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F.Y. B.Sc. (Sem. II) (CBCS)

BIOCHEMISTRY

[201]: CELL BIOLOGY

Unit 1
Introduction to Cell, Cell Morphology and Cell Theories

Prepared By

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CELL

The cell is structural & functional unit of all living things. All cells come from pre-existing cells by division. (Spontaneous Generation does not occur). Cells contains hereditary information which is passed from cell to cell during cell division. All cells are basically the same in chemical composition.

HISTORY OF CELL BIOLOGY

- 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 & 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).

First Cells Seen in Cork

- 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 cellular 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 Anton van Leeuwenhoek, who in 1674 described the algae Spirogyra. Van Leeuwenhoek probably also saw bacteria.

Formulation of the Cell Theory

- In 1838, Theodor Schwann and Matthias Schleiden were enjoying after-dinner coffee and talking about their studies on cells. It has been suggested that when Schwann heard Schleiden describe plant cells with nuclei, he was struck by the similarity of these plant cells to cells he had observed in animal tissues.
- The two scientists went immediately to Schwann's lab to look at his slides. Schwann published his book on animal and plant cells the next year, a treatise devoid of acknowledgments of anyone else's contribution, including that of Schleiden (1838). He summarized his observations into three conclusions about cells:

    - The cell is the unit of structure, physiology, and organization in living things.
    - The cell retains a dual existence as a distinct entity and a building block in the construction of organisms.
    - Cells form by free-cell formation, similar to the formation of crystals (spontaneous generation).

- We know today that the first two tenets are correct, but the third is clearly wrong. The correct interpretation of cell formation by division was finally promoted by others and formally enunciated in Rudolph Virchow's powerful dictum, *Omnis cellula e cellula*: "All cells only arise from pre-existing cells".

Modern Cell Theory

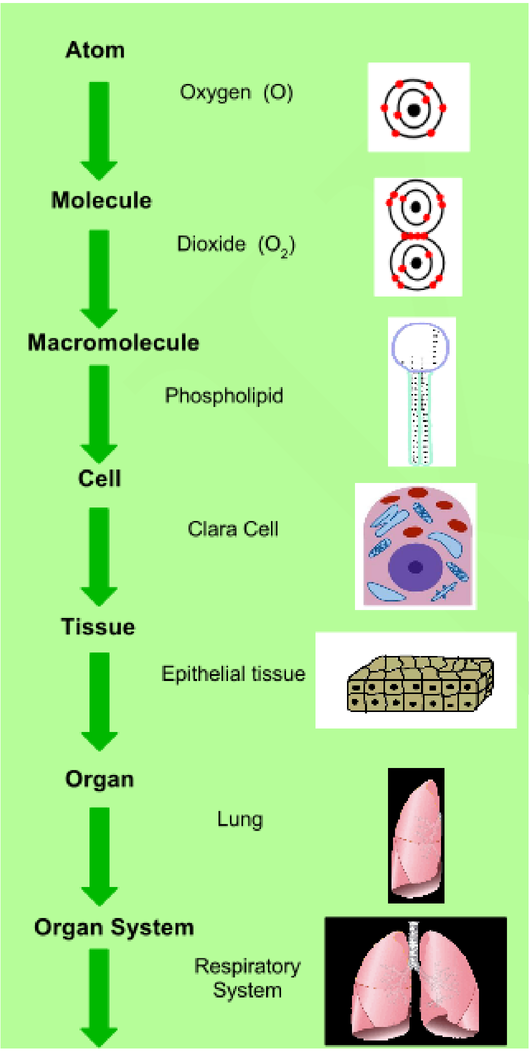
- All known living things are made up of cells.
- The cell is structural & functional unit of all living things.
- All cells come from pre-existing cells by division. (Spontaneous Generation does not occur).
- Cells contains hereditary information which is passed from cell to cell during cell division.
- All cells are basically the same in chemical composition.
- All energy flow (metabolism & biochemistry) of life occurs within cells.
- 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 co-workers, 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 in the way that the structure of DNA was the significant breakthrough of molecular biology.
- In an avalanche of progress in the study of cells, the coming decade included the characterization of the minimal media requirements for cells and development of sterile cell culture techniques. It was also aided by the prior advances in electron microscopy, and later advances such as the development of transfection methods, the discovery of green fluorescent protein in jellyfish, and discovery of small interfering RNA (siRNA), among others.
- The study of the structure and function of cells continues today, in a branch of biology known as cytology. Advances in equipment, including cytology microscopes and reagents, have allowed this field to progress, particularly in the clinical setting.

