MEDICAL UNIVERSITY – PLEVEN
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LECTURE No1

Nature and Subjects of Biophysics

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I. The subject of Biophysics

The subjects of biophysics are the physical principles underlying all processes of living systems. This also includes the explanation of interactions of various physical influences on physiological functions, which is a special subarea, called environmental biophysics.

Biophysics is an interdisciplinary science somewhere between biology and physics, as may be concluded from its name, and is furthermore connected with other disciplines, such as mathematics, physical chemistry, and biochemistry.

The term "biophysics" was first used in 1892 by Karl Pearson in his book *The Grammar of Science.*

What type of science is biophysics ?

Biology, by definition, claims to be a comprehensive science relating to all functions of living systems.

Hence, biophysics, like genetics, biochemistry, physiology etc., should be considered as a specialized subarea of biology.

This view has not remained undisputed by physicists, since physics is not confined to subjects of inanimate matter. Biophysics can be considered, with equal justification, as a specialized part of physics.

It would be futile to try to balance those aspects against each other. Both of them are justified. Biophysics cannot flourish unless cooperation is ensured between professionals from either side.

Biophysics is by no means some sort of a melting pot for various physical methods and their applications to biological problems.

The use of a magnifying glass has just as little to do with biophysics as the use of most up-to-date optical or electronic measuring instruments. Biophysical research, of course, requires modern methods, just as other fields of science do.

The nature of biophysics is actually defined by the scientific problems and approaches rather than by the applied methods.

British biophysicist Hill described the modern biophysicist in these terms: “Biological phenomena, like many others, show aspects and relations susceptible of physical analysis and interpretation. Biophysicists are people whom physical intuitions come naturally, who can state a problem in physical terms, who can recognize physical relations when they turn up, who can express results in physical terms. These intellectual quantities, more than any special facility with physical instruments and methods, are essential to the make-up of a biophysicist. Equally essential, however, are the corresponding qualities, intuitions, and experience of the biologist. A physicist who cannot develop the biological approach, who has no curiosity about vital processes and functions, who is not willing to spend time in learning the habits of living things, who regards biology simply as a branch of physics has no important future in biophysics”.

II. Historical background

In terms of science history, biophysical thought can be traced back to early phases of philosophical speculations on nature, that is back to antiquity.

This applies to the earliest mechanistic theories of processes of life and to insights into their dynamics (e.g. Heraclitus in the 5^{th} century B.C).

The promotion of scientific research in the Renaissance also includes biophysical considerations. Leonardo da Vinci (1452-1519), for example, investigated mechanical principles of bird flight in order to use the information for engineering design; research which would be termed bionics today.

A comprehensive biomechanical description of functions, such as mobility of limbs, bird's flight, swimming movement, etc., was given in a book by Alfonso Borelli (1608-1679) *De motu animalium* published in 1680. He founded a school in Pisa of *iatro-mathematics* and *iatro-physics* in which the human body was perceived as a mechanical machine, and where attempts were made to draw medical conclusions from that perception (Iatric - Greek term for medical art).

Iatro-physics has often been considered as a mechanistic forerunner of MEDICAL BIOPHYSICS.

Parallels to processes of life were established not only in the area of tempestuous progress of mechanics but at all levels throughout the development of physics.

The physics of electricity was studied in direct relationship with phenomena of electrophysiology - frog experiments undertaken by Luigi Galvani (1737-1798) .

Medical observations played a role in the discovery of the first law of thermodynamics by J. R. Mayer (1814-1878). Calorimetric studies of heat generation of mammals were conducted in Paris by A. L. Lavoisier (1743-1794) and P. S. de Laplace (1749-1827) as early as about 1780.

Reference should also be made to investigations of Thomas Young (1773-1829), and later Hermann v. Helmholtz (1821-1894) on the optical aspects of the human eye and on the theory of hearing.

These activities added momentum to the development of physiology which thus became the first biological platform for biophysics.

There have been many instances in which biologically induced problems had stimulating effects upon progress in physics and physical chemistry.

Brown's motion, discovered in pollen grains and subsequently calculated by A. Einstein, is an example.

Research on osmotic processes were largely stimulated by the botanist W. Pfeffer.

