Chapter 1.1

Cell Structure and Functions

Objectives:

At the end of the chapter, the reader should be able to

- Describe the structure of the cell
- Describe the functions of the cell membrane and the cell organelles

Introduction:

Cell is the basic structural and functional unit of all living organisms. Robert Hooke observed "row of empty boxes" when he viewed a slice of cork through his microscope and he coined the term cell. A cell consists of three basic structures: cell membrane, cytoplasm and nucleus. The nucleus is separated from the cytoplasm by a nuclear membrane, and the cytoplasm is separated from the surrounding fluids by a cell membrane, also called the plasma membrane.

Cell membrane

The cell membrane is a lipid bilayer membrane having a thickness of 7.5 to 10 nm, into which various protein molecules are inserted. Lipids constitute about 45% of the dry weight of the membrane and protein constitutes about 50% and carbohydrate constitutes 5%. Cell membrane maintains a constant intracellular environment such as constant cell volume and ionic composition which is essential for functioning of the organelles.

Lipid bilayer: This forms a permeability barrier between the interstitial fluid and the cell cytoplasm. The permeability of a substance depends on whether it is lipid-soluble or water-soluble. The lipid bi layered membrane is a semipermeable membrane because lipid soluble substances like oxygen and alcohol pass easily through it, whereas water soluble substances like urea and glucose do not pass easily.

Membrane proteins: These are of two types: **Integral proteins** and peripheral proteins. Integral proteins also called transmembrane proteins are those that span the entire thickness of the membrane. They serve as channel proteins, ion pumps, carriers, receptors, enzymes and some have antigenic functions. **Peripheral proteins** are those that are inserted lightly in the outer or inner border

Table 1.1.1: Functions of cell membrane

Integral proteins	• Act as channels or pores for diffusion of substances • Act as ion pumps • Act as carriers for transporting substance that cannot pass through the lipid layer • Act as receptors for water-soluble chemicals, such as peptide hormones • Act as enzyme proteins • Possess antigenic functions
Peripheral proteins	• Function as enzymes or as controllers of transport of substances through the cell membrane.
Carbohydrate moiety	• Repels other negative objects as they have negative electrical charge • Helps in attaching cells to one another due to the presence of glycocalyx • Act as receptor substances for binding hormones, such as insulin which in turn may activate a cascade of intracellular enzymes • May enter into immune reactions

of the membrane. They function as enzymes or as controllers of transport of substances through the cell membrane. Carbohydrate moieties are attached to the outer surface of the cell and they have several important functions. (Tab.1.1.1)

Cell organelles:

Various organelles such as mitochondria, endoplasmic reticulum, Golgi apparatus, ribosome, peroxisome, lysosome and centriole are present in a cell.

Mitochondria are the **"powerhouse"** of the cell. Each mitochondrion has outer and inner mitochondrial membranes and the inner cavity is filled with mitochondrial matrix that contains lot of enzymes. These enzymes participate in the oxidative reactions that occur inside the mitochondria, and the energy that is released is used to form the high-energy compound ATP. Mitochondria also have strands of DNA and are capable of self-replication. (Fig 1.1.1)

Endoplasmic reticulum (ER) consists of a network of tubular and vesicular structures in the cytoplasm which interconnect with one another. They are bilayered and the space in between the membrane is filled with an endoplasmic matrix. Endoplasmic reticulum is of two types namely rough and smooth endoplasmic reticulum. When the surface of ER is speckled with ribosomes, it is called rough endoplasmic or granular endoplasmic as it gives a **"rough"** or **"granular"** appearance to it. Rough endoplasmic reticulum is concerned with protein synthesis. When ribosomes are not attached to the surface of endoplasmic reticulum, it is called smooth endoplasmic reticulum or agranular endoplasmic reticulum as its surface has **"smooth"** or **"agranular"** appearance. Smooth endoplasmic reticulum is concerned with the synthesis of lipids. In muscle tissue, it is called sarcoplasmic reticulum.

Golgi apparatus has membranes similar to that of agranular endoplasmic reticulum and is located close to the nucleus. It has three or four stacked layers of thin flat enclosed vesicles. Golgi apparatus transports substances from endoplasmic reticulum to golgi apparatus and processes them to form lysosomes, secretory vesicles, and other cytoplasmic components. In short, it is the site for the packing of secretory products into the secretory granules and transports them to other organelles and cell surface.

Lysosomes are membrane-bound organelles that are formed by breaking off from Golgi apparatus. They contain enzymes which are responsible for intracytoplasmic digestion of the (i) damaged cellular structures, (2) food particles ingested by the cell, and (3) unwanted matter such as infective organisms and foreign bodies. Lysosomes are hence called **suicidal bags.**

