books

When the life sciences get physical

An Introduction to Systems Biology
Design Principles of Biological Circuits

Uri Alon
Chapman & Hall/CRC/Taylor & Francis, Boca Raton, FL, 2007. $49.95 paper (301 pp.). ISBN 978-1-58488-642-6

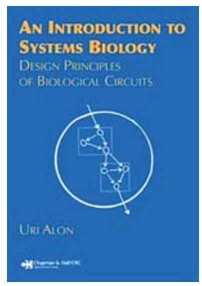
Systems Biology
Properties of Reconstructed Networks

Bernhard Ø. Palsson
Cambridge U. Press, New York, 2006. $75.00 (322 pp.). ISBN 978-0-521-85903-5

Reviewed by Nigel Goldenfeld

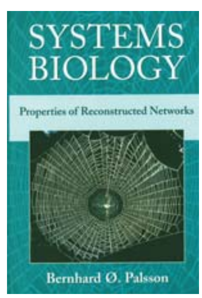
For some of us physicists, the recent explosion of interest in biology by our colleagues is something of a mystery—perhaps even a betrayal. Biology seems to offer none of the aesthetic elegance and beauty that is the hallmark of such cherished creations as the general theory of relativity and the standard model of strong, weak, and electromagnetic interactions. Neither does biology provide the breathtaking precision with which physical experiment and theory can agree in such phenomena as quantum electrodynamics or Josephson effects. And don't even think about summarizing all of biology on a T-shirt; biology textbooks, unlike those for physics, generally describe reactions and structures in monstrous detail, without an equation in sight. So why the allure of the subject among physicists? And what meaningful contributions can physical scientists make to the field?

One answer is the emergence of a new science of biological circuits, or systems biology, which has become advanced enough, both scientifically and promotionally, that textbooks are warranted. Uri Alon's *An Introduction to Systems Biology: Design Principles of Biological Circuits* and Bernhard Ø. Palsson's *Systems Biology: Properties of Reconstructed Networks* are two recent offerings by leaders in this new field. These texts deserve serious attention from any quantitative scientist or physicist who hopes to learn about modern biology. Both books are well written; each has a different focus. Thus they could be used together to create an accessible course for beginners, with the instructor's choice of topics from each book.



The books are a welcome departure from the typical biology textbook. First, they emphasize quantitative modeling rather than nomenclature; second, they concentrate on essentials of the modeling rather than on exhaustive lists of components that offer no meaningful integration; and third, the approaches described in the texts make nontrivial quantitative predictions that can be and have been verified.

Alon's book is the better place for physicists to start. It assumes no prior knowledge of or even interest in biology. Yet right from chapter 1 the author succeeds in explaining in an intellectually exciting way what the cell does and what degrees of freedom enable it to function. The book proceeds with detailed discussions of some of the key network motifs, circuit-element designs that are believed to be repeated over and over again in biological systems. Those motifs include autoregulation, feed-forward loops, positive-feedback loops, and kinetic proofreading. The discussions in all cases introduce the particular motif, use simple differential equations in most cases as a way to model it, and offer plenty of comparisons with experimental data.



Alon does not forget to ask a question physicists obsess over: Are any general physical principles at work in biology? Alon does not overplay that point but has included a nice chapter on robustness. He focuses on concrete examples such as chemotaxis and developmental pattern formation. He also devotes a chapter to explaining the precision with which biological processes can so accurately identify the right molecules amidst a sea of potentially confusing "wrong" targets. The basis of this process is kinetic proofreading, a concept first presented by physicist John Hopfield, and one that is based on simple nonequilibrium kinetics.

Alon ends his book with an epilogue on simplicity in biology. He draws the detailed strands together into an appealing and inspiring overview of biology. Without the preceding attention to biological detail, this exercise would be vacuous.

One final aspect of *An Introduction to Systems Biology* that must be mentioned is the wonderful set of exercises that accompany each chapter. The exercises range from elementary to advanced research areas. For example, chapter 9 contains problems on the error-minimization capabilities of the genetic code, which I and several other physicists, including Alon, are still elucidating. I would have liked to see evolution play a more central role in the text—for example, in a chapter of its own that amplifies the important comments in the epilogue about the evolution of modularity. Perhaps when it's time for the second edition, there will be enough concrete material to further justify including the topic.

Palsson's *Systems Biology* presents a completely different perspective. The book focuses less on principles and more on techniques for reconstructing detailed, elaborate, and predictive circuit models of biological systems. During the past 10 years these techniques have become feasible for entire organisms, thanks to the availability of fully sequenced genomes. It is now possible to map out the metabolic networks of bacteria such as *Escherichia coli* and simpler eukaryotes. However, other networks in organisms control other

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cellular processes, including transcription (writing out mRNA from DNA) and life-cycle events such as cell division and death. Systems biology will eventually need to deal with the systems of systems.

