COMMITTEE I
Unity of Science: Organization and
Change in Complex Systems

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ORGANIZATION AND CHANGE IN EUKARYOTIC CELLS

by

Claude A. Villee, Jr.
Andelot Professor of Biological Chemistry
Department of Biological Chemistry and
Laboratory of Human Reproduction & Reproductive Biology
Harvard Medical School
Boston, Massachusetts USA

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I. Introduction. Change and Resistance to Change in Living Systems: Homeostasis.

Living systems represent islands of order, of low entropy, in a vast sea of disorder. The low entropy of living systems must be maintained by the constant expenditure of energy by the living system. Moreover, the living system changes with time in defined ways as it undergoes growth, differentiation, maturation, ageing and death. Living systems may change in other ways in response to trauma or disease. Both of these types of changes are ultimately regulated by the turning on and turning off of specific genes in specific tissues as time progresses or by differential changes in gene activity in different tissues of the same organism. The programmed ability to respond to changes in the environment by systems that tend to minimize the effects of these environmental changes, changes that tend to keep a system constant, is termed homeostasis, and this ability is one of the prime characteristics of all living things.

Cells of living beings are complex dynamic systems composed of thousands of different molecular compounds, which interact in many different ways as they carry out specific functions in an organized and coherent form. In the first part of this paper the most relevant aspects of this interplay between change and organization at the cellular level are described, concluding with some brief considerations about cell differentiation and the origin of life.

II. Cellular and Subcellular Complexity.

A. Microtrabecular Lattice.

There have been many surprises as we have learned more and more about the structure and function of living things. The electron microscope and

its various improved forms have revealed a dazzling complexity at the subcellular level which parallels the remarkable complexity of the atomic nucleus now becoming apparent (Alberts, 1983). What originally, by rather primitive light microscopy, appeared to be simply the nucleus and the cytoplasm of the cell has been resolved by electron microscopy to reveal a wealth of subcellular organelles - mitochondria, endoplasmic reticulum, lysosomes, peroxisomes, chloroplasts, and others (Marx, 1983). Even the apparently formless background of the cytoplasm of the cell, which had appeared to be structurally homogeneous by conventional electron microscopy, has been shown to have an internal structure when examined by high voltage electron microscopy (Buckley and Porter, 1967). The cytoplasmic ground substance contains a microtravecular lattice, an irregular three-dimensional lattice of very slender protein threads that extend throughout the cytoplasm and are attached to the cell membrane (Wolosewick and Porter, 1979). These interlinked filaments form a three-dimensional spider web in which are suspended the several kinds of intracellular organelles. Microtubules and microfilaments are coated with a protein similar to that composing the individual lattice filaments. Microtubules, microfilaments, endoplasmic reticulum and mitochondria are integrated with the lattice and are suspended in it. This microtrabecular lattice links the cellular organelles into a highly organized structural and functional unit which appears to play an important role in cell movement. Enzymes that were previously believed to be dissolved in the cytoplasm may in fact be bound to this microtrabecular lattice; indeed, bound in a nonrandom orientation. That is, enzymes that

act in sequence may be located on the lattice in a spatial orientation so that they can pass substrate molecules from one enzyme to the next. The microtrabecular lattice serves as a sort of intracellular musculature and undergoes local contractions that change its shape and redistribute and reorient the intracellular organelles as the cell goes about its various functions (Goldman and Follett, 1970; Goldman, et al, 1979). This can be seen most readily in the movement of granules within the pigment cells in the skin of fishes, frogs and reptiles that occur under hormonal or nervous control. These movements of the pigment granules enable the animal to lighten or darken its skin color rapidly to match the color of its surroundings.

B. Nuclear Matrix

Just as the cytoplasm of eukaryotic cells has been shown to be permeated by the highly ordered subcellular skeleton of filaments and membranes, the nucleus has also been shown to contain an organized proteinaceous skeleton that probably plays a role in the proper positioning of gene sequences important for replication, transcription and chromosomal integrity (Maul, 1982). This nuclear skeleton, termed the nuclear matrix, makes up about 10% of the mass of the nucleus. It contains neither lipids nor histones, but is composed of some 20 proteins (some of which are phosphorylated), together with many minor proteins. The laminar polypeptides with molecular weights of 62, 66 and 69 kilodaltons migrate to the cytoplasm during mitosis.

We can now recognize three clearly different matrix systems - the nuclear matrix, the cytoplasmic matrix, and an extracellular matrix present in tissues such as bone, cartilage, ligaments, tendons and dense connective tissue.