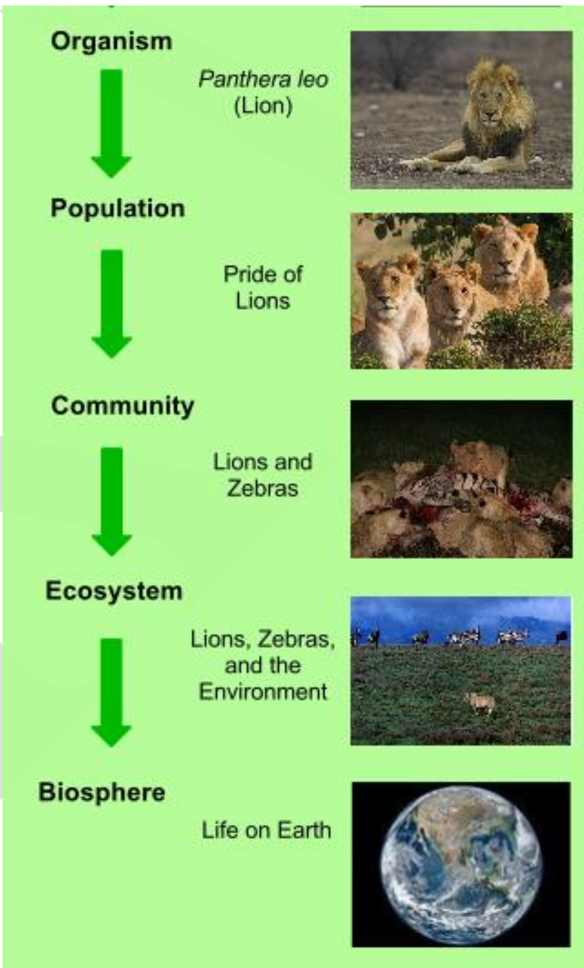
A Timeline

1595 – Jansen credited with 1st compound microscope
1655 – Hooke described 'cells' in cork.
1674 – Leeuwenhoek discovered protozoa. He saw bacteria some 9 years later.
1833 – Brown described the cell nucleus in cells of the orchid.
1838 – Schleiden and Schwann proposed cell theory.
1840 – Albrecht von Roelliker realized that sperm cells and egg cells are also cells.
1856 – N. Pringsheim observed how a sperm cell penetrated an egg cell.
1858 – Rudolf Virchow (physician, pathologist and anthropologist) expounds his famous conclusion: *omnis cellula e cellula*, that is cells develop only from existing cells [cells come from pre-existing cells]
1857 – Kolliker described mitochondria.
1879 – Flemming described chromosome behaviour during mitosis.
1883 – Germ cells are haploid, chromosome theory of heredity.
1898 – Golgi described the Golgi apparatus.
1938 – Behrens used differential centrifugation to separate nuclei from cytoplasm.

