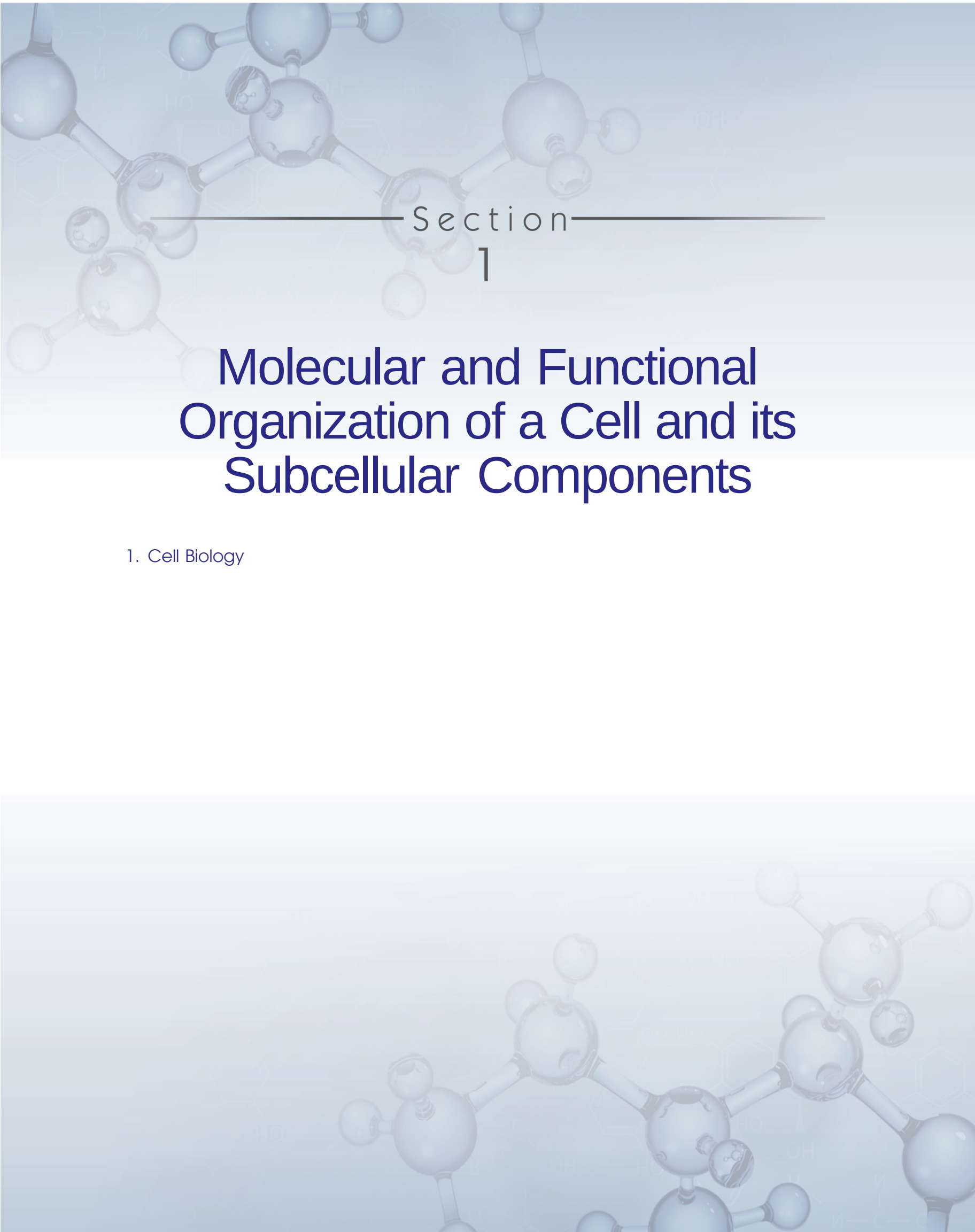


The background of the slide features a complex, semi-transparent molecular structure. It consists of numerous spheres of varying sizes, representing atoms, connected by lines representing chemical bonds. The spheres are primarily light blue and white, with some darker blue accents. The overall structure is intricate, resembling a network of interconnected molecules or a large protein complex. The text 'Section 1' is centered over this background, with a horizontal line passing through the word 'Section'.

Section

1

Molecular and Functional Organization of a Cell and its Subcellular Components

1. Cell Biology

Cell Biology

Competency achievement: The student after reading the chapter should be able to:

BI1.1: Describe the molecular and functional organization of a cell and its subcellular components.

HISTORY

Cell biology is the branch of biology that deals with the study of structural and functional unit of cell and subcellular organelles and its relation to the metabolism, growth, differentiation, heredity and evolution. The cell theory, or cell doctrine, states that all organisms are composed of similar units of organization, called cells. **The concept was formally articulated in 1839 by Schleiden and Schwann and has remained as the foundation of modern biology.** The idea predates other great paradigms of biology including Darwin's theory of evolution (1859), Mendel's laws of inheritance (1865), and the establishment of comparative biochemistry (1940). While the invention of the telescope made the Cosmos accessible to human observation, the microscope opened up smaller worlds, showing what living forms were composed of. **The cell was first discovered and named by Robert Hooke in 1665.** He remarked that it looked strangely similar to cellula or small rooms which monks inhabited, thus deriving the name. However, what Hooke actually saw was the dead cell walls of plant cells (cork) as it appeared under the microscope. Hooke's description of these cells was published in *Micrographia*. The cell walls observed by Hooke gave no indication of the nucleus and other organelles found in most living cells. The first man to witness a live cell under a microscope was Antonie van Leeuwenhoek, who in 1674 described the algae *Spirogyra*. Van Leeuwenhoek probably also saw bacteria.

As with the rapid growth of molecular biology in the mid-20th century, cell biology research exploded in the 1950's. It became possible to maintain, grow, and manipulate cells outside of living organisms. The first continuous cell line to be so cultured was in 1951 by George Otto Gey and coworkers, derived from cervical cancer cells taken from Henrietta Lacks, who died from her cancer in 1951. The cell line, which was eventually referred to as HeLa cells, have

been the watershed in studying cell biology, that the structure of DNA was the significant breakthrough of molecular biology.

The cell content was named as '**protoplasm**' by the scientist Purkinje in 1839. Scientist O Hertwig in 1892 stated that "The cell is an accumulation of a living substance 'protoplasm' possessing a nucleus and a cell membrane. Both the constituents are equally important and the disappearance of one or the other destroys the cell theory."

CELLS

The entire organism consists of cells. All multicellular organisms contain billions or trillions of cells organized into complex structures, but many organisms consist of a single cell. Even simple unicellular organisms exhibit all the characteristic properties of life, representing that the cell is the fundamental unit of life.

In general, two types of cells exist in nature. They are:

1. Prokaryotic cells, and
2. Eukaryotic cells

Prokaryotic cells

Prokaryotic cells (Greek *pro*—primitive or primary, and *karyon*—nucleus) do not have a well-defined nucleus or have nucleic acid but nuclear membrane is absent, e.g. bacteria. Eukaryote cells have a membrane-bound well-defined nucleus and other cell organelles. The two groups of prokaryotes, bacteria and archaea, contain organisms that exist as single cells, being simple in structure. As you recall, prokaryotes do not have a nucleus or other membrane-bound organelles. Fig. 1.1 shows a stylized prokaryotic cell, illustrating what a typical bacterium would look like (*E. coli*, here).

Structure of prokaryotic cell

Prokaryotic structural components consist of macromolecules such as DNA, RNA, proteins, polysaccharides, phospholipids and other. The macromolecules that make up cell material are made-up of primary subunits such as nucleotides, amino

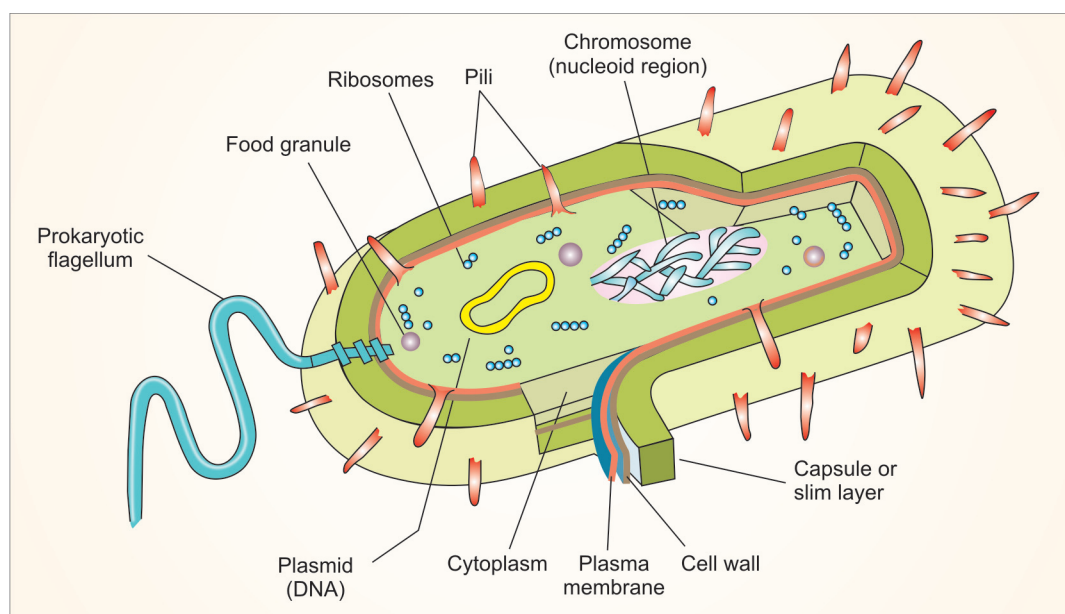


Fig. 1.1: Structure of prokaryotic cell

Table 1.1: Macromolecules that make up cell material

Macromolecules	Primary subunits	Place in cell
Proteins	Amino acids	Flagella, pili, cell walls, cytoplasmic membranes, ribosomes, cytoplasm
Polysaccharides	Sugars (carbohydrates)	Capsules, inclusions (storage), cell walls
Phospholipids	Fatty acids	Membranes
Nucleic acids (DNA/RNA)	Nucleotides	DNA: Nucleoid (chromosome), plasmids rRNA: Ribosomes; mRNA; tRNA: Cytoplasm

acids and sugar (Table 1.1). It is the sequence in which the subunits are put together in the macromolecule, called the **primary structure**.

