M.Sc.- I Semester-I CBOP-1: CHG – 190

General Chemistry-I, Semester-I (4 Credits)

SECTION-I: Theory Course (2 Credits, 24 L, 6T)

(Any one option is to be selected by candidate)

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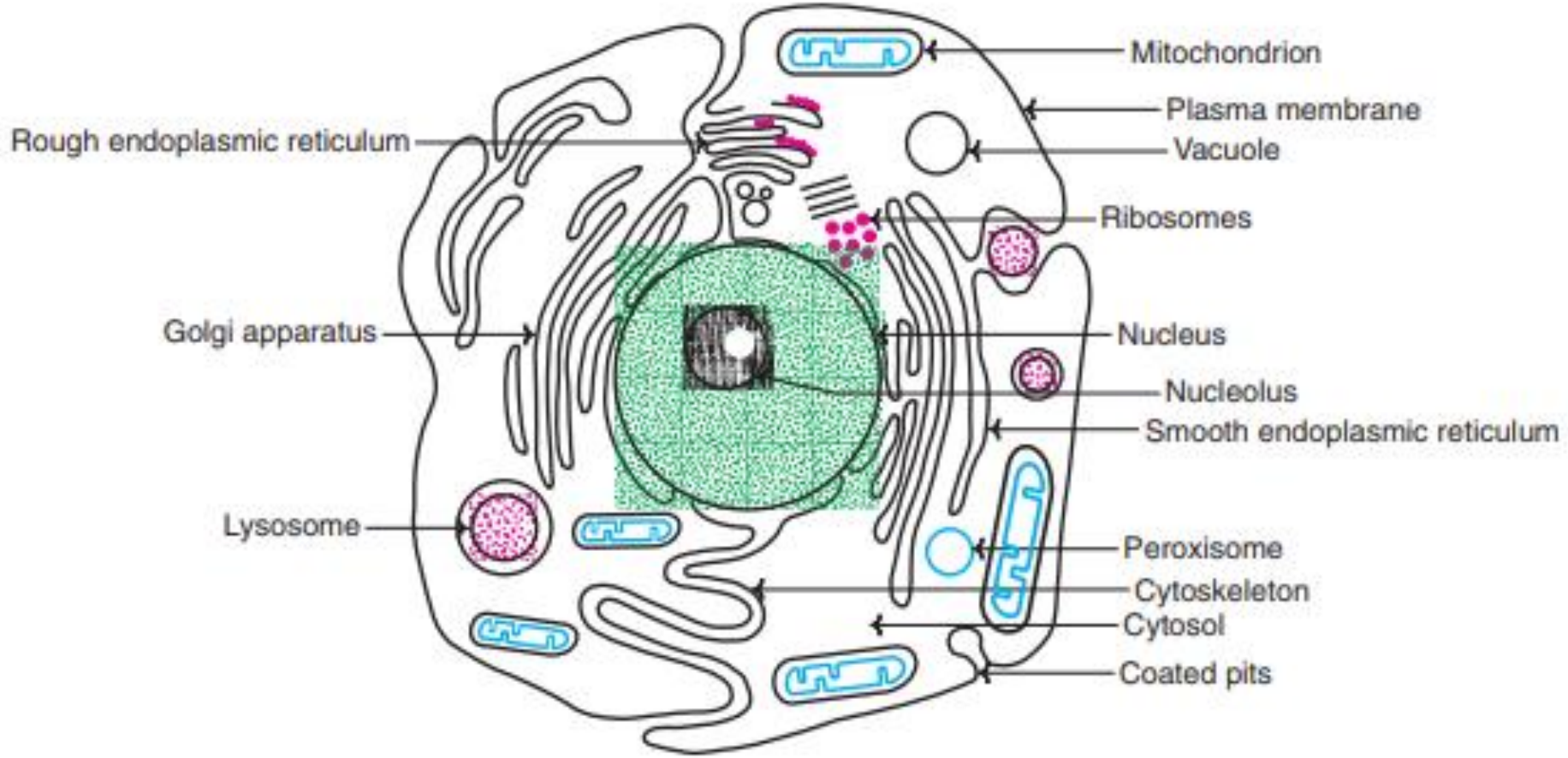
Elective Option-C: Introduction to Chemical Biology-I

