

ited audience, a useful companion to other computational biology books currently available. Parts of the book read quite well although, given its nature, it gets quite dense in places. This is an exciting time to move into the field of computational molecular biology, motivate others to move into this field, or simply keep an eye on the practical developments emerging from this rapidly evolving field. Reading all or parts of this book can help meet some of these goals.

Computational Molecular Biology is the first in a series of books on computational biology published by the MIT Press. Additional titles forthcoming within the next year or two include *Computational Modeling of Genetic and Biochemical Networks*; *Gene Regulation and Metabolism: Post-Genomic Computational Approaches*; *Current Topics in Computational Biology*; *Comparative Genomics: The Domains of Life*; and *The Handbook of Computational Molecular Biology and Bioinformatics*. This is a series worth watching for anyone interested in the growing field of computational biology.

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Molecules, Magnets, and Mathematics

*Signs of Life—How Complexity
Pervades Biology*

By Ricard Sole and Brian Goodwin

New York: Basic Books (2001). 315 pp. \$30.00

With the sequencing of the human genome, Molecular and Cellular Biology has reached a turning point. In the past half century, sophisticated tools have been developed for both identifying genes and studying their function. Analysis of the function of individual genes has yielded great insight into the molecular mechanisms underlying phenomena ranging from the development of the embryo to the molecular basis of learning. It is therefore not surprising that this reductionist strategy has captured the hearts and minds of the majority of biologists. However, to what extent can complex biological phenomena at many different scales be understood by identifying and studying their component parts in isolation?

A growing number of researchers are suggesting that a complementary approach is required to understand the complexity that pervades much of biology. This approach, sometimes loosely called the “science of complexity,” emphasizes the study of emergent phenomena. It is generally expressed in the form of mathematical and computational models, and often draws extensively on analogies with theories of certain physical phenomena. This can intimidate biological researchers not well-versed in these disciplines. *Signs of Life* tackles this problem by providing an inspiring and stimulating account of this approach designed to be accessible to

biologists (and others) with only minimal mathematical training.

The authors develop the idea that complexity arises when the behavior of a system is not given simply by the sum of its parts. An essential ingredient in such systems is nonlinearity, and it is often useful to talk about phenomena that “emerge” at a higher level of structure as a consequence of interactions between individual components. Some relatively simple physical systems provide a useful starting point for showing the power of mathematical tools for describing such emergent phenomena. After reviewing some of these, the book moves on to illustrate how mathematical models can provide insight into biological systems from the molecular level to cellular, organismic, and finally social and cultural level. By the end one is left with a strong sense that there really are coherent themes that characterize complexity across many biological systems at many levels of analysis.

A classic example of complexity emerging from simple underlying components is the Ising model of the magnetization of iron. Each iron atom acts as a miniature magnet that can line up one way or the other, and a macroscopic block of iron is magnetic when the majority of atoms are lined up in the same direction. Iron atoms exert forces on each other, tending to cause each atom to become lined up with other atoms nearby. At high temperatures, these forces are overcome by thermal energy and the overall pattern is disordered, but as the temperature decreases, atoms start to fall into line with each other. At a certain “critical” temperature, an abrupt change in the overall level of magnetization occurs. A crucial simplification of the Ising model (introduced by Ising in his Ph.D. thesis in 1926) is that atoms interact only with their nearest neighbors. The behavior of this model was exactly solved first for one dimension, and then for two dimensions in a mathematical tour-de-force by Onsager. Its behavior in three dimensions can only be explored by simulation, but the model is a remarkably good predictor of reality. A key finding is that near the critical temperature extremely complex spatial patterns of magnetization can occur, which can have a fractal character. Thus, as the temperature changes the system moves between two “boring” states (random at high temperature, unidirectional at low temperatures) via a small temperature range where very interesting patterns spontaneously emerge.

What have simple things like Ising models got to do with the messy world of biology? Consider a simple model for when a forest fire is likely to spread from one edge of the forest to another. When trees are at low density the probability of fire spreading to an adjacent tree is low, and a fire that starts at one end is likely to burn out before it gets too far. When trees are at high density the fire spreads quickly from one end of the forest, causing total but rapid devastation. Models of forest fires show that, as in the Ising model, there is a critical density of trees at which the likelihood of the fire spreading from one edge of the forest to the other abruptly changes from low to high. Around this critical density, the forest fire takes an extraordinarily long time to weave in and out in a complex pattern through the forest before it dies off. The pattern of burnt trees in such a ravaged forest displays fractal geometry. Similar

models have been used to explore the spread of an epidemic in a population, and the firing of populations of neurons in the brain. If movement of the interacting agents is included, it becomes easy to see how to model for instance the foraging behavior of ants, the synchronous firing of fire flies, and the spatial pattern of aggregating *Dictyostelium* amoebae. The list goes on and the book invites you to explore chapters on different levels of biological complexity that are used to illustrate recurrent themes related to Ising models, fractal patterns, power spectra, attractors, and self-organizing systems teetering on the brink between order and chaotic behavior.

Unfortunately, buzz-words like chaos, emergence, and self-organization suggest to many science which is trendy but lacking substance. While this is alas occasionally true, *Signs of Life* also does an excellent job of lucidly describing mathematical modeling work (such as reaction-diffusion systems) which has withstood the test of time. The form of explanation used in the book consists of boxed material containing formal mathematical statements for each model, while the main text describes each model purely qualitatively. This strategy works well and makes the book useful for both those who like equations and those who don't.

Molecular biologists guided by their "reductionist philosophy" continue to make new and important discoveries at a pace that shows no signs of slowing. The identification of individual genes and development of tools for their manipulation remain essential steps for testing hypotheses related to the function of the genes. However, the continuing productivity of molecular biologists is what keeps this community largely unaware and mostly skeptical of the pragmatic value of the kind of insights theoreticians can provide. Theoreticians on their part often see the molecular biologists as misguided in their search for an understanding of biological complexity in the analysis of its molecular components. Poor communication between the two communities ultimately keeps them in the dark about what the other can offer, resulting in a lost opportunity for both groups. For the molecular biologists, it is an opportunity to put their data in the context of a broader theoretical framework that helps understand the robustness of a dynamic system, to understand how it is able to adapt or regulate under different environmental situations or, for example, to understand how the activity of specific genes affects the parameters of a self-organizing patterning mechanism. For the theoretical biologist, better communication with biologists is likely to provide more opportunities to rigorously test their models and to collect relevant experimental data that is so often missing simply because the theoreticians and molecular biologists often ask very different kinds of questions.

The broad survey of modeling work presented in *Signs of Life* will hopefully stimulate some biologists to explore the cited references and perhaps incorporate conceptual frameworks inspired by the mathematical and computational models into their own research. In fields such as evolution, ecology, neuroscience, and structural biology, there is already an active community of researchers who have embraced such approaches and move back and forth from experimental studies to theory. Unfortunately, in developmental biology there is still little com-

munication between theoreticians and "wet" biologists. As developmental biologists spend more time understanding how complex networks of genes affect the behavior and fate of cells, computational tools that are being developed for studying such networks are going to be particularly useful for the study of pattern formation and morphogenesis. Work on somitogenesis described in the book, as well as work on pattern formation by Turing and Meinhardt, provides a glimpse of some particularly productive areas for interactions between theoreticians and experimental biologists (e.g., see <http://www.eb.tuebingen.mpg.de/abt.4/meinhardt/theory.html>). Books such as *Signs of Life* are a small step toward better communication between biologists and theoreticians who study complexity in biology, a step that we believe will eventually result in a richer understanding of biology for us all.

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