To the instructor

Physicist: "I want to study the brain. Tell me something helpful."
Biologist: "Well, first of all, the brain has two sides. . . ."
Physicist: "Stop! You've told me too much!"
— V. Adrian Parsegian

This book is the text for a course that I have taught for several years to undergraduates at the University of Pennsylvania. The class mainly consists of second- and third-year science and engineering students who have taken at least one year of introductory physics and the associated math courses. Many have heard the buzz about synthetic biology, superresolution microscopy, or something else, and they want a piece of the action.

Many recent articles stress that future breakthroughs in medicine and life science will come from researchers with strong quantitative backgrounds, and with experience at systems-level analysis. Answering this call, many textbooks on "Mathematical Biology," "Systems Biology," "Bioinformatics," and so on have appeared. Few of these, however, seem to stress the importance of physical models. And yet there is something remarkably—unreasonably—effective about physical models. This book attempts to show this using a few case studies.

The book also embodies a few convictions, including[1]

- The study of living organisms is an inspiring context in which to learn many fundamental physical ideas—even for physical-science students who don't (or don't yet) intend to study biophysics further.
- The study of fundamental physical ideas sheds light on the design and functioning of living organisms, and the instruments used to study them. It's important even for life-science students who don't (or don't yet) intend to study biophysics further.

In short, this is a book about how *physical science and life science illuminate each other.*

I've also come to believe that

- Whenever possible, we should try to relate our concepts to familiar experience.
- All science students need some intuitions about probability and inference, in order to make sense of methods now in use in many fields. These include likelihood maximization and Bayesian modeling. Other universal topics, often neglected in undergraduate syllabi, include the notion of convolution, long-tail distributions, feedback control, and the Poisson process (and other Markov processes).

[1]See also "To the Student."

- Algorithmic thinking is different from pencil-and-paper analysis. Many students have not yet encountered it by this stage of their careers, yet it's crucial to the daily practice of almost every branch of science. Recent reports have commented on this disconnect and recommended changes in curricula (e.g., Pevzner & Shamir, 2009; National Research Council, 2003). The earlier students come to grips with this mode of thought, the better.
- Students need explicit discussions about Where Theories Come From, in the context of concrete case studies.

This book is certainly not intended as a comprehensive survey of the enormous and protean field of Biophysics. Instead, it's intended to develop the *skills and frameworks* that students need in many fields of science, engineering, and applied math, in the context of understanding how living organisms manage a few of their remarkable abilities. I have tried to tell a limited number of stories with sufficient detail to bring students to the point where they can do research-level analysis for themselves. I have selected stories that seem to fit a single narrative, and that seem to open the most doors to current work. I also tried to stick with stories for which the student can actually do all the calculations, instead of resorting to "Smith has shown. . . ."

Students in the course come from a wide range of majors, with a correspondingly wide range of backgrounds. This can lead to some tricky, yet valuable, cross-cultural moments, like the one in the epigraph to this section. I have found that a little bit of social engineering, to bring together students with different strengths, can start the process of interdisciplinary contact at the moment when it is most likely to become a habit.

Ways to use this book

Most chapters end with "Track 2" sections. Some of these contain material appropriate for students with more advanced backgrounds. Others discuss topics that are at the undergraduate level, but will not be needed later in the book. They can be discussed a la carte, based on your and the students' interests. The main, "Track 1," sections do not rely on any of this material. Also, the *Instructor's Guide* contains many additional bibliographic references, some of which could be helpful for starting projects based on primary literature.

This book could serve as the basis of a course on the science underpinning contemporary biological physics. Or it can be used as a supplement in more specialized courses on physics, biophysics, or several kinds of engineering or applied math. Although Track 1 is meant as an undergraduate course, it contains a lot of material not generally included in undergraduate physics curricula. Thus, it could easily form the basis of a graduate course, if you add all or part of Track 2, and perhaps some reading from your own specialty (or work cited in the *Instructor's Guide*).