1. Role in DNA Replication

It is now realized that the double helix of chromosomal DNA is a very long fiber - with a length measured in meters, and that it must be folded and refolded very carefully to fit inside a nucleus only a few micrometers in diameter and yet be able to undergo replication rapidly without getting tangled with adjacent chromosomes (Hoagland, 1979). The evidence now suggests that this is achieved by having the ends of the chromosomes attached to the inner edge of the nuclear membrane in specific places.

To obtain a sample of nuclear matrix the tissue or group of cells is homogenized and the nuclei are separated from the remainder of the cell by centrifugation. The nuclei are then treated with nonionic detergents and 2M NaCl to remove lipids and histones and then are digested with deoxyribonuclease. Before being treated with deoxyribonuclease the chromosomes can be shown to be attached to the matrix at multiple sites. This organizes the DNA into topologically independent supercoiled domains. After the nuclei have been digested with deoxyribonuclease the nuclear matrix retains the shape of the nucleus and has three features - an outer lamina, a residual nucleolus, and a fibrillar network. This nuclear matrix may provide a structural support for the replication of DNA. It has been shown experimentally that newly synthesized DNA is tightly associated with the matrix. Other workers have found that the structural genes are preferentially associated with the matrix in those cells in which the genes are actively transcribed. Based on findings such as these, many investigators have concluded that the nuclear matrix serves some

crucial role in organizing and regulating nuclear events (Maul, 1982). Other investigators suggest that they may be artifacts produced by the isolation process. Comparable structures have been isolated by a different method from both metaphase and nondividing cells.

When nuclei are lysed by a gentle low salt procedure the resulting nuclei have their histones depleted, and then when they are digested with restriction endonucleases, about 70% of the DNA is solubilized. Analyses of the solubilized versus the residual DNA shows that one type of DNA appears to be found exclusively associated with the nuclear matrix whereas all other DNA fragments are found primarily in the soluble supernatant. This nuclear matrix-bound fragment is rich in adenine and thymine and is derived from a non-transcribed "spacer" sequence upstream from the histone I gene. A similar adenine- and thymine-rich fragment from the HSP70 heat shock gene has been shown to be associated with the nuclear matrix. Other adenine- and thymine-rich fragments of DNA have also been shown to be bound to the matrix. From these findings it has been inferred that the loops of DNA in interphase nuclei are maintained by way of these sequence specific associations with matrix proteins and that the associations are not changed as a function of transcriptional activity. These results support the hypothesis that the nucleus is indeed highly ordered and organized and that changes in this organization may play a role in controlling nuclear functions.

The average human diploid nucleus with a radius of 2.6 micrometers and a volume of 75 cubic micrometers contains 5.5×10^9 base pairs of DNA, which would extend 1.7×10^6 micrometers, or 1.7 meters. This length is

equal to 650,000 x the nuclear radius! Clearly, the replication of DNA must be organized in space in such a way that the resultant daughter chromosomes remain untangled and can segregate properly during mitosis. The replication of DNA in eukaryotes is ordered chronologically; that is, different sections of the genome appear to replicate at specific times during the S phase according to a schedule which is the same for each consecutive cycle of division. The chronological and topological ordering of DNA replication may be a function of the structural components of the nucleus called the nuclear matrix. These ubiquitous proteins, which are not dissolved by salt, are sensitive to proteolysis and hence must be isolated in the presence of protease inhibitors. The nuclear matrix is composed of three major polypeptides of 62, 66 and 69 kilodaltons. These proteins appear by tryptic peptide mapping to be structurally related and perhaps derived from a common precursor or evolved from closely related genes. It is now clear that they are also related immunologically, for they cross-react with monospecific antibodies.

The replication sites of DNA are bound to the nuclear matrix. The transcription of DNA and the synthesis of the several kinds of RNA also appear to be located on the nuclear matrix. Newly synthesized RNA is localized in the nuclear matrix and all of the heterogeneous nuclear RNA (the precursor of messenger RNA) is bound to the nuclear matrix. RNA is transported from the nucleus to the cytoplasm through nuclear pore complexes which are linked by way of the nuclear matrix to the sites of RNA synthesis.

