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Module on

Biochemical basis of life

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Biochemistry is an experimental science that focuses on the chemical basis of life. It explains life and life functions in chemical terms. Life is a dynamic phenomenon that integrates a large number of chemical/biochemical reactions aimed at sustaining a continuous flow of energy to cells, tissues, organs and organ systems. In biochemical terms, life is an open system that allows the flow of metabolites in and out of the system in which cyclical events are sustained in perpetuation of its existence. The laws of biochemistry govern all living organisms and living processes. By controlling information flow through biochemical signaling and the flow of chemical energy through metabolism biochemical processes give rise to the complexity of life.

Fundamental properties of life

All organisms consist of one or more cells – complex, organized assemblages of molecules enclosed within membranes. These cells are quite similar in size, sensitivity, growth and development, reproduction and regulation and Homeostasis. One of the most fruitful approaches to understanding biological phenomenon has been to purify an individual chemical component, such as a protein, from a living organism and to characterize its structural and chemical characters. By the late 18th century, chemists had concluded that the composition of living matter is strikingly different from that of the inanimate world and it was thought that only living beings could produce the molecules of life. Antonie Lavoisier (1743-1794) noted the related chemical simplicity of the "plant and animal worlds"; the latter, he knew, were composed of compounds rich in the elements carbon, oxygen, nitrogen, and phosphorous. Then, in 1828, Friedrich Wohler published a paper on the synthesis of urea, proving that organic compounds can be created artificially. Experiments recreating the atmosphere of primitive earth, with the energy sources and temperatures thought to be prevalent at that time, have led to the spontaneous formation of amino acids and other biologically significant molecules.

During the first half of the 20th century, parallel biochemical investigations of glucose breakdown in yeast and in animal muscle cells revealed remarkable chemical similarities in these apparently very different cell types; the breakdown of glucose in yeast and muscle cells involved the same ten chemical intermediates.Subsequent studies of many other biochemical processes in many different organisms have confirmed the generality of this observation, neatly summarized by Jacques Monad; “What is true of *E.coli* is true of the elephant”. The current understanding that all organisms share a common evolutionary origin is based in part on this observed universality of chemical intermediates and transformations. However the question where the signal of life starts remained unsolved. With recent developments in biochemical sciences, the composition of a cell, which is the constituent of all organisms, can be traced back to simple chemical elements such as hydrogen, oxygen, nitrogen, and carbon, phosphorous,sulphur, iron, copper and many others. It is fairly easy to obtain all these chemical constituents by chemical methods. But it has not been possible to reassemble the chemical elements and constitute a living cell again. Consequently there are two possibilities; 1) Is life a distinct and discrete entity separate from the complex chemistry of living organisms? 2) Is life an expression and result of complex organization of several chemical substances and molecules integrated in a right perspective? The first possibility is completely untouched by scientists. However, the second possibility has gained momentum in recent years. Whether it will solve the riddle of life or not is not certain, but biochemistry has certainly an explanation for the basis of life in the organisms.

Biomolecules are compounds of carbon with a variety of functional groups.

The chemistry of living organisms is organized around carbon, which accounts for more than half the dry weight of cells. Carbon can form single bonds with hydrogen atoms, and both single and double bonds with oxygen and nitrogen atoms. Of greatest significance in biology is the stability of carbon atoms to form very stable carbon-carbon single bonds. Each carbon atom can form single bonds with up to four other carbon atoms. Two carbon atoms also share two or three electron pairs, thus forming double or triple bonds

Covalently linked carbon atoms in biomolecules can form linear chain, branched chains, and cyclic structures. To these carbon skeletons are added groups of other atoms, called functional groups, which confer specific chemical properties on the molecule. It seems likely that the bonding versatility of carbon was a measure factor in the selection of carbon compounds for the molecular machinery of cells during the origin and evolution of living organisms. No other chemical element can form molecules of such widely different sizes and shapes or with such a variety of functional groups.

