

A Study of Enzymes

Volume I Enzyme Catalysis, Kinetics, and Substrate Binding

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Vere scire, esse per causas scire
(To know truly, is to know by causes)

Francis Bacon (1561—1626)

Dedicated to my loyal, loving wife, Josette, without whose persistence this task would never have been completed; and also to my students and colleagues, whose sometimes lively discussions, requests, and whose very insistence forced me to bring to a close these writings of several years. My gratitude to my brother George, for his mathematical critique, to Gerald for many of the figures and schemes drawn by computer, and to Rose and Lori for much of the typing.

PREFACE

Volume I has been completed first. It is largely a summary of almost 4 decades of our own work, and accordingly many of the examples and illustrations are drawn from our own published works. Although not every topic in Enzyme Kinetics or in Equilibrium Substrate Binding will be covered herein, there is enough breadth and scope to cover much that has been of interest to us and enzymologists, in general. It has been used as a text in Biochemistry 707 (Topics in Biophysical Chemistry, with Special Emphasis on Enzyme Kinetics), and might form the nucleus of a similar course, but hopefully it should be of some interest to graduate students and to teachers and researchers alike, if they find enzymology the fascinating and absorbing subject that it has been to this author over these past years.

Interestingly, the subject still appears to be in a remarkable state of flux as witnessed by the very recent questioning of the generality of a very important concept, viz., that of the "rate-limiting step" in certain steady-state enzymatic reactions by D. Northrop (606,607) and the possibility of a more consistent redefinition by W. Ray (608). In Chapter 6 (on Kinetic Isotope Effects) this interesting problem will be briefly touched upon in relation to the recent attempts to utilize the potential mechanistic applications of "kinetic isotope effects".

Even the subject of "equilibrium ligand binding", which superficially might be considered to be in a current state of almost static development, has been the very recent subject of a vigorous controversy in regard to the correct estimation of molecular receptor capacity by Scatchard plots in certain binding studies (Klotz, 620; and Feldman, 621). The subject of "equilibrium ligand binding" will be developed in Chapter 8, and Klotz's arguments (620) will be very briefly presented there.

Volume II on Enzyme Mechanisms will follow, with the aid of my colleagues and associates, and will present selected studies which are currently being vigorously pursued by a number of approaches and techniques which are at the "cutting edge" of biochemistry.

SELECTED BIBLIOGRAPHY

A number of excellent reviews and monographs have been written on the subject of "Enzyme Kinetics" and "Equilibrium Ligand Binding Measurements"; some of these are presented below, as well as a few specific references which will prove to be valuable in our discussions. In addition, a few general references to mathematics, and chemical kinetics which have been found useful by the author, also listed below. Finally, some references are cited to the "Mechanism of Action of Enzymes", and which will have a bearing on these writings and those to follow.

Thus, refer to the following references:

1. Enzyme kinetics

A. Reviews: References 7, 9, 10, 22, 40, 51, 52, 82, 96, 103, 164, 169, 184, 202, 489, 494, 554, 555—557, 568, 569, 574, 602, 693, 773, 774, 935, 963.

B. Some specific references: References 4, 8, 11, 14, 15, 17—20, 24, 26, 31, 38, 39, 42—47, 49, 50, 53—58, 60—62, 64—66, 68, 69, 71, 84, 157, 158, 165—168, 180, 181, 203—227, 490, 508, 581, 584, 585, 588—591, 601, 606—608, 610, 617—619, 625, 629, 630, 639, 653, 657, 658, 680, 681—685, 689, 690, 692, 812, 813, 841, 842, 936.

2. Mathematical references: References 170—179, 228—230, 382, 621.

3. Chemical kinetics: References 231—236, 577, 587, 592, 595, 609, 631, 634, 640—642, 644, 659, 684.

4. Equilibrium ligand binding measurements: References 58, 59, 74, 113, 115, 144—148, 237—249, 573, 596, 599, 600, 602, 603, 611, 620—624, 632, 633, 638, 646—648, 650, 652, 655, 687, 722, 938.

