BTY 101 CELL BIOLOGY

UNIT 1

Differences between prokaryotic and eukaryotic cell

Biotic components of the environment include all forms of life from minute bacteria to towering giant Sequoias. However, at the microscopic level, all living organisms are made up of the same basic unit – the cell.

Eventual advancements in science and technology shed more light into the cell, with new findings and discoveries about its structure and cellular components. During the 1950s, scientists postulated the concept of prokaryotic cells and eukaryotic cells, with earlier groundwork being laid by Edouard Chatton, a French Biologist in 1925.

Anatomically, cells vary with respect to their classification, therefore, prokaryotic cells and eukaryotic cells differ from each other quite drastically. Read on to explore how they differ from each other.

Prokaryotic Cell

The term "prokaryote" is derived from the Greek word *"pro", (meaning: before) and "karyon" (meaning: kernel). It translates to "before nuclei."

Prokaryotes are one of the most ancient groups of living organisms on earth, with fossil records dating back to almost 3.5 billion years ago.

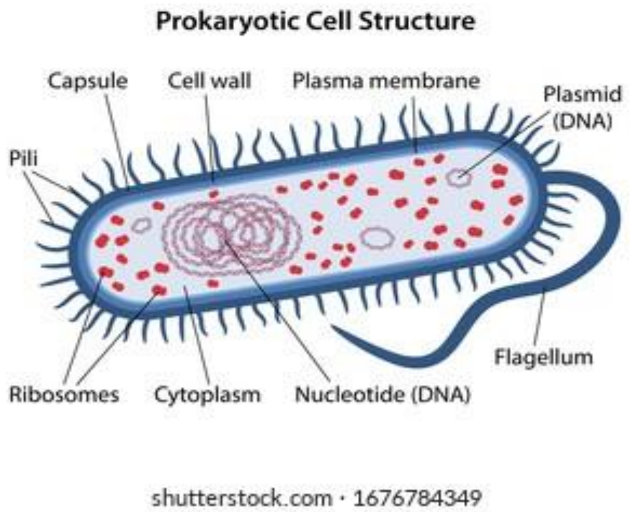
These prokaryotes thrived in the earth's ancient environment, some using up chemical energy and others using the sun's energy. These extremophiles thrived for millions of years, evolving and adapting. Scientists speculate that these organisms gave rise to the eukaryotes.

Prokaryotic cells are comparatively smaller and much simpler than eukaryotic cells. The other defining characteristic of prokaryotic cells is that it does not possess membrane-bound cell organelles such as a nucleus. Reproduction happens through the process of binary fission.

Structurally, prokaryotes have a capsule enveloping their entire body, and it functions as a protective coat. This is crucial for preventing the process of phagocytosis (where the bacteria gets engulfed by other eukaryotic cells, such as macrophages) The pilus is a hair-like appendage found on the external surface of most prokaryotes and it helps the organism to attach itself to various environments. The pilus essentially resists being flushed, hence, it is also called attachment pili. It is commonly observed in bacteria.

Right below the protective coating lies the cell wall, which provides strength and rigidity to the cell. Further down lies the cytoplasm that helps in cellular growth, and this is contained within the plasma membrane, which separates the interior contents of the cell from the outside environment. Within the cytoplasm, ribosomes exist and it plays an important role in protein synthesis. It is also one of the smallest components within the cell.

Some prokaryotic cells contain special structures called mesosomes which assist in **cellular respiration**. Most prokaryotes also contain plasmids, which contain small, circular pieces of DNA. To help with locomotion, flagella are present, though, pilus can also serve as an aid for locomotion. Common examples of Prokaryotic organisms are bacteria and archaea. Also, all members of Kingdom Monera are prokaryotes.



Eukaryotic Cell

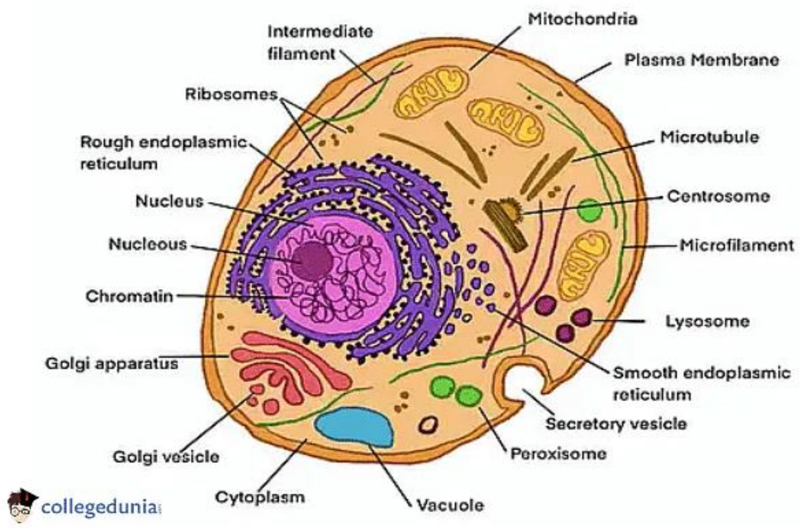
The term "Eukaryotes" is derived from the Greek word "*eu*", (meaning: good) and "*karyon*" (meaning: kernel), therefore, translating to "**good or true nuclei**." Eukaryotes are more complex and much larger than prokaryotes. They include almost all the major kingdoms except kingdom monera.

Structurally, eukaryotes possess a cell wall, which supports and protects the plasma membrane. The cell is surrounded by the plasma membrane and it controls the entry and exit of certain substances.

The nucleus contains DNA, which is responsible for storing all genetic information. The nucleus is surrounded by the nuclear membrane. Within the nucleus exists the nucleolus, and it plays a crucial role in synthesising proteins. Eukaryotic cells also contain mitochondria, which are responsible for the creation of energy, which is then utilized by the cell.

Present in only plant cells, chloroplasts are the subcellular sites of photosynthesis. The endoplasmic reticulum helps in the transportation of materials. Besides these, there are also other **cell organelles** that perform various other functions and these include ribosomes, lysosomes, Golgi bodies, cytoplasm, chromosomes, vacuoles and centrosomes.

Examples of eukaryotes include almost every unicellular organism with a nucleus and all multicellular organisms.



Difference between Prokaryotic and Eukaryotic Cells

Though these two classes of cells are quite different, they do possess some common characteristics. For instance, both possess cell membranes and ribosomes, but the similarities end there. The complete list of differences between prokaryotic and eukaryotic cells is summarized as follows:

	Prokaryotes	**Eukaryotes**
Type of Cell	Always unicellular	Unicellular and multi-cellular
Cell size	Ranges in size from 0.2 μm – 2.0 μm in diameter	Size ranges from 10 μm – 100 μm in diameter

Cell wall	Usually present; chemically complex in nature	When present, chemically simple in nature
Nucleus	Absent. Instead, they have a nucleoid region in the cell	Present
Ribosomes	Present. Smaller in size and spherical in shape	Present. Comparatively larger in size and linear in shape
DNA arrangement	Circular	Linear
Mitochondria	Absent	Present
Cytoplasm	Present, but cell organelles absent	Present, cell organelles present
Endoplasmic reticulum	Absent	Present
Plasmids	Present	Very rarely found in eukaryotes
Ribosome	Small ribosomes	Large ribosomes

Lysosome	Lysosomes and centrosomes are absent	Lysosomes and centrosomes are present
Cell division	Through binary fission	Through mitosis
Flagella	The flagella are smaller in size	The flagella are larger in size
Reproduction	Asexual	Both asexual and sexual
Example	Bacteria and Archaea	Plant and Animal cell

Cell Organelles

The cellular components are called cell organelles. These cell organelles include both membrane and non-membrane bound organelles, present within the cells and are distinct in their structures and functions. They coordinate and function efficiently for the normal functioning of the cell. A few of them function by providing shape and support, whereas some are involved in the locomotion and reproduction of a cell. There are various organelles present within the cell and are classified into three categories based on the presence or absence of membrane.

Organelles without membrane*:* The Cell wall, Ribosomes, and Cytoskeleton are non-membrane-bound cell organelles. They are present both in the **prokaryotic cell** and the eukaryotic cell.

Single membrane-bound organelles: Vacuole, Lysosome, Golgi Apparatus, Endoplasmic Reticulum are single membrane-bound organelles present only in a eukaryotic cell.

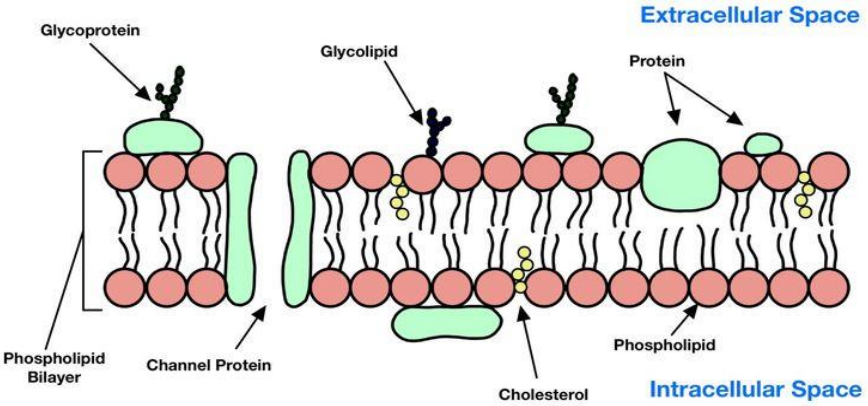
Double membrane-bound organelles: Nucleus, mitochondria and chloroplast are double membrane-bound organelles present only in a eukaryotic cell.

List of Cell Organelles and their Functions

Plasma Membrane

The plasma membrane is also termed as a Cell Membrane or Cytoplasmic Membrane. It is a selectively permeable membrane of the cells, which is composed of a lipid bilayer and proteins.

The plasma membrane is present both in plant and animal cells. It functions as the selectively permeable membrane, by permitting the entry of selective materials in and out of the cell according to the requirement. In an animal cell, the cell membrane functions by providing shape and protects the inner contents of the cell. Based on the structure of the plasma membrane, it is regarded as the fluid mosaic model. According to the fluid mosaic model, the plasma membranes are subcellular structures, made of a lipid bilayer in which the protein molecules are embedded.



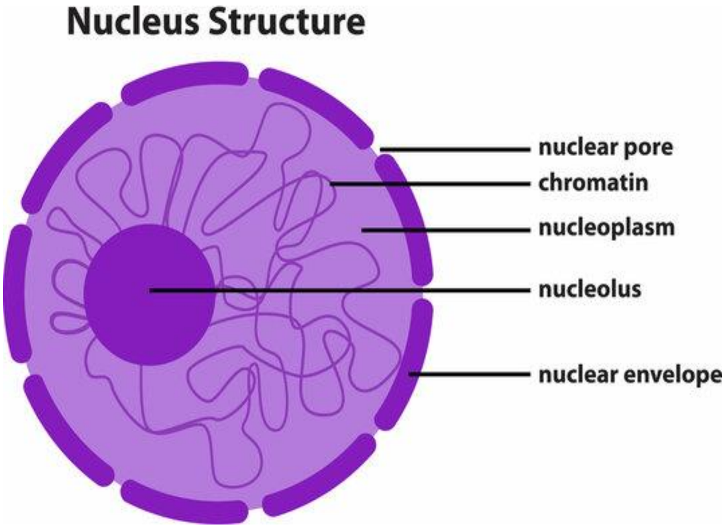
Cytoplasm

The cytoplasm is present both in plant and animal cells. They are jelly-like substances, found between the cell membrane and nucleus. They are mainly composed of water, organic and inorganic compounds. The cytoplasm is one of the essential components of the cell, where all the cell organelles are embedded. These cell organelles contain enzymes, mainly responsible for controlling all metabolic activity taking place within the cell and are the site for most of the chemical reactions within a cell.

