Preface

Over the past two decades, there has been a growing dialog between biologists and an ever-increasing number of physicists, mathematicians, and engineers. The reason for this mutual interest attraction is obviously the modern biology's pre-eminent role on the front lines of scientific research.

The connection between the physical and biomedical sciences has been developing rapidly over the past few decades, especially since the groundbreaking discoveries in molecular genetics. There is clearly a need for a continuing dialog and a cross-fertilization between life sciences and physical sciences. As a result of the naturally interdisciplinary nature of the life sciences numerous new border areas are being created and developed. Therefore, disciplines such as: mathematical biology, biophysics, computational biology, bio-statistics, biological physics, theoretical biology, biological chemistry (and of course bio-chemistry), and biomedical engineering have been undergoing exponential growth.

Diversity present in biological systems is a simple result of the multitude of possible combinations of the finite number of structural elements. The functioning of biological systems should also follow from this complexity with specific organization of complex molecular systems providing specific functions while they continue to be governed by fundamental physical laws. The principle of complexity begetting function is familiar to physicists and has often been referred to as an emergent phenomenon. It is a characteristic feature of atomic systems to display new emergent properties as they become more complex. This property is at the core of the instability of living organisms which acquire new functional features as their structural complexity grows with size from single-cell organisms to multi-cellular organisms.

This hierarchical, interconnected, but a coherently operating system of systems that sustains life poses a great scientific challenge not only to understand how its pieces work but also how the whole is organized internally to achieve specific functional advantages. Our quest to understand biology using physical laws and engineering principles is greatly aided by the rapid development of sophisticated experimental techniques that physics and technology has supplied for the use by biologists. Some of the most prominent examples are listed below:

- Light microscope (resolution: 400–600 nm) with various modern upgrades such as confocal, phase contrast, or cryomicroscopy.
- Electron microscope (10–100 nm)
- Neutron scattering (1–10 Å)
- X-ray crystallography (1 Å)
- Patch clamp electrophysiology
- STM, AFM, TEM
- NMR, MRI, fMRI
- Fluorescence spectroscopy
- Microwave absorption
- Laser light scattering
- Synchrotron radiation scattering
- Laser tweezers, etc.

Many other techniques that originated in physical laboratories have made their way to become standard equipment used by molecular biologists and chemists. From their original inventions as probes of physical phenomena these experimental techniques are then frequently adapted to molecular biology and eventually some of them are further transformed into diagnostic and therapeutic tools in modern medicine. X-ray machines are used for the detection of abnormalities, NMR, now called magnetic resonance imaging (MRI) by medical practitioners helps in the detection of tumor growth, which in turn can be treated by radiation from radioactive sources. Electrical manifestations of the activity of the heart are monitored by the cardiologist, who uses electrocardiography (ECG) and, likewise, brain activity is studied through the use of electroencephalography (EEG). Ultrasound has found applications in both diagnostics (e.g., fetal development) and therapeutics (gall and kidney stone shattering).

These techniques have allowed biologists to gain spectacular insights into the inner workings of cells, tissues and organisms. In addition, new physical concepts developed principally by nonlinear physicists are being used as an appropriate theoretical framework within which living systems can be better understood. These concepts involve hallmarks of biological structures such as: nonlinearity, self-organization, self-similarity, cooperativity, and collective behavior (synergy) as well as emergence and complexity mentioned above.

Attempts at applying physical laws to living systems can be traced to the early creators of modern science. Galileo analyzed the structure of animal bones using physical principles, Newton applied his optics to color perception, Volta and Cavendish studied animal electricity, and Lavoisier demonstrated that the process of respiration is a physiological example of an oxidative chemical reaction. Robert Mayer was inspired by physiological studies to formulate the first law of thermodynamics. A particularly fruitful area of application of physics to physiology is hydrodynamics where, for example, blood flow was analyzed by Poiseuille using fluid dynamics principles and air flow in the lungs has been described consistently with the laws of aerodynamics. An important figure in the history of biophysics is that of the German physicist and physiologist Hermann von Helmholtz who laid the foundations for the fundamental theories of vision and hearing. The list of physicists who made a large impact on biology and physiology is very long, so we only name a few of the most well-known figures who have crossed this now rapidly thinning boundary between physics and biology. Delbrück, Kendrew, von Bekesy, Crick, Meselson, Hartline, Gamow, Schrödinger, Hodgkin, Huxley, Fröhlich, Davydov, Cooper and Szent-György (1972) have undoubtedly pushed the frontier of the life sciences in the direction of exact quantitative analysis. Of particular importance to membrane biophysics is the patch-clamp technique which is a refinement of the voltage clamp. E. Neher and B. Sakmann developed the patch clamp in the late 1970s and early 1980s and received the Nobel Prize in Physiology or Medicine in 1991 for this work. This discovery made it possible to record the currents of single ion channels for the first time, proving their involvement in fundamental cell processes such as action potential conduction in nerve cell's axons.

