

Preface

From the Preface to the Third Edition, by Russell K. Hobbie:

Between 1971 and 1973 I audited all the courses medical students take in their first two years at the University of Minnesota. I was amazed at the amount of physics I found in these courses and how little of it is discussed in the general physics course.

I found a great discrepancy between the physics in some papers in the biological research literature and what I knew to be the level of understanding of most biology majors or premed students who have taken a year of physics. It was clear that an intermediate-level physics course would help these students. It would provide the physics they need and would relate it directly to the biological problems where it is useful.

This book is the result of my having taught such a course since 1973. It is intended to serve as a text for an intermediate course taught in a physics department and taken by a variety of majors. Since its primary content is physics, I hope that physics faculty who might shy away from teaching a conventional biophysics course will consider teaching it. I also hope that research workers in biology and medicine will find it a useful reference to brush up on the physics they need or to find a few pointers to the current literature in a number of areas of biophysics. (The bibliography in each chapter is by no means exhaustive; however, the references should lead you quickly into a field.) The course offered at the University of Minnesota is taken by undergraduates in a number of majors who want to see more physics with biological applications and by graduate students in physics, bio-

physical sciences, biomedical engineering, physiology, and cell biology.

Because the book is intended primarily for students who have taken only one year of physics, I have tried to adhere to the following principles in writing it:

1. Calculus is used without apology. When an important idea in calculus is used for the first time, it is reviewed in detail. These reviews are found in the appendices.
2. The reader is assumed to have taken physics and to know the basic vocabulary. However, I have tried to present a logical development from first principles, but shorter than what would be found in an introductory course. An exception is found in Chapters 14–18, where some results from quantum mechanics are used without deriving them from first principles. (My students have often expressed surprise at this change of pace.)
3. I have not intentionally left out steps in most derivations. Some readers may feel that the pace could be faster, particularly after a few chapters. My students have objected strongly when I have suggested stepping up the pace in class.
4. Each subject is approached in as simple a fashion as possible. I feel that sophisticated mathematics, such as vector analysis or complex exponential notation, often hides physical reality from the student. I have seen electrical engineering students who could not tell me what is happening in an RC circuit but could solve the equations with Laplace transforms.

The Fourth Edition follows the tradition of earlier editions. The book now has a second author: Bradley

J. Roth of Oakland University. Both of us have enjoyed this collaboration immensely. We have added a chapter on sound and ultrasound, deleting or shortening topics elsewhere, in order to keep the book only slightly longer than the Third Edition. Some of the deleted material is available at the book's website: <http://www.oakland.edu/~roth/hobbie.htm>.

The Fourth Edition has 44% more end-of-chapter problems than the Third Edition; most highlight biological applications of the physical principles. Many of the problems extend the material in the text. A solutions manual is available to those teaching the course. Instructors can use it as a reference or provide selected solutions to their students. The solutions manual makes it much easier for an instructor to guide an independent-study student. Information about the Solutions manual is available at the book's website.

Chapter 1 reviews mechanics. Translational and rotational equilibrium are introduced, with the forces in the heel and hip joint as clinical examples. Stress and strain, hydrostatics, incompressible viscous flow, and the Poiseuille–Bernoulli equation are discussed, with examples from the circulatory system. The chapter concludes with a discussion of Reynolds number.

Chapter 2 is essential to nearly every other chapter in the book. It discusses exponential growth and decay and gives examples from pharmacology and physiology (including clearance). The logistic equation is discussed. Students are also shown how to use semilog and log-log graph plots and to determine power-law coefficients using a spreadsheet. The chapter concludes with a brief discussion of scaling.

Chapter 3 is a condensed treatment of statistical physics: average quantities, probability, thermal equilibrium, entropy, and the first and second laws of thermodynamics. Topics treated include the following: the Boltzmann factor and its corollary, the Nernst equation; the principle of equipartition of energy; the chemical potential; the general thermodynamic relationship; the Gibbs free energy; and the chemical potential of a solution. You can plow through this chapter if you are a slave to thoroughness, touch on the highlights, or use it as a reference as the topics are needed in later chapters.

Chapter 4 treats diffusion and transport of solute in an infinite medium. Fick's first and second laws of diffusion are developed. Steady-state solutions in one, two and three dimensions are described. An important model is a spherical cell with pores providing transport through the cell membrane. It is shown that only a small number of pores are required to keep up with the rate of diffusion toward or away from the cell, so there is plenty of room on the cell surface for many different kinds of pores and receptor sites. The combination of diffusion and drift (or solvent drag) is also discussed. Finally, a simple random-walk model of diffusion is introduced.

Chapter 5 discusses transport of fluid and neutral solutes through a membrane. This might be a cell mem-

brane, the basement membrane in the glomerulus of the kidney, or a capillary wall. The phenomenological transport equations including osmotic pressure are introduced as the first (linear) approximation to describe these flows. Countercurrent transport is described. Finally, a hydrodynamic model is developed for right-cylindrical pores. This model provides expressions for the phenomenological coefficients in terms of the pore radius and length. It is also used to calculate the net force on the membrane when there is flow.

After reviewing the electric field, electric potential, and circuits, *Chapter 6* describes the electrochemical changes that cause an impulse to travel along a nerve axon or along a muscle fiber before contraction. Two models are considered: electrotonus (when the membrane obeys Ohm's law) and the Hodgkin–Huxley model (when the membrane is nonlinear). Saltatory conduction in myelinated fibers is described. The dielectric properties of the membrane are modeled in terms of its molecular structure. Some simple changes to the membrane conductivity give rise to a periodically repeating action potential. Finally, a general relationship is developed between diffusive transport, resistance and capacitance for a given geometry.