1. Overview of Biochemical Concepts (03 L)



The cell speaks : *"I am the unit of biological activity; Organized into subcellular organelles; Assigned to each are specific duties; Thus, I truly represent life!"*

✓The living matter is composed of mainly six elements—

- Carbon
- Hydrogen
- Oxygen
- Nitrogen
- Phosphorus and
- Sulfur
- These elements together constitute about 90% of the dry weight of the human body.
- Several other functionally important elements are also found in the cells.
- These include Ca, K, Na, Cl, Mg, Fe, Cu, Co, I, Zn, F, Mo and Se.

Carbon- a unique element of life

- Carbon is the most predominant and versatile element of life.
- It possesses a unique property to form infinite number of compounds.
- This is attributed to the ability of carbon to form stable covalent bonds and C-C chains of unlimited length.
- It is estimated that about 90% of compounds found in living system invariably contain carbon.

Chemical molecules of life

- Life is composed of lifeless chemical molecules.
- A single cell of the bacterium, Escherichia coli contains about 6,000 different organic compounds.
- It is believed that man may contain about 1,00,000 different types of molecules although only a few of them have been characterized.

Complex biomolecules

•The organic compounds such as amino acids, nucleotides and monosaccharides serve as the monomeric units or building blocks of complex biomolecules—proteins, nucleic acids (DNA and RNA) and polysaccharides, respectively.

•The important biomolecules (macromolecules) with their respective building blocks and major functions are given in Table 1.1.

•As regards lipids, it may be noted that they are not biopolymers in a strict sense, but majority of them contain fatty acids.

TABLE 1.1 The major complex biomolecules of cells		
Biomolecule	**Building block (repeating unit)**	**Major functions**
1. Protein	Amino acids	Fundamental basis of structure and function of cell (static and dynamic functions).
2. Deoxyribonucleic acid (DNA)	Deoxyribonucleotides	Repository of hereditary information.
3. Ribonucleic acid (RNA)	Ribonucleotides	Essentially required for protein biosynthesis.
4. Polysaccharide (glycogen)	Monosaccharides (glucose)	Storage form of energy to meet short term demands.
5. Lipid	Fatty acids, glycerol	Storage form of energy to meet long term demands; structural components of membranes.

Chemical composition of man

•The chemical composition of a normal man, weighing 65 kg, is given in Table 1.2.

•Water is the solvent of life and contributes to more than 60% of the weight.

• This is followed by protein (mostly in muscle) and lipid (mostly in adipose tissue).

•The carbohydrate content is rather low which is in the form of glycogen.

TABLE 1.2 Chemical composition of a normal man (weight 65 kg)

Constituent	*Percent (%)*	*Weight (kg)*
Water	61.6	40
Protein	17.0	11
Lipid	13.8	9
Carbohydrate	1.5	1
Minerals	6.1	4

THE CELL

- The cell is the structural and functional unit of life.
- It may be also regarded as the basic unit of biological activity.
- The concept of cell originated from the contributions of Schleiden and Schwann (1838).
- However, it was only after 1940, the complexities of cell structure were exposed.

Prokaryotic and eukaryotic cells

•The cells of the living kingdom may be divided into two categories

1. Prokaryotes (Greek : pro – before; karyon – nucleus) lack a well defined nucleus and possess relatively simple structure. These include the various bacteria.
2. Eukaryotes (Greek : eu – true; karyon – nucleus) possess a well defined nucleus and are more complex in their structure and function.

- The higher organisms (animals and plants) are composed of eukaryotic cells. A comparison of the characteristics between prokaryotes and eukaryotes is listed in Table 1.3.