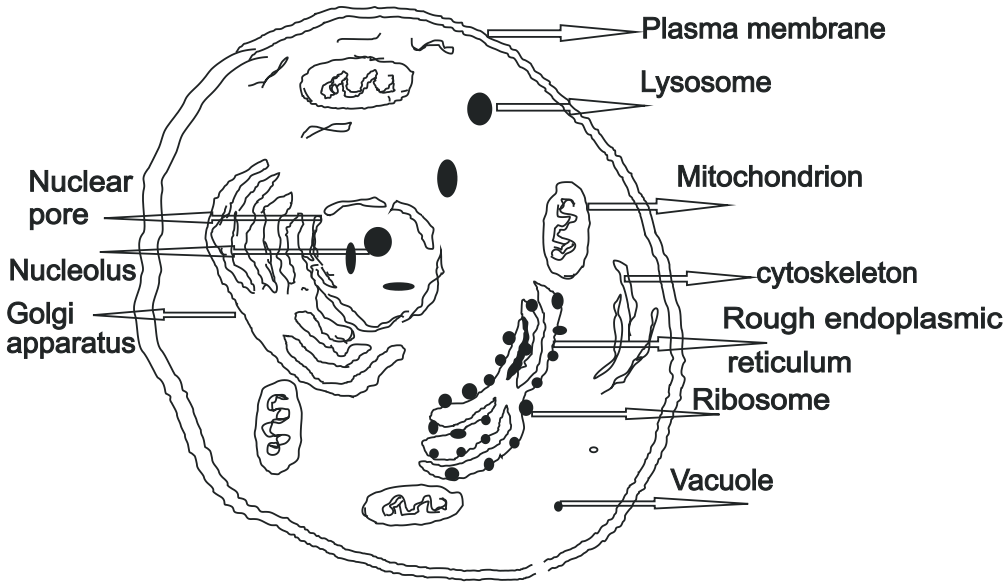

Fig. 1.1.1 Human cell

Ribosomes are composed of a mixture of RNA and proteins. Ribosomes are usually present on the surface of endoplasmic reticulum and they are also present as free ribosomes in the cytoplasm. Their function is to synthesize new protein molecules.

Peroxisomes are small spherical organelles formed by pinching off from the smooth endoplasmic reticulum. They contain oxidases and catalases which play a role in reducing oxidative injury in the cell.

Centrosomes are cylindrical structures located near the nucleus of the cell. They are made up of microtubules. Each microtuble has two centrioles placed at right angles to each other. Centrosomes regulate chromosome movement during cell division.

Cytoskeleton is an intracellular system of fibers which maintain the structural integrity of the cell, and allow desired change in cell shape for cell mobility and participation of cell in various physiological activities. Cytoskeleton comprises microfilaments, microtubules and intermediate filaments which are made up of different cell proteins. Cytoskeleton serves three functions: mechanical support; anchor organelles; and help move substances.

Nucleus

Nucleus is the **control centre** of a cell. It is commonly located at the center of the cell and is surrounded by a bilayered nuclear membrane and contains large quantities of DNA. The nuclear membrane has many nuclear pores which serve as passages for the exchange of materials between the cytoplasm and the nucleoplasm. The nucleus contains nucleolus, a patchwork of granules that are rich in RNA. There may be multiple nucleoli in a nucleus, especially in developing cells. Nucleoli do not have a limiting membrane and they synthesize ribosomes. Nucleus regulates cell functions. The DNA in the nucleus is responsible for transmission of hereditary features and the RNA is essential for protein synthesis. Nucleus is the main regulator of cell division.

Intercellular junctions

Intercellular junctions can be classified as follows:

(i) Occluding Junctions - Tight Junctions (Zona Occludens)

(ii) Anchoring Junctions - Actin filament attachment sites: Cell-cell junctions (Zonula Adherens) & Cell-matrix junction (Focal Adhesions) and Intermediate filament attachment sites: Cell-cell junction (Desmosomes) & Cell-matrix junction (Hemidesmosomes)

(iii) Channel Forming Junctions - Gap junctions

(iv) Signal Relaying Junctions - Chemical synapse. (Fig.1.1.2)

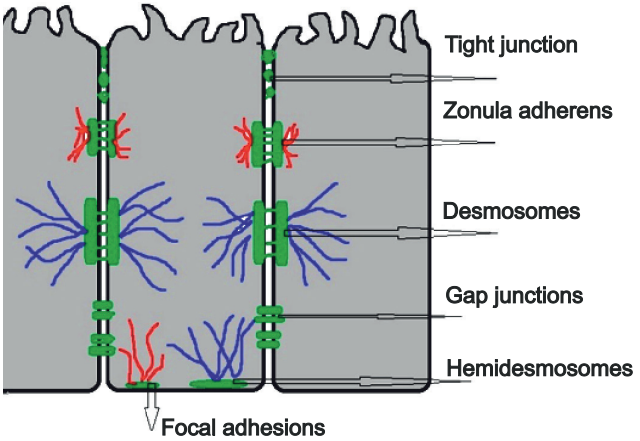

Fig. 1.1.2 Intercellular junctions

Tight junctions seal gap between epithelial cells. Zonula Adherens junction connects actin filament bundle in one cell with that in the next cell. Focal adhesion anchors actin filaments in cell to extracellular matrix. Desmosomes are cell structure specialized for cell-to-cell adhesion. They connect intermediate filament in one cell to those in the next cell. Hemidesmosomes look like half-desmosomes that attach cells to the underlying basal lamina. They anchor intermediate filament in a cell to extracellular matrix. Gap junctions allow the passage of small water soluble molecules from cell to cell.

Chapter 1.2

Body Fluid Compartments

Objectives:

At the end of the chapter, the reader should be able to

- List the various body fluid compartments
- Enumerate the differences in composition between the various fluid compartments
- Describe the methods of measurement of body fluid compartments
- List the applied aspects

Introduction:

A knowledge about the body fluid compartments is essential for the medical and paramedical personnel to identify the signs of dehydration and the nature of electrolyte imbalance in a patient, and it forms the basis for preferential choice of intravenous fluids. In an average 70 kg adult man, Total Body Water (TBW) is about 60% of his body weight or 42L. This TBW varies with age, gender and BMI (Body Mass Index). Generally, in males, water constitutes 55-60% of body weight (BWt) and in females, 45-50% of body weight. In a fetus, water constitutes 85-90% of body weight, in a newborn, 75-80% of body weight and it progressively decreases with advance in age. An interesting fact is that muscle comprises 50%, skin comprises 30%, and blood comprises 10% of TBW.

