Lectures 1- 3

CELL AND BODY FLUIDS

Levels of organization

Human body, like any other multicellular organism, is organized, into the following levels:

1- Chemical levels: They are the atomic and molecular levels. An atom is the smallest unit of matter. A molecule is made up of two or more (similar or different) atoms that are chemically bonded together. Compounds are molecules made up of two or more different atoms. An ion is an atom or molecule that has an electrical charge.

2- Cellular levels: They involve the organelles and cell levels. Cells are the basic structural and functional units of a living organism.

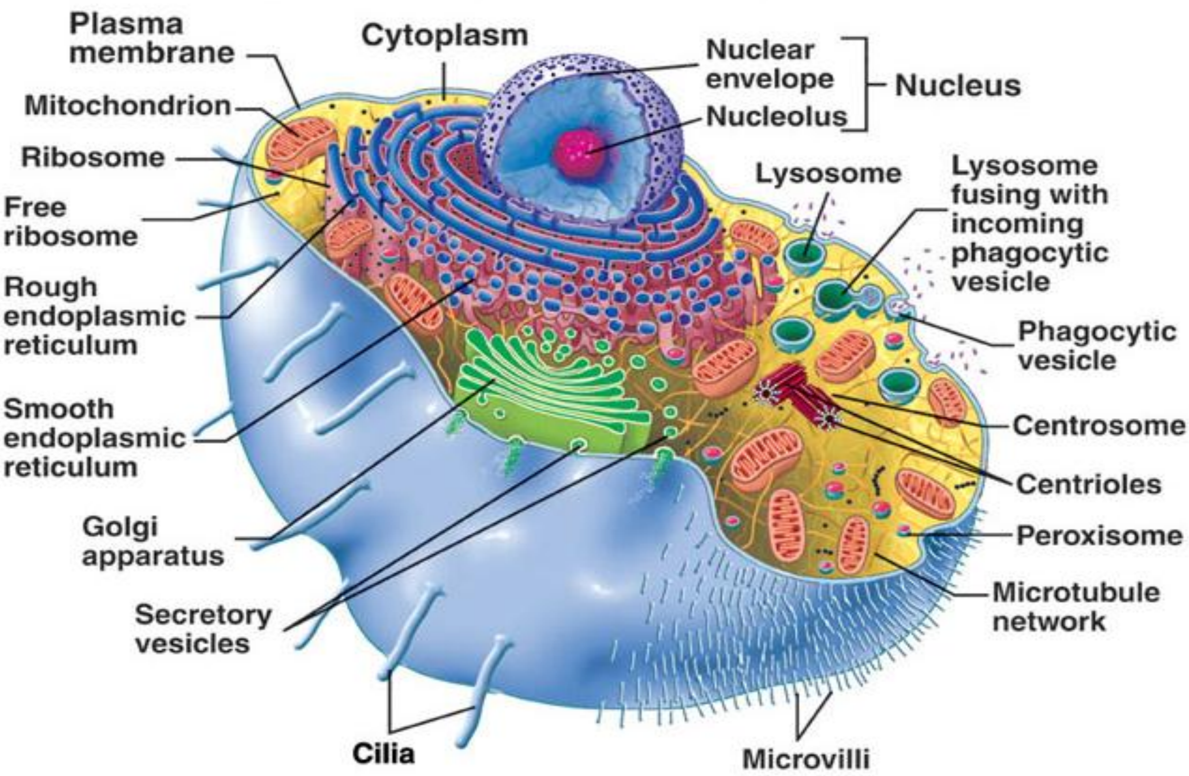
3- Tissue level: Tissues are groups of cells that have a similar structure and act together to perform a specific function. There are four types of tissues. They are epithelial, connective, muscle and nervous tissues.

4- Organ level: An organ is an independent group of tissues that performs a specific function in the body. The lungs, heart, kidneys, liver, and stomach are examples of organs. Some organs and tissues serve a purpose in only one body system. Other organs serve more than one function and, hence, are belong to more than one body system.

5- System level: Body systems are groups of organs and tissues that work together to perform important functions for the body. Examples are digestive system, cardiovascular system, respiratory system, ... etc.

6- Organismal level: The whole living person.

Systems	Examples of organs
Integumentary	Skin, hair and nails
Skeletal	Bones and joints
Muscular	Smooth, cardiac, and skeletal muscles
Circulatory	Heart, arteries and veins
Respiratory	Lungs, trachea, bronchi, diaphragm, larynx, ...
Digestive	Stomach, intestines, liver, pancreas, esophagus, ...
Urinary	Kidneys, ureters, urinary bladder, urethra, ...
Immune	Lymph nodes, bone marrow, thymus, ...
Nervous	Brain, spinal cord, nerves, ...
Endocrine	Pituitary gland, thyroid, adrenals, pancreas, ...
Reproductive	Penis, vagina, prostate, ovaries, uterus, ...



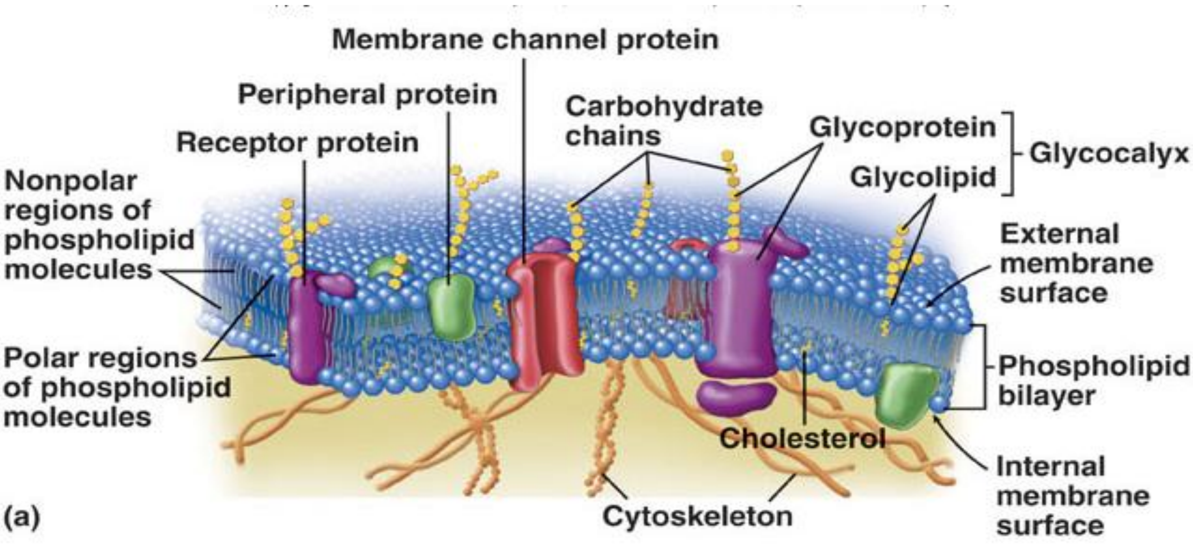
Cell

In eukaryotic organisms, a typical cell is composed of a plasma membrane which encloses the cytoplasm and organelles. The cytoplasm is the fluid that fills the cell. It includes the cytosol, cytoskeleton, proteins, ions and macromolecular structures. The organelles are suspended in the cytosol. The largest organelle is the nucleus which is bounded by a nuclear membrane and contains the genetic material (DNA). There are other organelles like ribosomes, endoplasmic reticulum, Golgi complex, mitochondria, lysosomes, vacuoles, ...

