Cell Biology: Cellular Organization, Division and Processes
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Lecture – 1
Introduction to Cell Biology, Cell Components, Organization and Processes, Part I

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Hello everyone. I am Shikha Laloraya, Professor of Biochemistry at IISc. Today is the introductory lecture to the course on Cell biology: cellular organization, division and processes. I will be introducing you to the basics of cell components and organization and I will be giving a general overview of the macromolecules that compose the cell, of membranes, organelles, and the processes that occur within the cell.

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So why should we study cell biology? All organisms are made up of cells. Focusing on the cell is a starting point to get a detailed understanding of the organism as a whole. And cell biology is a fundamental discipline in Life Sciences and in biomedical research. In order to understand the diseased state of a cell or an organism, one must first understand normal cell function.

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So, what is cell biology? This discipline is the study of cells, which is the basic unit of life that all organisms are made up of: we study the structure of cells, the molecules, the compartments within the cell and their organization. The function, that is, the cellular energetics and metabolism, the decoding and release a genetic information in the form of newly synthesized molecules. And also, the division of the cell that is reproduction of the cell, replication and segregation of the genetic material, and its regulation, and we also study intercellular communication, both intra as well as intercellular signalling.

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So, in this lecture as I mentioned, I will be talking in the first part, about the composition of cells, various molecules: small molecules as well as macromolecules, and certain definitions of cells and different types of cells that we study, and model systems, a little bit about introduction to ATP as well.

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So, a cell is a basic unit of life. Cells were first seen in sections of cork by Robert Hooke a long time ago. Around the same time, Leeuwenhoek saw living cells using a simple microscope. And he also saw some microbes moving around in pond water, and therefore he referred to them as small animals or animalcules, which is just a translation of the Dutch word that he used for it. And he also observed many other types of cells in muscles, sperm, RBC, etc.

Schleiden and Schwann were biologists, a botanist and a physiologist, who were studying plants and animals. respectively. And they defined cells as elementary particles of organisms in both plants and animals. And from their observations, they concluded that some organisms are unicellular, whereas others are multicellular. The cell theory was proposed by Schwann, synthesizing both of their observations. And it was stated that the cell is a unit of structure, physiology and organization in living things. A cell can either have a distinct identity or it can be a building block in the construction of multicellular organisms, and somewhat erroneously it was stated that cells formed by free cell formation similar to formation of crystals or by spontaneous generation, which we now know is not true.

And hence a correction of this came about by Virchow, who was a pathologist, who proposed that all cells come from pre-existing cells. Fleming, who was an anatomist, described the process of cell division and he observed that cell reproduction involves transmission of chromosomes from parent to daughter cells by mitosis, followed by the division of the cell into two cells.

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So, as per the current cell theory, the cell is the fundamental structural and functional unit of living beings. All organisms are made up of one or more cells. Cells arise from pre-existing cells by cell division. Cells carry hereditary information that is passed on to daughter cells during cell division, and all cells have more or less similar chemical composition and structural organization with a few small differences that we will discuss in this class.

And, there are various reactions that occur inside cells that require energy and this involves energy flow among the molecules present within the cells.

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So, the basic components of any cell are mainly three: the genetic material or the DNA, and the cytoplasm, and these contents they are surrounded by the plasma membrane. So, this is the very basic and there are simple cells known as prokaryotes, which have only these and they do not have any intracellular membranes. Some cells however, also have a cell wall, such as fungi or plant cells.

And then there are other cells known as eukaryotes, in which the genetic material is enclosed in a compartment known as the nucleus, which is a membrane-bound compartment. So, you have prokaryotes, an example of which is the *E. coli* bacterium, and eukaryotes, two different kinds are shown here: the budding yeast *Saccharomyces cerevisiae* and an animal cell, which is much larger than the other two.

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So, this slide summarizes some of the properties of prokaryotes versus eukaryotes. Prokaryotes are almost always unicellular, and various eukaryotes can be unicellular or multicellular; prokaryotes are rather small, ranging from 0.2 microns to about 2 microns in diameter and these are all general rules, they have a nucleoid, there is no nuclear membrane, the DNA is usually circular. And this is surrounded by cytoplasm which has ribosomes, mitochondria are absent, centrosomes are absent, and examples of this class are Eubacteria and Archaea bacteria.

Eukaryotes are somewhat slightly larger cells, they can range in size approximately from 10 microns to even 100 microns, of course, some cells are much larger, and they have a nucleus which is a membrane bound compartment that has the DNA.   The DNA is often linear, organized in chromosomes and the cytoplasm has got ribosomes and several membrane-bound organelles such as the endoplasmic reticulum, lysosomes, Golgi apparatus, peroxisomes, etc. Mitochondria are present and they produce ATP.   And they also have centrosomes, generally. So, examples of eukaryotes are animals, plants, yeasts or fungi and protists or protozoa.