2. Mechanism of Action of Steroid Hormones

A fascinating problem at present is the question of how steroid hormones control the expression of specific genes in their target tissues. It is believed, and there is experimental evidence to support it, to involve specific binding protein receptors and acceptors which take up the steroid hormone and bind the steroid-receptor complex to specific gene locations. For example, estrogens bind to salt insoluble nuclear subfractions in their target tissues which have been shown to be nuclear matrix. Similar studies with other tissues also show the binding of steroid hormones to salt resistant nuclear protein fractions; that is, the androgens bind to the nuclear matrix in the prostate, the glucocorticoids to the nuclear matrix in fibroblasts and liver, and so on.

III. Information Flow

A. Introns and Exons

The central dogma of biology states that information flows from DNA (deoxyribonucleic acid) through mRNA (messenger RNA) to proteins. This is substantially true in the relatively simple coliform bacteria, Escherichia coli, in which many of the early studies of molecular biology were made. However, when scientists turned to other forms of life, and particularly to eukaryotic organisms, some surprises occurred. One of the first was that most eukaryotic genes were found to contain very long sequences of nucleotides that do not end up in the corresponding mature messenger RNAs. During the processing of messenger RNA after it has been transcribed from DNA in the nucleus, the RNA is split at precise points,

certain segments are removed, and the remaining segments are spliced back together again. The sequences that are retained in the mature RNA are called exons and the discarded ones are called introns. The gene for the globin component of hemoglobin ~~contains two introns~~ produces a messenger RNA after the deletion of two introns. The gene for ovalbumin (egg white protein) contains seven introns and the gene specifying another egg white protein, conalbumin, contains 16 introns. The apparently unused introns may be collectively much longer than the functional exons. The ovalbumin gene contains about 7700 base pairs despite the fact that its mature messenger RNA contains only 1859 bases. It remains unclear why a cell should contain 5841 apparently wasted and useless bases in just one of its many genes.

B. RNA Viruses and Reverse Transcriptase

Another surprise came with the discovery that certain viruses contain only RNA and not DNA. It was then discovered that a class of enzymes called reverse transcriptases can synthesize DNA using RNA as the template. The resulting DNA can then be used in a regular transcription system to produce many copies of RNA which will be available for the multiplying virus.

C. DNA Codes and Prions

The establishing of the genetic code which assigned each of the possible triplet codons to a specific amino acid appeared to be universal as systems from bacteria to the human were analyzed and all found to use the same genetic code. However, examination of the details of the coding relationships in the DNA of both yeast mitochondria and human mitochondria led to the unexpected finding that some of these codons are different from

the accepted universal code (Grizell, 1983). For example, in yeast mitochondria the sequence AUA codes for methionine rather than for isoleucine and the sequence UGA codes for tryptophan instead of serving as it does in the nucleus as a terminator code. An even greater shock has come with the recent finding that the agents of certain diseases such as scrapie of sheep, the kuru of New Guinea cannibals and of Alzheimer's disease which originally were thought to be caused by a virus may be caused not by viruses, but by small protein particles called prions. Prions have not yet been found to contain any nucleic acid. It is not clear yet how prions may cause disease, but they may do it by affecting genetic expression, rather than by actually transmitting genetic information. It is not at all clear how such particles could be self-replicating, which is a condition required of any particle that transmits genetic information.

Thus our understanding of the organization of living systems and of the factors that control changes in the system has grown remarkably in the past few years, but it seems likely that there will be many more surprises in store for us before the final chapter is written.

IV. Cell Structure

Early biologists thought that the inside of a cell was filled with a homogeneous jelly-like material that they called protoplasm. With their primitive microscopes they could recognize only a few structures within the cell such as the nucleus. Our present perception of the world within the cell has been greatly expanded, and we know that each cell is a highly organized, complex structure with its own control center, its own power

plants, its own internal transport system, its own factories for synthesizing a variety of needed materials, places for packaging these biosynthetic products, and even a "self-destruct" system within the cell (Fawcett, 1981). The various subcellular organelles are enclosed by membranes which effectively partition the cytoplasm into specific compartments. These membrane barriers make possible the accumulation of specific chemicals and enzymes in certain compartments. The chemical contents within that compartment may be quite different from the chemical environment in the general cytoplasm or inside other organelles.

A. Endoplasmic Reticulum

Proteins are synthesized on the ribosomes attached to the rough endoplasmic reticulum (Avers, 1981). Since the ribosomes are the site of protein synthesis, the amount of rough endoplasmic reticulum is especially large in those cells that synthesize proteins for export from the cell, such as those in the pancreas that secrete digestive enzymes.