Plasma Membrane

The plasma (or cell) membrane is thin, flexible, double-layer membrane. This phospholipid bilayer consists of a polar 'head' end, which is hydrophilic (water loving) situated on the outer and inner surfaces of the cell, and fatty acid 'tails', which are hydrophobic (water hating) facing each other. Lipids, proteins, and carbohydrates are floating across the surface of plasma membrane. This is known as the fluid mosaic model.

Membrane proteins are either integral or peripheral. They form channels, receptors, pores or gates. They play a role in cell signaling, enzyme activity and recognition of foreign or other body cells.

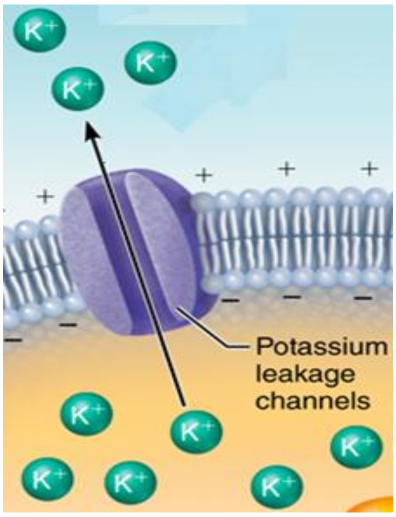


Functions of plasma membrane

The plasma membrane is a physical barrier. It surrounds the cell and protects its components. It provides structural support and gives the cell its shape. It is selectively semipermeable which means that certain molecules (like water, oxygen, and carbon dioxide) are allowed to pass through the membrane while others (like ions and polar molecules) cannot pass through and they must go through specific channels or pores in the membrane. The shape of plasma membrane changes to allow molecules to enter (endocytosis) or exit (exocytosis) the cell. Plasma membrane also facilitates communication and signaling between cells. Various proteins and carbohydrates function in recognition of other foreign or body cells. The membrane has receptors to bind molecules such as hormones or other chemicals (ligands). Electrical signal in nerve and muscle cells is transmitted along their plasma membrane.

Ion channels

Certain plasma membrane proteins act as ion channels. Each channel only allows certain types of ions to enter or exit the membrane. The most common types of ion channels are:



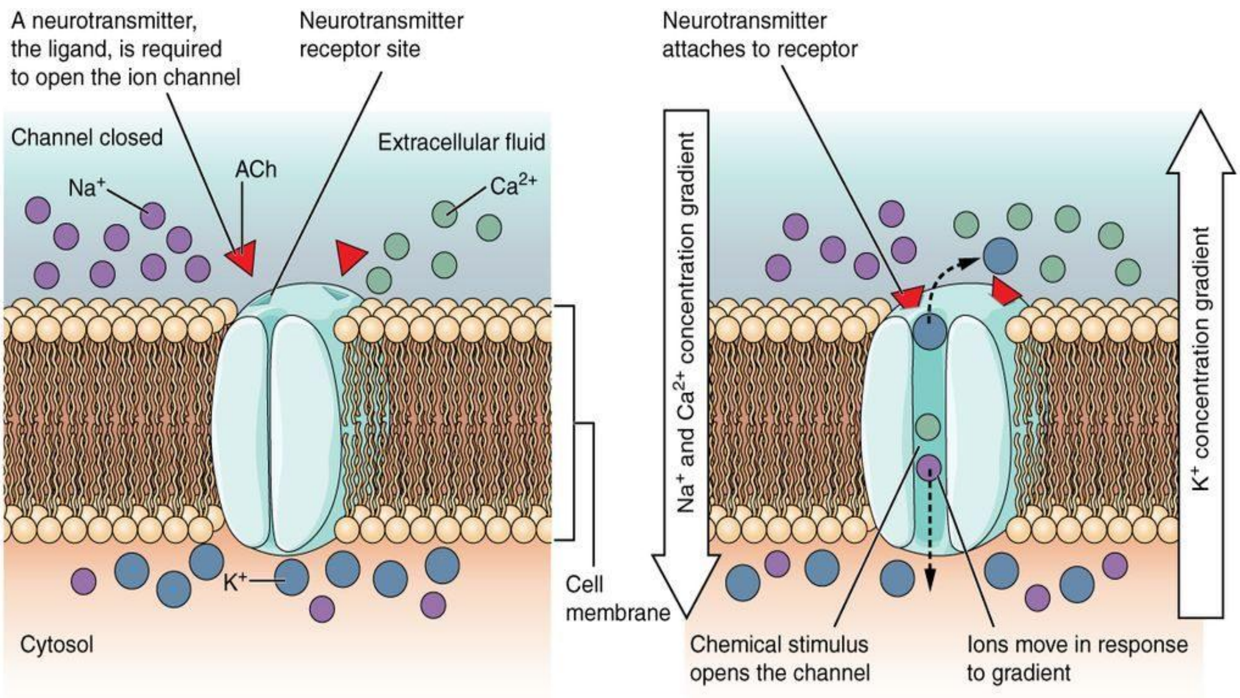
Leakage Channels

Leakage channels are the simplest type of ion channel with constant permeability. Examples are potassium and chloride channels in neurons. Some leakage channels are shut off by ligands.

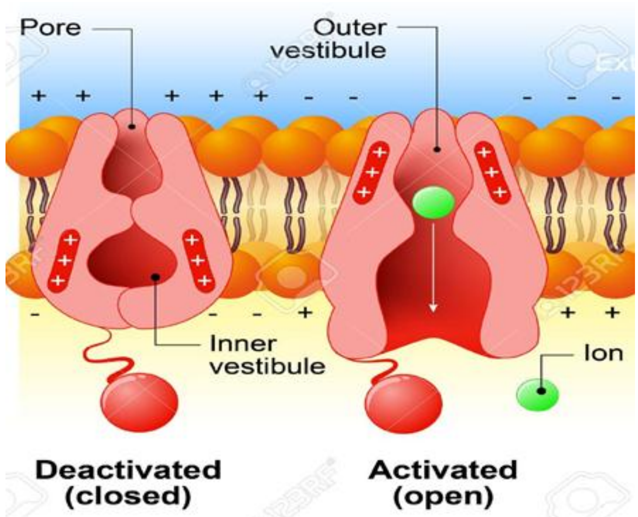
Gated Channels

There are three main types of gated channels: chemically-gated (or ligand-gated) channels, voltage-gated channels, and mechanically-gated channels.

