

Feature Book Review

Physics in a Beautiful Context

Review of: *Physical Biology of the Cell*, by Rob Phillips, Jane Kondev, and Julie Theriot; 2009; 807 pp; Garland Science, Taylor & Francis Group (New York, NY); ISBN 978-0-8153-4163-5

Reviewed by Raquell M. Holmes, Center for Cell Analysis and Modeling, University of Connecticut Health Center, Farmington, CT 06032

INTRODUCTION

Like many of the readers, my training during college and graduate school focused on experimental methods for studying cellular, molecular, and developmental systems. This training included little formal education in physics and mathematics beyond the minimal requirement, a single semester of calculus and one to two semesters of physics. If the reader is anything like me, we are now wishing that our experience included a much stronger introduction to the fundamental principles and rules of physics and mathematics, particularly as they apply to biology.

Physical Biology of the Cell, written by Rob Phillips, Jane Kondev, and Julie Theriot and illustrated by Nigel Orme, bridges the fields of biology and physics. This poetically written book is one of an increasing number of texts attempting to fill the gap in resources available for understanding cellular systems from the vantage of mathematics and physics. The authors identify three audience types: the physicist curious about biology, biologists curious about physics, and those interested in learning both. However, this is not a book for novices, since it assumes that the reader has a background in at least one, if not both, of these fields. As a result, the authors reference biological structures and physical examples as if they are familiar, if not well-known, quantities. This makes *Physical Biology of the Cell* most clearly appropriate for use in an advanced physics course for undergraduates who have taken cell biology. The examples chosen throughout the text to describe biological phenomena or systems are drawn from physics. Without familiarity with

the physics models, readers with a biology background may lack the intuitions associated with the physics references, and therefore need to learn simultaneously physics and math presented. Consequently, schools developing curricula in biophysics or mathematical biology may want to consider this book for capstone classes.

The book is written as four parts: “The Facts of Life,” “Life at Rest,” “Life in Motion,” and “The Meaning of Life,” covering the essentials of cell and molecular biology; understanding mechanical equilibrium at multiple scales; modeling dynamics of motion; and bioinformatics. Each section is filled with illustrations that add significantly to our ability to see the relationships between biology, physics and mathematics. The problem sets provided at the end of each chapter are useful for developing homework assignments. Special sections that add insights to each topic are distributed throughout the text. For example, “Estimates” helps readers brush up on estimates of biological quantities such as the amount of energy required from glucose carbon bonds to manufacture physical structures in the cell; “Experiments Behind the Facts” explains how methods such as fluorescence correlation spectroscopy and fluorescence redistribution after photobleaching are used to measure diffusive dynamics; “The Math Behind the Models” helps us understand the mathematics used to describe the physics, i.e., Taylor Series; and “Tricks Behind the Math” shares tips on simplifying mathematical descriptions through substitutions and equivalencies. These special sections are not evenly distributed throughout the four parts of the book. In fact, the number and distribution of the types of special sections seems to mirror an assumption that the readers are more comfortable with mathematical models than understanding the experiments that produce the data that are modeled.

The mathematics used in *Physical Biology of the Cell* goes from simple algebra to linear algebra (matrices, Eigen-values) and both ordinary and partial differential equations. Although the first equation is $\frac{1}{2}kx^2$, which describes a simple spring, the final equation is the steady state solution for a genetic switch: $f'(u^*)f^*(v^*) < 1$. To their credit, the authors do

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Address correspondence to: Raquell Holmes (rholmes@uchc.edu).

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List 1. Sample of notation and symbols used in text

Notation	Name	Meaning
Σ	Capital Sigma	A summation sequence
$n!$	Factorial	The value is equal to the number (n) times all the positive whole numbers less than it. $3! = 3 \times 2 \times 1$
Ω	Omega	Used to indicate states for any given object, typically identified as L
$\langle \dots \rangle$	Average	Used to indicate the average for an object
Π	Capital Pi	Multiplication sequence, similar to Capital Sigma
F	Force	Bold indicates a vector

an excellent job of introducing mathematical notation (List 1). As a result, instead of cringing when a new Greek symbol is introduced, you actually begin to search for words that give you a new understanding of the math presented. It is nice that such descriptions are built directly into the discussion. Although the notation is not always consistently explained, the willingness to describe such notation speaks to the authors' desire to create a way for readers new to this physics and mathematics to develop a better understanding of both.