TABLE 1.3 Comparison between prokaryotic and eukaryotic cells

Characteristic	*Prokaryotic cell*	*Eukaryotic cell*
1. Size	Small (generally 1-10 μm)	Large (generally 10-100 μm)
2. Cell membrane	Cell is enveloped by a rigid cell wall	Cell is enveloped by a flexible plasma membrane
3. Sub-cellular organelles	Absent	Distinct organelles are found (e.g. mitochondria, nucleus, lysosomes)
4. Nucleus	Not well defined; DNA is found as nucleoid, histones are absent	Nucleus is well defined, surrounded by a membrane; DNA is associated with histones
5. Energy metabolism	Mitochondria absent, enzymes of energy metabolism bound to membrane	Enzymes of energy metabolism are located in mitochondria
6. Cell division	Usually fission and no mitosis	Mitosis
7. Cytoplasm	Organelles and cytoskeleton absent	Contains organelles and cytoskeleton (a network of tubules and filaments)

EUKARYOTIC CELL

- The human body is composed of about 10^{14} cells.
- There are about 250 types of specialized cells in the human body e.g. erythrocytes, nerve cells, muscle cells, E cells.
- An eukaryotic cell is generally 10 to 100 Pm in diameter.
- A diagrammatic representation of a typical rat liver cell is depicted in Fig.1.1.
- The plant cell differs from an animal cell by possessing a rigid cell wall (mostly composed of cellulose) and chloroplasts. The latter are the sites of photosynthesis.