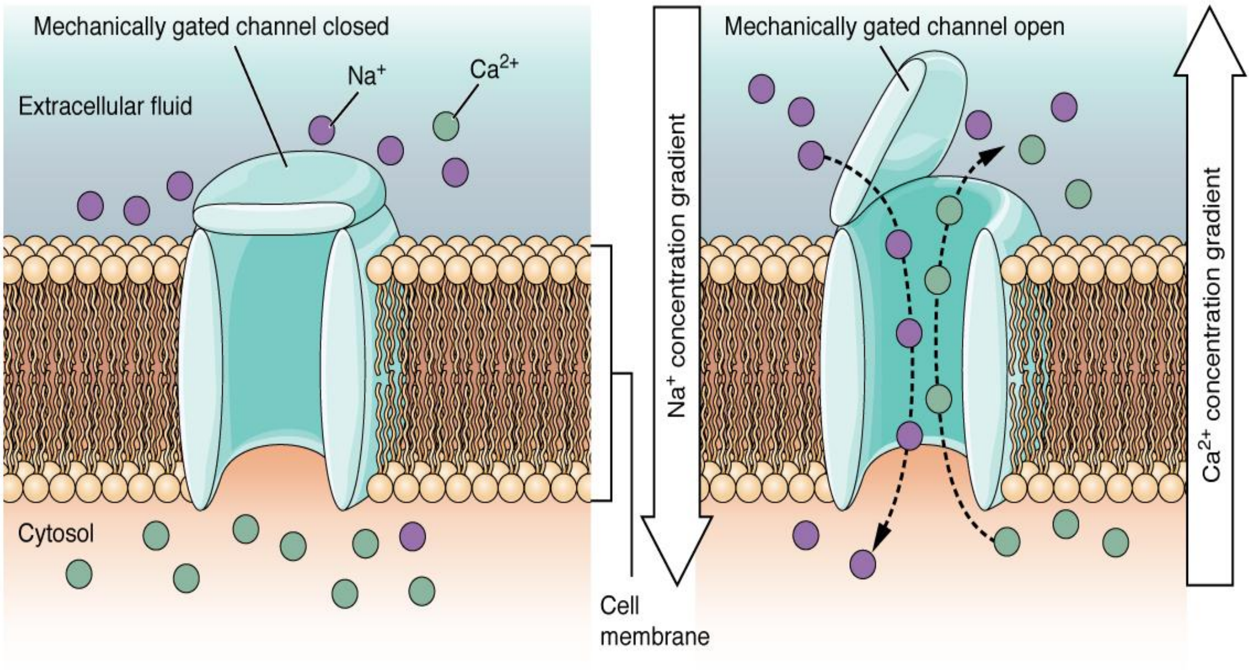
Ligand-gated ion channels are opened or closed when certain chemical ligand binds to the protein structure. They can be activated by ligands that appear in the extracellular area or by interactions on the intracellular side.



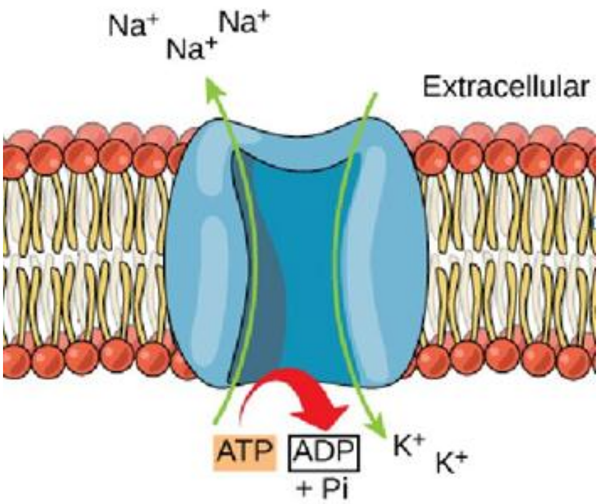
Voltage-gated ion channels, also known as voltage-dependent ion channels, are opened or closed by changing the membrane potential. Many of these channels are also time-dependent (they do not respond immediately to a voltage change, but only after a delay). Voltage-gated channels are essential for the generation and propagation of action potentials.



Mechanically-gated channels open in response to physical deformation of the receptor, as in sensory receptors of touch and pressure.



Ion pumps are not ion channels, but are membrane proteins that perform active transport by using cellular energy (ATP) to "pump" the ions against their concentration gradient i.e. they carry ions from the membrane side of lower concentration to the other side of higher concentration.

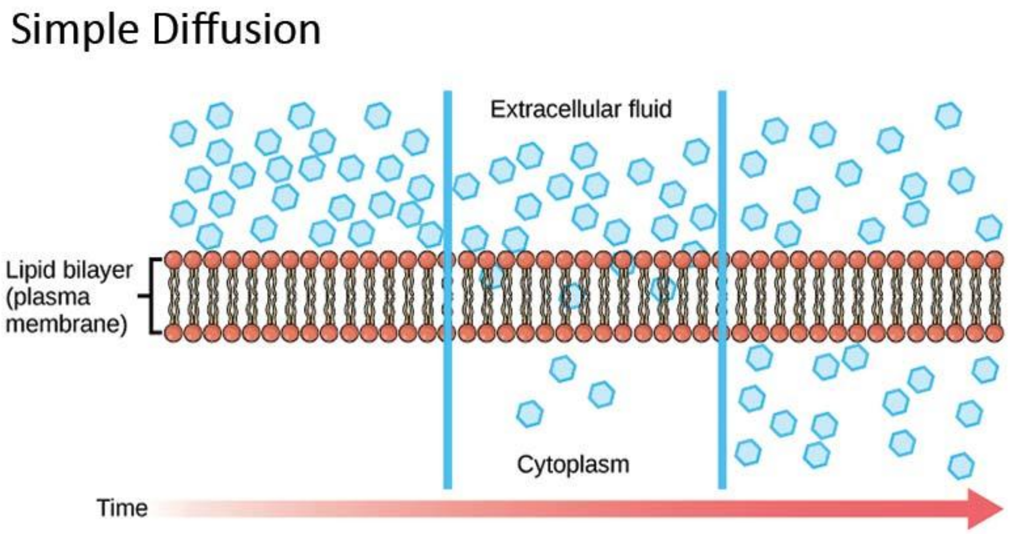


Membrane transport:

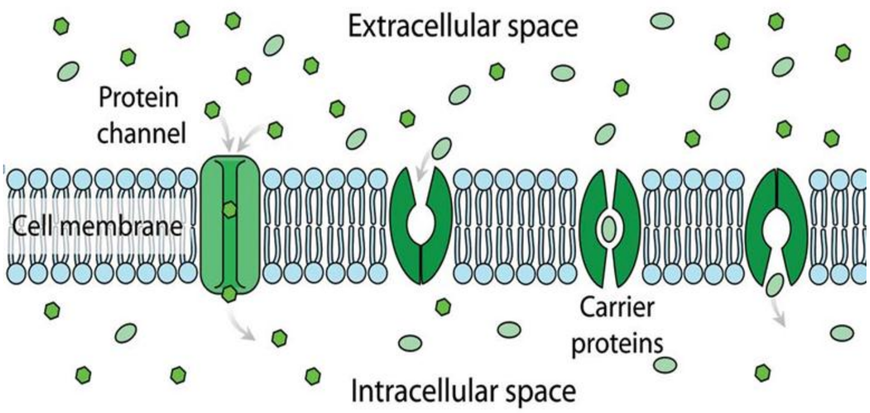
Movement across membranes is either a passive process (in which there is no energy expenditure) or an active process (in which energy is required).
Passive processes:

1. Diffusion: Net movement of a substance down a concentration gradient (graded concentration change over a distance in a particular direction) which is a random molecular movement results from intrinsic kinetic energy and is affected by temperature and molecular size and it continues until a dynamic equilibrium is reached. There are several types of diffusion:

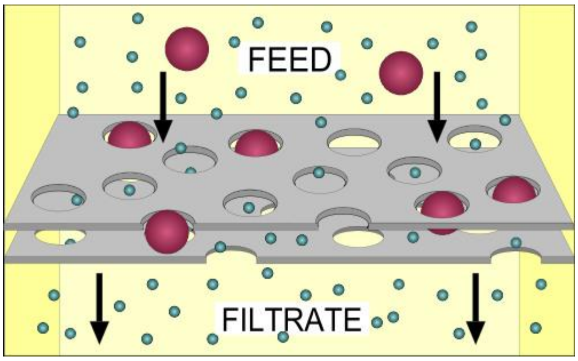
a. Simple diffusion:
Nonpolar substances that are lipid soluble pass directly through lipid bilayer. Polar and charged particles can diffuse if they can fit through pores.



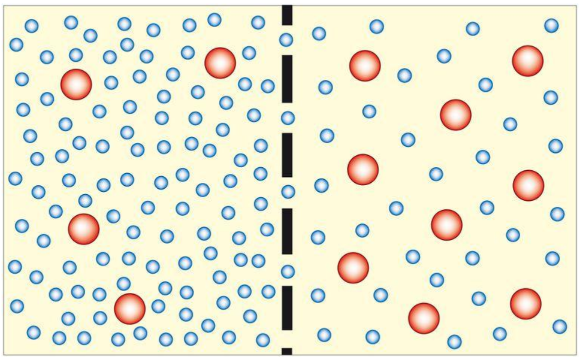
b. Facilitated diffusion: Lipid insoluble molecules too large to diffuse through membrane pores can move passively with carrier molecules which is selective (specific) and limited by number of carrier molecules present (saturated).



2. Filtration: Water and solutes are forced through a membrane or capillary by hydrostatic pressure (pressure gradient pushes solute-containing fluid out).

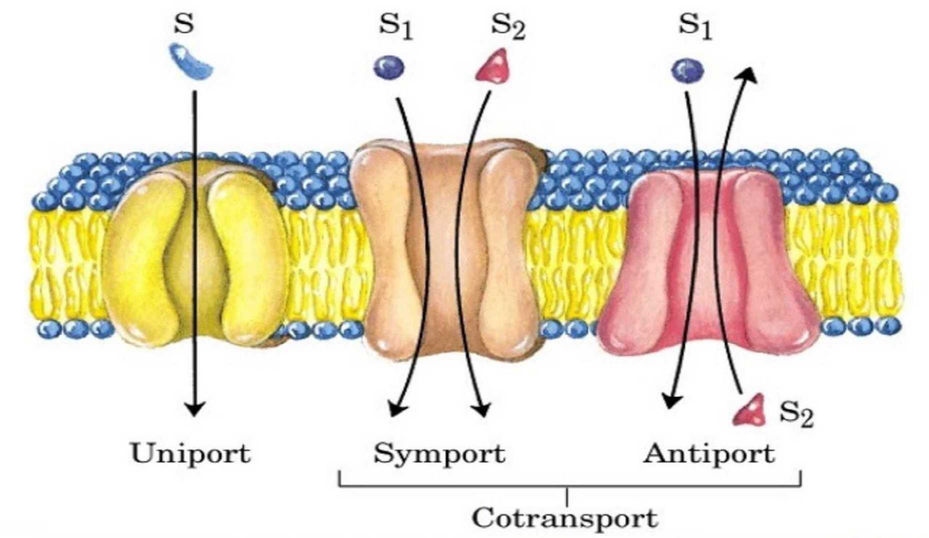


3. Osmosis: Is diffusion of a solvent through a selectively permeable membrane.

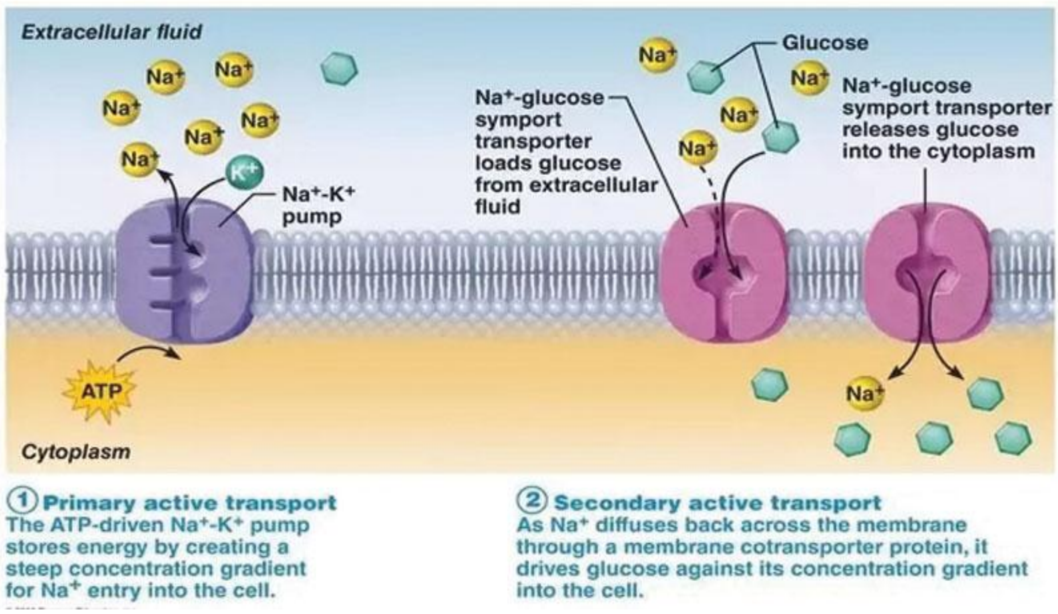


Active Processes:

1. Primary active transport: Transporters utilize energy from ATP to pump molecules against their concentration gradients (from area of low concentration to area of high concentration). If only one molecule is transported; this is called "uniport". If two or more molecules are transported; this is called "multiport". If all molecules are transported in the same direction; this is called "symport", and if they are transported in opposite directions; it is called "antiport".