A prokaryotic cell has five essential structural components—a **nucleoid (DNA)**, **ribosomes**, **cell membrane**, **cell wall**, and some sort of **surface layer**, which may or may not be an inherent part of the wall.

Characteristics and functions of typical bacterial cell structures

1. Flagella help in swimming movement, they consist of protein.
2. Sex pilus stabilizes mating bacteria during DNA transfer by conjugation made up of protein.
3. Common pili or fimbriae attachment to surface; protection against phagotrophic engulfment of protein.
4. Capsule (includes slime layers and glycocalyx) attachment to surface; protection against phagocytic engulfment, occasionally killing or digestion; reserve of nutrient or protection against desiccation of polysaccharide or occasionally polypeptide.
5. A gram-positive bacterium prevents osmotic lysis of cell protoplast and confers rigidity and shape on cells.

6. Gram-negative bacteria peptidoglycan prevents osmotic lysis and confers rigidity and shape; outer membrane is permeability barrier and has various functions.
7. Chromosome and plasmid extrachromosomal genetic material is DNA.

Eukaryotic cells

Eukaryotic (Greek *eu*—true, *karyon*—nucleus) cells (Fig. 1.2) are the type of living cells that form the organisms of all of the life kingdoms except monera. They are generally larger than bacterial cells. Eukaryotic cells have membrane-bound organelles. Their DNA is organized into linear threads called chromosomes which are located within a membrane, and the entire unit is called a nucleus. Organelles that might be found in a cell include ribosomes (80S), mitochondria, chloroplast and Golgi bodies. The cell surface membrane and the membranes which form organelles in eukaryotic cells, all have the same basic structure, known as the fluid mosaic model. Such membranes provide control of the entry and exit of substances into cells and organelles and such control is a result of the phospholipid bilayer and membrane proteins.

Functions

- **Cell body** contains:
 - **Nucleus**, which provides the genetic code for the production of neurotransmitter substances, e.g. acetylcholine and enzymes, e.g. cholinesterase.
 - **Dense groups of ribosomes and endoplasmic reticulum called Nissl granules** for production and transport of proteins and neurotransmitters.
- **Synaptic knob** at end of dendrite contains:
 - Many mitochondria to provide ATP for active refilling of synaptic vesicles.
 - Numerous vesicles for modification and release of chemical transmitters across the synapse.
- **Double nuclear envelope to enclose and protect DNA** (normally visible as chromatin granules).

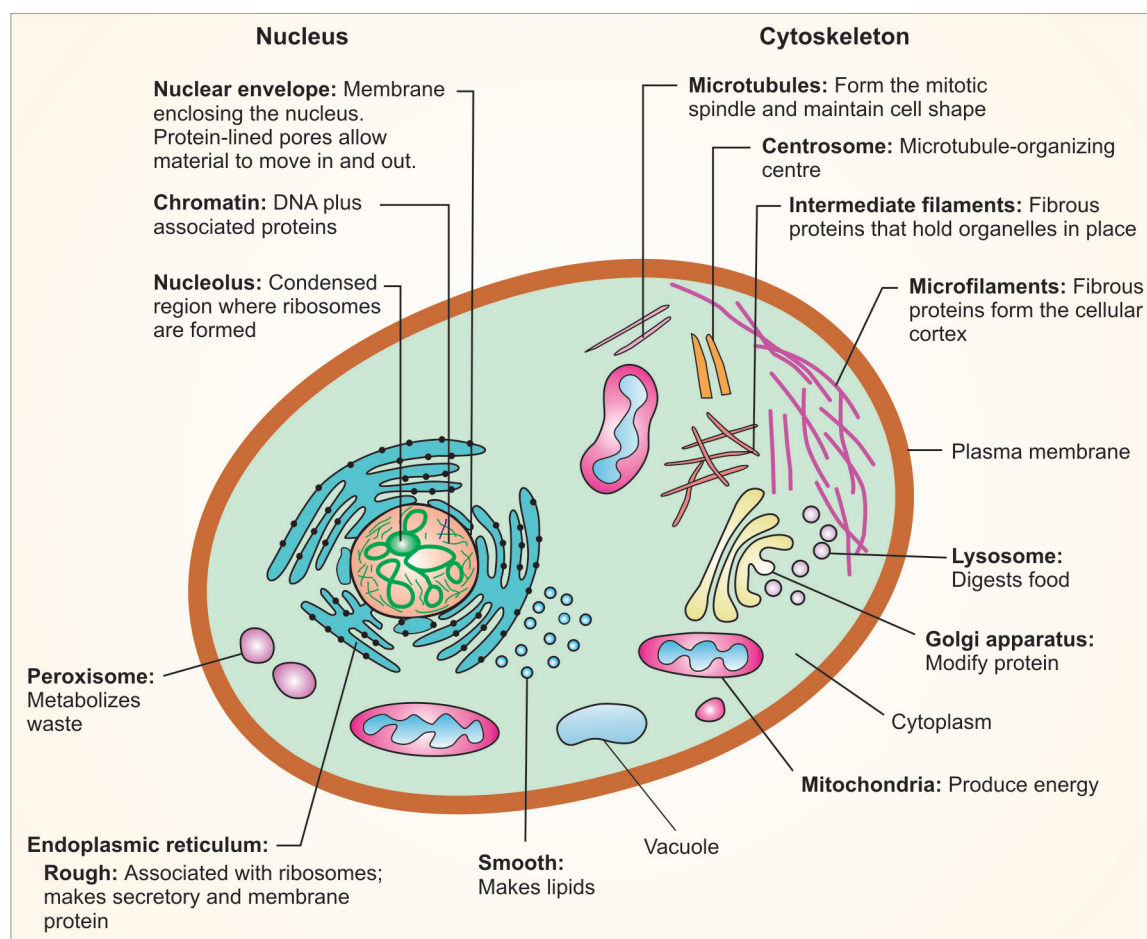


Fig. 1.2: Eukaryotic cell

- **Nuclear pores** allow entry of substances such as nucleotides for DNA replication and exit of molecules such as mRNA during protein synthesis.
- Normally, the nuclear pores are plugged by an RNA/protein complex. Small molecules pass through the pores by diffusion, whereas large molecules such as partly complete ribosomes pass through actively.
 - The matrix contains 70S ribosomes for protein manufacture, e.g. enzymes.
 - DNA codes for proteins.
 - Enzymes, e.g. decarboxylase formation of metabolism, e.g. in Krebs cycle.
- Endoplasmic reticulum is of two types:
 - Rough endoplasmic reticulum is a synthesizer of protein.
 - Smooth endoplasmic reticulum is a synthesizer of lipid.
- **Golgi body** consists of flattened cisternae (membrane-bound cavities) which may be stacked on top of each other and which may invaginate and fuse to form vesicles. This allows internal transport. Vesicles contain materials to be secreted. Vesicles protect the molecules as they are transported across the cytoplasm to the cell surface membrane.
- **Ribosomes** provide sites for the binding of mRNA which allows translation of the DNA code. There are two sites for the binding of 2 tRNA molecules. Ribosomes recognise the initiation and termination codons on mRNA. Ribosomes are capable of moving along the mRNA strand. This allows decoding of the mRNA and synthesis of a polypeptide chain.

- **Lysosomes** are vesicles which contain hydrolytic enzymes, collectively known as lysozymes. When released, these enzymes can break down old organelles, storage molecules or, indeed, the whole cell, when it dies.

All bacterial cells and archaea have a plasma membrane to regulate what enters and leaves the cell. The membrane is a phospholipid bilayer with proteins embedded in it. Most bacteria and archaea also have a cell wall exterior to the plasma membrane. Their DNA, though in a discrete region in the cell, is not separated by a membrane. Bacterial DNA is a circular molecule loose within the cell. It may be concentrated toward the middle and will attach to the plasma membrane before the cell divides. Though, there are few organelles, ribosomes are the sites of protein synthesis. Prokaryotic cells are able to carry out all functions we recognize as fundamental to life, such as reproduction and energy transduction but are much more simple in structure than eukaryotic cells.

Differences between prokaryotic and eukaryotic cells have been summarised in Table 1.2.

