Biological Physics: Contents and Preface

Philip C. Nelson  
*University of Pennsylvania, nelson@physics.upenn.edu*

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Biological Physics: Contents and Preface

Abstract
Contents; To the Student; To the Instructor

Keywords
biophysics

Disciplines
Physical Sciences and Mathematics | Physics

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Biological Physics Student Edition 2020: Contents and Prefaces

Philip C. Nelson
University of Pennsylvania, nelson@physics.upenn.edu

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Abstract
Brief Contents; Detailed Contents; To the Student; To the Instructor

Keywords
biophysics; biological physics; physical biology; neuroscience; biophysical chemistry; molecular motors; single-molecule; ion channel; statistical physics; mechanobiology; self-assembly; entropic forces; molecular machines; molecular biophysics

Disciplines
Biochemistry, Biophysics, and Structural Biology | Physical Sciences and Mathematics | Physics

Comments
Web resources

The book’s Web site (www.physics.upenn.edu/biophys/BPse/) contains links to the following resources in the Student section:

- Color figures for those viewing a b/w printout.
- Errata will appear as needed.

Detailed contents

To the student xiii
To the instructor xviii

PART I Mysteries, Metaphors, Models

Chapter 1 What the ancients knew 2
1.1 Heat 2
   1.1.1 Heat is a form of energy 2
   1.1.2 Just a little history 4
   1.1.3 Preview: The concept of free energy 6
1.2 How life generates order 8
   1.2.1 The puzzle of biological order 8
   1.2.2 Osmotic flow as a paradigm for free energy transduction 11
   1.2.3 Preview: Disorder as information 13
1.3 Excursion: Commercials, philosophy, pragmatics 14
1.4 How to do better on exams (and discover new physical laws) 16
   1.4.1 Most physical quantities carry dimensions 16
   1.4.2 Dimensional analysis can help you catch errors and recall definitions 18
   1.4.3 Dimensional analysis can also help you formulate hypotheses 19
   1.4.4 Units and graphs 20
   1.4.5 Some notational conventions involving flux and density 22
1.5 Other key ideas from physics and chemistry 22
   1.5.1 Molecules are small 22
   1.5.2 Molecules are particular spatial arrangements of atoms 24
   1.5.3 Molecules have well-defined internal energies 24
   1.5.4 Low-density gases obey a universal law 26
Big Picture 27
Key Formulas 27
Chapter 2 | What’s inside cells  34

2.1 Cell physiology  36
  2.1.1 Internal gross anatomy  38
  2.1.2 External gross anatomy  42

2.2 The molecular parts list  43
  2.2.1 Small molecules  43
  2.2.2 Medium-sized molecules  45
  2.2.3 Big molecules  47
  2.2.4 Macromolecular assemblies  49

2.3 Bridging the gap: Molecular devices  51
  2.3.1 The plasma membrane  51
  2.3.2 Molecular motors  53
  2.3.3 Enzymes and regulatory proteins  54
  2.3.4 The overall flow of information in cells  55

Big Picture  57

PART II  Diffusion, Dissipation, Drive

Chapter 3 | The molecular dance  66

3.1 The probabilistic facts of life  66
  3.1.1 Discrete distributions  67
  3.1.2 Continuous distributions  68
  3.1.3 Mean and variance  70
  3.1.4 Addition and multiplication rules  71

3.2 Decoding the ideal gas law  74
  3.2.1 Temperature reflects the average kinetic energy of thermal motion  74
  3.2.2 The complete distribution of molecular velocities is experimentally measurable  77
  3.2.3 The Boltzmann distribution  77
  3.2.4 Activation barriers control reaction rates  80
  3.2.5 Relaxation to equilibrium  82

3.3 Excursion: A lesson from heredity  83
  3.3.1 Aristotle weighs in  84
  3.3.2 Identifying the physical carrier of genetic information  84
  3.3.3 Schrödinger’s summary: Genetic information is structural  90

Big Picture  94

Key Formulas  95

Chapter 4 | Random walks, friction, and diffusion  101

4.1 Brownian motion  102
  4.1.1 Just a little more history  102
  4.1.2 Random walks lead to diffusive behavior  103
  4.1.3 The diffusion law is model independent  109
  4.1.4 Friction is quantitatively related to diffusion  110
4.2 Excursion: Einstein's role 112

