A MATHEMATICAL MODEL FOR THE REACTION MECHANISM OF THE ENZYME ALCOHOL DEHYDROGENASE

by

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June 1972

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SUMMARY

1. A set of simultaneous non-linear differential equations was derived from stoichiometric equations which describe the Theorell-Chance mechanism for liver alcohol dehydrogenase.

2. Assuming that the concentrations of the intermediate complexes remained constant, an explicit solution involving three unknown parameters was obtained for the differential equations. Relaxation of the assumptions to permit the concentration of one of the intermediates to change linearly with time gave rise to a four-parameter solution. The values of the unknown parameters in the two types of solution were estimated from experimental data by the method of least squares.

3. A computer program was written to provide a numerical solution of the differential equations and the solution was used to obtain estimates of the velocity constants for the Theorell-Chance mechanism. The validity of this model for liver alcohol dehydrogenase was checked under different experimental conditions. This mechanism appears to be valid for the reaction when NAD concentrations between 80 μM and 240 μM are used.

4. The reaction of yeast alcohol dehydrogenase was also examined in relation to the Theorell-Chance mechanism. Estimates of velocity constants were obtained and numerical solutions from the computer program compared with experimental data. The results of this investigation appear to support an alternative mechanism involving the formation of a ternary complex as proposed by Theorell and Chance.

DECLARATION

I hereby declare that the work presented in this thesis has been performed by myself except where otherwise stated, and that it has not been submitted in any previous application for any degree.

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June 1972

ACKNOWLEDGEMENTS

I wish to thank my supervisors, Professor D.J.D. Nicholas (biochemistry) and Professor A.T. James and Mr. W.B. Taylor (statistics), for their help and advice with this work. Thanks are also due to Mrs. Helen Brereton for technical assistance with the biochemical work.

INTRODUCTION

Enzymes are naturally occurring organic compounds which increase the rates of certain chemical reactions while themselves remaining unchanged. The study of enzymes is of great interest since, to quote DIXON and WEBB (1964):

> "Life depends on a complex network of chemical reactions brought about by specific enzymes, and any modification of the enzyme pattern may have far reaching consequences for the living organism."

Usually an enzyme is detected by its reactions with a substrate. The amount present is estimated from the reaction velocity.

Many workers have studied the relationships between the rate of enzymic reaction and various environmental factors, such as concentration of enzyme and of substrate, temperature and pH. These observations may be used to formulate kinetic equations which describe the reaction.

This investigation is concerned with the formulation of mathematical models of enzymic reactions, and with the testing of these models by comparing predictions based upon them with data obtained from actual experiments.