STRUCTURE OF CELL

Cells vary in shape and size. Usually, they are microscopic, but some of them are also visible to naked eyes. They range from 0.2 to 0.5 μ in diameter. Cells can be of any shape. Their shape usually reflects the functions it carries out in an

Table 1.2: Differences between prokaryotic and eukaryotic cells

Prokaryotic cells	Eukaryotic cells
The size is 0.1–5.0 nm.	The size is 5–100 nm.
Cell wall, if present, contains mucopeptide or peptidoglycan.	Cell wall, if present, contains cellulose, peptidoglycan is absent.
A typical nucleus is absent.	A typical nucleus made of nuclear envelope, chromatin, nucleoplasm.
DNA content is low.	DNA lies inside the nucleus, mitochondria and plastids.
DNA is naked or without any association with histone proteins.	DNA is associated with histones.
Introns are commonly absent in DNA, RNA, therefore, does not require splicing.	Introns are quite common. RNA, therefore, requires splicing before becoming operational.
Sexual reproduction is absent.	Sexual reproduction is commonly present.
Cell division does not show distinction of interphase and M phase.	A distinction of interphase and mitotic phase occurs during cell cycle.
Endocytosis and exocytosis are absent.	They occur in eukaryotic cells.
Flagella are smaller. A distinction of axoneme and sheath is absent in the flagellum.	Flagella are longer. A flagellum shows distinction of axoneme and sheath.
Cytokinesis is absent.	Cytokinesis or cytoplasmic streaming is common.
Ribosome—small size (70S).	Large size; smaller size (70S) in organelles.

organism, e.g. nerve cells which have to transmit impulses to long distances; muscle cells are elongated cells may be flat, spindle, cuboidal shaped and of other shapes as well. All cells have certain common features. Presence of nucleus in cells is one such main feature. Nucleus in cells is control centre. Bacteria and blue-green algae are devoid of a typical nucleus. Viruses have no recognisable structure. They are so small that usually they are not visible without the help of an electron microscope. They do not have cytoplasm; however, they are crystal of nucleoprotein.

Cells can grow duplicate, process in sequence, respond to stimuli, and carry out an array of chemical reactions. These abilities define life. The living matter, i.e. protoplasm is composed of mainly six elements—carbon, hydrogen, oxygen, nitrogen, phosphorus and sulfur.

So, each cell is a small container of chemicals and water wrapped in a membrane. There are 100 trillion cells in a human, and each contains all of the genetic information necessary to manufacture a human being or any living organism. This information is encoded within the nucleus of cell in the form of DNA.

Cell organelles

1. Nucleus
2. Endoplasmic reticulum
3. Golgi apparatus
4. Mitochondria
5. Lysosomes
6. Peroxisomes
7. Plasma membrane

Nucleus

Structure

Nucleus (Fig. 1.3) is a largest, double-membrane bound cell organelle found in eukaryotic cells. The nucleus appears to be dense, spherical organelle. It occupies about 10% of the total volume of the cell. In mammalian cells, the average diameter of the nucleus is approximately 6 micrometers. Nuclear membrane is made up of two membranes, the outer

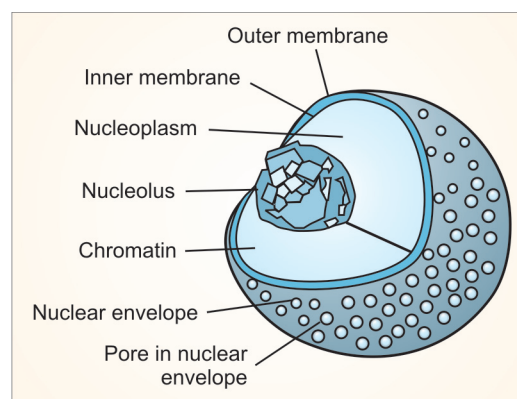


Fig. 1.3: Structure of nucleus

membrane and the inner membrane. The outer membrane of the nucleus is continuous with the membrane of the rough endoplasmic reticulum. The space between these layers is known as the perinuclear space. The nuclear envelope separates the genetic material of the cell from the cytoplasm. It also serves as a barrier to prevent passage of macromolecules freely between the nucleoplasm and the cytoplasm. The nuclear envelope is perforated with numerous pores called nuclear pores. The nuclear pores are composed of many proteins known as nucleoproteins. The nuclear pores regulate the passage of the molecules between the nucleus and cytoplasm. The pores allow the passage of molecules of only about 9 nm wide. The genes are arranged on the chromosomes.

A human cell has nearly 6 feet of DNA, which is divided into 46 individual molecules. The nucleus constitutes the genetic material of the cell and maintains the integrity of the genes which regulate the gene expression, in turn, regulating the activities of the cell. Therefore, the nucleus is known as the **control center of the cell**. The nucleolus is not surrounded by a membrane, it is a densely stained structure found in the nucleus. During cell division, the nucleolus disappears. The number of nucleoli is different from species to species but within a species the number is fixed. Studies suggest that nucleolus may be involved in cellular aging and senescence.

The larger molecules are transferred through active transport. A fluid filled in nucleus is called nucleoplasm which is a viscous semi-solid fluid and is similar to the composition of the cytoplasm. DNA and RNA are found in the nucleus. The DNA molecules are in complex with a large variety of proteins (histones) constitutes chromatin. During cell-division the chromatin forms well-defined chromosomes.

Functions

1. It is responsible for protein synthesis, cell division, growth and differentiation.
2. The nucleus provides a site for genetic transcription that is segregated from the location of translation in the cytoplasm, allowing levels of gene regulation that are not available to prokaryotes.
3. Nucleolus produces ribosomes and is known as protein factories. It also regulates the integrity of genes and gene expression.
4. The main function of the cell nucleus is to control gene expression and mediate the replication of DNA during the cell cycle.

Endoplasmic reticulum

Structure

The endoplasmic reticulum (ER) (Fig. 1.4) is a series of interconnected membranous sacs and tubules that collectively modifies proteins and synthesizes lipids. The membrane of the ER, which is a phospholipid bilayer embedded with proteins, is continuous with the nuclear envelope. However, these two functions are performed in separate areas of the ER—the rough ER and the smooth ER.

- **Smooth endoplasmic reticulum**, ribosomes are not attached with its surface and differ in function with respect to rough ER.
- **Rough endoplasmic reticulum** has ribosomes attached throughout the surface. These are present in cells, which are active in protein synthesis.

Biomedical importance of ER

A malfunction of the ER stress response caused by aging,

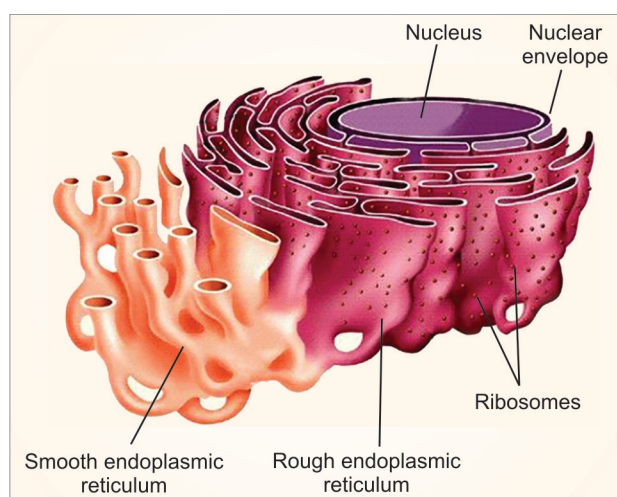


Fig. 1.4: Structure of endoplasmic reticulum

genetic mutations, or environmental factors can result in various diseases, such as diabetes, inflammation, and neurodegenerative disorders including Alzheimer's disease, Parkinson's disease, and bipolar disorder. Further mitochondrial DNA can be damaged by free radicals. Age-related degenerative disorders such as Parkinson's disease; cardiomyopathy may have a component of mitochondrial damage.

Functions

(a) Common to both ER

1. Forms the skeletal framework
2. Active transport of cellular materials
3. Metabolic activities due to presence of different enzymes
4. Provides increased surface area for cellular reactions
5. Formation of nuclear membrane during cell division
6. Detoxification of various drugs is an important function of ER. Microsomal cytochrome P-450 hydroxylates drugs such as benzpyrine, aminopyrine, aniline, morphine, phenobarbitone, etc.

(b) Functions of smooth ER

1. Lipid synthesis,
2. Glycogen synthesis, and
3. Steroid synthesis like cholesterol, progesterone, testosterone, etc.

(c) Functions of rough ER

1. It provides site for protein synthesis, and
2. It helps in transport of proteins.

Golgi complex (apparatus)

Structure

Golgi apparatus (Fig. 1.5) was discovered by an Italian biologist **Camillo Golgi** in the year **1898**. They are also called **dictyosomes**. The Golgi organelle is a network of flattened smooth membranes and vesicles. It may be considered as the converging area of endoplasmic reticulum. The Golgi complex has a **proximal** or **cis** compartment, a **medial** compartment and a **distal** or **trans** compartment.