4.3 Other random walks 113
  4.3.1 The conformation of polymers 113
  4.3.2 Vista: Random walks on Wall Street 117

4.4 More about diffusion 117
  4.4.1 Diffusion rules the subcellular world 117
  4.4.2 Diffusion follows a differential equation 119
  4.4.3 Precise statistical prediction of random processes 122

4.5 Functions, derivatives, and snakes under the rug 125
  4.5.1 Functions describe the details of quantitative relationships 122
  4.5.2 A function of two variables can be visualized as a landscape 124

4.6 Biological applications of diffusion 125
  4.6.1 The permeability of artificial membranes is diffusive 125
  4.6.2 Diffusion sets a fundamental limit on bacterial metabolism 127
  4.6.3 The Nernst relation sets the scale of membrane potentials 128
  4.6.4 The electrical resistance of a solution reflects frictional dissipation 131
  4.6.5 Diffusion from a point gives a spreading, Gaussian profile 131

Big Picture 133
Key Formulas 133
Track 2 135
Problems 140

Chapter 5 | Life in the slow lane: The low Reynolds number world 149

5.1 Friction in fluids 149
  5.1.1 Sufficiently small particles can remain in suspension indefinitely 149
  5.1.2 The rate of sedimentation depends on solvent viscosity 151
  5.1.3 It’s hard to mix a viscous liquid 152

5.2 Low Reynolds number 154
  5.2.1 A critical force demarcates the physical regime dominated by friction 154
  5.2.2 The Reynolds number quantifies the relative importance of friction and inertia 156
  5.2.3 The time-reversal properties of a dynamical law signal its dissipative character 159

5.3 Biological applications 161
  5.3.1 Swimming and pumping 161
  5.3.2 To stir or not to stir? 166
  5.3.3 Foraging, attack, and escape 167
  5.3.4 Vascular networks 168
  5.3.5 Viscous drag at the DNA replication fork 170

5.4 Excursion: The character of physical Laws 172

Big Picture 173
Key Formulas 173
Track 2 175
Problems 178

Chapter 6 | Entropy, temperature, and free energy 184

6.1 How to measure disorder 184

6.2 Entropy 187
  6.2.1 The Statistical Postulate 187
  6.2.2 Entropy is a constant times the maximal value of disorder 188

6.3 Temperature 190
  6.3.1 Heat flows to maximize disorder 190
  6.3.2 Temperature is a statistical property of a system in equilibrium 191

Jump to Contents Index Notation
8.2.2 $\Delta G$ gives a universal criterion for the direction of a chemical reaction 284
8.2.3 Kinetic interpretation of complex equilibria 289
8.2.4 The primordial soup was not in chemical equilibrium 290

8.3 Dissociation 291
8.3.1 Ionic and partially ionic bonds dissociate readily in water 291
8.3.2 The strengths of acids and bases reflect their dissociation equilibrium constants 292
8.3.3 The charge on a protein varies with its environment 293
8.3.4 Electrophoresis can give a sensitive measure of protein composition 295

8.4 Self-assembly of amphiphiles 297
8.4.1 Emulsions form when amphiphilic molecules reduce the oil–water interface tension 297
8.4.2 Micelles self-assemble suddenly at a critical concentration 299

8.5 Excursion: On fitting models to data 302

8.6 Self-assembly in cells 303
8.6.1 Bilayers self-assemble from amphiphiles 303
8.6.2 Vista: Macromolecular folding and aggregation 308
8.6.3 Another trip to the kitchen 310

Big Picture 312
Key Formulas 312
Track 2 314
Problems 316

PART III Molecules, Machines, Mechanisms

Chapter 9 | Cooperative transitions in macromolecules 321

9.1 Elasticity models of polymers 321
9.1.1 Why physics works (when it does work) 322
9.1.2 Four phenomenological parameters characterize the elasticity of a long, thin rod 324
9.1.3 Polymers resist stretching with an entropic force 326

9.2 Stretching single macromolecules 329
9.2.1 The force–extension curve can be measured for single DNA molecules 329
9.2.2 A two-state system qualitatively explains DNA stretching at low force 331

9.3 Eigenvalues for the impatient 333
9.3.1 Matrices and eigenvalues 333
9.3.2 Matrix multiplication 336

9.4 Cooperativity 336
9.4.1 The transfer matrix technique allows a more accurate treatment of bend cooperativity 336
9.4.2 DNA also exhibits linear stretching elasticity at moderate applied force 339
9.4.3 Cooperativity in higher-dimensional systems gives rise to infinitely sharp phase transitions 340