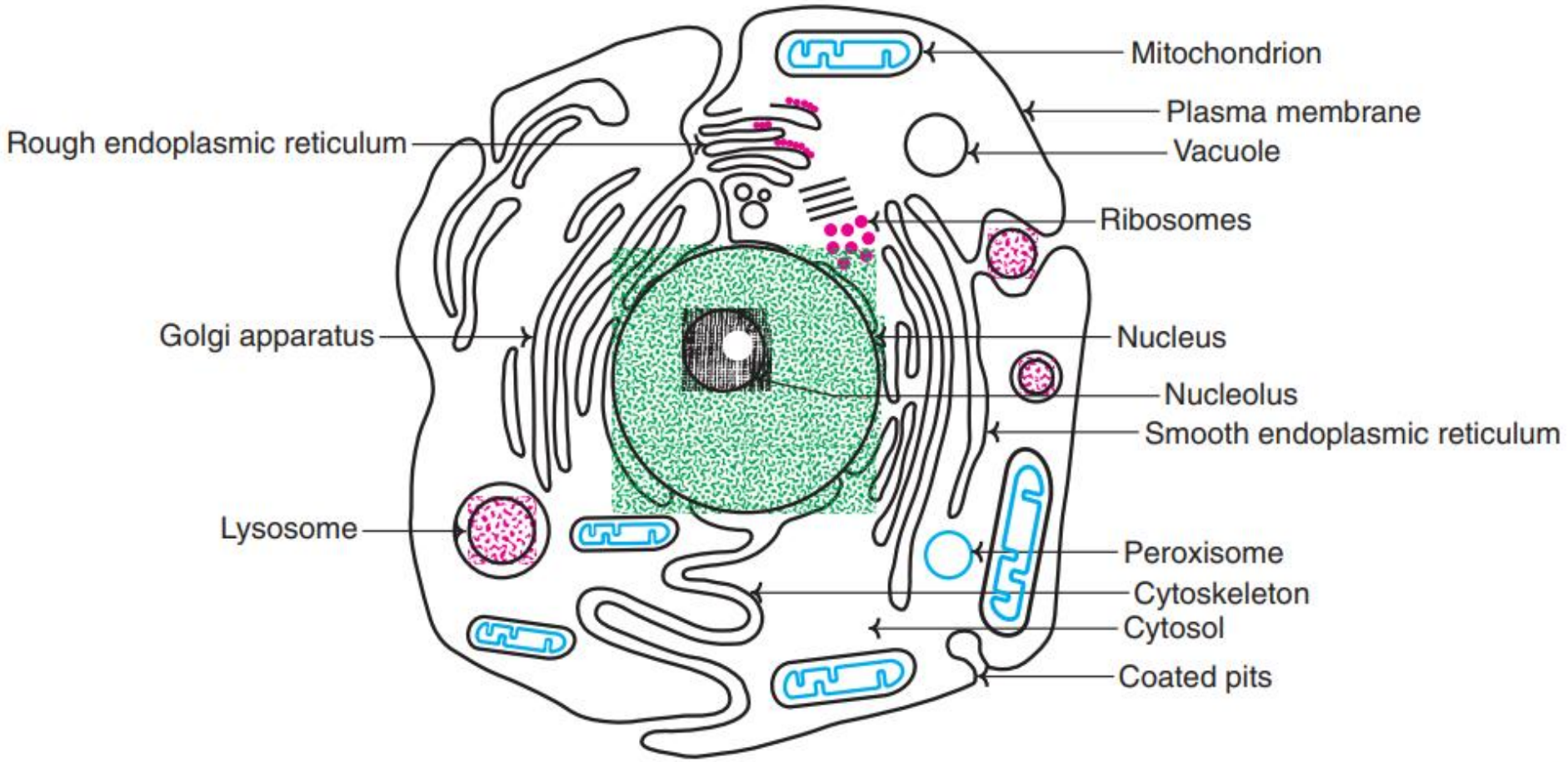


Fig. 1.1 : *Diagrammatic representation of a rat liver cell.*

•The cell consists of well defined subcellular organelles, enveloped by a plasma membrane.
•By differential centrifugation of tissue homogenate, it is possible to isolate each cellular organelle in a relatively pure form.
•The distribution of major enzymes and metabolic pathways in different cellular organelles is given in the chapter on enzymes (Refer Fig.6.6).
•**Nucleus:** Nucleus is the largest cellular organelle, surrounded by a double membrane nuclear envelope.
•The outer membrane is continuous with the membranes of endoplasmic reticulum. At certain intervals, the two nuclear membranes have nuclear pores with a diameter of about 90 nm.
•These pores permit the free passage of the products synthesized in the nucleus into the surrounding cytoplasm.

TABLE 6.6 Distribution of certain enzymes and metabolic pathways in cellular organelles

Organelle	*Enzyme/metabolic pathway*
Cytoplasm	Aminotransferases; peptidases; glycolysis; hexose monophosphate shunt; fatty acid synthesis; purine and pyrimidine catabolism.
Mitochondria	Fatty acid oxidation; amino acid oxidation; Krebs cycle; urea synthesis; electron transport chain and oxidative phosphorylation.
Nucleus	Biosynthesis of DNA and RNA.
Endoplasmic reticulum (microsomes)	Protein biosynthesis; triacylglycerol and phospholipid synthesis; steroid synthesis and reduction; cytochrome P_{450}; esterase.
Lysosomes	Lysozyme; phosphatases; phospholipases; hydrolases; proteases; lipases; nucleases.
Golgi apparatus	Glucose 6-phosphatase; 5′-nucleotidase; glucosyl- and galactosyl-transferases.
Peroxisomes	Catalase; urate oxidase; D-amino acid oxidase; long chain fatty acid oxidation.

•Nucleus contains DNA, the repository of genetic information.

•Eukaryotic DNA is associated with **basic protein (histones)** to form **nucleosomes**.

•An assembly of **nucleosomes** constitutes **chromatin fibres** of **chromosomes** (Greek: chroma – colour; soma – body).

•Thus, a single human **chromosome** is composed of about a **million nucleosomes**.

•The number of chromosomes is a characteristic feature of the species.

•Humans have **46 chromosomes**, compactly packed in the **nucleus.**

•The **nucleus of the eukaryotic cell** contains a dense body known as **nucleolus**.

•It is rich in **RNA**, particularly the **ribosomal RNA** which enters the **cytosol** through **nuclear pores**.

•The ground material of the nucleus is often referred to as **nucleoplasm**.

•It is rich in enzymes such as **DNA polymerases** and **RNA polymerases**.

Mitochondria:

•The mitochondria (Greek: mitos – thread; chondros – granule) are the centres for the cellular respiration and energy metabolism.

•They are regarded as the power houses of the cell with variable size and shape.