B. Golgi Complex

The Golgi complex consists of layers of platelike membranes which may be distended to form vesicles or sacs which are filled with cell products (Holtzman and Novikoff, 1984). The Golgi complex functions as a processing and packaging center and is most highly developed in cells that are specialized to secrete products. As proteins are synthesized in the rough endoplasmic reticulum, they are sealed off in little packets of membrane forming vesicles. These pass through the endoplasmic reticulum to the Golgi complex and there fuse to form new Golgi complex membranes.

Within the Golgi complex the proteins secreted may be concentrated by the action of its membranes or the proteins may undergo modification such as having carbohydrate residues added or having certain amino acid residues removed. The protein is then packaged within a sac made of Golgi complex membranes and these secretory vesicles are released from the Golgi complex and moved to the cell membrane. They fuse with the cell membrane, releasing their contents to the exterior of the cell. An actively secreting cell such as a goblet cell in the lining of the digestive system that secretes mucus may completely renew all of its membranes every 30 minutes.

C. Lysosomes

Another type of subcellular organelle is the lysosome, which contains intracellular digestive enzymes (DeDuve, 1963). These include a variety of hydrolases that can cleave peptides, carbohydrates, lipids or nucleotides. These lysosomes are dispersed throughout the cytoplasm. When a white blood cell eats bacteria, debris or dead cells, the foreign matter is surrounded by a vesicle consisting of part of the cell membrane. One or more of the cell's lysosomes then fuse with the vesicle containing the foreign matter and the enzymes from the lysosomes digest the proteins, polysaccharides, lipids and nucleic acids which made up the dead cell or bacterium. When a cell dies, the lysosomes release their enzymes into the cytoplasm and these enzymes then break down the cell itself. This self-destruct system accounts for the rapid deterioration of cells following the death of the organism. Christine deDuve, the Belgian biochemist who discovered lysosomes, referred to them as "suicide bags."

D. Mitochondria

Most of the enzymatic reactions of cellular respiration occur within the mitochondria and, as you might expect, mitochondria are more numerous in cells that are very active. Mitochondria may be spherical, rod-shaped, sausage-shaped, or thread-like. Each mitochondrion is bounded by a double membrane. The outer membrane forms the smooth, outer boundary, whereas the inner membrane is folded repeatedly into parallel plates or cristae that extend into the center of the mitochondrial cavity. The shelf-like cristae contain many of the enzymes involved in cellular respiration. Other enzymes involved in cellular respiration are located within the semifluid matrix inside the inner compartment (Margulis, 1981).

E. Peroxisomes

Another type of subcellular membrane-bounded organelle is the peroxisome which contains enzymes that utilize oxygen in metabolic reactions. Some reactions produce hydrogen peroxide, but before the cell can be damaged by this potentially lethal compound the hydrogen peroxide is split by superoxide dismutase to yield water and oxygen.

F. Microtubules and Microfilaments

Most cells contain in their cytoplasm hollow cylindrical cytoplasmic subunits called microtubules which are important in maintaining and controlling the shape of the cell (Fawcett, 1981). Microtubules also play important roles in cellular movements such as the movement of the chromosomes on the spindle formed during mitosis. Microtubules are also the major structural components of cilia and flagella. They are composed of the protein tubulin made up of two subunits. Microtubules can grow in length

by the addition of more subunits or can shorten by the disassembly of subunits. The microtubules present within the axons of nerve cells play an important role in the rapid transport of proteins and other molecules down the axon to its tip where these substances are released.

Microfilaments are solid cytoplasmic strands that are composed of protein molecules. These protein filaments play additional roles in maintaining cell structure and permitting cell movement (Wessels, 1971). The cytoplasm of skeletal muscle fibers contain long, thin filaments, the myofibrils of two types - one composed of the protein actin and the other composed of the protein myosin. The interaction of these two is the basis of the process of muscle contraction. Microfilaments made of actin are also associated with such cellular movements as the flowing of cytoplasm in amoebas (Lazarides and Revell, 1978). The assembly of microfilaments and microtubules form a flexible cellular framework termed the cytoskeleton. Each kind of animal cell contains two centrioles, organelles that play a role in cell division. Each centriole is a hollow cylinder made up of nine triple microtubules.

Within the nucleus and readily visible in a stained cell in the light microscope is the nucleolus, a compact, spherical body rich in RNA and the site where ribosomal RNA is synthesized.