Nucleus

The nucleus is a double-membraned organelle found in all eukaryotic cells. It is the largest organelle, which functions as the control centre of the cellular activities and is the storehouse of the cell's DNA. By structure, the nucleus is dark, round, surrounded by a nuclear membrane. It is a porous membrane (like cell membrane) and forms a wall between cytoplasm and nucleus. Within the nucleus, there are tiny spherical bodies called nucleolus. It also carries an essential structure called chromosomes.

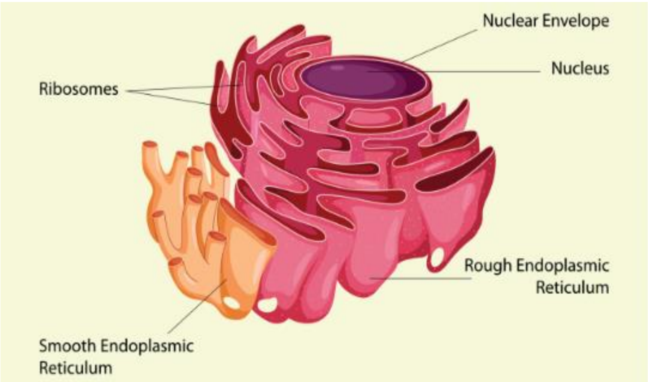
Chromosomes are thin and thread-like structures which carry another important structure called a gene. Genes are a hereditary unit in organisms i.e., it helps in the inheritance of traits from one generation (parents) to another (offspring). Hence, the nucleus controls the characters and functions of cells in our body. The primary function of the nucleus is to monitor cellular activities including **metabolism** and growth by making use of DNA's genetic information. Nucleoli in the nucleus are responsible for the synthesis of protein and RNA.



Endoplasmic Reticulum

The Endoplasmic Reticulum is a network of membranous canals filled with fluid. They are the transport system of the cell, involved in transporting materials throughout the cell.
There are two different types of Endoplasmic Reticulum:

1. Rough Endoplasmic Reticulum – They are composed of cisternae, tubules, and vesicles, which are found throughout the cell and are involved in protein manufacture.
2. Smooth Endoplasmic Reticulum – They are the storage organelle, associated with the production of lipids, steroids, and also responsible for detoxifying the cell.

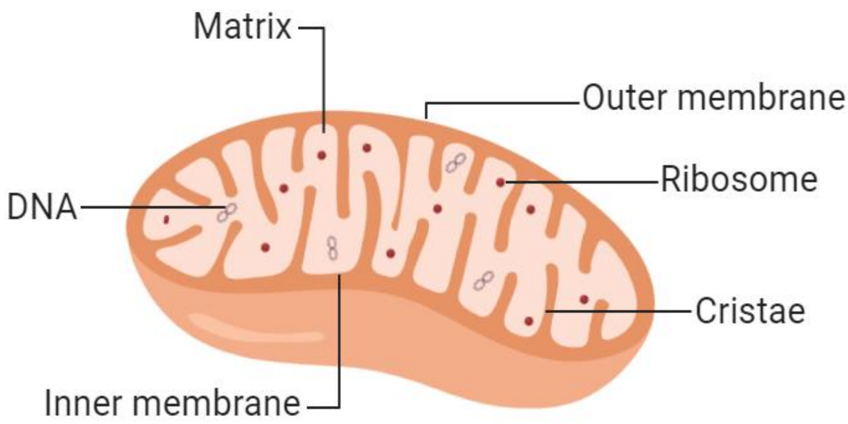


Mitochondria

Mitochondria are called the powerhouses of the cell as they produce energy-rich molecules for the cell. The mitochondrial genome is inherited maternally in several organisms. It is a double membrane-bound, sausage-shaped organelle, found in almost all eukaryotic cells.

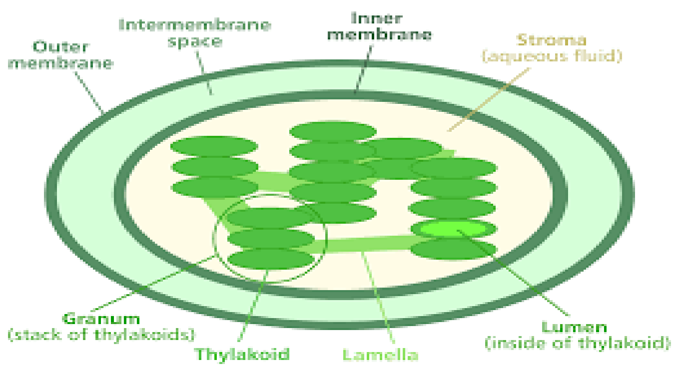
The double membranes divide its lumen into two distinct aqueous compartments. The inner compartment is called a 'matrix' which is folded into cristae whereas the outer membrane forms a continuous boundary with the cytoplasm. They usually vary in their size and are found either round or oval in shape. Mitochondria are the sites of **aerobic respiration** in the cell, produces energy in the form of ATP and helps in the transformation of the molecules.

For instance, glucose is converted into adenosine triphosphate – ATP. Mitochondria have their own circular DNA, RNA molecules, ribosomes (the 70s), and a few other molecules that help in protein synthesis.



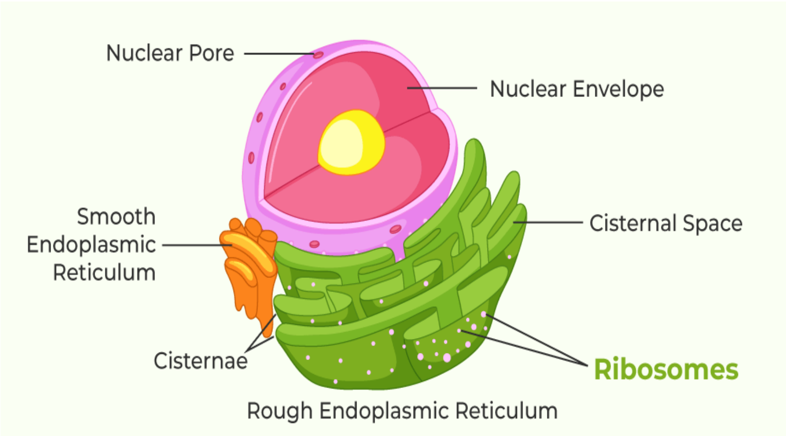
Plastids

Plastids are large, membrane-bound organelles which contain pigments. Based on the type of pigments, plastids are of three types:



- Chloroplasts – Chloroplasts are double membrane-bound organelles, which usually vary in their shape – from a disc shape to spherical, discoid, oval and ribbon. They are present in mesophyll cells of leaves, which store chloroplasts and other carotenoid pigments. These pigments are responsible for trapping light energy for photosynthesis. The inner membrane encloses a space called the stroma. Flattened disc-like chlorophyll-containing structures known as thylakoids are arranged in a stacked manner like a pile of coins. Each pile is called a granum (plural: grana) and the thylakoids of different grana are connected by flat membranous tubules known as stromal lamella. Just like the mitochondrial matrix, the stroma of chloroplast also contains a double-stranded circular DNA, 70S ribosomes, and enzymes which are required for the synthesis of carbohydrates and proteins.
- Chromoplasts – The chromoplasts include fat-soluble, carotenoid pigments like xanthophylls, carotene, etc. which provide the plants with their characteristic color – yellow, orange, red, etc.
- Leucoplasts – Leucoplasts are colorless plastids which store nutrients. Amyloplasts store carbohydrates (like starch in potatoes), aleuroplasts store proteins, and elaioplasts store oils and fats.

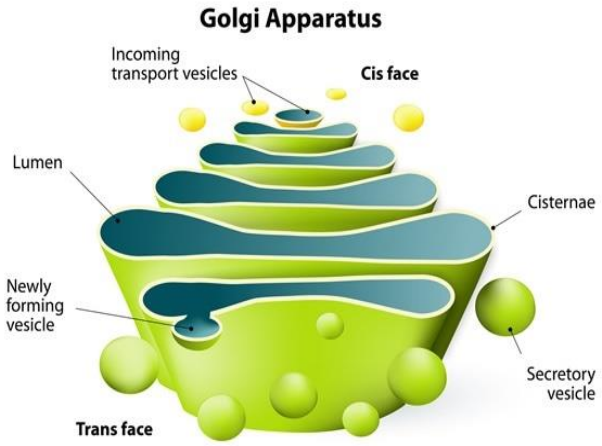
Ribosomes



Ribosomes are non membrane-bound and important cytoplasmic organelles found in close association with the endoplasmic reticulum. Ribosomes are found in the form of tiny particles in a large number of cells and are mainly composed of 2/3rd of RNA and 1/3rd of protein. They are named as the 70s (found in prokaryotes) or 80s (found in eukaryotes) The letter S refers to the density and the size, known as Svedberg's Unit. Both 70S and 80S ribosomes are composed of two subunits. Ribosomes are either encompassed within the endoplasmic reticulum or are freely traced in the cell's cytoplasm. Ribosomal RNA and Ribosomal proteins are the two components that together constitute ribosomes. The primary function of the ribosomes includes protein synthesis in all living cells that ensure the survival of the cell.

Golgi Apparatus

Golgi Apparatus is also termed as Golgi Complex. It is a membrane-bound organelle, which is mainly composed of a series of flattened, stacked pouches called cisternae. This cell organelle is primarily responsible for transporting, modifying, and packaging proteins and lipids to targeted destinations. Golgi Apparatus is found within the cytoplasm of a cell and is present in both plant and animal cells.



Micro bodies

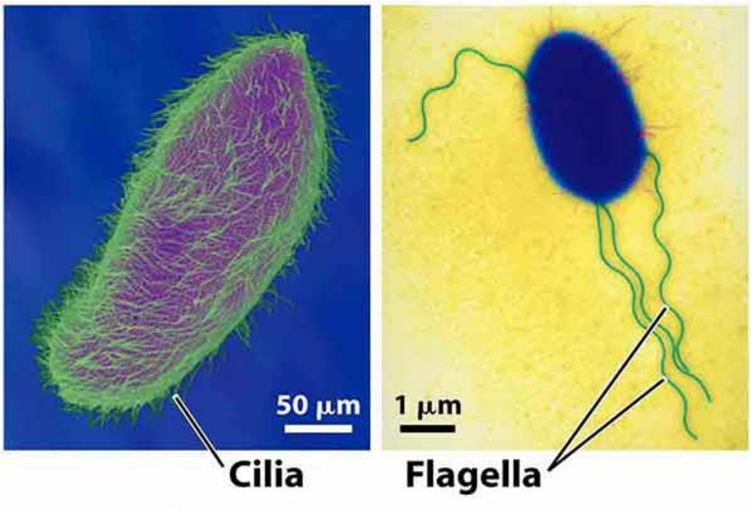
Micro bodies are membrane-bound, minute, vesicular organelles, found in both plant and **animal cells**. They contain various enzymes and proteins and can be visualized only under the electron microscope.

Cytoskeleton

It is a continuous network of filamentous proteinaceous structures that run throughout the cytoplasm, from the nucleus to the plasma membrane. It is found in all living cells, notably in the eukaryotes. The cytoskeleton matrix is composed of different types of proteins that can divide rapidly or disassemble depending on the requirement of the cells. The primary functions include providing the shape and mechanical resistance to the cell against deformation, the contractile nature of the filaments helps in motility during cytokinesis.