9.5 Thermal, chemical, and mechanical switching 341
9.5.1 The helix–coil transition can be observed by using polarized light 341
9.5.2 Three phenomenological parameters describe a given helix–coil transition 343
9.5.3 Calculation of the helix–coil transition 346
9.5.4 DNA also displays a cooperative “melting” transition 350
9.5.5 Applied mechanical force can induce other cooperative structural transitions in macromolecules 351

9.6 Allostery 352
9.6.1 Hemoglobin binds four oxygen molecules cooperatively 352
9.6.2 Allostery often involves relative motion of molecular subunits 355
9.6.3 The native “state” of a protein is really a continuous distribution of substates 356

Big Picture 357
Key Formulas 358
Track 2 360

Jump to Contents Index Notation
Chapter 10 | Enzymes and molecular machines 377

10.1 Survey of molecular devices found in cells 378
   10.1.1 Terminology 378
   10.1.2 Enzymes display saturation kinetics 378
   10.1.3 All eukaryotic cells contain cyclic motors 381
   10.1.4 One-shot machines assist in cell locomotion and spatial organization 382

10.2 Purely mechanical machines 384
   10.2.1 Macroscopic machines can be described by an energy landscape 384
   10.2.2 Microscopic machines can step past energy barriers 388
   10.2.3 The Smoluchowski equation gives the rate of a microscopic machine 390

10.3 Molecular implementation of mechanical principles 396
   10.3.1 Three ideas 397
   10.3.2 The reaction coordinate gives a useful reduced description of a chemical event 397
   10.3.3 An enzyme catalyzes a reaction by binding to the transition state 399
   10.3.4 Mechanochemical motors move by random-walking on a two-dimensional landscape 403

10.4 Kinetics of real enzymes and machines 404
   10.4.1 The Michaelis–Menten rule describes the kinetics of simple enzymes 405
   10.4.2 Modulation of enzyme activity 408
   10.4.3 Two-headed kinesin as a tightly coupled, perfect ratchet 409
   10.4.4 Molecular motors can move even without tight coupling or a power stroke 418

10.5 Vista: Other molecular machines 422

Big Picture 422
Key Formulas 424
Track 2 425
Problems 433

Chapter 11 | Machines in membranes 443

11.1 Electroosmotic effects 443
   11.1.1 Before the ancients 443
   11.1.2 Ion concentration differences create Nernst potentials 444
   11.1.3 Donnan equilibrium can create a resting membrane potential 447

11.2 Ion pumping 449
   11.2.1 Observed eukaryotic membrane potentials imply that these cells are far from Donnan equilibrium 449
   11.2.2 The Ohmic conductance hypothesis 452
   11.2.3 Active pumping maintains steady-state membrane potentials while avoiding large osmotic pressures 454

11.3 Mitochondria as factories 458
   11.3.1 Busbars and driveshafts distribute energy in factories 458
   11.3.2 The biochemical backdrop to respiration 459
   11.3.3 The chemiosmotic mechanism identifies the neighborhood of the mitochondrial inner membrane as a busbar 462
   11.3.4 Evidence for the chemiosmotic mechanism 463
   11.3.5 Vista: Cells use chemiosmotic coupling in many other contexts 467

11.4 Excursion: “Powering up the flagellar motor” by H. C. Berg and D. Fung 468

Big Picture 469
Key Formulas 470
Track 2 471
Problems 473
Chapter 12 | Nerve impulses 477

12.1 The problem of nerve impulses 478
   12.1.1 Phenomenology of the action potential 478
   12.1.2 The cell membrane can be viewed as an electrical network 481
   12.1.3 Membranes with Ohmic conductance lead to a linear cable equation with no traveling wave solutions 485

12.2 Simplified mechanism of the action potential 489
   12.2.1 The puzzle 489
   12.2.2 A mechanical analogy 490
   12.2.3 Just a little more history 492
   12.2.4 The time course of an action potential suggests the hypothesis of voltage gating 495
   12.2.5 Voltage gating leads to a nonlinear cable equation with traveling wave solutions 498

