ELEMENTS OF BIOPHYSICS

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biophysics

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Translated from the Russian
by Artavaz Beknazarov

Mir Publishers
Moscow

БИОФИЗИКА
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Издательство «Наука» Москва

First published 1983
Revised from the 1981 Russian edition

На английском языке

Preface to the English Edition

This book is intended for students and post-graduates—biologists and physicists—who study biophysics. The book has emerged from the lectures given by the author for many years at the Moscow Physico-Technical Institute and from two monographs published earlier. The first of these monographs, *Molecular Biophysics*, was published in Russian in 1975 and in English by Academic Press in 1977. The second, *General Biophysics*, was issued in Russian in 1978 and is being prepared for publication by Academic Press. A considerable part of the book has been written anew. At the same time, the above two monographs are recommended to the reader for a more thorough study of the subject. They are provided with extensive bibliography.

In my opinion, biophysics is not a subsidiary branch of biology but a legitimate part of the physical sciences. Biophysics is the physics of living things. Accordingly, an attempt has been made to divorce biophysics from physiology, though these fields overlap to a considerable extent. Though the book is devoted mainly to the theoretical problems of biophysics, it also deals with the most important experimental findings.

I am well aware of the difficulties associated with the writing of an encyclopedic course of biophysics by one author. Today, biophysics is a very vast, complicated and diversified branch of natural science and one cannot be, so to say, a jack-of-all-trades, a specialist equally well versed in all the problems dealt with in biophysics.

This unavoidably leads to deficiencies of exposition. The author will appreciate all critical remarks from the reader.

The author expresses his gratitude to Professors L. A. Blumenfeld and A. B. Rubin who read the manuscript and made valuable suggestions.

M. Volkenshtein
Moscow, March 1982

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Chapter 1 Goals and Methods of Biophysics

1.1. The Place of Biophysics in Natural Sciences

We shall adopt the definition of physics as a science dealing with the study of the structure and properties of concrete forms of matter—substances and fields, and of the forms of existence of matter—space and time. This definition does not imply any discrimination between living organisms and inanimate matter. It does not reduce the entire natural science to physics, but it indicates that the basic theoretical foundations of any branch of natural science are of a physical nature. Such foundations have already been discovered in chemistry and today we know that chemistry is concerned with the study of the structure of the electronic shells of atoms and molecules and of its change in the course of their interactions. Accordingly, theoretical chemistry is based at present on quantum and statistical mechanics, on thermodynamics and physical kinetics.

Biology is a science dealing with living organisms which are immeasurably more complicated than nonliving matter. Therefore, we have still to travel a long path before we can get a more penetrating insight into the deep-seated physical laws and principles governing biological phenomena.

Based on what has been said above, we define biophysics as the physics of life phenomena studied at all levels, from molecules and cells to the biosphere as a whole. Such a definition of biophysics contrasts with its being regarded as a subsidiary branch of biology and physiology. The content of biophysics is not necessarily associated with the application of physical instruments in a biological experiment. A clinical thermometer, an electrocardiograph, and a microscope are all physical instruments, but physicians and biologists who employ these devices are not at all concerned with biophysics.

A biophysical investigation commences with the physical formulation of a problem pertaining to living organisms. This means that such a problem is formulated on the basis of the general laws of physics and the atomic and molecular structure of substances.

Thereby, the ultimate goal of biophysics consists in substantiating theoretical biology. At the same time, biophysics is concerned with the solution of numerous theoretical and practical (applied) problems of a more specific nature.

The formulation of the biophysical task is possible so far only in a limited number of cases. Living systems are so complex that biological knowledge is mostly insufficient for physical approaches to be worked out. Biology, however, is progressing at a very rapid rate and the development of biophysics is inseparably tied up with the advancement of biology.

Biophysics is a science of the 20th century. This is not to say that biophysical problems had not been solved at all before. Maxwell enunciated his theory of colour vision, Helmholtz measured the velocity of propagation of the nervous impulse. Many other examples could be cited. However, only in our time has biophysics switched over from the study of the physical properties of living organisms and of their physical stimulation (light, sound, electricity) to the investigation of the fundamental problems—heredity and variability, ontogenesis and phylogenesis, metabolism and bioenergetics. This has been made possible only as a result of the vigorous development of biology and biochemistry.

The objectives of biophysics are analogous to those of biology. They consist in understanding and interpreting life phenomena. Being a part of physics, biophysics is inseparable from biology. The biophysicist must have both physical and biological knowledge. For the work in the field of biophysics to be successful, a general understanding of living matter is desirable, which can be achieved through the knowledge of the fundamentals of zoology and botany, physiology and ecology. Physicists often neglect the descriptive sections of biology. The knowledge of zoology and botany is fundamentally significant; without Linnaeus the Darwin theory of evolution could not have originated.