G. Cell Membrane

Even with the primitive early microscope, it was possible to recognize that cells have a cell membrane which separates the complex structures within the cell from the surrounding environment. The cell contains a host of specific proteins, lipids, carbohydrates and inorganic ions and the

concentrations of these in cellular components must be maintained relatively constant if the cell is to continue to remain alive. The cell membrane is not simply an inanimate wall, but rather a complex structure that permits selective interactions between the cell and its environment (Lodish and Rothman, 1979). The cell membrane regulates the passage of materials into and out of the cell, enabling the cell to maintain the concentrations of many of its constituents different from those in the surrounding environment. The cell membrane prevents the passage of certain substances and permits or even facilitates the passage of others.

Cells can, in a sense, talk to each other. The cell membrane receives information that permits the cell to sense changes in its environment and respond appropriately to these changes. Cell surfaces are equipped with a variety of receptor proteins that receive chemical messages from other cells. These receptor proteins bind specifically with certain hormones, growth factors and neurotransmitters, and the binding triggers the specific response of the cell.

The cell membrane is really thin, about 6 to 10 nanometers in thickness, and is composed of a fluid lipid bilayer in which are imbedded a variety of globular proteins (Singer and Nicholson, 1972). The lipid components of the cell membrane include phospholipids, glycolipids and cholesterol, all of which are asymmetrical, elongated molecules with one hydrophilic end and one hydrophobic end. The bilayer is arranged so that the nonpolar hydrophobic ends of the lipids meet, overlap and interdigitate with each other, whereas the polar hydrophilic ends are directed towards the outside of the membrane. The two sheets of the

lipid bilayer differ in their chemical composition. The outer layer is especially rich in choline phospholipids and glycolipids, whereas the internal fluid layer is rich in other types of phospholipids. The fatty acids of the outer choline-rich lipid layer are primarily saturated fatty acids whereas the inner layer is rich in polyunsaturated fatty acids.

Imbedded in the bilayer lipid fluid matrix are proteins which can move around like "protein icebergs in a lipid sea". The lipids serve as a general permeability barrier to ions and polar molecules, whereas the membrane proteins carry out specific functions such as chemical transport and transmission of messages. The plastic quality of the lipid bilayer permits the cell to respond to a wide variety of external stimuli. The membrane proteins that protrude from the outer surface away from the cytoplasm are largely glycoproteins; that is, proteins to which sugar residues are attached (Unwin and Henderson, 1984). Thus nearly all cells are "sugar-coated" like breakfast cereal. Little or no sugar is attached to the inner surface of the cell membrane or to any of the intracellular membranes. Membrane proteins can move laterally within the membrane and can change their position on the cell surface.

V. Cell Differentiation

Organisms such as human beings are composed of an exceedingly large number ($>10^9$) of individual cells and of many kinds of cells. Each kind of cell is specialized and adapted to carry out certain functions important for the survival and growth of the human being. One of the central questions in biology at the present time concerns the molecular basis of

this process of cellular differentiation. Put more simply: What kind of processes occur during development that insure that a single fertilized egg cell will develop into all of these many types of cells, each in the proper place in the organism, each with its appropriate spectrum of enzymes, and each with its characteristic structure, so that the net result is a human being? We now have a good idea of how a single gene can code for the production of a single kind of enzyme and how the activity of the enzyme in the cell can result in the conversion of a precursor molecule into the product, the right kind of product for that cell. However, we have very little idea of how a gene may determine the structural feature of a cell or tissue or how the malfunctioning of genes during development may lead to a tremendous alteration in the structure of the body, such as that seen in anencephaly, spina bifida, cleft palate or club foot. What is truly remarkable is that these mistakes in the developmental process happen relatively rarely.

VI. The Origin of Life

Another important problem in present day biology is the question of how life got started on the planet earth (Ambrose, 1982). We now know that living things come only from other living things, but under the very different conditions than that obtained when the earth was young; living things may indeed have developed from nonliving things. The concept that the first living things evolved from nonliving things and suggestions as to what the sequence of events may have been were put forward by Haldane, Beutner and Oparin in the early 30's. The earth originated some five

billion years ago and was probaly very hot and molten when it was first formed. Conditions consistent with life may have appeared on the planet only three billion years ago. Twenty-two different amino acids were isolated from Precambrian rocks from South Africa that are dated at about 3.1 billion years old. It seems likely that in the early period of the earth's development there was essentially no free oxygen in the atmosphere. All of the oxygen atoms were combined as water or as oxides. The primitive atmosphere of the earth would have been strongly reducing and would have included the gases methane, ammonia and water.