2. Secondary active transport: It does not expend energy by itself. Instead, it utilizes concentration gradient resulting from primary active transport in certain location to move other substances in another location.



3. Bulk Transport (or vesicular transport):

a. Exocytosis:
Substance is released from vesicle (membranous sac which fuses with plasma membrane and releases its contents to outside).

b. Endocytosis:
Large substances progressively enclosed by membrane and taken into cell like phagocytosis (engulfing hard substances), pinocytosis (ingestion of fluids) and
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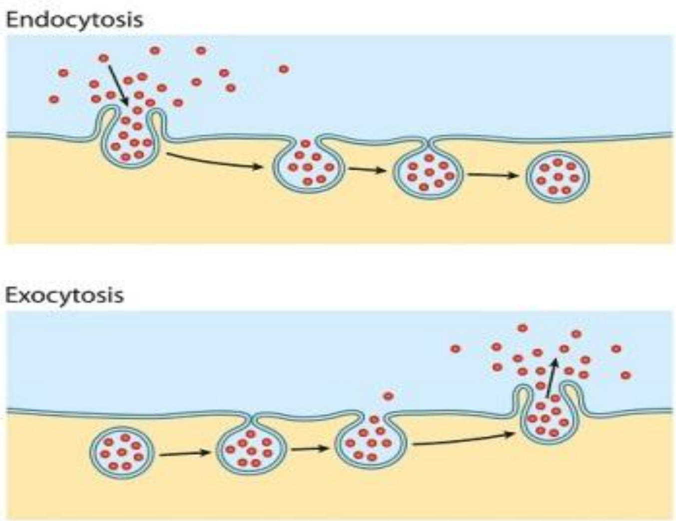
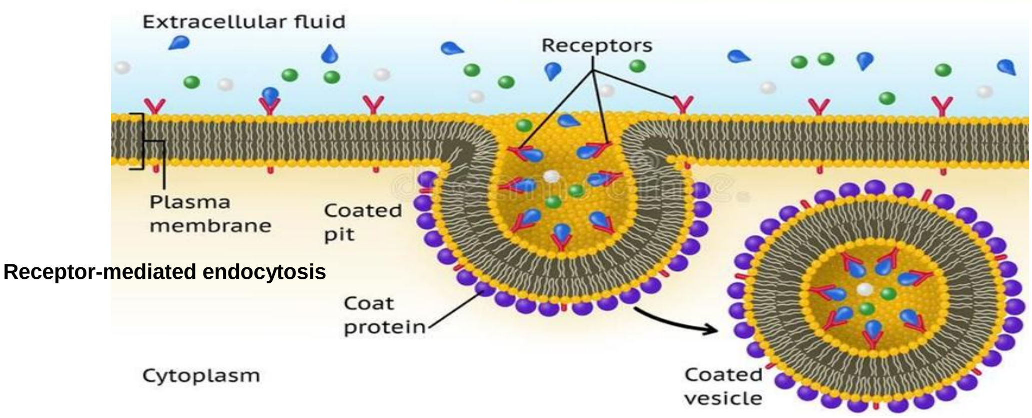




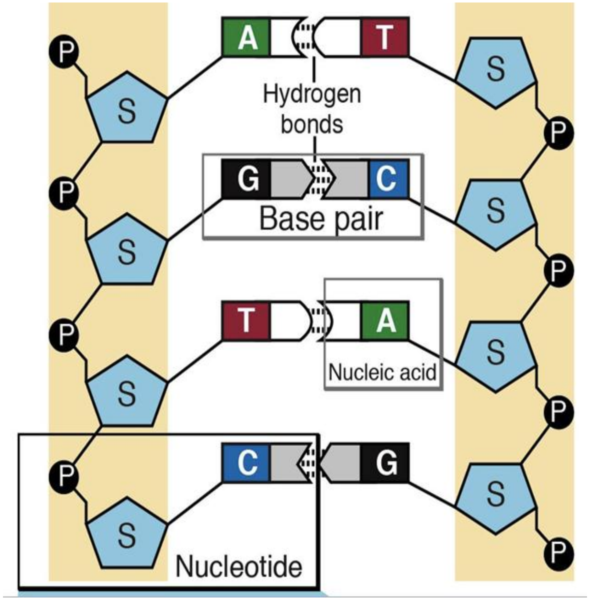
Functions of some organelles and inclusions

Cell components	Functions
Ribosomes	They convert genetic code into an amino acid sequence and build protein polymers from amino acid monomers.
Rough endoplasmic reticulum (studded with ribosomes)	It folds the proteins into the proper shape, makes any necessary chemical additions or processing and packages up proteins in a transport vesicle to be sent to the Golgi complex.
Smooth endoplasmic reticulum (has no ribosomes)	It creates lipids and breaks down toxins.
Golgi Complex	It fully modifies proteins, mixes them with other chemical constituents. These proteins may be secreted outside the cell (defensive proteins, hormones, neurotransmitters, ... etc.), go to the lysosomes (as hydrolytic enzymes...) or embedded in the cellular membrane to be structural components.
Mitochondria	They provide energy in the form of ATP.
Lysosomes	They store hydrolases enzymes which break apart polymers by catalyzing hydration reactions. So, they function in internal and/or external digestion, recycling the worn out organelles, autolysis (self-digestion).
Vacuoles	They hold excess water, toxins, wastes, and byproducts so they cannot affect the chemistry of the rest of the cell.
Cytoskeleton (microfilaments, microtubules, intermediate filaments)	They provide shape and support, site for specific enzymes, cell movement, intracellular transportation.
Centrioles	They aid in cellular reproduction.
Chromosomes	They contain genetic information.
Cilia	They move fluid or particles over the surface of the cell.
Glycogen granules	They store glycogen.
Microvilli	They increase cell surface and act as a site for secretion, absorption and cellular adhesion.
Nucleolus	It is the site for the formation of ribosomes.
Peroxisomes	They carry out metabolic reactions, act as sites for destruction of hydrogen peroxide; protect the cell from harmful substances, such as alcohol and formaldehyde.
Secretory vesicles	They secrete hormones, neurotransmitters.
Lipid droplets (adiposomes)	They store cholesterol and acyl-glycerols for membrane formation and maintenance.