1939 – Siemens produced the first commercial transmission electron microscope.
1952 – Gey and co-workers established a continuous human cell line.
1955 – Eagle systematically defined the nutritional needs of animal cells in culture.
1957 – Meselson, Stahl and Vinograd developed density gradient centrifugation in cesium chloride solutions for separating nucleic acids.
1965 – Ham introduced a defined serum-free medium. Cambridge Instruments produced the first commercial scanning electron microscope.
1976 – Sato and colleagues publish papers showing that different cell lines require different mixtures of hormones and growth factors in serum-free media.
1981 – Transgenic mice and fruit flies are produced. Mouse embryonic stem cell line established.
1995 – Tsien identifies mutant of GFP with enhanced spectral properties
1998 – Mice are cloned from somatic cells.
1999 – Hamilton and Baulcombe discover siRNA as part of post-transcriptional gene silencing (PTGS) in plants

LEVELS OF ORGANIZATION IN BIOLOGY





- The simplest unit in this hierarchy is the atom, like oxygen. Two or more atoms is a molecule, like a dioxide. Many small molecules may combine in a chemical reaction to make up a macromolecule, such as a phospholipid. Multiple macromolecules form a cell, like a club cell. A group of cells functioning together as a tissue, for example, Epithelial tissue.
- Different tissues make up an organ, like a lung. Organs work together to form an organ system, such as the Respiratory System. All of the organ systems make a living organism, like a lion.
- A group of the same organism living together in an area is a population, such as a pride of lions. Two or more populations interacting with each other form a community, for example, lion and zebra populations interacting with each other.
- Communities interacting not only with each other but also with the physical environment encompass an ecosystem, such as the Savanna ecosystem. All of the ecosystems make up the biosphere, the area of life on Earth.

STRUCTURAL ORGANIZATION OF PROKARYOTIC AND EUKARYOTIC CELL

- **Prokaryotic cells** comprise bacteria and archaea. They typically have a diameter of 0.1–5 µm, and their DNA is not contained within a nucleus. Instead, their DNA is circular and can be found in a region called the **nucleoid**, which floats in the cytoplasm. Prokaryotes are organisms that consist of a single prokaryotic cell.
- **Eukaryotic cells** are found in plants, animals, fungi, and protists. They range from 10–100 µm in diameter, and their DNA is contained within a membrane-bound **nucleus**. Eukaryotes are organisms containing eukaryotic cells.

	Prokaryotic Cells	**Eukaryotic Cells**
Nucleus	No	Yes
DNA arrangement	Circular	Linear
Size (diameter)	0.1–5 µm	10–100 µm
Unicellular	Always	Sometimes
Multicellular	Never	Usually

PROKARYOTES

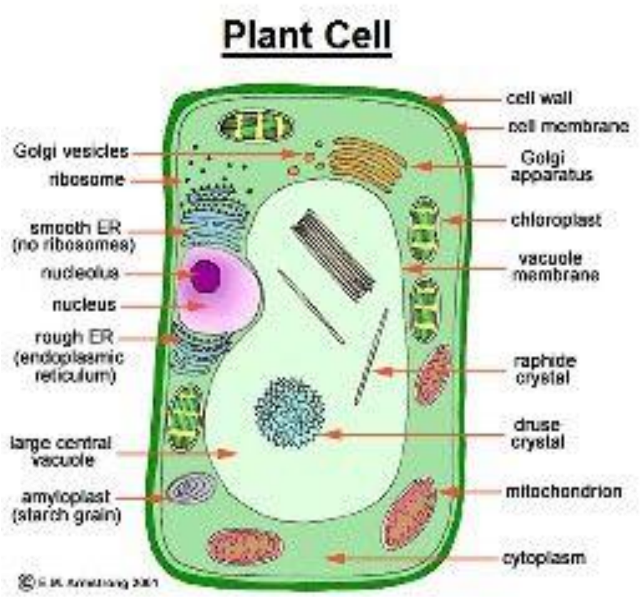
- A **prokaryote** is a typically unicellular organism that lacks a nuclear membrane-enclosed nucleus. The word *prokaryote* comes from the Greek πρό (*pro*, 'before') and κάρυον (*karyon*, 'nut' or 'kernel'). In the two-empire system arising from the work of Édouard Chatton, prokaryotes were classified within the empire **Prokaryota**.
- But in the three-domain system, based upon molecular analysis, prokaryotes are divided into two domains: *Bacteria* (formerly Eubacteria) and *Archaea* (formerly Archaebacteria). Organisms with nuclei are placed in a third domain, Eukaryota.
  - In the study of the origins of life, prokaryotes are thought to have arisen before eukaryotes.

