Transport across the Cell Membrane

In cellular biology, membrane transport refers to the collection of mechanisms that regulate the passage of solutes such as ions and small molecules through biological membranes, which are lipid bilayers that contain proteins embedded in them.

Transport across the Cell Membrane

One of the great wonders of the cell membrane is its ability to regulate the concentration of substances inside the cell. These substances include ions such as Ca^{++}, Na^{+}, K^{+}, and $Cl^{–}$; nutrients including sugars, fatty acids, and amino acids;

and waste products, particularly carbon dioxide (CO_2), which must leave the cell. The membrane's lipid bilayer structure provides the first level of control. The phospholipids are tightly packed together, and the membrane has a hydrophobic interior. This structure causes the membrane to be selectively permeable. It lets some substances pass through rapidly and some substances pass through more slowly, but prevent other substances passing through it at all.

. In the case of the cell membrane, only relatively small, nonpolar materials can move through the lipid bilayer (remember, the lipid tails of the membrane are nonpolar). Some examples of these are other lipids, oxygen and carbon dioxide gases, and alcohol. However, water-soluble materials—like glucose, amino acids, and electrolytes—need some assistance to cross the membrane because they are repelled by the hydrophobic tails of the phospholipid bilayer.

All substances that move through the membrane do so by one of two general methods, which are categorized based on whether or not energy is required. ***Passive transport*** is the movement of substances across the membrane without the expenditure of cellular energy. In contrast, ***active transport*** is the movement of substances across the membrane using energy from adenosine triphosphate (ATP).

*PASSIVE TRANSPORT or DIFFUSION:

The molecules move down a concentration gradient. Molecules have kinetic energy, which makes them move about randomly. As a result of diffusion molecules reach an equilibrium where they are evenly spread out. Diffusion is a PASSIVE process which means no energy is used to make the molecules move, they have a natural kinetic energy.

Diffusion is important to cells because it allows them to gain the useful substances they require to obtain energy and grow, and lets them get rid of waste products.

Three common types of passive transport include **simple diffusion, osmosis,** and **facilitated diffusion.**

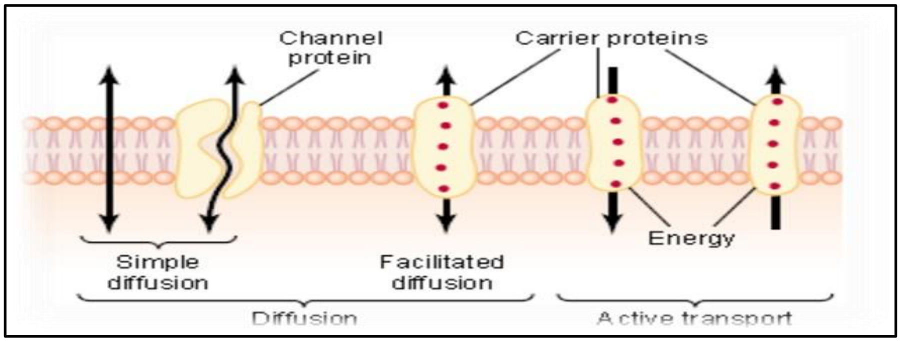
Simple Diffusion is the movement of particles from an area of higher concentration to an area of lower concentration.

Whenever a substance exists in greater concentration on one side of a semipermeable membrane, such as the plasma membrane, any substance that can move down its concentration gradient across the membrane will do so.

It is further devided into:

1- Simple diffusion through lipid layer

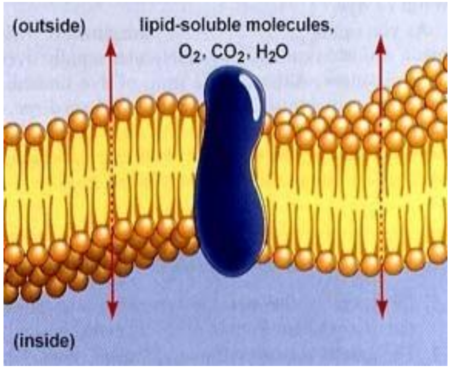
2- Simple diffusion through protein layer
3- Facilitated or carrier-mediated diffusion



Simple Diffusion through Lipid Bilayer

Lipid layer of the cell membrane is permiable to lipid soluble substances like oxygen, carbon dioxide and alcohol.
The diffusion through lipid layer is directly proportional to the solubility.

1. Oxygen – Non-polar so diffuses very quickly.
2. Carbon dioxide – non Polar but very small so diffuses quickly.
3. Water – Polar but also very small so diffuses quickly.