This book is not a sequel to my earlier one (Nelson, 2014). Indeed there is very little overlap between these books, which partly explains why certain topics are not covered here. Still other topics will appear in a forthcoming book on light, imaging, and vision. A few of the many other recent books with overlapping goals are listed in "To the student"; others appear at the ends of chapters.

There are many ways to organize the material: by organism type, by length scale, and so on. I have tried to arrange topics in a way that gradually builds up the framework needed to understand an important and emblematic system in Chapter 11.

Computer-based assignments

The difference between a text without problems and a text with problems is like the difference between learning to read a language and learning to speak it.
—Freeman Dyson

All of the problems set in this book have been tested on real students. Many ask the student to use a computer. One can learn some of the material without doing this, but I think it's important for students to learn how to write their own short codes, from scratch. It's best to do this not in the vacuum of a course dedicated to programming, but in the context of some problems of independent scientific interest—for example, biophysics. The book's companion Web site features a collection of real experimental datasets to accompany the homework problems. Many reports stress the importance of students working with such data (for example, see National Research Council, 2003).

To do research, students need skills relevant for data visualization, simulation of random variables, and handling of datasets, all of which are covered in this book's problems. Several general-purpose programming environments would work well for this, depending on your own preference, for example, *Mathematica*®, MATLAB®, Octave, Python, R, or Sage. Some of these are free and open source. It's hugely motivating when that beautiful fit to data emerges, and important for students to have this experience early and often.

In my own course, many students arrive with no programming experience. A separate *Student's Guide* gives them some computer laboratory exercises and other suggestions for how to get started. The *Instructor's Guide* gives solutions to these exercises, and to the Problems and Your Turn questions in this book. Keep in mind that programming is very time consuming for beginners; you can probably only assign a few of the longer problems in a semester, and your students may need lots of support.

Classroom demonstrations

One kind of experiential learning is almost unique to physical science classes: We bring a piece of apparatus into the class and show the students some surprising *real* phenomenon—not a simulation, not a metaphor. The *Instructor's Guide* offers some suggestions for where to give demonstrations.

New directions in education

Will life-science students really need this much background in physical science? Although this is not a book about medicine per se, nevertheless many of its goals mesh with recent guidelines for the preparation of premedical students, and specifically for the revised MCAT exam (American Association of Medical Colleges, 2014):[2]

[2] See also American Association of Medical Colleges / Howard Hughes Medical Institute, 2009. Similar competencies are listed in the context of biology education in another recent report

1. “Achieving economies of time spent on science instruction would be facilitated by breaking down barriers among departments and fostering interdisciplinary approaches to science education. Indeed, the need for increased scientific rigor and its relevance to human biology is most likely to be met by more interdisciplinary courses.”
2. Premedical students should enter medical school able to
   - “Apply quantitative reasoning and appropriate mathematics to describe or explain phenomena in the natural world.”
   - “Demonstrate understanding of the process of scientific inquiry, and explain how scientific knowledge is discovered and validated,” as well as “knowledge of basic physical and chemical principles and their applications to the understanding of living systems.”
   - “Demonstrate knowledge of how biomolecules contribute to the structure and function of cells.”
   - “Apply understanding of principles of how molecular and cell assemblies, organs, and organisms develop structure and carry out function.”
   - “Explain how organisms sense and control their internal environment and how they respond to external change.”
3. At the next level, students *in* medical school need another set of core competencies, including an understanding of technologies used in medicine.
4. Finally, practicing physicians need to explain to patients the role of complexity and variability, and must be able to communicate approaches to quantitative evidence.

This book may be regarded as showing one model for how physical science departments can address these goals in their course offerings.

Standard disclaimers

This is a textbook, not a monograph. Many fine points have been intentionally banished to Track 2, to the *Instructor's guide*, or even farther out into deep space. The experiments described here were chosen simply because they illustrated points I needed to make. The citation of original works is haphazard. No claim is made that anything in this book is original. No attempt at historical completeness is implied.

(American Association for the Advancement of Science, 2011), for example, “apply concepts from other sciences to interpret biological phenomena,” “apply physical laws to biological dynamics,” and “apply imaging technologies.”