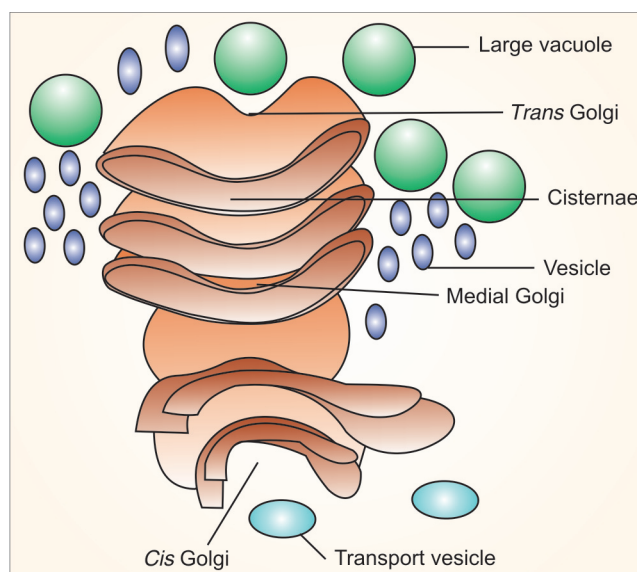


Fig. 1.5: Structure of Golgi apparatus

Functions

1. The main function of the Golgi apparatus is to **modify, sort and package** the macromolecules that are synthesized by the cells for secretion purposes within the cell.
2. It mainly modifies the proteins that are prepared by the rough endoplasmic reticulum.
3. They are also involved in the transport of lipid molecules around the cell.
4. The Golgi complex is, thus, referred as post office where the molecules are packaged, labelled and sent to different parts of the cell.
5. It imports substances like nucleotides from the cytosol of the cell. The modifications brought about by the Golgi body might form a signal sequence. This determines the final destination of the protein.
6. The Golgi complex also plays an important role in the production of proteoglycans. The proteoglycans are molecules that are present in the extracellular matrix of the animal cells.
7. It is also a major site of synthesis of carbohydrates. These carbohydrates include the synthesis of glycosaminoglycans, Golgi body attaches to these polysaccharides which then attaches to a protein produced in the endoplasmic reticulum to form proteoglycans.
8. The Golgi complex involves in the sulfation process of certain molecules. The process of phosphorylation of molecules by the Golgi complex requires the import of ATP into its lumen.

Mitochondria

Mitochondria are the **powerhouse** of the cell, where energy released from oxidation of foodstuffs is trapped as chemical energy in the form of ATP.

Structure

The mitochondria (Fig. 1.6) (Greek *mitos*—thread, *chondros*—granule) are the centers for the cellular respiration and energy metabolism. The mitochondria are spherical rod-shaped bodies, vary in diameter from 0.5–1.0 μ and may be up to 7 μ long. They are bounded by a double membrane.

This membrane is made up of lipoprotein. The outer membrane is smooth, but the inner membrane is convoluted or folded internally to form cristae. Mitochondria are filled with a fluid known as matrix. Mitochondria contain cytochromes, dehydrogenase enzymes, respiratory pigment flavin and some other enzymes that participate in lipid metabolism and the Krebs cycle. They usually occur in large number in nerve cells, muscle cells and secretory cells. Thus, mitochondria are actually the **powerhouse** or **batteries of a cell**, and therefore, of the organism as a whole.

Various enzymes found in mitochondria along with their locations have been summarised in Table 1.3.

Table 1.3: Location of enzymes in mitochondria

Mitochondria, outer membrane	Monoamine oxidase, Acyl-CoA synthetase
In between outer and inner membrane	Adenylate kinase
Inner membrane, outer surface	Glycerol-3-phosphate dehydrogenase
Inner membrane, inner surface	Succinate dehydrogenase
Soluble matrix	Enzymes of citric acid cycle

Functions

- Mitochondria acts as high energy storage center taking active part in metabolism.
- The mitochondria convert the potential energy of different food materials into a kind of energy that can be used to carry out different activities of cell like reabsorption, growth reproduction, respiration, etc.
- This occurs by a process of cellular respiration, also known as aerobic respiration, which is dependent on the presence of oxygen.
- The two separate biochemical pathways are called the Krebs citric acid and electron transfer chain.
- The synthesis of ATP by the mitochondria is brought about by the conjugation of two separate biochemical pathways, each involving many enzymes.

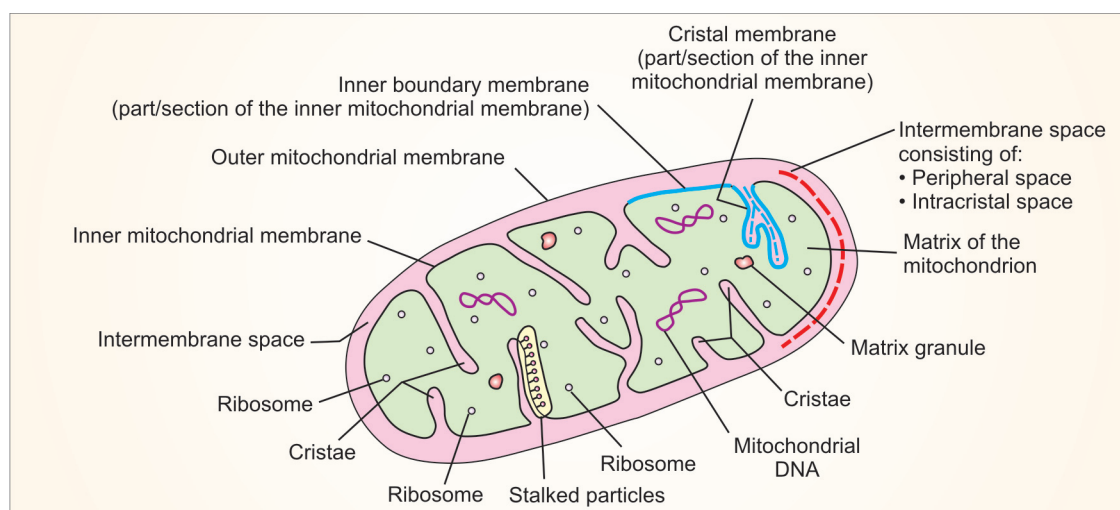


Fig. 1.6: Structure of mitochondria

- In Krebs cycle, the products are exposed to successive dehydrogenation. Cytochrome provides a mechanism whereby the electrons resulting from the oxidation of hydrogen are transported to oxygen functioning as acceptor for hydrogen ions to form water.
- The citric acid is a collection of about 10 enzymes which works together to remove energy from pyruvic acid molecules in a series of easy stages. This might be through a process of slow and controlled burning, in which the heat energy is trapped in ATP molecules.
- **The major function of mitochondria is the production of energy during the production of adenosine triphosphate (ATP) through the citric acid cycle.**

Lysosomes

- **Lysosomes** (Fig. 1.7) are membrane-bound, dense granular structures containing **hydrolytic enzymes** responsible mainly for intracellular and extracellular digestion.
- Lysosomes are formed by budding of the Golgi apparatus, and the hydrolytic enzymes within them are formed in the endoplasmic reticulum.
- The word 'lysosome' is made up of two words: 'lysis' meaning breakdown, and 'soma' meaning body.
- It is an important cell organelle responsible for the inter- and extracellular breakdown of substances.
- They are more commonly found in animal cells, while only in some lower plant groups (slime molds and saprophytic fungi).
- Lysosomes occur freely in the cytoplasm. In animals, they are found in all cells **except in the RBCs**.
- They are found in abundance in cells related to enzymatic reaction such as cells of liver, pancreas, kidney, spleen, leucocytes, macrophages, etc.

Structure of lysosomes

- Lysosomes are without any characteristic shape or structure, i.e. they are **pheomorphic**.
- They are mostly globular or granular in appearance.

- Each lysosome is 0.2–0.5 μm in size and is surrounded by a single lipoprotein membrane unique in composition.
- Membrane contains highly glycosylated lysosome-associated membrane proteins (LAMP) and lysosomal integral membrane proteins (LIMP).
- LAMPs and LIMPs form a coat on the inner surface of the membrane.
- They protect the membrane from attack by the numerous hydrolytic enzymes retained inside.
- The lysosomal membrane has a hydrogen proton pump which is responsible for maintaining pH conditions of the enzyme, i.e. acidic medium maintained by the proton pump that pumps H^+ inside the lumen, ensuring the functionality of the lysosomal enzymes.
- Inside the membrane, the organelle contains the enzymes in the crystalline form.

Lysosomal enzymes

For degradation of extra- and intracellular material, lysosomes fitted with enzymes called **hydrolases**. **It contains about 40 varieties of enzymes** which are classified into the following main types, namely:

- Proteases: Digest proteins
- Lipases: Digest lipids
- Amylases: Digest carbohydrates
- Nucleases: Digest nucleic acids
- Phosphomonoesterases: Catalyse the hydrolysis of phosphoryl ($\text{P}=\text{O}$) bonds

Collectively, the group of enzymes is called **hydrolases**, which cause breakdown of substrates by the addition of water molecules. Most of the **lysosomal enzymes act in acidic medium**.

Types of lysosomes

Lysosomes are of two types:

- Primary
 - Small sac-like structures enclosing enzymes synthesized by the rough endoplasmic reticulum.

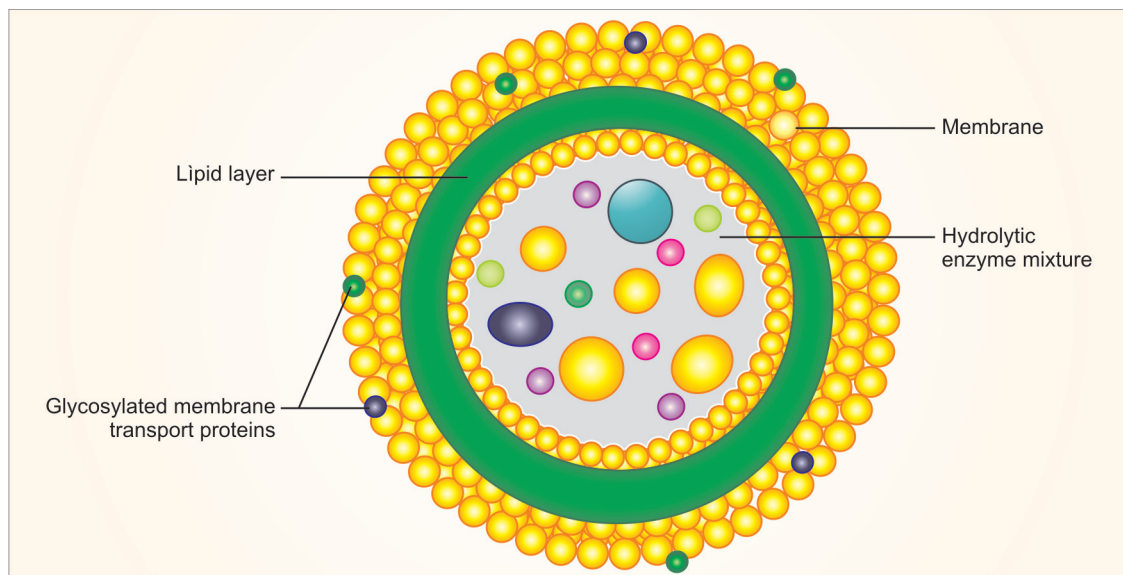


Fig. 1.7: Lysosome

- Simply called storage granules storing enzymes.
- Secondary
 - Formed by the fusion of primary lysosome with phagosomes.
 - Contain engulfed material plus enzymes
 - Materials are progressively engulfed.