Consider substances that can easily diffuse through the lipid bilayer of the cell membrane, such as the gases oxygen (O_2) and CO_2. O_2 generally diffuses into cells because it is more concentrated outside of them, and CO_2 typically diffuses out of cells because it is more concentrated inside of them. Neither of these examples requires any energy on the part of the cell, and therefore they use passive transport to move across the membrane. Because cells rapidly use up oxygen during metabolism, there is typically a lower concentration of O_2 inside the cell than outside. As a result, oxygen will diffuse from the interstitial fluid directly through the lipid bilayer of the membrane and into the cytoplasm within the cell. On the other hand, because cells produce CO_2 as a byproduct of metabolism, CO_2 concentrations rise within the cytoplasm; therefore, CO_2 will move from the cell through the lipid bilayer and into the interstitial fluid, where its concentration is lower. This mechanism of molecules spreading from where they are more concentrated to where they are less concentration is a form of passive transport called simple diffusion (Figure 3.15).

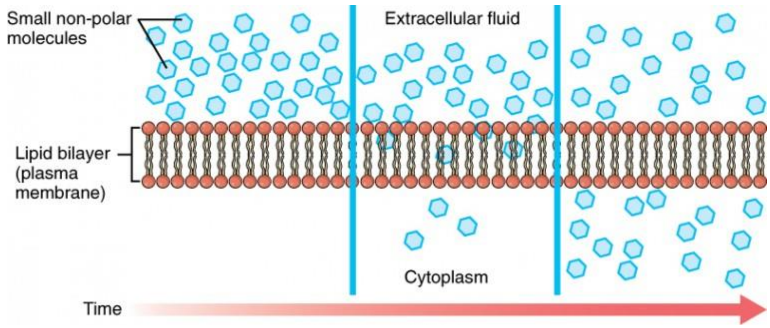


Figure 3.15. Simple Diffusion across the Cell (Plasma) Membrane

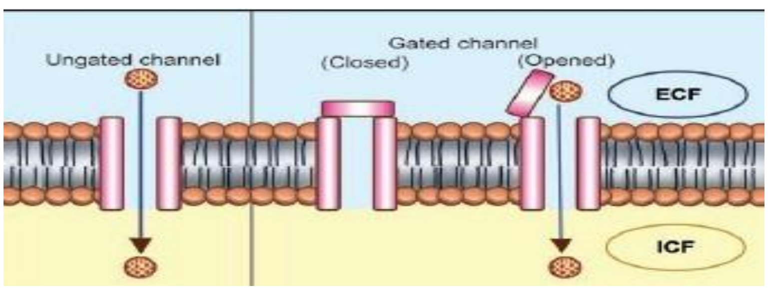
The structure of the lipid bilayer allows only small, non-polar substances such as oxygen and carbon dioxide to pass through the cell membrane, down their concentration gradient, by simple diffusion.

Simple Diffusion through Protein Layer

Proteins form the channels for diffusion of substances which are water soluble:

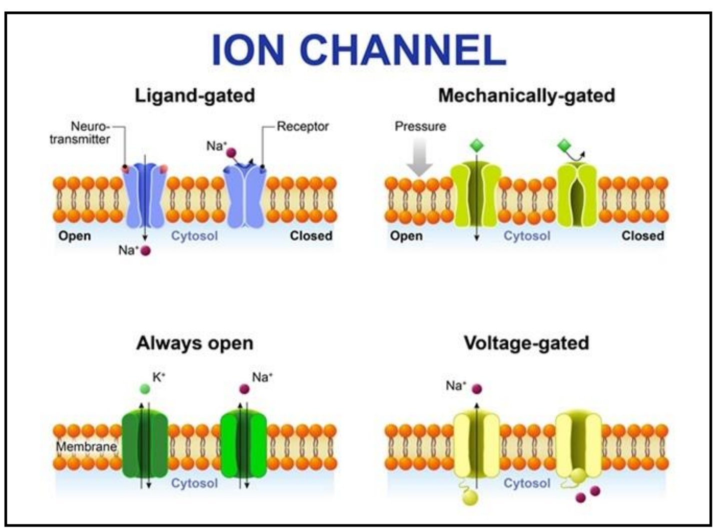
-Some channels are continuously open are called Ungated channels.

-Some channels are always closed and are called Gated channels.



Gated channels: These are further devided into:

1- Voltage-gated channels.
2- ligand-gated channels.
3- mechanically gated channels.



Osmosis is the diffusion of water through a semipermeable membrane (Figure 3.16). Water can move freely across the cell membrane of all cells, either through protein channels or by slipping between the lipid tails of the membrane itself. However, it is concentration of solutes within the water that determine whether or not water will be moving into the cell, out of the cell, or both.