•Mitochondria are rod-like or filamentous bodies, usually with dimensions of 1.0 x 3 Pm.

•About 2,000 mitochondria, occupying about 1/5th of the total cell volume, are present in a typical cell.

•The mitochondria are composed of a double membrane system (Refer Fig.11.5).

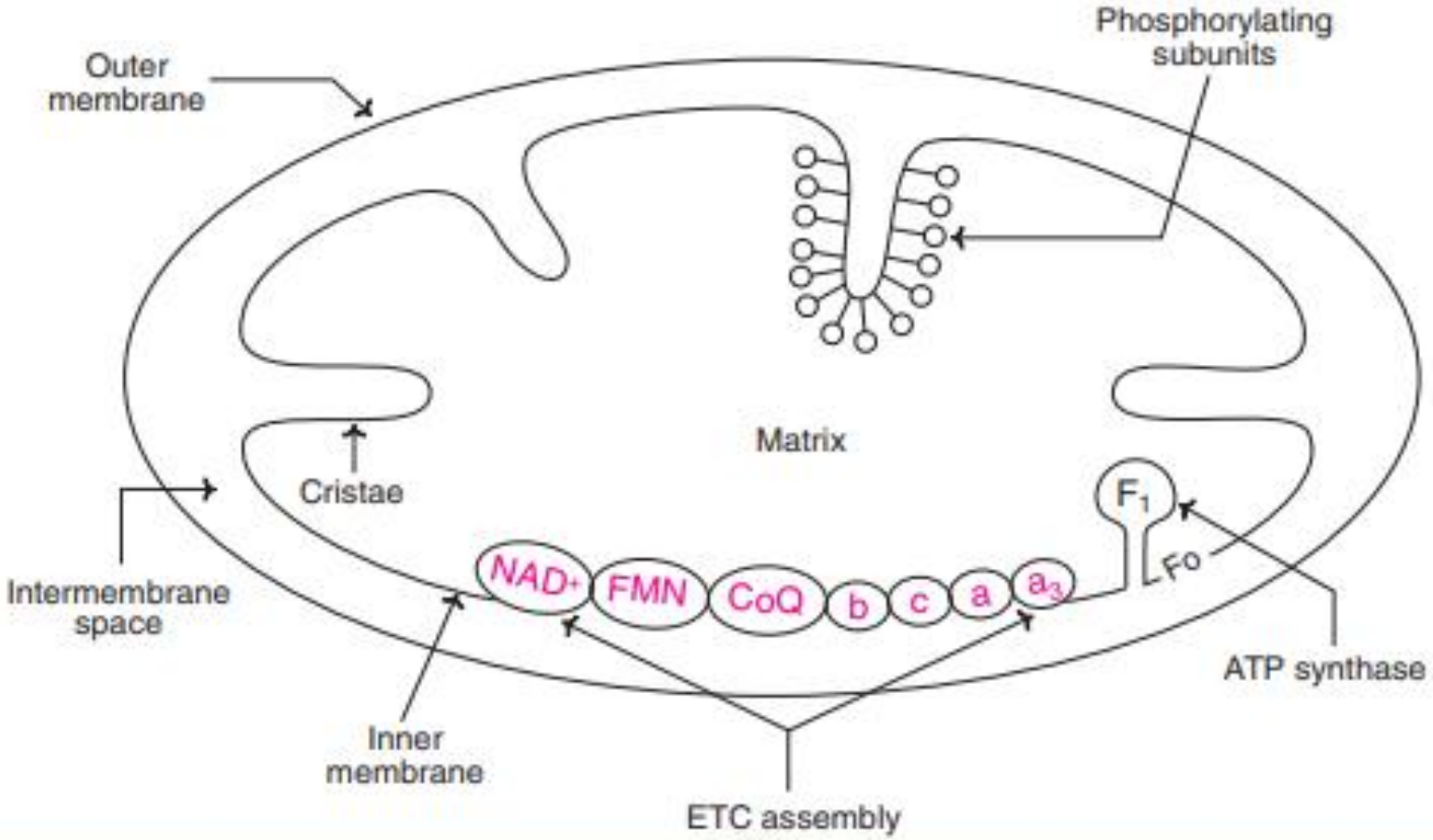


Fig. 11.5 : *Structure of mitochondrion depicting electron transport chain (ETC) (F_o, F_1—Protein subunits).*

•The outer membrane is **smooth** and completely envelops the organelle.