The T dependence of rate constants of chemical reactions was initially formulated in terms of phenomenology by S. Arrhenius (1859-1927), and has, ever since, been applied to a great number of functions of life, including phenomena as sophisticated as processes of growth.

Studies of physiochemical foundations of cellular processes have continued to be important in biophysical research, especially after the introduction of the principles of non-equilibrium thermodynamics. Biological membranes, as highly organized anisotropic structures, are always attractive subjects for biophysical investigations.

This brief view of the history and the development of biophysics allows us now to draw the following conclusions about its nature and relevance: biophysics seems to be quite a new branch of interdisciplinary science, but, in fact, biophysical questions have always been asked in the history of science.

Biophysics relates to all levels of biological organization, from molecular processes to ecological phenomena. Hence, all the other biological subareas are penetrated by biophysics, including biochemistry, physiology, cytology, morphology, genetics and ecology.

A decisive impetus has been given to biophysical research through the discovery of X-rays and their application to medicine.

It was attributable to close cooperation between physicists, biologists, and medical scientists which paved the way for the emergence of radiation biophysics which also made substantive contributions to the growth of modern molecular biology.

The year 1948 saw the publication of Norbert Wiener's book *Cybernetics* dealing with control and communications in men and machines.

While regulation and control of biological systems had been subjects of research before, biocybernetics has given further important inspiration to Biophysics.

In the 1970s, biological system theory moved very close to thermodynamics. It should be mentioned that the expansion of classical thermodynamics to cover non-equilibrium systems with non-linear equations of motion was strongly stimulated by biological challenges.

The word "bionics" was coined by a synthesis of "biology" and "technics" at a conference in Dayton, USA, in 1960.

III. Areas of study

The main subdivisions of biophysics, according to the International Union for Pure and Applied Biophysics, are as follows:

1. *Molecular biophysics*: it is closely related to molecular biology. It studies the structure and physicochemical properties of biological molecules. The aim is to establish the physical mechanisms responsible for the biological functionality of molecules.

2. *Cellular biophysics* studies cellular structures and bioenergetics. It aims to examine the physical properties of biological membranes (permeability, resting potential generation, nervous impulse propagation, muscle contraction, photobiological processes - photosynthesis, bioluminescence, vision).

3. Biophysics of complex systems – also known as theoretical biophysics. It studies the general physicobiological problems and physicomathematical modeling of biological processes:

- theory of dissipative non-linear dynamic systems (thermodynamics of irreversible processes)

- theory of bioenergetic phenomena

- modeling processes of biological development: evolution, ontogenesis, carcinogenesis, immunity

4. Environmental biophysics - effect of physical factors on biological systems

Molecular Structure of Biological Systems

Quantum-mechanical approaches allow us to explain molecular bonds and processes of energy transfer in biological systems.

Two kinds of physical behavior meet at the molecular level of biological structures:

1. *Microphysical -* based on the individual behavior of single small particles like atoms, molecules or supramolecular structures. These processes are mostly stochastic;

2. *Macrophysical -* the kind of behavior of "large" bodies. The "macrophysics" is ruled by the laws of classical physics. Our daily experiences with macrophysical systems teach us that their behavior is generally deterministic.

Let us consider a simple mechanical wheelwork. The knowledge of its design and construction allows a precise prediction of the behavior of the system. This prediction is based on the laws of classical mechanics.

In contrast to this, a chemical reaction with a small number of molecules in a homogeneous phase depends on stochastic collisions of the individual molecules with each other. Since this process is stochastic, it is only predictable in a statistical way.

This stochastic behavior of molecular systems can be transformed into a deterministic one, if the number of participating stochastic events is large, or if the degrees of freedom of the single reactions are extremely limited.

The increase of stochastic events can be realized by

- an increasing number of participating molecules,
- enlarging the volume, where the reaction takes place,
- an increase of the time interval of observation.

The limitation of the degree of freedom of a biochemical reaction is realized by a property of the system which is called *anisotropy*. In contrast to isotropic systems, like simple solutions, in anisotropic systems the mobility of molecules in various directions is not identical, but is restricted in some directions, and promoted in others.

