

FEATURES OF BIOPHYSICS IN BIOLOGICAL SYSTEMS.

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Resume

Biophysics is the field that applies the theories and methods of physics to understand how biological systems work. Biophysics has been critical to understanding the mechanics of how the molecules of life are made, how different parts of a cell move and function, and how complex systems in our bodies—the brain, circulation, immune system, and others— work. Biophysics is a vibrant scientific field where scientists from many fields including math, chemistry, physics, engineering, pharmacology, and materials sciences, use their skills to explore and develop new tools for understanding how biology—all life—works.

Keywords: biophysics, biological system, analysis, neuroscience, biomechanics.

ОСОБЕННОСТИ БИОФИЗИКИ В БИОЛОГИЧЕСКИХ СИСТЕМАХ.

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Резюме. Биофизика — это область, которая применяет теории и методы физики для понимания того, как работают биологические системы. Биофизика сыграла решающую роль в понимании механики создания молекул жизни, того, как движутся и функционируют различные части клетки, а также того, как работают сложные системы нашего тела — мозг, кровообращение, иммунная система и другие. Биофизика — это динамичная научная область, в которой ученые из многих областей, включая математику, химию, физику, инженерное дело, фармакологию и материаловедение, используют свои навыки для изучения и разработки новых инструментов для понимания того, как работает биология — вся жизнь.



Ключевые слова: биофизика, биологическая система, анализ, нейронаука, биомеханика.

Biophysics is that branch of knowledge that applies the principles of physics and chemistry and the methods of mathematical analysis and computer modeling to biological systems, with the ultimate goal of understanding at a fundamental level the structure, dynamics, interactions, and ultimately the function of biological systems. Biophysics seeks to explain biological function in terms of the physical properties of specific molecules. The size of these molecules varies from small fatty acids and sugars (~1 nm = 10⁻⁹ m), to macromolecules like proteins (5–10 nm), starches (>1000 nm), and the enormously elongated DNA molecules (over 10,000,000 nm = 1 cm long but only 20 nm wide). These building blocks of living organisms, assemble into cells, tissues, and whole organisms by forming complex individual structures with dimensions of 10, 100, 1000, 10,000 nm and larger. Thus, proteins assemble into the casein micelles of milk, which aggregate to form the curd of cheese; proteins and ribonucleic acids assemble into ribosomes, the machinery for building proteins; lipids and proteins assemble into cell membranes, the external barriers and internal surfaces of cells; and proteins and DNA wind up into chromosomes, the carriers of the genetic code.

Much effort in biophysics is directed to determining the structure and dynamics of specific biological molecules and of the larger architecture into which they assemble. Some of this effort involves inventing new methods and building new instruments for viewing these dynamic structures in action. In addition, biophysicists are increasingly concerned with the mechanical properties of biological systems, on length scales from nanometers to meters.

Biophysics is relevant to medicine, and many biophysicists direct their investigations towards biomolecules that play a key role in disease. At Michigan, examples include Alzheimer's disease, ALS ("Lou Gehrig's disease"), HIV, diabetes, breast cancer, and multiple sclerosis. Consequently, although the central focus of Biophysics is on basic science rather than medical applications, many of our biophysicists have close interactions with medical school faculty, and many hold appointments in the medical school.

The biological questions of interest to biophysics are as diverse as the organisms of biology:

- How do linear polymers of only 20 different amino acids fold into proteins with precise three-dimensional structures and specific biological functions?



- How does a single, enormously long DNA molecule untwist and exactly replicate itself during cell division?
- How does RNA fold into complex 3-D structures and carry out highly sophisticated transactions when it is composed of four chemically-similar nucleotides?
- How are sound waves, or photons, or odors, or flavors, or touches, detected by a sensory organ and converted into electrical impulses that provide the brain with information about the external world?
- How does a muscle cell convert the chemical energy of ATP hydrolysis into mechanical force and movement?
- How does the cell membrane, a lipid barrier impermeable to water-soluble molecules, selectively transport such molecules through its non-polar interior?

Biophysics seeks to answer these questions using a highly interdisciplinary approach that combines chemical and biochemical analysis for identifying molecules and spectroscopic techniques and computational methods to examine relationships between their physical properties and biological function. In so doing, Biophysics explains biological functions in terms of molecular mechanisms: precise physical descriptions of how individual molecules work together like tiny “nanomachines” to produce specific biological functions.

Physical scientists use mathematics to explain what happens in nature. Life scientists want to understand how biological systems work. These systems include molecules, cells, organisms, and ecosystems that are very complex. Biological research in the 21st century involves experiments that produce huge amounts of data. How can biologists even begin to understand this data or predict how these systems might work?

This is where biophysicists come in. Biophysicists are uniquely trained in the quantitative sciences of physics, math, and chemistry and they are able tackle a wide array of topics, ranging from how nerve cells communicate, to how plant cells capture light and transform it into energy, to how changes in the DNA of healthy cells can trigger their transformation into cancer cells, to so many other biological problems.