Functions of lysosomes

These serve two major functions:

1. Intracellular digestion:
 - To digest food, the lysosome membrane fuses with the membrane of food vacuole and transmits the enzymes inside.
 - The digested food then diffuses through the vacuole membrane and enters the cell to be used for energy and growth.
2. Autolytic action:
 - Cell organelles that need to be got ridden are covered by vesicles on vacuoles by the process of **autophagy** to form **autophagosome**.
 - The autophagosome is then destroyed by the action of lysosomal enzymes.

Processes in which lysosomes play very important roles are:

- (a) Heterophagy: The taking into the cell of exogenous material by phagocytosis or pinocytosis and the digestion of the ingested material after fusion of the newly formed vacuole with a lysosome.
- (b) Autophagy: A normal physiological process that deals with the destruction of cells in the body. It is essential for maintaining the homeostasis, for normal functioning by protein degradation, turnover of destroyed cell organelles for new cell formation.
Yoshinori Ohsumi, a Japanese cell biologist, was awarded the Nobel Prize in Physiology or Medicine in the year 2016 for his discoveries on how cells recycle their content, a process known as autophagy, a Greek term for 'self-eating'.
- (c) Extracellular digestion: Primary lysosomes secrete hydrolases outside by exocytosis resulting in degradation of extracellular materials, e.g. saprophytic fungi.
- (d) Autolysis: It refers to the killing of an entire set of cells by the breakdown of the lysosomal membrane. It occurs during amphibian and insect metamorphosis.
- (e) Fertilization: The acrosome of the sperm head is a giant lysosome that ruptures and releases enzymes on the surface of the egg. This provides the way for sperm entry into the egg by digesting the egg membrane.
- (f) As janitors (**sweepers**) of the cell: Lysosomes remove 'junk' that may accumulate into the cell to prevent diseases.

Peroxisomes

Peroxisomes contain enzymes that oxidize certain molecules normally found in the cell, notably fatty acids and amino acids. Those **oxidation reactions produce H_2O_2 , which is the basis of the name peroxisome**. The peroxisomes are

single membrane, found in eukaryotic cell. They are approximately $0.5\ \mu$ in diameter. They are rich in leukocytes and platelets. They also have antioxidant enzymes, e.g. catalase and peroxidase. The free radicals damage molecules, cell membranes, tissues and genes. Catalase protects the cell from the toxic effects of H_2O_2 , by converting it into H_2O and O_2 . Peroxidase destroys the unwanted peroxides and other free radicals. Now, it has been shown that liver peroxisomes have an uncommonly active α -oxidative system capable of oxidizing long chain fatty acids (C 16 to 18 or $>C\ 18$). The α -oxidation enzymes of peroxisomes are rather unique in that the first step of the oxidation is catalyzed by a flavoprotein, an 'acyl-CoA oxidase'.



Malfunctioning of peroxisomes causes '**Zellweger syndrome**', a rare inherited metabolic disorder. Children with this syndrome usually do not survive beyond the first year of life. It is caused by mutations in any one of at least 12 genes; mutations in the PEX1 gene are the most common cause. Peroxisomes are organelles found in almost every cell of the body and are needed for the formation of organs like liver, kidneys and brain.

Plasma membrane

The cell membrane is selectively-permeable to ions and organic molecules and controls the movement of substances in and out of cells. The principal components of a plasma membrane are lipids (phospholipids and cholesterol), proteins, and carbohydrates. Chemically, the plasma membrane is composed of a wide variety of proteins, lipids in the form of cholesterol, phospholipid and sphingolipid and carbohydrates in the form of glycoproteins. Between various types of cells, there may not only be differences in the type and amount of lipids, carbohydrates and proteins but the amount of these chemicals may vary between each monolayer of the plasma membrane.

Fluid mosaic model of membrane structure

The fluid mosaic model of membrane structure (Fig. 1.8) proposed by **Singer** and **Nicholson** in **1972**. Biological membranes are very small (7–10 nm). **The Fluid Mosaic Model is generally accepted as describing how membranes are arranged**. In fluid mosaic model, the plasma membrane is a mosaic of components—phospholipids, cholesterol, and proteins (Table 1.4) that travel freely and fluidly in the plane of the membrane. A phospholipid is a lipid made up of glycerol, two fatty acid tails, and a phosphate-linked head group. Normal membranes usually involve two layers of phospholipids with their tails pointing inward, an arrangement called a phospholipid bilayer. The Fluid Mosaic Model states that membranes are composed of a phospholipid bilayer with various protein molecules.

The fluid part represents a few parts of the membrane which can move freely, if they are not attached to other parts of the cell. The mosaic parts illustrate the 'patchwork' of proteins that is found in the phospholipid bilayer. Two types of protein are found in plasma membrane—'intrinsic' that

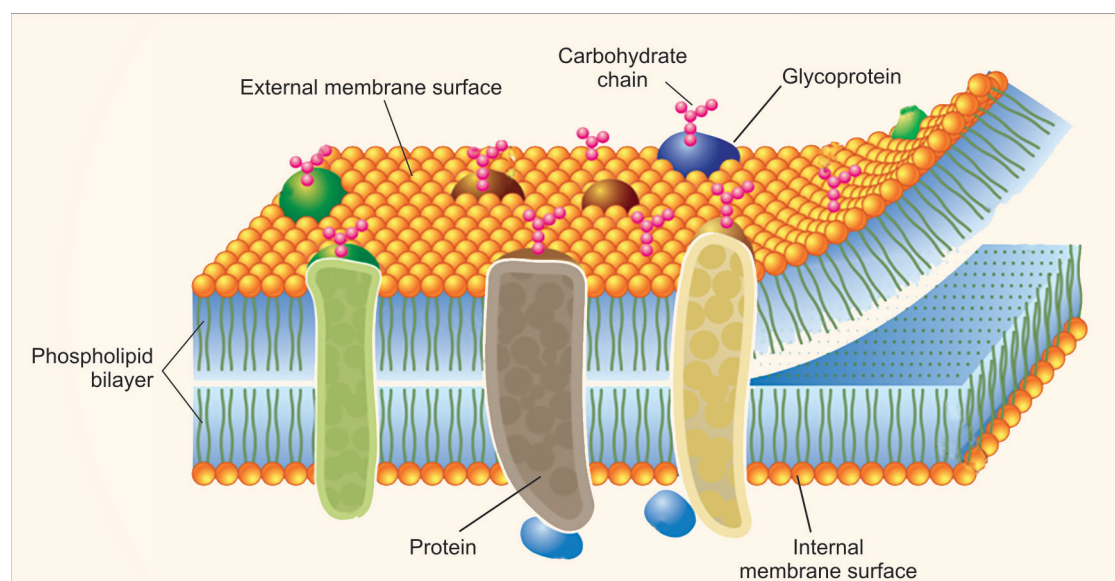


Fig. 1.8: Fluid mosaic model of plasma membrane

Table 1.4: Location of components of the plasma membrane

Component	Location
Phospholipids	Main fabric of the membrane
Cholesterol	Tucked between the hydrophobic tails of the membrane phospholipids
Integral proteins	Embedded in the phospholipid bilayer; may or may not extend through both layers
Peripheral proteins	On the inner or outer surface of the phospholipid bilayer, but not embedded in its hydrophobic core
Carbohydrates	Attached to proteins or lipids on the extra-cellular side of the membrane (forming glycoproteins and glycolipids)

are completely span in lipid bilayer, ‘extrinsic’, they are partly embedded in the bilayer.

Components of plasma membrane have been summarised in Table 1.5.

There are **three main factors** that influence cell membrane fluidity.

- **Temperature:** The temperature will affect how the phospholipids move and how close together they are found. They are found more rapidly together and when it is hot they move farther apart.
- **Cholesterol:** Lipid composed of four fused carbon rings, is found alongside phospholipids in the core of the membrane.
- **Unsaturated fatty acids:** The increased concentration of unsaturated fatty acids in the cell membrane is responsible for increased fluidity. They act as a buffer, increasing fluidity at low temperatures and decreasing fluidity at high temperatures.

Carbohydrate groups are here only on the external surface of the plasma membrane and are attached to proteins, forming glycoproteins, or lipids, forming glycolipids. The scope of proteins, lipids, and carbohydrates in the plasma membrane

differs between unusual types of cells. For a typical human cell, though, proteins account for about 50% of the composition by mass, lipids (of all types) account for about 40%, and the residual 10% comes from carbohydrates.

