Chapter 4
Cell Membranes

4.1. The Ultrastructure of Animal Cells

This schematic represents an idealized animal cell, e.g., a liver cell.

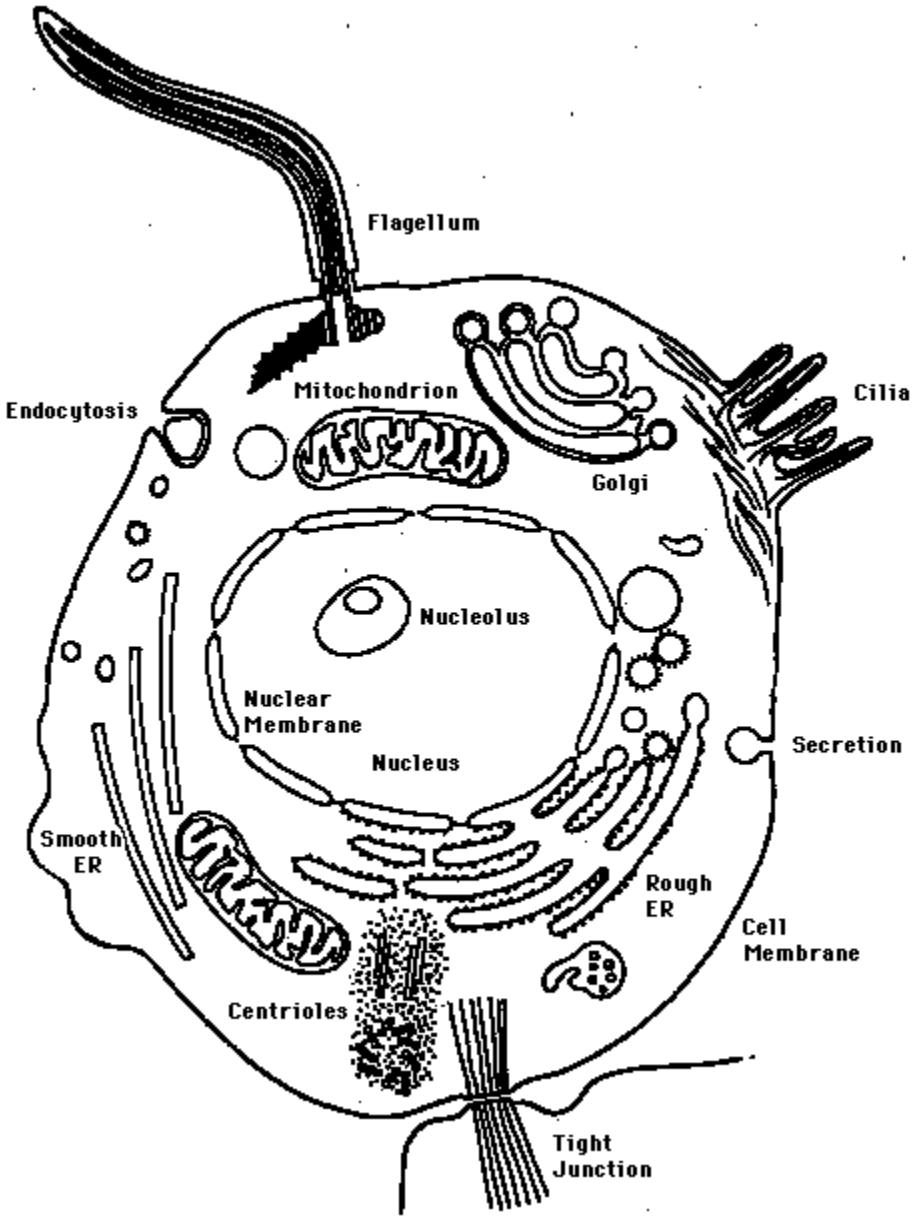


Fig.4.1. Ultrastructure of Animal Cells

4.2. Cell Membranes

One universal feature of all cells is an outer limiting membrane called the **plasma membrane**. In addition, all **eukaryotic cells** contain elaborate systems of **internal**

membranes which set up various **membrane-enclosed compartments** within the cell. Cell membranes are built from **lipids** and **proteins**.

4.2.1. The Plasma Membrane

The plasma membrane serves as the interface between the machinery in the interior of the cell and the **extracellular fluid** (ECF) that bathes all cells. The lipids in the plasma membrane are chiefly phospholipids like **phosphatidyl ethanolamine** and **cholesterol**. Phospholipids are **amphiphilic** with the hydrocarbon tail of the molecule being **hydrophobic**; its polar head **hydrophilic**. As the plasma membrane faces watery solutions on both sides, its phospholipids accommodate this by forming a **phospholipid bilayer** with the hydrophobic tails facing each other.

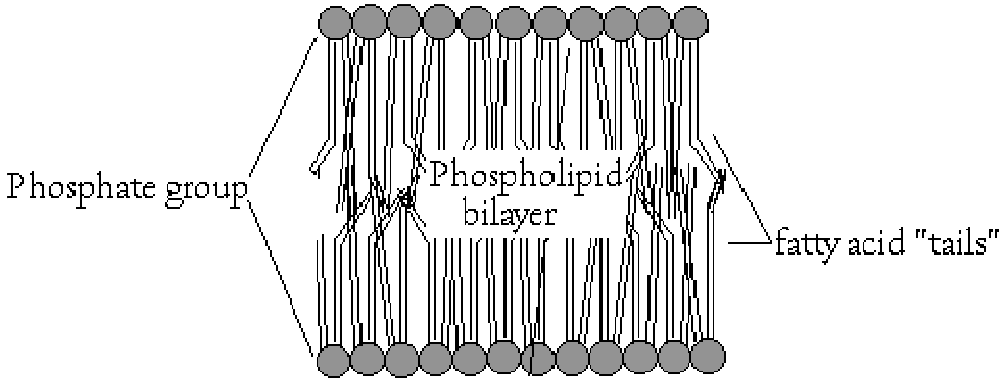


Fig.4.2a. Phospholipid Bilayer of Plasma Membrane

(a) Integral Membrane Proteins

Many of the proteins associated with the plasma membrane are tightly bound to it. Some are attached to lipids in the bilayer. In others - the **transmembrane proteins** - the polypeptide chain actually traverses the lipid bilayer. Fig.4.2b shows a transmembrane protein that passes through the bilayer. All **G-protein**-coupled receptors (e.g., receptors of **peptide hormones**, each span the plasma membrane 7 times.