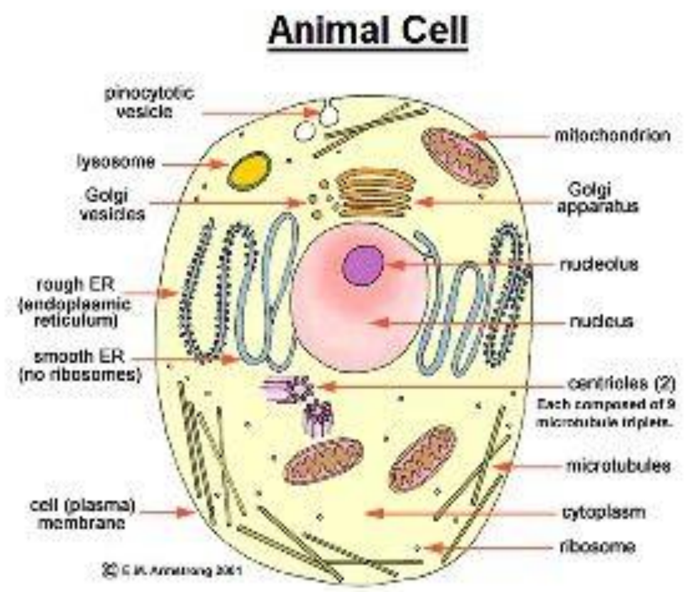
- Prokaryotes lack mitochondria, or any other eukaryotic membrane-bound organelles; and it was once thought that prokaryotes lacked cellular compartments, and therefore all cellular components within the cytoplasm were unenclosed, except for an outer cell membrane.
- But bacterial microcompartments, which are thought to be simple organelles enclosed in protein shells, have been discovered, along with other prokaryotic organelles. While typically being unicellular, some prokaryotes, such as cyanobacteria, may form large colonies.
- Others, such as myxobacteria, have multicellular stages in their life cycles. Prokaryotes are asexual, reproducing without fusion of gametes, although horizontal gene transfer also takes place.
- Molecular studies have provided insight into the evolution and interrelationships of the three domains of life.
- The division between prokaryotes and eukaryotes reflects the existence of two very different levels of cellular organization; only eukaryotic cells have an enveloped nucleus that contains its chromosomal DNA, and other characteristic membrane-bound organelles including mitochondria.
- Distinctive types of prokaryotes include extremophiles and methanogens; these are common in some extreme environments.

EUKARYOTES

- **Eukaryotes** (/juːˈkærioʊts, -əts/) are organisms whose cells have a nucleus enclosed within a nuclear envelope. Eukaryotes belong to the domain **Eukaryota** or **Eukarya**; their name comes from the Greek εὖ (*eu*, "well" or "good") and κάρυον (*karyon*, "nut" or "kernel").The domain Eukaryota makes up one of the three domains of life; the prokaryotes Bacteria and Archaea make up the other two domains. The eukaryotes are usually now regarded as having emerged in the Archaea or as a sister of the now cultivated Asgard archaea.
- Eukaryotes represent a tiny minority of the number of organisms; however, due to their generally much larger size, their collective global biomass is estimated to be about equal to that of prokaryotes.
- Eukaryotes emerged approximately 2.1-1.6 billion years ago, during the Proterozoic eon, likely as flagellated phagotrophs.
- Eukaryotic cells typically contain other membrane-bound organelles such as mitochondria and Golgi apparatus; and chloroplasts can be found in plants and algae. Prokaryotic cells may contain primitive organelles.
- Eukaryotes may be either unicellular or multicellular, and include many cell types forming different kinds of tissue; in comparison, prokaryotes are typically unicellular. Animals, plants, and fungi are the most familiar eukaryotes; other eukaryotes are sometimes called protists.
- Eukaryotes can reproduce both asexually through mitosis and sexually through meiosis and gamete fusion. In mitosis, one cell divides to produce two genetically identical cells.
- In meiosis, DNA replication is followed by two rounds of cell division to produce four haploid daughter cells.
- These act as sex cells or gametes. Each gamete has just one set of chromosomes, each a unique mix of the corresponding pair of parental chromosomes resulting from genetic recombination during meiosis