5. Mechanism of action of enzymes: References 103, 190, 191, 202, 250—270, 297, 494, 518, 555—557, 571, 572, 575, 576, 578—580, 582, 583, 588, 593, 598, 602—605, 612—616, 626—628, 635—637, 645, 649, 651, 655, 656, 660, 683, 686, 688, 807, 954, 966.

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He is a member of the American Society of Biochemistry and Molecular Biology, the American Chemical Society Division of Biochemistry (Chemistry), Sigma Xi, Phi Beta Kappa, American Association for the Advancement of Science, and the New York Academy of Sciences. He has been a member of the Subcommittee on Enzymes, Committee on Biological Chemistry, Division of Chemistry and Chemical Technology, National Academy of Sciences and National Research Council; and also a member of the Physiological Chemistry Study Section, Division of Research Grants, National Institutes of Health, Public Health Service, Department of Health, Education and Welfare. His long list of publications reflect these research interests.

TABLE OF CONTENTS

Volume I

Section I: Enzyme Catalysis and Steady-State Kinetics

Chapter 1

Historical Introduction, Theories of Enzyme Catalysis, and Some Elementary Considerations of Enzyme Kinetics

I.	Introduction	3
II.	Historical Development of Enzyme Kinetics	4
III.	Some Theoretical Aspects of Enzyme Catalysis	4
	A. Reactions in Sequence and Covalent Catalysis	5
	B. Proximity and Orientation Effects	5
	C. Bifunctional and Acid-Base Catalysis and Other Electronic Effects, e.g., Push-Pull Mechanism, Facilitated Proton Transfer, and Neighboring- Group Effects	6
	D. Electrostatic Effects	7
	E. Induced-Fit Mechanism of the Enzyme and Strain or Distortion Theory of the Substrate Bound to the Enzyme. (Relation of Energy Derived from Substrate Binding and Catalysis)	8
	F. Productive and Nonproductive Binding of Substrates	9
	G. Electro-Mechano-Chemical Model and Energy Funnel Model	9
IV.	Some Elementary Considerations of Enzyme Kinetics	10
	A. One-Substrate Reactions Having a Single Intermediate	10
	B. Inhibition by High Substrate Concentration	13
	C. Integrated Form of the Michaelis-Menten Equation and Applications	16
	D. Classical Single-Substrate Inhibition Systems of Linear Reciprocal Form in their Primary Plots and Linear in their Secondary Replots	20
	1. Competitive Inhibition	20
	2. Noncompetitive Inhibition	22
	3. Uncompetitive Inhibition	26
V.	Partial and Mixed Type of Inhibition in Single-Substrate Systems	26
	A. Partial Competitive Inhibition	26
	B. Partial Noncompetitive Inhibition	29
	C. Mixed Type of Inhibition	32
	D. Tightly Bound Inhibitors	34
	E. Tightly Bound Cofactors or Substrates	36
VI.	Effect of Temperature	37
	A. Theory of Absolute Reaction Rates	42
VII.	Kinetics of Immobilized Enzymes	47
VIII.	Some Practical Considerations in Enzyme Assays and Enzyme Kinetic Measurements	52

Chapter 2

A Description of Steady-State Kinetics and Quasi- or Rapid Equilibrium Kinetics by a Development of the Rate Expressions for Several Selected Mechanisms and Their Characteristics