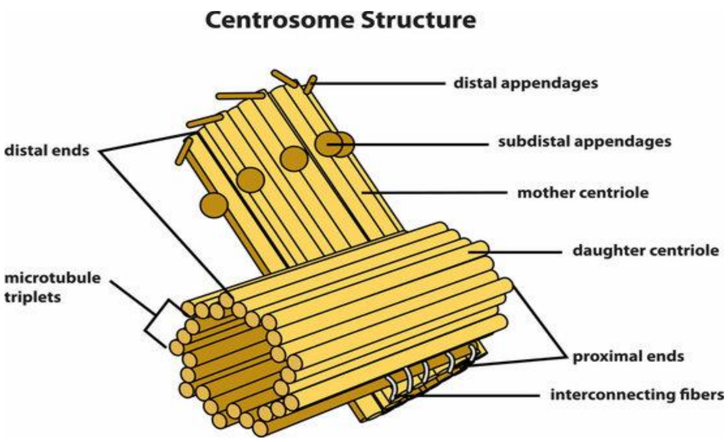
Cilia and Flagella

Cilia are hair-like projections, small structures, present outside the cell wall and work like oars to either move the cell or the extracellular fluid. Flagella are slightly bigger and are responsible for the cell movements. The eukaryotic flagellum structurally differs from its prokaryotic counterpart. The core of the cilium and flagellum is called an axoneme, which contains nine pairs of gradually arranged peripheral **microtubules** and a set of central microtubules running parallel to the axis. The central tubules are interconnected by a bridge and are embedded by a central sheath. One of the peripheral microtubular pairs is also interconnected to the central sheath by a radial spoke. Hence there are a total of 9 radial spokes. The cilia and flagella emerge from centriole-like structures called basal bodies.



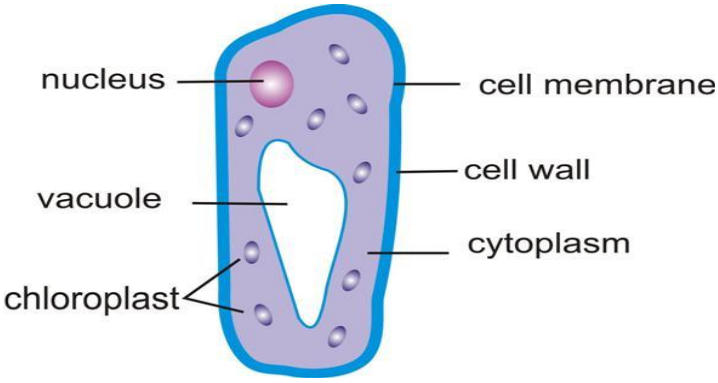
Centrosome and Centrioles

The centrosome organelle is made up of two mutually perpendicular structures known as centrioles. Each centriole is composed of 9 equally spaced peripheral fibrils of tubulin protein, and the fibril is a set of interlinked triplets. The core part of the centriole is known as a hub and is proteinaceous. The hub connects the peripheral fibrils via radial spoke, which is made up of proteins. The centrioles from the basal bodies of the cilia and flagella give rise to spindle fibres during cell division.



Vacuoles

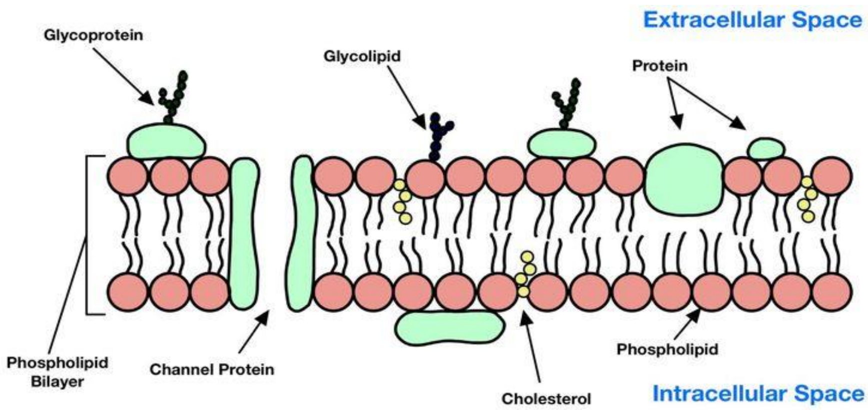
Vacuoles are mostly defined as storage bubbles of irregular shapes which are found in cells. They are fluid-filled organelles enclosed by a membrane. The vacuole stores the food or a variety of nutrients that a cell might need to survive. In addition to this, it also stores waste products. The waste products are eventually thrown out by vacuoles. Thus, the rest of the cell is protected from contamination. The animal and **plant cells** have different size and number of vacuoles. Compared to the animals, plant cells have larger vacuoles.



UNIT – 2

Plasma membrane

Plasma membrane is also referred to as the cell membrane. It is the membrane found in all cells, that separate the inner part of the cell from the exterior. A cell wall is found to be attached to the plasma membrane to its exterior in plant and bacterial cells. Plasma membrane is composed of a lipid layer which is semipermeable. It is responsible to regulate the transportation of materials and the movement of substances in and out of the cell.



Plasma Membrane Functions

- This membrane is composed of a phospholipid bilayer implanted with proteins. It forms a stable barrier between two aqueous compartments, which are towards the outside and inside of a cell in plasma membrane.
- The embedded proteins perform specialized functions which include cell-cell recognition and selective transport of molecules.
- Plasma membrane renders protection to the cell along with providing a fixed environment within the cell. It is responsible for performing different functions.
- In order for it allow movement of substances such as white and red blood cells, it must be flexible such that they could alter the shape and pass through blood capillaries.
- In addition, it also anchors the cytoskeleton to render shape to a cell and in associating with extracellular matrix and other cells to assist the cells in forming a tissue.
- It also maintains the cell potential. Plasma membrane is responsible for interacting with other, adjacent cells which can be glycoprotein or lipid proteins.

- The membrane also assists the proteins to monitor and maintain the chemical climate of the cell, along with the assistance in the shifting of molecules across the membrane.

Lipid bilayer Function

- Lipid bilayer is a fine membrane comprising double layers of lipid molecules, the membranes form a continuous barrier around cells.
- The lipid bilayer serves as a barrier keeping proteins, ions and various other molecules where it is required and prevent its inaccurate diffusion.
- These are impermeable to most of the hydrophilic molecules. In particular, bilayers are impermeable to ions that allow cells to regulate pH and salt concentrations by transportation of ions across its membrane with the use of ion pumps.

Plasma Membrane – Components

Parts of Plasma membrane

It is composed of the following constituents:

- **Phospholipids** – forms the ultimate fabric of the membrane
- **Peripheral proteins** – present on the outer or inner surface of phospholipid bilayer but are not implanted in the hydrophobic core
- **Cholesterol** – folded between the hydrophobic tails of phospholipid membrane
- **Carbohydrates** – found to be attached to the lipids or proteins on the extracellular side of the membrane, leading to the formation of glycolipids and glycoproteins
- **Integral proteins** – found to be implanted in the phospholipid bilayer

Phospholipids spontaneously self-organize into a bilayer. These interactions with water enables formation of plasma membrane.

- Proteins are packed between the lipids which constitute the membrane. Such transmembrane proteins enables their passing into cells through channels, gates or pores which otherwise could not enter.
- Hence, cells regulate the molecule flow and also perform other roles such as cell recognition and signaling.
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- Carbohydrates usually seen in the plasma membrane form a part of glycoproteins which take form when carbohydrates associate with proteins.
- The glycoproteins are significantly involved in the interaction taking place between cells which includes cell adhesion.

Structure Of Plasma Membrane – Bio membrane structure

- Plasma membrane is a fluid mosaic of proteins, lipids and carbohydrates. The plasma membrane picture provided above shows the detailed structure of the plasma membrane.
- It is impermeable to ions and water-soluble molecules crossing membranes only through carriers, transmembrane channels and pumps.
- The transmembrane proteins nourish the cell with nutrients, regulate the internal ion concentration and set up a transmembrane electrical potential.
- Change in a single amino acid in one Cl^- channel and plasma membrane pump can lead to human disease cystic fibrosis.
- On the basis of location of the membrane in the body, lipids can make up anywhere from 20-80% of the membrane, the rest being proteins.
- It is composed of a phospholipid bilayer, which is two layers of phospholipids back-to-back. Phospholipids are lipids with a phosphate group associated with them.
- The phospholipids have one head and two tails where the head is polar and water-loving or hydrophilic. Tails on the other hand are nonpolar and water-fearing or hydrophobic.

Phospholipids of Plasma membrane

- Phospholipids constitute a main element of biological membranes, they are the most abundant lipids found in the membrane.
- In addition to membrane changes, these components are also operational in signaling hubs.
- The assemblage of distinct phospholipids is a defining trait of various compartments of the cell which aim at the phospholipid-binding proteins to those compartments.
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- Phosphatidylethanolamine (PE), Phosphatidylcholine (PC), Sphingomyelin and Phosphatidylserine (PS) usually comprise the framework of biological membranes of animal cells which are stabilized by cholesterol.
- The phospholipids mentioned are distributed asymmetrically between the two halves of the bilayer membrane.
- The inner leaflet of the membrane consists of the phosphatidylserine and phosphatidylethanolamine predominantly while the outer leaflet mainly comprises the sphingomyelin and phosphatidylcholine.

Fluid Mosaic Model

The description of the structure of plasma membrane can be carried out through the fluid mosaic model as a mosaic of cholesterol, carbohydrates, proteins and phospholipids.

First proposed in 1972 by Garth L. Nicolson and S.J. Singer, the model explained the structure of plasma membranes.

- The model evolved with time however, it still accounts for the functions and structure of plasma membranes the best way.
- The model describes plasma membrane structure as a mosaic of components which includes proteins, cholesterol, phospholipids, and carbohydrates; it imparts a fluid character on the membrane.
- Thickness of the membrane is in the range of 5-10nm. The proportion of constituency of plasma membrane i.e., the carbohydrates, lipids and proteins vary from cell to cell.
- For instance, the inner membrane of the mitochondria comprises 24% lipid and 76% protein, in myelin, 76% lipid is found and 18% protein.

Phospholipids

- The chief fabric of this membrane comprises phospholipid molecules that are amphiphilic.
- The hydrophilic regions of such molecules are in touch with the aqueous fluid outside and inside the cell.
- The hydrophobic or the water-hating molecules on the other hand are non-polar in nature.
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- One phospholipid molecule comprises a three-carbon glycerol backbone along with 2 fatty acid molecules associated to carbons 1 and 2, and one phosphate-containing group connected to the third carbon.
- This organisation provides a region known as head to the molecule on the whole.
- The head, which is a phosphate-containing group possesses a polar character or a negative charge while the tail, another region containing fatty acids, does not have any charge.
- They tend to interact with the non-polar molecules in a chemical reaction however, do not typically interact with the polar molecules.
- The hydrophobic molecules when introduced to water, have the tendency to form a cluster.
- On the other hand, hydrophilic areas of the phospholipids have the tendency to form hydrogen bonds with water along with other polar molecules within and outside the cell.
- Therefore, the membrane surface interacting with the exterior and interior of cells are said to be hydrophilic.
- On the contrary, the middle of the cell membrane is hydrophobic and does not have any interaction with water.
- Hence, phospholipids go on to form a great lipid bilayer cell membrane separating fluid inside the cell from the fluid to the exterior of the cell.

Proteins

- The second major component is formed by the proteins of the plasma membrane.
- Integrins or integral proteins integrate fully into the structure of the membrane, along with their hydrophobic membrane, ranging from regions interacting with hydrophobic regions of phospholipid bilayer.
- Typically, single-pass integral membrane proteins possess a hydrophobic transmembrane segment consisting of 20-25 amino acids.
- Few of these traverses only a portion of the membrane linking with one layer whereas others span from one to another side of the membrane, thereby exposing to the flip side.
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- Few complex proteins consist of 12 segments of one protein, highly convoluted to be implanted in the membrane.
- Such a type of protein has a hydrophilic region/s along with one or more mildly hydrophobic areas.
- This organisation of areas of the proteins has the tendency to align the protein along with phospholipids where the hydrophobic area of the protein next to the tails of the phospholipids and hydrophilic areas of protein protrudes through the membrane is in touch with the extracellular fluid or cytosol.

