Systems Biology for 21st-Century Quantitative Scientists

Review of *Physical Models of Living Systems*, by Philip Nelson; 2015; W. H. Freeman (New York); ISBN-13: 978-1-4641-4029-7

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INTRODUCTION

Physical Models of Living Systems is a relatively short book compared with typical biological science books. It is unique in its quantitative view toward biology, tailored especially (albeit not exclusively) to those with training in physics and related disciplines. In an era of explosive development in the biological sciences, this is a desirable viewpoint to adopt, especially given the new professional opportunities offered by the rapidly evolving fields of modern biology and systems science.

In some aspects, biology in the 21st century seems to face similar developments and challenges as chemistry 100 years ago. Inclusion of quantitative, physics-based approaches in chemistry education and research led to the development of physical chemistry as an explicit core area and is today reflected in any form of chemistry education. A similar trend is now observed in biology and has attracted to the life sciences large numbers of scientists from quantitative science areas such as mathematics, physics, chemistry, engineering, and computer science. In turn, the contributions made by those scientists have made biological methodology and understanding more quantitative. This positive-feedback loop reinforces the synergy between the development of quantitative biological science and the influx of quantitative scientists to biology.

The new wave of systems biology in the early 21st century was accompanied by the publication of many textbooks. *Physical Models of Living Systems* is one of them. It presents an unusual selection of examples ranging from molecular to epidemiological phenomena, and it attempts to associate these examples elegantly with analogous processes from physics whenever this is possible. The author is renowned scientist Philip Nelson, a physicist by training and a biophysicist by profession, active in teaching and research. His previous biophysics textbook, *Biological Physics* (Nelson, 2013), published a little more than a decade ago, has received acclaim from the biophysics community (Dobson, 2004). Though the two books are unrelated in scope and subject matter, similar organizational principles are adopted in both. That said, the author carried forward some noteworthy and well-conceived "signature" structural elements, like the "Signpost" preamble to every chapter.

Most textbooks in biophysics focus on introducing the body of knowledge by using an approach similar to that of most biochemistry textbooks. While it is essential to teach factual knowledge in any scientific subject, of course, this is no longer sufficient, especially for those thinking of extending their expertise from the physical into the biological sciences or vice versa. We must also teach how to apply the theory and principles to real-world problems. Therefore, a widening gap can be felt between standard-style textbooks and actual research conducted by professional scientists. In contrast to such texts, *Physical Models of Living Systems* attempts to connect the information found in the standard biophysical textbooks with current academic research topics. In fact, the book feels personal in its selection of topics and the training journey on which it takes its readership. In our opinion, the combination of this uniqueness

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with technical accuracy makes the book a noteworthy and valuable addition to resources for advanced biophysics education.

CONTENT: SELECTED MODERN BIOLOGY EXAMPLES, WITH SOME INTERSPERSED "CLASSICS"—AND A HEALTHY DOSE OF BAYESIAN STATISTICS TO GO WITH IT

The book presents 11 chapters, accompanying end-of-chapter problem sets, and a set of appendices in just 330 pages. However, readers should not be fooled by this relatively small size, as the book conveys rich information, is clearly structured, and provides comprehensive data sets that are subject to analysis in the problem sections in the form of a free and uncomplicated Web download. (Note that the companion website is www.macmillanlearning.com/Catalog/studentresources/nelsonphysicalmodels1e). A teacher companion website is also offered, with additional information exclusively for instructors.

After an exquisitely motivating anecdote told beautifully in the prologue, in which insight into HIV infection dynamics was elegantly drawn from analogies with liquid inflow and outflow calculations, the first two chapters pursue this story further to introduce some basic principles of modeling in part 1 ("First Steps"). Part 2 ("Randomness in Biology," five chapters) focuses on introducing important statistics background material needed for modeling biological processes. After this necessarily more "standard" treatment, reward awaits in Part 3 ("Cellular Processes"), in which a selection of worked examples that are amenable to quantitative or semiquantitative modeling allows previously acquired knowledge to be put to use while more principles are introduced in passing. This journey through worked examples—including their selection—contributes to the book's uniqueness and suitability for interdisciplinary and cross-disciplinary (re)training.