While increasingly present in many areas of physiology, biology, and medical research physics is helpful in providing deeper insight into the phenomena studied by these sciences, in some fields of investigation physics has actually provided the primary stimulus for development. One such area is electrophysiology where membranes of nerve cells are characterized by a voltage gradient called the action potential. The propagation of action potentials along the axons of nerve cells is the key observation made in the investigation of brain physiology. A physical theory of action potential propagation was developed by Huxley and Hodgkin, who earned a Nobel Prize for their discovery. Likewise, the structure of DNA, discovered by Crick and Watson, that ushered in a new area of molecular biology, would not have been possible without both experimental and theoretical tools developed by physicists. In this case, it was X-ray crystallography that revealed the double helix structure of DNA. More recently, investigations of DNA sequences have been pursued in the hope of revealing a molecular basis of genetically inherited diseases. Gel electrophoresis and fluorescent labeling techniques are the crucial methods perfected by physicists and biochemists for the studies of DNA sequences.

This book is intended to provide a broad overview of membrane biophysics. Membrane biophysics uses the methods of biophysics, biochemistry, and cell biology to study how membranes of living organisms function. The objects of study described here belong to the realm of biology, the language of description will be that of physics with a sprinkling of mathematics and chemistry where needed. Since life itself is a nonlinear far-from-equilibrium process, some aspects of the book will involve nonlinear physics.

Biophysics is the study of the physics of certain complex macromolecular systems—cells and organisms—whose functioning takes place under conditions of insignificant temperature and pressure changes. Biophysicists seek to understand biophysical processes by accounting for intra-molecular and intermolecular interactions, and their resulting electronic and structural conformational changes; and by studying the transfer of electrons, protons, metallic ions and various biomolecules and the associated energetical transformations within biological systems. In order for these solutes to enter into a cell, their transfer across biological membranes must take place. In solid-state physics, such problems are solved by the methods of quantum mechanics, statistical physics and both equilibrium and non-equilibrium thermodynamics. However, since isolated biophysical systems are not found in nature, the description is complicated by the openness of livings systems and their far-from-equilibrium nature. It is clear that studies of biological systems have been advanced and largely dominated in the past by biochemistry, molecular and structural biology, as well as genetics. This has accrued tremendous benefits, the most obvious appears to be the precise information regarding the chemical composition of cells, in terms of macromolecules, and other structural components, followed by finding the reaction pathways in the production of the synthesized components and culminating in the discovery of the genetic code mechanism. We are now witnessing a paradigm shift where physical methods of both measurement and theoretical interpretation of biological mechanisms are starting to make a profound effect on the field of cell biology. Membrane biophysics is one of the best examples of this paradigm shift.

This book is focused on a detailed description of the diverse mechanisms and phenomena associated with cellular membranes. General membrane phenomena, mechanisms, and other properties will be discussed in Chap. 1. This will be followed by a discussion regarding transmembrane electrical potentials, ionic gradients, ion transport, specificities and directionalities in ion movements, membrane's capacitive effects and related aspects, etc. in Chap. 2. Chapter 3 will focus on the issue of lipid organization in membranes, lipid phase properties, and the thermodynamics of membranes, etc. Chapter 4 will provide a description of transport phenomena in membranes including the question how crucial electrical properties of membranes get compromised due to agents residing inside membranes or external agents interacting with membranes. Various classes of specific ion channels or non-specific pores used by ion flows temporarily appearing inside membranes will be explained here. Natural membrane proteins, antimicrobial peptides, chemotherapy drugs, certain types of lipids, other biomolecules, etc., will be analyzed in order to explain how those agents coexist with lipids and other membrane constituents to generate various membrane events, mainly those which are responsible for changing the membrane transport properties. Chapter 5 will bring additional aspects regarding the mechanisms underlying the generation of membrane transport events and provide a general picture of energetics responsible for statics and dynamics of lipids and membrane residing agents. This chapter will summarize all aspects of the regulation of membrane protein functions based on the electrical and mechanical properties of membranes and membrane proteins. Chapter 6 will attempt to explain how membrane-based nanotechnology can be used in drug delivery into cellular interiors. Electrical and mechanical properties of membranes determine the interactions between nanoparticles and membranes and lead to possible delivery methods beyond the membrane subject to the presence of other agents that induce membrane transport events. Novel membrane-based nanotechnology will be discussed in this chapter as a new dimension in developing drug delivery strategies. A number of serious diseases involving cell membrane structures and functions will be discussed in Chap. 7. Information regarding the physical, chemical, and biological processes that are involved in disease initiation and progression will be provided in this chapter. Finally, certain diseases such as cancer, Alzheimer's disease, bacterial infections, and some other membrane based disorders and their potential treatments will be discussed in the context of membrane biophysics in this chapter.

The authors hope that this monograph will be of use as a source of valuable information and conceptual inspiration to both students of biophysics and expert researchers.

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