I.	Procedures for the Derivation of Rate Expressions	57
	A. Straight Elimination Procedure for Steady-State Kinetics	57

B.	The Determinant Procedure for Steady-State Kinetics	57
C.	King-Altman Schematic Method (Symbolic Matrix Method) for Deriving Steady-State Rate Equations for Enzyme-Catalyzed Reactions	65
1.	A Random Steady-State Bisubstrate Reaction to Yield Reversibly a Single Product	70
D.	Two-Substrate Systems of the First Degree	78
1.	The Theorell-Chance Mechanism for Liver Alcohol Dehydrogenase	79
2.	Dalziel's Empirical Approach	88
3.	Quasi- or Rapid Equilibrium Kinetics for a Random Two-Substrate Two-Product Reaction	93
4.	Overall Velocity Expressions for Random Two-Substrate Two-Product Reactions	94
5.	Product Inhibition Patterns in the Case of Dead-End Complexes	96
6.	Special Case of Independent Binding of Two Substrates	97
7.	Steady-State Mechanism for a Compulsory Order of Addition of the Two Substrates and Dissociation of the Two Products that is, an Ordered Bi Bi System and Illustration of Cleland's Symbolism	98
8.	Rapid Equilibrium Ordered Bi Bi System	106
9.	A Case Where a Product is Released between the Additions of the Two Substrates	113
E.	An Ordered Ter Ter Sequence — A Case of a Three-Substrate System of the First Degree	119
1.	A Steady-State Kinetic Analysis of the Prolyl-4-Hydroxylase Reaction	125
2.	Alternate Nomenclature	127
3.	Random Three-Substrate (Terreactant) Rapid (Quasi-) Equilibrium System	132

Chapter 3

Inhibition and Product Inhibition

I.	Single-Substrate Cases — A Summary	139
II.	Multisubstrate Cases	141
A.	Ordered Bi Bi System	142
B.	Rapid or Quasi-Equilibrium of Random Types (Two-Substrate Reactions)	150
C.	Product Inhibition Patterns for an Ordered Ter Ter Mechanism	154
1.	Product Inhibition Patterns for Prolyl-4-Hydroxylase	159

Chapter 4

Effects of pH and Temperature

I.	Effect of pH on the Reaction Velocity	163
A.	Introduction	163
B.	pH Effects in the Steady-State and in Aqueous Solution	165
1.	Single Substrate, Single Product Rapid Equilibrium Systems with only One ES Complex	165
a.	All Forms of E Bind S ⁰ , However Only HES Yields Product	165
b.	Substrate S Ionizes with the HS Species as the Active Substrate	170

c.	All Forms of E Bind the Substrate, but Only HES and ES Yield the Product	170
d.	All Forms of E Bind S^0 , and All Forms of ES Yield Product P^0	173
e.	System C (Scheme II) with the Addition of an $ES \rightleftharpoons EP$ Step ..	173
2.	A Two-Substrate Reaction Illustrated by Brewers' Yeast Glucose 6-Phosphate Dehydrogenase	175
II.	Effect of Temperature on the Reaction Velocity	180
A.	The Measured Arrhenius Energy of Activation as Determined from Data at One Given pH Value	183
B.	Enzyme Inactivation Kinetics	184

Chapter 5

Effect of Metal Cofactors on the Reaction Velocity

I.	Unireactant Cases	191
A.	Case 1. Exclusive or Obligatory Interaction of the Free Metal with the Free Enzyme	191
B.	Case 2. Plus A Metal-Free (and Kinetically Active) E-S Complex	192
C.	Interaction of the Cation with the Substrate Prior to Reaction with the Enzyme	194
II.	Bireactant Cases	196
A.	Case I: Random Quasi-Equilibrium with Independent Binding of Substrates	197
1.	Without Enzyme-Magnesium Complexes and Product Inhibition	197
a.	Without Enzyme-Magnesium Complexes, with Product Inhibition, and Formation of "Dead-End" Complexes	199
b.	Without Enzyme-Magnesium Complexes, with Product Inhibition, but "Dead-End" Complexes are not Formed	201
2.	With Enzyme-Magnesium Complexes and Associated Reactions which are Significant Compared to Total Enzyme Concentration	202
B.	Case II. Random Quasi-Equilibrium without Independent Binding of Substrates Two General Mechanisms will be Considered Here, Case 1 Without "Dead-End" Complexes and Case 2 with "Dead-End" Complexes	207
1.	Without "Dead-End" Complexes	207
2.	With "Dead-End" Complexes	210
III.	Steady-State Kinetic Analysis of Kinase-Type of Catalyzed Reactions	212
A.	Illustrated by the Isoenzymes of Calf and Human ATP-Creatine Transphosphorylase (Creatine Kinase)	212
B.	Illustrated by the Adenylate Kinases from Rabbit and Calf Muscle and from Calf Liver	222
1.	Kinetic Analysis	225
2.	Kinetics of the Rabbit Muscle ATP-AMP Transphosphorylase	227
3.	Kinetics of the Calf Muscle and Calf Liver ATP-AMP Transphosphorylase Isoenzymes	232
C.	Some Comments on Other ATP Transphosphorylases or Kinases	237
IV.	Calculations of the Equilibrium Concentrations of the Various Ionic and Complex Species of the Substrates and Thermodynamic Functions Associated with the Catalyzed Equilibria of Kinase Type of Reactions	238