Biochemists trained "classically" (say, before 2000) will recognize some paradigmatic teaching examples, like the genetic switch system used in lambda bacteriophages and the *trp* operon of *Escherichia coli*. However, avoiding the traditional biochemistry treatment, Nelson touches upon them almost as an aside, alongside other examples and embedded in the context of the aspects of cellular processes he chooses to discuss: randomness, feedback control, switches, and oscillators. This "personal touch" helps keep the text fresh and unexpected, although it also makes it challenging. With regard to biological background, for example, independent additional reading and interest will generally be required to completely understand all the very diverse examples Nelson uses, especially for readers who did not have advanced biology courses in high school or college. Dedicated students, whether they are working toward a new profession in modern biology or simply embarking on a self-motivated cross-disciplinary journey, will not shy away from this challenge and will also greatly appreciate how far this new text "stretches" into new biology topics, including synthetic biology.

Ambitious and interdisciplinary technical texts benefit particularly from experienced authors and publishers, and this book is a good example of this. Nelson uses structural style elements consistently, which is helpful without being overly rigid. Each chapter is introduced by a "Signpost" preamble and ends with a short recap of the "Big Picture," "Key Formulas," and a "Further Reading" list. Information for those looking for more advanced material is appended in "Track 2" sections that are not required for the subsequent "Problem Set" sections, except for questions that are also labeled accordingly. Illustrations are depicted in thumbnail format in the page margin wherever they are referenced, even if the full-sized version is found elsewhere. Because this book is written as a textbook (not a research text), only limited space is available in each example for critical discussion of alternative models. However, Nelson devotes ample space to explaining the vital importance of clearly defining the assumptions underpinning each model, the perils of overfitting in quantitative modeling and simulation, and the option to quickly use dimensions (units) to verify the consistency of calculations, an approach often applied in practice, to flag avoidable errors without much extra effort.

BEST TARGET READERSHIP: SCIENTISTS AND ENGINEERS OF ALL AGES WITH ADVANCED TRAINING IN PHYSICS

A list of books introduced in the preface by the author offers a good overview regarding prior knowledge that is recommended, generally, for effectively using this book. The list covers a wide range of sciences, from biology through mathematics and chemistry to computer science. Throughout the book, the author exemplifies and discusses how quantitative skills (mathematics and computation) can be applied effectively to constructing quantitative models for complex biological problems. Prospective readers should be aware that, in doing so, the author uses various quantitative skills that likely exceed those taught in the curricula of typical undergraduate biology and chemistry programs in the U.S. higher education system.

With chemistry and biology majors, we would recommend the following prerequisite knowledge based on "average" college/university students and curricula standards that we are familiar with in the United States. (A more cursory use of the book may, of course, be possible with less preliminary knowledge—and, conversely, exceptionally bright students will often be able to synthesize background knowledge they are missing just from context.) As a prerequisite in biology, the student needs at least one semester of a cell and molecular biology course in addition to an introductory college biology course. As a physical chemistry prerequisite, we expect that it will be sufficient to have taken at least one semester of a biophysical or physical chemistry course in which basic thermodynamics and chemical kinetics are covered in the context of biochemistry. Similarly, as long as one has a solid understanding of calculus-based introductory college physics together with the aforementioned prerequisites, we believe devoted students will not strictly require additional advanced senior-level physics courses. Of course, more advanced knowledge and understanding in biology/chemistry/physics will always be beneficial, and it also will not render this text boring (noteworthy for teachers considering this text for their courses).