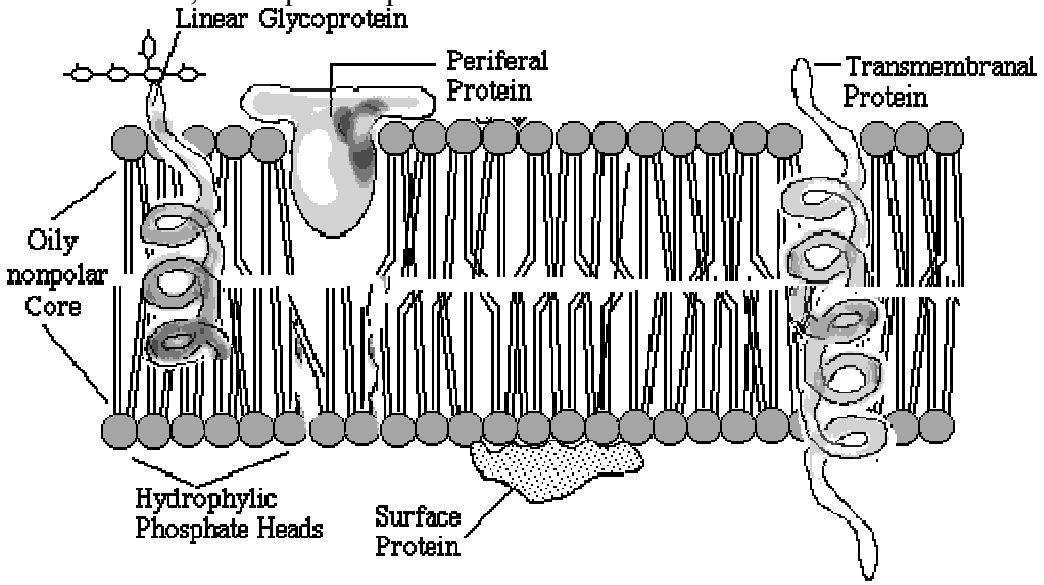


Fig.4.2b. Membrane Proteins

In all these cases, the portion within the lipid bilayer consists primarily of hydrophobic amino acids. These are usually arranged in an **alpha helix** so that the polar -C=O and -NH groups at the **peptide bonds** can interact with each other rather than with their hydrophobic surroundings.

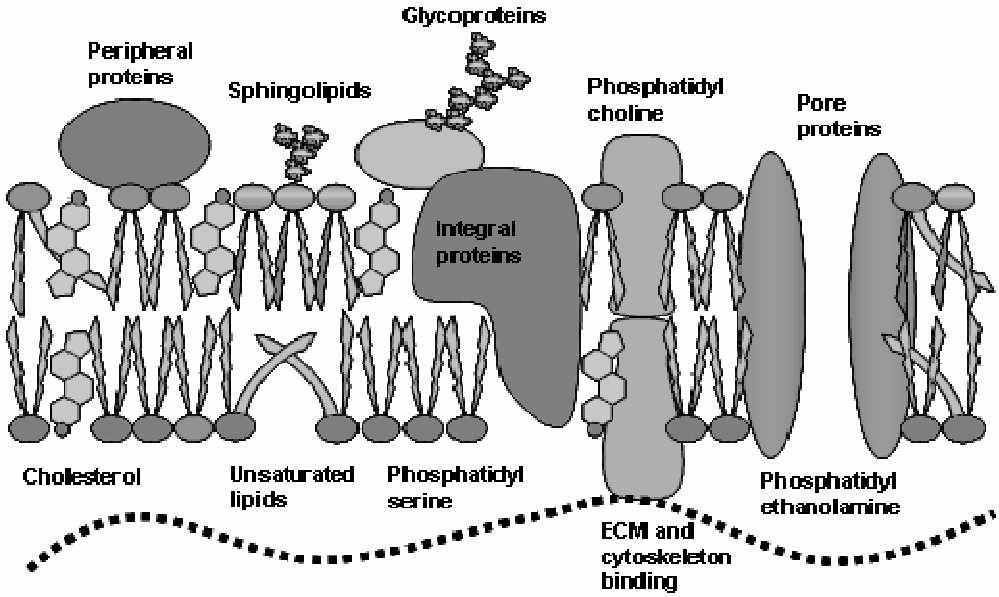
Those portions of the polypeptide that project out from the bilayer tend to have a high percentage of **hydrophilic amino acids**. Furthermore, those that project into the aqueous surroundings of the cell are usually **glycoproteins**, with many hydrophilic sugar residues attached to the part of the polypeptide exposed at the surface of the cell. Some transmembrane proteins that span the bilayer several times form a **hydrophilic channel** through which certain **ions** and **molecules** can enter (or leave) the cell.

(b) Peripheral Membrane Proteins

These are more loosely associated with the membrane. They are usually attached **noncovalently** to the protruding portions of integral membrane proteins.