Chapter 7 shows how an electric potential is generated in the medium surrounding a nerve or muscle cell. This leads to the current dipole model for the electrocardiogram. The model is refined to account for the anisotropy of the electrical conductivity of the heart. We then discuss electrical stimulation, which is important for pacemakers, stimulating nerve and muscle cells, and defibrillation. Finally, the model is extended to the electroencephalogram.

Chapter 8 shows how the currents in a conducting nerve or muscle cell generate a magnetic field, leading to the magnetocardiogram and the magnetoencephalogram. Some bacteria (and probably some higher organisms) contain magnetic particles used for determining spatial orientation in the earth's magnetic field. The mechanism by which these bacteria are oriented is described. The detection of weak magnetic fields and the use of changing magnetic fields to stimulate nerve or muscle cells are also discussed.

Chapter 9 covers a number of topics at the cellular and membrane level. It begins with Donnan equilibrium, where the presence of an impermeant ion on only one side of a membrane leads to the buildup of a potential difference across the membrane, and the Gouy–Chapman model for how ions redistribute near the membrane to generate this potential difference. The Debye–Hückel model is a simple description of the neutralization of ions by surrounding counterions. The Nernst–Planck equation provides the basic model for describing combined diffusion and drift in an applied electric field. It also forms the basis for the Goldman–Hodgkin–Katz model for zero total current in a membrane with a constant electric field. Gated membrane channels are then discussed. Noise is inescapable in all signalling situations. After

developing the basic properties of shot noise and Johnson noise, we show how a properly adapted shark can detect very weak electric fields with a reasonable signal-to-noise ratio. The chapter concludes with a discussion of the basic physical principles that must be kept in mind when assessing the possibility of biological effects of weak electric and magnetic fields.

Chapter 10 describes feedback systems in the body. It starts with the regulation of breathing rate to stabilize the carbon dioxide level in the blood, moves to linear feedback systems with one and two time constants, and then to nonlinear models. We show how nonlinear systems described by simple difference equations can exhibit chaotic behavior, and how chaotic behavior can arise in continuous systems as well. Examples of feedback systems include Cheyne-Stokes respiration, heat stroke, pupil size, oscillating white-blood-cell counts, waves in excitable media, and period doubling and chaos in the heart.

Chapter 11 shows how the method of least squares underlies several important techniques for analyzing data. These range from simple curve fitting to discrete and continuous Fourier series, power spectra, correlation functions, and the Fourier transform. We then describe the frequency response of a linear system and the frequency spectrum of noise. We conclude with a brief discussion of testing data for chaotic behavior and the important concept of stochastic resonance.

Armed with the tools of the previous chapter, we turn to images in *Chapter 12*. Images are analyzed from the standpoint of linear systems and convolution. This leads to the use of Fourier analysis to describe the spatial frequencies in an image and the reconstruction of an image from its projections. Both Fourier techniques and filtered backprojection are discussed.

Chapter 13 is new in the Fourth Edition. It discusses acoustics, hearing, and medical ultrasound.

Chapter 14 discusses the visible, infrared, and ultraviolet regions of the electromagnetic spectrum. The scattering and absorption cross sections are introduced and are used here and in the next three chapters. We then describe the diffusion model for photon transport in turbid media. Biological examples of infrared scattering include the near infrared, optical coherence tomography, Raman scattering, and the far infrared. Thermal radiation emitted by the body can be detected; the emission of infrared radiation by the sun includes ultraviolet light, which injures skin. Protection from ultraviolet light is both possible and prudent. The definitions of various radiometric quantities have varied from one field of research to another. We present a coherent description of radiometric, photometric and actinometric definitions. We then turn to the eye, showing how spectacle lenses are used to correct errors of refraction. The chapter closes with a description of the quantum limitations to dark-adapted vision.

Chapter 15, like Chapter 3, has few biological examples but sets the stage for later work. It describes how photons and ionizing charged particles such as electrons lose energy in traversing matter. These interaction mechanisms, both in the body and in the detector, are fundamental to the formation of a radiographic image and to the use of radiation to treat cancer.

Chapter 16 describes the use of x rays for medical diagnosis and treatment. It moves from production to detection, to the diagnostic radiograph. We discuss image quality and noise, followed by angiography, mammography, fluoroscopy, and computed tomography. After briefly reviewing radiobiology, we discuss therapy and dose measurement. The chapter closes with a section on the risks from radiation.

Chapter 17 introduces nuclear physics and nuclear medicine. The different kinds of radioactive decay are described. Dose calculations are made using the fractional absorbed dose method recommended by the Medical Internal Radiation Dose committee of the Society of Nuclear Medicine. Auger electrons can magnify the dose delivered to a cell or to DNA. This can potentially provide new methods of treatment. Diagnostic imaging includes single photon emission tomography and positron emission tomography. Therapies include brachytherapy and internal radiotherapy. A section on the nuclear physics of radon closes the chapter.

Chapter 18 develops the physics of magnetic resonance imaging. We show how the basic pulse sequences are formed and used for slice selection, readout, image reconstruction and to manipulate image contrast. We close with chemical shift imaging, flow effects, functional MRI, and diffusion and diffusion tensor MRI.

Biophysics is a very broad subject. Nearly every branch of physics has something to contribute, and the boundaries between physics and engineering are blurred. Each chapter could be much longer; we have attempted to provide the essential physical tools. Molecular biophysics has been almost completely ignored: excellent texts already exist, and this is not our area of expertise. This book has become long enough.

We would appreciate receiving any corrections or suggestions for improving the book.

Finally, thanks to our long-suffering families. We never understood what these common words really mean, nor the depth of our indebtedness, until we wrote the book.

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