Biophysical Journal Volume 68 April 1995 1634

Book Review

Biophysical Thermodynamics of Intracellular Processes: Molecular Machines of the Living Cell by L. A. Blumenfeld and A. N. Tikhonov

Springer-Verlag, New York, 1994. 178 pages. $69.00

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This book is aimed at a large audience from students to scientists working in the fields of biophysics and biochemistry. It is about more than thermodynamics, as indicated by the titles of the principal chapters, which are "Thermodynamics and Chemical Kinetics of Living Systems," "Molecular Machines: Mechanics and/or Statistics?," "Principles of Enzyme Catalysis," and "Energy Transduction in Biological Membranes." The book does not give much background on thermodynamics and, in fact, is quite critical of thermodynamics. For example, after pointing out that the equilibrium constant for the oxidation of glucose to carbon dioxide is very large, the authors state that "it would be incorrect (or even meaningless) to use the equilibrium thermodynamics approach." This seems to miss the point that thermodynamics is useful in analyzing the energetic changes in the various steps along the way, and even in better understanding the steps in the mechanism of a single enzymatic reaction. They never mention the use of apparent equilibrium constants K' written in terms of sums of species at specified pH or the Haldane relation, which shows that the maximum velocities and Michaelis constants of the forward and reverse reactions of an enzyme-catalyzed reaction are related to the apparent equilibrium constant. They state that the conventional thermodynamics approach does not take into account the time scales of the processes considered (p. 44), but this is not true. A mixture of substrates can be in equilibrium at a certain pH and, when acid is added, the equilibrium is adjusted rapidly to an equilibrium state at a different pH. When an an enzyme that catalyzes a reaction between the substrates is added to the mixture, a different equilibrium state is achieved more slowly. Thermodynamics can be used for quantitative analysis of both of these processes, which have quite different time scales. Because biochemical reactants like ATP are made up of sums of species, they can be treated like one entity at a specified pH. New thermodynamic properties and symbols are required when biochemical reactions at a specified pH are discussed, so that these quantities and symbols will not get mixed up with those used in discussing chemical reactions. These thermodynamic quantities and symbols are recommended in IUPAC and IUBMB reports (Wadsö, I., H. Gutfreund, P. Privlov, J. T. Edsall, W. P. Jencks, G. T. Strong, and R. L. Biltonen. Recommendations for measurement and presentation of biochemical equilibrium data prepared by the Interunion Commission on Biothermodynamics. *J. Biol. Chem.* 1976. 251:6879–6885; and Alberty, R. A., A. Cornish-Bowden, Q. H. Gibson, R. N. Goldberg. G. G. Hammes, W. Jencks, K. F. Tipton, R. Veech, H. V. Westerhoff, and E. C., Webb. Recommendations for Nomenclature and Tables in Biochemical Thermodynamics. *Pure Applied Chem.* 1994. 66:1641–1666).

The authors are also quite critical of thermodynamics in a long section dealing with the violation of the mass action law (p. 60), in which they claim that the equilibrium constant for $PQ = P + Q$ is a characteristic of a single PQ molecule. The second law and the concept of an equilibrium constant are based on the consideration of systems with large number of molecules, so called macroscopic systems. Their solution to problems that are encountered in biology is the concept of "molecular machines." These "molecular machines are enthalpy-driven constructions," and so there are real disadvantages here in ignoring the effect of entropy changes in biochemical reactions, some of which occur because of entropy changes rather than enthalpy changes.

Chapter 4 discusses the relaxation concept of enzyme catalysis. This seems to be heavily based on the idea the enzymatic paths of the direct ($S \rightarrow P$) and reverse ($P \rightarrow S$) chemical transformations are different. This idea violates the principle of detailed balance (microscopic reversibility) that is a part of both classical mechanics and quantum mechanics. The last chapter on energy transduction in biological membranes is the longest and may be the most useful because of the detailed discussion of research in this field; this chapter has over 200 references.

An Afterword points out that the crucial word in the title of this book is "machines." Of course, that raises the question as to what is meant by "machine," but I think that this emphasis on machines throughout the book has its dangers. According to one dictionary, "a machine is a device consisting of fixed and moving parts that modifies mechanical energy and transmits it in a more useful form." Operations of real machines are not discussed in terms of entropy, but we know that on the molecular scale, entropy is very important and may determine whether a change in state can occur. Thinking about enzyme-catalyzed reactions, for example, in terms of structures is certainly useful, but it would seem to be a good idea to make thermodynamic and kinetic calculations in ways that have shown their utility in dealing with molecules in aqueous environments.