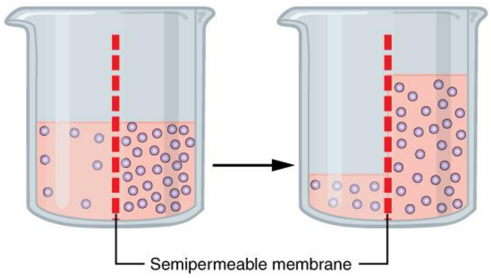


Figure 3.16. Osmosis

Osmosis is the diffusion of water through a semipermeable membrane down its concentration gradient. If a membrane is permeable to water, though not to a solute, water will equalize its own concentration by diffusing to the side of lower water concentration (and thus the side of higher solute concentration). In the beaker on the left, the solution on the right side of the membrane is hypertonic.

Solutes within a solution create osmotic pressure, a pressure that pulls water. Osmosis occurs when there is an imbalance of solutes outside of a cell versus inside the cell. The more solute a solution contains, the greater the osmotic pressure that solution will have. A solution that has a higher concentration of solutes than another solution is said to be *hypertonic.* Water molecules tend to diffuse into a hypertonic solution because the higher osmotic pressure pulls water (Figure 3.17). If a cell is placed in a hypertonic solution, the cells will shrivel or *crenate* as water leaves the cell via osmosis. In contrast, a solution that has a lower concentration of solutes than another solution is said to be *hypotonic.* Cells in a hypotonic solution will take on too much water and swell, with the risk of eventually bursting, a process called *lysis*. A critical aspect of homeostasis in living things is to create an internal environment in which all of the body's cells are in an isotonic solution, an environment in which two solutions have the same concentration of solutes (equal osmotic pressure). When cells and their extracellular environments are isotonic, the concentration of water molecules is the same outside and inside the cells, so water flows both in and out and the cells maintain their normal shape (and function). Various organ systems, particularly the kidneys, work to maintain this homeostasis.

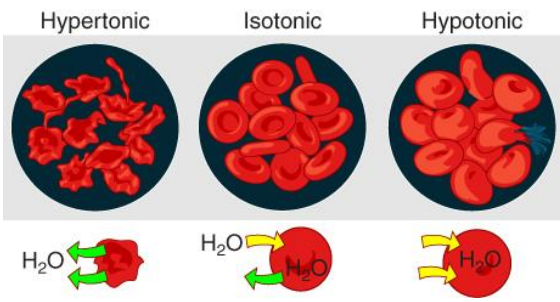


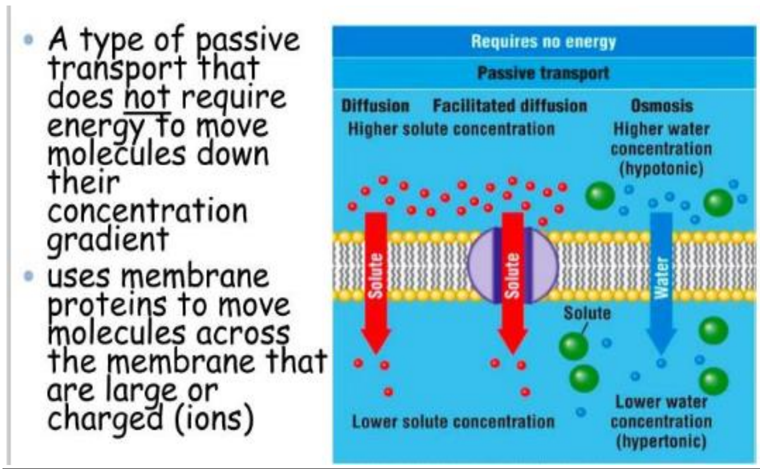
Figure 3.17. Concentration of Solutions

A hypertonic solution has a solute concentration higher than another solution. An isotonic solution has a solute concentration equal to another solution. A hypotonic solution has a solute concentration lower than another solution.

Facilitated Diffusion:

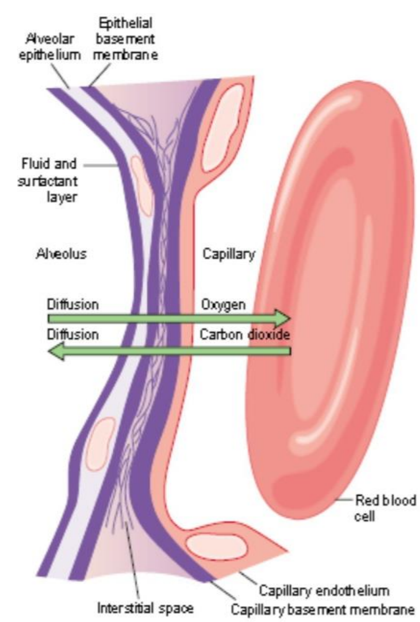
Is the diffusion process used for those substances that cannot cross the lipid bilayer due to their size and/or polarity (Figure 3.18). A common example of facilitated diffusion is the movement of glucose into the cell, where it is used to make ATP. Although glucose can be more concentrated outside of a cell, it cannot cross the lipid bilayer via simple diffusion because it is both large and polar. To resolve this, a specialized carrier protein called the glucose transporter will transfer glucose molecules into the cell to facilitate its inward diffusion. There are many other solutes that must undergo facilitated diffusion to move into a cell, such as amino acids, or to move out of a cell, such as wastes. Because facilitated diffusion is a passive process, it does not require energy expenditure by the cell.