E.g. enzymatic reactions, where the participating enzymes are orientated in membranes or the reactions of charged or polar reactants in strong electric fields of electrical double layers.

In many fields the biological organism works as an amplifier of the microphysical stochastics. A molecular mutation, for examples, leads to a reaction chain, which finally ends with a phenomenological alteration of the organism. Or, as another example: a few molecular events in the pigments of optical receptors can lead to perception and to reaction in behavior.

The visible "biological structure", as known in the fields of anatomy, morphology and histology, now appears as concentration profiles or as systems of electric charges or electromagnetic fields. Instead of visible and measurable lengths, diameters or distances, as common in the visible world, in the microphysical world so-called ***effective parameters*** are used.

The ***effective parameters*** are exactly defined and can be measured with arbitrary exactness, but they do not correspond to some visible boundaries.

A single ion, for example, has no diameter in the sense of the diameter of a cell, or a cell nucleus, which can be measured by a microscopic scale but a define effective parameter like hydration radius and Debye-Huckel radius, which really are important parameters for functional explanations.

- **Intramolecular Bonds**
- Any representation of the dynamics of molecular and supramolecular structures has to begin with the atom, its organization and energy states and with interactions between atoms in a molecule. The molecule is initially assumed to be thermally unaffected. The thermal energy of movement will be introduced as an additional parameter later.

- ***Covalent bond***

- The most important chemical bond is the covalent bond. It can only occur if two mutually approaching atoms have unpaired electrons in their valence shells. This means that both relevant orbits are each occupied by one electron only, thus leaving space for another electron. In this case the Pauli exclusion principle is not violated. Figuratively speaking, an electron pair with anti-parallel spin quantum numbers is formed, being common to both atoms and forming a type of molecular orbital.

- Molecular orbitals may sometimes result in a considerable charge displacement within the molecule. Simply, this can be illustrated by considering that the electron pairs common to two atoms in a covalent bond are distributed asymmetrically. In other words, the molecular orbital of the bond is shifted toward one of the two covalently bonded atoms. The atom with the greater probability of the presence of the electron pair is more strongly "electronegative" than the other one.

- In this respect, a series of atoms with an increasing degree of *electronegativity* can be constructed. In the periodic system of elements this series is directed toward increasing atomic numbers within the periods as well as within the groups. Hence, the following relation applies:

H < C < N < O < F, and J < Br < Cl < F.

In this way, the displacement of bonding angles within a water molecule can be explained. Because of the strong electronegativity of the oxygen atom in relation to the hydrogen atom, a dipole O—H results and, consequently, the two hydrogen atoms will repel each other. This polarization effect contributes directly to the bonding energy. About 22% of the bonding energy in a C—O bond, and 39% in a H—O bond are attributable to this effect.

Ionic Bonds

If the polarization effect of covalent bonds is pushed to the extreme, it is no longer possible to refer to a molecular orbit, nor to bonding electrons. There occurs a total transmission of an electron from the valency orbital of one atom to that of the other.

This causes a full separation of charges - ions are generated, which attract each other electrostatically. With the loss of the molecular orbitals there also occurs a loss of the molecular identity. Strictly speaking, it makes no sense to use the term NaCl-molecule. In solutions, the molecular character of this salt is just expressed by the stoichiometric relation of the number of anions and cations.

A crystal of NaCl, on the other hand, can be considered as a super molecule, because in this case the ions are arranged in an electrostatic lattice. The ionic bond, in contrast to the covalent bond, can be considered simply from an electrostatic point of view *(Coulomb's law).*

It defines the force F with which two point charges q_1 and q_2 repel each other at a distance x in a vacuum (k = 8.854 10^{12} C V^{-1} m^{-1}). The equation also makes it possible to calculate the bonding force, as the negative value of the force (—F) which is required to separate two ions. This force, however, is not measurable directly. It is better therefore to transform this equation in such a way that it can provide information on the bonding energy or, which is the same, on the energy of ionization.

The *bonding energy* is equivalent to the work which is necessary to move a given ion from its bonding place up to an infinite distance from the counter ion. A work differential *(dW),* which has a very small, but finite value, can be calculated from the product of force (F) and a corresponding distance.