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Book Reviews

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Review of A Primer of Population Genetics, 3rd edn, by Daniel L. Hartl, SinauerAssociates, Inc., MA, U.S.A.$29.95 (paperback), 200 pp. + 73 illustrations. ISBN: 0-87893-304-2.

What can one say about a classic? This book is a concise introduction to population genetics that has become a staple in the intellectual diet of specialists and non-specialists alike. Its logical structure and comprehensive content are revealed by its four main headings: Genetic Variation, The Causes of Evolution, Molecular Population Genetics, and The Genetic Architecture of Complex Traits. Only a rudimentary knowledge of mathematics is required. The author skillfully guides the reader through complex mathematical results, appealing to biological intuition rather than mathematical rigor. The role of empirical evidence in both forming and supporting the theory is appropriately given considerable attention. I highly recommend this book to anyone wishing to gain a basic understanding of both classical and modern population genetics. It is also quite useful to the specialist as a general reference.

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An Introduction to Chaos in Nonequilibrium Statistical Mechanics, by J. R. Dorfman, Cambridge University Press, Cambridge, 1999. £20.95 (paperback), ISBN: 0521655897.

It has been almost a quarter of a century since chaos theory burst on to the scientific scene, if one collectively takes the publications of Li-York (1975), May (1976), and Feigenbaum (1978) as an indicator. The mathematical theory of nonlinear dynamical systems has continued to keep the fascination of mathematicians and scientists alike; it even caught the fancy of the general public which has made James Gleick's 'Chaos: Making of a New Science' a bestseller. However, to most mathematicians and physicists, with the exception of a few experts, the earlier promise of understanding the nature of turbulence and finishing the foundation of statistical physics still seems elusive. The mathematics involved in the latter subject, known as smooth ergodic theory, a subfield of nonlinear dynamical systems, becomes increasingly technical and is out of reach for the average applied mathematicians and physicists. It is against this backdrop, that the book by Professor Dorfman has been long awaited. The unique feature of this book is its exposition of sophisticated material at a rather elementary level. Working through this book will be a pleasure to readers with sufficient exposure to the mathematical theory of nonlinear dynamical systems. To readers with a background in statistical physics and interested in its theoretical basis, it will be a wonder to see some familiar themes being played with more cogency. I recommend it highly.

A review of this book aimed at an audience of theoretical physicists is bound to be very positive. But why is it recommendable to mathematical biologists? My reasoning is that biology has entered the cellular and molecular age. It is a fact that most mathematical biologists trained today have a heavy dose of differential equations, but are relatively weak in statistical mechanics, and even more so with thermodynamics. It is also significant to point out that while most mathematical biologists are interested in time-dependent phenomena, the introductory courses on classical statistical mechanics only deal with equilibrium! The part of statistical physics which is more relevant to biology is the nonequilibrium part. Hence with a background in dynamical systems, mathematical biologists should go directly to the center of the action, by-passing the large disciplinary apparatus in equilibrium statistical mechanics centering round computing partition functions, and catch a glimpse of the part of modern theoretical physics which will surely be the foundation for the theories of life. This book just might serve as such a 'tunnel'.

The first five chapters of the book focus on topics familiar in most textbooks on statistical mechanics: Liouville's equation, the Boltzmann equation and the H-theorem, Gibb's mixing, the BBGKY hierarchy, and entropy. While dealing with traditional subjects, the presentation is definitely nontraditional. It is much more mathematically cogent. My favorite part is a simple toy example, originally given by Mark Kac (the academic grandfather of the author via T. Berlin; Kac, 1985), on the mathematical nature of Boltzmann's work (Figure 1). It is unfortunate that this elegant example is not included in the usual statistical mechanics textbooks. The example nicely shows how one can devise a stochastic model for a complex deterministic system whose dynamics is not even chaotic; in fact it is periodic! This is the power of the statistical treatment; it is the contribution of Boltzmann (Lebowitz, 1993), not only to statistical physics, but to nonlinear dynamics as well.