The Beauty

Part I of the book, "The Facts of Life," contains biology and physical/mathematical concepts that could be reasonably expected for cell and molecular biology students. The authors spend the first few chapters of the book focusing on developing the readers' sense of scale for size and time with the bacteria *E. coli* as the standard unit for size (List 2). The biological time scales span across months of fly development to seconds and nanoseconds for ion transport and enzyme catalysis. With quantitative intuitions for size and time, it is then possible to better evaluate which forces and reactions of biological systems can be ignored, or are significant and need to be accounted for in a mathematical model.

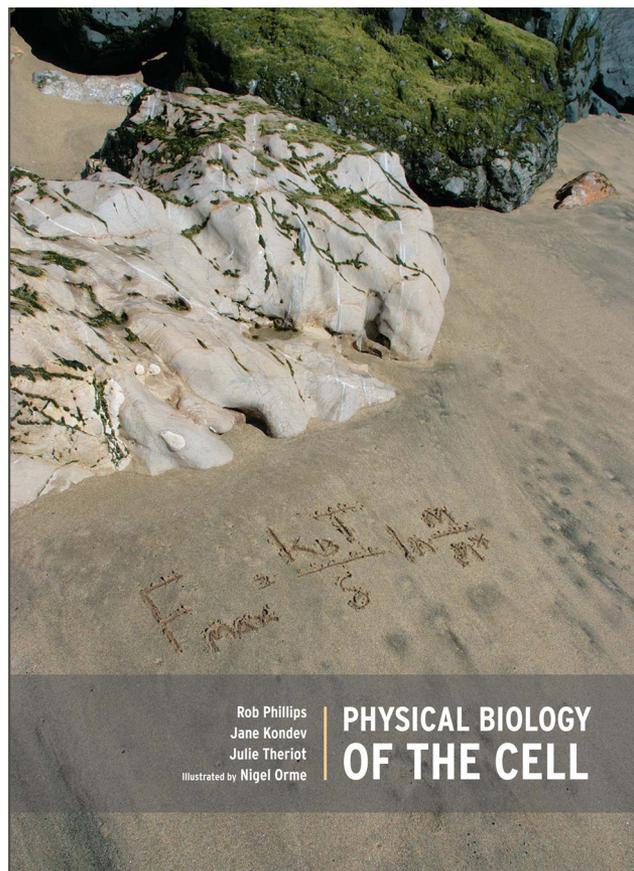
The illustrations are deftly used to highlight the variety of models scientists use as functional abstractions of complex biological objects. These models describe physical properties, and do not require computers to be understood or solved. For example, the first mathematical model introduced is the spring, a physical object whose behavior is characterized by harmonic oscillations. The mathematical model that describes the behavior of this simple harmonic oscillator is $\frac{1}{2}kx^2$.

List 2. *E. coli* measurements used as base for standard estimates^a

Quantity of interest	Symbol	Rule of thumb
Cell volume	$V_{E.coli}$	$\approx 1 \text{ um}^3$
Cell cycle time	$t_{E.coli}$	$\approx 3000 \text{ s}$
Genome length	$N_{bp}^{E.coli}$	$\approx 5 \times 10^6 \text{ bp}$

^a Extracted from Table 1.1 of *Physical Biology of the Cell*.

The allusion to a spring or to an oscillating system thus brings with it the association of the mathematical model. This is similar to saying a protein behaves like a single substrate enzyme whose behavior is characterized by Michaelis-Menten kinetics. This statement brings with it the mathematical model $v = v_{max} = \frac{[S]}{K_m + [S]}$. Yet, this same enzyme might be described by models of charge state or folding properties, each model abstraction with its own mathematical description. The challenge for readers then is to become familiar with the physics representations of familiar objects. For example, we can begin to see the circadian clock as an oscillating spring, and know that we can describe its behavior with the equation above.