Biophysicists work to develop methods to overcome disease, eradicate global hunger, produce renewable energy sources, design cutting-edge technologies, and solve countless scientific mysteries. In short, biophysicists are at the forefront of solving age-old human problems as well as problems of the future.



Data Analysis and Structure

The structure of DNA was solved in 1953 using biophysics, and this discovery was critical to showing how DNA is like a blueprint for life.

Now we can read the sequences of DNA from thousands of humans and all varieties of living organisms. Biophysical techniques are also essential to the analysis of these vast quantities of data.

Computer Modelling

Biophysicists develop and use computer modeling methods to see and manipulate the shapes and structures of proteins, viruses, and other complex molecules, crucial information needed to develop new drug targets, or understand how proteins mutate and cause tumors to grow.

Molecules in Motion

Biophysicists study how hormones move around the cell, and how cells communicate with each other. Using fluorescent tags, biophysicists have been able to make cells glow like a firefly under a microscope and learn about the cell's sophisticated internal transit system.

Neuroscience

Biophysicists are building computer models called neural networks to model how the brain and nervous system work, leading to new understandings of how visual and auditory information is processed.

Bioengineering, Nanotechnologies, Biomaterials

Biophysics has also been critical to understanding biomechanics and applying this information to the design of better prosthetic limbs, and better nanomaterials for drug delivery.

Imaging

Biophysicists have developed sophisticated diagnostic imaging techniques including MRIs, CT scans, and PET scans. Biophysics continues to be essential to the development of even safer, faster, and more precise technology to improve medical imaging and teach us more about the body's inner workings.

Medical Applications

Biophysics has been essential to the development of many life-saving treatments and devices including kidney dialysis, radiation therapy, cardiac defibrillators, pacemakers, and artificial heart valves.

Ecosystems

Environmental biophysics measures and models all aspects of the environment from the stratosphere to deep ocean vents. Environmental biophysicists research the



diverse microbial communities that inhabit every niche of this planet, they track pollutants across the atmosphere, and are finding ways to turn algae into biofuels. Biophysicists are teachers and researchers in biology, physics, engineering, and many other fields. They work in universities, hospitals, tech startups, and engineering companies developing new diagnostic tests, drug delivery systems, or potential biofuels. Biophysicists develop computer models to find out why a new flu strain eludes the immune system or they make 3D models of new protein structures to better understand how they work. They practice law in specialized fields like intellectual property, write about science for print and online publications, and work in government to advise legislatures. Those who are trained in biophysics have unlimited career possibilities.

Mainstream biophysics has traditionally focused on biological systems as *single entities*, such as a macromolecule, a membrane, a cell, or a tissue. The objective is typically to study physical properties of the system, such as force-extension curves of macromolecules or elastic properties of cells, or to use physical approaches to obtain information about biologically relevant properties, such as the structure of macromolecular complexes. This single-entity view of biophysics that has proved to be so prolific, however, cannot capture the origins of *emergent behavior*. Systems biophysics, in contrast, emphasizes the focus on how the system properties emerge from the relations between constituent elements. These types of approaches are needed, for instance, to study how mutations affect the molecular properties of the cellular components; how the mutated components affect different signaling pathways; and how these modified pathways confer cell-growth advantages during tumor progression and metastasis.

Systems biophysics is not a new field. The study of emergent behavior in terms of the properties of the components has led to historical breakthroughs. A most notable example is the work of A. L. HODGKIN and A. F. HUXLEY on the ionic mechanisms underlying the initiation and propagation of action potentials in the squid giant axon, for which they were awarded the **Nobel Prize in Physiology or Medicine in 1963**. After a series of experiments, HODGKIN and HUXLEY developed a circuit model that was able to capture how the squid axon carried an action potential in terms of the electrical properties of the cell membrane, voltage-gated conductivities for different ions, and electrochemical gradients. This model has been exceptionally successful, not just in describing but also in predicting a large number of neuronal properties, to the extent that modern investigations have confirmed many aspects of the model that were assumptions at the time.



Conclusion

Linus Pauling noted that “life is a relationship among molecules and not a property of any molecule”. The ultimate goal of systems biophysics is precisely to work out those relationships. New tools, and especially new frameworks and conceptual developments, are still needed to accurately determine the cellular behavior in terms of the physical properties of the molecular interactions. Even relatively simple systems, like the lac operon, have proved to be substantially more complex than originally speculated. Major challenges are still present on how to integrate thermodynamic and structural information with massive data in order to obtain at least information at the mesoscopic level. New approaches have to be able to describe the complex assembly dynamics of the multiple cellular components that carry out the cellular function over scales ranging from milliseconds to hours and days and they need to account for processes as diverse as protein-protein interaction, binding to DNA, transcription, translation, degradation and macromolecular assembly of signaling complexes at membranes and scaffolds.

Achieving this goal, at least partially, has important implications, as it is a prerequisite for the rational identification of therapeutic molecular targets and eventually for bridging prediction of clinical outcomes with molecular properties.

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