•The inner membrane is folded to form cristae (Latin – crests) which occupy a larger surface area.

•The internal chamber of mitochondria is referred to as **matrix or mitosol**.

•The components of electron transport chain and oxidative phosphorylation (flavoprotein, cytochromes b, c1, c, a and a3 and coupling factors) are buried in the inner mitochondrial membrane.

•The matrix contains several enzymes concerned with the energy metabolism of carbohydrates, lipids and amino acids (e.g., citric acid cycle, E-oxidation).

•The matrix enzymes also participate in the synthesis of heme and urea.

•Mitochondria are the principal producers of ATP in the aerobic cells.

•ATP, the energy currency, generated in mitochondria is exported to all parts of the cell to provide energy for the cellular work.

•The mitochondrial matrix contains a circular double stranded DNA (mtDNA), RNA and ribosomes.

•Thus, the mitochondria are equipped with an independent protein synthesizing machinery.

•It is estimated that about 10% of the mitochondrial proteins are produced in the mitochondria.

•The structure and functions of mitochondria closely resemble prokaryotic cells.

•It is hypothesized that mitochondria have evolved from aerobic bacteria.

Endoplasmic reticulum:

•The network of membrane enclosed spaces that extends throughout the cytoplasm constitutes endoplasmic reticulum (ER).

•Some of these thread-like structures extend from the nuclear pores to the plasma membrane.

•A large portion of the ER is studded with ribosomes to give a granular appearance which is referred to as rough endoplasmic reticulum.

•Ribosomes are the factories of protein biosynthesis.

•During the process of cell fractionation, rough ER is disrupted to form small vesicles known as microsomes.

•It may be noted that microsomes as such do not occur in the cell.

•The smooth endoplasmic reticulum does not contain ribosomes.

•It is involved in the synthesis of lipids (triacylglycerols, phospholipids, sterols) and metabolism of drugs, besides supplying Ca2+ for the cellular functions.

Golgi apparatus:

•Eukaryotic cells contain a unique cluster of membrane vesicles known as dictyosomes which, in turn, constitute Golgi apparatus (or Golgi complex).

•The newly synthesized proteins are handed over to the Golgi apparatus which catalyse the addition of carbohydrates, lipids or sulfate moieties to the proteins.

•These chemical modifications are necessary for the transport of proteins across the plasma membrane.

•Certain proteins and enzymes are enclosed in membrane vesicles of Golgi apparatus and secreted from the cell after the appropriate signals.

•The digestive enzymes of pancreas are produced in this fashion.

•Golgi apparatus are also involved in the membrane synthesis, particularly for the formation of intracellular organelles (e.g. peroxisomes, lysosomes).

Lysosomes:

•Lysosomes are spherical vesicles enveloped by a single membrane.

•Lysosomes are regarded as the digestive tract of the cell, since they are actively involved in digestion of cellular substances—namely proteins, lipids, carbohydrates and nucleic acids.

•Lysosomal enzymes are categorized as hydrolases.

•These include the enzymes (with substrate in brackets)— D-glucosidase (glycogen), cathepsins (proteins), lipases (lipids), ribonucleases (RNA).

•The lysosomal enzymes are responsible for maintaining the cellular compounds in a dynamic state, by their degradation and recycling.

•The degraded products leave the lysosomes, usually by diffusion, for reutilization by the cell.

•Sometimes, however, certain residual products, rich in lipids and proteins, collectively known as lipofuscin accumulate in the cell.

•Lipofuscin is the age pigment or wear and tear pigment which has been implicated in ageing process.

•As the cell dies, the lysosomes rupture and release hydrolytic enzymes that results in post-morteum autolysis.

• The digestive enzymes of cellular compounds are confined to the lysosomes in the best interest of the cell.