(c) Membrane Proteins are often Restricted in their movements

A lipid bilayer is really a film of oil. Thus we might expect that structures immersed in it would be relatively free to float about. For some membrane proteins, this is the case. Our understanding of the plasma membrane is based on the **Fluid Mosaic Model** by **Singer-Nicholson** (1972*)*which refers to the fluidlike qualities of the **phospholipid** sheets and the dynamic behaviour of proteins that seem to float in or on a "sea" of phospholipids. The fluid mosaic model pictures the membrane as a phospholipid bilayer with many proteins, some integral to the membrane, others attached more loosely. Note the many other components, such as cholesterol; and the attachement sites for the extracellular environment (*via* glycoproteins) and intracellular cytoskeleton.



For others proteins, however, their mobility is limited: Some of the proteins exposed at the interior face of the plasma membrane are tethered to cytoskeletal elements like actin microfilaments. Some proteins are the exterior face of the plasma membrane are anchored to components of the **extracellular matrix** like **collagen**. Integral membrane

proteins cannot pass through the **tight junctions** found between some kinds of cells (e.g., epithelial cells).

4.2.2. Transport across Cell Membranes

All cells acquire the molecules and ions they need from their surrounding **extracellular fluid** (**ECF**). There is an unceasing traffic of **molecules** and **ions** in and out of the cell through its **plasma membrane**. Examples: glucose, Na^+, Ca^{2+} . In eukaryotic cells, there is also **transport in** and **out** of membrane-bounded intracellular compartments such as the nucleus, **endoplasmic reticulum**, and **mitochondria**. Examples: proteins, mRNA, Ca^{2+}, ATP

(a) Two Problems to be Considered

(i) Relative Concentrations

Molecules and ions move spontaneously down their concentration gradient (i.e., from a region of higher to a region of lower concentration) by **diffusion**. Molecules and ions can be moved **against** their concentration gradient, but this process, called **active transport**, requires the expenditure of energy (usually from ATP).

(ii) Lipid Bilayers are Impermeable to Most Essential Molecules and Ions

The lipid bilayer is permeable to **water** molecules and a few other small, uncharged, molecules like oxygen (O_2) and carbon dioxide (CO_2). These diffuse freely in and out of the cell. The diffusion of water through the plasma membrane is of such importance to the cell that it is given a special name **osmosis**. Lipid bilayers are **not** permeable to **ions** such as K^+, Na^+, Ca^{2+} (called **cations** because when subjected to an electric field they migrate toward the cathode [the negatively-charged electrode]) Cl^-, HCO_3^- (called **anions** because they migrate toward the anode [the positively-charged electrode]) small **hydrophilic molecules** like glucose **macromolecules** like proteins and RNA.

(b) Solving these Problems

Mechanisms by which cells solve the problem of transporting ions and small molecules across their membranes:

(i) Facilitated Diffusion: Transmembrane proteins create a water-filled pore through which ions and some small hydrophilic molecules can pass by diffusion. The channels can be opened (or closed) according to the needs of the cell.

(ii) Active Transport: Transmembrane proteins, called transporters, use the energy of ATP to force ions or small molecules through the membrane **against** their concentration gradient.

4.2.3. Facilitated Diffusion of Ions

Facilitated diffusion of ions takes place through proteins, or assemblies of proteins, embedded in the plasma membrane. These transmembrane proteins form a water-filled channel through which the ion can pass **down** its concentration gradient. The trans-membrane channels that permit facilitated diffusion can be opened or closed. They are said to be **"gated"**. Some types of gated ion channels:

- Ligand-gated
- Mechanically-gated
- Voltage-gated
- Light-gated

(a) Ligand-Gated Ion Channels

Many ion channels open or close in response to binding a small Signalling molecule or **"ligand"**. Some ion channels are gated by extracellular ligands; some by intracellular ligands. In both cases, the ligand is **not** the substance that is transported when the channel opens.

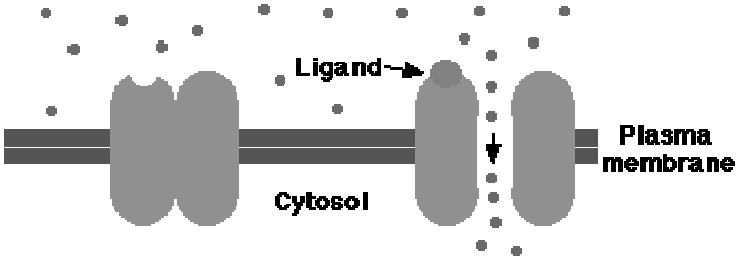


Fig.4.3. Ligand-Gated Ion Diffusion

(i) External Ligands

External ligands (shown here in green) bind to a site on the extracellular side of the channel. **Examples:**

- **Acetylcholine** (**ACh**). The binding of the neurotransmitter acetylcholine at certain synapses opens channels that admit Na^+ and initiate a nerve impulse or muscle contraction.
- **Gamma amino butyric acid** (**GABA**). Binding of GABA at certain synapses — designated $GABA_A$ — in the central nervous system admits Cl^- ions into the cell and inhibits the creation of a nerve impulse.

(ii) Internal Ligands

Internal ligands bind to a site on the channel protein exposed to the cytosol.

Examples:

- "Second messengers", like **cyclic AMP** (**cAMP**) and **cyclic GMP** (**cGMP**), regulate channels involved in the initiation of impulses in neurons responding to odours and light respectively.
- **ATP** is needed to open the channel that allows chloride (Cl^-) and bicarbonate (HCO_3^-) ions out of the cell. This channel is defective in patients with **cystic fibrosis**. Although the energy liberated by the hydrolysis of ATP is needed to open the channel, this is **not** an example of active transport; the ions diffuse through the open channel following their concentration gradient.