12.3 The full Hodgkin–Huxley mechanism and its molecular underpinnings 501
   12.3.1 Each ion conductance follows a characteristic time course when the membrane potential changes 502
   12.3.2 The patch clamp technique allows the study of single ion channel behavior 505

12.4 Nerve, muscle, synapse 512
   12.4.1 Nerve cells are separated by narrow synapses 513
   12.4.2 The neuromuscular junction 514
   12.4.3 Vista: Neural computation 515

Big Picture 516
Key Formulas 516
Track 2 519
Problems 520

Epilogue 525

Appendix A | Global list of symbols and units 527
A.1 Notation 527
A.2 Named quantities 528
A.3 Dimensions 532
A.4 Units 533

Appendix B | Numerical values 535
B.1 Fundamental constants 535
B.2 Magnitudes 535
B.3 Specialized values 537

Acknowledgments 540
Credits 543

Bibliography 546
Index 556
To the student

This is a book for life science students who are willing to use calculus. This is also a book for physical science and engineering students who are willing to think about cells. I believe that in the future every student in both groups will need to know the essential core of the others’ knowledge.

I attend many conferences and seminars, where I listen to physicists, biologists, chemists, and engineers, as well as physicians, mathematicians, and entrepreneurs. After a while, I began to wonder how this diverse group manages to overcome the Tower-of-Babel syndrome. Slowly I began to realize that, even though each discipline carries its immense load of experimental and theoretical detail, still the headwaters of these rivers are manageable, and come from a common spring, a handful of simple, general ideas. Armed with these few ideas, I found that one can understand an enormous amount of front line research. This book explores these first common ideas, ruthlessly suppressing the more specialized ones for later.

Specifically, first-year physics generally consists of a semester about mechanics followed by a semester about electricity, and neither feels particularly “life-like.” In this book, you’ll find that mechanics becomes much more relevant to cell and molecular biology when we acknowledge the incessant thermal motion that dominates the nanoworld. Similarly, electricity also becomes more life-like when we acknowledge… thermal motion.

In fact, my own undergraduate education postponed the introduction of many such basic ideas to the last year of my degree (or even later) and many programs still have this character: We meticulously build a sophisticated mathematical edifice before introducing many of the Big Ideas. My colleagues and I became convinced that this approach did not serve the needs of our students. Many of our undergraduate students start research in their very first year and need the big picture early. Many others create interdisciplinary programs for themselves and may never even get to our specialized, advanced courses. In this book, I hope to make the big picture accessible to any student who has taken first-year physics and calculus (plus a smattering of high school chemistry and biology), and who is willing to stretch. When you’re done, you should be in a position to read current work in Science and Nature. You won’t get every detail, of course. But you will get the sweep.

When we began to offer this course, we were surprised to find that many of our graduate students wanted to take it, too. Accordingly, many sections in this book have “Track–2” addenda addressing this more mathematically experienced group.

Physical science versus life science
At the dawn of the twentieth century, it was already clear that, chemically speaking, you and I are not much different from cans of soup. And yet we can do many complex and even fun things we do not usually see cans of soup doing. At that time, people

---

1 For example, see Chapters 4, 9, and 10.
2 For example, see Chapters 7, 11, and 12.
had very few correct ideas about how living organisms create order from food, do work, and even compute things—just a lot of inappropriate metaphors drawn from the technology of the day.

By mid-century, it began to be clear that the answers to many of these questions would be found in the study of very big molecules. In the twenty-first century, ironically, the situation is inverted: The problem is now that we have way too much information about those molecules! We are drowning in information; we need an armature, a framework, on which to organize all those zillions of facts.

Some may dismiss physics as “reductionist,” tending to strip away all the details that make frogs different from, say, neutron stars. Others believe that right now some unifying framework is essential to see the big picture. I think that the tension between the developmental/historical/complex sciences and the universal/ahistorical/reductionist ones has been enormously fruitful and that the future belongs to those who can switch fluidly between both kinds of brains.

Setting aside philosophy, it’s a fact that the past 25 years has seen a revolution in physical techniques to get inside the nanoworld of cells, tweak them in physical ways, and measure quantitatively the results. At last, a lot of physical ideas lying behind the cartoons found in cell biology books are getting the precise tests needed to confirm or reject them.

Why all the math?

