – Influenza virus penetrates into animal cell via endocytosis
- Nervous Control – release of acetylcholine via exocytosis
- Hormonal Control – Insulin release

Endocytosis

Endocytosis occurs by an infolding or invagination of the cell surface membrane to form a vesicle allowing the cell to acquire macromolecules and particulate matter. There are 3 types of endocytosis in animal cells:

- Phagocytosis
- Pinocytosis
- Receptor-mediated Endocytosis

Phagocytosis

Phagocytosis is loosely termed as "Cell eating". Filaments in cytoskeleton react with ATP to help form pseudopodia**.** Pseudopodia extends outwards and wraps around solid particle (engulfing). Packages particle within membrane enclosed sac to form phagosome/ phagocytic vesicle/ food vacuole.

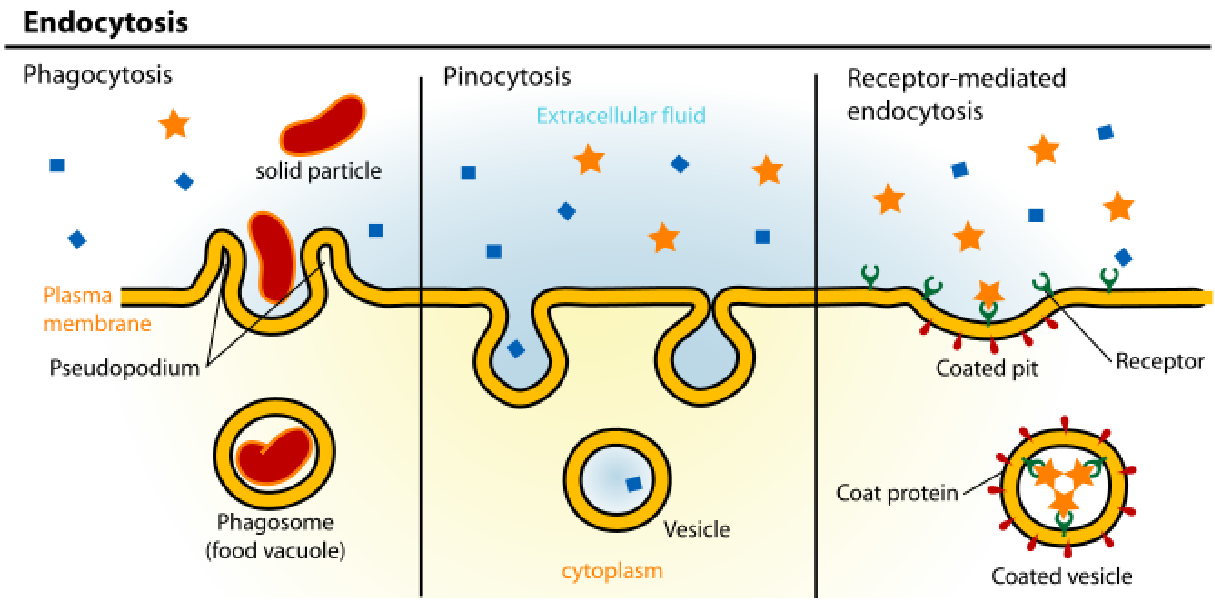
This phagocytic vesicle is subsequently fused with a lysosome containing hydrolytic enzymes to digest the solid contents**.** Cells that specialize in this process are termed phagocytes e.g. white blood cells engulfing bacteria by phagocytosis.

Pinocytosis

Pinocytosis is loosely termed as "Cell drinking". A small area of plasma membrane invaginates to form a narrow channel which extracellular fluid is taken up by cell and tiny fluid containing vesicles are formed into the interior of cells. e.g. human egg cell takes up nutrients from surrounding by pinocytosis

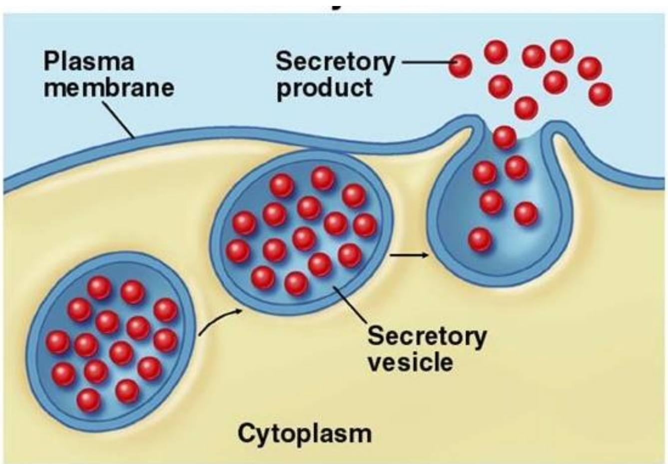
Receptor-mediated endocytosis

Specific receptor sites (proteins) are embedded in membranes that are exposed to the extracellular fluid. The receptor proteins are usually clustered in regions of the membrane called coated pits. Receptor-mediator endocytosis helps cell to acquire bulk quantities of specific substances even though they may not be in very high concentration in the extracellular fluid. e.g. Human cells use the process to take in cholesterol for use in the synthesis of membranes and as a precursor for the synthesis of other steroids.



Exocytosis

Exocytosis is the secretion of macromolecules (waste materials, undigested remains or useful products) by the fusion of vesicles with the plasma membrane.



Process

A transport vesicle that has budded from the Golgi apparatus moves along the fibers of the cytoskeleton to the plasma membrane. When the phospholipid bilayer of the transport vesicle comes into contact with the phospholipid bilayer of the plasma membrane, lipid molecules begin to rearrange themselves so that the two membranes fuse. Materials in the secretary vesicle are then released to the outside of the cell. Exocytosis is often used for the export of manufactured products. Common in cells of the stomach and intestine that release enzymes and mucus. e.g. pancreas – Hormone insulin is manufactured and secreted directly into blood by exocytosis. Neurones – exocytosis releases acetylcholine that stimulates other neurones/ muscle cells.