(b) Mechanically-Gated Ion Channels

Examples:

- Sound waves bending the cilia-like projections on the hair cells of the inner ear open up ion channels leading to the creation of nerve impulses that the brain interprets as sound.
- Mechanical deformation of the cells of stretch receptors opens ion channels leading to the creation of nerve impulses.

(c) Voltage-Gated Ion Channels

In so-called "excitable" cells like **neurons** and **muscle cells**, some channels open or close in response to changes in the charge (measured in volts) across the plasma membrane.

Example: As an impulse passes down a neuron, the reduction in the voltage opens sodium channels in the adjacent portion of the membrane. This allows the influx of Na^+ into the neuron and thus the continuation of the nerve impulse.
Some 7000 sodium ions pass through each channel during the brief period (about 1 millisecond) that it remains open. This was learned by use of the patch clamp technique.

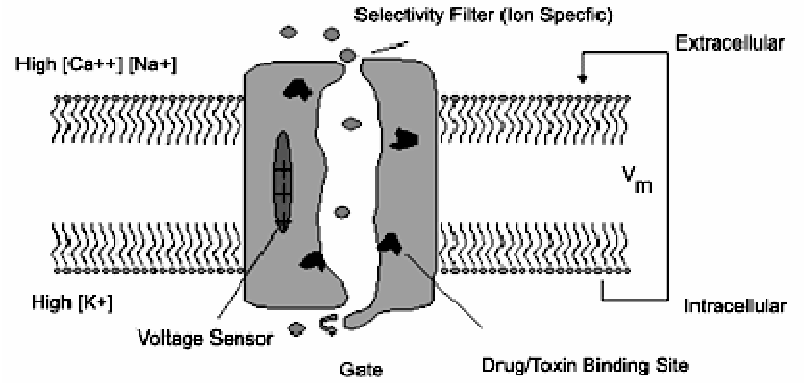


Fig.4.4. Voltage-Gated Ion Channels

4.2.4. Facilitated Diffusion of Molecules

Some small, hydrophilic organic molecules, like sugars, can pass through cell membranes by facilitated diffusion. Once again, the process requires transmembrane proteins. In some cases, these — like ion channels — form water-filled pores that enable the molecule to pass in (or out) of the membrane following its concentration gradient.

Example:

- **Maltoporin**. This **homotrimer** in the outer membrane of *E. coli* forms pores that allow the disaccharide maltose and a few related molecules to diffuse into the cell.
- The plasma membrane of human red blood cells contain transmembrane proteins that permit the diffusion of glucose from the blood into the cell.

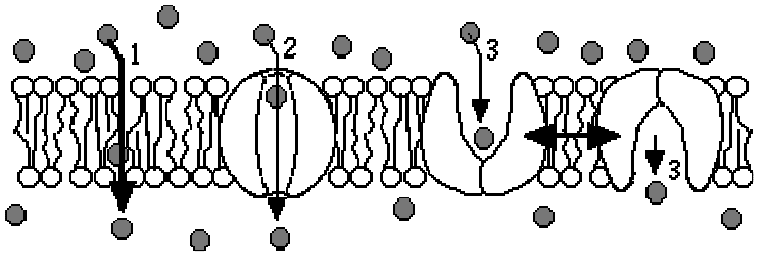


Fig.4.5. Facilitated Diffusion of Molecules

Note that in all cases of facilitated diffusion through channels, the channels are **selective**; that is, the structure of the protein admits only certain types of molecules through. Whether all cases of facilitated diffusion of small molecules use channels is yet to be proven. Perhaps some molecules are passed through the membrane by a conformational change in the shape of the transmembrane protein when it binds the molecule to be transported. In either case, the interaction between the molecule being transported and its transporter resembles in many ways the interaction between an enzyme and its substrate.

4.2.5. Active Transport

Active transport is the pumping of molecules or ions through a membrane **against** their concentration gradient. It requires a transmembrane protein (usually a complex of them) called a **transporter** and energy. The source of this energy is **ATP**.
The energy of ATP may be used directly or indirectly.

- **Direct Active Transport.** Some transporters bind ATP directly and use the energy of its hydrolysis to drive active transport.
- **Indirect Active Transport.** Other transporters use the energy already stored in the gradient of a directly-pumped **ion**. Direct active transport of the ion establishes a concentration gradient. When this is relieved by facilitated diffusion, the energy released can be harnessed to the pumping of some other ion or molecule.

(A) Direct Active Transport

(a) The Na^+/K^+ ATPase

The cytosol of animal cells contains a concentration of potassium ions (K^+) as much as 20 times higher than that in the extracellular fluid. Conversely, the extracellular fluid contains a concentration of sodium ions (Na^+) as much as 10 times greater than that within the cell. These concentration gradients are established by the active transport of both ions. And, in fact, the same transporter, called the Na^+/K^+ ATPase, does both jobs. It uses the energy from the hydrolysis of ATP to actively transport 3 Na^+ ions out of the cell for each 2 K^+ ions pumped into the cell. This accomplishes several vital functions:

- It helps establish a net charge across the plasma membrane with the interior of the cell being negatively charged with respect to the exterior. This **resting potential** prepares nerve and muscle cells for the propagation of action potentials leading to nerve impulses and muscle contraction.
- The accumulation of sodium ions outside of the cell draws water out of the cell and thus enables it to maintain osmotic balance (otherwise it would swell and burst from the inward diffusion of water).
- The gradient of sodium ions is harnessed to provide the energy to run several types of indirect pumps.

The crucial roles of the Na^+/K^+ ATPase are reflected in the fact that almost one-third of all the energy generated by the mitochondria in animal cells is used just to run this pump.