STRUCTURAL AND FUNCTIONAL DIVERSITIES IN EUKARYOTIC CELLS, PLANT VS ANIMAL CELL





DIFFERENCE BETWEEN ANIMAL CELL AND PLANT CELL

ANIMAL CELL	PLANT CELL
Generally small in size	plant cells are larger than animal cells
Cell wall is absent	The plasma membrane of plant cell has rigid wall of cellulose
Except the protozoa *euglena* no animal cell possess plastid	Plastids are present
Vacuole in animal cells is many and small	Most mature plant cell have a large central sap vacuole
Animal cell have single highly complex Golgi apparatus	Plant cell have simpler unit of Golgi apparatus, called dictyosome
Animal cell have centrosome and centrioles.	Plant cell lack centrioles and centrosome

OVERVIEW OF VIRUSES, VIRIODS AND PRIONS

OVERVUEW OF VIRUSES

- The discipline of virology studies viruses, a unique group of infectious agents whose distinctiveness resides in their simple, acellular organization and pattern of multiplication.
- Despite this simplicity, viruses are major causes of disease. For instance, many human diseases are caused by viruses, and more are discovered every year, as demonstrated by the appearance of SARS in 2003, new avian influenza viruses over the past 5 to 6 years, and the H1N1 (swine) influenza virus in 2009. However, their simplicity also has made them attractive model organisms. They served as models for understanding DNA replication, RNA synthesis, and protein synthesis.

- Therefore, the study of viruses has contributed significantly to the discipline of molecular biology. In fact, the field of genetic engineering is based in large part on the use of viruses and viral enzymes such as the retroviral enzyme reverse transcriptase.
- Viruses can exist either extracellularly or intracellularly. When extracellular, they are inactive (with one known interesting exception: because they possess few, if any, enzymes and cannot reproduce outside of living cells.
- When intracellular, viruses exist primarily as replicating nucleic acids that induce the host to synthesize viral components from which progeny virions are assembled and eventually released.
- Viruses can infect all cell types. Numerous viruses infect bacteria. They are called bacteriophages, or phages for short. Fewer archaeal viruses have been identified.
- Most known viruses infect eukaryotic organisms, including plants, animals, protists, and fungi. Viruses have been classified into numerous families based primarily on genome structure, life cycle, morphology, and genetic relatedness.
- These families have been designated by the International Committee for the Taxonomy of Viruses (ICTV), the agency responsible for standardizing the classification of viruses.

