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Book Review: *Proteins: A Theoretical Perspective of Dynamics, Structure, and Thermodynamics*

Proteins: A Theoretical Perspective of Dynamics, Structure, and Thermodynamics. C. L. Brooks III, M. Karplus, and B. M. Pettitt.

This treatise, published as Vol. LXXI of the Advances in Chemical Physics series, is an enlightening introduction to the new and rapidly developing field of molecular dynamics of proteins. Written in clear language, with relatively few equations and a comprehensive reference list, it discusses methodology and numerical procedures applied, elaborates on the major results obtained to date, and concludes with a comparison between molecular dynamics calculations and experiment. In the methodology section, the authors cover the semiempirical potential energy functions and the variety of dynamical simulation techniques (classical and stochastic trajectories, normal mode analysis, and Monte Carlo energy minimization) as they apply to proteins. The authors are careful to point out both merits and possible pitfalls in the various methods. Results obtained in several groups are logically organized in a hierarchial fashion: From small motions of side chains, through larger backbone motions, to large motions of rigid structures, e.g., double helices and domains. Hence the incredibly complex motions in proteins unfold for longer and longer time scales. The influence of additional solvent molecules on the vacuum simulations is discussed. The qualitative agreement with experiment of such detailed calculations is remarkable. It is noted that the theoretical results actually contain much more information than can conceivably be generated by experiment.

Although barely older than one decade, the field of protein dynamics has already changed our concept of proteins dramatically. While the impression given by classical *X*-ray studies is of rigid, well-defined protein structures which are all-important to their function (i.e., the lock-and-key picture for enzyme–substrate activity), it is becoming increasingly clear from molecular dynamics simulations that protein fluctuations can have relatively large magnitudes and that these play a crucial role in protein activity. This is observed for all length and time scales: The rotation of a

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small side chain depends on motion in some "protein coordinate(s)" to provide a path with low activation barrier. The structure of myoglobin determined from *X*-ray crystallography shows no clear paths for ligand entry and escape and imply that these paths are largely determined by protein fluctuations. The activity of the enzyme lysozyme results from a "hinge-bending" motion of a whole domain. This resembles a huge jaw which opens to allow the substrate to enter.

Beyond the conceptual and scientific interest in the field of protein dynamics there is the potential for many practical applications. Because function depends on motion as well as structure, it is conceivable that pharmaceutical companies in the future would employ a molecular dynamics expert to assess drug activity, just as quantum chemistry is used today as a tool for estimating its structure. Likewise, an expensive genetic engineering project may be preceded by a molecular dynamics calculation which would evaluate the functional change resulting from specific mutations.

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Book Review: *Noise in Nonlinear Dynamical Systems*

Noise in Nonlinear Dynamical Systems. Vol. 1. Theory of continuous Fokker Planck systems. Vol 2. Theory of noise induced processes in special applications. Vol. 3. Experiments and simulations. Frank Moss and P. V. E. McClintock, eds., Cambridge University Press, 1989.

The three volumes comprising this monograph contain a series of longish articles on a number of aspects related to the effects of noise on the behavior of dynamical systems. Since this general area is the focus of considerable and intense investigation at the present time, much of the material must be regarded as being tentative, representing the state of the art. Nevertheless, the monograph is a most valuable introduction to what is known about the effects of noise on physical systems for an audience acquainted with the fundamentals of probability theory.

While it is clearly impossible to review all of the articles in these volumes, a description of a few of these can provide a little of the flavor of the set. The leadoff article in the first volume, written by R. Landauer, reviews some of the history of noise in general and the Kramers' problem in particular. This is followed by an extensive article on the application of Markov methods in the analysis of nonlinear dynamical systems by Stratonovich. Unfortunately, the material in the article is quite condensed and does not begin to achieve the clarity found in the author's pioneering books on random noise. Sancho and San Miguel then review some aspects of the theory of Langevin equations with colored noise. Related material is found in articles by Grigolini (on the projection-operator approach to the Fokker Planck equation), by Lindeberg, West, and Masoliver (on non-Markovian first passage time problems), and by Hänggi (on mathematical techniques for treating colored noise based on functional calculus). Although the focus of considerable research effort, much remains to be learned about colored noise effects in general, and, in particular, for models in which the assumed correlations take some form other than a simple exponential. The subject has not yet sufficiently gelled to enable predictions on how long the cited articles will still represent relevant reviews of impor-

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tant research directions. Other topics in the first volume include techniques for solving the Fokker–Planck equation based mainly on eigenfunction expansions and continued fraction techniques, by Risken and Vollmer, the use of potentials for analyzing multidimensional nonequilibrium systems, discussed by Graham, and the theory of transition phenomena in multidimensional systems, as described by Ebeling and Schimansky-Geier. The general ideas in Risken and Vollmer's article are covered in considerably greater detail by Risken in his book on the Fokker–Planck equation. An added bonus in the first volume is a translation of the original article by Pontryagin, Andronov, and Vitt (1933) on the use of the backward equation in analyses of first passage times of systems satisfying the Fokker–Planck equation.

Volume 2 of the set contains still more specialized material exemplified by a discussion of stochastic processes in quantum mechanics by Fox, the Kramers' problem by Büttiker, two articles on the effects of noise on discrete systems, one by Knobloch and Weiss, and the second a most interesting and slightly more comprehensive contribution by Talkner and Hänggi. Other topics represented include a discussion of some effects of modulated control parameters by Lücke, a provocative article on both theoretical and practical applications of period doubling bifurcations by Wiesenfeld, and a description of symmetry-breaking transitions by Kondepudi. Recent work on the theory of noise-induced transitions is described in an introductory manner by Horsthemke and Lefever, and some mechanisms for these transitions in chemical systems are suggested in an article by Kapral and Celarier. Related material is found in an exposition by Dykman, Krivoglaz, and Soskin. The remainder of the volume contains material related to noise effects on a ring-laser gyroscope, and a description of some applications to optical systems. Volume 3 of this set is devoted to such experimental systems as bistable transitions in liquid He II, an electrohydrodynamic instability of liquid crystals, three articles on the role of fluctuations in the operation of lasers, and finally, a set of three articles on simulations of noisy dynamical systems. This last volume will probably be the most transient of the three.

As can be seen from the sampling of articles cited above, the editors have certainly chosen a number of authors most eminently qualified to describe some of the most recent work on stochastic effects on dynamical systems. Quite generally the resulting articles are authoritative and provide a useful introduction to the subject matter at only a slightly more sophisticated level than, say, Gardiner's monograph on stochastic processes in the physical sciences. Some topics that might have warranted inclusion as full-length articles but are not discussed in great detail include recent work on stochastic resonance and some of the ideas introduced into the analysis of noisy systems by Matkowsky and Schuss, and their collaborators. In ten years much of the material in these volumes will be outdated, but at the present time they represent a useful description of where the general field is at. The editors are to be commended for their efforts in putting together a most useful introduction to modern research in some aspects of statistical physics by a number of distinguished expositors.

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