Most biomolecules can be regarded as derivatives of hydrocarbons, with hydrogen atoms replaced by a variety of functional groups to yield different families of organic compounds. Typical of these are alcohols, which have one or more hydroxyl groups; amines, with amino groups; aldehydes and ketones, with carbonyl groups; and carboxylic acids, with carboxyl groups. Many biomolecules are polyfunctional, containing two or more different kinds of functional groups, each with its own chemical characteristics and reactions. The chemical 'personality' of a compound is determined by the chemistry of its functional groups and their disposition in three-dimensional space.

Cells contain a universal set of small molecules

Dissolved in the aqueous phase (cytosol) of all cells is a collection of 100-200 different organic molecules of molecular weight ranging from 100-500, the central metabolites in the major pathways occurring in nearly every cell-the metabolites and pathways that have been conserved throughout the course of evolution. This collection of molecules includes the common amino acids, nucleotides, sugars and their phosphorylated derivatives, and a number of mono, di and tricarboxylic acids. The molecules are polar or charged, water soluble, and present in micromolar to milli molar concentrations. They are trapped within the cell because the plasma membrane is impermeable to them-although specific membrane transporters can catalyse the movement of some molecules into and out of the cell or between compartments in eukaryotic cells. There are other small biomolecules, specific to certain types of cells or organisms. For example, vascular plants, in addition to the universal set, small molecules called secondary metabolites, which play a specific role in plant life. These metabolites include compounds that give plants their characteristic scents, and compounds such as morphine, quinine, nicotine and caffeine that are valued for their physiological effects on humans but used for other purposes by plants. It is impossible to pinpoint as to which of the myriads of biomolecule is living, because none of these, independently, can be expressive of life. The entire collection of small molecules in a given cell has been called that cell's metabolome, in parallel with the term "genome". If we know the composition of a cell's metabolome, we could predict which enzymes and metabolic pathways were active in that cell.

Macromolecules are the major constituents of cells

Many biological molecules are macromolecules, polymers of high molecular weight assembled from relatively simple precursors. Carbohydrates (polysaccharides), Proteins, lipids and nucleic acids carbohydrates are produced by the polymerisation of relatively small compounds with molecular weights of 500 or less. The number of polymerised units can range from tens to millions.

Biomolecules first arose by chemical evolution

Biochemistry has largely concentrated on as to how these simple components came into being and ultimately organized themselves into an object expressive of life processes. Apart from their occurrence in living organisms, organic compounds, including the basic biomolecules such as amino acids and carbohydrates, are found in only trace amounts in the earth's crust, the sea, and the atmosphere. How did the first living organisms acquire their characteristic organic building blocks? In 1924, the Russian biochemist Aleksadr I. Oparin proposed a theory for the origin of life early in the history of Earth, postulating that the atmosphere was very different from that of today, rich in methane, ammonia and water, and essentially devoid of oxygen. It was a reducing atmosphere, in contrast to the oxidizing environment of our era. In 1929 English biologist J.B.S. Haldane published a paper in which he proposed that ultraviolet light or heat energy from volcanoes acting on a primitive reducing atmosphere containing ammonia, methane and water vapour produced oceans with the consistency of a hot dilute soup containing the building blocks of life. In Oparin's theory, electrical energy from lightening discharges or heat energy from volcanoes caused ammonia, methane, water vapour, and other components of the primitive atmosphere to react, forming simple organic compounds. These compounds then dissolved in ancient seas, which over many millennia became enriched with a large variety of simple organic substances. Thus according to his hypothesis contemporary cells were created chemically before life began. In 1953, Stanley L. Miller and Harold C.Urey at the University of Chicago, set up an experimental investigation into the molecular origins of life, that simulated the Oparian-Haldane "early earth". The origin of water is uncertain, but it seems to have been present on the earth during the prebiotic period. A large number of molecules thus formed existed in the outer space. Many molecules like Acetonitrile (CH_3CN),Acetyledehyde (CH_3CHO),Ammonia (NH_3), carbon-monoxide (CO),carbon monosulphide (CS), Carbonyl sulphide

(OCS), Formaldehyde (HCHO), Hydroxy radicle (OH) and many more which have been reportedly discovered from the interstellar space are apparently precursors of macromolecules. From this extremely rich pool of molecules the prebiotic cell picked up organic molecules by a process of accretion (a process of growth by continuous coherence). There have been several reports indicating the presence of organic molecules in meteorites and microfossils in the most ancient terrestrial rocks. In nature UV light and very high temperature either from volcanoes or hot springs could serve as a source of energy for the process of accretion. Proteinaceous amino acids have been recovered in samples from the terrestrial lava as well as from the moon. The fact that amino acids can be formed under prebiotic conditions suggests that these should be found where life does not exist now although the conditions are congenial.

