



University of Pennsylvania
ScholarlyCommons

Department of Physics Papers


Department of Physics

1-1-2014

Biological Physics: Contents and Preface

Philip C. Nelson

Follow this and additional works at: https://repository.upenn.edu/physics_papers

 Part of the [Physics Commons](#)

From the book *Biological Physics: Energy, Information, Life with new art by David Goodsell* (W H Freeman and Co 2014)

This paper is posted at ScholarlyCommons. https://repository.upenn.edu/physics_papers/1
For more information, please contact repository@pobox.upenn.edu.

Biological Physics: Contents and Preface

Abstract

Contents; To the Student; To the Instructor

Keywords

biophysics

Disciplines

Physical Sciences and Mathematics | Physics

Comments

From the book *Biological Physics: Energy, Information, Life with new art* by David Goodsell (W H Freeman and Co 2014)



Biological Physics

Energy, Information, Life

With new art by David Goodsell

Philip Nelson

University of Pennsylvania

with the assistance of Marko Radosavljević and Sarina Bromberg



W. H. Freeman and Company
New York

*Not chaos-like together crush'd and bruis'd,
But, as the world, harmoniously confus'd:
Where order in variety we see,
And where, though all things differ, all agree.*
— Alexander Pope, 1713

Contents

To the Student	xv
To the Instructor	xx
Acknowledgments	xxiv

Part I Mysteries, Metaphors, Models

Chapter 1	What the Ancients Knew	3
1.1	Heat	3
1.1.1	Heat is a form of energy	4
1.1.2	Just a little history	6
1.1.3	Preview: The concept of free energy	8
1.2	How life generates order	9
1.2.1	The puzzle of biological order	9
1.2.2	Osmotic flow as a paradigm for free energy transduction	12
1.2.3	Preview: Disorder as information	14
1.3	Excursion: Commercials, philosophy, pragmatics	15
1.4	How to do better on exams (and discover new physical laws)	18
1.4.1	Most physical quantities carry dimensions	18
1.4.2	Dimensional analysis can help you catch errors and recall definitions	20
1.4.3	Dimensional analysis can also help you formulate hypotheses	22
1.4.4	Some notational conventions involving flux and density	22
1.5	Other key ideas from physics and chemistry	23
1.5.1	Molecules are small	23
1.5.2	Molecules are particular spatial arrangements of atoms	25
1.5.3	Molecules have well-defined internal energies	26
1.5.4	Low-density gases obey a universal law	27
	The big picture	28
	Track 2	30
	Problems	31

Chapter 2 | What's Inside Cells**35**

- 2.1 Cell physiology 37
 - 2.1.1 Internal gross anatomy 40
 - 2.1.2 External gross anatomy 43
- 2.2 The molecular parts list 45
 - 2.2.1 Small molecules 46
 - 2.2.2 Medium-sized molecules 48
 - 2.2.3 Big molecules 50
 - 2.2.4 Macromolecular assemblies 54
- 2.3 Bridging the gap: Molecular devices 54
 - 2.3.1 The plasma membrane 55
 - 2.3.2 Molecular motors 58
 - 2.3.3 Enzymes and regulatory proteins 58
 - 2.3.4 The overall flow of information in cells 59
- The big picture 62
- Track 2 63
- Problems 64

Part II Diffusion, Dissipation, Drive**Chapter 3 | The Molecular Dance****69**

- 3.1 The probabilistic facts of life 69
 - 3.1.1 Discrete distributions 70
 - 3.1.2 Continuous distributions 71
 - 3.1.3 Mean and variance 73
 - 3.1.4 Addition and multiplication rules 75
- 3.2 Decoding the ideal gas law 78
 - 3.2.1 Temperature reflects the average kinetic energy of thermal motion 78
 - 3.2.2 The complete distribution of molecular velocities is experimentally measurable 82
 - 3.2.3 The Boltzmann distribution 83
 - 3.2.4 Activation barriers control reaction rates 86
 - 3.2.5 Relaxation to equilibrium 87
- 3.3 Excursion: A lesson from heredity 89
 - 3.3.1 Aristotle weighs in 89
 - 3.3.2 Identifying the physical carrier of genetic information 90
 - 3.3.3 Schrödinger's summary: Genetic information is structural 96
- The big picture 101
- Track 2 104
- Problems 105