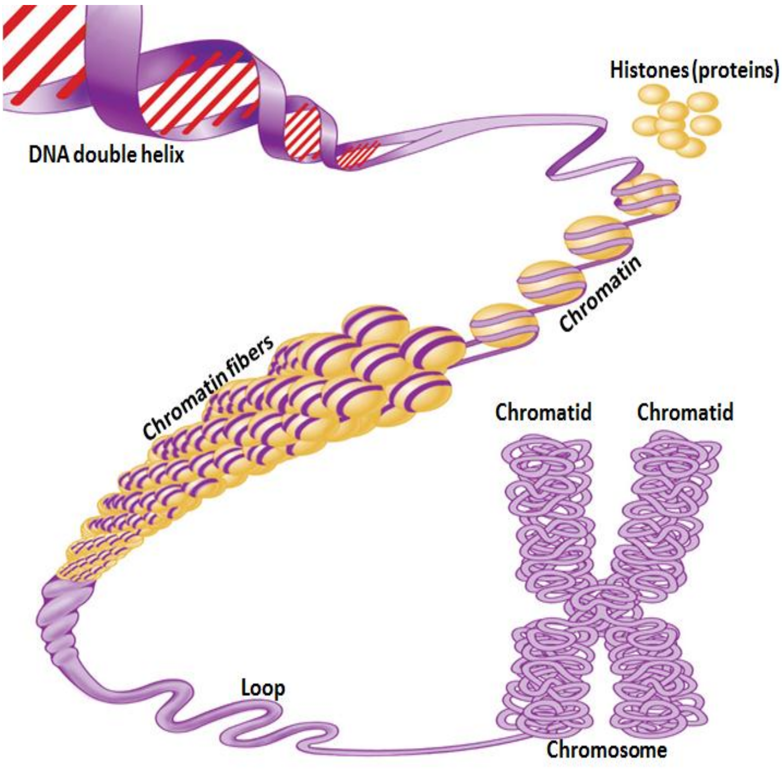
Chromosomes

Nucleic acids are components of DNA and they have two major functions: The production of proteins and transmission genetic information from one generation to the next. Two strands of DNA are arranged as double helix resembling a ladder. The genes are sections of DNA. The genetic information is encoded in a linear sequence of chemical subunits, called nucleotides.

Nucleotides consist of three molecules: deoxyribose, phosphate and base. Deoxyribose is a five-carbon cyclic sugar. Phosphate is an inorganic, negatively charged molecule. Base is a nitrogen–carbon ring structure. The DNA contains four types of bases. They are adenine (A), thymine (T), guanine (G) and cytosine (C). Our genes are different due to the difference in the order of these bases. Every base is connected to the deoxyribose of the strand by covalent bond. The bases on one strand of DNA are joined to their complement bases on the other strand by hydrogen/polar bonds. The complement of A is T, and the complement of G is C.



The nucleic acid is combined with protein molecules known as histones. The DNA and histones together make up the nucleosomes contained within the cell nucleus. Several nucleosomes form the chromatin. The chromatins are extensively twisted, folded and packed to form the chromatids. Two chromatids are joined by a centromere to make a chromosome.



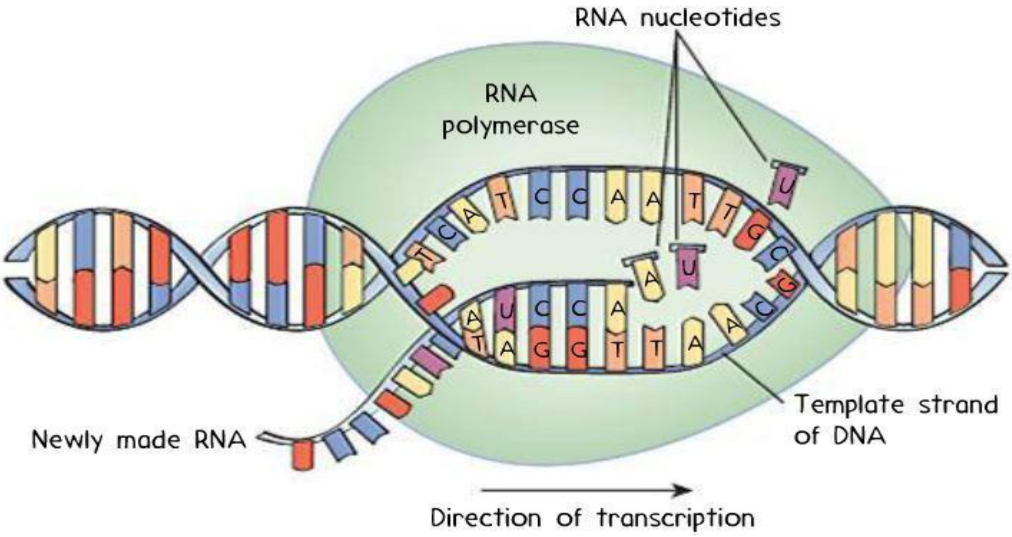
Each nucleated cell within the human body has 46chromosomes, arranged in 23 pairs. Of those 23 pairs, one pair determines the gender of the person. Females have a pair of X chromosomes. Males have one X and one Y chromosomes. The remaining 22 pairs of chromosomes are known as autosomes. Autosome can be defined as the chromosomes that determine physical/body characteristics.

Genes that occupy corresponding positions (loci) on both chromatids are called alleles. A pair of identical alleles is homozygous while a dissimilar pair is heterozygous. The genotype is the chemical composition of DNA while the phenotype is the observable traits. A dominant genotype shows its phenotype even if it is present on only one of the paired chromosomes. A recessive genotype does not show its phenotype unless it is present on both chromosomes.