The biggest gap remains between molecules in a state of solution to a state of organized cell. Prebiotic formation of molecules may be understood but their biotic transformation when life first appeared is indeed a puzzling phenomenon. Chemical affinities of these molecules assembling themselves as organized cells are possible and explainable with modern development in bond chemistry. Formation of proteinoid (thermal proteins)droplets as a result of aggregation of molecules in contact with water has been suggested by Sidney Fox(1950) at the University of Miami. Whether such proteinoid droplets would pocesses the enzymatic ability or the active transformation mechanism so characteristic of a living cell membrane has not been demonstratively checked.

It is true that amino acids could just be joined to each other with a consequent loss of water resulting in a peptide bond which is characteristic of protein molecule, but the origin of a living cell from such inanimate molecule is highly speculative. The origin of proteinoid type of molecules is very well documented even by laboratory experiments and the next step could have been towards the direction of interaction of such molecules to form membrane like structure. However, the sequencing of amino acids which is a genetically determined property is rather difficult to take place in the absence of a suitable genetic messenger. Nevertheless, it is quite understandable that the proteiniod type of molecules or prototype of a modern living cell might have arisen with frequent distribution in space and time. Their interaction in due course, led to the better evolved cellular characteristic features as operational in cells.

A second major direction is towards the development of a catalytic system to hasten the flow of energy. Addition of iron (Fe^{+++}) molecules to the proteiniods could enhance their ability as forerunners of enzymes. But, in the absence of a proper genetic signal, this could take place with hit and trial methods only. There is no direct evidence to indicate whether the biochemical information or the genetic signal originated first.

Besides the simple proteiniod or a prototype of nucleic acids, a cell still requires a host of components to be full of life. There must be a system to extract energy from the surroundings as well as maintain the energy budget.

Perhaps the origin of another molecule called adenine (6-amino purine) must have taken place much earlier than the prototype of the living cell evolved. Miller and Urey demonstrated the formation of simple biomolecules. But the further chemical evolution would depend on the polymerization or condensation of these monomer units into polymer, e.g., nucleic acid bases can be synthesized under supposed prebiotic conditions. In particular adenine is formed by the condensation of HCN, a plentiful component of the prebiotic atmosphere in a reaction catalyzed byNH_3. The other bases have been synthesized by similar reactions involving HCN and H_2O. Sugars have been synthesized by the polymerization of formaldehyde (CH_2O) in reactions catalyzed by divalent cations, alumina or clays. Adenine is not only a constituent of information molecules like DNA and RNA but is also present in energy rich compounds such as FAD (Flavine adenine dinucleotide), NAD^+ and $NADP^+$ (nicotinamide adeine dinucleotide), cAMP (Cyclic adenosine 3,5 monophosphate), and others.

If complex molecules were produced from simpler one, how might they have become organized into cells?

Macromolecules aggregate into membrane-enclosed droplets (coaservates and microspheres) as a result of intermolecular forces, which exhibit some features of living systems such as organisation, selective permeability, and energy use.

The spontaneous self-assembly of macromolecules into coaservates and microspheres, indicates that the occurrence of similar structures under primitive conditions would probably give rise to more organized structures, called protocells.