Carbohydrates

- The third most important component of the plasma membrane are carbohydrates.
- hey are generally found on the outside of the cells and linked either to lipids to form glycolipids or proteins to form glycoproteins.
- The chain of this carbohydrate can comprise two to sixty monosaccharide units which could be branched or straight.
- Carbohydrates alongside peripheral proteins lead to the formation of concentrated sites on the surface of the cell which identify each other.
- This identification is crucial to cells as they permit the immune system to distinguish between the cells of the body and the foreign cells/tissues.
- Such glycoproteins and glycoproteins are also observed on the surface of viruses, which can vary thereby preventing the immune cells to identify them and attract them.
- On the exterior surface of cells, these carbohydrates, their components of both glycolipids and glycoproteins are together known as glycocalyx, which is extremely hydrophilic in nature attracting huge quantities of water on the cell surface.
- This helps the cell to interact with its fluid-like environment and also in the ability of the cell to acquire substances dissolved in water.

Micellar model of Plasma membrane

In 1963, Hilleir and Hoffman suggested that biological membranes can have a non-lamellar pattern. As per them, the plasma membrane has a mosaic of globular subunits referred to as micelles that are densely packed with a central core of lipid molecules with a hydrophilic polar end.

- As lipid micelles have a tendancy towards spontaneous linking, they are probable building blocks for membranes.
- The protein components of the membrane in this model can establish a monolayer on either sides of the plane of lipid micelles.
- It is suggested that the gaps between the globular micelles form water-filled pores which are partially lined by polar groups of micelles and partially by polar groups of associate protein molecules.

Cell Transport and Its Types

The movement of a substance across the cell membrane is known as cell transport. The substance can move either in or out of the cells. There are various molecules that pass through the plasma membrane or the cell membrane. The plasma membrane is highly selective in nature.

Introduction to types of transport

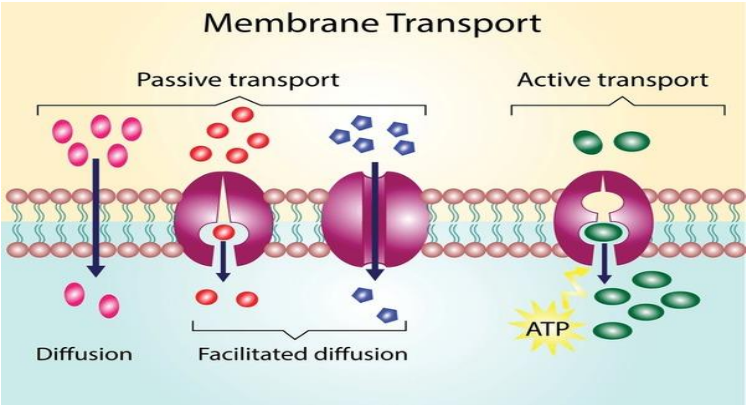
Types of transport across cell membranes are listed below.

- Active Transport
- Passive Transport
- Facilitators

Active Transport: Active transport requires energy in the form of ATP, solute from lower concentration to higher concentration transport through cell membrane.

Passive Transport: Passive transport does not require any energy and it transmits solute from high concentration to lower concentration through the transport through cell membrane.

Facilitators: The facilitators will allow the diffusion process to take place through the membrane made up of glycoprotein.



Types of Active Transports

The active transports are classified into four types based on their action mechanism. They are listed below

1. Anti-port Pumps

2. Symport Pumps

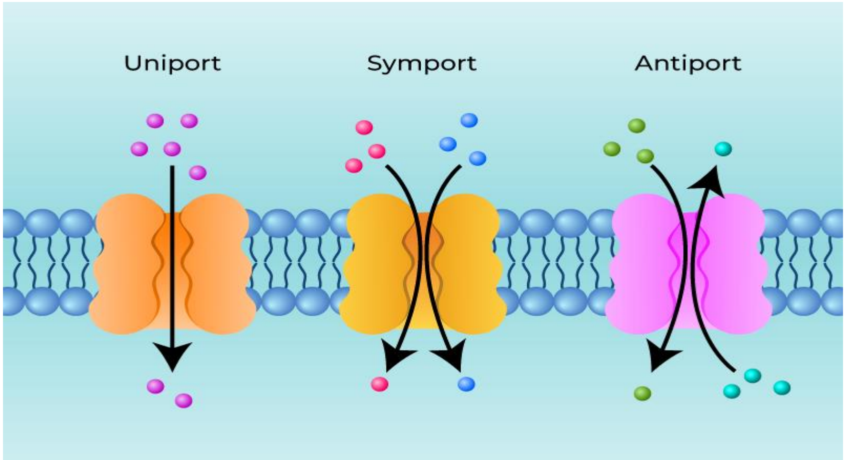
3. Endocytosis

4. Exocytosis

Anti-port Pumps: The transmembrane is made up of co-transporter protein. This will pump a substance in one direction and transport the substance to another direction. The ATP molecules are enough to perform this process. An example of an antiport pump is the sodium-potassium pump.

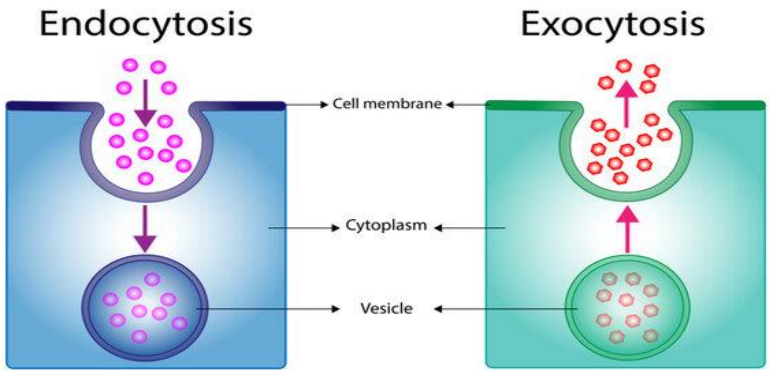
Symport Pumps: The molecules of two different substances can move in the same direction related to each other through the protein transmembrane. Here, the movement of molecules or substances occurs from higher concentration to lower concentration. An example of symport pumps transport is a sodium-glucose transport protein

Uniport Pumps: when a particular type of molecule moves across a membrane, through carrier protein, independent of other molecule, the diffusion is called uniport.



Endocytosis: The larger molecules or large substances of extracellular fluid will enter into the cell through the process of endocytosis. The cell utilizes its protein membrane to fold the membrane into the pockets. The pocket formed around the larger molecules enters the cell. These membrane packets, which carry materials inside the cells are termed vesicles.

Exocytosis: The process of exocytosis is the opposite of endocytosis. The vesicle present inside the cell moves outside of the cell membrane is known as exocytosis. This is commonly occurring, when the cell needs to export a molecule, enzymes and hormones In eukaryotic cells, the protein products are made up of endoplasmic reticulum. The Golgi apparatus helps in packaging and removing these substances.



Transport Mechanism Across Cell Membrane

- The chemical structure of the cell membrane is flexible, it is because of the rapid growth of cells and cell division.
- The cell membrane is also known as a formidable barrier. This allows and blocks the dissolved substances or solutes to pass through the membrane.
- The Lipid soluble molecules and some other molecules can fill the membrane, but the bilayer lipid effectively repels the entry of larger water-soluble molecules.
- In order to make the cell live, the electrically charged ions must be imported or exported from the cell.

Transport systems

- The transport systems are carried out by different intrinsic proteins to perform the transportation of vital substances in cells.
- The types of intrinsic proteins are open channels, facilitators, and pumps. The open channel allows the ion to directly diffuse into the cell.
- Facilitators will allow the little chemical transformation. It helps to diffuse solutes to pass the lipid screen.
- The pump will force solutes to pass through the membrane if they are not concentrated enough to diffuse into the cell membrane spontaneously.
- The large particles, which are pumped or diffused can occur only by opening or closing the membrane.

Diffusion in the cell membrane

- The major principle behind the movement of solutes transport across the cell membranes is based on the diffusion process.
- According to the diffusion process, dissolved substances transported across membranes through a concentration gradient. This does not require external energy to move from a higher concentration to a lower concentration.
- This diffusion continues and starts decreasing gradually till it attains the equilibrium state.
- The random diffusion occurs from both places at an equal ratio during the equilibrium state.
- A solute at a high concentration has high free energy. These are capable to do more work than the solute at low concentration.
- While performing the diffusion process, the solutes lose their free energy.
- So, the solutes are unable to return to the high concentration, after attaining the lower concentration or equilibrium state.
- But, it is possible to perform the transport of ions across the cell membrane to higher concentrations through an ion pump.

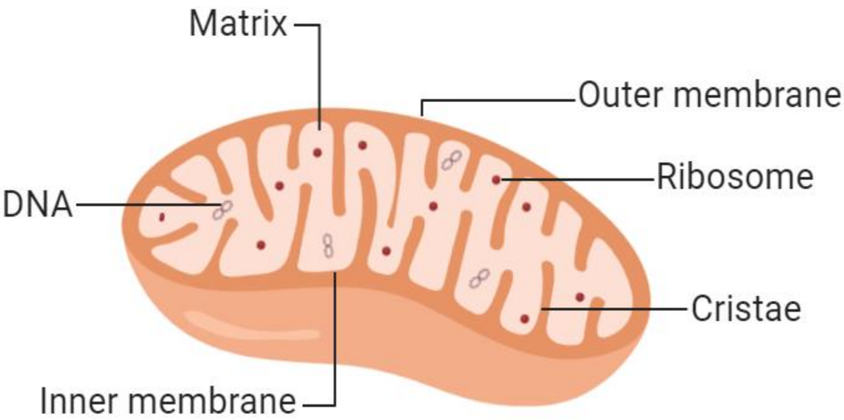
Role of pumps in transport

- For many substances, the concentration present inside the cells is different from the concentration present outside the cell.
- This can create the concentration gradient and solutes start diffusing from higher concentration to lower concentration of cell through the lipid bi layer, membrane channel, and diffusion facilitators.
- The changes in protein help to take place to facilitate diffusion. For the healthy cell function, some solutes in each side of the membrane must remain at different concentrations.
- If the cells undergo diffusion and approach equilibrium, they must be pumped back to their gradient concentration using active transport.
- The membrane proteins, which serve as pumps will provide the energy for transport across plasma membrane for cell metabolism or diffusion of other solutes.

UNIT - 3

Mitochondria

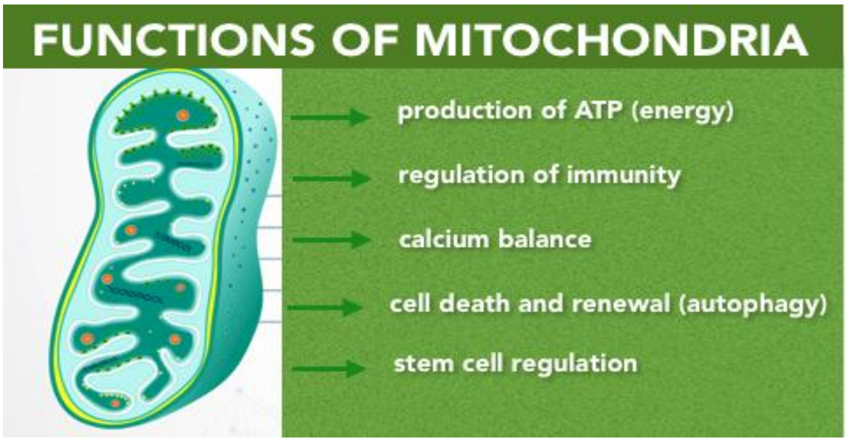
Mitochondria are the powerhouse of cells as they generate energy for cell functioning. The structure of mitochondria is unique. The mitochondrion is a rod or sausage-shaped structure found in animal and plant cells. It is a small organelle whose size is between 0.5 to 1 micrometre in diameter. Hence, it cannot be seen under a microscope unless stained. Unlike other organelles, it has two layers; inner and outer. Each layer performs different functions.



