

Biophysics Searching for Principles

William Bialek
Princeton U. Press, 2012. \$95.00
(640 pp.). ISBN 978-0-691-13891-6

The title of William Bialek's text, *Biophysics: Searching for Principles*, makes an important point: Even the top practitioners in the field do not completely agree on its main principles or where to find them. Many classic textbooks present biophysics as grounded in structural biology and biophysical chemistry, which focus on nucleic acids, proteins, lipids, and their assemblies. That view was memorably articulated by Adrian Parsegian in the PHYSICS TODAY article "Harness the hubris: Useful things physicists could do in biology" (July 1997, page 23). According to Parsegian, biophysicists should make themselves useful to biologists by starting at the bottom, modeling and cataloging the forces of interaction between small biomolecules, before tackling the big molecules—or the big problems—in biology.

However, not all biophysicists want to start on the bottom rung. As Robert Austin famously wrote in an accompanying counterpoint to the Parsegian article, "Forget that! I want to do the big problems. . . . Don't tell me that I should be a good little boy and work on sugars first." In that spirit, an increasing number of biophysics textbooks stake their claims on big problems in biology. Philip Nelson's *Biological Physics: Energy, Information, Life* (W. H. Freeman, 2003) presents the subject as the application of statistical physics to fundamental biological problems at the molecular and cellular levels. Uri Alon's *An Introduction to Systems Biology* (Chapman & Hall/CRC, 2006) explores the design principles that allow complex biological networks to regulate their own function. And *Physical Biology of the Cell* by Rob Phillips and coauthors (Garland Science, 2008) boldly rewrites much of cell biology in the language of physics.

Bialek's *Biophysics* seeks and articulates a set of physical principles that underlie the capture and processing of information by biological systems of all types. The John Archibald Wheeler/Battelle Professor of Physics at Princeton University, Bialek is easily one of the best-known physicists working in biology. He is highly regarded for his work on the encoding of information in

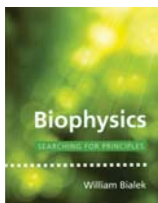
the nervous system and for his studies of noise and information in other signaling contexts such as gene regulatory networks and morphogenesis.

Drawing upon that work, *Biophysics* combines quantitative modeling with the analysis of laboratory data to explore themes of signal, noise, and information processing from the biomolecular scale up to the level of neurons and animals. The book arose from a set of lectures taught to physics graduate students and is naturally aimed at the same group. Consequently, students will need a solid grasp of graduate statistical physics (especially noise and fluctuations), basic quantum mechanics, and some Matlab skills. Each chapter contains many novel, intriguing, and challenging homework problems, usually mathematical and often open-ended.

At the outset, Bialek reviews some of the past successes of biological physics and argues that physicists can and will find interesting problems throughout biology. He then jumps into photon counting in vision, analyzing vision as a complex sequence of signal-processing steps, each highly optimized from a physics standpoint. Exploring vision through the principle of physical optimization makes for a fascinating thread that encompasses many decades' worth of ingenious and precise experiments and analysis.

On the topic of noise, Bialek develops the general principle that sensory and regulatory systems have mechanisms for managing thermal noise, particle number fluctuation, and other types of background, and that those mechanisms in many cases reduce noise almost to its fundamental physical limits. Examples include reaction dynamics in photosynthetic enzymes, bacterial chemotaxis, embryonic development, and bat echolocation.

Bialek also explores the distinction made in systems biology between robust and fine-tuned: Systems biology generally takes the view that reliable performance by a biological system arises robustly from good system design such as feedback control and will not depend on the precise values of underlying parameters such as reaction rates. Examples here include protein folding, DNA binding sites, the Hodgkin-Huxley equations, morphogen gradients, and chemotactic adaptation. And he presents the principle of efficient representation, the view that sensory systems represent and transmit the information that they gather in a way that is optimal, subject



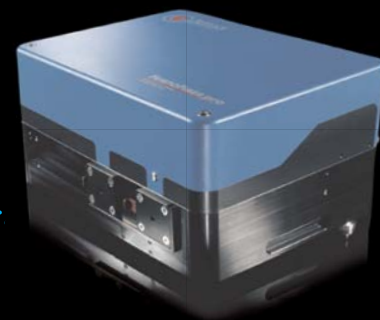
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to physical limits. This idea is made quantitative through information theory, which Bialek presents in tutorial fashion before exploring examples from such areas as embryogenesis, neural spike train encoding, bacterial growth, and animal learning.

Although *Biophysics* occasionally wanders into such well-trodden biophysical chemistry territory as alpha helices and hemoglobin cooperativity, the book makes no pretense of explaining biology and biochemistry. Even the 20 amino acids are not seen until halfway through the book. Experimental techniques are thinly described. This is not a book about the nuts and bolts. In fact many of the author's diagrams are so abstract or schematic that they bear little relation to the system's chemical or physical function or configuration as conventionally described. The physicist reader will not learn the language of biology. On the other hand, physicists who are seeking an exciting intellectual path through the complexity of biology will deeply appreciate Bialek's clear vision of the big ideas and his expert guidance through their many applications.

Stephen J. Hagen
University of Florida
Gainesville

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