Body fluid compartments:

Body fluid compartments include the intracellular compartment and the extracellular compartment. (Fig1.2.1)

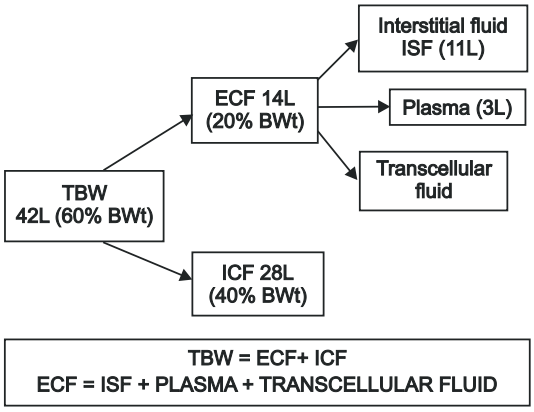

Fig. 1.2.1 Compartments of TBW in a 70 kg man

The intracellular compartment (ICF) is the largest fluid compartment and it forms 2/3rd of TBW (28L). It accounts for 40% of body weight and is separated from extracellular fluid by cell membrane. ICF contains large quantities of cations namely potassium, magnesium and anions such as phosphates and proteins. Besides, ICF has other ions such as sodium, chloride and sulphate in lesser quantities. Table 1.2.1

Table 1.2.1: Ionic composition of body fluids (m osm/L)

	Ions	Plasma	ISF	ICF
Cations	Sodium	142	139	14
	Potassium	4.2	4	140
	Magnesium	0.8	0.7	20
	Calcium	1.3	1.2	0
Anions	Chloride	108	108	4
	Bicarbonate	24	28.3	10
	Phosphate	2	2	11
	Protein	1.2	0.2	4

Extracellular fluid space (ECF) also called the *"milieu interior "forms* 1/3rd of TBW (14L) and accounts for 20% of body weight. ECF is further divided by capillary membrane into two compartments namely interstitial fluid compartment (15%) which forms 3/4th of ECF (11L) and plasma (5%) which forms 1/4th of ECF (3L). The chief cation in ECF is sodium and the chief anions are chloride and bicarbonate. The difference between ICF and ECF constituents is maintained by the $Na^+ K^+$ ATPase pump.

Interstitial Fluid (Tissue fluid), a part of ECF, transports substances between the cells and blood plasma. Interstitial fluid is formed by plasma filtration at capillaries, as governed by Starling's forces. A balance between the two processes of capillary filtration and reabsorption is assisted by the local lymphatic drainage.

ECF also has a small transcellular fluid compartment which includes cerebrospinal fluid, synovial (joint), gastrointestinal, biliary, pleural, pericardial, and intraocular fluids.

Measurement of body fluid compartments: Indicator Dilution Principle is used to measure the body fluid compartments. This is based on the relationship between the amount of substance administered (I), the volume of space in which the substance is distributed (V) and the final plasma concentration of the substance (C). Since some of the substance gets metabolized and excreted, the i.e. /

Volume of fluid compartment = (Amount administered – Amount metabolized and excreted)/ final plasma concentration.

$$\text{Volume of fluid space (V)} = \frac{I}{C} \quad \frac{\text{Amount administered}}{\text{Final Concentration}}$$

Substances used to measure TBW include tritium oxide ($3H_2O$), deuterium oxide ($2H_2O$), antipyrine, urea and thiourea. Substances used to measure ECF volume are inulin, sucrose, mannitol, radioactive sodium, radioactive chloride, radioactive iothalamate and thiosulfate ion. Different substances penetrate ECF space to various extents. Therefore, the volume of ECF determined by various substances is designated as the space occupied by that substance. Example: sucrose space, thiocyanate space etc.

Blood volume:

Blood constitutes 6-8% of body weight in healthy adult males. Blood volume of 5L or 60-80ml/kg BW comprises plasma volume (55%) and red cell mass (PCV 45%). Measurement of plasma volume is done using substances that do not leave the vascular compartment and do not enter blood cells. They are Evans blue or T-1824 and Radio Iodinated human Serum Albumin. Calculation of blood volume can be done after determining plasma volume using the isotope method and if hematocrit or PCV is already known.

BV = Plasma volume/ 1-Hematocrit.

Applied aspects:

Disturbances of volume and composition of body fluids (osmolarity) can occur in various clinical conditions. **Dehydration** is water loss or ECF volume contraction. The causes could be (blood loss) hemorrhage, plasma loss through burns; Gastrointestinal fluid loss through vomiting and diarrhea. **Over hydration** is water gain or ECF volume expansion. E.g. Edema or swelling as in renal failure (retention of salt & water), heart disease and hypoproteinemia. Edema is excess accumulation of fluid in the body tissues particularly extracellular fluid compartment.

