ON THE KINETICS OF ENZYME REACTIONS

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The Abel type differential equation governing the kinetics of the enzyme reactions is derived. Approximate solutions of this equation corresponding to the transient phase of the reaction, before a steady state is reached, are considered. It is shown that in several cases it is possible to obtain explicit, approximate solutions to the transient phase.

1. Introduction. The Law of Mass Action is modelled by a set of simultaneous, ordinary differential equations of the first order. It is shown elsewhere (Darvey et al., 1977) that in the case of a two step, bimolecular reaction, these equations reduce to a single Abel equation (Murphy, 1960) of the first kind. In this article we shall consider the kinetics of the simplest, reversible, enzyme reaction of the type

\[ E + S \xrightleftharpoons[k_2]{k_1} X \xrightleftharpoons[k_4]{k_3} P + E. \] (1)

Here \( S, P, X \) and \( E \) denote respectively the substrate, product, a single intermediate compound, and the enzyme. The \( k_i, i = 1, 2, 3, 4 \) are the velocity constants. Since no confusion can arise in the present work, we shall employ the same notation for the concentrations of the various compounds. We shall be interested particularly in the initial stages of the reaction, that is, before a steady state is reached. This occurs usually in a very short time interval (say of the order of 1 sec, and perhaps much less) and some of the approximation employed herein will depend on this fact.

The differential equations governing enzyme kinetics have been studied
by numerous authors since the theory was formulated by Michaelis and Menten (1913). Approximate equations were analysed by Swoboda (1957) for the partially irreversible case when \( k_4 = 0 \). Some aspects of the fully reversible reaction were considered by Darvey and Matlak (1967).

Nevertheless, the general theory underlying the mathematical structure describing the reaction (1) does not appear to be well understood. We shall show below that besides the well known exact solution of Miller and Alberty when \( k_1 = k_4 \) it is possible to derive new solutions to which the biochemical situation closely approximates.

We are interested here only in analytic approximations. Numerical integration of Abel's equations presents problems of its own because of numerical values commonly encountered in biochemical reactions. It will be discussed in another publication.

2. Derivation and Reduction of Biochemical Abel Equation. In the case of the reaction (1), the Law of Mass Action gives

\[
\begin{align*}
\dot{S} &= -k_1ES + k_2X, \\
\dot{P} &= k_3X - k_4EP, \\
\dot{X} &= -\dot{E} = k_1ES + k_4EP - (k_2 + k_3)X.
\end{align*}
\] (2)

Here dots denote differentiation with respect to the time \( t \). If the initial (\( t = 0 \)) concentrations of the substrate and of the enzyme are \( S_0 \) and \( E_0 \) respectively, and those of \( X \) and \( P \) are zero, it follows immediately that

\[
S_0 = S + X + P \quad \text{and} \quad E_0 = E + X.
\] (3)

These two conservation laws or first integrals enable us to eliminate the variables \( X \) and \( E \) from (2) to give two first order equations

\[
\begin{align*}
\dot{S} &= -k_1(E_0 - S_0 + S + P)S + k_2(S_0 - S - P), \\
\dot{P} &= -k_4(E_0 - S_0 + S + P)P + k_3(S_0 - S - P),
\end{align*}
\] (4)

which form the basis of discussion of the enzyme reaction before the steady state stage is reached. On adding the two equations (4) and putting

\[ U = S + P, \]