I said it in Hebrew, I said it in Dutch,
I said it in German and Greek;
But I wholly forgot (and it vexes me much)
That English is what you speak!
— Lewis Carroll

Life science students may wonder whether all the mathematical formulas in this book are really needed. This book’s premise is that the way to be sure that a theory is correct is to make quantitative predictions from a simplified model, then test those predictions experimentally. The following chapters supply many of the tools to do this. Ultimately, I want you to be able to walk into a room with an unfamiliar problem, pull out the right tool, and solve the problem. I realize this is not easy, at first.

Actually, it’s true that physicists sometimes overdo the mathematical analysis. In contrast, the point of view in this book is that beautiful formulas are usually a means, not an end, in our attempts to understand Nature. Usually only the simplest tools, like dimensional analysis, suffice to see what’s going on. Only when you’ve been a very good scientist, do you get the reward of carrying out some really elaborate mathematical calculation and seeing your predictions come to life in an experiment. Your other physics and math courses will give you the background you’ll need for that.

Features of this book

I have tried to adhere to some principles while writing the book. Most of these are boring and technical, but there are four that are worth pointing out here:

• When possible, relate the ideas to everyday phenomena.
• Say what’s going on. Instead of just giving a list of steps, I have tried to explain why we are taking these steps, and how we might have guessed that a step would prove fruitful. This exploratory (or discovery-style) approach involves more words than you may be used to in physics texts. The goal is to help you make the difficult
transition to choosing your own steps.

- **No black boxes.** The dreaded phrase “Smith has shown” hardly ever appears in Track–1. Almost all mathematical results mentioned are actually derived here, or taken to the point where you can get them yourself as homework problems. When I could not obtain a result in a discussion at this level, I usually omitted it altogether.

- **No fake data.** When you see an object that looks like a graph, almost always it really is a graph. That is, the points are somebody’s actual laboratory data, usually with a citation. The curves are some actual mathematical function, usually derived in the text (or in a homework problem). Graphlike sketches are clearly labeled as such. In fact, every figure carries a pedantic little tag giving its logical status, so you can tell which are actual data, which are reconstructions, and which are an artist’s sketches.

Real data are generally not as pretty as fake data. You need the real thing in order to develop your critical skills. For one thing, some simple theories don’t work as well as you might believe just from listening to lectures. On the other hand, some unimpressive-looking fits of theory to experiment actually do support strong conclusions; you need practice looking for the relevant features.

Please take a moment now to check the two appendices. They include a list of all the symbols used in the text to represent physical quantities, definitions of all the units, and numerical values for many physical quantities, some of them useful in working the problems.

**Why the history?**

This is not a history book, and yet you will find many ancient results discussed. (Many people take “ancient” to mean “before Internet,” but in this book I use the more classical definition “before television.”) The old stuff is not there just to give the patina of scholarship. Rather, a recurring theme of the book is the way in which physical measurements have often disclosed the existence and nature of molecular devices in cells long before traditional biochemical assays nailed down their precise identities. The historical passages document case studies where this has happened; in some cases, the gap has been measured in decades!

Even today, with our sophisticated toolkit of molecular biology, the traditional knock-out-the-gene-and-see-what-kind-of-mouse-you-get experimental strategy can be much slower and more difficult to interpret than a more direct, reach-in-and-grab-it approach. In fact, the menu of ingenious new tools for applying physical stresses to functioning cells or their constituents (all the way down to the single-molecule level) and quantitatively measuring their responses has grown rapidly in recent decades, giving unprecedented opportunities for deducing what must be happening at the molecular level. Scientists who can integrate the lessons of both the biochemical and biophysical approaches will be the first ones to see the whole picture. Knowing how it has worked in the past prepares you for Your Turn.

**Learning this subject**

If your previous background in physical science is a first-year undergraduate course in physics or chemistry, this book will have a very different feel from the texts you’ve read so far. This subject is rapidly evolving; my presentation won’t have that authoritative, stone-tablets feeling of a fixed, established subject, nor should it. Instead, I offer you the
excitement of a field in flux, a field where you personally can make new contributions
without first hacking through a jungle of existing formalism for a decade.

If your previous background is in life sciences, you may be accustomed to a writing
style in which facts are delivered to you. But in this book, many of the assertions,
and most of the formulas, are supposed to follow from the previous ones, in ways you
can and must check. In fact, you will notice the words we, us, our, let’s throughout
the text. Usually in scientific writing, these words are just pompous ways of saying
I, me, my, and watch me; but in this book, they refer to a team consisting of you
and me. You need to figure out which statements are new information and which
are deductions, and work out the latter ones. Sometimes, I have flagged especially
important logical steps as “Your Turn” questions. Most of these are short enough
that you can do them on the spot before proceeding. It is essential to work these out
yourself in order to get the skill you need in constructing new physical arguments.