Chapter 1.3

Homeostasis

Objectives:

At the end of the chapter, the reader should be able to

- Define homeostasis
- Describe the basic concept of homeostasis
- Explain the feedback mechanisms involved in maintaining homeostasis
- List the disturbances in homeostasis

Introduction:

Homeostasis is all about a balancing act!! It's a balance between demands placed on the body and the physiological response to those demands. **Claude Bernard** (1813-1878), a **French Physiologist** explained the concept of milieu interieur. He recognised that many animals regulate their internal environment even if the external environment changes. **Walter B Canon** (1871- 1945) coined the term 'homeostasis' in 1926.(*Homoios: similar, stasis: position*). In short, homeostasis refers to maintaining internal stability within an organism and returning to a particular stable state after a fluctuation.

Basic concept of homeostasis:

In a multicellular organism, extracellular fluid (ECF) forms the internal environment. ECF is nothing but a thin layer of fluid around the cell and this ECF is in constant motion. There is continuous movement of blood in the circulatory system, movement of fluid between blood capillaries and interstitial fluid and movement of fluid between interstitial fluid and the cell.

Why is homeostasis required?

For optimal cellular activity. Optimal is the level at which enzyme systems function best.

What should be maintained as a constant?

Temperature, volume, pH, electrolyte composition, nutrients and the concentration of waste products have to be maintained a constant in the ECF.

When does homeostasis have to be achieved?

Whenever there is any change in the internal environment, for example as while performing exercise: Metabolic activities require a supply of materials (oxygen, nutrients, salts, etc.,) that must be replenished and the waste products that are produced must be expelled.

What are the systems that help in achieving homeostasis?

Almost every system helps in achieving homeostasis. Respiratory system helps in acquiring oxygen required for the body, gastrointestinal system including the liver help in digesting, metabolizing and absorbing the nutrients required for the body and musculoskeletal system helps in moving and acquiring food for the body. Excretory, Respiratory and Integumentary systems help in removing the waste products from the body. Nervous system, Endocrine glands and Immune system help in regulating the various body functions.

How is homeostasis achieved?

It is by a biological control system which regulates some physiological variable at or near constant value either by a negative feedback mechanism or a positive feedback mechanism

Components of a biological control system: It comprises a **'Receptor'** which is capable of detecting changes, **'Integrating center'** which assesses input and initiates response and an **'Effector'** which corrects changes to internal environment. (Fig.1.3.1)

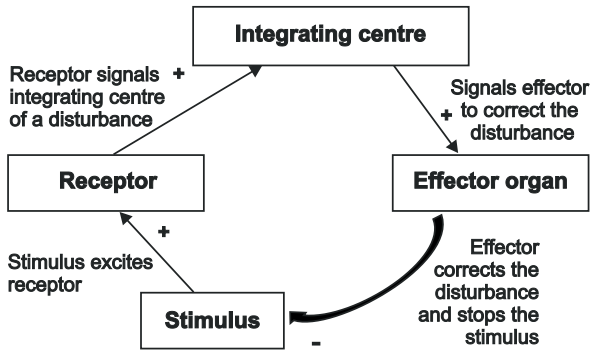

Fig. 1.3.1 Biological control system

Negative feedback mechanism:

The response counteracts the stimulus shutting off the response. i.e the response is negative to the initial stimulus. (Fig.1.3.2)

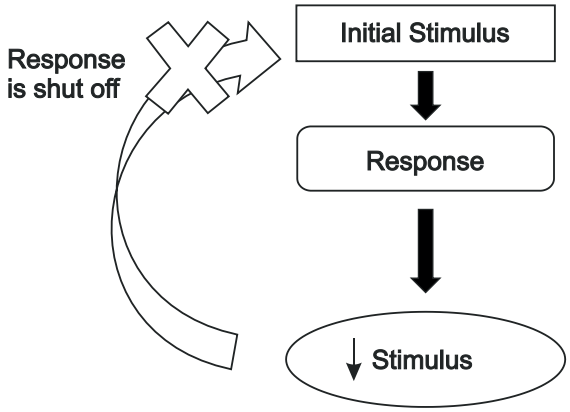

Fig. 1.3.2 Negative feedback mechanism

Eg; temperature regulation. Though heat is lost through radiation, conduction and convection mechanisms, any increase in temperature may activate the heat loss mechanisms such as increase in sweating and vasodilation resulting in further heat loss so that the temperature returns back to normal. Other examples include: regulation of blood glucose level and regulation of blood pressure.

Positive feedback mechanism:

The response reinforces the stimulus and an outside factor is required to shut off the response. (Fig.1.3.3)

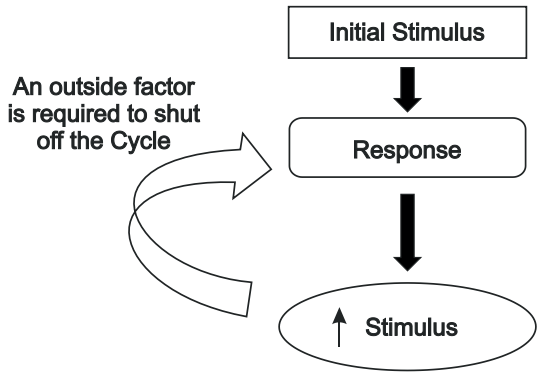

Fig. 1.3.3 Positive feedback mechanism

Eg: Parturition reflex. Stretch of the cervix by the fetal head leads to oxytocin release which causes uterine contraction leading to further descent of fetal head leading to further stretch of the cervix leading to further oxytocin release by positive feedback mechanism until the fetus is born. (Fig.1.3.4)