Despite serious difficulties, modern biophysics has made great advances in the explanation of a number of biological phenomena. We have learnt a lot about the structure and activity of biologically functional molecules, about the properties and mechanisms of the function of cellular structures, such as membranes, bioenergetic organelles, mechanochemical systems. Physico-mathematical models of biological processes are being successfully constructed, including those of ontogenesis and phylogenesis. General theoretical approaches to life phenomena have been worked out, which are based on thermodynamics, information theory, the theory of automatic control. All these topics will be examined in this book in varying degrees of detail. In accordance with the definition of biophysics as the physics of life phenomena, we shall resort to physical laws rather than to the physiological classification. For example, the reception of external stimuli by sense organs is considered in various sections of the book—vision in a chapter devoted to photobiological phenomena; the senses of hearing and touch in a chapter dealing with mechanochemical processes; the sense of smell is treated in connection with the physics of molecular recognition.

1.2. Physics and Biology

We may ask: Is contemporary physics sufficient for the solution of biological problems, for the substantiation of theoretical biology? Perhaps, biophysics will need a new, as yet non-existent physics? There occurred situations in the history of science, when the earlier developed theory reached its limits of applicability and it proved necessary to build up a fundamentally new set of concepts. It is exactly in this way that the theory of relativity and quantum mechanics emerged. The possibility is not excluded *a priori* that true biophysics must be built up on the basis of the yet unknown future physics, essentially different from modern physics.

We put aside the concept of *vitalism*, according to which biological phenomena are basically incomprehensible on the basis of physics and chemistry since there exists a certain mysterious "vital force", or entelechy, or a biological field, which are not amenable to a physical interpretation. The vital-force theory has nothing to do with science; it denies the unity of nature and, in the final run, leads to theology. Vitalistic conceptions are no longer existent today in modern science.

While discussing the possibilities of a physical interpretation of life phenomena, i.e., the impact of physics on the present-day and further development of biology, we should not forget about the influence of biology on physics. The law of conservation of energy, which is the first law of thermodynamics, was discovered by Mayer, Joule, and Helmholtz. As is known, Mayer's conceptions were based on observations of living organisms, human beings. It is less widely known that Helmholtz too used biological phenomena, being guided by a distinct antivitalistic conception. He wrote, "According to Stahl, the forces that are operating in a living body are in essence the physical and chemical forces of the organs and substances, but some living soul or life force inherent in the body is capable of binding or releasing their activity ... I have found that the Stahl theory ascribes to any living body the properties of a so-called *perpetuum mobile* (a perpetual-motion machine) ... Thus, I have run across the question of what relationships exist between the various natural forces if it is assumed that the *perpetuum mobile* is absolutely impossible...". Not only biophysics but physics too as a whole had to overcome the vital-force theory in the course of their development.

Let us consider the concepts of the interrelationship between physics and biology that have been worked out by the physicists of the twentieth century—Bohr and Schrödinger.

Bohr treated this problem on the basis of the *principle of complementarity*, a special case of which is the Heisenberg uncertainty principle. Bohr maintained that the biological laws proper are complementary to the laws obeyed by inanimate things. The physicochemical properties of a living organism and the life phenomena cannot be studied simultaneously—the cognition of one excludes that of the other. Life should be looked upon as the basic postulate of biology that does not lend itself to further analysis, just as the existence of a quantum of action forms the elementary basis of nuclear physics. Thus, Bohr believed that biological and physico-chemical investigations are complementary to each other, i.e., are incompatible, though not contradictory. This concept is not vitalistic since it denies the existence of a limit to the application of physics and chemistry for the solution of biological problems. Bohr wrote that *no single result of a biological investigation can be described* unambiguously unless the physical and chemical concepts are resorted to.

Bohr's view changed with the progress of modern biology. Later, he spoke of a complementarity between the physico-chemical considerations practically employed in biology and the concepts that are directly associated with the unity of the organism and go beyond the framework of physics and chemistry. The utilization of the concept of complementarity in biology was advocated by Bohr through reference not to the postulative nature of the life concept but to the extreme complexity of the organism as a whole system. In other words, not a fundamental but rather a practical, i.e., surmountable, complementarity is meant. This cannot be disputed.