Mitochondria Structure

- **Outer Membrane -** It is made of proteins. The membrane allows small protein-like molecules to pass through it.
- **Intermembrane Space -** It is the space between outer and inner membranes.
- **Inner Membrane -** This membrane is made of phospholipids and does not allow molecules to pass through it. Special transporters (carrier molecules) are required to transport substances. Here, ATP production takes place.
- **Cristae -** These are the irregular folds of the inner membrane. They increase the space for chemical reactions to take place by increasing the surface area of the membrane.
- **Matrix -** It is fluid within the inner membrane. This fluid has several enzymes required for ATP production. It also contains ribosomes, mitochondrial DNA, inorganic and organic molecules, etc.

Functions of Mitochondria



The most common function of Mitochondria is energy generation. However, it performs several other vital functions of the body. These include the following.

Energy Generation

Mitochondria help produce ATP molecules which are the energy units of cells. Most energy production takes place in the cristae or folds of the inner membrane. It generates energy by converting chemical energy from food.

Cell Death

Apoptosis or cell death is an essential part of the regeneration of new cells. As cells damage or become old, they are destroyed by the mitochondria, and new cells are formed. It releases enzymes like Cytochrome C, which helps in cell degeneration.

Heat Production

In extreme colds, the body generates its heat by utilising tissue fat. Mitochondria release energy in the form of heat in cold climatic conditions.

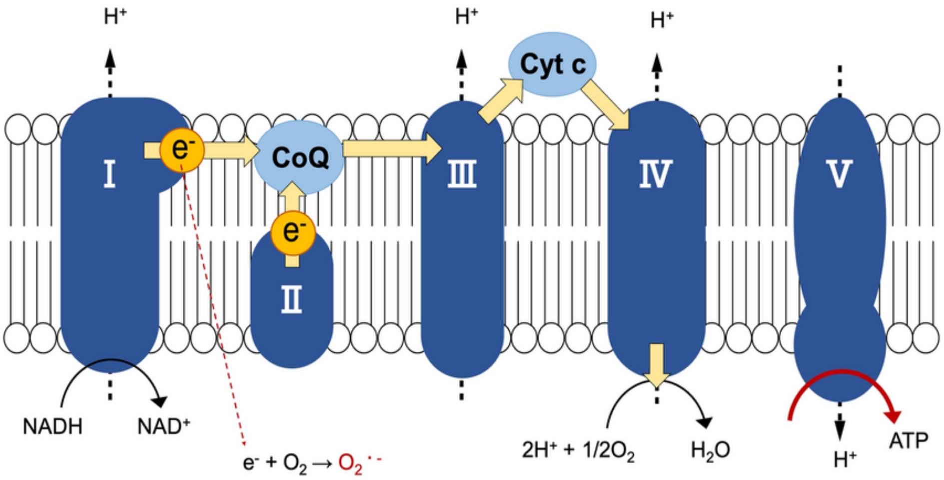
Storing Calcium

Calcium is involved in several cellular processes. For example, releasing neurotransmitters for nerve conduction and muscle movement, blood clotting, fertilisation, hormone signalling, steroid synthesis, and cellular metabolism. As calcium is so important for the body, cells regulate it tightly. Mitochondria help in the absorption of calcium ions and store them until they are used.

Mitochondrial respiratory chain

Electron Transport Chain is a series of compounds where it makes use of electrons from electron carrier to develop a chemical gradient. It could be used to power oxidative phosphorylation. The molecules present in the chain comprises enzymes that are protein complex or proteins, peptides and much more.

Large amounts of ATP could be produced through a highly efficient method termed oxidative phosphorylation. ATP is a fundamental unit of metabolic process. The electrons are transferred from electron donor to the electron acceptor leading to the production of ATP. It is one of the vital phases in the electron transport chain. Compared to any other part of cellular respiration the large amount of ATP is produced in this phase.



Electron transport is defined as a series of redox reaction that is similar to the relay race. It is a part of aerobic respiration. It is the only phase in glucose metabolism that makes use of atmospheric oxygen. When electrons are passed from one component to another until the end of the chain the electrons reduce molecular oxygen thus producing water. The requirement of oxygen in the final phase could be witnessed in the chemical reaction that involves the requirement of both oxygen and glucose.

Electron Transport Chain in Mitochondria

A complex could be defined as a structure that comprises a weak protein, molecule or atom that is weakly connected to a protein. The plasma membrane of prokaryotes comprises multi copies of the electron transport chain.

Complex 1- NADH-Q oxidoreductase: It comprises enzymes consisting of iron-sulfur and FMN. Here two electrons are carried out to the first complex aboard NADH. FMN is derived from vitamin B2.

Q and Complex 2- Succinate-Q reductase: FADH2 that is not passed through complex 1 is received directly from complex 2. The first and the second complexes are connected to a third complex through compound ubiquinone (Q). The Q molecule is soluble in water and moves freely in the hydrophobic core of the membrane. In this phase, an electron is delivered directly to the electron protein chain. The number of ATP obtained at this stage is directly proportional to the number of protons that are pumped across the inner membrane of the mitochondria.

Complex 3- Cytochrome c reductase: The third complex is comprised of Fe-S protein, Cytochrome b, and Cytochrome c proteins. Cytochrome proteins consist of the heme group. Complex 3 is responsible for pumping protons across the membrane. It also passes electrons to the cytochrome c where it is transported to the 4th complex of enzymes and proteins. Here, Q is the electron donor and Cytochrome C is the electron acceptor.

Complex 4- Cytochrome c oxidase: The 4th complex is comprised of cytochrome c, a and a3. There are two heme groups where each of them is present in cytochromes c and a3. The cytochromes are responsible for holding oxygen molecule between copper and iron until the oxygen content is reduced completely. In this phase, the reduced oxygen picks two hydrogen ions from the surrounding environment to make water.

Oxidative Phosphorylation

Oxidative phosphorylation is the final step in cellular respiration. It occurs in the mitochondria. It is linked to a process known as electron transport chain. The electron transport system is located in the inner mitochondrial membrane. The electrons are transferred from one member of the transport chain to another through a series of redox reactions.

➢ Oxidative Phosphorylation Steps

The major steps of oxidative phosphorylation in mitochondria include:

➢ Delivery of Electrons by NADH and FADH2

Reduced NADH and FADH2 transfer their electrons to molecules near the beginning of the transport chain. After transferring the electrons, they get oxidised to NAD+ and FAD and are utilised in other steps of cellular respiration.

➢ Electron Transport and Proton Pumping

The electrons move from a higher energy level to a lower energy level, thereby releasing energy. Some of the energy is used to move the electrons from the matrix to the intermembrane space. Thus, an electrochemical gradient is established.

➢ Splitting of Oxygen to form Water

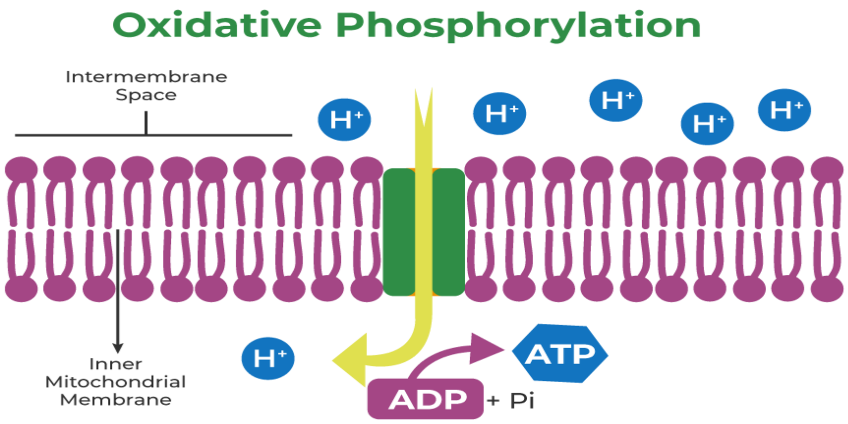
The electrons are then transferred to the oxygen molecule which splits into half and uptakes H+ to form water.

➢ ATP Synthesis

The H+ ions pass through an enzyme called ATP synthase while flowing back into the matrix. This controls the flow of protons to synthesize ATP.

➢ Chemiosmosis

- Oxidative phosphorylation uses the chemical reactions that release energy to drive a chemical reaction that requires energy.
- These 2 sets of reactions are coupled and interrelated.
- The electrons that flow through electron transport chain is an exergonic process and the synthesis of ATP is an endergonic process.
- These two processes are ingrained within a membrane. As a result, energy will be transmitted from the electron transport chain to ATP synthase by the movement of proteins. This process is termed as chemiosmosis.
- Endergonic Process is a chemical reaction in which energy is absorbed. There will be a change in free energy and it is always positive.
- Exergonic Process is a chemical reaction in which there will be a positive flow of energy from the system to the surrounding environment.
- Chemical reactions are also considered exergonic when they are spontaneous.



Chloroplast

Plants form the basis of all life on earth and are known as producers. Plant cells contain structures known as plastids which are absent in animal cells. These plastids are double-membraned cell organelles which play a primary role in the manufacturing and storing of food. There are three types of plastids –

- Chromoplasts- They are the colour plastids, found in all flowers, fruits and are mainly responsible for their distinctive colours.
- Chloroplasts- They are green coloured plastids, which comprise green-coloured pigments within the plant cell and are called chlorophyll.
- Leucoplasts- They are colourless plastids and are mainly used for the storage of starch, lipids and proteins within the plant cell.

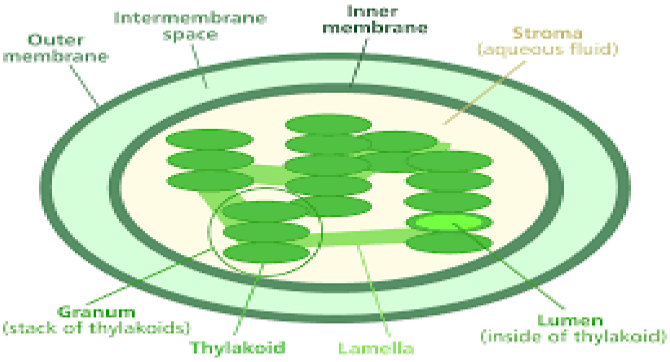
Chloroplast Definition

"Chloroplast is an organelle that contains the photosynthetic pigment chlorophyll that captures sunlight and converts it into useful energy, thereby, releasing oxygen from water. "

The chloroplast diagram below represents the chloroplast structure mentioning the different parts of the chloroplast. The parts of a chloroplast such as the inner membrane, outer membrane, intermembrane space, thylakoid membrane, stroma and lamella can be clearly marked out.

Structure of Chloroplast

Chloroplasts are found in all higher plants. It is oval or biconvex, found within the mesophyll of the **plant cell**. The size of the chloroplast usually varies between 4-6 µm in diameter and 1-3 µm in thickness. They are double-membrane organelle with the presence of outer, inner and intermembrane space. There are two distinct regions present inside a chloroplast known as the grana and stroma.



- Grana are made up of stacks of disc-shaped structures known as thylakoids or lamellae. The grana of the chloroplast consists of chlorophyll pigments and are the functional units of chloroplasts.
- Stroma is the homogenous matrix which contains grana and is similar to the cytoplasm in cells in which all the organelles are embedded. Stroma also contains various enzymes, DNA, ribosomes, and other substances. Stroma lamellae function by connecting the stacks of thylakoid sacs or grana.