Each time the text introduces a formula, take a moment to look at it and think
about its reasonableness. If it says $x = yz/w$, does it make sense that increasing $w$
should decrease $x$? How do the units work out? At first, I’ll walk you through these
steps; but from then on, you need to do them automatically. When you find me using
an unfamiliar mathematical idea, please talk to your instructor as soon as possible
instead of just bleeping over it. Other helpful resources are listed below.

Beyond the questions in the text, you will find problems at the ends of the chapters.
They are not as straightforward as they were in first-year physics; often you will need
some common sense, some seat-of-the-pants qualitative judgment, even some advice
from your instructor to get off to the right start. Most students are uncomfortable
with this approach at first—it’s not just you!—but in the end this skill is going to be
one of the most valuable ones you’ll ever learn, no matter what you do later in life.
It’s a high-technology world out there, and it will be your oyster when you develop
the agility to solve open-ended, quantitative problems.

The problems also get harder as you go on in the text, so do the early ones even
if they seem easy.

$T_2$

Some sections and problems are flagged with this symbol. These are For
Mature Audiences Only. Of course, I say it that way to make you want to read
them, whether or not your instructor assigns them. These Track–2 sections take
the mathematical development a bit further. They forge links to what you are learning/will
learn in other physics courses. They also advertise some of the cited research literature.
The main (Track–1) text does not rely on these sections; it is self-contained. Even
Track–2 readers should skip the Track–2 sections on the first reading.

Many students find this course to be a stiff challenge. The physics students have
to digest a lot of biological terminology; the biology students have to brush up on
their math. It’s not easy, but it’s worth the effort: Interdisciplinary subjects like this
one are among the most exciting and fertile. I’ve noticed that the happiest students
are the ones who team up to work together with another student from a different
background and do the problems together, teaching each other things. Give it a try.
To the instructor

This low-cost reissue of *BP* is intended to be plug-compatible with the 2014 edition; even the numbering of problems has been left unchanged. However, I have taken the opportunity to add many updates and clarifications.

Once upon a time, my department asked their undergraduate students what they needed but were not getting from us. One of the answers was, “a course on biological physics.” Our students could not help noticing all the exciting articles in *The New York Times*, all the cover articles in *Physics Today*, and so on; they wanted a piece of the action. This book emerged from their request.

The book also serves to introduce much of the conceptual material underlying the young fields of nanotechnology and soft materials. It’s not surprising—the molecular and supramolecular machines in each of our cells are the inspiration for much of nanotechnology, and the polymers and membranes from which they are constructed are the inspiration for much of soft-materials science. Moreover, the foundational ideas of mechanobiochemistry are now a standard part of premedical education (American Association of Medical Colleges, 2017).

This text was intended for use with a wildly diverse audience. It is based on a course I have taught to a single class containing students majoring in physics, biology, biochemistry, biophysics, materials science, and chemical, mechanical, and bioengineering. I hope the book will prove useful as a main or adjunct text for courses in any science or engineering department. My students also vary widely in experience, from sophomores to third-year graduate students. You may not want to try such a broad group, but it works at Penn. To reach them all, the course is divided into two sections; the graduate section has harder and more mathematically sophisticated problems and exams. The structure of the book reflects this division, with numerous Track–2 sections and problems covering the more advanced material. These sections are placed at the ends of the chapters and are introduced with a special symbol: T2. The Track–2 sections are largely independent of one another, so you can assign them à la carte. I recommend that all students skip them on the first reading.

The only prerequisites for the core, Track–1, material are first-year physics, and a perhaps distant memory of high school chemistry and biology. The *concepts* of calculus are used freely, but very little of the technique; only the very simplest differential equations need to be solved. More important, the student needs to possess or acquire a fluency in throwing numbers around, making estimates, keeping track of units, and carrying out short derivations. The Track–2 material and problems should be appropriate for senior physics majors and first-year graduate students.

For a one-semester class of less experienced students, you will probably want to skip one or both of Chapters 9 and 10 (or possibly 11 and 12). For more experienced students, you can instead skim the opening chapters quickly, then spend extra time on the advanced chapters.

