

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, 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 structural 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. 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.² 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.

¹See the Bibliography at the back of this book.

²In a similar vein, do not, under any circumstances, read “To the Instructor.”