Journal of Statistical Physics, Vol. 52, Nos. 1/2, 1988

Book Review: *The Fluctuating Enzyme*

The Fluctuating Enzyme. G. R. Welch, ed., Wiley, New York, 1986.

The idea that the role of the protein in enzymatic catalysis is not merely geometrical but also dynamical is central in the modern study of biophysical kinetics. According to this point of view, the protein is not just a static structure, forming the "keyhole" that complements the shape of its substrate: It also participates actively in the reactive event through the dynamics of conformational change. This can occur in two ways: First, through fluctuations around the thermal equilibrium state. In this mechanism the reaction takes place from the wings of the thermal distribution. The second mechanism is through the relaxation of a non-equilibrium state toward equilibrium, where the distribution function is evolving in time.

The volume under review is a collection of nine theoretical papers dealing with the above-mentioned questions. Although, as the title implies, it leans toward the first mechanism, the second point of view is also represented (Blumenfeld, Burbajev, and Davydov). Consequently, the theoretical tools utilized are mainly those of thermodynamics and statistical mechanics and, to a lesser extent, methods of stochastic processes.

The experimental phenomena in enzyme kinetics that support this point of view are the distributions of proton-exchange rates in enzymes (Lumry and Gregory) and in polypeptides (Ikegami), the quenching of fluorescence of tryptophan residues in globular proteins and of the porphyrin moiety in heme proteins (Careri and Gratton, Somogyi and Damjanovich), the viscosity dependence of the catalytic rate and the mean square atomic displacement as obtained from X-ray diffraction (Gavish), laser enhancement of enzyme activity (Fröhlich), and enthalpy–entropy compensation (Lumry and Gregory). The main ideas are summarized in the last chapter (Welch and Kell).

Unfortunately, the experimental evidence for conformational motion is still rudimentary. In particular, for enzymes lacking a prosthetic group,

0022-4715/88/0700-0519$06.00/0

there is usually no good spectroscopic marker for the time course of protein conformational change. As a result, most theories tend to be somewhat abstract. In heme proteins, good spectroscopic markers do exist, for example, in the absorption (Blumenfeld, Burbajev, and Davydov) and magnetic circular dichroism (Volkenstein) spectra. Hence time-dependent data are reported (Blumenfeld *et al.*). However, perhaps because it is outside the scope of the book, major results on ligand rebinding to heme proteins gathered by absorption, Raman, and IR spectroscopy, and results from Mössbauer spectra of heme proteins, are mentioned only in passing, while more space is devoted to less central issues. Also not represented are some important molecular dynamics calculations.

Theories of enzyme activity should ultimately deal with the dynamics of conformational change in the time domain. In order to do so, more detailed time-resolved data are needed.

Noam Agmon
National Institutes of Health
Bethesda, MD 20892, USA
and The Hebrew University of Jerusalem
Jerusalem 91904, Israel