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So, prokaryotes, as I already mentioned do not have a nucleus, they have genetic material and it is kind of known as a nucleoid attached to the cell membrane and they include Archaea and various kinds of bacteria, some of which are shown here. One of them is *E. coli*, which I am mentioning because it is a very popular model organism in cell biology and molecular biology research.

There are 2 types of bacteria based on their staining properties, gram negative or gram positive, which refers to the staining by crystal violet where the gram negative give a light pink color whereas the gram positive ones are stained purple because they have, the gram positive bacteria have, a thick peptidoglycan layer shown here and no outer membrane. Whereas gram negative bacteria have a very thin peptidoglycan layer and they also have an outer lipid membrane.

Another class of interesting bacteria are cyanobacteria, which are photosynthetic bacteria, they have thylakoid membranes and also the enzyme Rubisco, which fixes atmospheric CO_2.

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Coming to the origin of eukaryotes, it is believed that they arose from a predatory cell such as an archaea-derived anaerobic ancestor, that engulfed an aerobic eubacterium, that later on evolved into a mitochondrion. Another similar event that happened was the acquisition of cyanobacteria from this derived cell to finally produce plant cells. The cyanobacterium may have evolved into chloroplasts found in current day plant cells.

The nuclear genome in eukaryotes, is derived both from the archaeabacterial as well as the eubacterial genomes.

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This slide show the diversity of eukaryotes. As mentioned, eukaryotes can be either uni or multicellular. Shown at the top are various unicellular eukaryotes such as yeast, a model system in cell and molecular biology research, the green alga *Chlamydomonas,* and a protist *Paramecium*.   A transition to multicellularity occurred early on; shown at the bottom is the alga *Volvox*, which has got 16 germ cells and about 2000 somatic cells.

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Various organisms have been used for research in cell biology starting with the bacterium *E. coli*, the yeasts: budding yeast as well as fission yeast, and various other multicellular organisms such as *C. elegans*, *Drosophila*, frogs, zebrafish, human cell lines, mice and so on, and also *Arabidopsis,* which is a model plant organism. The model organism is chosen based on its suitability for the question being asked.

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So, living systems only have a subset of elements. For example, in the human body, of course the major molecule present is water. But among the elements, the most common elements are carbon, hydrogen, nitrogen, oxygen and often these are linked by covalent bonds to form molecules and there are other elements in smaller quantities such as ions: sodium, potassium, magnesium, calcium, and so on, and various trace elements, which are present in very small quantities.

As we already mentioned, water is the major constituent of cells, about 70%, and water molecules they form a hydrogen bonded network because of its being a dipole and we will come to this in the next slide. Cells also have various kinds of small as well as large organic molecules, small molecules such as sugars, fatty acids, amino acids, nucleotides, which make up the macromolecules, which are larger polysaccharides, lipids -come together to form membranes, proteins and nucleic acids, and also various kinds of ions. Inside the cell the molecules bind to each other by noncovalent bonds such as electrostatic bonds, hydrogen bonds, van der Waals interactions, and also very importantly, hydrophobic force in water, it pushes nonpolar groups away from the hydrogen-bonded water network.

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So just to recap, about the structure of atoms, atoms of course they are the smallest particles that retain the properties of an element. Each atom has at its centre a positively charged nucleus, which has got positively charged protons and neutral neutrons and the nucleus is surrounded by a cloud of electrons, electrons are negatively charged, an atom overall is neutral. So the number of protons and electrons are equal.

And this is a highly schematic representation, I mean, you cannot be sure about the positions of the electrons as is depicted here but in fact, the properties of these subatomic particles are described by quantum mechanics, which we will not be covering in this course. But most importantly, it is important to know that the electrons determine the chemical behaviour of an atom in terms of the types of bonds it forms or interacts with other atoms.

Once again, this is a highly schematic representation of hydrogen, carbon, and oxygen; their atomic numbers and weights as shown and in fact, the nucleus is much much smaller than what is shown here, in relation to the electron cloud. Now electrons, they can only exist in certain discrete states called orbitals, and each can accommodate only a certain number of electrons. For example, the innermost shell can have only 2 electrons, the second can have up to 8 electrons, as well as the third and so on.

An unfilled electron shell is less stable than a filled one and hence when there is an incomplete shell then this atom tries to complete this shell by taking up electrons or sharing electrons, and this number of electrons is termed as a valence. Now a carbon atom for example, it can share 4 electrons and therefore it can form 4 bonds with other molecules, which have tetrahedral symmetry as shown here in case of methane.