The Energy Barrier

The requirement for physics and mathematics knowledge increases significantly in Parts Two and Three, respectively, "Life at Rest" and "Life in Motion." At the onset of Part Two, the authors take the time to introduce the reader to thermal energy. Thermal energy is discussed as a totality in terms of the Boltzmann constant times Temperature, $k_B T$ and is fundamental to the determination of the energy of a system, regardless of whether that system is a molecular bond, a protein, or a tissue. Thermal energy is the basis for statistical mechanics. Essentially, statistical mechanics takes into ac-

count the possible states of a system and determines which is most probable based on the fluctuations in thermal energy of those states.

Thermal energy is introduced by defining the conversion factor for $k_B T$ in relation to ATP. We learn that the carbon bonds and ATP of the glycolytic process can be viewed as $k_B T$ (thermal energy) in a different unit scale $k_B T = 0.6$ kcal/mol or $k_B T = 0.6$ kcal/mol. $k_B T = 2.5$ kJ/mol.

With the linkage between the thermal energy in physics and the chemical bonds of biology made, the authors proceed to look across cellular systems in Part Two by examining equilibrium, motion, and minimized energy states of biological structures. Fluctuations at the membrane due to cytoskeletal forces are used as a brief example of when one can consider a dynamic process to be in mechanical equilibrium. In Part Three, the authors look at dynamic systems involving biochemical reactions, diffusion, and membrane potentials.

From Part Two on, the text consistently makes use of functions, differential equations, vectors, and linear algebra. It is also at this point that I wish my skills in differentials, integration, and functions were better. The careful attention to explicit descriptions of mathematical principles and notations with numerous easy-to-recognize biological examples has me wanting to delve further into the text and examples. However, the authors' assumption that we are on mathematically familiar ground is a bit too early for this math-friendly, but differential-equation challenged reader.

Bioinformatics from a Different View

Part Four, "The Meaning of Life," covers the relatively more familiar topic of bioinformatics: the nature of sequences, homology, sequence comparisons, scoring weights, and probabilities. In these chapters, topics are presented in a less familiar way, by developing analogies and examples based on molecular energies, an approach in line with the statistical mechanics used throughout the book. This treatment is most visible in the section on molecular specificity and fidelity, which highlights that the specificity of molecular interactions exceeds what would be predicted

by a thermodynamic model. The authors continue to highlight the contributions of a statistical mechanics approach to understanding networks and dynamics and conclude with a call to the use and role of quantitative models in biology.

Challenges

The book provides passionate prose, beautiful figures, and illustrations of cell biology that begin with relatively simple mathematics followed with increasing dependence on deciphering functions, matrices, and other mathematics learned in linear algebra, third-semester calculus, and probabilities. This increased dependence on mathematics is consistent with the book's theme of physical biology. The very nature of physics is built on mathematical descriptions. Yet, the physics of statistical mechanics in this text is something learned in upper-level physics courses that are not commonly taken by biology majors. Although the book makes the math more accessible by embedding the mathematical descriptions and notation throughout the text, once the concepts are introduced, later chapters assume the reader has mastered them. This makes surfing or skipping chapters difficult and left me wishing for an electronic version that could be used to search for the first instance of the word or symbol. A glossary of the commonly used mathematical notation would eliminate the need to search for the initial description and be an additional tool for those of us still learning to master linear algebra, ordinary calculus, and calculus of variations. For those of us with less than a full year of calculus or physics (or with these courses in the ancient history section of our brains), the mathematics associated with the statistical mechanics is likely to be the energy barrier that must be overcome to make full use of the text. Yet, with that said, I believe any cellular, molecular biologist who looks at *Physical Biology of the Cell* will find biological images, experiments, and discussion related to one of their favorite systems. "The Facts of Life" and "Life as Motion" are particularly worthwhile to examine as complementary additions to existing curricula with an eye to providing students with quantitative views of biology.