Movement of molecules is still PASSIVE just like ordinary diffusion, the only difference is, the molecules go through a protein channel instead of passing between the phospholipids.



FACTORS THAT DETERMINE THE RATE OF DIFFUSION:

1. The steepness of the concentration gradient.
2. Temperature.
3. Solubility of the substance.
4. Permeability of the cell membrane.
5. Thickness of the cell membrane
6. Size of the molecule.
7. Size of the ions.
8. Charge of the ions.



SPECIAL TYPES OF PASSIVE TRANSPORT

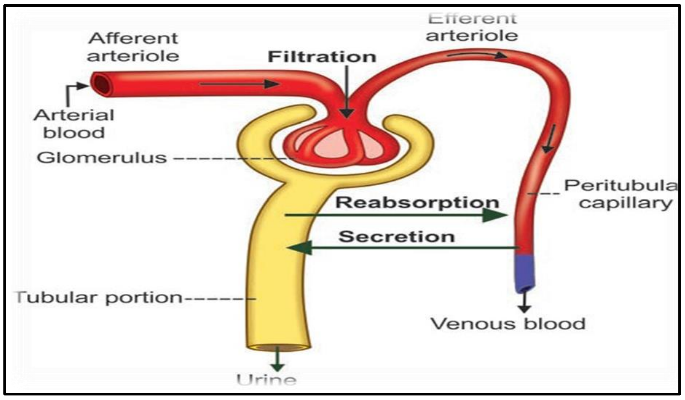
In adddition to diffusion,there are some special types of passive transport,i.e: Bulk flow, Filtration.

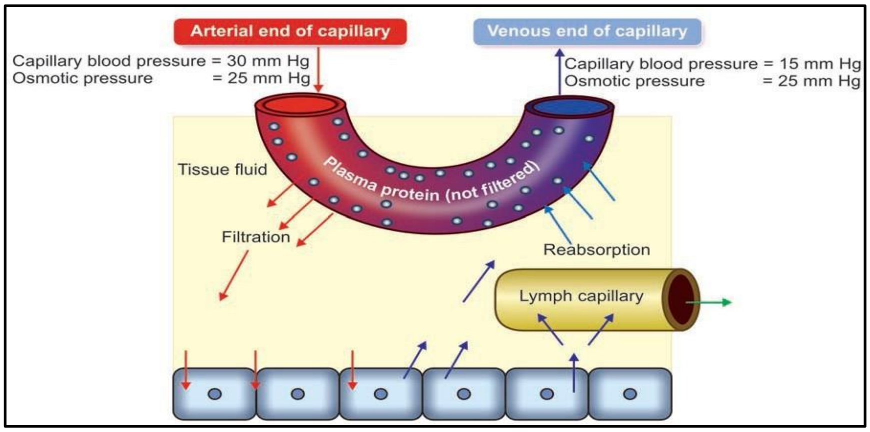
BULK FLOW:

Bulk flow is the movement of large quantity of substances from a region of high pressure to the region of low pressure.
It is due to the pressure gradient of the substances across the cell membrane

FILTRATION:

Movement of water and solutes from an area of high hydrostatic pressure to an area of low hydrostatic pressure is called Filtration.





Cells can gain or lose water by the process of osmosis. This depends on the water concentration of the solution inside the cell compared to water concentration of the solution outside the cell.

Solutions with a high concentration of solute molecules, such as sugars or salts, have a low concentration of water molecules and vice versa.

*ACTIVE TRANSPORT:

Active Transport

For all of the transport methods described above, the cell expends no energy. Membrane proteins that aid in the passive transport of substances do so without the use of ATP. During active transport, ATP is required to move a substance across a membrane, often with the help of protein carriers, and usually *against* its concentration gradient. One of the most common types of active transport involves proteins that serve as pumps. Energy from ATP is required for these membrane proteins to transport substances—molecules or ions—across the membrane, usually against their concentration gradients (from an area of low concentration to an area of high concentration). The *sodium-potassium pump*, which is also called N^+/K^+ ATPase, transports sodium out of a cell while moving potassium into the cell. The Na^+/K^+ pump is an important ion pump found in the membranes of many types of cells. These pumps are particularly abundant in nerve cells, which are constantly pumping out sodium ions and pulling in potassium ions to maintain an electrical gradient across their cell membranes. An *electrical gradient* is a difference in electrical charge across a space. In the case of nerve cells, for example, the electrical gradient exists between the inside and outside of the cell, with the inside being negatively-charged (at around -70 mV) relative to the outside. The negative electrical gradient is maintained because each Na^+/K^+ pump moves three Na^+ ions out of the cell and two K^+ ions into the cell for each ATP molecule that is used (Figure 3.19). This process is so important for nerve cells that it accounts for the majority of their ATP usage.

