Contents

Preface *page* ix

Part One: Basic steady state enzyme kinetics

1 Derivation of a rate equation 3
- 1.1 The role of 'diastase' in the early development of a theory 3
- 1.2 The basic assumptions on which derivation of an equation is based 7
- 1.3 The Briggs-Haldane steady state treatment of enzyme kinetic behavior 9
- 1.4 Estimation of steady state parameters 12
- 1.5 Problems for chapter 1 13

Appendix: A brief look at statistical analysis
- 1.A.1 Definition of a few statistical terms 14
- 1.A.2 Linear regression 15
- 1.A.3 Non-linear regression in enzyme kinetic analysis 18

References for chapter 1 20

2 A closer look at the basic assumptions 22
- 2.1 Why must the substrate concentration greatly exceed that of the enzyme? 22
- 2.2 What if the substrate concentration does not greatly exceed that of the enzyme? 23
- 2.3 Examination of the entire time-course of an enzymic reaction 25
- 2.4 A precise definition of steady-state velocity 27
- 2.5 Problems for chapter 2 28

References for chapter 2 28

3 Enzyme inhibition 30
- 3.1 A general model of enzyme inhibition 30

3.2 Quantitative estimates of steady state parameters in enzyme inhibition 34
3.3 Competitive inhibition: A limiting case of inhibition 35
3.4 Uncompetitive inhibition: A different limiting case 37
3.5 Substrate inhibition 38
3.6 Problems for chapter 3 41
Appendix: A brief discussion of polyonomial regression 42
References for chapter 3 43
4 Reversible enzyme-catalyzed reactions 44
4.1 Derivation of a rate equation by matrix inversion 44
4.2 Reformulation of the complete rate equation 50
4.3 The effect of product inhibition 52
4.4 Use of the King-Altman method to derive the rate equation 53
4.5 Problems for chapter 4 55
References for chapter 4 56
Part Two: Enzyme reaction sequence
5 Multi-reactant enzymic reactions 59
5.1 Three distinct two substrate, two product reaction sequences 59
5.2 The connection matrix method for deriving rate equations 61
5.3 Reformulation of the rate equations for multi-reactant enzymes 69
5.4 Problems for chapter 5 75
References for chapter 5 76
6 Analysis of multi-reactant enzyme kinetics 77
6.1 Analysis of the kinetic behavior of an enzymic reaction in the absence of products 77
6.2 Product inhibition as a tool in the analysis of reaction sequences 82
6.3 A reaction sequence with abortive complexes 87
6.4 Problems for chapter 6 91
References for chapter 6 91
7 Prediction of reaction sequence 92
7.1 The enzyme kineticist and the mystery novel 92
7.2 Product inhibition patterns: The clues with which the enzyme kineticist works 94
7.3 Problems for chapter 7 100
References for chapter 7 102
8 Enzyme-catalyzed isotopic exchange 103

8.1 Isotopic exchange in an ordered reaction sequence 104
8.2 Isotopic exchange in a random enzyme sequence 110
8.3 Problems for chapter 8 113
References for chapter 8 113
9 Kinetic isotope effect on steady state parameters 114
9.1 The basis for the kinetic isotope effect on rate constants 114
9.2 Use of the kinetic isotope effect in steady state enzyme kinetic studies 115
9.3 Problems for chapter 9 118
References for chapter 9 119
10 The effect of pH on enzyme kinetics 120
10.1 Michaelis pH functions of a simple amino acid 120
10.2 Michaelis pH functions of an enzyme 123
10.3 The effect of pH on steady state enzymic parameters 124
10.4 Effect of substrate ionization on steady state parameters 126
10.5 Problems for chapter 10 128
References for chapter 10 129
Part Three: Non-hyperbolic enzyme kinetics
11 The causes of non-hyperbolic enzyme kinetics 133
11.1 Random enzyme reaction sequences 133
11.2 The kinetic behavior of allosteric enzymes 137
11.3 Multiple enzymes catalyzing the conversion of a single substrate 138
11.4 Problems for chapter 11 138
References for chapter 11 139
12 Analysis of non-hyperbolic enzyme kinetics 140
12.1 The use of analytical geometry to analyze a substrate-saturation curve 141
12.2 Analysis of the rate equation which is a 2:2 rational function 141
12.3 Analysis of the Lineweaver-Burk plot of a 2:2 rational polynomial 143
12.4 Analysis of the Hanes plot of a 2:2 rational polynomial 149
12.5 The kinetic behavior of higher order rational polynomials 151
12.6 Problems for chapter 12 151
References for chapter 12 152
13 The effect of subunit interactions on enzyme kinetics 153
13.1 The effect of subunit interactions on rate constants 153

13.2 The effect of sequential subunit interactions 155
13.3 The effect of partially concerted subunit interactions 158
13.4 The effect of fully concerted subunit interactions 160
13.5 The effect of exclusive allosteric subunit interactions 162
13.6 Problems for chapter 13 164
References for chapter 13 165

Part Four: Control of multi-enzyme systems

14 Control of linear multi-enzyme systems 169
14.1 Definition of the parameters of metabolic control 170
14.2 Application of the sensitivity theory to the control of linear multi-enzyme systems 173
14.3 The relationship between sensitivity theory and metabolic control theory 179
14.4 The effect of feedback and feed forward loops on the control of a linear pathway 183
14.5 The quantitative estimation of control coefficients 185
14.6 Problems for chapter 14 186
Appendix 186
References for chapter 14 187

15 Control of branched multi-enzyme systems 189
15.1 Application of the sensitivity theory to branched pathways 189
15.2 Flux control in substrate cycles 194
15.3 Problems for chapter 15 197
Appendix 198
References for chapter 15 198

16 Biochemical systems theory 199
16.1 Power law formulation of control of a linear multi-enzyme system 199
16.2 Power law formulation of control of linear multi-enzyme pathways when enzyme activities are variable 205
16.3 Power law formulation for branched pathways 207
16.4 The future of metabolic control in biology 209
16.5 Problems for chapter 16 210
Appendix 210
References for chapter 16 211

Part Five: Solutions to problems

Author index 241
Subject index 244