The chloroplast structure consists of the following parts:

Membrane Envelope

It comprises inner and outer lipid bilayer membranes. The inner membrane separates the stroma from the intermembrane space.

Intermembrane Space

The space between inner and outer membranes.

Thylakoid System (Lamellae)

The system is suspended in the stroma. It is a collection of membranous sacs called thylakoids or lamellae. The green coloured pigments called chlorophyll are found in the thylakoid membranes. It is the sight for the process of light-dependent reactions of the photosynthesis process. The thylakoids are arranged in stacks known as grana and each granum contains around 10-20 thylakoids.

Stroma

It is a colourless, alkaline, aqueous, protein-rich fluid present within the inner membrane of the chloroplast present surrounding the grana.

Grana

Stack of lamellae in plastids is known as grana. These are the sites of conversion of light energy into chemical energy.

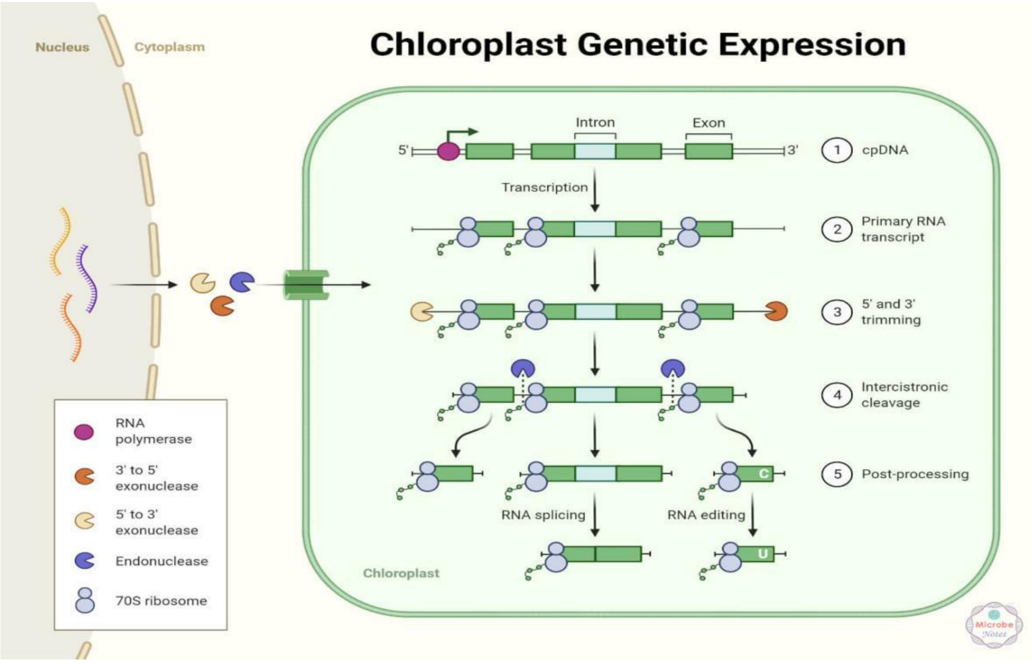
Chlorophyll

It is a green photosynthetic pigment that helps in the process of photosynthesis.

Semi-autonomous nature of chloroplast

Like the mitochondria, they are also known as semi-autonomous cell organelles as they have their DNA and complete machinery to synthesize some of the required proteins.

- While some other proteins depend upon nuclear DNA and cytoplasmic ribosomes.
- Chloroplast and mitochondria are the only two organelles having their DNA.



Functions of Chloroplasts

- Chloroplasts are the sites for photosynthesis, which comprises a set of light-dependent and light-independent reactions to harness solar energy and convert it into chemical energy.
- The components of chloroplast participate in several regulatory functions of the cell as well as in photorespiration.
- Chloroplasts also provide diverse metabolic activities for plant cells, including the synthesis of fatty acids, membrane lipids, isoprenoids, tetrapyrroles, starch, and hormones.
- Plants lack specialized immune cells—all plant cells participate in the plant response.
- The chloroplasts with the nucleus and cell membrane and ER are the key organelles of pathogen defense.
- Chloroplasts can serve as cellular sensors.

Calvin Cycle

Photosynthesis is the biochemical process that occurs in all green plants or autotrophs producing organic molecules from carbon dioxide (CO2). These organic molecules contain many carbon-hydrogen (C–H) bonds and are highly reduced compared to CO2.

There are two stages of Photosynthesis –

Light-dependent reactions – As the name suggests, it requires light and mainly occurs during the daytime.

Light-independent reactions – It is also called the dark reaction or Calvin cycle or C3 cycle. This reaction occurs both in the presence and absence of sunlight.

Calvin cycle is also known as the C3 cycle or light-independent or dark reaction of photosynthesis. However, it is most active during the day when NADPH and ATP are abundant. To build organic molecules, the plant cells use raw materials provided by the light reactions:

1. Energy: ATP provided by cyclic and noncyclic photophosphorylation, which drives the endergonic reactions.

2. Reducing power*:* NADPH provided by photosystem I is the source of hydrogen and the energetic electrons required to bind them to carbon atoms. Much of the light energy captured during photosynthesis ends up in the energy-rich C—H bonds of sugars.

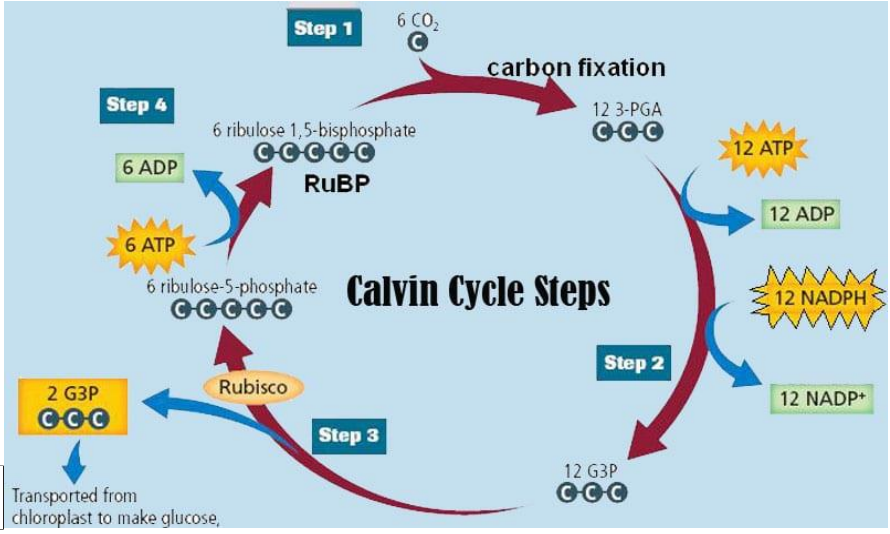
Plants store light energy in the form of carbohydrates, primarily starch and sucrose. The carbon and oxygen required for this process are obtained from CO2, and the energy for carbon fixation is derived from the ATP and NADPH produced during the photosynthesis process.

The conversion of CO2 to carbohydrate is called Calvin Cycle or C3 cycle and is named after Melvin Calvin who discovered it. The plants that undergo the Calvin cycle for carbon fixation are known as C3 plants.

Calvin Cycle requires the enzyme ribulose-1,5-bisphosphate carboxylase/oxygenase commonly called RuBisCO. It generates the triose phosphates, 3-phosphoglycerate (3-PGA), glyceraldehyde-3P (GAP), and dihydroxyacetone phosphate (DHAP), all of which are used to synthesize the hexose phosphates fructose-1,6-bisphosphate and fructose 6-phosphate.

C3 Cycle Diagram

The Calvin cycle diagram below shows the different stages of Calvin Cycle or C3 cycle that include carbon fixation, reduction, and regeneration.



Stages of C3 Cycle

Calvin cycle or C3 cycle can be divided into three main stages:

Carbon fixation

The key step in the Calvin cycle is the event that reduces CO2.

CO2 binds to RuBP in the key process called carbon fixation, forming two-three carbon molecules of phosphoglycerate. The enzyme that carries out this reaction is ribulose bisphosphate carboxylase/oxygenase, which is very large with a four-subunit and present in the chloroplast stroma. This enzyme works very sluggishly, processing only about three molecules of RuBP per second (a typical enzyme process of about 1000 substrate molecules per second). In a typical leaf, over 50% of all the protein is RuBisCO. It is thought to be the most abundant protein on the earth.

Reduction

It is the second stage of Calvin cycle. The 3-PGA molecules created through carbon fixation are converted into molecules of simple sugar – glucose.

This stage obtains energy from ATP and NADPH formed during the light-dependent reactions of photosynthesis. In this way, Calvin cycle becomes a pathway in which plants convert sunlight energy into long-term storage molecules, such as sugars. The energy from the ATP and NADPH is transferred to the sugars.

This step is known as reduction since electrons are transferred to 3-PGA molecules to form glyceraldehyde-3 phosphate.

Regeneration

It is the third stage of the Calvin cycle and is a complex process that requires ATP. In this stage, some of the G3P molecules are used to produce glucose, while others are recycled to regenerate the RuBP acceptor.

Products of C3 Cycle

- One molecule of carbon is fixed at each turn of the Calvin cycle.
- One molecule of glyceraldehyde-3 phosphate is created in three turns of the Calvin cycle.
- Two molecules of glyceraldehyde-3 phosphate combine together to form one glucose molecule.
- 3 ATP and 2 NADPH molecules are used during the reduction of 3-phosphoglyceric acid to glyceraldehyde-3 phosphate and in the regeneration of RuBP.
- 18 ATP and 12 NADPH are consumed in the production of 1 glucose molecule.

UNIT - 4

Mitosis

"Mitosis is that step in the cell cycle where the newly formed DNA is separated and two new cells are formed with the same number and kind of chromosomes as the parent nucleus."

Cell division is the driving process of reproduction at the cellular level. Most eukaryotic cells divide in a manner where the ploidy or the number of chromosomes remains the same, except in the case of germ cells where the number of chromosomes is halved.

Mitosis is the phase of the cell cycle where the nucleus of a cell is divided into two nuclei with an equal amount of genetic material in both the daughter nuclei. It succeeds the G2 phase and is succeeded by cytoplasmic division after the separation of the nucleus.

Mitosis is essential for the growth of the cells and the replacement of worn-out cells. Abnormalities during mitosis may alter the DNA, resulting in genetic disorders.

Features of Mitosis

1. In each cycle of cell division, two daughter cells are formed from the parent cell.
2. The cell is also known as equational cell division because the chromosome number in the parent cell and daughter cell is the same.
3. In plants, mitosis leads to the growth of vegetative parts of the plant like root tip, stem tip, etc.
4. Segregation and combination do not occur in this process.

The processes occurring during mitosis have been divided into different stages.

Stages of Mitosis

Right before prophase, the cell spends most of its life in the interphase, where preparations are made before the beginning of mitosis (the DNA is copied). However, since the actual process involves the division of the nucleus, the prophase is technically the first stage of this process.

The different stages of mitosis occurring during cell division are given as follows-

- **Interphase**

Before entering mitosis, a cell spends a period of its growth under interphase. It undergoes the following phases when in interphase:

- G1 Phase: This is the period before the synthesis of DNA.
- S Phase: This is the phase during which DNA synthesis takes place.
- G2 Phase: This is the phase between the end of DNA synthesis and the beginning of the prophase.

Prophase

Prophase immediately follows the S and G2 phases of the cycle and is marked by condensation of the genetic material to form compact mitotic chromosomes composed of two chromatids attached at the centromere.

The completion of the prophase is characterised by the initiation of the assembly of the mitotic spindle, the microtubules and the proteinaceous components of the cytoplasm that help in the process.