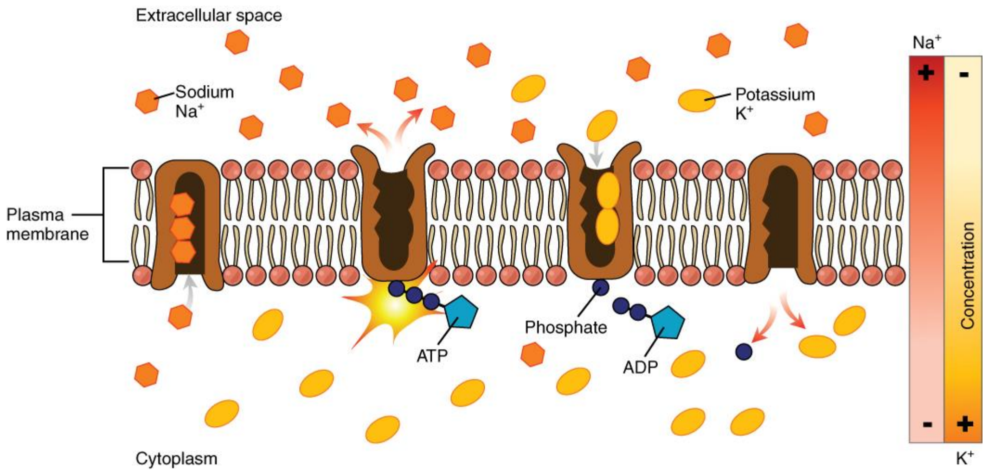
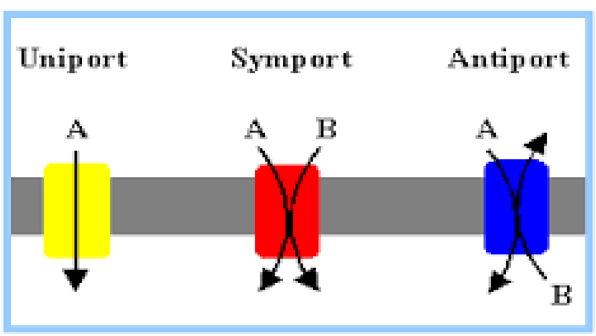


Figure 3.19. Sodium-Potassium Pump

The sodium-potassium pump is found in many cell (plasma) membranes. Powered by ATP, the pump moves sodium and potassium ions in opposite directions, each against its concentration gradient. In a single cycle of the pump, three sodium ions are extruded from and two potassium ions are imported into the cell.

Carrier Proteins of Active Transport

There are several types of membrane transport proteins:-
uniports and **cotransport** **(Symport & Antiport)**.
Uniports can move solutes from one side to another, change the position of the proteins. Cotransport systems can simultaneously sending two solutes across the lipid bilayer. Solutes are sent in the same direction or opposite directions Transport proteins does not need to be acts natural direction.



Mechanism of active transport

When a substance to be transported across the cell membrane comes near the cell, it combines with the carrier protein of the cell membrane and forms substance-protein complex. This complex moves towards the inner surface of the cell membrane. Now, the substance is released from the carrier proteins. The same carrier protein moves back to the outer surface of the cell membrane to transport another molecule of the substance.

Substances transported by active transport:

Substances, which are transported actively, are in ionic form are sodium, potassium, calcium, hydrogen, chloride and iodide while Substances in non-ionic form are glucose, amino acids and urea.

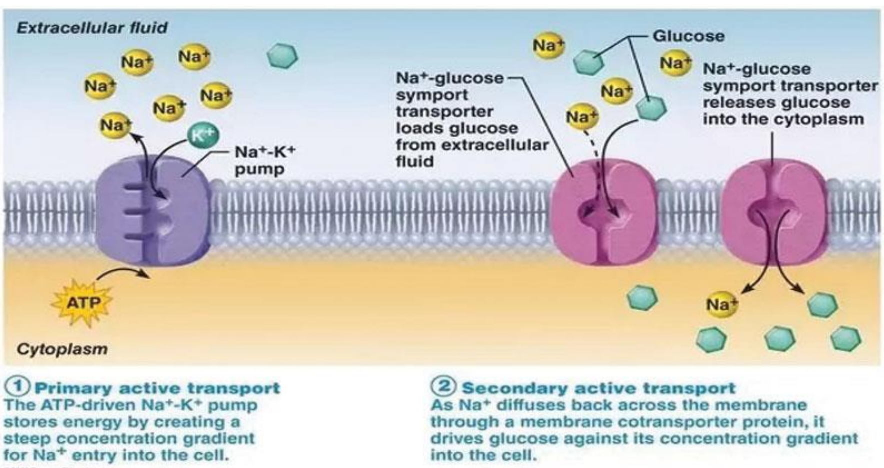
TYPES ACTIVE TRANSPORT:

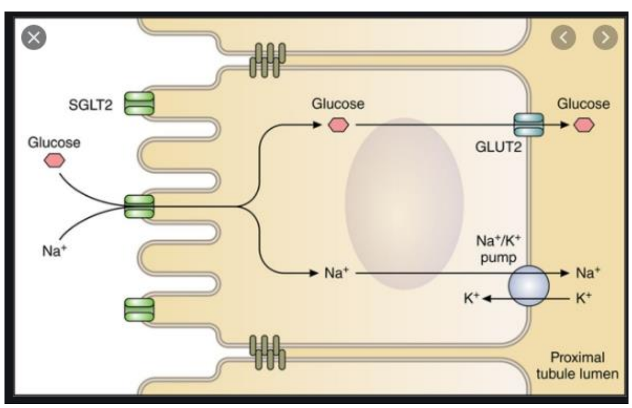
A- Primary active transport

In **primary active transport**, the energy is derived directly from the breakdown of ATP to **transport** molecules across a membrane against their concentration gradient.
Therefore, all groups of ATP-powered pumps contain one or more binding sites for ATP, which are always present on the cytosolic face of the membrane.
Primary active transport is also called direct active transport or uniport. Substances that are transported across the cell membrane by primary active transport include metal ions, such as Na+, K+, Mg2+, and Ca2+.
Most of the enzymes that perform this type of transport are transmembrane ATPases.

B- Secondary active transport

In the **secondary active transport**, the energy is derived secondarily from energy that has been stored in the form of ionic concentration **differences** between the two sides of a membrane.
Secondary active transport is the transport of a substance with sodium ion, by means of a common carrier protein. When sodium is transported by a carrier protein, another substance is also transported by the same protein simultaneously, either in the same direction (of sodium movement) or in the opposite direction. Thus, the transport of sodium is coupled with transport of another substance.
One molecule helps set up the needed gradient to allow for the movement of many chemicals into and out of the cell. The energy derived from the pumping of protons across a cell membrane is frequently used as the energy source in secondary active transport.





In humans, sodium (Na+) is a c-transported ion across the plasma membrane, whose electrochemical gradient is then used to power the active transport of a second ion or molecule against its gradient.

Importance of Active Transport:-

This process is vital for living organisms and is important for the following reasons:
(1) Absorption of most nutrients from the intestine
(2) Rapid and selective absorption of nutrients by cells
(3) Maintaining a membrane potential
(4) Maintaining water and ionic balance between cells and extracellular fluids.

SPECIAL TYPES OF ACTIVE TRANSPORT

Membrane transport of Macromolecules can divide into

1. Endocytosis
2. Exocytosis
3. Transcytosis.

- Endocytosis is the process of capturing a substance or particle from outside the cell by engulfing it with the cell membrane, and bringing it into the cell.

- There are three types of endocytosis:

- Phagocytosis ("cellular eating"): A cell engulfs a particle in a vacuole, the vacuole fuses with a lysosome to digest the particle Larger bacteria, larger antigens and other larger foreign bodies are taken inside the cell by means of phagocytosis. Only few cells in the body like neutrophils, monocytes and the tissue macrophages show phagocytosis. Among these cells, the macrophages are the largest phagocytic cells.

- Pinocytosis ("cellular drinking"): Molecules are taken up when extracellular fluid is "gulped" into tiny vesicles

- Receptor-mediated endocytosis: is the transport of macromolecules with the help of a receptor protein. Surface of cell membrane has some pits which contain a receptor protein called **clathrin.** Binding of ligands to receptors triggers vesicle formation, A **ligand** is any molecule that binds specifically to a receptor site of another molecule

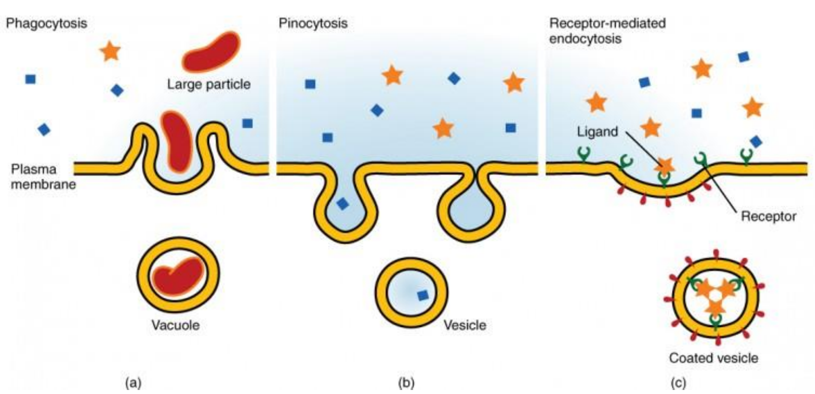


Figure 3.20. Three Forms of Endocytosis

Endocytosis is a form of active transport in which a cell envelopes extracellular materials using its cell membrane. (a) In phagocytosis, the cell takes in a large particle. (b) In pinocytosis, the cell takes in small particles in fluid. (c) In contrast, receptor-mediated endocytosis is quite selective. When external receptors bind a specific ligand, the cell responds by endocytosing the ligand.