Saturated and unsaturated fatty acids: Fatty acids are what make up the phospholipid tails. Saturated fatty acids are chains of carbon atoms that have single bonds between them. This makes them straight and easy to pack tightly. Unsaturated fats are chains of carbon atoms that have some double bonds between them.

Double bonds create kinks (twists) in the chain, making them not as easy to pack tightly.

There are two possible kinks that can occur:

1. *Cis-unsaturated fats*, where both sides of the chain remain on the same side.
2. *Trans-unsaturated fats*, where the sides of the chain are opposite from each other.

The kinked shape of *cis*-unsaturated fats makes it more difficult to pack tightly.

Showing saturated fatty acids are easier to stack compared to unsaturated fatty acids, which are difficult to stack because of the kinks in their carbon chains.

This plays a role in membrane fluidity, because the kinks increase the space in between the phospholipids, making them harder to freeze at lower temperatures.

Phospholipids: Phospholipids (Fig. 1.9) are attracted to each other, but they are also constantly in motion and bounce around a little of each other.

The spaces created by the membrane’s fluidity are very small, so it is still an effective barrier. For this reason, and the ability of proteins to help with transport across the membrane, the cell membrane is also known as *semi-permeable*.

Some of the molecules can cross the membrane and some of them need the help of other molecules or processes. One way of distinguishing between these categories of molecules is based on how they react with water.

Table 1.5: Components of the plasma membrane

Component	Composition	Function	Mechanism	Example
Phospholipid molecules	Phospholipid bilayer	Provides permeability barrier, matrix for proteins	Excludes water-soluble molecules from nonpolar interior of bilayer	Bilayer of cell is impermeable to water soluble molecules, like glucose
Transmembrane proteins	Carriers	Transport molecules across membrane against gradient	'Escort' molecules through the membrane in a series of conformational changes	Glycophorin carrier for sugar transport
	Channels	Passively transport molecules across membrane	Create a tunnel that acts as a passage through membrane	Sodium and potassium channels in nerve cells
	Receptors	Transmit information into cell	Signal molecules bind to cell surface portion of the receptor protein; this alters the portion of the receptor protein within the cell, inducing activity	Specific receptors bind peptide hormones and neurotransmitters
Interior protein	Spectrins	Determine shape of cell	Form supporting scaffold beneath membrane, anchored to both membrane and cytoskeleton	Red blood cell
	Clathrins	Anchor certain proteins to specific sites, especially on the exterior cell membrane in receptor-mediated endocytosis	Proteins line coated pits and facilitate binding to specific molecules	Localization of low-density lipoprotein receptor within coated pits
Cell surface markers	Glycoproteins	'Self'-recognition	Create a protein/carbohydrate chain shape characteristic of individual	Major histocompatibility complex protein recognized by immune system
	Glycolipid	Tissue recognition	Create a lipid/carbohydrate chain shape characteristic of tissue	A, B, O blood group markers

Molecules, that are **hydrophilic (water loving)**, are capable of forming bonds with water and are called polar molecules. The opposite can be said for molecules that are **hydrophobic (water fearing)**, they are called non-polar molecules.

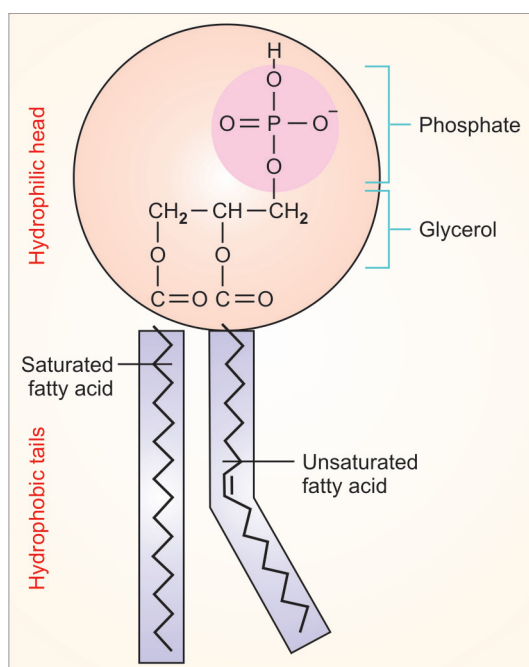


Fig. 1.9: Structure of a phospholipid

These are of four types:

1. Small, non-polar molecules (e.g. oxygen and carbon dioxide) can pass through the lipid bilayer and do so by squeezing through the phospholipid bilayers. They don't need proteins for transport and can diffuse across quickly.
2. Small, polar molecules (e.g. water): This is a little more difficult than the molecule type above. Recall that the interior of the phospholipid bilayer is made up of the hydrophobic tails. It won't be easy for the water molecules to cross, but they can cross without the help of proteins. This is somewhat slower process.
3. Large, non-polar molecules (e.g. carbon rings): These rings can pass through but it is also a slow process.
4. Large, polar molecules (e.g. simple sugar—glucose) and ions: The charge on ion, and the size and charge of large polar molecules, makes it too difficult to pass through the non-polar region of the phospholipid membrane without help.

Membrane functions

- **Protective:** It forms the outermost boundary of the cell organelles keeping them in a safe zone.
- **Digestive:** Takes in nutrients and excretes waste products.
- **Property of selective permeability:**
 - Non-polar molecules (gases like O₂, CO₂ and N₂, lipids, steroid hormones, alcohol can dissolve non-polar more rapidly across the membrane).

- Membranes serve as barriers that separate the contents of a cell from the external environment or the contents of individual organelles from the remainder of the cell.
- The proteins in the cell membrane are involved in the transport of substances across the membrane.

Summary of cell organelles

Various cell organelles play vital and very important role in human body which have been summarised in Table 1.6.

Table 1.6: Summary of cell organelles	
Organelles	Functions
Nucleus	DNA replication, transcription
Endoplasmic reticulum	Biosynthesis of proteins, glycoproteins, reticulum lipoproteins, drug metabolism, ethanol oxidation, synthesis of cholesterol (partial)
Golgi body	Maturation of synthesized protein
Lysosome	Degradation of proteins, carbohydrates, lipids and nucleotides
Mitochondria	Electron transport chain, ATP generation, TCA cycle, beta-oxidation of fatty acids, ketone body production, urea synthesis (part), heme synthesis (part), gluconeogenesis (part), pyrimidine synthesis (part)
Cytosol	Protein synthesis, glycolysis, glycogen metabolism, HMP shunt pathway, transaminations fatty acid synthesis, cholesterol synthesis, heme synthesis, urea synthesis, pyrimidine synthesis, purine synthesis

TRANSPORT ACROSS CELL MEMBRANE

These biological membranes are semipermeable in nature, that is, their permeability properties ensure that the specific molecules and ions readily enter the cell and the waste products leave the cell. These movements of solutes into the cell are mediated through the action of specific transport

proteins that are present on the cell membrane. Such proteins are, therefore, required for movements of ions, such as Na^+ , K^+ , Ca^{2+} , and Cl^- , as well as metabolites such as pyruvate, amino acids, sugars, nucleotides and water.

Types of transport process

There are two ways in which substances can enter or leave a cell:

1. Active transport, and
2. Passive transport

ACTIVE TRANSPORT

It is the movement of solutes across a membrane against a concentration gradient (i.e. from a region of lower concentration to one of higher concentrations). It is an endergonic process that, in most cases, is coupled to the hydrolysis of ATP.

Types of active transport

Active transport is the term used to describe the process of moving materials through the cell membrane that requires the use of energy. There are three main types of active transport, viz.

1. Sodium-potassium pump,
3. Endocytosis, and
2. Exocytosis.

Sodium-potassium pump

Sodium-potassium pump (Fig. 1.10) is a structure known as cell membrane pump that uses energy to transport sodium and potassium ions into and out of the cell. There are other varieties of cell membrane pump, however, the Na^+-K^+ pump plays a vital role in maintaining cell's homeostasis.

The pump is powered by molecule of ATP. The ATP allows the shape of the pump to change, emptying its contents either into or out of the cell. Following are the steps that the Na^+-K^+ pump uses to function.

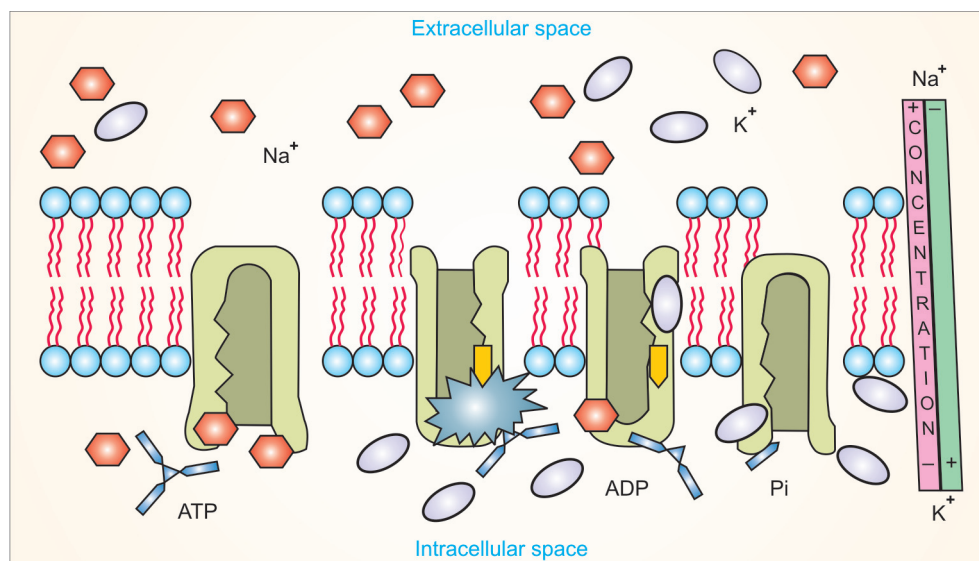


Fig. 1.10: Action of the sodium-potassium pump

1. Three Na^+ ions formed inside cell bind to the pump.
2. The phosphate group from a molecule of ATP binds to the pump.
3. The pump changes shape and the sodium ions are released outside the cell.
4. Two K^+ ions bind to the pump.
5. The phosphate group is released from the pump and the pump again changes shape and releases the ions inside the cell.