Chapter 4 | Random Walks, Friction, and Diffusion 108

- 4.1 Brownian motion 109
 - 4.1.1 Just a little more history 109
 - 4.1.2 Random walks lead to diffusive behavior 110
 - 4.1.3 The diffusion law is model independent 117
 - 4.1.4 Friction is quantitatively related to diffusion 118
- 4.2 Excursion: Einstein's role 121
- 4.3 Other random walks 122
 - 4.3.1 The conformation of polymers 122
 - 4.3.2 Vista: Random walks on Wall Street 126
- 4.4 More about diffusion 127
 - 4.4.1 Diffusion rules the subcellular world 127
 - 4.4.2 Diffusion obeys a simple equation 128
 - 4.4.3 Precise statistical prediction of random processes 131
- 4.5 Functions, derivatives, and snakes under the rug 132
 - 4.5.1 Functions describe the details of quantitative relationships 132
 - 4.5.2 A function of two variables can be visualized as a landscape 134
- 4.6 Biological applications of diffusion 135
 - 4.6.1 The permeability of artificial membranes is diffusive 135
 - 4.6.2 Diffusion sets a fundamental limit on bacterial metabolism 138
 - 4.6.3 The Nernst relation sets the scale of membrane potentials 139
 - 4.6.4 The electrical resistance of a solution reflects frictional dissipation 142
 - 4.6.5 Diffusion from a point gives a spreading, Gaussian profile 142
- The big picture 144
- Track 2 147
- Problems 153

Chapter 5 | Life in the Slow Lane: The Low Reynolds-Number World 158

- 5.1 Friction in fluids 158
 - 5.1.1 Sufficiently small particles can remain in suspension indefinitely 158
 - 5.1.2 The rate of sedimentation depends on solvent viscosity 160
 - 5.1.3 It's hard to mix a viscous liquid 161
- 5.2 Low Reynolds number 163
 - 5.2.1 A critical force demarcates the physical regime dominated by friction 164
 - 5.2.2 The Reynolds number quantifies the relative importance of friction and inertia 166
 - 5.2.3 The time-reversal properties of a dynamical law signal its dissipative character 169

- 5.3 Biological applications 172
 - 5.3.1 Swimming and pumping 172
 - 5.3.2 To stir or not to stir? 177
 - 5.3.3 Foraging, attack, and escape 178
 - 5.3.4 Vascular networks 179
 - 5.3.5 Viscous drag at the DNA replication fork 182
- 5.4 Excursion: The character of physical Laws 184
 - The big picture 185
- Track 2 187
- Problems 190

Chapter 6

Entropy, Temperature, and Free Energy

195

- 6.1 How to measure disorder 196
- 6.2 Entropy 199
 - 6.2.1 The Statistical Postulate 199
 - 6.2.2 Entropy is a constant times the maximal value of disorder 200
- 6.3 Temperature 202
 - 6.3.1 Heat flows to maximize disorder 202
 - 6.3.2 Temperature is a statistical property of a system in equilibrium 203
- 6.4 The Second Law 206
 - 6.4.1 Entropy increases spontaneously when a constraint is removed 206
 - 6.4.2 Three remarks 209
- 6.5 Open systems 210
 - 6.5.1 The free energy of a subsystem reflects the competition between entropy and energy 210
 - 6.5.2 Entropic forces can be expressed as derivatives of the free energy 213
 - 6.5.3 Free energy transduction is most efficient when it proceeds in small, controlled steps 214
 - 6.5.4 The biosphere as a thermal engine 216
- 6.6 Microscopic systems 217
 - 6.6.1 The Boltzmann distribution follows from the Statistical Postulate 218
 - 6.6.2 Kinetic interpretation of the Boltzmann distribution 220
 - 6.6.3 The minimum free energy principle also applies to microscopic subsystems 223
 - 6.6.4 The free energy determines the populations of complex two-state systems 225