Other examples include LH (Lutenising hormone) surge: Increased LH secretion leads to ovulation. Normally, estrogen inhibits LH, but before ovulation,

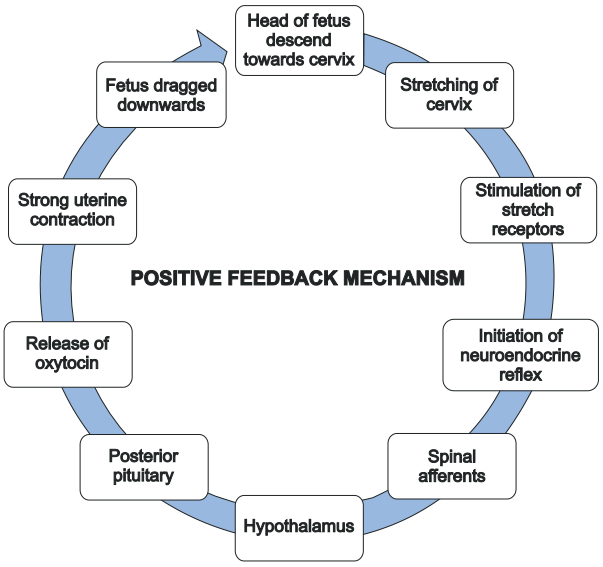

Fig. 1.3.4 Positive feedback mechanism

estrogen provides positive feedback to LH resulting in LH surge. Action potential – opening of voltage gated sodium channels – positive feedback – further sodium influx – depolarization.

Positive feedback mechanisms may be harmful at times. Fall in blood pressure beyond a certain level will reduce the blood flow to the heart muscle through the coronary blood vessels which in turn will reduce the efficiency of cardiac pumps leading to further decrease in coronary blood flow. This **vicious cycle** repeats leading to death.

Quality of a negative feedback control can be assessed in terms of gain. It is the degree to which the control system maintains homeostasis.

Gain = Correction/Error.

System with large gain is more capable of maintaining homeostasis. Gain is more for temperature regulating mechanisms.

Applied aspects:

Most diseases and/or disorders result from homeostatic imbalance. Homeostatic mechanisms may fail due to aging (Homeostenosis). With aging, body organs and control systems become less efficient, the internal environment becomes less and less stable and there is greater risk of illness/injury. It may also fail due to congenital metabolic disorders, chromosomal abnormalities and environment factors such as UV radiation and chemical pollutants.

Chapter 1.4

Transport Across Cell Membrane

Objectives:

At the end of the chapter, the reader should be able to

- List the various types of transport across cell membrane
- Explain in detail about active and passive transport
- Brief about sodium potassium pump
- List the applied aspects

Introduction:

Cell membrane also called the plasma membrane is made up of lipid bilayer. This double layered cell membrane is interspersed with globular protein molecules. Any substance has to cross the cell membrane to enter or leave the cell. There are various mechanisms by which substances are transported across cell membranes.

Types of transport:

Fig.1.4.1 depicts the different modes of transport across cell membranes.

Passive	Active	Vesicular

• Simple Diffusion
• Facilitated Diffusion
• Osmosis
	• Primary
	• Secondary
	  • Co (symport)
	  • Counter (antiport)
		• Excytosis
		• Endocytosis
		• Pinocytosis
		• Phagocytosis
		• Receptor mediated endocytosis

Fig. 1.4.1 Types of transport

Passive transport: Diffusion is passive transport of substances from an area of higher concentration to lower concentration.

Simple diffusion shows continuous random movement of molecules which occur using kinetic energy. Simple diffusion can occur by two pathways. (Fig.1.4.2) Movement of lipid soluble substances is faster and it occurs directly through lipid bilayer. E.g.

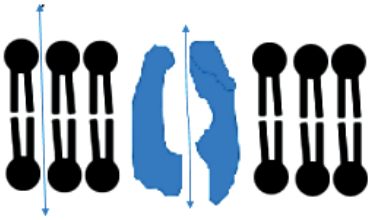

Fig. 1.4.2 Simple diffusion

oxygen, carbon dioxide, steroid hormones etc., Lipid insoluble substances move through channel proteins. These protein channels are either continuously open or gated. Gated channels are either voltage gated or ligand gated. E.g. Movement of water molecules through aquaporin channels and this movement is influenced by ADH in the kidney.

Facilitated diffusion is mediated through carrier protein and is energy independent. It occurs down the concentration/electrical gradient and is faster than simple diffusion. (Fig.1.4.3) Facilitated diffusion is specific and it shows saturation kinetics and is susceptible to competitive inhibition. E.g. transport of glucose from ECF to ICF by glucose transporter protein (GLUT)

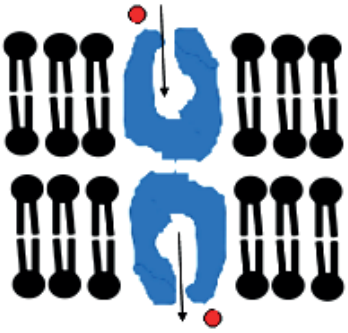

Fig. 1.4.3 Facilitated diffusion

Osmosis is diffusion of pure solvent from an area of high water concentration (low solute concentration) to an area of low water concentration (high solute concentration) through a semipermeable membrane. The pressure necessary to prevent solvent migration is called osmotic pressure.

