
PREFACE

All too often, textbooks of enzymology present enzyme kinetics simply as a catalogue of standard mechanisms and their rate laws. Little effort is made to give the reader what one might call a “gut-feeling” for the connection between a mechanism and its rate law; that is, how a mechanism is reflected in the form of its rate law, and how a rate law predicts the behavior of its corresponding mechanism. Furthermore, these kinetic treatments seldom provide adequate conceptual resources for the analysis of real-world enzyme kinetic data, which frequently reflect underlying mechanisms that deviate from standard mechanisms. In this book, I aim to develop a distinctly different treatment of enzyme kinetics.

The two overarching goals of this book are to present (1) theoretical aspects of enzyme kinetics within a conceptual framework that underscores the connections between mechanism and rate law and (2) practical aspects of enzyme kinetics with a focus on mechanism-independent methods of data analysis.

An underlying premise of this book is that the conceptual understanding of an enzyme mechanism, independent of any mathematical treatment, allows a more informed use of the mechanism’s rate law, for both experimental design and data analysis. Such an understanding can be achieved through the construction and analysis of free energy diagrams for enzymatic mechanisms. This approach is used throughout this book to provide conceptual underpinnings for single-substrate reactions with one or two intermediate species, enzyme inhibition, and mechanisms of two-substrate reactions.

Analysis of enzyme kinetic data is presented in this book as a process based on a mechanism-independent approach, the goal of which is to provide an alternative to the standard analytical approach in which mechanisms are imposed on a data set. Instead, an analytical method is presented that allows the mechanism to emerge from the data. Significantly, this approach reveals departures from non-ideal behavior in enzyme kinetic data that reflect non-standard mechanisms.

Another goal of this book is to provide a resource for practitioners of enzymology who work in early stage drug discovery. So, throughout this book, the theoretical and

practical principles just described are presented in the context of drug discovery, using examples and case studies drawn from the literature.

Finally, it is my hope that this book will provide enzymologists, at all stages of their careers, with a new way of thinking about the theory and practice of enzyme kinetics.

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