The nuclear envelope starts disintegrating.

Prometaphase

In the prometaphase, the nuclear envelop disintegrates. Now the microtubules are allowed to extend from the centromere to the chromosome. The microtubules attach to the kinetochores which allow the cell to move the chromosome around.

Metaphase

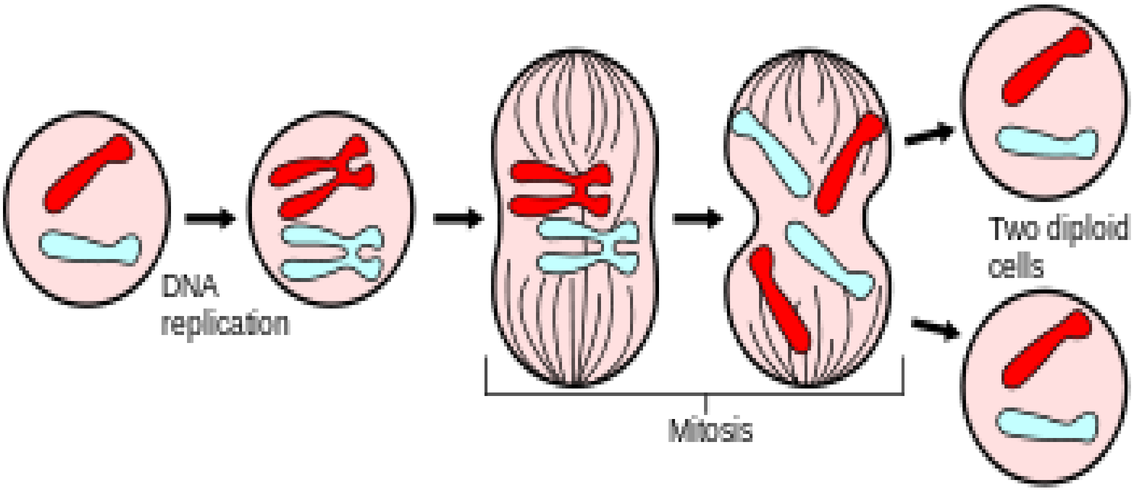
At this stage, the microtubules start pulling the chromosomes with equal force and the chromosome ends up in the middle of the cell. This region is known as the metaphase plate. Thus, each cell gets an entire functioning genome.

Anaphase

The splitting of the sister chromatids marks the onset of anaphase. These sister chromatids become the chromosome of the daughter nuclei. The chromosomes are then pulled towards the pole by the fibres attached to the kinetochores of each chromosome. The centromere of each chromosome leads at the edge while the arms trail behind it.

➢ Telophase

The chromosomes that cluster at the two poles start coalescing into an undifferentiated mass, as the nuclear envelope starts forming around it. The nucleolus, Golgi bodies and ER complex, which had disappeared after prophase start to reappear.Telophase is followed by cytokinesis, which denotes the division of the cytoplasm to form two daughter cells. Thus, it marks the completion of cell division.



Functions of Mitosis

Following are the two important functions of mitosis:

1. Mitosis helps in the development of an organism. In single-celled organisms, mitosis is the process of asexual reproduction.
2. Mitosis helps in the replacement of damaged tissues. The cells near the damaged cells begin mitosis when they do not sense the neighbouring cells. The dividing cells reach each other and cover the damaged cells.

Significance of Mitosis

1. Mitosis is responsible for the development of the zygote into an adult.
2. Equal distribution of chromosomes to each daughter cell.
3. It is responsible for the growth and development of an individual.
4. It maintains the constant number of chromosomes in all body cells of an organism.
5. Mitosis is required for asexual reproduction, vegetative propagation in plants and is also responsible for the repair and regeneration of damaged tissues.

6. Mitosis helps in maintaining the purity of the genome as no recombination or crossing over takes place.
7. It is responsible for the repair and regeneration of old and damaged cells in animals e.g. gut epithelium, blood cells, etc.

Meiosis

"Meiosis is the type of cell division that results in four daughter cells, each with half the number of chromosomes of the parent cell."

Meiosis is the process in which a single cell divides twice to form four haploid daughter cells. These cells are the gametes – sperms in males and egg in females. The process of meiosis is divided into 2 stages. Each stage is subdivided into several phases.

- **Meiosis I:**
  - Prophase I
  - Metaphase I
  - Anaphase I
  - Telophase I
  - Cytokinesis I
- **Meiosis II:**
  - Prophase II
  - Metaphase II
  - Anaphase II
  - Telophase II
  - Cytokinesis II

Stages of Meiosis

Meiosis cell division takes place in the following stages:

Meiosis I

Prophase I

- The nuclear envelope disintegrates.
- Chromosomes begin to condense.
- Spindle fibres appear.

Prometaphase II

Spindle fibres attach to the chromosomes at the centromere.

Metaphase I

The homologous chromosomes align at the equatorial plate ensuring genetic diversity among offspring.

Anaphase I

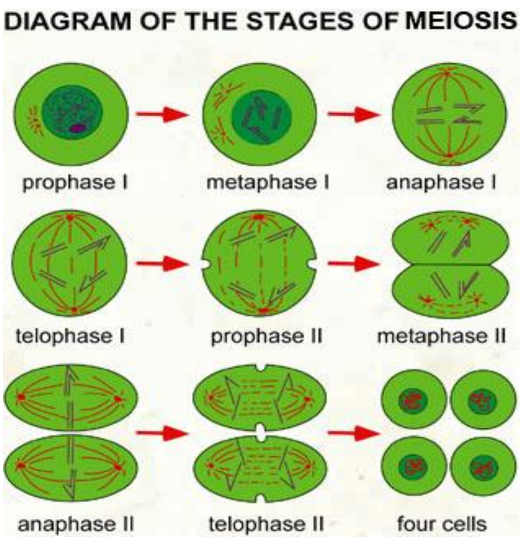
The homologous chromosomes are pulled towards the opposite poles.

Telophase I

- Spindle fibres disappear.
- Nuclear envelope is reformed.

Cytokinesis I

The cytoplasm and the cell division result in 2 non-identical haploid daughter cells.



Meiosis II

Prophase II

- The chromatin condenses into chromosomes.
- Nuclear envelope disintegrates.
- Centrosomes migrate to either poles.
- Spindle fibres are reformed.

Metaphase II

The chromosomes align along the equatorial plate. On the contrary, the chromosomes in metaphase I were in homologous pairs.

Anaphase II

Sister chromatids are pulled to the opposite poles.

Telophase II

Nuclear envelope redevelops and the spindle fibres disappear.

Cytokinesis II

The cytoplasm and cell divide producing 4 non-identical haploid daughter cells.

Features of Meiosis

- It results in the formation of four daughter cells in each cycle of cell division.
- The daughter cells are identical to the mother cell in shape and size but different in chromosome number.
- The daughter cells are haploid.
- Recombination and segregation take place in meiosis.
- The process occurs in the reproductive organs and results in the formation of gametes.
- The process is divided into two types-Meiosis-I reduces the chromosome number to half and is known as reductional division. Meiosis-II is just like the mitotic division.

Significance

1. Meiosis is responsible for the formation of sex cells or gametes that are responsible for sexual reproduction.
2. It activates the genetic information for the development of sex cells and deactivates the sporophytic information.
3. It maintains the constant number of chromosomes by halving the same. This is important because the chromosome number doubles after fertilization.
4. In this process independent assortment of maternal and paternal chromosomes takes place. Thus the chromosomes and the traits controlled by them are reshuffled.
5. The genetic mutation occurs due to irregularities in cell division by meiosis. The mutations that are beneficial are carried on by natural selection.
6. Crossing over produces a new combination of traits and variations.

Cell cycle regulation mechanism

The cell cycle is the sequence of events occurring in an ordered fashion which results in cell growth and cell division.

- The cycle begins at the end of each nuclear division and ends with the beginning of the next.
- A cell cycle acts as a unit of biological time that defines the life history of the cell.
- The cell cycle is a continuous process that includes all significant events of the cell, ranging from duplication of DNA and cell organelles to subsequent partitioning of the cytoplasm.
- In addition, the process of cell growth where the cell absorbs nutrients and prepares for its cell division is also a part of the cell cycle.
- The process of the cell cycle occurs in various phases, all of which are specialized for a particular stage of the cell.
- The overall process and steps of the cell cycle might differ in eukaryotic and prokaryotic organisms as a result of the differences in their cell complexity.
- Three main cycles are involved in the cell cycle; chromosome cycle, cytoplasmic cycle, and centrosome cycle.
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- The chromosome cycle involves DNA synthesis that alternates with mitosis. During this cycle, the double-helical DNA of the cell replicates to form two identical daughter DNA molecules. This is followed by mitosis to separate the cell into two daughter cells.
- The cytoplasmic cycle involves cell growth that alternates with cytokinesis. During growth, the cell accumulates nutrients and growth factors and doubles the contents of the cytoplasm. Eventually, the cytoplasm divides via cytokinesis to equally divide the cytoplasmic contents into two cells.
- The final cycle is the centrosome cycle where the centrosome is divided so that it can be inherited reliably and duplicated accordingly to form two poles of the mitotic spindle fibers.
- The cell cycle is regulated by various stimulatory and inhibitory factors that decide whether the cell needs to divide or grow.
- The cell cycle is divided into different phases (according to Howard and Pelc), each of which is defined by various processes.

Cell Cycle Regulation

1. Cyclins

- Cyclins are a group of proteins that together work to regulate different phases of the cell cycle as core regulators.
- These proteins regulate the various phases of the cell cycle by either activating the cyclin-dependent kinases or by activating some other enzymes or complexes.
- Cyclins are specific to different phases as work to regulate different phases of the cycle.
- In humans, four different cyclins are known, G1 cyclins, G1/S cyclins, S cyclins, and M cyclins. These cyclins, as the name suggests, regulate different phases.
- The term 'cyclin' was given to this class of proteins because of the varying concentration of these proteins in the cell during the cell cycle.

Mechanism

- The concentration of these cyclins usually remains low for the most part but peaks dramatically if they are needed during the cycle.
- The activation of the cyclin proteins is stimulated by the binding of the growth factors to the receptors on the cell, which activate the transcription of the cyclin genes.

- Most of the cyclin proteins act by binding themselves to the cyclin-dependent kinases, which form a complex. The complex is then responsible for the regulation of the cell cycle.
- Some cyclin proteins like the cyclin D of the G1 phase (or G1 cyclin) act as rate-limiting proteins for cell cycle progression. G1 cyclins accelerate G1 transition by the overexpression of the cyclin genes.
- Even though cyclins do not have any enzymatic activity on their own, they induce different processes in the cell cycle by providing binding sites for other enzymes.

2. Cyclin-dependent kinases (CDKs)

- Cyclin-dependent kinases (CDKs) are a group of enzymes that work to regulate different processes in the cell cycle after activation by the binding of a cyclin molecule.
- CDKs are a part of the CMGC group of enzymes consisting of serine or threonine units that are characterized by their dependency on protein subunits.
- The activity of these enzymes is only observed after the binding of a cyclin molecule followed by the phosphorylation of the threonine unit.

Mechanism

- The cyclin molecules that bind to these kinases provide additional sequences to the enzymes that are required for their enzymatic activity.
- The CDKs usually have specificity towards different cyclin molecules, and the binding of cyclin to the CDK molecule determines the specificity of the enzyme towards its substrate.
- The mechanism of action of these enzymes might differ among different kinases regulation different phases of the cell cycle.
- The activated CDKs in the interphase undergo phosphorylation and cause inactivation of the retinoblastoma protein (Rb).
- The inactivation of Rb causes depression of multiple genes encoding proteins that are necessary for DNA synthesis.
- The regulation of the cell cycle is also brought by the inhibition of the CDKs in which case, CDK inhibitors are involved.
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- CDK regulating the cell cycle is negatively regulated by the binding of other smaller proteins of the Cip/Kip families of inhibitors.
- These are also specific to the enzymes and act by distorting the cyclin interface and the ATP-binding pocket of the enzyme.
- These prevent the activation of CDKs, which causes a negative regulation of the cell cycle.