Active transport: It is a process by which substances are transported against concentration (from lower concentration to higher concentration), electrical or pressure gradient with expenditure of energy. It requires ATP and carrier protein (pumps). Two types of active transport are: primary active transport and secondary active transport. Secondary active transport is of two subtypes namely co–transport / symport and countertransport / antiport.

Primary active transport is a type of active transport in which energy is directly derived from hydrolysis of ATP or other high energy phosphate compounds. E.g. Na^+K^+ ATPase pump which is present in all animal cell membranes which

catalyzes ATP dependent transport of sodium out of a cell in exchange for potassium entering inside the cell. (Fig.1.4.4) Other examples include Ca^{++}ATPase (cell cytosol) and H^+K^+ ATPase (stomach for acid secretion). Na^+ K^+ ATPase pump has the following functions: Maintains cell volume; Acts as an electrogenic pump and plays a major role in genesis of action potential; Stores energy for secondary active transport and allows passive movement of Cl^-, HCO_3^-, H_2O etc.,

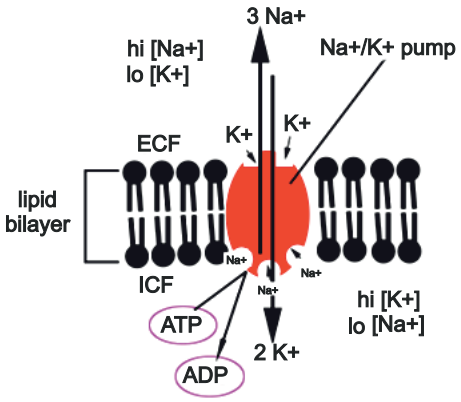

Fig. 1.4.4 Na^+K^+ ATPase pump

Secondary active transport is a coupled transport and the energy needed for "uphill" movement is obtained from "downhill" transport of sodium ions. Hydrolysis of ATP by Na^+K^+ ATPase pump is required indirectly to maintain sodium gradient. In symport (Co-transport), the carrier binds two substrates and transports them together across the cell membrane in the same direction. E.g. sodium glucose symport in intestine and renal tubules by sodium glucose transporter protein S.G.L.T. (Fig.1.4.5)

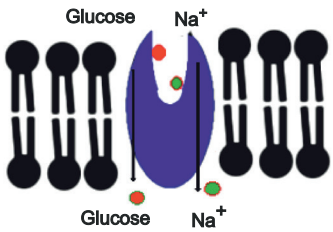

Fig. 1.4.5 Secondary active transport (co)

In antiport, carriers exchange one solute for another across the cell membrane. E.g. Cation exchanger: Na^+/ Ca^{++} in cell membrane (Fig.1.4.6) and Na^+/ H^+ in renal tubules; Anion exchanger: Cl^-/ HCO_3^- in RBC membrane.

Vesicular transport is the mode of transport for macromolecules. It is energy and calcium dependent.

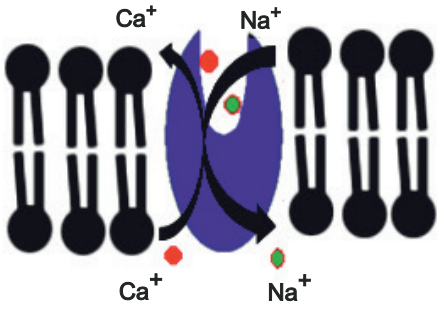

Fig. 1.4.6 Secondary active transport (counter)

There are various types namely exocytosis, endocytosis, pinocytosis, phagocytosis and receptor mediated endocytosis. **Exocytosis** is a process in which substance is transported out of the cell by fusion of the vesicle with cell membrane and expulsion of its contents. E.g. protein secretion from the cell. **Endocytosis** is a process in which substance is transported into the cell by invagination of a portion of cell membrane trapping macromolecules from outside and forming a vesicle around the substance. **Pinocytosis** is endocytosis for small soluble substances and is visible only under electron microscope. It is also called 'cell drinking'. E.g. thyroglobulin entry in follicular cells. Phagocytosis is endocytosis for large insoluble particles like dead cell, bacterium, tissue debris etc., It is seen in tissue macrophages and WBC (neutrophil). It is also called 'cell eating'. **Receptor mediated endocytosis** is a type of vesicular transport in which clathrin coated pits on cell membranes act as receptors which mediate the endocytosis process. E.g. internalisation of LDL cholesterol, nerve growth factor etc., Transcytosis also called cytopempsis involves both exocytosis and endocytosis. E.g. protein crosses capillary endothelial wall by endocytosis and interstitial side by exocytosis.

Applied aspects:

- Symport : Oral rehydration therapy is based on cotransport of glucose and sodium into intestinal epithelial cells via the SGLT protein which help in rapid absorption and restoration of body fluid volume.

- Antiport: Ouabain, digitalis in cardiac muscle blocks Na^+K^+ATPase pump thereby depressing Na^+/ Ca^{++} antiport mechanism leading to an increase in intracellular Ca^{++} which has a positive inotropic effect. Hence, this is used in heart failure.

