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The Place that Ultrastructural Studies in Biology and Medicine

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ABSTRACT

As we delve deeper and deeper into the study of the functions of biological systems, we end up at the level of electronic interactions, and it is possible that eventually all biological phenomena will be considered in this respect. To ensure biological differentiation, biological systems have taken the path of constructing certain macromolecules, which themselves are capable of variability in many parameters, and also the path of organising small molecules and ions, implying their interaction either among themselves or with these macromolecules. It is at the level of these molecular structures that the most fruitful studies of the main types of biological activity are now being carried out.

Keywords: Ultrastructural Studies; Biological Systems; Macromolecules

Introduction

As we delve deeper and deeper into the study of the functions of biological systems, we end up at the level of electronic interactions, and it is possible that eventually all biological phenomena will be considered in this respect [1-7]. To ensure biological differentiation, biological systems have taken the path of constructing certain macromolecules, which themselves are capable of variability in many parameters, and also the path of organising small molecules and ions, implying their interaction either among themselves or with these macromolecules [8]. It is at the level of these molecular structures that the most fruitful studies of the main types of biological activity are now being carried out. Biological phenomena can be viewed as the spatial and temporal distribution of different types of activity; the study of biological ultrastructure aims to establish which spatial structures are compatible with these activities [1]. Attempts have often been made to find a single basic recurrent spatial structure that is compatible with all bio-logical phenomena; however, all the structures proposed so far have only limited application. There is some periodicity of structure, in particular the phenomenon of regular repetition of the subunits from which the macromolecule is built, but at the same time we are confronted with an apparent disorderedness in both sequence and configuration, and this disorderedness completely destroys all attempts to declare this or that orderliness of structure as a fundamental property of life [1,4]. If such a fundamental property exists, we have not yet been able to identify it, but the reason for this may simply be that our knowledge of biological phenomena is not sufficiently detailed or has not yet penetrated to a level where this single principle underlying all phenomena can be identified.

At present it seems more expedient to study individual systems and their organisation, but it must always be borne in mind that, having established the organisation of a given system, we may find that it has a wider significance and is to some extent peculiar to other systems, the study of which is more difficult.Life at the molecular level is now understood to depend entirely on the behaviour of macromolecules, and even the most primitive organisms now existing are highly complex molecular complexes. However, the form in which life first

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emerged was probably much more primitive than any of the current manifestations of life. The problem of the origin of life is the subject of much research and debate, but, although there is some agreement on the possible ways of formation of simple organic compounds, the question of the origin of macromolecules and life itself is still largely at the level of arbitrary assumptions. From methane, ammonia and water can be obtained a number of organic molecules of biological importance, if in the presence of reducing agents to pass through them an electric discharge. Further interactions between the thus obtained relatively simple products, which are in gaseous form, in aqueous solution or adsorbed state, can lead to the formation of more complex molecules, but to reproduce in the laboratory processes that would allow in the absence of enzyme systems to obtain even more complex biological macromolecules, we do not yet know how.

We do not even know yet what level of molecular complexity is required for the emergence of life in its simplest form; it may be that some primitive forms of life existed before the emergence of macromolecules in their present form and even contributed to the evolution of the latter. This process could have lasted for an inconceivably long time, and it is possible that during this process there were successive changes in the environment which will never be repeated again and which cannot be repeated even under experimental conditions. At the same time, it is possible that some elements of this process still take place today, but the very existence of life has changed the environment so much that the fate of certain intermediate products has completely changed. This also applies to life itself: the existence of the original primitive forms of life may now be completely impossible because of the changed environment [9]. We are even farther from the experimental reproduction of the further step/- the transition from complex molecules to cellular organisms. Apparently, at a certain stage in the evolution of biological systems, the phenomena occurring in colloidal solutions and, in particular, the formation of coacervates played an important role' these phenomena could serve as a basis for the process of compartmentalisation, which resulted in the possibility of a local increase in the concentration of some molecules, but the details of these processes can again be considered only at the level of general reasoning.

The questions of what should now be considered the simplest form of life and what factors led to the development of the more complex forms that now dominate nature are also more a matter of debate and hypothesis than of rigorous scientific reporting. The simplest nucleoprotein viral particle could be considered alive in the sense that it contains all the regulatory factors necessary for its self-reproduction in a suitable environment, and that no other agent is able to ensure the construction of viral particles in the same or any other environment [10,11]. However, a suitable medium for the reproduction of a viral particle is the cellular organism, which is much more complex than the viral particle itself. The simplest form of cellular life may have been a sort of sac of macromolecular compounds, protected from the influence of the environment, but capable of receiving raw materials from it and of depositing metabolic wastes into it. This need for access to the external environment, which persisted despite the growth of the cellular organism, may have been the stimulus for both cell division and differentiation, leading to the development of specialised digestive and excretory systems.