•Escape of these enzymes into cytosol will destroy the functional macromolecules of the cell and result in many complications.

•The occurrence of several diseases (e.g. arthritis, muscle diseases, allergic disorders) has been partly attributed to the release of lysosomal enzymes.

•Inclusion cell (I-cell) desease is a rare condition due to the absence of certain hydrolases in lysosomes.

•However, these enzyme are syntherized and found in the circulation. I-cell disease is due to a defect in protein targetting, as the enzymes cannot reach lysosomes.

Peroxisomes:

•Peroxisomes, also known as microbodies, are single membrane cellular organelles.

•They are spherical or oval in shape and contain the enzyme catalase.

•Catalase protects the cell from the toxic effects of H_2O_2 by converting it to H_2O and O_2.

•Peroxisomes are also involved in the oxidation of long chain fatty acids (> C18), and synthesis of plasmalogens and glycolipids.

•Plants contain glyoxysomes, a specialized type of peroxisomes, which are involved in the glyoxylate pathway.

•Peroxisome biogenesis disorders (PBDs), are a group of rare diseases involving the enzyme activities of peroxisomes.

•The biochemical abnormalities associated with PBDs include increased levels of very long chain fatty acids (C24 and C26) and decreased concentrations of plasmalogens.

•The most severe form of PBDs is Zellweger syndrome, a condition characterized by the absence of functional peroxisomes. The victims of this disease may die within one year after birth.

Cytosol and cytoskeleton:

•The cellular matrix is collectively referred to as cytosol.

•Cytosol is basically a compartment containing several enzymes, metabolites and salts in an aqueous gel like medium.

•More recent studies however, indicate that the cytoplasm actually contains a complex network of protein filaments, spread throughout, that constitutes cytoskeleton.

•The cytoplasmic filaments are of three types – microtubules, actin filaments and intermediate filaments.

•The filaments which are polymers of proteins are responsible for the structure, shape and organization of the cell.

Integration of Cellular Functions:

- The eukaryotic cells perform a wide range of complex reactions/functions to maintain tissues, and for the ultimate well-being of the whole organism.
- For this purpose, the various intracellular processes and biochemical reactions are tightly controlled and integrated.
- Division of a cell into two daughter cells is good example of the orderly occurrence of an integrated series of cellular reactions.
- Apoptosis is the programmed cell death or cell suicide. This occurs when the cell has fulfilled its biological functions.

•Apoptosis may be regarded as a natural cell death and it differs from the cell death caused by injury due to radiation, anoxia etc.

•Programmed cell death is a highly regulated process.

Summary

1. Life is composed of lifeless chemical molecules. The complex biomolecules, proteins, nucleic acids (DNA and RNA), polysaccharides and lipids are formed by the monomeric units amino acids, nucleotides, monosaccharides and fatty acids, respectively.
2. The cell is the structural and functional unit of life. The eukaryotic cell consists of well defined subcellular organelles, enveloped in a plasma membrane.
3. The nucleus contains DNA, the repository of genetic information. DNA, in association with proteins (histones), forms nucleosomes which, in turn, make up the chromosomes.

4. The mitochondria are the centres for energy metabolism. They are the principal producers of ATP which is exported to all parts of the cell to provide energy for cellular work.
5. Endoplasmic reticulum (ER) is the network of membrane enclosed spaces that extends throughout the cytoplasm. ER studded with ribosomes, the factories of protein biosynthesis, is referred to as rough ER. Golgi apparatus are a cluster of membrane vesicles to which the newly synthesized proteins are handed over for further processing and export.

6. Lysosomes are the digestive bodies of the cell, actively involved in the degradation of cellular compounds. Peroxisomes contain the enzyme catalase that protects the cell from the toxic effects of H_2O_2. The cellular ground matrix is referred to as cytosol which, in fact, is composed of a network of protein filaments, the cytoskeleton.
7. The eukaryotic cells perform a wide range of complex functions in a well coordinated and integrated fashion. Apoptosis is the process of programmed cell death or cell suicide.