In 1945 Schrödinger published a book called *What is Life?* which exerted a substantial impact on the development of biophysics and molecular biology. Several problems of fundamental significance are treated in detail in this book. The first of these is the thermodynamic foundations of life. At first glance there is a distinct contradiction between the evolution of an isolated physical system towards the state of maximum entropy, i.e., disorder (the second law of thermodynamics), and biological evolution which goes from the simple to the complex. Schrödinger stated that the living organism "feeds on negative entropy". This means that the organisms and the biosphere as a whole are not isolated but open systems which exchange both matter and energy with the outside world. The nonequilibrium state of an open system is maintained through the outflow of the entropy into the surroundings. The second problem is the general structural features of organisms. In Schrödinger's words, an organism is an *aperiodic crystal*, i.e., a highly ordered system, like a solid body, but devoid of the periodicity in the arrangement of cells, molecules, and atoms. This statement is valid for the structure of organisms, cells, and biological macromolecules (proteins, nucleic acids). As we shall see, the concept of the aperiodicity of a crystal is essential to the treatment of life phenomena on the basis of information theory. The third problem is the conformity of biological phenomena to the laws of quantum mechanics. While discussing the results of the radiobiological investigations carried out by Timofeev-Ressovsky, Delbrück, and others, Schrödinger pointed out the quantum nature of radiation mutagenesis. At the same time, the applications of quantum mechanics in biology are not trivial since living organisms are essentially macroscopic. Schrödinger posed the question: "Why are atoms small?" It is obvious that this question is meaningless if no point of reference is specified. They are small in comparison with our measures of length—the metre, the centimetre. But these measures are determined by the dimensions of the human body. Hence, Schrödinger says, the question should be reformulated: why are atoms much smaller than the organisms? In other words, why are the organisms built up of a large numbers of atoms? Indeed, the number of atoms in the smallest bacterial cell *Mycoplasma laidlawii* is of the order of 10^9. The answer to the question is that the orderliness necessary for life is possible only in a macroscopic system; otherwise, the order would be destroyed by fluctuations. And, finally, Schrödinger posed the question of the stability of the substance of genes, which is made up of the light atoms, C, H, N, O, and P, during the lifetime of numerous generations. The answer to this question was later provided by molecular biology which established the double-helical structure of deoxyribonucleic acid (DNA).

We shall not dwell on the works of some physicists who maintained that biological phenomena do not conform to the laws of physics (Elsasser, Wigner, and others). The erroneousness of these works was disclosed in scientific literature.

There is every ground today to assert that modern physics is not approaching its limits of applicability for the treatment of biological phenomena. It is hardly probable that such limits will be reached in the future. On the contrary, the advancement of biophysics as a part of modern physics points to its unlimited possibilities. One has, of course, to introduce new physical conceptions but not new principles and laws.

1.3. Living and Inanimate Nature

Let us first define a living organism as an open, self-regulating, self-reproducing and developing heterogeneous system whose most important functional substances are biopolymers—proteins and nucleic acids. A living organism is a historical system in the sense that it is the result of the phylogenetic evolution and itself covers the path of ontogenetic development—from zygote to old age and death.

The conventional physics of inanimate matter has nothing to do with history. The electron, atom, and molecule are characterized by constant physical properties, irrespective of their origin. Of course, conventional physics deals with kinetic, dynamic processes. The individual past history of a physical body is not considered, however.

What has been said above does not mean that there are no historical problems in the physics of inanimate nature. The origin of living matter itself, its evolution, and the individual development of each species is a part of the development of the Universe as a whole, a part of the development of the solar system, a part of the development of the Earth. Hence, there is every reason to consider the similarity and differences between biophysics, on the one hand, and cosmology, astrophysics, and geophysics, on the other. This is instructive because these different branches of physics may enrich each other with unified approaches to the solution of historical problems.

According to modern concepts, the history of the Universe begins with a small cluster of high-density plasma. About 2×10^{10} years ago this plasma cluster began to expand explosively, electrons and nuclons emerging from photons and neutrinos; as the Universe cooled, light and then heavy atoms were formed. Evidently, the expansion of Universe is a continuous and irreversible process. The forces of gravity made possible the formation of stars and galaxies. On high gravitational compression the temperature of a star rises up to the moment when there occur thermonuclear processes. These processes are responsible for the evolution of stars, for catastrophic events (so-called cataclysms of nature), such as the appearance of supernovae. The Sun is a star which is in a certain stage of evolution; the formation of the planets is one of the consequences of the development of the sun. According to present-day findings, the Earth exists for about 4.5×10^9 years and the life on the Earth for about 3.5×10^9 years.

Cosmology and astrophysics are based on the theory of relativity and quantum (nuclear) physics, on thermodynamics and statistical mechanics. The evolution of stars is not linked up with their "struggle for existence", i.e., with their interactions with the environment and with competing interrelationships. This is a non-Darwinian evolution. Accordingly, it might seem that there is nothing common between biophysics and astrophysics.

There are, however, two points of similarity. First, the evolution of both the Universe and the biosphere involves an irreversible and continuous *generation of new information*. New information appears as a result of the memorizing of an accidental choice. Second, the irreversible development in both cases does mean the presence of *instabilities*. A new stage in the evolution of a star, a planet, the biosphere, biogeocenosis, a biological species or population arises as