Chapter 1.5

Bioelectric Potentials

Objectives:

At the end of the chapter, the reader should be able to

- Define bioelectric potential
- Describe the genesis and ionic basis of resting membrane potential
- Describe the ionic basis of action potential
- Define local potential
- List the differences between action potential and local potential

Introduction:

Beating of heart, functioning of nervous system and contraction of muscles etc are all associated with electrical phenomena and they are studied by Electrocardiography (ECG), Electro Encephalo Graphy (EEG) and ElectroMyoGraphy (EMG). To initiate, regulate, coordinate and perform complex biological activities throughout our body, a uniform messaging system is required. These messaging units are bioelectric potentials. It is the language spoken and understood by all the cells in our body. All cells are separated from their environments by their cell membrane. This lipid bilayer membrane is a barrier between intracellular and extracellular environments. This not only serves as a barrier between two fluid environments but also separates two electrical environments.

Genesis of resting membrane potential: Difference in electrical charge across the cell membrane in a cell under resting condition is called resting membrane potential (RMP). Potential/ Voltage difference exists between the cell interior and the surrounding medium due to concentration difference of ions in ICF and ECF. (ECF has more of Na^+, Cl^- and ICF has more of K^+, $Prot^-$, PO_4^{3-}). Charged particles in and around the cell interact resulting in the development of potential and it should be noted that there is no potential difference deep in the cytoplasm. In short, bioelectric potential exists between interior and exterior of the cell membrane and it is always negative at rest. RMP ranges from -9mV to -90mV. RMP of skeletal muscle and large diameter peripheral nerve is -90mV and RMP of smooth muscle and thin nerve is -40 to -60 mV.

Ionic basis of RMP:

RMP is due to ionic imbalance across cell membrane which is effected by

(i) **diffusion potential** of potassium [tendency of potassium ions to flow out of the cell, together with the indiffusibility of anions present inside the cell]. Diffusion potential is the potential difference that is created due to diffusion of ions from areas of high concentration to low concentration. Initial concentration gradient leads to diffusion resulting in an electrical gradient which ultimately causes repulsion leading to diffusion in the opposite direction. This process continues until an equilibrium is attained. At this equilibrium potential, there is no net movement of ions because the opposing forces acting upon it are exactly balanced. In short, the potential level across the cell membrane that prevents net diffusion of an ion in either direction is termed as equilibrium potential.

(ii) **Membrane permeability** is determined by specific membrane transport /gated channels. In the ICF, anionic protein molecules dominate and the channels for such anionic protein molecules are either non-existent or closed. It is because of these intracellularly-trapped, negatively charged

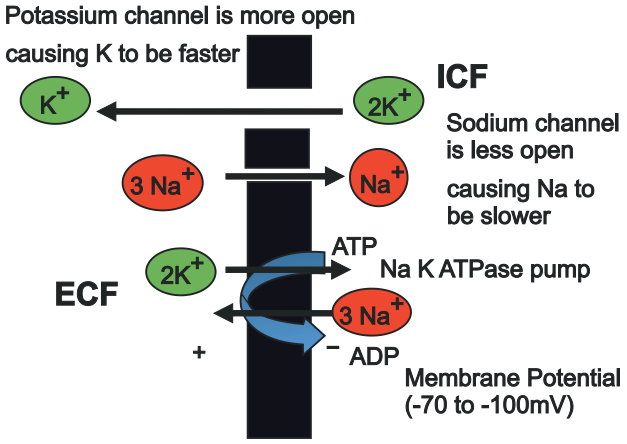

Fig. 1.5.1 Resting membrane potential

molecules that the intracellular compartment ends up being a bit more negative than the extracellular compartment. In the ECF, chloride ions dominate and invariably the chloride channels are closed. Now, the only ions that can move across cell membranes are sodium and potassium. In a resting cell, many of the potassium channels remain open and most of the sodium channels are closed. (Fig. 1.5.1) Hence, the cell membrane is more permeable for potassium at rest.

To counteract this (iii) **Sodium potassium pump** moves 3 sodium ions out and 2 potassium ions into the cell resulting in slight intracellular negativity. Sodium potassium pump is an active transport mechanism which transports sodium & potassium in opposite directions creating an imbalance in distribution of positive ions and resulting in differences in electrical charge across the cell membrane i.e., resting membrane potential. In short, RMP is due to ionic imbalance across cell membrane which is effected by (i)Diffusion potential of potassium ions [tendency of the potassium ions to flow out together with the indiffusibility of anions] (ii)More open potassium channels than sodium and (iii) By operation of Na^+ K^+ pump.

Local potential:

Cell membrane at rest is said to be polarized. Depolarization is a decrease in the electronegativity of the interior of a resting cell. Repolarization is the return of RMP after depolarization. Hyperpolarization is an increase in electronegativity within a cell. Potential changes from RMP do occur. If depolarisation is less than the firing level, it ends up in local potential. If depolarisation is beyond firing level, it results in action potential. Local changes in membrane potential can be either in depolarising or hyperpolarising direction. Local potential is also called Graded potential [magnitude of deviation from RMP is proportional to magnitude of stimulus]. Examples of Graded potential include End plate potential, EPSP, IPSP, and Receptor potential. The differences between graded potential and action potential is given in Table.1.5.1.

Action potential:

Cell is said to be polarised at rest. Action potential is a brief, all or none , reversal of membrane potential. It has a threshold, refractory period and is conducted without decrement. Sequence of changes in the membrane potential which spread rapidly along a nerve fiber when a threshold stimulus is applied results in action potential. There are three stages namely: resting stage, depolarisation stage and repolarisation stage. Latent period is the time taken by an impulse to travel from stimulating electrode to recording electrode.