Chapter 6 treats a classical subject in textbooks on nonequilibrium statistical mechanics, the Green–Kubo formula, which gives the relationship between equilibrium thermal fluctuations and relaxation kinetics. A great example from biophysics

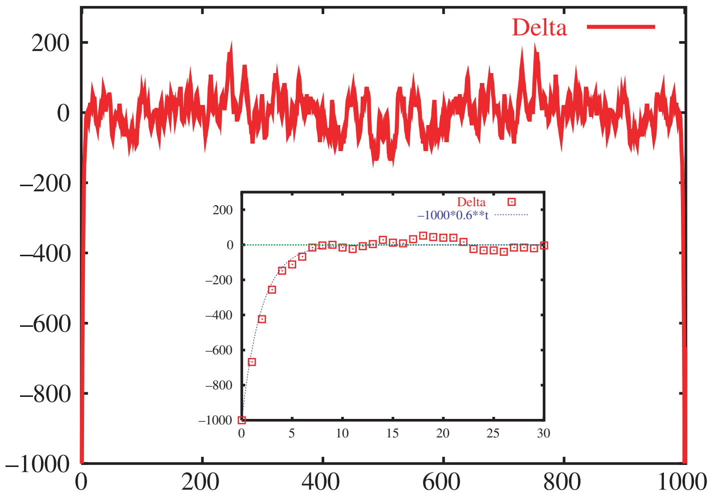

Figure 1. The Kac's ring, $\nu_{k(t)}|\nu = \pm 1; k = 1, 2, \ldots, 1000; t = 1, 2, \ldots,$ is a 1000-dimensional linear deterministic system with a periodic dynamics (Kac, 1959). The $\Delta(t) = \sum_{k=1}^{1000} \nu_{k(t)}$ plotted here is a one-dimensional projection which clearly shows a periodicity of 1000, and a time-reversibility with a symmetry at $t = 500$. These are important known properties of a Hamiltonian system. However, it is also clear that the dynamical system is 'irreversible' within the time frame of 0–10, and highly 'stochastic' within the time frame of 10–500. An approximated stochastic analysis can be easily devised which gives a prediction, without any fitting parameter, shown in the inset (the dotted line). This example demonstrates how a simple stochastic analysis can give quite an accurate description of the statistical aspects of a large, deterministic system. This is Boltzmann's approach. For more details, see the book under review.

demonstrates precisely this relationship: the pair of methods known as fluorescence correlation spectroscopy (FCS) and fluorescence photobleaching recovery (FPR) are two optical methods for measuring membrane protein diffusion via fluctuations and correlation functions, and via perturbations and relaxation kinetics, respectively (Elson, 1985).

Chapters 7 and 8 discuss standard concepts in nonlinear dynamics: Lyapunov exponents, the baker's transformation, Arnold's cat, and Kolmogorov entropy. However, the relationship between chaos and irreversibility presented in the book is usually not found in regular textbooks.

The material in the remainder of the book, starting with Chapter 9, is usually only presented with sophisticated mathematical background in measure theory and abstract differentiable dynamical systems on manifolds. These represent the heart and soul of modern ergodic theory, and the author is admirably accomplished in presenting the difficult material in an accessible way. His approach relies heavily on the work of Sinai, Ruelle, and the late Robert Bowen (SRB) which leads the readers directly to the recent development by Gallavotti–Cohen (Gallavotti, 1999). The workers of this school have found a nonlinear, nonequilibrium, but stationary dynamical system as a model for a thermodynamic nonequilibrium steady-state.

The focus of this approach, followed by the book chapters, is on the system's entropy production, its average rate and its fluctuations due to chaos. It is important to point out that, while there is a vast literature on nonequilibrium statistical mechanics, most books only deal with transient processes and transport properties. Very few books treating nonequilibrium steady-states exist. However, it is the nonequilibrium steady-state which is most relevant to biochemical networks (Hill, 1995), biological energy and signal transductions, and physiological homeostasis.