As functions become increasingly complex, there is a need for even more specialised molecular structures, more complex metabolic processes and much more extensive regulatory systems [11,12]. In medicine we seek to understand, adjust and repair quite complex systems, but much of what we now know was originally established through the study of relatively simply organised living things.Our knowledge of how complex macromolecules are synthesised from relatively simple precursors in living systems is now continuously expanding [13-15]. The sites of synthesis, the nature of the precursor molecules, the basic steps of molecular transformations, the enzymes and substrates required - all this is now largely elucidated, although many details of the mechanisms involved remain unknown. We already know the basic role of each type of macromolecule [8-9,14]. We know that the main source of information in living systems are nucleic acids and that the chromosomes of each cell of a given organism, apparently, contain all the information necessary for the development of the whole organism, although each cell itself can use only a small fraction of this information [6,9,12,16,17]. The information contained in the chromosome structure can probably be blocked directly by proteins. Apparently, proteins are also involved in each step of the utilisation of "free" information, but the details of the mechanisms controlling the release and utilisation of information are still unknown [10].

Some regulation is undoubtedly exerted by the environment, as has been shown, for example, in tissue culture and embryo tissue transplantation experiments. Transplanted tissue may begin to develop along a new path according to the site to which it is transplanted, and in cells grown in culture it is possible to induce strong changes by altering the conditions in the artificial medium. Such changes in the character of growth, however, are not unlimited. Thus epithelial tissue transplanted to an unusual site or transferred to an artificial medium retains to a large extent its characteristic features. Other external conditions, such as the composition of the nutrient medium, may also influence the realisation of individual genetic potencies, but the very potencies to develop along any of the paths that a given organism may take are inherent in its genetic material. Turning to a narrower field, it should be noted that we have now fully appreciated the importance of the exact conformation of protein molecules, which determines the infinite variety of enzymatic activities and immunological reactions [3,5,18].

The important role of the spatial distribution of enzymes and the nature of all substrates and environmental factors in the regulation of metabolic processes is also unquestionable, although we cannot yet describe it in detail [6,17,19]. It is now established that in completely

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different organisms there are enzymes with almost identical structure, performing the same functions, but in some other organisms slightly modified molecules can be used for the same purpose [9,20]. In some cases, it is possible to establish the limits of changes compatible with the preservation of the activity of the molecule, which makes it possible to identify changes that are pathological in nature. These pathological changes in structure may be congenital, i.e. due to the fact that the instructions necessary for the construction of a given molecule were originally incorrectly recorded in the chromosome of a given organism; however, genetic instructions may also be altered by external factors, such as radiation [39]. The nature of the consequences of such disturbances can be quite varied. In the most severe cases, sometimes even with relatively small genetic changes, the development of the organism completely ceases or, at the same time, the development of the organism is affected. In the most severe cases, sometimes even with relatively small genetic changes, the development of the organism ceases altogether or the organism becomes severely dysfunctional; an example is sickle-cell anemia, in which a relatively small change in the sequence of amino acids in the polypeptide chain of hemoglobin so drastically alters the configuration of the molecule that the haem group completely loses its ability to bind oxygen.

In other blood diseases the effect of comparable molecular disturbances is reduced to a decrease in the efficiency of the corresponding function, so that the disturbance itself may remain undetected and manifest itself only under unfavourable conditions. It may be thought that in a number of cases molecular disturbances do not directly affect the fulfilment of function, but merely make the process sensitive to the action of other factors, usual or unusual for the environment in which the organism lives. It has been suggested that this situation may be observed in some forms of cancer, in particular lung cancer, and the reaction of different people to unfavourable conditions (air pollution, cigarettes) may vary greatly [11]. Small changes in the structure of molecules may also underlie individual differences in response to a number of external factors, such as differences in sensitivity to the action of drugs. Thus, in seemingly completely similar organisms, numerous macromolecular systems may differ in detail, giving each organism a unique individuality.Such individuality is particularly evident in immunological responses, which again are based on relatively small differences in molecular configuration; it is possible that these same differences also account for some individual variability in responses to external influences. Environmental factors, such as pH, the nature of ions and their concentration, to some extent directly determine the molecular con- figurations and molecular interactions, thus regulating the course of metabolic processes.

Direct regulation is also carried out by hormones, which are secreted into the blood and lymph and stimulate or inhibit vital metabolic processes [5,20,21].In large organisms the co-ordination of all the regulatory systems is carried out by the nervous system. Sometimes it can be a simple reflex arc consisting of an excitable receptor (sensitive neuron) and an effector (motor neuron), ending, say, at a neuromuscular junction, which in response to excitation coming through the nerve terminal, causes muscle contraction [2].Considerable progress has been made in elucidating the molecular basis of most of the activities occurring in such a nervous circuit, but much more complex nervous systems, such as the mammalian brain, in addition to the unimaginable complexity of the same activities, also provide for the analysis, storage and reproduction of information. The molecular basis of such high forms of nervous system activity has begun to attract serious attention, but the experimental data available in this field allow only very preliminary general assumption to be/ made [2].

Disturbances in the regulation and co-ordination of metabolic processes are undoubtedly of the most direct relevance to medical problems; particularly severe consequences are observed when nervous co-ordination is disturbed. Small biochemical disturbances and minor anomalies of molecular configuration can be amplified to such an extent as to lead to serious psychiatric disorders. Perhaps the problems of psychiatry and seem so confusing because we still know very little about the fundamental processes occurring in the brain [2,18,22]. It is because of such subtle disturbances [23-39] in biological systems that the study of the structure of molecules and the spatial localisation of biochemical processes can be of particular value to medicine.

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