VIROIDS

- **Viroids** are small infectious pathogens. They are composed solely of a short strand of circular, single-stranded RNA. Unlike viruses, they have no protein coating. All known viroids are inhabitants of angiosperms, and most cause diseases, whose respective economic importance on humans varies widely.
- The first discoveries of viroids in the 1970s triggered the historically third major extension of the biosphere—to include smaller lifelike entities —after the discoveries, in 1675 by Antonie van Leeuwenhoek (of the "subvisible" microorganisms) and in 1892 by Dmitri Iosifovich Ivanovsky (of the "submicroscopic" viruses). The unique properties of viroids have been recognized by the International Committee on Taxonomy of Viruses, in creating a new order of subviral agents.
- The first recognized viroid, the pathogenic agent of the potato spindle tuber disease, was discovered, initially molecularly characterized, and named by Theodor Otto Diener, plant pathologist at the U.S Department of Agriculture's Research Center in Beltsville, Maryland, in 1971. This viroid is now called Potato spindle tuber viroid, abbreviated PSTVd. Soon thereafter was discovered the *Citrus exocortis viroid* (CEVd), and together understanding of PSTVd and CEVd shaped the concept of the viroid.[Fl 1]
- Although viroids are composed of nucleic acid, they do not code for any protein. The viroid's replication mechanism uses RNA polymerase II, a host cell enzyme normally associated with synthesis of messenger RNA from DNA, which instead catalyses "rolling circle" synthesis of new RNA using the viroid's RNA as a template. Some viroids are ribozymes, having catalytic properties that allow self-cleavage and ligation of unit-size genomes from larger replication intermediates
- With Diener's 1989 hypothesis that viroids may represent "living relics" from the widely assumed, ancient, and non-cellular RNA world—extant before the evolution of DNA or proteins—viroids

have assumed significance beyond plant pathology to evolutionary science, by representing the most plausible RNAs capable of performing crucial steps in abiogenesis, the evolution of life from inanimate matter.

- The human pathogen hepatitis D virus is a subviral agent similar to a viroid

PRIONS

- **prions** are misfolded proteins with the ability to transmit their misfolded shape onto normal variants of the same protein. They characterize several fatal and transmissible neurodegenerative diseases in people and many other animals.
- It is not known what causes the normal protein to misfold, but the abnormal three-dimensional structure is suspected of conferring infectious properties, collapsing nearby protein molecules into the same shape. The word *prion* derives from "proteinaceous infectious particle". The hypothesized role of a protein as an infectious agent stands in contrast to all other known infectious agents such as viroids, viruses, bacteria, fungi, and parasites, all of which contain nucleic acids (DNA, RNA, or both).
- Prion isoforms of the prion protein (PrP), whose specific function is uncertain, are hypothesized as the cause of transmissible spongiform encephalopathies (TSEs), including scrapie in sheep, chronic wasting disease (CWD) in deer, bovine spongiform encephalopathy (BSE) in cattle (commonly known as "mad cow disease") and Creutzfeldt–Jakob disease (CJD) in humans. All known prion diseases in mammals affect the structure of the brain or other neural tissue; all are progressive, have no known effective treatment, and are always fatal.
- Until 2015, all known mammalian prion diseases were considered to be caused by the prion protein (PrP); however in 2015 multiple system atrophy (MSA) was hypothesized to be caused by a prion form of alpha-synuclein.
- Prions form abnormal aggregates of proteins called amyloids, which accumulate in infected tissue and are associated with tissue damage and cell death. Amyloids are also responsible for several other neurodegenerative diseases such as Alzheimer's disease and Parkinson's disease.[11][12] Prion aggregates are stable, and this structural stability means that prions are resistant to denaturation by chemical and physical agents: they cannot be destroyed by ordinary disinfection or cooking. This makes disposal and containment of these particles difficult.
- A prion disease is a type of proteopathy, or disease of structurally abnormal proteins. In humans, prions are believed to be the cause of Creutzfeldt–Jakob disease (CJD), its variant (vCJD), Gerstmann–Sträussler–Scheinker syndrome (GSS), fatal familial insomnia (FFI), and kuru There is also evidence suggesting prions may play a part in the process of Alzheimer's disease, Parkinson's disease, and amyotrophic lateral sclerosis (ALS); these have been termed *prion-like diseases*. Several yeast proteins have also been identified as having prionogenic properties. Prion replication is subject to epimutation and natural selection just as for other forms of replication, and their structure varies slightly between species.