Endocytosis

Endocytosis is a process by which cells can take in large particles and deposit them into the cell; this process is accomplished by forming membrane-bound sacs that pinch off from the cell's membrane.

Endocytosis can be used to bring large particles, such as glucose, into a cell. Also, this process can be used by white blood cells to ingest viruses or bacteria and then digest them in their lysosomes. There are two sub-categories of endocytosis: pinocytosis and phagocytosis.

Pinocytosis brings liquids into the cell whereas phagocytosis is responsible for transporting large particles or other solids into the cell.

Exocytosis

Exocytosis is very similar to endocytosis except that it deposits materials from inside the cell on the outside instead of the other way around. Vesicles once formed in the **Golgi bodies**, filled with materials to be sent outside the cell, and then fuse with the cell membrane and release their contents outside the cell.

PASSIVE TRANSPORT

Passive transport is a method of transporting materials that does not use energy. Because of this, it is generally found only when particles move down their concentration gradient, from an area of higher concentration to an area of lower concentration. One of the most common types of passive transport is **osmosis**, which is solely responsible for moving water through a cell's membrane. Other kinds of particles can also move through the cell membrane as well. They are usually very small particles such as oxygen and simply pass between the spaces in the lipid bilayer of a cell's membrane.

Passive transport really is not a very complicated process and as such is fairly easy to understand. However, it is a vital process that all cells need to survive.

Types of passive transport

There are three types of passive transport:

1. Simple diffusion,
2. Facilitated diffusion, and
3. Ion channels

1. Simple diffusion

The process of the net movement of solutes from high concentration to low concentration is known as diffusion which means movement of small or lipophilic molecules, e.g. O_2 , CO_2 , etc. The differences of concentration between

the two regions are termed as concentration gradient and the diffusion continues till the gradient has been vanished. Diffusion occurs down the concentration gradient.

Examples of diffusion in biology

- Gas exchange at the alveoli—oxygen from air to blood, carbon dioxide from blood to air
- Gas exchange for respiration—oxygen from blood to tissue cells, carbon dioxide in opposite direction

2. Facilitated diffusion

Movement of large or charged molecules (e.g. ions, sucrose, etc.) via membrane proteins (Fig. 1.11). Substances that are too large or polar diffuse across the lipid bilayer through membrane proteins called carriers, permeases, channels and transporters. Unlike active transport, this process does not involve chemical energy. So, the passive mediated transport is totally dependent upon the permeability nature of cell membrane. **Facilitated diffusion is similar to an enzyme-catalyzed reaction.** Like enzymes, facilitative transporters are specific for the molecules, for example, sugars (Fig. 1.12) and amino acids that do not penetrate the lipid bilayer.

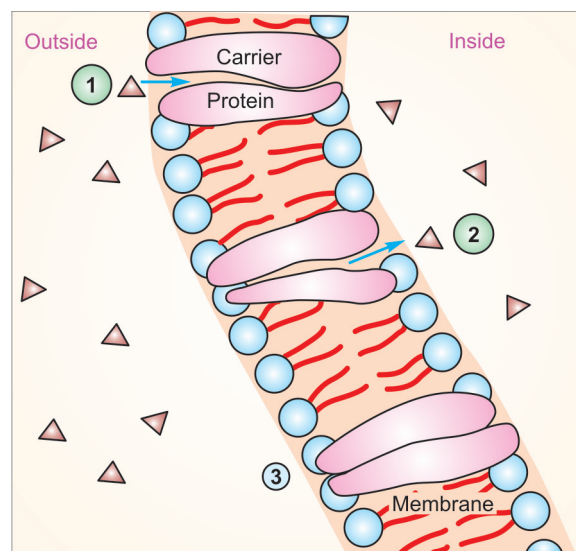


Fig. 1.11: Facilitated diffusion. A carrier protein speeds up the rate at which a solute crosses a membrane from higher solute concentration to lower solute concentration. (1) Molecule enters carrier. (2) Molecule is transported across the membrane and exits on inside. (3) Carrier returns to its former state.

3. Ion channels

The two main groups of ion channels are:

1. The voltage-gated channels such as the sodium and potassium channels of the nerve axons and nerve terminals.
2. The extracellular ligand-activated channels which include channels such as GABA and glycine receptor channels.

Glucose transporter

If the molecule is changed on entering the cell (glucose + ATP $\rightarrow$ glucose phosphate + ADP), then the concentration gradient of glucose will be kept high, and there will be a steady one-way traffic.

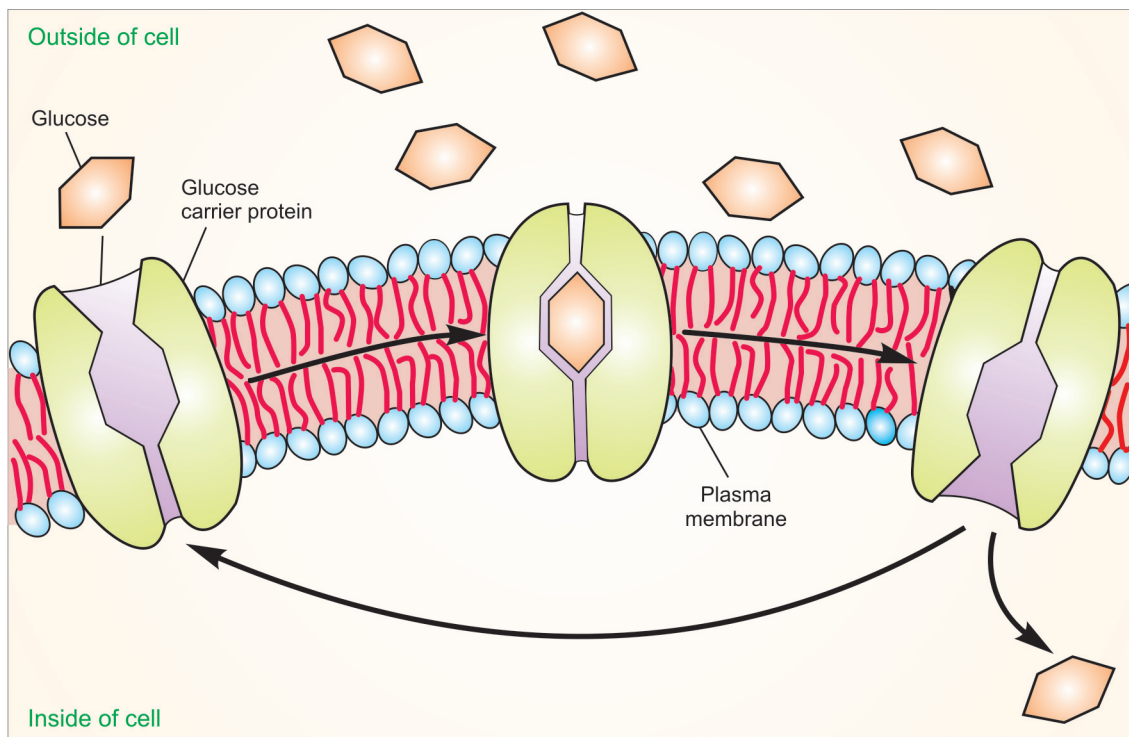


Fig. 1.12: Facilitated diffusion with glucose molecule

ACTIVE TRANSPORTERS

The active transporters (Fig. 1.13) are—(a) uniport, (b) symport, and (c) antiport.

(a) Uniport

Uniport carriers mediate transport of a single solute pumped in same directions across a membrane. Example: GLUT1 glucose carrier.

(b) Symport

Symport uses the downhill movement of one solute species from high to low concentration to move another molecule uphill from low concentration to high concentration. Example: Glucose transporter SGLT1, which co-transport one glucose (or galactose) molecule into the cell for every two sodium ions it imports into the cell.

(c) Antiport

In antiport, two species of ions or solutes are pumped in opposite directions across a membrane. One of these species is allowed to flow from high to low concentration which yields the entropic energy to drive the transport of the other solute from a low concentration region to a high one. Example: The sodium–calcium exchanger or antiporter, which allows three sodium ions into the cell to transport calcium out.