Probably the most challenging area of prerequisite for many "average" students will be mathematics, especially for those whose major academic background so far has been in the biological sciences, in which the influx of modern biological knowledge that emerged in the past decade has not necessarily included the necessary additional applied mathematics training. Specifically, consistent with most biological phenomena being dynamic and stochastic, two major mathematical topics are encountered throughout the entire book: differential equations and probability theory. To prepare potential students from "classic" biology curricula, we would recommend one semester of a differential equations course followed by an introductory course in calculus-based probability theory as prerequisites for this book. The author suggests in the preface the classic *Basic Training in Mathematics: A Fitness Program for Science Students* (Shankar, 1995), which some students will have encountered, as a complementary book, and which in our view will provide sufficient mathematical background, especially for differential equations. Regarding probability theory, we think that *Chance in Biology: Using Probability to Explore Nature* (Denny and Gaines, 2000), also listed in the suggested reading material by the author, definitely provides a sufficient background on probability for understanding the textbook. However, we also note that Nelson devotes a considerable portion of the book (part 2) to introducing aspects of randomness, Bayesian statistics, and value distributions, possibly similar in scope to material covered in some specialist courses in biophysics, bioinformatics, systems biology/chemistry, or other science and engineering courses. Thus, some readers may find themselves sufficiently equipped for these topics without having taken a formal course in probability theory.

Similarly, computational programming is a central theme of this book and is assumed to be a skill of interest to the students engaging in solving the problem sets. Nelson shows how computational programming can be used effectively in modeling biological systems at the cellular and molecular levels. While he mentions that many students without programming experience enroll in his course, we would caution instructors in biology and chemistry programs that they will definitely need to teach basic programming skills alongside this book unless their students have some prior programming experience. Computer programming tools suggested by the author are Mathematica, Matlab, Octave, Python, R, and Sage. The website accompanying the book provides several resources for students, including a free downloadable Matlab guide for students (Nelson and Dodson, 2015), coauthored with Tom Dodson, that will provide basic skills in applying Matlab to the study of the book. In addition, the author recently also copublished with Jesse M. Kinder a specialist book, *A Student's Guide to Python for Physical Modeling* (Kinder and Nelson, 2015), which can be considered as (independent) additional material for teaching programming or encouraging students to acquire these skills independently.

For undergraduate readers, we believe the prerequisites above are a minimum, and not all undergraduate biology programs offer the corresponding courses within their curricula. Therefore, in our view, this book is not generally appropriate as a textbook for the majority of undergraduate students who major in biology alone. In contrast, this book may be used effectively in a senior-level course within biological science, physical science, interdisciplinary science, and engineering programs that focus on quantitative biology. (Such programs can be found under many names—biophysics, systems biology, computational biology, or bioinformatics, to name just a few.) Finally, when using this book at the undergraduate level, particularly at public and/or low-income institutions, one must also carefully consider the cost and availability of this and additional supplementary texts students may require in independent study alongside these advanced topics and costs associated with licenses for commercial computer software (e.g., Matlab). We also noticed that in the preface the author implies that this book could be a useful resource for premedical students preparing for the MCAT. Even though the MCAT has emphasized quantitative and analytical skills since 2015, the skills needed for the MCAT are at a level far below that of this book.

Another group of "students" should be strongly considered as a prime target audience for this excellent and inspiring book. Beginning graduate students and professional researchers in academe or industry, university faculty, and "mature students" who are either planning to pursue research in computational modeling of physical processes in biology or just looking to stimulate their intellect by venturing away from their specialty for a little while will all greatly enjoy this journey. We know we did.

CONCLUSION

In our view, this overall excellent book will be of best use in a capstone class in specialized undergraduate biological science programs that include strong physics training, such as computational biology, systems biology, biophysics, or mathematical biology. In addition, many graduate students in those areas will enjoy the different and stimulating perspective that the book offers, and its format makes it amenable to self-study or faculty-assisted study. Possibly the most exciting place for this book, however, will be in the offices of professional or postgraduate researchers and teachers, who find themselves faced with the new challenges and excitement of an increasingly quantitative modern view of the biological world and the desire to immerse themselves in these challenges by conceiving, and/or even just enjoying, the intriguing examples of quantitative physical views of living systems that are exquisitely presented in this text.

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