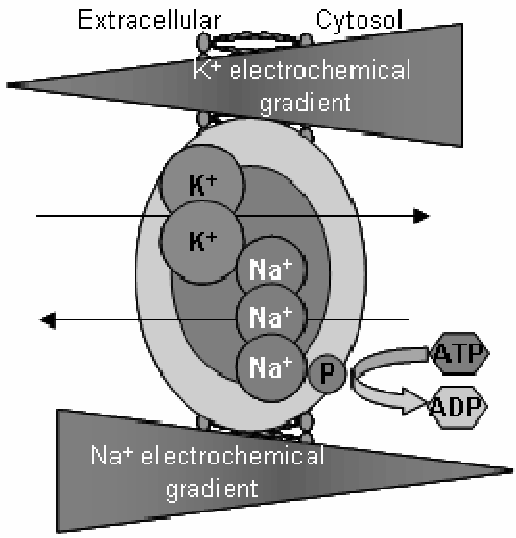


Fig.4.6a. The Na^+/K^+ ATPase

(b) The H^+/K^+ ATPase

The parietal cells of your stomach use this pump to secrete gastric juice. These cells transport protons (H^+) from a concentration of about 4 x 10^{-8} M within the cell to a concentration of about 0.15 M in the gastric juice (giving it a pH close to 1). Small wonder that parietal cells are stuffed with mitochondria and uses huge amounts of energy as they carry out this three-million fold concentration of protons.

(c) The Ca^{2+} ATPases

In resting skeletal muscle, there is a much higher concentration of calcium ions (Ca^{2+}) in the sarcoplasmic reticulum than in the cytosol. Activation of the muscle fibre allows some of this Ca^{2+} to pass by facilitated diffusion into the cytosol where it triggers contraction. After contraction, this Ca^{2+} is pumped back into the sarcoplasmic reticulum. This is done by a Ca^{2+} ATPase that uses the energy from each molecule of ATP to pump 2 Ca^{2+} ions. A Ca^{2+} ATPase is also located in the **plasma membrane** of all eukaryotic cells. It pumps Ca^{2+} out of the cell helping to maintain the ~10,000-fold concentration gradient of Ca^{2+} between the cytosol (~ 10^{-7}M) and the ECF (~ 10^{-3}M). Pumps are designated **P-type ion transporters** because they use the same basic mechanism: a conformational change in the proteins as they are reversibly phosphorylated by ATP. And all three pumps can be made to run backward. That is, if the pumped ions are allowed to diffuse back through the membrane complex, ATP can be synthesized from ADP and inorganic phosphate.

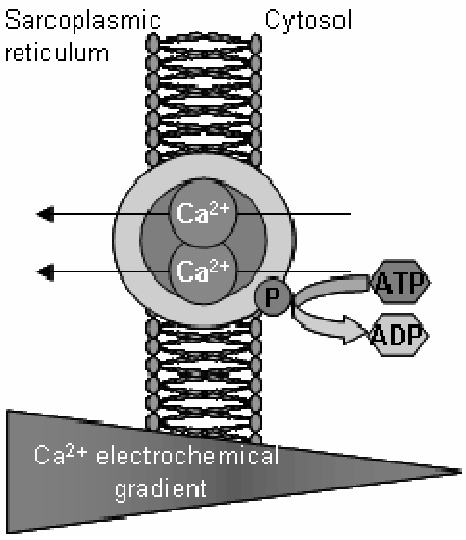


Fig.4.6b. The Ca^{2+} ATPases

(d) ABC Transporters

ABC ("**A**TP-**B**inding **C**assette") transporters are transmembrane proteins that expose a ligand-binding domain at one surface and a ATP-binding domain at the other surface. The ligand-binding domain is usually restricted to a single type of molecule.

The ATP bound to its domain provides the energy to pump the ligand across the membrane. The human genome contains 48 genes for ABC transporters. Some examples include:

- **CFTR** — the cystic fibrosis transmembrane conductance regulator

- **TAP**, the transporter associated with antigen processing.
- the transporter that liver cells use to pump the salts of bile acids out into the bile.
- ABC transporters that pump chemotherapeutic drugs out of cancer cells thus reducing their effectiveness.

ABC transporters must have evolved early in the history of life. The ATP-binding domains in **archaea, eubacteria**, and **eukaryotes** all share a homologous structure, the ATP-binding "cassette".

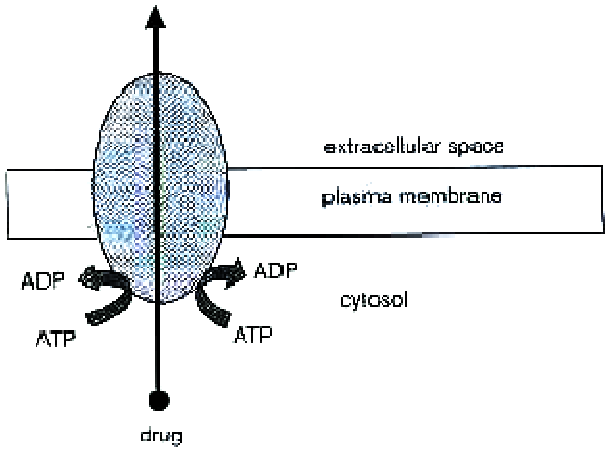


Fig.4.6c. ABC Transporters

(A) Indirect Active Transport

Indirect active transport uses the **downhill flow** of an ion to pump some other molecule or ion against its gradient. The driving ion is usually sodium (Na^+) with its gradient established by the Na^+/K^+ ATPase.

(a) Symport Pumps

In this type of indirect active transport, the driving ion (Na^+) and the pumped molecule pass through the membrane pump in the **same** direction.