Oparin suggested that the carbon atoms in the earth's crust were present as metallic carbides which could react with water to form acetylene. Acetylene can polymerize to form compounds composed of long chains of carbon atoms. High energy radiation, such as cosmic rays, can catalyze the synthesis of organic compounds. This was shown by Melvin Calvin's experiments in which solutions of carbon dioxide and water were irradiated in a cyclotron and formic, oxalic and succinic acids, which contain 1, 2 and 4 carbons respectively, were obtained. These compounds are intermediates in metabolic pathways of living organisms.

Irradiating solutions of inorganic compounds with ultraviolet light or passing electric charges through the solutions to simulate lightning also produces organic compounds. Stanley Miller and Howard Urey (1952) exposed a mixture of water vapor, methane, ammonia and hydrogen gases to electric discharges for a week and demonstrated the production of organic compounds, including D and L amino acids. Other theorists believe that the early atmosphere consisted of water vapor, carbon dioxide, carbon monoxide, nitrogen and some

free hydrogen. When this mixture of gases was subjected to electric charges, even greater amounts of organic compounds were formed, including (surprisingly enough) nucleotide bases of DNA and RNA. Amino acids and some other compounds are produced on earth at the present time by lightning discharges or ultraviolet radiation, but any such organic compound produced would be phagocytized by protists or degraded by molds and bacteria that now abound on earth. Under the original presumably sterile and anoxic conditions, the compounds could have persisted.

The details of the chemical reactions that could give rise, without the intervention of living things, to carbohydrates, fats and amino acids have been described by Oparin, Calvin and others. They believe that most, and perhaps all, of the reactions by which organic substances were formed probably occurred in the sea which contained a rich pool of precursors. The sea became a sort of dilute broth in which the molecules collided, reacted and aggregated to form larger molecules. As more has been learned about the role of hydrogen bonds and other weak intramolecular forces in the pairing of specific nucleotide bases and the effectiveness of these processes in the transfer of biological information it has become clear that similar forces could have operated early in evolution before living organisms first appeared. Oparin's theory continues with the suggestion that the forces of intermolecular attraction and the tendency for certain molecules to form liquid crystals might provide an explanation for the spontaneous formation of large, complex specific molecules. It has now been shown that such reactions can take place with the molecules adhering to particles of

clay as well as in free solution in the water, and that the particles of clay may help direct reactions in a certain direction (Cairns-Smith, 1982).

Once some of the protein molecules had been formed and had achieved the ability to catalyze reactions; that is, once they were enzymes, the rate of formation of additional molecules would be greatly speeded up. Eventually when they had combined with nucleic acids the complex protein molecules should acquire the ability to catalyze the synthesis of molecules like themselves. Such hypothetical autocatylic particles made of nucleic acids and proteins could have been something like a modern virus, or perhaps a plasmid.

A major step in the evolution of these prebiotic systems was the development of a protein-lipd membrane surrounding the aggregate that permitted the accumulation of some molecules and the exclusion of others from the surrounding medium. Of course, another major evolutionary step was the development of the genetic code. No feature of a living cell could be maintained for more than one generation, if that long, without an informational basis. Thus, any credible theory of the origin of life must suggest ways whereby not only the nucleic acids, but the informational content of the nucleic acids, as well as the read-out mechanisms by which the information is translated into cellular structures, would have originated.

The first living organism having arisen in a sea of organic molecules and in contact with an atmosphere lacking oxygen probably obtained energy by fermenting these organic substances. The first

organisms, therefore, were almost certainly heterotrophs. From these early heterotrophs probably evolved the autotrophs which were able to make their own organic molecules by chemosynthesis or photosynthesis. One of the byproducts of photosynthesis is gaseous oxygen. All of the oxygen in the atmosphere is now produced by photosynthesis and, according to this, it always has been produced by photosynthesis. Other inorganic sources of oxygen, such as the photolysis of water vapor by ultraviolet light, might have contributed some of the oxygen in the early atmosphere.

Although at one time it was generally believed that living things have some unique "vital force" that governs their existence, there is no doubt at present that living things are subject to the same principles and laws of physics and chemistry as are nonliving things. Living things are typically much more complex in their organization and structure than are nonliving systems. Our understanding of the complexities of the structure of the atomic nucleus had to wait until the appropriate technology was developed - cyclotrons, linear accelerators and other types of atom smashers. Similarly, our understanding of the complex structure of the cell became possible only with the invention and development of electron microscopes and a variety of physical and chemical micromethods. Our understanding of the structure and organization of living things has increased by quantum jumps in recent decades, but much remains to be done to achieve an equivalent understanding of the nature of changes in living systems and the factors controlling these changes.

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