

Imperfect in practice

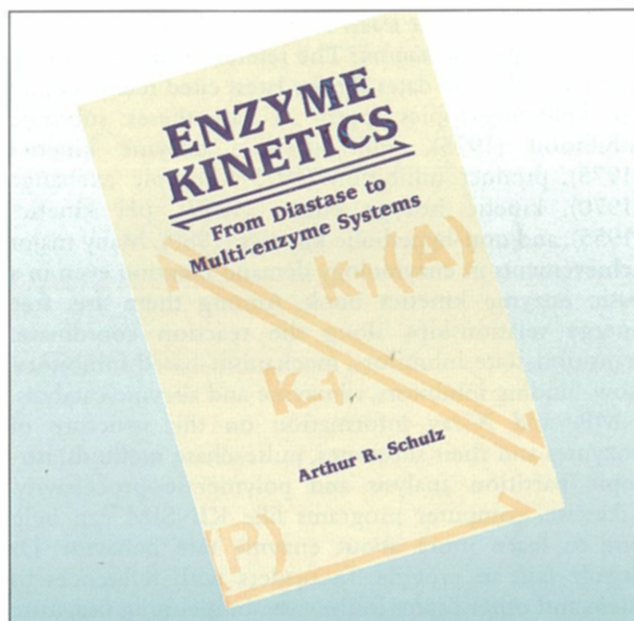
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Enzyme Kinetics: From Diastase to Multi-Enzyme Systems by Arthur R. Schulz. Cambridge University Press, 1994, 246 pages. \$29.95 paperback (ISBN 0-521-44950-2; \$59.95 cloth (ISBN 0-521-44500-0)).

Enzymology is an extraordinarily diverse field that has grown in sophistication through recent advances in structural biology, transition-state theory and physical organic chemistry, as well as through the application of recombinant DNA expression and site-directed mutagenesis. The scope of enzymology has expanded through the recognition that nature employs nucleic acids as biological catalysts and that humans can design catalytic antibodies exhibiting novel activities. Thus, new books may have great value in expanding the awareness of efforts to discover the mechanistic origins of catalytic rate enhancement, and in disclosing the salient features of regulatory interactions. Given the variety of robust theoretical and experimental approaches that are now at the disposal of those seeking to analyze biological catalysis, a good monograph can be particularly valuable in organizing concepts and exemplifying the advantages and/or weaknesses of particular strategies. It was with such optimism and expectation that this reviewer accepted the invitation to review the monograph written by Dr Schulz. Unfortunately my optimism was not rewarded.

What is the scope of this new book? The following topics are concisely covered: Derivation of a rate equation; A closer look at the basic assumptions; Enzyme inhibition; Reversible enzyme-catalyzed reactions; Multi-reactant enzyme kinetics; Analysis of multi-reactant enzyme kinetics; Prediction of reaction sequence; Enzyme-catalyzed isotopic exchange; Kinetic isotope effect on steady state parameters; The effect of pH on enzyme kinetics; The causes of non-hyperbolic enzyme kinetics; Analysis of non-hyperbolic enzyme kinetics; The effect of subunit interactions on enzyme kinetics; Control of linear multi-enzyme systems; Control of branched multi-enzyme systems; and Biochemical systems theory. The first thirteen chapters deal with classical enzyme kinetics, and the last three chapters quite obviously reflect the author's interests in the control of multi-enzyme processes. A few exercises or problems are included at the end of each chapter, and the last part of the book presents solutions to these problems.

For whom did the author intend the book? In the preface, the author states: "It is hoped that [this book] will be useful not only to the reader who is enrolled in a formal course in enzyme kinetics or enzyme chemistry, but also to readers who wish to familiarize themselves with enzyme kinetics in a self-study program, and also to those readers



who wish to review the principles of steady state enzyme kinetics. . . . A deliberate objective has been to present the fundamentals of enzyme kinetics in general terms rather than in terms of specific enzymes. The basis for this approach is the conviction that an objective investigation of the kinetic behavior of an enzyme-catalyzed reaction should be pursued in a manner which is cognizant of basic principles rather than an attempt to 'fit' the data obtained with one enzyme to the behavior of some other enzyme."

Does the book meet its objectives? In other words, will the novice gain sufficient conceptual mastery from this monograph to design useful experiments for characterizing enzyme catalysis? The first thirteen chapters are a briefer and no more recent treatment than Segal's *Enzyme Kinetics* (Wiley-Interscience, Inc., 1975). Both lack practical suggestions regarding the acquisition and analysis of rate data, and both fail to present any experimental findings on enzymes. Enzyme kinetics is by its nature practical, and students are ill served by theory unconnected to practice. Interestingly, for the material explored in the current monograph, Fromm's *Initial Rate Enzyme Kinetics* (Springer-Verlag, Inc., 1975) remains a far more rigorous single-authored treatment and also provides valuable practical advice on experimental design. One best learns enzymology by linking kinetic behavior to chemical and structural information, something done extremely well by Cleland who, although he has not published a text, has published a number of excellent chapters (although none more

recent than 1977 is cited in Schulz's book) describing a mix of classical and recent theoretical developments; they invariably consider experimental results obtained for a range of relevant enzymes. This book suffers by comparison to Cleland's book chapters and to the other older texts.

Does the book help the reader to comprehend the current literature on enzyme mechanism? The references in this monograph are old, and dates for the latest cited references on the following topics appear in parentheses: substrate inhibition (1975), multi-substrate enzyme kinetics (1975), product inhibition (1975), isotopic exchange (1970), kinetic isotope effects (1977), pH kinetics (1955), and non-hyperbolic kinetics (1980). Many major achievements in enzymology demand mention even in a basic enzyme kinetics book. Among them are: free energy relationships along the reaction coordinate; transition-state inhibitors, mechanism-based inhibitors, slow-binding inhibitors, ribozyme and abzyme catalysis, NMR and X-ray information on the structure of enzymes and their substrates, pulse-chase methods, isotopic partition analysis and polymerase processivity. Likewise, computer programs like KINSIM can help one to learn more about enzyme rate behavior. Dr Schulz fails to provide his readers with references to these and other topics in the ever-burgeoning literature on enzyme kinetics and mechanism.

Will the experienced enzymologist gain additional insights? Those concerned with mathematical treatments of multi-enzyme pathways may find this book of interest. Beyond regulation *per se*, the design of industrial enzyme reactors requires some understanding of enzymes in linear or branched pathways. Among the concepts developed in the last chapters are: flux control coefficients, elasticity coefficients, application of sensitivity theory, effects of feed-back and feed-forward loops on linear pathway control, flux control in substrate cycles, and power law formulations of linear and branched pathway dynamics. Again, by not considering practical constraints on differentiating rival mechanisms, the author does not add substantially to concepts already developed in the references cited.

In summary, *Enzyme Kinetics: From Diastase to Multi-Enzyme Systems* cannot be highly recommended for introductory courses on enzyme kinetics and mechanism. In the absence of any contemporary theoretical or experimental perspective, this monograph is also unlikely to become a resource of enduring value for experienced investigators.

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