Chapters 11 and 12 address macroscopic transport properties from the escape rate point of view in chaotic dynamics. This link is important: it ties the mathematical analysis of the nonlinear dynamical system to physically measurable properties of macroscopic thermodynamic systems.

While this book provides a unique introduction to nonequilibrium statistical mechanics for mathematical biologists, it offers no insight on how to develop actual models for nonequilibrium systems which are abundant in cellular and molecular biology. This is no fault of the author. The fact is that, based on Hamiltonian systems, the Boltzmann approach to molecular systems and their thermodynamics, though being successful with gases and fluids, is nearly useless in dealing with biological macromolecular systems and processes in aqueous solution at constant temperature. The large number of water molecules completely overwhelm the biologically important macromolecules. Fortunately, modeling such isothermal systems can be accomplished by a stochastic approach based on the Fokker–Planck equations (Risken, 1984), which should be considered as the time-dependent version of Gibbs' equilibrium statistical mechanics (Qian, 2001a). It is important to point out that, following the recent work of Lebowitz and Spohn (1999), many results from the dynamical systems (Boltzmann) approach are easily obtained from the stochastic approach. This is very significant to mathematical biologists who are interested in real modeling: it provides the practical stochastic approach with a sound theoretical foundation. Lebowitz and Spohn's results, in addition to other results on Fokker–Planck equations including an H-theorem-like inequality (Qian, 2001a,b,c), suggest that the stochastic approach is not inferior, but complementary to Boltzmann's approach to irreversibility. Dorfman's book also clearly points out that both approaches invoke a stochastic element *a priori* in dealing with molecular collisions.

In summary, this book successfully gives its audience a unique and accessible up-to-date exposition of the mathematical foundation of Boltzmann's statistical mechanics based on the modern ergodic theory of chaotic dynamical systems. This book will be valuable to applied mathematicians and theoretical physicists alike; it might also serve a particular niche in providing a new generation of mathematical biologists, who are faced with the increasing cellular and molecular nature of biological research, with a unique education on an important branch of theoretical physics. In the past, equilibrium statistical mechanics and thermodynamics has provided physical sciences with a molecular foundation. We expect nonequilibrium statistical mechanics and thermodynamics, as promised (Nicolis and Prigogine, 1977), will provide the biological and life sciences their ultimate molecular basis.

REFERENCES

Elson, E. L. (1985). Fluorescence correlation spectroscopy and photobleaching recovery. *Ann. Rev. Phys. Chem.* **36**, 379–406.

Gallavotti, G. (1999). *Statistical Mechanics: A Short Treatise*, New York: Springer.

Hill, T. L. (1995). *Free Energy Transduction and Biochemical Cycle Kinetics*, New York: Springer.

Kac, M. (1959). *Probability and Related Topics in Physical Sciences*, Lectures in Applied Mathematics, Vol 1, London: Interscience.

Kac, M. (1985). *Enigmas of Chance*, New York: Harper & Row.

Lebowitz, J. L. (1993). Boltzmann's entropy and time's arrow. *Physics Today* **46(9)**, 32–38.

Lebowitz, J. L. and H. Spohn (1999). A Gallavotti–Cohen-type symmetry in the large deviation functional for stochastic dynamics. *J. Stat. Phys.* **95**, 333–365.

Nicolis, G. and I. Prigogine (1977). *Self-Organization in Nonequilibrium Systems*, New York: Wiley.

Risken, H. (1984). *The Fokker–Planck Equation: Methods of Solution and Applications*, New York: Springer.

Qian, H. (2001a). *Equations for Stochastic Macromolecular Mechanics of Single Proteins: Equilibrium Fluctuations, Transient Kinetics and Nonequilibrium Steady-State*, submitted for publication.

Qian, H. (2001b). *Mathematical Formalism for Isothermal Linear Irreversibility*, submitted for publication.

Qian, H. (2001c). *Nonequilibrium Steady-State Circulations and Heat Dissipation Functional*, accepted for publication.

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