Appendix

I.	Derivation of Equations 20 and 24 from Chapter 1 Corresponding to the Mechanism of Scheme II for Inhibition by High Substrate Concentration	245
II.	Derivation of Equation 79 from Chapter 1 for Inhibition of Enzyme (E) by Antienzyme (I) with a Stoichiometry of 2E:1 I	248

Section II: Enzyme Kinetics and Substrate Binding

Chapter 6

Some Remarks on Isotope Exchange Studies and Kinetic Isotope Effects

I.	Isotope Exchange Studies	253
A.	A*-P Exchange in an Ordered BiBi System at Chemical Equilibrium	254
II.	Kinetic Isotope Effects	262
A.	Isotope Effects on Chemical Equilibria	262
B.	Isotope Effects on Rates of Chemical Reactions	265
1.	Primary Isotope Effects	265
2.	Secondary Isotope Effects	270
C.	The Northrop Method for Determination of the Absolute Magnitude of Hydrogen Isotope Effects in Enzyme-Catalyzed Reactions	272
1.	A Simple Enzyme Kinetic Mechanism with a Single Substrate-Single Product and Single ES Intermediate	272
a.	Nomenclature for Apparent Isotope Effects	273
b.	Calculation of Intrinsic Isotope Effects	273
2.	An Enzyme Kinetic Mechanism with Reversible Steps and Multiple Intermediate Complexes	275
3.	Isotope Effects on the Equilibrium Constant	277
4.	Apparent Kinetic Isotope Effects in Bisubstrate Reactions	278
5.	Some Applications of the Northrop Approach or Modifications Thereof	279

Chapter 7

Non-Michaelis-Menten Kinetics and Allosteric Kinetics

I.	Some General Remarks	283
II.	Mechanisms which may Lead to Non-Michaelis-Menten Behavior, but do not Yield Sigmoidal Kinetics	284
A.	Michaelis-Menten Kinetics Involving a Series of Intermediates which Yield Hyperbolic Reaction Velocity Expressions	284
B.	Catalysis by Two Enzymes which may Lead to Nonhyperbolic Kinetics but not Sigmoidal Kinetics	285
C.	If the Substrate Contains an Impurity that Forms an Inactive Complex with it, Sigmoidal Kinetics may not Result	285
D.	If the Substrate Contains an Impurity which Combines with the Enzyme, Forming Inactive EI, Sigmoidal Kinetics may not Occur	287
E.	The Enzyme Contains an Impurity which Forms an Inactive EI	288
III.	Mechanisms which may Lead to a Non-Michaelis-Menten Behavior and which are Sigmoidal in Nature	288
A.	The Enzyme Contains an Impurity which may Combine with the Substrate	288
B.	Two Forms of the Same Enzyme	289
C.	Consider the Case Where Two Molecules of Substrate May Bind to One Molecule of Enzyme	290