Palsson is a founder of systems biology and he presents an accessible account that is structured in three parts: reconstruction of biological networks from data, mathematical aspects of reconstruction, and results of the approach. Palsson's goal is to model the rate of reactions and the concentrations of the reactants. Without detailed information on kinetic constants, one can nevertheless make progress by focusing on steady states. The challenge is to enumerate what a physicist would call the phase diagram of a biological network as a function of external constraints such as resource availability and other factors, such as biomass generation, that express what biological systems may have evolved to optimize. The end-use of the modeling technique is metabolic engineering: How does a modification to the genome of an organism—by knocking out a particular gene, for example—affect the organism's operating state? Models, Palsson emphasizes, can drive discovery: When systems biology models yield predictions that disagree with experiment, one can pinpoint what aspects of the organism have not been properly represented or modeled. In this way, systems biology helps in the design of experiments that, in turn, lead to better models.

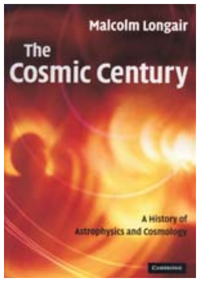
Systems Biology is a very readable introduction to the subject, even though some of the most promising results in the field became available after it had been published. The book's technical level is advanced undergraduate physics or engineering, but a higher level of scientific maturity will be needed to fully appreciate the thoughtful discussions about levels of description and the modeling enterprise in general. There are no exercises, although those will be forthcoming on a website dedicated to the book, according to the author.

Alon's and Palsson's books make it clear that this is an exciting time for biology. The authors expose readers to enough material that the research literature in quantitative systems biology should become accessible. Alon's book should become a standard part of the training of graduate students in biological physics; Palsson's will undoubtedly play a similar role for students of metabolic engineering and perhaps biological physics.

The Cosmic Century

A History of Astrophysics and Cosmology

Malcolm Longair
Cambridge U. Press, New York, 2006. $65.00 (545 pp.). ISBN 978-0-521-47436-8



Recent advances in physics and astronomy have brought about in our knowledge of the universe a revolution comparable to the one that occurred at the end of the 16th century and through the 17th century during the times of Tycho Brahe, Johannes Kepler, Galileo, and Isaac Newton. Since the first part of the 20th century, we have been able to answer some of the questions that humankind has always asked: How old is the universe, and how did it start? What makes stars evolve, shine, and die? And how do galaxies, planets, and elements form?

However, in the past 50 years the rate of astronomical discoveries has increased rapidly, thanks to powerful new observatories on the ground and in space. The entire range of wavelengths emitted by celestial objects, from radio waves to gamma rays, can now be observed. The data can be analyzed, stored, and distributed by powerful computers. So, what have we found? Perhaps the most striking result is that the universe appears to be filled predominantly with forms of energy and matter different from the normal baryonic matter of everyday objects. What determines the dynamics and the evolution of the universe is subject to natural laws that researchers do not yet fully comprehend. Once again astronomy is posing some of the most fundamental questions for physics.

In *The Cosmic Century: A History of Astrophysics and Cosmology*, Malcolm Longair has written a very timely book, directed toward students, researchers, and lecturers; I enjoyed experiencing all three roles while reading it. It is a lucid and in-depth presentation of the subject and introduces topics at various levels of complexity. *The Cosmic Century* is different from most books on astrophysics and cosmology that are either for the general public or for a specialized audience. The author covers the historical advances in the field with regard to their impact on the astrophysical worldview. In its 16 chapters describing observations and theory, the book takes us through the logical developments and the interactions between data and interpretation. At an even deeper level are the notes and appendixes to the chapters, in which Longair treats specific subjects in greater detail, often with the appropriate mathematics.

Longair is, in my opinion, uniquely qualified to write this tour de force. As a professor of natural philosophy and head of the Cavendish Laboratory at the University of Cambridge, he has conducted significant research in high-energy astrophysics, astrophysical cosmology, and the history of physics. He is a brilliant lecturer and prolific writer. Among his books are *Theoretical Concepts in Physics: An Alternative View of Theoretical Reasoning in Physics for Final-Year Undergraduates* (Cambridge U. Press, 1984) and *Galaxy Formation* (Springer, 1998). He has contributed to some of the major astronomical projects on the ground and in space, including the *Hubble Space Telescope*. His service on many of the committees involved in setting priorities for astronomical research has given him a wonderful insight into how modern astronomy is done and what it may offer as future advances.

Parts 1 and 2 of the book give a very useful account of the progress from astronomy to astrophysics in the last part of the 19th century by introducing the advances in spectroscopy and in the classification of stellar spectra. He summarizes the development of theories of stellar structure and evolution in a manner particularly useful for many physicists who have joined that subfield.

After describing the theoretical and observational advances of the early 20th century, the author introduces readers to modern astronomy in part 3. In this section he narrates with great authority the opening up of the entire electromagnetic spectrum to astronomical observations and the impact of that achievement on the theory of stellar evolution. In addition, Longair covers the physics of the interstellar medium and cluster and galaxy evolution, a subject close to his own research.

The last portion of the book, parts 4 and 5, describes the advances of astrophysical cosmology over the past 50 years—from our knowledge of the origin of the universe, including the development of structure and its evolution, to our measurement of cosmological parameters.

Longair's style very effectively engages the reader in the story of this wonderful adventure of the human mind. I think *The Cosmic Century* would be of great value to anybody who has