When an atom forms covalent bonds with other atoms, these bonds they have a defined orientation in space relative to one another and these reflect the orientations of the orbits of the shared electrons. So, the covalent bonds between multiple atoms are characterized by specific bond angles, and they also have specific bond length and bond energies.

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So, we already mentioned covalent bonds. Covalent bonds are formed when 2 atoms share a pair of electrons, there can be single bonds where there is sharing of 2 electrons, each donated by each participating atom. And this type of bond allows rotation around the bond axis, which is not seen in double bonds and triple bonds. Double bonds result from the sharing of 2 pairs of electrons; they are more rigid. Whereas triple bonds result from the sharing of 3 pairs of electrons; 3 electrons are donated by each atom, it is even more rigid and does not permit free rotation.

Interesting property of covalent bonds are: some covalent bonds are polar. So, when atoms of 2 different elements form a covalent bond, these 2 atoms attract the shared electrons to different extents, the pair of electrons is shared unequally with a partial transfer between the atoms. And this results in a polar covalent bond.

Molecules are held to each other with noncovalent bonds inside cells and one important bond is the hydrogen bond which results from an interaction in which an electropositive hydrogen atom is partially shared by 2 electronegative atoms. This is a directional bond, it is strongest when all the 3 atoms are in a straight line and they can be weakened by water because it can form competing hydrogen bonds.

Ionic bonds are formed when electrons are transferred from one atom to another, thus, in the end each of them has a charge, and van der Waals interactions are weak interactions. These are interactions or attractions between 2 neutral atoms at a close range, and it arises from the formation of induced transient dipoles; there is a fluctuation in the electron cloud and it produces a transient dipole that can induce an oppositely polarized dipole in a nearby atom. And these are very weak interactions but they are not weakened by water. And finally, hydrophobic forces are caused by pushing away of nonpolar groups out of the hydrogen-bonded water network, these are nonspecific but they are very important for protein folding.

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So, water molecule of course is very important in cells, as I already mentioned. Water is a dipole; it has got polar covalent bonds and overall it has a net neutral charge but the electrons are asymmetrically distributed. The oxygen nucleus draws electrons away from hydrogen towards itself and thus imparts a weak positive charge to the hydrogen and there is excess of electron density on the oxygen atom, which creates weak negative regions with a tetrahedral symmetry shown here as delta (δ) minus.

So once again, the hydrogen bond, it is an interaction between a hydrogen, which has got a positive charge that shares a polarized covalent bond with a more electronegative atom such as this oxygen here which is referred to as a donor, and with an atom with a partial negative charge, which is the acceptor, which is a part of another dipole. So, due to the polarized nature, water molecules can form hydrogen bonds.

They form such types of hydrogen bonded lattice; the hydrogen bonds are of course much weaker than covalent bonds and as I already mentioned, they would be strongest when the 3 atoms are in a straight line. Water molecule can bond with 4 others to form a transient flickering cluster, inside the aqueous medium.

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There are also small organic molecules, the carbon-based molecules, present within cells. Carbon can form large molecules, it is a small atom, it has 4 electrons and 4 vacancies in its outermost shell and it can form 4 covalent bonds with other atoms. A carbon can also join to other carbon atoms by very stable covalent carbon-carbon bonds; it can form rings and chains and it can in fact form large molecules with no obvious upper limit to their size.

These carbon-based compounds in cells are referred to as organic molecules and they also have various chemical groups which are reactive and these are common in biological molecules such as hydroxyl, carboxyl, amino, phosphate, etc. Examples of these types of organic molecules in cells are sugars, fatty acids, nucleotides, amino acids, and we will take an example of amino acids here, which are building blocks for larger macromolecules term polypeptides or proteins. Shown here are two amino acids.

So here is a central carbon, it is bonded to 4 different groups: amino, hydrogen, carboxylic, and a side chain. Now this side chain can vary and based on what the side chain is, there are 20 common amino acids in proteins, which are mentioned over here and you can sort of recap your biochemistry. It is important to know the structures of some of these amino acids, but there are 4 different groups: nonpolar, polar, acidic, and basic, and their names are mentioned here in their single letter abbreviation.

So, two amino acids, they can actually come together and form a peptide bond by the removal of one water molecule, and this forms what we would call as a dipeptide and you can in fact have a chain of such amino acids referred to as a polypeptide, which is forming a protein.

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This process of peptide bond formation is quite complex and it happens within a large complex known as the ribosome. So here is the messenger RNA, which is transcribed from DNA, which stores the genetic material, and it is complementary to the gene sequence from which it is derived and within the ribosome, transfer RNA molecules bring the amino acids, and they are hooked up in this chain of polypeptide. So, this is where the peptide bond formation occurs.