Protein production

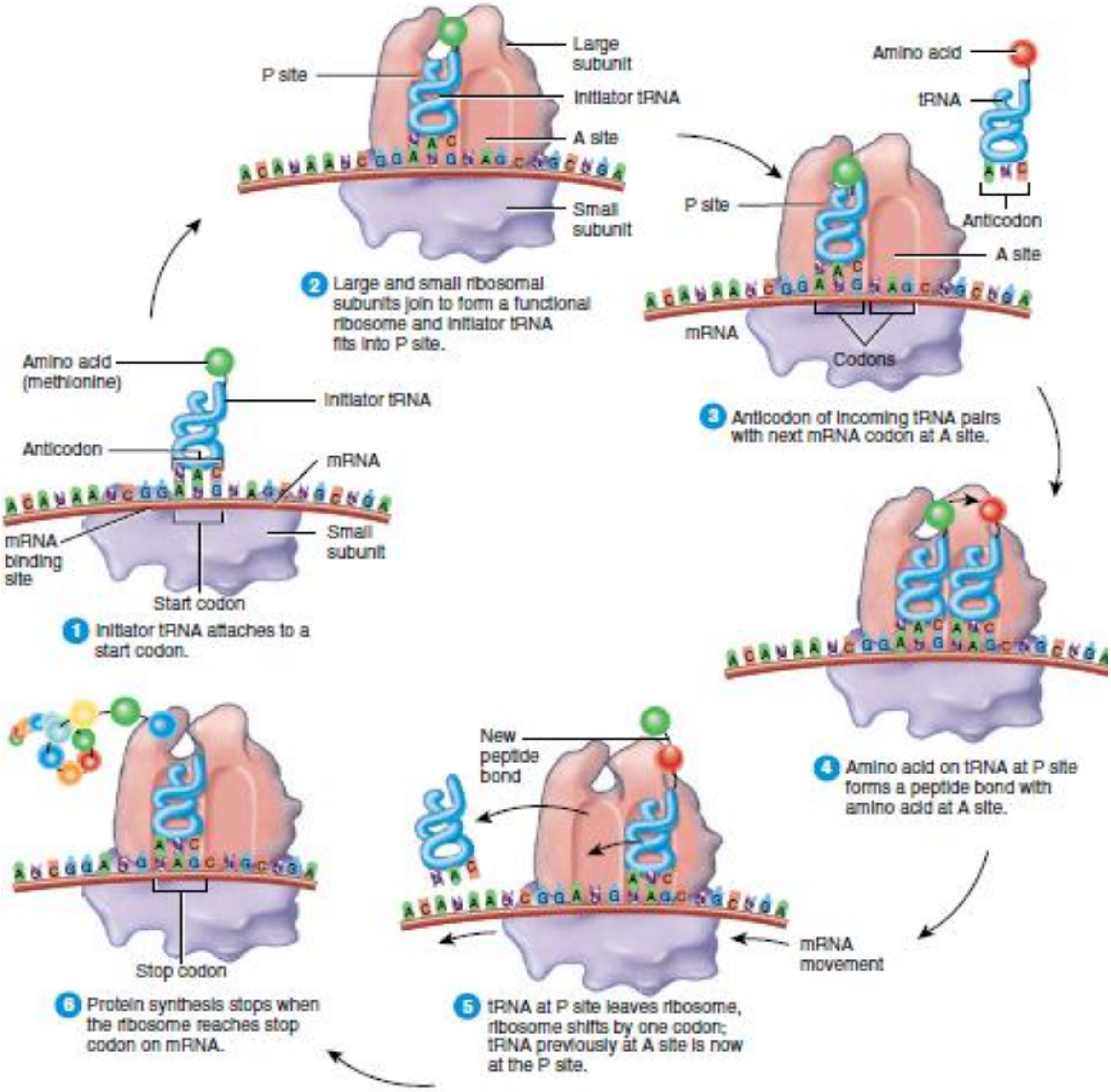
The genetic information for protein synthesis is encoded in the DNA. The double strands are separated and DNA is copied onto RNA. This is called "transcription".

Transcription occurs in the nucleus. The separated bases on each strand join to bases in RNA strands. The RNA strand also contains four bases. They are adenine (A), guanine (G), cytosine (C) and uracil (U). There is no thymine in RNA. Guanine in DNA pairs up with cytosine in RNA and vice versa. Thymine in DNA pairs up with adenine in RNA, but adenine in the DNA pairs up with uracil in RNA.



The DNA acts a template to synthesize mRNA, rRNA and tRNA. The mRNA (messenger RNA) transfers the information from DNA to the ribosomes to make proteins, the rRNA (ribosomal RNA) together with the ribosomal proteins, makes up the ribosomes, the tRNA (transfer RNA) is responsible for matching the code of the mRNA with amino acids. The base code of mRNA is "translated" to a specific amino acid sequence of a protein. Translation occurs in the cytoplasm.

The functional ribosomes are formed by joining of two subunits; the small and the large subunits. The mRNA is attached to the small subunit while the initiator tRNA is fit to the P-site on the large subunit. Every three successive bases on mRNA are called a "codon". The tRNA molecules are small strands. Each tRNA strand is composed of just three bases (triplet). This triplet is known as an "anticodon". One end of the tRNA carries a specific amino acid while the other end (anticodon) recognizes its corresponding codon of the mRNA strand and attaches to it by base-pairing. Then, the ribosome moves along the mRNA strand, the initiator tRNA moves from P-site to A-site and the second tRNA moves to fit P-site. The second tRNA carries a specific amino acid according to its triplet code. The first and second amino acids are joined by a peptide bond and, then, the first tRNA anticodon is separated from the mRNA strand to go back into the cytoplasm. The ribosome continues to move along the strand of mRNA and the process continues in the same way until it is stopped by a special codon known as a termination codon. The new protein is released from the ribosome, and the ribosome subunits are separated.



Body fluids

Human body is primarily composed of water. In male, about 60% of body weight is water (and in female, it is about 55%). Total body water (TBW) decreases with age. Adipose tissue is low in water content; thus, obese individuals have less body water than normal weight individuals.

In turn, TBW is divided into two major compartments: intracellular fluid (ICF) and extracellular fluid (ECF). The ICF compartment represents fluid contained within all cells in the body (approximately 65% of TBW). The ECF compartment includes all fluids outside of cells (approximately 35% of TBW) .

ECF is further divided into :

a. Blood plasma (blood without cells) about 20% of ECF

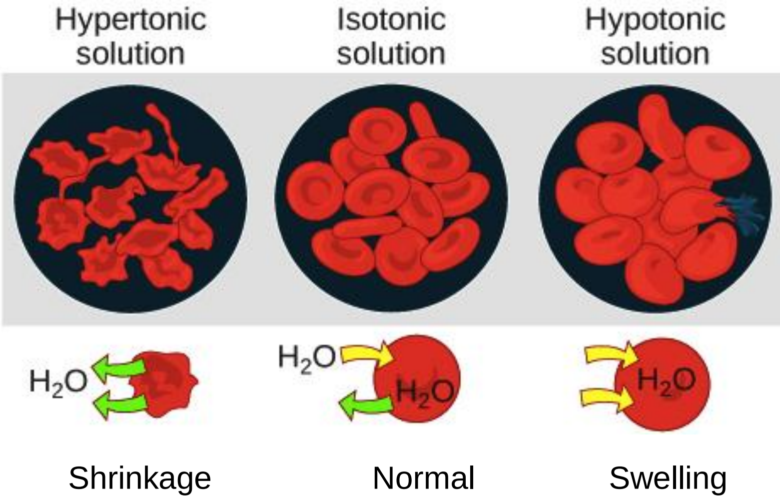
b. Interstitial fluid (ISF) (fluid between cells) about 70% of ECF

c. Transcellular fluid (synovial, intraocular, pericardial, cerebrospinal, and epithelial fluids) about 10% of ECF

The amount of solutes dissolved by a solution is described as "concentration". Tonicity is the concentration of a solution as compared to another solution. The total concentration of all solutes (electrolytes) in a solution is called "osmolarity". The ECF osmolarity is about 280 mmol/L. Osmotic pressure is the amount of pressure required to prevent net movement of water into a solution.