Ionic basis of action potential:

Depolarising stage: Stimulus triggers sodium channels to open and allow inward sodium diffusion causing the cell membrane to depolarise. As the threshold point is reached [-70 to -50 mV], voltage

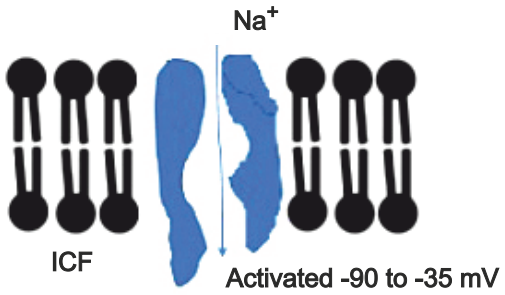

Fig. 1.5.2 Depolarising stage

Table.1.5.1. Differences between graded potential and action potential

Graded Potential	Action Potential
Graded response	All or none response
Can be summated	Cannot be summated
Has no threshold	Has a threshold
Conducted with decrement	Propagated without decrement
Depolarisation/ hyperpolarisation	Depolarisation

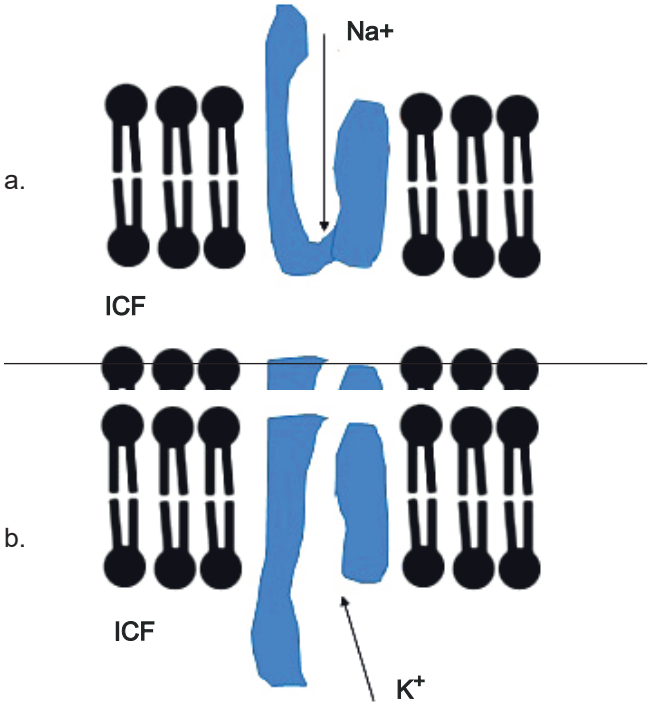

Fig. 1.5.3 Repolarising stage

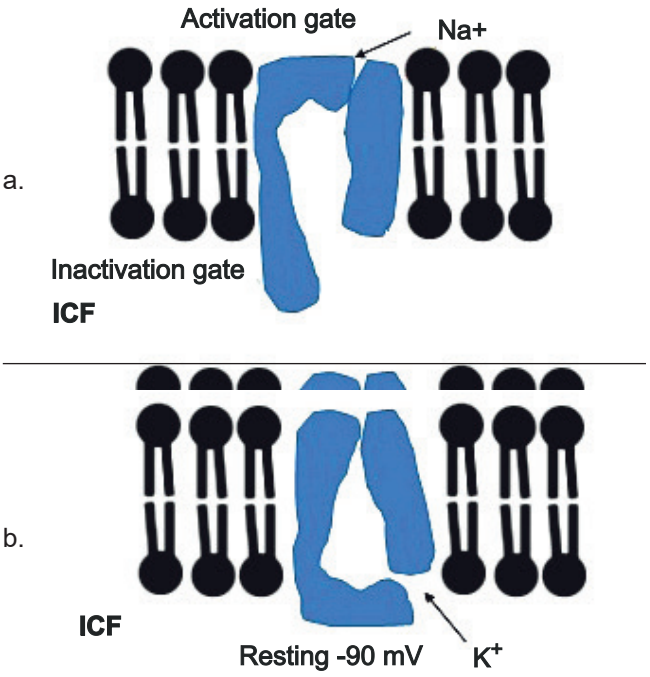

Fig. 1.5.4 Hyper polarising & Resting stage

gated sodium channels open. Activation gate opens and the permeability increases to 500 – 5000 times and is a rapid process. (Fig.1.5.2)

Repolarising stage: The same increase in voltage [-70 to -50 mV] closes the inactivation gate of the sodium channel and opens the activation gate of potassium channel with a delay of 10,000th of a sec. (Fig.1.5.3)

Hyper polarising stage: Potassium channels remain open for several milliseconds after repolarisation. (Fig.1.5.4) After hyperpolarisation, RMP is restored by Na^+K^+ pump and return of ion channels to resting state.

Action potential elicited at one point on an excitable membrane excites adjacent portions of membrane. Local current flow triggers voltage sensitive sodium channels in the next segment to open; sodium rushes inside the cell resulting in action potential. AP never moves back because of the refractory period of the previous segment. AP travels in all directions away from stimulus. Transmission of depolarisation along muscle fibre results in muscle impulse. Propagation of AP in myelinated nerve fibre is faster when compared with unmyelinated fibre due to saltatory conduction.

Applied aspects:

ECG, EEG and EMG are the record of electrical activities of heart, nerve and muscle respectively. Induced electrical activities called as Evoked potentials can also be recorded and interpreted which has wide applications in clinical set up.