D.	The Case of the Substrate also Acting as a Modifier	290
E.	Two-Substrate Random Steady-State Systems	291
F.	Two-Substrate Mechanisms with Alternative Pathways	291
G.	The Case of Interacting Subunits and Allosteric Kinetics	292
H.	The "Induced-Fit" Model for Interacting Subunits	296
I.	Some Observations on Allosteric Kinetics	299

Chapter 8

Equilibrium Ligand Binding — Multiple Equilibria

I.	The Relationship Between the Equilibrium Constants for Ligand Binding in the Absence of Interactions	302
II.	Some General Equations for Ligand Binding for the Case of a Single Set of Sites with the Same Intrinsic Binding Constant	304
III.	Some Reduced Equations for a Single Set of Binding Sites with No Interactions	305
IV.	Competitive Binding of Two Ligands, A and B, at the Same Sites of the Protein	306
V.	Case of Multiple Classes of Binding Sites	308
	A. The Case of m Classes of Independent Sites for Binding A	308
	B. The Case for Two Independent Sites	313
VI.	Equilibrium Substrate Binding as Illustrated by the ATP-Transphosphorylase Enzymes (e.g., Creatine Kinase and Adenylate Kinase)	317
	A. Equilibrium Binding of $1,N^6$ -Etheno Analogues of Adenine Nucleotides as Measured by UV-Difference Spectroscopy	329
VII.	Structural Relationships of the Nucleotide-Magnesium Complexes to the Transphosphorylase Enzymes	336

Chapter 9

Some Complex Kinetic Mechanisms and Treatment of Enzyme Kinetic Data

I.	Some Complex Kinetic Mechanisms	341
	A. Simplification Procedures Applicable to Complex King-Altman Patterns	341
	1. Addition of Multiple Lines Connecting Two Corners	341
	a. Steady-State Equation for Monod, Wyman, and Changeux Model	341
	2. Reduction of Matrices to a Point	344
	a. A Case of an Alternative Substrate, I, which can Substitute for Substrate A in a Bisubstrate Steady-State Mechanism such as a "Ping-Pong BiBi" Mechanism	344
	3. Steady-State Systems with Rapid Equilibrium Segments	348
	a. An Ordered BiBi System where the Binding and Dissociation of the First Substrate (A) and the Last Product (Q) are Exceedingly Fast Compared to the Other Steps	348
	B. Hybrid and Mixed Mechanisms	352
	1. Hybrid "Ping-Pong — Random" BiBi System	352
	2. An Ordered Three-Substrate System with a Rapid Equilibrium Random Sequence in Ligands A and B and in R and Q	355
II.	Treatment of Enzyme Kinetic Data	359
	A. Graphical Analyses for Obtaining Provisional Estimates of the Kinetic Parameters	359

B.	Statistical Analyses	363
1.	The Least-Square Method.....	363
2.	Weighted Least-Square Plots and Variances	366
3.	Some Comments on Statistical Analysis of Multisubstrate Reactions.....	372
4.	A Few Comments on Computer Fitting of pH and Initial Rate Data	374

Chapter 10

Kinetics of the Transient Phase or Pre-Steady-State Phase of Enzymic Reactions

I.	Introduction	377
II.	Analysis of Rapid Reaction Rate Data.....	377
III.	Kinetics of the Transient Phase	382
IV.	Rapid Flow Methods	386
A.	Measurements of the Steady-State Kinetics (in Baker's Yeast) of Oxidation of the Cytochrome Chain by Molecular Oxygen	390
B.	Pre-Steady-State Kinetics of Oxidation of Cytochrome-C Oxidase by Molecular Oxygen in Intact Yeast Cells	395
V.	Relaxation Methods	401
A.	Analyses of Relaxation Times	404
1.	First Order Reaction	404
2.	Second Order Reaction	406
3.	Expressions for Relaxation Times with Two or More Steps	408
VI.	Concluding Remarks	412