If a solution has a higher concentration of solutes (less water) than another it is said to be hypertonic. A hypotonic solution has a lower concentration of solutes and more water than another solution. Isotonic solutions contain the same concentration of solutes.

If a cell is surrounded by a hypertonic ECF, water will leave the cell, and the cell will shrink (ICF volume is decreased). If the ECF is isotonic, there is no net water movement, so there is no change in the size of the cell. When a cell is placed in a hypotonic ECF, water will enter the cell, and the cell will swell (ICF volume is increased).



	ECF volume	ECF osmolarity	ICF volume
Loss of isotonic fluid Hemorrhage Diarrhea Vomiting	Decrease	No change	No change
Loss of hypotonic fluid Dehydration Diabetes insipidus Alcoholism	Decrease	Increase	Decrease
Gain of isotonic fluid Isotonic saline	Increase	No change	No change
Gain of hypotonic fluid Hypotonic saline Water intoxication	Increase	Decrease	Increase
Gain of hypertonic fluid Hypertonic saline Hypertonic mannitol	Increase	Increase	Decrease

Exchange of fluids and solutes through capillary membrane

Four forces control movement of fluid through capillary wall (called Starling forces):

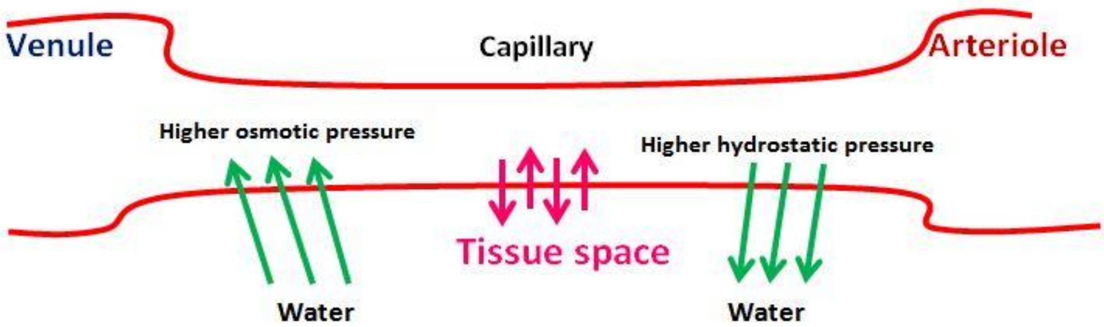
-Capillary hydrostatic pressure (Pc) moves water out of the capillary.

-Capillary osmotic pressure (πc) moves water into the capillary.

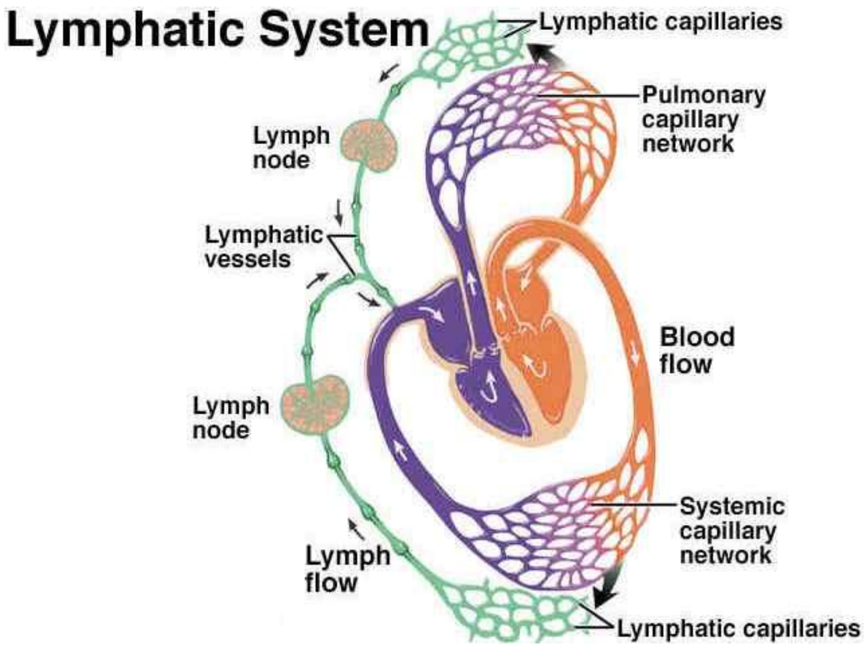
-Tissue space hydrostatic pressure (Pif) moves water out of tissue space (into the capillary).

-Tissue space osmotic pressure (πif) moves water into tissue space (out of the capillary).

At the arterial end of a capillary, hydrostatic pressure is higher than osmotic pressure. So, fluids exit a capillary. Midway along the capillary, there is no pressure difference. So, solutes diffuse according to their concentration gradient: Oxygen and nutrients (glucose and amino acids) diffuse out of the capillary; carbon dioxide and wastes diffuse into the capillary. Red blood cells and plasma proteins remain in the capillary. At the venule end of the capillary, osmotic pressure is greater than blood pressure, and fluids move back to the capillary. The same amount of fluids that left the capillary return to it.



Some excess tissue fluids containing electrolytes and some escaped proteins is collected by lymphatic capillaries. The tissue fluid which is contained within the lymphatic vessels is called lymph. Lymph returns to the systemic venous blood when the major lymphatic vessels enter subclavian veins in shoulder region.



Edema

Edema is an abnormal accumulation of fluid in the interstitium or in one or more cavities of the body. It is clinically shown as swelling. Edema may be due to increased pressure difference (e.g. hypertension and pregnancy, hypoalbuminemia, liver cirrhosis and inflammation). It may be caused by increased blood vessel wall permeability (e.g. in inflammation and allergy). Another cause of edema is the obstruction of lymphatic system (e.g. tumors or surgical removal of lymph nodes).