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So, as already mentioned most of the macromolecules in cells are polymers. Macromolecules in cells are very abundant and their roles range from information, regulatory, as well as structural roles. Examples given earlier were polysaccharides, nucleic acids, and proteins. We will take the example of proteins here, as I already mentioned, they are polymers of amino acids, they are formed by a condensation reaction by loss of a water molecule and linkage via a peptide bond, which is a CO-NH bond, which is somewhat partially planer.

These polypeptides can fold into different structures, common secondary structures are alpha helix formed by hydrogen bonding between amino acids on the same chain and also beta-pleated sheets are another type of secondary structural element. They can fold via noncovalent interactions into these precise stable shapes, and these shapes are crucial for their functions. So, you can also have another level of folding termed the 3-dimensional tertiary structure, where the secondary structural elements are further organized in 3-dimensional space and different polypeptides can come together and associate with each other again by noncovalent bonds. Different subunits of protein complexes come together in this way. In addition, different protein complexes can form complexes with other molecules other macromolecules as well and form large molecular machines capable of performing complex tasks, such as the ribosome that we just mentioned.

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So, in a cell, chemical reactions occur in aqueous environment in a dynamic network of water molecules, which are bound via hydrogen bonds. The chemical reactions within cells can generate order, for example synthesis of macromolecules and their assembly, and they also release heat. The synthesis requires energy and that comes from oxidation of food and organic molecules.

Many different reactions are constantly being performed in a living cell and this is referred to as metabolism. It can be anabolic or biosynthetic, where small molecules are used, along with energy to synthesize other larger molecules, or catabolic, that is break down of food into small molecules to generate energy, which are then utilized for biosynthesis. Activated carrier molecules are produced by oxidation of food molecules; these molecules they store energy as chemical bond energy in the form of energy-rich covalent bonds. And this can be used for energy requiring reactions of biosynthesis. Examples of such activated carriers are ATP (adenosine triphosphate), NADH, NADPH, $FADH_2$, Acetyl Coenzyme A, and various other molecules. ATP is a common energy currency in cells. ATP hydrolysis is coupled to synthesis of biological polymers. Of course, ATP also provides building blocks for nucleic acids.

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ATP is formed in cells via reactions driven by the energy released during the oxidative breakdown of food and it is synthesized by this fascinating molecular machine termed ATP synthase, which is present in the mitochondria. It has got 3 phosphate groups, they are linked in a series by 2 phospho-anhydride bonds, and breaking these bonds releases large amounts of useful energy, which is used for energy requiring reactions.

The terminal phosphate group of ATP is often split off by hydrolysis, sometimes transferring this phosphate to other molecules and releasing useful energy that drives energy requiring biosynthetic reactions. Energy released from this hydrolysis occurs because cleavage of this bond, it separates off one of the negatively charged phosphates and it relieves some of the electrostatic repulsion in the molecule.

The standard free energy of hydrolysis of ATP has a value of -30.5 kilojoules per mole and in fact, in cells this value is even more negative because the concentrations of ATP, ADP, and Pi are lower in cells, and inspite of this negative delta G value, ATP is kinetically stable towards non enzymatic breakdown, at pH of 7, because the activation energy for ATP hydrolysis is relatively high, so it does not spontaneously occur and this can only occur when it is catalyzed by an enzyme, which is referred to as an ATPase.

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Enzymes are a class of biological catalysts that accelerate reactions within the cells. Enzymes are mostly proteins, although there are RNA catalysts termed as ribozymes that also exist in cells. Enzymes bind substrates in such a way that lowers the activation energy of the reaction that needs to occur; they have a much higher affinity for the unstable transition state than for the stable form of the substrate and this binding lowers the energy of the transition state.

Enzymes are highly specific; they only catalyze a specific type of reaction using particular substrates, so they are not interchangeable. Coenzymes are small organic molecules that work with enzymes to enhance the reaction rates. Coenzymes are recycled to participate in multiple enzymatic reactions. For example, nicotine amide adenine dinucleotide, or NAD^+, it is an electron carrier in oxidation reduction reactions.

This can accept 2 electrons and a hydrogen ion from one substrate to form NADH that can then donate these 2 electrons to another substrate reforming NAD^+.

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We have discussed various molecules present inside cells. So is a cell just to bag of chemicals that react? In fact, the molecules inside cells are ordered and highly organized. Cellular processes follow established chemical and physical principles; they are not entirely magical as it might seem. These processes are inter-connected and they serve a purpose. Cells can grow and replicate themselves.

So, a living cell can be defined as a complex chemical system, bounded by a membrane that performs complex processes, that are purposeful, and often interdependent, in order to maintain itself and that can grow and reproduce, that is make another copy of itself. Thus, a cell is a minimal self-replicating unit of living matter. Stay tuned for the next lecture.