- 6.7 Excursion: “RNA folding as a two-state system” by J. Liphardt, I. Tinoco, Jr., and C. Bustamante 226
 - The big picture 229
- Track 2 232
- Problems 239

Chapter 7 | Entropic Forces at Work 245

- 7.1 Microscopic view of entropic forces 246
 - 7.1.1 Fixed-volume approach 246
 - 7.1.2 Fixed-pressure approach 247
- 7.2 Osmotic pressure 248
 - 7.2.1 Equilibrium osmotic pressure follows the ideal gas law 248
 - 7.2.2 Osmotic pressure creates a depletion force between large molecules 251
- 7.3 Beyond equilibrium: Osmotic flow 254
 - 7.3.1 Osmotic forces arise from the rectification of Brownian motion 255
 - 7.3.2 Osmotic flow is quantitatively related to forced permeation 259
- 7.4 A repulsive interlude 260
 - 7.4.1 Electrostatic interactions are crucial for proper cell functioning 261
 - 7.4.2 The Gauss Law 263
 - 7.4.3 Charged surfaces are surrounded by neutralizing ion clouds 264
 - 7.4.4 The repulsion of like-charged surfaces arises from compression of their ion clouds 269
 - 7.4.5 Oppositely charged surfaces attract by counterion release 272
- 7.5 Special properties of water 273
 - 7.5.1 Liquid water contains a loose network of hydrogen bonds 273
 - 7.5.2 The hydrogen-bond network affects the solubility of small molecules in water 276
 - 7.5.3 Water generates an entropic attraction between nonpolar objects 280
- The big picture 281
- Track 2 283
- Problems 290

Chapter 8 | Chemical Forces and Self-Assembly 294

- 8.1 Chemical potential 294
 - 8.1.1 μ measures the availability of a particle species 295
 - 8.1.2 The Boltzmann distribution has a simple generalization accounting for particle exchange 298

8.2	Chemical reactions	299
8.2.1	Chemical equilibrium occurs when chemical forces balance	299
8.2.2	ΔG gives a universal criterion for the direction of a chemical reaction	301
8.2.3	Kinetic interpretation of complex equilibria	306
8.2.4	The primordial soup was not in chemical equilibrium	307
8.3	Dissociation	308
8.3.1	Ionic and partially ionic bonds dissociate readily in water	308
8.3.2	The strengths of acids and bases reflect their dissociation equilibrium constants	309
8.3.3	The charge on a protein varies with its environment	311
8.3.4	Electrophoresis can give a sensitive measure of protein composition	312
8.4	Self-assembly of amphiphiles	315
8.4.1	Emulsions form when amphiphilic molecules reduce the oil–water interface tension	315
8.4.2	Micelles self-assemble suddenly at a critical concentration	317
8.5	Excursion: On fitting models to data	321
8.6	Self-assembly in cells	322
8.6.1	Bilayers self-assemble from two-tailed amphiphiles	322
8.6.2	Vista: Macromolecular folding and aggregation	327
8.6.3	Another trip to the kitchen	330
	The big picture	332
	Track 2	335
	Problems	337

Part III Molecules, Machines, Mechanisms

Chapter 9 | Cooperative Transitions in Macromolecules 341

9.1	Elasticity models of polymers	342
9.1.1	Why physics works (when it does work)	342
9.1.2	Four phenomenological parameters characterize the elasticity of a long, thin rod	344
9.1.3	Polymers resist stretching with an entropic force	347
9.2	Stretching single macromolecules	350
9.2.1	The force–extension curve can be measured for single DNA molecules	350
9.2.2	A two-state system qualitatively explains DNA stretching at low force	352