Out of the crucial events leading to the formation of the first cell must have been the development of an outer membrane. The need for containment is easily fulfilled by a class of molecules that has the simple physiochemical property of being amphipathic i.e., consisting of hydrophobic and hydrophilic parts, when such molecules are placed in water; they aggregate, arranging their hydrophobic portions as much in contact with one another as possible and their hydrophilic portions in contact with the water. Amphipathic molecules of appropriate shape spontaneously aggregate to form bilayers, creating small closed vesicles whose aqueous contents are isolated from the external medium. All present-day cells are surrounded by a plasma membrane consisting of amphipathic molecules. Presumably, the first membrane bound cells were formed by spontaneous assembly of phospholipid molecules from the prebiotic soup enclosing a self-replicating mixture of RNA and other molecules. It is possible to think of prokaryotic anaerobes as the first animate objective cells formed under prebiotic conditions. Modern enzyme system including hydrogenase and ferredoxin (iron and sulfur containing enzymes) must have a precursor enzyme operating in those anaerobic prototype living cells essentially in view of extremely reducing conditions present during the precellular period. The cells able to utilize the vast resources of light energy from the sun, must have originated at a much later stage. The formation of the pigment system with the heme group was prerequisite to the formation of an autotrophic cell. Supposedly photosynthesis emerged approximately 2 billion years ago. At that time, the earth's atmosphere was anaerobic and reducing. It contained a substantial amount of CO_2 formed as a result of decomposition of organic compounds by primary heterotrophs and O_2 traces in the upper layers which were caused by radiation and ultraviolet effects on water vapours. Photosynthetic bacteria that are comparatively more ancient, from the evolutionary point of view, were capable of utilizing only reducing components. the original electron(hydrogen) donor for these photosynthetic organisms was probably H_2S, yielding elemental sulfur as the by product, but at some point cells developed the enzymatic capacity to use H_2O as the electron donor in photosynthetic reactions producing O_2.

On the contrary cyanobacteria were utilizing oxidized compounds such as water. The changing process involved not only functional but also structural changes of the photosynthetic apparatus. As is well known, photosynthesis occurs in special organelles in chromatophores of purple and green bacteria and in chloroplasts of higher plants and green algae. However, chromatophores show only an orderly lamellar structure, whereas chloroplast shows a differentiation into grana and stroma. A cyanobacterial cell is the first cell formed with an oxygenic type of photosynthesis and able to evolve oxygen. As a matter of fact, cyanobacteria are credited with the responsibility of filling up our atmosphere with oxygen. The mechanism of splitting of water molecule and consequent release of oxygen is least understood today, but a cyanobacterial cell must have created the need to do so.The cyanobacteria are the modern descendants of the early photosynthetic O_2 producers. One important landmark along this evolutionary road occurred when there was a transition from small cells with relatively simple internal structures called prokaryotic cells, to a flourishing of larger radically more complex eukaryotic cells such as found in higher animals and plants. The fossil record show that earliest eukaryotic cells evolve about 1.5 billion years ago. These major changes must have occurred as prokaryotes gave rise to eukaryotes. First, as cells acquired more DNA, mechanisms evolved to fold it compactly into discrete complexes with specific proteins and to divide it equally between daughter cells at cell division. These DNA-Protein complex are called chromosomes become especially compact at the time of cell division.

Secondly, the cells became larger and intracellular membrane organelles developed. Eukaryotic cells have a nucleus which contains most of the cell's DNA, enclosed by a double layer membrane. The DNA is thereby kept in a compartment separate from the rest of the contents of the cell, the cytoplasm, where most of the cell' metabolic reactions occur.

Finally, primitive eukaryotic cells, which were incapable of photosynthesis or of aerobic metabolism pooled their assets with those of aerobic bacteria or photosynthetic bacteria to form symbiotic associations that became permanent. Some aerobic bacteria evolved into the mitochondria of modern eukaryotes and some photosynthetic cyanobacteria became the chloroplast of modern cells.

Functions of Biomolecules

1. **Carbohydrates:** Carbohydrates are the most widely distributed and abundant biological molecule on earth. They have a central role in the metabolism of organisms. Carbohydrate biosynthesis in plants starting from carbon dioxide and water with the help of light energy, i. e., photosynthesis, is the basis for the existence of all other organisms which depend on the intake of organic substances with food. Carbohydrates are essential for life in both plants and animals. They are involved in energy storage and production, structure and signaling. The fundamental monomer of carbohydrates is called a monosaccharide. Monosaccharides can be linked together by glycosidic linkages, which are covalent bonds formed through condensation reactions. Monosaccharides are linked together to form disaccharides, slightly larger oligosaccharides, or the largest class of carbohydrates, the polysaccharides. The polysaccharides have two major functions; as energy-yielding fuel store and as extracellular structural elements with specific binding sites for particular proteins. Shorter polymers of sugars (oligosaccharides) attached to proteins or lipids at the cell surface serve as specific cellular signals.