Examples:

- **The Na^+/glucose transporter**: This transmembrane protein allows sodium ions and glucose to enter the cell together. The sodium ions flow **down** their concentration gradient while the glucose molecules are pumped **up** theirs. Later the sodium is pumped back out of the cell by the Na^+/K^+ ATPase. The Na^+/glucose transporter is used to actively transport glucose out of the intestine and also out of the kidney tubules and back into the blood.
- All the **amino acids** can be actively transported, for example out of the kidney tubules and into the blood and the reuptake of Glucose from the synapse back into the presynaptic neuron by sodium-driven symport pumps.
- **The Na^+/iodide transporter**: This symporter pumps iodide ions into the cells of the thyroid gland (for the manufacture of thyroxine) and also into the cells of the mammary gland (to supply the baby's need for iodide).
- The **permease** encoded by the lac operon of *E. coli* that transports lactose into the cell.

(b) Antiport Pumps

In antiport pumps, the driving ion (again, usually sodium) diffuses through the pump in one direction providing the energy for the active transport of some other molecule or ion in the opposite direction. **Example**: Ca^{2+} ions are pumped out of cells by a sodium-driven antiport pump. An antiport pump in the vacuole of some plants harnesses the outward facilitated diffusion of protons (themselves pumped into the vacuole by a **H^+ ATPase**) to the active inward transport of sodium ions. This sodium/proton antiport pump enables the plant to sequester sodium ions in its vacuole. Transgenic tomato plants that overexpress this sodium/proton antiport pump are able to thrive in saline soils too salty for conventional tomatoes.

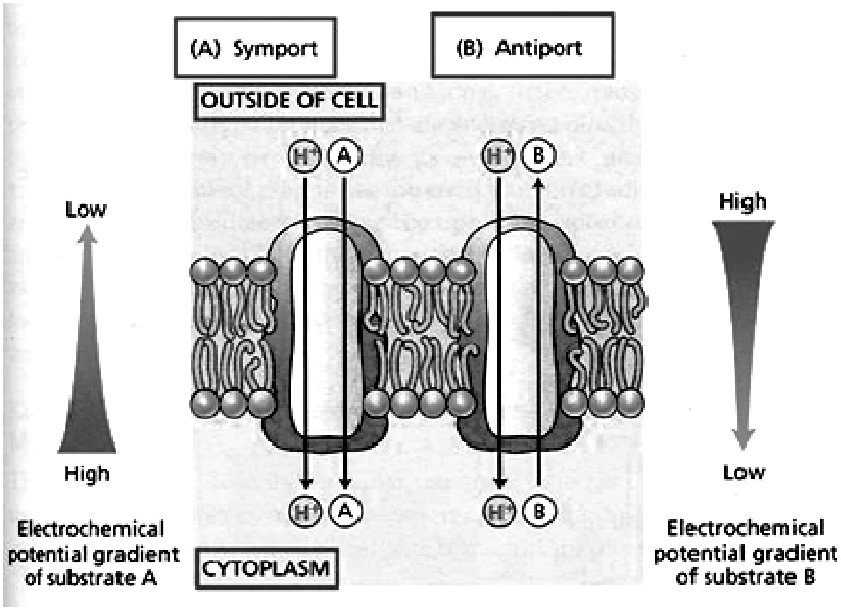


Fig.4.6d. Symport and Antiport

(c) Some Inherited Ion-Channel Diseases

A growing number of human diseases have been discovered to be caused by inherited mutations in genes encoding channels.

Some examples:

- **Chloride-channel** diseases
  - Cystic fibrosis
  - inherited tendency to kidney stones (caused by a different kind of chloride channel than the one involved in cystic fibrosis)
- **Potassium-channel** diseases
  - some inherited life-threatening defects in the heartbeat
  - a rare, inherited tendency to epileptic seizures in the newborn.
  - several types of inherited **deafness**.
- **Sodium-channel** diseases
  - inherited tendency to certain types of muscle spasms
  - Liddle's syndrome. Inadequate sodium transport out of the kidneys, because of a mutant sodium channel, leads to elevated **osmotic pressure** of the blood and resulting hypertension (high blood pressure).

4.2.6. Osmosis

Osmosis is a special term used for the diffusion of water through cell membranes. Although water is a polar molecule, it is able to pass through the lipid bi-layer of the plasma membrane. Transmembrane proteins that form hydrophilic channels accelerate the process, but even without these, water is still able to get through. Water passes by diffusion from a region of higher to a region of lower concentration. Note that this refers to the concentration of water, NOT the concentration of any solutes present in the water. Water is never transported actively; that is, it never moves against its concentration gradient. However, the concentration of water can be altered by the active transport of solutes and in this way the movement of water in and out of the cell can be controlled. **Example**: the re-absorption of water from the kidney tubules back into the blood depends on the water following behind the active transport of Na^+.

(a) Hypotonic Solutions

If the concentration of water in the medium surrounding a cell is greater than that of the cytosol, the medium is said to be **hypotonic**. Water enters the cell by osmosis.

A red blood cell placed in a hypotonic solution (e.g., pure water) bursts immediately ("haemolysis") from the influx of water. Plant cells and bacterial cells avoid bursting in hypotonic surroundings by their strong cell walls. These allow the buildup of **turgor** within the cell. When the turgor pressure equals the osmotic pressure, osmosis ceases.

(b) Isotonic Solutions

When red blood cells are placed in a 0.9% salt solution, they neither gain nor lose water by osmosis. Such a solution is said to be **isotonic**. The extracellular fluid (ECF) of mammalian cells is isotonic to their cytoplasm. This balance must be actively maintained because of the large number of organic molecules dissolved in the cytosol but not present in the ECF. These organic molecules exert an osmotic effect that, if not compensated for, would cause the cell to take in so much water that it would swell and might even burst. This fate is avoided by pumping sodium ions out of the cell with the Na^+/K^+ ATPase.