9.3	Eigenvalues for the impatient	354
9.3.1	Matrices and eigenvalues	354
9.3.2	Matrix multiplication	357
9.4	Cooperativity	358
9.4.1	The transfer matrix technique allows a more accurate treatment of bend cooperativity	358
9.4.2	DNA also exhibits linear stretching elasticity at moderate applied force	361
9.4.3	Cooperativity in higher-dimensional systems gives rise to infinitely sharp phase transitions	363
9.5	Thermal, chemical, and mechanical switching	363
9.5.1	The helix–coil transition can be observed by using polarized light	364
9.5.2	Three phenomenological parameters describe a given helix–coil transition	366
9.5.3	Calculation of the helix–coil transition	369
9.5.4	DNA also displays a cooperative “melting” transition	373
9.5.5	Applied mechanical force can induce cooperative structural transitions in macromolecules	375
9.6	Allostery	376
9.6.1	Hemoglobin binds four oxygen molecules cooperatively	376
9.6.2	Allostery often involves relative motion of molecular subunits	379
9.6.3	Vista: Protein substates	380
	The big picture	382
	Track 2	384
	Problems	396

Chapter 10

Enzymes and Molecular Machines

401

10.1	Survey of molecular devices found in cells	402
10.1.1	Terminology	402
10.1.2	Enzymes display saturation kinetics	403
10.1.3	All eukaryotic cells contain cyclic motors	404
10.1.4	One-shot machines assist in cell locomotion and spatial organization	407
10.2	Purely mechanical machines	409
10.2.1	Macroscopic machines can be described by an energy landscape	409
10.2.2	Microscopic machines can step past energy barriers	413
10.2.3	The Smoluchowski equation gives the rate of a microscopic machine	415

- 10.3 Molecular implementation of mechanical principles 422
 - 10.3.1 Three ideas 423
 - 10.3.2 The reaction coordinate gives a useful reduced description of a chemical event 423
 - 10.3.3 An enzyme catalyzes a reaction by binding to the transition state 425
 - 10.3.4 Mechanochemical motors move by random-walking on a two-dimensional landscape 431
- 10.4 Kinetics of real enzymes and machines 432
 - 10.4.1 The Michaelis–Menten rule describes the kinetics of simple enzymes 433
 - 10.4.2 Modulation of enzyme activity 436
 - 10.4.3 Two-headed kinesin as a tightly coupled, perfect ratchet 437
 - 10.4.4 Molecular motors can move even without tight coupling or a power stroke 446
- 10.5 Vista: Other molecular motors 451
 - The big picture 451
- Track 2 455
- Problems 464

Chapter 11

Machines in Membranes

469

- 11.1 Electroosmotic effects 469
 - 11.1.1 Before the ancients 469
 - 11.1.2 Ion concentration differences create Nernst potentials 470
 - 11.1.3 Donnan equilibrium can create a resting membrane potential 474
- 11.2 Ion pumping 476
 - 11.2.1 Observed eukaryotic membrane potentials imply that these cells are far from Donnan equilibrium 476
 - 11.2.2 The Ohmic conductance hypothesis 478
 - 11.2.3 Active pumping maintains steady-state membrane potentials while avoiding large osmotic pressures 481
- 11.3 Mitochondria as factories 486
 - 11.3.1 Busbars and driveshafts distribute energy in factories 487
 - 11.3.2 The biochemical backdrop to respiration 487
 - 11.3.3 The chemiosmotic mechanism identifies the mitochondrial inner membrane as a busbar 491
 - 11.3.4 Evidence for the chemiosmotic mechanism 492
 - 11.3.5 Vista: Cells use chemiosmotic coupling in many other contexts 496

- 11.4 Excursion: “Powering up the flagellar motor” by H. C. Berg and D. Fung 497
 - The big picture 499
- Track 2 501
- Problems 503

Chapter 12 | Nerve Impulses 505

- 12.1 The problem of nerve impulses 506
 - 12.1.1 Phenomenology of the action potential 506
 - 12.1.2 The cell membrane can be viewed as an electrical network 509
 - 12.1.3 Membranes with Ohmic conductance lead to a linear cable equation with no traveling wave solutions 514
- 12.2 Simplified mechanism of the action potential 518
 - 12.2.1 The puzzle 518
 - 12.2.2 A mechanical analogy 519
 - 12.2.3 Just a little more history 521
 - 12.2.4 The time course of an action potential suggests the hypothesis of voltage gating 524
 - 12.2.5 Voltage gating leads to a nonlinear cable equation with traveling wave solutions 527
- 12.3 The full Hodgkin–Huxley mechanism and its molecular underpinnings 532
 - 12.3.1 Each ion conductance follows a characteristic time course when the membrane potential changes 532
 - 12.3.2 The patch clamp technique allows the study of single ion channel behavior 536
- 12.4 Nerve, muscle, synapse 545
 - 12.4.1 Nerve cells are separated by narrow synapses 545
 - 12.4.2 The neuromuscular junction 546
 - 12.4.3 Vista: Neural computation 548
 - The big picture 549
- Track 2 552
- Problems 553

