STEADY-STATE ENZYME KINETICS

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ERRATA

1. Page 4, line 9. Substitute 'thereby' for 'hereby'.
2. Page 8, equation 1.5. Delete the three stray arrowheads in the lower centre part of the equation.
3. Page 37, equation 2.37. In the extreme R.H.S. of the equation substitute $E_1 + P$ for $E_0 + P$.
4. Page 57, equation 3.51. The R.H.S. numerator should read $V_f A$ not $V_f A$.
5. Page 60, 15th line up. Substitute A for A .
6. Page 67, equation 3.87. Substitute K_1 and K_2 for k_1 and k_2 .
7. Page 85, equation 4.55. For ③ read ④ , and for ④ read ③ .
8. Page 126, equation 5.57. In the last term of the equation substitute $\sigma_{A^2Q} Q$ for $\sigma_{AQ}^2 Q$.
9. Page 166, equation 7.35. R.H.S. should read $\phi[1 - \exp(-\varepsilon'_{\lambda}cd)]$.
10. Page 166, 6th line up. Substitute $(OD \leq 0.05)$ for $(A \leq 0.05)$.
11. Page 170, equation 7.46. Extreme R.H.S. should read $k_2 B$.
12. Page 174, line between equations 7.59 and 7.60. For $(\bar{y} = v^{-1})$ substitute $(\bar{y} = \bar{v}^{-1})$.
13. Page 179, first part of equation 7.74. R.H.S. should read $\Sigma v^3 / \Sigma v^4$.
14. Page 190, line following equation 8.36. Delete 'a'.
15. Page 199, line following equation 8.65. Substitute $\bar{v}$ for v .
16. Page 202, equation 9.3. For $\frac{dv_0}{dA}$ substitute $\frac{d^2v_0}{dA^2}$.
17. Page 219, equations 9.71 and 9.72. For v substitute $\bar{v}$.
18. Page 229, line below equation 9.116. For v_T substitute v_{τ} .
19. Page 233, last line. Insert 'T' between 'two' and 'protomers'.

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Preface

‘Kinetics deals with the rate of chemical reaction, with all the factors which influence the rate of reaction and with the explanation of the rate in terms of the reaction mechanism’ (Frost and Pearson). This succinct definition of chemical kinetics applies with equal validity to the study of the initial rates of enzyme-catalysed reactions, the subject matter of this book. It indicates the two main reasons why biochemists are interested in enzyme kinetics. First, kinetics provides the most definitive method of determining the mechanism of reaction, in the sense that any conclusion about the mechanism (which can, of course, depend on non-kinetic experiments) must be consistent with the kinetic behaviour of the enzyme; and second, the mechanism, and its associated constants, allows the biochemist to discuss the behaviour of the enzyme in a cellular environment more meaningfully and, at a more practical level, to devise efficient assays either for, or incorporating, the enzyme.

This book is almost exclusively concerned with the first function of enzyme kinetics, namely to define the mechanism of reaction. It will be noted that the method adopted is essentially negative; proposed mechanisms of reaction can be excluded as inconsistent with the kinetic data, but consistent mechanisms cannot be distinguished. The role of the enzyme kineticist is, therefore, to postulate mechanisms and by analysis predict their behaviour. The licence that is thereby provided to the rational imagination is at once the chief attraction and the principal danger of the method, for science in general, and biochemistry in particular, is seldom rational except by hindsight and the kineticist must be continually reminded of the complexity and unpredictability of enzyme behaviour. The attraction remains the satisfaction of creating working models and, under its compulsion, there has grown up a large body of enzyme kinetic theory. Formidable kinetic problems lie ahead in biochemistry not only to do with individual enzymes but also with the co-operative activity of groups of enzymes. Enzyme kinetic theory is therefore an essential part of the undergraduate curriculum, both explaining what is known and providing the necessary springboard for further investigation of enzyme activity.

It is true that undergraduates commonly regard enzyme kinetics as a difficult subject, largely because of its mathematical content. But it is my conviction, gained from teaching the subject for 10 years, that the mathematical description of kinetic ideas cannot be circumvented without delaying or even preventing the understanding of those ideas. And further, that most undergraduates come to realise, with a little practice, that the application of mathematics in steady-state enzyme kinetics is not intrinsically difficult but merely time-consuming. Indeed, at least 90% of the equations in this book can be derived with only the most elementary grounding in algebraic manipulation. Whether this simplicity will be retained as the student moves forward is an open question, but one, fortunately, that is not relevant here.

For the present, I have given expression to my conviction by developing kinetic ideas mathematically; I have, however, presented the argument as fully as possible so that the reader can pass from one stage to the next with the minimum of difficulty. In this connection, I should like to advise the reader to equip himself with pencil and paper; the actual experience of manipulating equations is invaluable, more, it is inescapable if real progress is to be made.

Another point arises here concerning the presentation. I have not attempted to give an exhaustive account of enzyme kinetics (indeed, a treatment of pre-steady-state kinetics is one notable omission); what I have attempted to do is to identify some of the basic ideas of steady-state kinetics and to explain them in a way that will enable the reader to apply the general principle involved to a particular problem that engages his attention. For this reason, the book should also be helpful to graduate students about to embark on kinetic studies themselves.

The layout of the book can be seen in the chapter headings and requires little comment. Chapter 1 is an introduction to the physical basis of enzyme action and provides examples of enzyme mechanisms that are discussed in detail elsewhere in the book. Chapters 2–8 deal with the kinetic behaviour of simple enzymes; in particular, Chapter 7 may be noted for its emphasis on practical considerations and Chapter 8 for its treatment of isotope transfer between the reactants and products of the enzyme-catalysed reaction. The last chapter describes the kinetic behaviour of oligomeric enzymes, a group of enzymes that are especially important for the regulation of metabolic activity.

Finally, thanks are due to Professor Walter Bartley and to my colleagues, notably Elizabeth Heyde, William Ferdinand, Neil Macfarlane and Julian Kinderlerer, for their help in discussing the problems of enzyme kinetics. I also remember many other friends and colleagues who have helped me, often very substantially; this book could not have been written without them.

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S.A.