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Biological Physics: Contents and Preface

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

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Abstract

Contents; To the Student; To the Instructor

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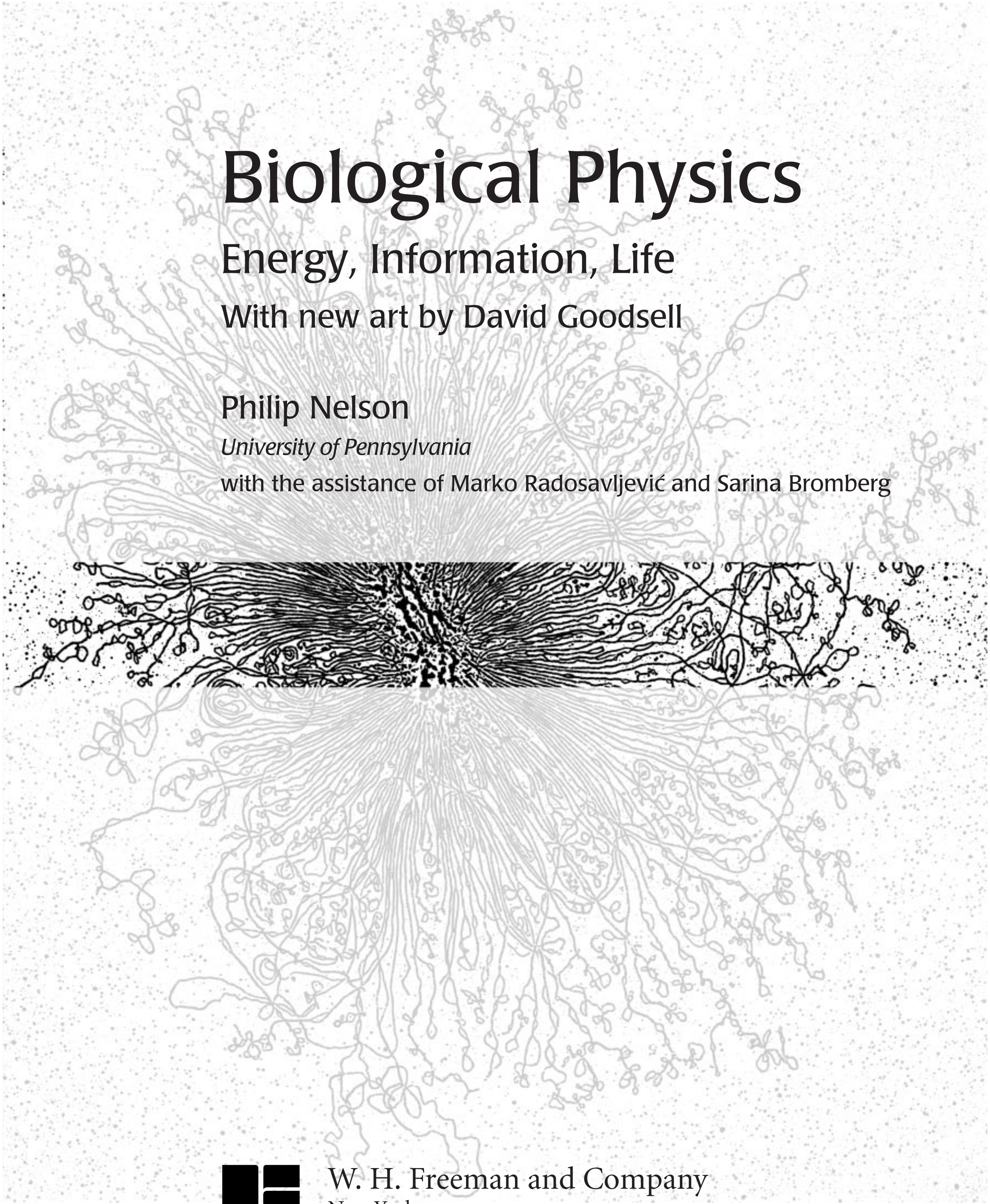

Biological Physics

Energy, Information, Life

With new art by David Goodsell

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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

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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.

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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!

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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.

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[1] See 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.

$\boxed{T_2}$ 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 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.

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- 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 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 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.

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