(c) Hypertonic Solutions

If red cells are placed in sea water (about 3% salt), they lose water by osmosis and the cells shrivel up. Sea water is **hypertonic** to their cytosol. Similarly, if a plant tissue is placed in sea water, the cell contents shrink away from the rigid cell wall. This is called **plasmolysis**. Sea water is also hypertonic to the ECF of most marine vertebrates. To avoid fatal dehydration, these animals (e.g., bony fishes like the cod) must continuously drink sea water and then desalt it by pumping ions out of their gills by active transport. (Marine reptiles — turtles and snakes — use special salt glands for the same purpose.)

4.2.7. Endocytosis

In endocytosis, the cell engulfs some of its extracellular fluid (**ECF**) including material dissolved or suspended in it. A portion of the plasma membrane is invaginated and pinched off forming a membrane-bounded **vesicle** called an **endosome**.

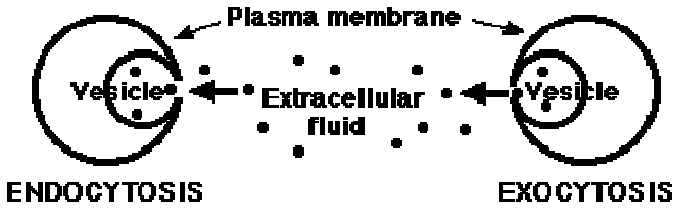


Fig.4.7a. Endocytosis and Exocytosis

(a) Phagocytosis

Phagocytosis ("cell eating"): results in the ingestion of particulate matter (e.g., bacteria) from the ECF. The endosome is so large that it is called a **phagosome** or **vacuole**. Phagocytosis occurs only in certain specialized cells (e.g., neutrophils, macrophages, the amoeba), and occurs sporadically. In due course, phagosomes deliver their contents to **lysosomes.** The membranes of the two organelles fuse. Once inside the lysosome, the contents of the phagosome, e.g. ingested bacteria, are destroyed by the degradative enzymes of the lysosome.

Phagocytic cells, like macrophages and neutrophils, are an early line of defense against invading bacteria. However, some bacteria have evolved mechanisms to avoid destruction even after they have been engulfed by phagocytes.

Two examples:

- *Salmonella enterica* is a bacterium that causes food poisoning in humans. Once engulfed by phagocytosis, it secretes a protein that prevents the fusion of its phagosome with a lysosome.
- *Mycobacteria* (e.g., the tubercle bacillus that causes tuberculosis) use a different trick. When the phagosome is first pinched off from the plasma membrane, it is coated with a protein called "TACO" (for tryptophan-aspartate-containing coat protein). This must be removed before the phagosome can fuse with a lysosome. Mycobacteria taken into a phagosome are able, in some way, to keep the TACO coat from being removed. Thus there is no fusion with lysosomes and the mycobacteria can continue to live in this protected intracellular location.

(b) Pinocytosis

In pinocytosis ("cell drinking"), the drop engulfed is relatively small. Pinocytosis occurs in almost all cells and continuously. A cell sipping away at the ECF by pinocytosis acquires a representative sample of the molecules and ions dissolved in the ECF. But pinocytosis also provides a much more elegant method for cells to pick up critical components of the ECF that may be in scant supply.

(c) Receptor-Mediated Endocytosis

Some of the integral membrane proteins that a cell displays at its surface are receptors for particular components of the ECF. For example, iron is transported in the blood complexed to a protein called **transferrin**. Cells have receptors for transferrin on their surface. When these receptors encounter a molecule of transferrin, they bind tightly to it. The complex of transferrin and its receptor is then engulfed by endocytosis. Ultimately, the iron is released into the cytosol. The strong **affinity** of the transferrin receptor for transferrin (its **ligand**) ensures that the cell will get all the iron it needs even if transferrin represents only a small fraction of the protein molecules present in the ECF. Receptor-

mediated endocytosis is many thousand times more efficient than simple pinocytosis in enabling the cell to acquire the macromolecules it needs.

Another Example: the Low-Density Lipoprotein (LDL) Receptor

Cells take up cholesterol by receptor-mediated endocytosis. Cholesterol is an essential component of all cell membranes. Most cells can, as needed, either synthesize cholesterol or acquire it from the ECF. Human cells get much of their cholesterol from the liver and, if your diet is not strictly "100% cholesterol-free", by absorption from the intestine. Cholesterol is a hydrophobic molecule and quite insoluble in water. Thus it cannot pass from the liver and/or the intestine to the cells simply dissolved in blood and ECF. Instead it is carried in tiny droplets of lipoprotein. The most abundant cholesterol carriers in humans are the **low-density lipoproteins** or **LDL**s. LDL particles are spheres covered with a single layer of phospholipid molecules with their hydrophilic heads exposed to the watery fluid (e.g., blood) and their hydrophobic tails directed into the interior. Over a thousand molecules of cholesterol are bound to the hydrophobic interior of LDL particles. One molecule of a protein, called **apolipoprotein B-100** (Apo B-100) is exposed at the surface of each LDL particle.