Appendix

Notes Added in Retrospect	413
Acknowledgment	415

References	419
------------------	-----

Index	457
-------------	-----

TABLE OF CONTENTS

Volume II

Section I: Some Theoretical Aspects of Enzyme Mechanisms

Chapter 1

Mechanical Force, Hydration, and Conformational Fluctuations in Enzymic Catalysis 3

Rufus Lumry

Chapter 2

Complexation and Catalysis in Biology 83

R. J. P. Williams

Chapter 3

Mechanistic Role of Biotin in Enzymatic Carboxylation Reactions 105

Albert S. Mildvan, David C. Fry, and Engin H. Serpersu

Chapter 4

Thiamin-Dependent Reactions (Mechanisms) 117

Clark J. Gubler

Section II: Allostery and Non-Michaelis-Menten Behavior

Chapter 5

Glycogen Phosphorylase and Glycogen Synthetase 139

Neil B. Madsen

Section III: Proteases-Structures and Mechanisms

Chapter 6

Calcium-Activated Neutral Protease 161

Kazutomo Imahori, Koichi Suzuki, and Seiichi Kawashima

Section IV: Dehydrogenases — Structure and Catalytic Mechanisms

Chapter 7

Glutamate Dehydrogenase (Bovine Liver) 173

Roberta F. Colman

Chapter 8

Dihydrofolate Reductase 193

John F. Morrison

Chapter 9

2-Oxoacid Dehydrogenases 227

Minoru Hamada and Hitoshi Takenaka

Section V: Flavoprotein Catalysis

Chapter 10

Old Yellow Enzyme 247

Lawrence M. Schopfer and Vincent Massey

Chapter 11	
D-Amino Acid Oxidase	271
Kunio Yagi	
Chapter 12	
Cytochrome c, Quinone, and Cytochrome P-450 Reductases	285
Mark S. Johnson and Stephen A. Kuby	
Section VI: Activated Oxygen Reactions	
Chapter 13	
Dioxygenases and Monooxygenases	313
Shozo Yamamoto and Yuzuru Ishimura	
Section VII: ATP-ases, Nucleotide Binding Carriers and Nucleotidyl Transferases	
Chapter 14	
Ca ²⁺ , Mg ²⁺ -ATPase (Microsomal)	345
Hitoshi Takenaka, Michihiro Sumida, and Minoru Hamada	
Chapter 15	
Mechanistic and Energetic Aspects of Carrier Catalysis — Exemplified with Mitochondrial Translocators	367
Martin Klingenberg	
Chapter 16	
Terminal Deoxynucleotidyl Transferase	391
Mukund J. Modak and Virendra N. Pandey	
Section VIII: Phosphotransferases — Structure and Mechanisms	
Chapter 17	
Adenylate Kinase	403
Minoru Hamada, Hitoshi Takenaka, Michihiro Sumida, and Stephen A. Kuby	
Chapter 18	
Phosphofructokinase and Fructose 6-Phosphate, 2-Kinase: Fructose 2,6-Bisphosphatase	445
Kosaku Uyeda	
Section IX: Emden-Meyerhof Reactions — Mechanism of Action	
Chapter 19	
Triose- and Hexose-Phosphate Isomerases	457
K. Ümit Yüksel and Robert W. Gracy	
Chapter 20	
Mechanistic Studies of Muscle Aldolase	485
D. J. Hupe	
Section X: Metalloenzymes	
Chapter 21	
Mechanism and Structure of Superoxide Dismutases	499
John A. Tainer, Victoria A. Roberts, Cindy L. Fisher, Robert A. Hallewell, and Elizabeth D. Getzoff	

Section XI: Hydrolases — Mechanisms

Chapter 22
Phospholipases 539
Gilbert Arthur and Patrick C. Choy

Chapter 23
Esterases (Including Choline Esterases) 563
Hiromichi Okuda

Chapter 24
Lipases 579
Hiromichi Okuda

Index 597