STRUCTURE AND FUNCTION OF CYTOSKELETON ELEMENTS

- The cytoskeleton is a network of filaments and tubules that extends throughout a cell, through the cytoplasm, which is all of the material within a cell except for the nucleus. It is found in all cells, though the proteins that it is made of vary between organisms. The cytoskeleton supports the cell, gives it shape, organizes and tethers the organelles, and has roles in molecule transport, cell division and cell signalling.
- Structure of the Cytoskeleton All cells have a cytoskeleton, but usually the cytoskeleton of eukaryotic cells is what is meant when discussing the cytoskeleton.
- Eukaryotic cells are complex cells that have a nucleus and organelles. Plants, animals, fungi, and protists have eukaryotic cells. Prokaryotic cells are less complex, with no true nucleus or organelles except ribosomes, and they are found in the single-celled organisms bacteria and archaea. The cytoskeleton of prokaryotic cells was originally thought not to exist; it was not discovered until the early 1990s.
- The eukaryotic cytoskeleton consists of three types of filaments, which are elongated chains of proteins: microfilaments, intermediate filaments, and microtubules.

Microfilaments

- Microfilaments are also called actin filaments because they are mostly composed of the protein actin; their structure is two strands of actin wound in a spiral.
- They are about 7 nanometres thick, making them the thinnest filaments in the cytoskeleton. Microfilaments have many functions. They aid in cytokinesis, which is the division of a cytoplasm of a cell when it is dividing into two daughter cells.
- They aid in cell motility and allow single-celled organisms like amoebas to move. They are also involved in cytoplasmic streaming, which is the flowing of cytosol (the liquid part of the cytoplasm) throughout the cell. Cytoplasmic streaming transports nutrients and cell organelles. Microfilaments are also part of muscle cells and allow these cells to contract, along with myosin. Actin and myosin are the two main components of muscle contractile elements.

Intermediate Filaments

- Intermediate filaments are about 8-12 nm wide; they are called intermediate because they are in-between the size of microfilaments and microtubules. Intermediate filaments are made of different proteins such as keratin (found in hair and nails, and also in animals with scales, horns, or hooves), vimentin, desmin, and lamin.
- All intermediate filaments are found in the cytoplasm except for lamins, which are found in the nucleus and help support the nuclear envelope that surrounds the nucleus. The intermediate filaments in the cytoplasm maintain the cell's shape, bear tension, and provide structural support to the cell.

Microtubules

- Microtubules are the largest of the cytoskeleton's fibres at about 23 nm. They are hollow tubes made of alpha and beta tubulin. Microtubules form structures like flagella, which are "tails" that propel a cell forward. They are also found in structures like cilia, which are appendages that increase a cell's surface area and, in some cases, allow the cell to move.
- Most of the microtubules in an animal cell come from a cell organelle called the centrosome, which is a microtubule organizing centre (MTOC). The centrosome is found near the middle of the cell, and microtubules radiate outward from it.
- Microtubules are important in forming the spindle apparatus (or mitotic spindle), which separates sister chromatids so that one copy can go to each daughter cell during cell division. They are also involved in transporting molecules within the cell and in the formation of the cell wall in plant cells.

FUNCTION OF CYTOSKELETON

- As described above, the cytoskeleton has several functions. First, it gives the cell shape. This is especially important in cells without cell walls, such as animal cells, that do not get their shape from a thick outer layer. It can also give the cell movement. The microfilaments and microtubules can disassemble, reassemble, and contract, allowing cells to crawl and migrate, and microtubules help form structures like cilia and flagella that allow for cell movement.
- The cytoskeleton organizes the cell and keeps the cell's organelles in place, but it also aids in the movement of organelles throughout the cell. For example, during endocytosis when a cell engulfs a molecule, microfilaments pull the vesicle containing the engulfed particles into the cell. Similarly, the cytoskeleton helps move chromosomes during cell division.
- One analogy for the cytoskeleton is the frame of a building. Like a building's frame, the cytoskeleton is the "frame" of the cell, keeping structures in place, providing support, and giving the cell a definite shape.