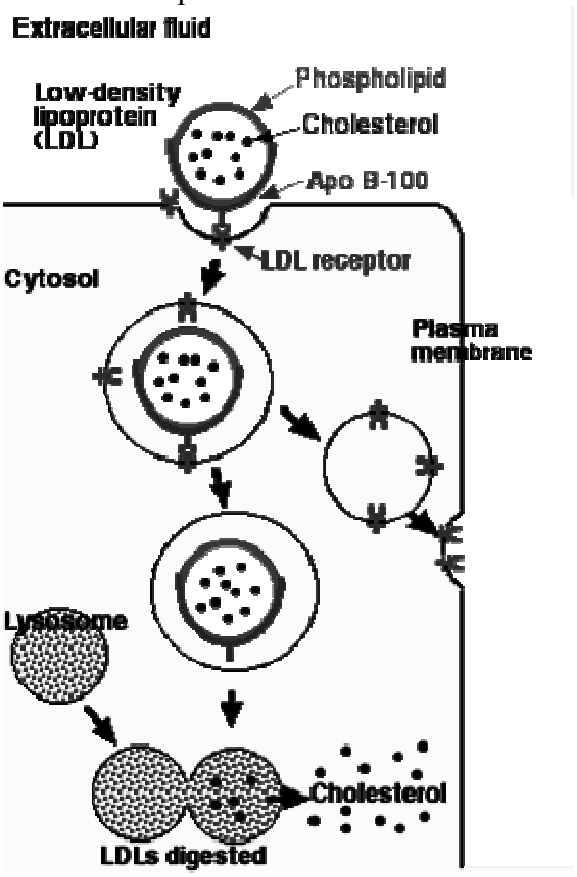


Fig.4.7b. Receptor-Mediated Endocytosis

The first step in acquiring LDL particles is for them to bind to **LDL receptors** exposed at the cell surface. These transmembrane proteins have a site that recognizes and binds to the apolipoprotein B-100 on the surface of the LDL. The portion of the plasma membrane with bound LDL is internalized by endocytosis. A drop in the pH (from ~7 to ~5) causes the LDL to separate from its receptor. The vesicle then pinches apart into two smaller

vesicles: one containing free LDLs; the other containing now-empty receptors. The vesicle with the LDLs fuses with a lysosome to form a **secondary lysosome**. The enzymes of the lysosome then release free cholesterol into the cytosol. The vesicle with unoccupied receptors returns to and fuses with the plasma membrane, turning inside out as it does so (exocytosis). In this way the LDL receptors are returned to the cell surface for reuse.

People who inherit two defective (mutant) genes for the LDL receptor have receptors that function poorly or not at all. This creates excessively high levels of LDL in their blood and predisposes them to **atherosclerosis** and heart attacks. The ailment is called **familial** (because it is inherited) **hypercholesterolemia**. Mutations in the **Apo B-100 gene** cause another form of inherited hypercholesterolemia. Other small hydrophobic molecules are also transported in the blood while bound to soluble proteins: The retinoid vitamin A (retinol) bound to the retinol-binding protein and the steroids **25[OH] vitamin D_3** bound to the vitamin D binding protein, **cortisol** bound to the corticosteroid binding **globulin** and **testosterone** and **estrogens** bound to the sex hormone binding globulin. There is growing evidence that, like cholesterol, they are taken into the cell by receptor-mediated endocytosis.

Some **intracellular** parasites exploit receptor-mediated endocytosis to sneak their way into their host cell. They have evolved surface molecules that serve as decoy ligands for receptors on the target cell surface. Binding to these receptors tricks the cell into engulfing the parasite.

Some examples:

- **Epstein-Barr Virus** (**EBV**). This virus causes **mononucleosis** and is a contributing factor in the development of **Burkitt's lymphoma**, a cancer of B lymphocytes. It binds to a receptor present on the surface of B cells .
- **Influenza virus**. The **hemagglutinin** on the surface of the virus binds to carbohydrate on the surface of the target cell tricking the cell into engulfing it .
- **Listeria monocytogenes**. This food-borne bacterium can be dangerous to people with defective immune systems as well as to pregnant women and their newborn babies. It has two kinds of surface molecules each a ligand for a different receptor on the target cell surface.
- **Streptococcus pneumoniae**. Epithelial cells like those in the nasopharynx have receptors that are responsible for transporting IgA and IgM antibodies from the blood to the cell surface. The pneumococcus exploits this receptor for a return trip into the cell.

(d) Exocytosis

Endocytosis removes portions of the plasma membrane and takes them inside the cell. To keep in balance, membrane must be returned to the plasma membrane. This occurs by **exocytosis**. Exocytosis is the reverse of **endocytosis**. In 30 minutes an active cell like a **macrophage** can endocytose an amount of plasma membrane equal to its complete plasma membrane. So the cell must have a mechanism to restore the normal amount of plasma membrane. Exocytosis is that mechanism.

(i) The Process

Membrane-bound vesicles move to the cell surface where they **fuse** with the plasma membrane. This accomplishes three things:

- It restores the normal amount of plasma membrane.
- Any molecules dissolved in the fluid contents of these vesicles are discharged into the extracellular fluid - this is called **secretion**. E.g. the various components of the extracellular matrix are secreted by exocytosis.
- Any integral membrane proteins exposed to the **interior** surface of the vesicles will now be displayed at the cell surface because the vesicles turn inside out as they fuse with the plasma membrane. Thus exocytosis does not simply replace plasma membrane but ensures that the plasma membrane will display its **characteristic cell-surface proteins**.

Exocytic vesicles are created from several sources:

- Some are simply endosomes traversing the cell.
- Others are pinched off from endosomes before they fuse with lysosomes.
- Others bud off from the endoplasmic reticulum and Golgi apparatus taking their products to the surface of the cell.
- The exocytosis of lysosomes supplies the membrane needed to repair wounds in the plasma membrane.

Some cells specialize in secretion. In cells that secrete large amounts of protein, for example, the protein accumulates in specialized secretory granules formed by the Golgi apparatus. These move to the cell surface and discharge their contents to the outside. E.g. Exocrine cells in the pancreas synthesize and secrete pancreatic digestive enzymes.