In contrast with endocytosis, ***exocytosis*** (taking "out of the cell") is the process of a cell exporting material using vesicular transport (Figure 3.21). Many cells manufacture substances that must be secreted, like a factory manufacturing a product for export. These substances are typically packaged into membrane-bound vesicles within the cell. When the vesicle membrane fuses with the cell membrane, the vesicle releases it contents into the interstitial fluid. The vesicle membrane then becomes part of the cell membrane. Cells of the stomach and pancreas produce and secrete digestive enzymes through exocytosis (Figure 3.22). Endocrine cells produce and secrete hormones that are sent throughout the body, and certain immune cells produce and secrete large amounts of histamine, a chemical important for immune responses.

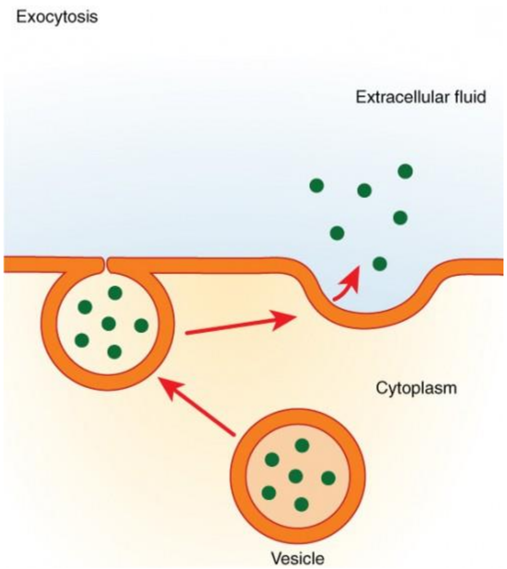


Figure 3.21. Exocytosis

Exocytosis is much like endocytosis in reverse. Material destined for export is packaged into a vesicle inside the cell. The membrane of the vesicle fuses with the cell membrane, and the contents are released into the extracellular space.

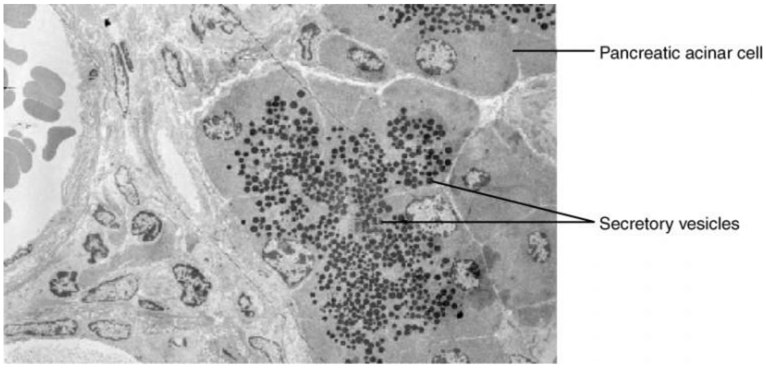


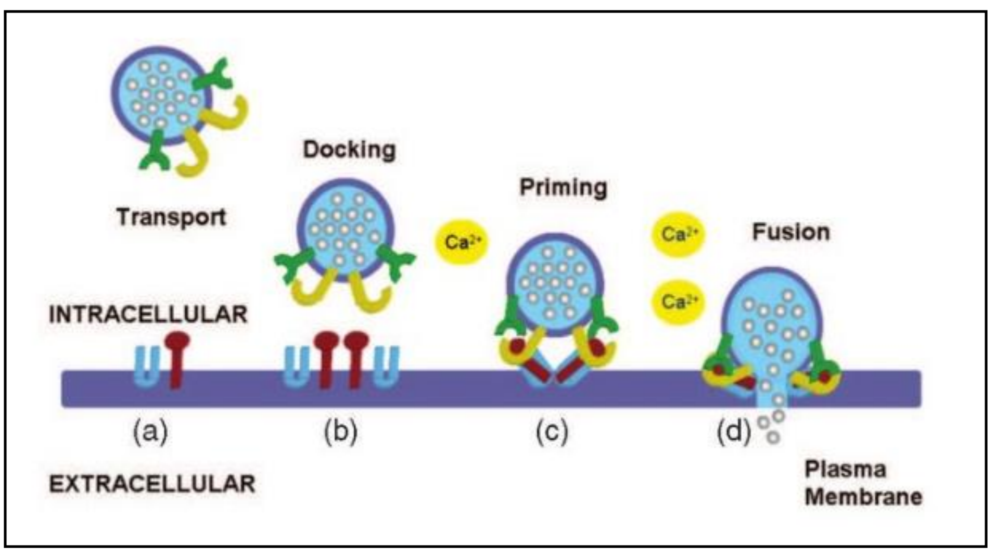
Figure 3.22. Pancreatic Cells' Enzyme Products