2. Proteins: Proteins, long polymers of α-amino acids, which are linked by peptide bonds and constitute the largest fraction (besides water) of cells. They are found everywhere – inside of cells, in membranes, and outside of cells – and play many roles for organisms. Proteins are perhaps the most versatile of all biomolecules, many proteins act as enzymes, and catalyze very specific chemical reactions. Life is possible due to coordination of various chemical reactions in living organisms. An example is the digestion of food, absorption of appropriate molecules and ultimately production of energy. All these reactions are catalyzed by enzymes. Other proteins have roles in the transport of substances (membrane proteins), protection (antibodies), attack (toxins),and structure (collagen). Of the literally millions of different types of proteins used by living organisms, all proteins are made from the same 20 amino acids, but have different sequences of amino acids.

3. **Lipids**: Lipids are a diverse group of molecules grouped together on the basis of their solubility in nonpolar solvents. Lipids include fatty acids, fats (oils) terpenes (steroids, cholestol), prostaglandins, and also complex molecules such as phosphoglycerides, sphingolipids and hybrid molecules such as lipoproteins or glycolipids. Certain fat soluble **vitamins (**A, E, and K), and hormones are also found in this class. Lipids serve as structural element, e.g., in the cell membrane. They store and transport metabolic energy in chemical form. They also form protection surface and fatty layers. In addition, they play an important role in cell-cell recognition and in the immune response. Individual lipid molecules are much smaller (M_r 750-1,500) and are not classified as macromolecules. However, large number of lipid molecules can associate noncovalently into very large structures. Cellular membranes are built of enormous noncovalent aggregates of lipid and protein molecules.

4.Nucleic acids

The nucleic acids DNA and RNA are responsible for storing and transmitting the genetic code of all organisms. DNA is a huge polymer that stores information in the sequence of its monomers, called nucleotides. The information in DNA is used to produce proteins. RNA is used to transfer the information of DNA to sites of protein synthesis and to translate the information into the amino acid sequences of proteins. DNA also serves as a partial record of the history of life, and allows us to peer into the past to discern evolutionary trends and relationships. The most common nucleic acids are deoxyribonucleic acid and ribonucleic acid. Their monomers are called nucleotides. The most common nucleotides are adenine, cytosine, guanine, and uracil. Adenine binds with thymine and uracil; Thymine binds only with adenine; and cytosine and guanine can bind only with each other.

Besides these four important biomolecule, another molecule which is known as the basic molecule of life is the water. Water constitutes more than half of the all living organisms and 90% of plant cells. The importance of water is well understood by the fact that primitive life originated in aqueous medium. It is not only a natural environment of most of the cells but also a natural solvent for the physical and chemical events taking place within and around the cell. It is the most significant molecule that connects the physical world with the biological processes.

Because of the immense increase in knowledge of food biochemistry in the recent years, metabolic pathways of living organisms are being clarified. These developments results in a better understanding of the biological materials which we use as food.

Biomolecules like amino acids, peptides and proteins are important constituents of food. They supply the required building blocks for protein biosynthesis. In addition they directly contribute to the flavor of food and are precursors for aroma compounds and colors formed during thermal or enzymatic reactions in production, processing and storage of food. Other food constituents, e.g.,carbohydrates, also take part in such reactions. Proteins also contribute significantly to the physical properties of food through their ability to build or stabilize gels, foams, emulsions and fibrillar structures. The nutritional energy value of proteins (17 kJ/g or 4 kcal/g) is as high as that of carbohydrate.

Water (moisture) is the predominant constituent in many foods. As medium water supports chemical reactions, and it is a direct reactant in hydrolytic processes. Therefore, removal of water from food or binding it by increasing the concentration of common salt or sugar retards many reactions and inhibits the growth of microorganisms, thus improving the shelf lives of a number of foods. Through physical interaction with proteins, polysaccharides, lipids and salts, water contributes significantly to the texture of food.