Example: ($\text{Na}^+ - \text{K}^+$)-ATPase (Fig. 1.14)

($\text{Na}^+ - \text{K}^+$)-ATPase active transport system is commonly found in the plasma membranes of higher eukaryotes, which was first characterized by Jens Skou. This transmembrane protein consists of two types of subunits—a 110-kD non-glycosylated α -subunit that contains the enzyme's catalytic activity and ion-binding sites, and a 55-kD glycoprotein β -subunit of

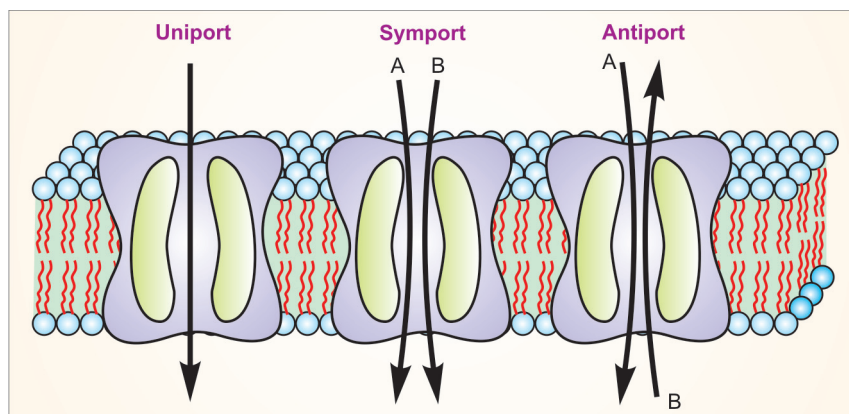


Fig. 1.13: Types of transport system (active transporters)

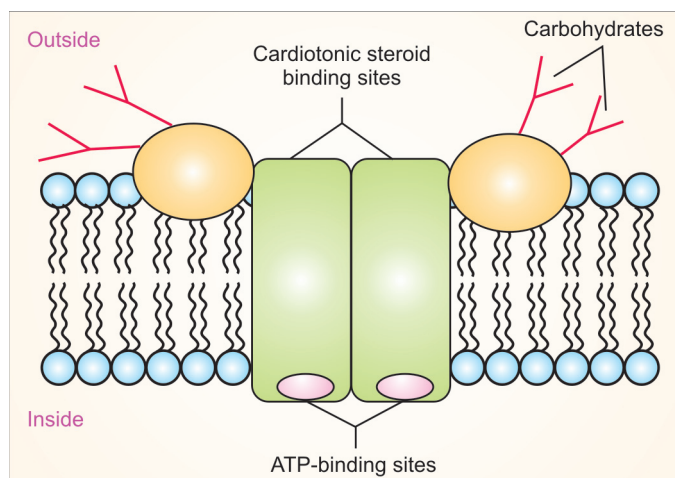
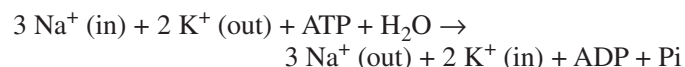


Fig. 1.14: Antiport— $(\text{Na}^+-\text{K}^+)\text{-ATPase}$

unknown function. Sequence analysis suggests that α -subunit has eight transmembrane α -helical segments and two large cytoplasmic domains. The β -subunit has a single transmembrane helix and a large extracellular domain. The protein may function as an $(\alpha\beta)$ 2 tetramer *in vivo*. The $(\text{Na}^+-\text{K}^+)\text{-ATPase}$ is also called the $(\text{Na}^+-\text{K}^+)\text{ pump}$ because it pumps 3 Na^+ out of and 2 K^+ into the cell in presence of hydrolysis of ATP. The overall stoichiometry of the reaction is:



There is yet another type of active transport, known as **ion gradient driven active transport**.

Ion gradient driven active transport

For example, cells of the intestinal epithelium take up dietary glucose by Na^+ -dependent symport. This process is an example of secondary active transport, because Na^+ gradient in these cells is maintained by the $(\text{Na}^+-\text{K}^+)\text{-ATPase}$. The Na^+ -glucose transport system concentrates glucose inside the cell. Glucose is then transported into the capillaries through a passive-mediated glucose uniport (which resembles GLUT1) (Fig. 1.15).

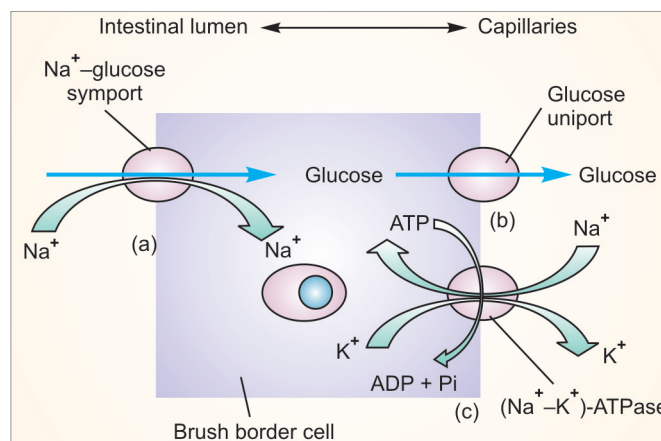


Fig. 1.15: Glucose transport across intestinal epithelium.

The brush-like villi lining the small intestine greatly increases the surface area (a), thereby facilitating the absorption of the nutrients. The brush border cells from which the villi are formed (b) concentrate glucose from the intestinal lumen in symport to Na^+ (c), a process that is driven by $(\text{Na}^+-\text{K}^+)\text{-ATPase}$, which is located on the capillary side of the cell and functions to maintain a low internal $[\text{Na}^+]$. The glucose is exported to the bloodstream via a passive-mediated uniport system similar to GLUT1.

Key Facts

- The cystic fibrosis transmembrane regulator (CFTR) is a chloride ion channel found on cell membranes. Mutation in this protein results in cystic fibrosis (CF). CF is the most common lethal genetic disease in Caucasians and results in viscous secretions of the respiratory tract with recurrent life-threatening pulmonary infections.
- “Apoptosis is a pathway of cell death in which cells activate enzymes that degrade the cell’s own nuclear DNA and nuclear and cytoplasmic proteins.” In other words, apoptosis is the process of programmed cell death (PCD), in which biochemical changes lead to cell changes such as cell shrinkage, nuclear fragmentation, chromatin condensation, and chromosomal DNA fragmentation, the ultimate consequence of which is cell death.
- Traumatic (not pre-planned or ‘programmed’) cell death, e.g. due to acute cellular injury is called necrosis.

Important Questions

Short Answer Type Questions

1. What is the clinical significance of sodium pump?
2. What do you understand by the term uniport?
3. Give examples of ‘uniport system’.
4. What do you understand by the term symport?
5. What are the examples of ‘symport system’?
6. What do you understand by the term antiport system?
7. Give an example of ‘antiport transport’.
8. Name the phospholipids which are found in membrane.
9. What are the salient features of facilitated diffusion?
10. Give an example of facilitated transport.
11. What is the structure of a cell membrane?

12. Write a short note on the following.

- a. Mitochondria
- b. Structure of cell membrane
- c. Lysosomes
- d. Endoplasmic reticulum
- e. Golgi apparatus
- f. Peroxisomes
- g. Facilitated transport
- h. Active transport
- i. Symport system
- j. Fluid mosaic model
- k. Diseases concerned with altered lysosomal function

Essay Type Questions

1. Draw a diagram of a cell and describe in detail the functions of various organelles.
2. Discuss at length the differences between eukaryotic and prokaryotic cells.
3. Discuss in detail about biomembrane with the help of a diagram.
4. Define active transport. Explain different types of active transport by giving examples.

Multiple Choice Questions

Read the following questions carefully and put a tick (✓) mark in the box against the correct option.

1. Peroxisomes are involved in one of the following.
 - (a) Oxidative reactions ☐
 - (b) In the production of free radicals ☐
 - (c) The site of post-translational modifications ☐
 - (d) Concerned with none of the above ☐
2. Phagocytosis is:
 - (a) Endosmosis ☐
 - (b) α -oxidation ☐
 - (c) β -oxidation ☐
 - (d) Respiratory burst ☐
3. Galactosyltransferase is a marker enzyme of any one of the following.
 - (a) Lysosomes ☐
 - (b) Mitochondria ☐
 - (c) Cell membrane ☐
 - (d) Golgi complex ☐
4. Sodium–potassium pump gets inhibited by any one of the following:
 - (a) Paracetamol ☐
 - (b) Folic acid ☐
 - (c) Digoxin ☐
 - (d) Erythromycin ☐
5. Lysosomes are known as ‘suicidal bags’ because of:
 - (a) Hydrolytic activity ☐
 - (b) Food vacuole ☐
 - (c) Parasitic activity ☐
 - (d) Catalytic activity ☐
6. Name the scientist who for the first time discovered electron microscope and in which year.
 - (a) E. Ruska and Max Knoll (1931) ☐
 - (b) Emil Adolf von Behring (1901) ☐
 - (c) Paul Ehrlich (1908) ☐
 - (d) Christian Eijkman (1929) ☐
7. Approximately how many protein molecules are found in one human cell?
 - (a) 25,000 ☐
 - (b) 50,000 ☐
 - (c) 1,00,000 ☐
 - (d) >1,00,000 ☐
8. Approximately how many fat molecules does cellular membrane contain?
 - (a) 2 lakhs ☐
 - (b) 10 lakhs ☐
 - (c) 50 lakhs ☐
 - (d) Crores ☐
9. In which syndrome male patients suffer from the development of breasts, small testes and failure of sperm formation?
 - (a) Down syndrome ☐
 - (b) Turner syndrome ☐
 - (c) Klinefelter syndrome ☐
 - (d) None of these ☐
10. In which syndrome, male patients have only a single X-chromosome and no Y-chromosome? Such individuals are described as XO. They have rudimentary female sex organs, short stature and a short webbed neck.
 - (a) Klinefelter syndrome ☐
 - (b) Turner syndrome ☐
 - (c) Down syndrome ☐
 - (d) None of these ☐
11. In which syndrome, a baby is born with an extra copy of a chromosome?
 - (a) Down syndrome ☐
 - (b) Klinefelter syndrome ☐
 - (c) Turner syndrome ☐
 - (d) None of these ☐

Answers

1. a 2. d 3. d 4. c 5. a 6. a 7. b 8. d 9. c 10. b 11. a