When teaching this course, I also assign supplementary readings from one of the standard cell biology texts. Cell biology inevitably contains a lot of nomenclature and iconography; both students and instructor must make an investment in learning
these. The payoff is clear and immediate: Not only does this investment allow one to communicate with professionals doing exciting work in many fields, it is also crucial for seeing what physical problems are relevant to biomedical research.

I have made a special effort to keep the terminology and notation unified, a difficult task when spanning several disciplines. Appendix A summarizes all the notation in one place. Appendix B contains many useful numerical values, more than are used in the text. (You may find these data useful in making new homework and exam problems.)

More details about how to get from this book to a full course can be found in the Instructor’s Guide. The Guide also contains solutions to all the problems and “Your Turn” questions, suggested class demonstrations, and the computer code used to generate many of the graphs found in the text. You can use this code to create computer-based problems, do class demos, and so on.

Errata to this book will appear at www.physics.upenn.edu/biophys/BPse/.

**Why doesn’t my favorite topic appear?**

It’s probably one of my favorite topics, too. But the text reflects the relentless pursuit of a few maxims:

- Keep it a course, not an encyclopedia. The book corresponds to what I actually manage to cover (that is, what the students actually manage to learn) in a typical 40-hour semester, plus about 20% more to allow flexibility.
- Keep a unified story line.
- Maintain a balance between recent results and the important classical topics. Choose those topics that open the most doors into physics, biology, chemistry, and engineering.
- Make practically no mention of quantum theory, which our students encounter only after this course. Fortunately, a huge body of important biological physics (including the whole field of soft biomaterials) makes no use of the deep quantum ideas.\(^4\)
- Restrict the discussion to concrete problems where the physical vision leads to falsifiable, quantitative predictions and where laboratory data are available. Every chapter presents some real experimental data.
- But choose problems that illuminate, and are illuminated by, the big ideas. Students want that—that’s why they study science.

There are certainly other topics meeting all these criteria but not covered in this book. I look forward to your suggestions as to which ones to add to the next edition.

Underlying the preceding points is a determination to present physical ideas as beautiful and important in their own right. Respect for these foundational ideas has kept me from relegating them to the currently fashionable utilitarian status of a mere toolbag to help out with other disciplines. A few apparently dilatory topics, which pursue the physics beyond the point (currently) needed to explain biological phenomena, reflect this conviction.

**Standard disclaimers**

This is a textbook, not a monograph. I am aware that many subtle subjects are presented in this book with important details burnished off. No attempt has been

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\(^4\)For that, see Nelson, 2017.
made to sort out historical priority, except in those sections titled “history.” The
experiments described here were chosen simply because they fit some pedagogical
imperative and seemed to have particularly direct interpretations. The citation of
original works is haphazard, except for my own work, which is systematically not
cited. No claim is made that anything in this book is original, although at times I just
couldn’t stop myself.

Is this stuff really physics?
Should it be taught in a physics department? If you’ve come this far, probably you have
made up your mind already. But I’ll bet you have colleagues who ask this question. The
text attempts to show, not only that many of the founders of molecular biology had
physics background, but conversely that historically the study of life has fed crucial
insights back into physics. It’s true at the pedagogical level as well. Many students
find the ideas of statistical physics to be most vivid in the life science context. In fact,
students tell me that this course helped them move on to full courses in statistical
physics or physical chemistry; it puts the pieces together for them in a new and helpful
way.

More important, I have found a group of students who are interested in studying
physics but feel turned away when their physics departments offer no connections to
the excitement in the life sciences. It’s time to give them what they need.

At the same time, your life sciences colleagues may ask, “Do our students need this
much physics?” The answer is, maybe not in the past, but certainly in the future. This
book tries to show that there is a quantitative, physical sciences approach to problems,
and it’s versatile. It’s not the only toolbox in the well-educated scientist’s mind, but
it’s one of the powerful ones. We need to teach it to everyone, not just to physical
science majors. I believe that the recent insularity of physics is only a temporary
aberration; both sides can only stand to prosper by renewing their once-tight linkage.

Last
I had the great good fortune to see statistical physics for the first time through the
beautiful lectures of Sam Treiman (1925–1999). Treiman was a great scientist and one
of the spiritual leaders of a great department. From time to time, I still go back to
my notes from that course. And there he is, just as before.