Epilogue 557

Appendix A | Global List of Symbols and Units 559

- Notation 559
- Named quantities 560
- Dimensions 565
- Units 565

Appendix B	Numerical Values	569
	Fundamental constants	569
	Magnitudes	569
	Specialized values	571
Appendix C	Additional Problems	575
	Problems for Chapter 1	575
	Problems for Chapter 2	577
	Problems for Chapter 3	578
	Problems for Chapter 4	579
	Problems for Chapter 5	584
	Problems for Chapter 6	586
	Problems for Chapter 7	588
	Problems for Chapter 8	592
	Problems for Chapter 9	594
	Problems for Chapter 10	596
	Problems for Chapter 11	602
	Problems for Chapter 12	604
	Credits	607
	Bibliography	609
	Index	623

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.

In the past few years, I have attended many conferences and seminars. Increasingly, I have found myself surrounded not only by physicists, biologists, chemists, and engineers, but also by physicians, mathematicians, and entrepreneurs. These people come together to learn from one another, and the traditional academic distinctions between their fields are becoming increasingly irrelevant to this exciting work. I want to share some of their excitement with you.

I began to wonder how this diverse group managed 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.

I also realized that my own undergraduate education had postponed the introduction of many of the basic ideas to the last year of my degree (or even later) and that 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. In part this reflected their own compartmentalized education: The physics students wanted to read the biology part and see it integrated with their other knowledge; the biology students wanted the reverse. To our amazement, we found that the course became popular with students at all levels from sophomore to third-year graduate, with the latter digging more deeply into the details. 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 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. Now, as we begin 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 life scientists 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 decade or two 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. At the same time, even some mechanisms not necessarily used by Nature have proved to be of immense technological value.

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, *The Hunting of the Snark*

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:

1. When possible, *relate the ideas to everyday phenomena*.
2. *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*.
3. *No black boxes*. The dreaded phrase “it can be 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.
4. *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.

Many chapters contain a section titled “Excursion.” These sections lie outside the main story line. Some are short articles by leading experimentalists about experiments they did. Others are historical or cultural essays. There are also two appendices. Please take a moment now to check them. 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 immensely sophisticated armamentum 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 perform and 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 the last decade, giving unprecedented opportunities for indirectly 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. Another helpful resource is the book by Shankar (Shankar, 1995).¹

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.

¹See the Bibliography at the back of this book.

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.

T₂ 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 new printing of *Biological Physics* includes updated versions of the beautiful art by David Goodsell, reflecting recent advances in structural biology.

A few years ago, 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.

Around the same time, many of my friends at other universities were beginning to work in this field and were keenly interested in teaching a course, but they felt uncomfortable with the existing texts. Some were brilliant but decades old; none seemed to cover the beautiful new results in molecular motors, self-assembly, and single-molecule manipulation and imaging that were revolutionizing the field. My friends and I were also daunted by the vastness of the literature and our own limited penetration of the field; we needed a synthesis. This book is my attempt to answer that need.

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.

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: $\boxed{T_2}$. 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 calculus and calculus-based physics, and a 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*, available from W. H. Freeman and Company. 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

<http://www.whfreeman.com/biologicalphysics>

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 42-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.
- 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 toolbox 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 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, some students take my course *after* courses in statistical physics or physical chemistry; they tell me that 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. Your colleagues may enjoy two recent eloquent articles on this subject (Alberts, 1998;

Hopfield, 2002), and the comprehensive NRC report (National Research Council, 2003). 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.