The pancreatic acinar cells produce and secrete many enzymes that digest food. The tiny black granules in this electron micrograph are secretory vesicles filled with enzymes that will be exported from the cells via exocytosis. LM × 2900. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)

Generally, exocytosis involves five steps for the expulsion of the intracellular substance.

1- Vesicle trafficking: It is the first step where the vesicles are transported to the cell membrane along with the microtubules of the cytoskeleton. Motor proteins, kinesins, dyneins and myosins mediate the movement of secretory vesicles.
2-Tethering: Once the vesicle reaches the cell membrane, it tends to contact with the cell membrane.
3-Docking: It is the third step, which involves the attachment between the cell membrane and the vesicle membrane. During this step, the phospholipid bilayer of both the membranes begins to merge.
4-Priming: It is the step that only occurs in the regulated exocytosis. Priming involves specific modifications in the molecules of the cell membrane, for the signalling process to stimulate exocytosis.
5-Fusion: Two types of fusion occur in exocytosis.

- **Complete fusion**: Here, the vesicle membrane entirely incorporates with the cell membrane. It makes the use of ATP that helps in the separation and fusion of the phospholipid membrane. The fusion results in a fusion pore that expels the content out of the cell membrane.
- **Kiss and run fusion**: It's the temporary fusion of the vesicle with the cell membrane and expels the contents out of the fusion pore. After the release of substances to the extracellular environment, the vesicle detaches from the bilayer cell membrane.



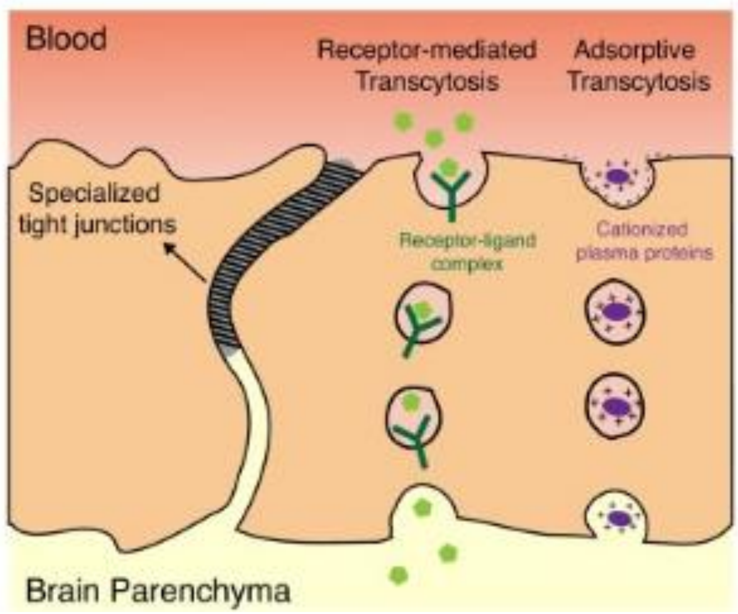
TRANSCYTOSIS:

Trans-cytosis is a transport mechanism in which an extracellular macromolecule enters through one side of a cell, migrates across cytoplasm of the cell and exits through the other side.

MECHANISM OF TRANSCYTOSIS

Cell encloses the extracellular substance by invagination of the cell membrane to form a vesicle. Vesicle then moves across the cell and thrown out through opposite cell membrane by means of exocytosis.

Example of this type of transport is the movement of proteins from capillary blood into interstitial fluid across the endothelial cells of the capillary. Many pathogens like human immuno deficiency virus (HIV) are also transported by this mechanism.



ACTIVE TRANSPORT VS FACILITATED DIFFUSION

Active transport mechanism is different from facilitated diffusion by two ways:

1. Carrier protein of active transport needs energy, whereas the carrier protein of facilitated diffusion does not need energy
2. In active transport, the substances are transported against the concentration or electrical or electrochemical gradient. In facilitated diffusion, the substances are transported along the concentration or electrical or electrochemical gradient.

Learning Objectives:

- Compare and contrast passive and active transport
- Describe the process of diffusion, osmosis, and facilitated diffusion
- Describe the process of the sodium/potassium pump and endo/exocytosis
- Describe the three types of endocytosis