3. Maturation-promoting factor (MPF)

- Maturation-promoting factor or M-phase promoting factor (MPF) is a large-sized diffusible protein that regulates the M-phase of a cell cycle.
- The protein consists of two subunits; an inert subunit and a kinase subunit. The kinase subunit is capable of activating the inert subunit as well as other molecules.
- MPF is the regulator of the G2/M transition where it activates activities like nuclear envelope breakdown and chromosome condensation.

Mechanism

- During the interphase, the inert subunit of MPF is inactive due to the presence of an enzyme, Wee1.
- The activation of the MPF unit is brought about by CDC25, which results in the binding of the cyclin molecule to the kinase subunit.
- After the binding of cyclin to cyclin-dependent kinase, and the activation of CDK, transition into the M phase begins.
- The MPF molecules then act by adding phosphate molecules to the nuclear
- Besides, it also triggers the formation of spindle fibers as a result of microtubule instability.
- The MPF kinase also phosphorylases several substances like histone H1, which then promotes chromosome condensation.
- The activity of MPF is further regulated by other components like p34. The phosphorylation of p34 regulates the activity of MPF.

4. Anaphase-promoting complex/cyclosome (APC/C)

- Anaphase-promoting complex (APC) is a protein that regulates the M phase of the cell cycle by inhibiting the action of MPF and causes the destruction of cyclin molecules.
- This molecule is important during the transition of a cell from metaphase to anaphase of the M phase.
- The APC is an enzyme that functions in the cell cycle by a different mechanism than CDKs.

Mechanism

- Instead of activation by phosphorylation and addition of phosphate group to the targets, APC adds ubiquitin on the target molecules. The target molecules are either S and M cyclins or securing.
- In the case of cyclins, the binding of ubiquitin on the surface causes the movement of the cell to the proteasome. In the proteasome, the cyclins are degraded, which allows the newly formed daughter cell to enter the G1 phase.
- Besides, it also triggers the separation of sister chromatids during the metaphase. It binds the ubiquitin tag to a protein, called securing.
- The binding of the tag causes the destruction of securin, which then releases the separase enzyme.
- The separase enzyme acts on the cohesion protein present at the site of connection between two sister chromatids. The separation of sister chromatids indicates anaphase.

5. p53

- p53, also called TP53 or tumor protein, is a gene that encodes for the protein that regulates cell proliferation and also acts as a tumor suppressor.
- The p53 gene is often termed the ‘guardian of the genome’ as it helps in conserving stability of the genome by preventing genome mutation.
- In eukaryotic organisms, it is important as it suppresses cancer.
- It also stimulates apoptosis if DNA damage is detected that is irreparable.

P53 Regulation and Signalling

Mechanism

- The presence of p53 ensures proper cell cycle as it prevents the division of cells with damaged DNA.

- The concentration of p53 in a normal cell is quite low; however, it increases due to DNA damage or stress signals.
- The p53 gene can perform one of three functions, cell cycle arrest, DNA repair, and apoptosis.
- The cell cycle arrest by p53 is mediated by the activation of p21/WAF1. The p21 binds to the G1 cyclin which arrests the cell in the G1 phase as the cyclin can no longer bind to its CDK.
- The p21 also interacts with proliferating cell nuclear antigen that inhibits DNA replication, causing cell-cycle arrest.
- Further, it also regulates the G2/M transition as p21 inhibits cyclin B, which is responsible for the activation of CDK in the G2/M checkpoint.
- In the case of DNA damage, the cell cycle arrest by p53 activates the transcription of proteins involved in DNA repair.

6. Retinoblastoma protein (Rb)

- Retinoblastoma protein is a nuclear phosphoprotein that helps in cell cycle regulation while also acting as a tumor suppression protein.
- The primary function of Rb is to prevent excessive cell growth during the cell cycle progression.
- It acts as a negative regulator of the cell cycle as inhibiting the process.
- The protein is expressed in both cycling and resting cells which functions by inhibiting a variety of nuclear proteins involved in the cell cycle.
- It regulates the transition of a cell from the G1 phase to the S phase by inhibiting DNA replication.

Mechanism

- The family of transcription factors, E2F is the primary target of Rb. These factors regulate the timing and levels of expression of different genes involved in the cell-cycle process.
- E2F factors target the proteins involved in replication like DNA polymerase and thymidine kinase.
- In the G0/G1 phase hypophosphorylated Rb binds to E2F which inactivates and prevents cell-cycle progression,
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- Similarly, in the S phase, the chronic activation of Rb leads to downregulation of the necessary DNA replication factors.

Cell cycle checkpoints

1. G1 Checkpoint

- The G1 checkpoint is the first checkpoint in the cell cycle of a mammalian cell and the start point in the yeast cell that determines whether the cell enters the cell cycle or not.
- The checkpoint is present between the G1 phase and S phase and is responsible for the entry of the cell in the division phase.
- Depending on the external and internal factors and stimuli, the decision of whether the cell enters the cell cycle or undergoes the G0 phase is determined.
- The checkpoints are essential in the cell cycle as they limit the chances of genomic instability arising due to DNA damage during the cycle.
- The G1 checkpoint is regulated by p53 which aids in the downregulation of tumors and cell lines.
- In order to cause G1 checkpoint arrest, the p53 regulates the transcription of CDK inhibitor p21.
- The arrest is stimulated by factors like a break in the DNA double-strand, which prevents the proliferation of irreparably damaged cells.
- The G1 checkpoint arrest is a positive feedback mechanism where the presence of breaks in the DNA strand enhances the expression of the p53 gene.
- Because of the proteins involved in the checkpoint, the G1 checkpoint is an important checkpoint during tumor suppression and prevention of excessive cell proliferation.
- Cells with reparable DNA damage are held at the checkpoint to provide time for repair while others are either signaled for apoptosis or moved to the G0 phase.

Cell cycle checkpoints

2. G2 Checkpoint

- The G2 checkpoint is the second checkpoint in the cell cycle where is present at the transition between G2 and S phase.

- The checkpoint prevents the entry of cells into the S phase of the cycle by preventing the activation of regulators like cyclins and CDKs.
- This checkpoint, like the G1 checkpoint, looks for DNA damage and breaks to prevent the proliferation of mutated or damaged cells.
- As the checkpoint helps maintain genomic stability, studies on the checkpoint help to understand the molecular mechanism of cancer.
- The target of the G2 checkpoint arrest is the CDK2 that usually drives the transition from G2 to the S phase.
- In the checkpoint, DNA damage triggers the activation of the ATM pathway, which causes phosphorylation of ATM and inactivation of checkpoint kinases.
- The checkpoint also involves the p53 genes which inactivate enzymes by the expression of p21 proteins.
- Additional pathways in the G2 checkpoint ensure the stability of the arrest by the expression of proteins like Rb and downregulation of several genes that code for proteins required for the S phase.

3. Metaphase Checkpoint (Spindle checkpoint)

- The metaphase checkpoint or M phase checkpoint or Spindle checkpoint is the checkpoint during mitosis which checks if all the sister chromatids are correctly attached to the spindle fibers.
- The checkpoint ensures that all the chromosomes of cells entering the anaphase are firmly attached to at least two spindle fibers from opposite poles of the cell.
- The separation of chromosomes in anaphase is an irreversible process, which is why this checkpoint is crucial in mitosis.
- The proteins in the checkpoint look for straggler chromosomes that can be detected in the cytoplasm.
- The checkpoint acts by negative regulation of CDC20 which prevents the activation of ubiquitin tag by the anaphase-promoting complex.
- There are different mechanisms to deactivate the checkpoint once all chromosomes are correctly attached.
- One of the important mechanisms is by transporting the motor complex proteins away from the kinetochores. The proteins are then redistributed to the spindle poles.

Apoptosis

"The term apoptosis can be defined as a natural biological process of programmed cell death in which the cells destroy themselves for maintaining the smooth functioning of the body."

There are two forms of cell death

1. Programmed death of cells called Apoptosis.
2. An uncontrolled death of cells called Necrosis.

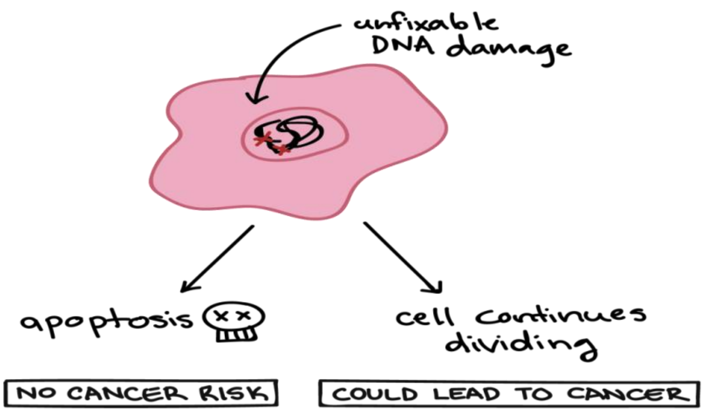
Both apoptosis and necrosis occur under different circumstances and involve different steps.

The term apoptosis is derived from the Greek word meaning dropping or falling off. It was first introduced by Kerr, Wyllie, and Currie.

Apoptosis is a biological process which occurs in all multicellular organisms including plants and animals. It removes the cells from the organisms that should no longer be a part of the organism. This process plays a major role in the development of humans and in developing and maintaining a healthy immune system.

On an average, 50 – 80 billion cells die every day in a human adult due to apoptosis. During this biological process, infected cells, pre-cancerous cells and other cancer cells are eliminated successfully and maintain the balance of cells in the human body. Therefore, it is an essential process that is responsible for the normal development of cells, cell cycle maturation and maintaining the regular functions and activities of cells.

Apoptosis occurs in all the vertebrates that have fingers and toes like digits. A slight mistake during apoptosis results in fused toes or fingers. The loss of the tail of a tadpole when it develops into a frog is yet another example of apoptosis.



Apoptosis Pathways

The process of apoptosis undergoes two pathways:

- Extrinsic Pathway
- Intrinsic Pathway

Extrinsic Pathway

This pathway triggers apoptosis in response to external stimuli, like, ligand binding at death receptors on the cell surface. These receptors are members of the Tumor Necrosis Factor gene family. The receptor binding initiates caspase activation.

Intrinsic Pathway

- This pathway triggers apoptosis in response to internal stimuli such as biochemical stress, DNA damage and lack of growth factors.

- This pathway is modulated by two groups of molecules- Bax, and Bcl-2. These groups of molecules determine whether a cell will survive or undergo apoptosis in response to the stimuli.

Significance of Apoptosis

Apoptosis is significant for the following reasons:

1. It helps to maintain homeostasis in the multicellular organisms.
2. Proper size of the body is maintained by apoptosis.
3. Apoptosis maintains the constancy of cell number in an organism.
4. The unwanted cells are eliminated from the body by apoptosis.
5. The dangerous T-lymphocytes are eliminated by apoptosis.
6. Programmed cell death is crucial for cell development.

Role Of Apoptosis

Apoptosis plays an important role in the body of an organism. Following are a few such roles performed by the process:

1. The separation of the fingers during the development of the foetus is due to apoptosis.

2. It results in the closure of the neural tube in the dorsal part.
3. Programmed cell death results in the removal of vestigial remnants such as pronephros.
4. During the determination of sex of the foetus, the Wolffian ducts are removed by cell death.
5. In the urachus, apoptosis allows the removal of redundant tissues between the bladder and umbilicus.