

A First Course on Kinetics and Reaction Engineering

Example 9.1

Problem Purpose

This problem illustrates the generation of a rate expression for an enzymatic reaction where the use of catalyst conservation is required. In doing so, it illustrates the derivation of the Michaelis-Menten rate expression.

Problem Statement

Michaelis-Menten kinetics can be used to describe the enzymatic rate of conversion of a substrate to a product with the overall, macroscopically observed reaction (1), where S is used to denote the substrate and P is used to denote the product. The mechanism is given in equations (2) and (3), where E denotes free (not complexed) enzyme and E-S denotes an enzyme-substrate complex.



Assume step (3) is irreversible and use the Bodenstein steady state approximation to derive a rate expression for the overall, macroscopically observed reaction.

Problem Analysis

The problem asks us to derive a rate expression based on a mechanism. The problem does not indicate that there is a rate-determining step, so we will use the Bodenstein steady state approximation. To do so, we will generate a rate expression that sets the net rate of generation of the product equal to the sum of its rates of generation in the mechanistic steps. We will then identify the reactive intermediates and set their net rates of generation equal to zero. The resulting equations will not be mathematically independent because a catalyst is involved, so we will replace one of them with the equation for conservation of catalyst. The resulting set of equations will be solved to obtain expressions for the concentrations of the reactive intermediates, and those will be substituted, as necessary, into the rate expression.

Problem Solution

We should first check the mechanism to make sure that there is a linear combination of the steps that is equal to the overall reaction. It can be seen by inspection that the sum of steps (2) and (3) gives reaction (1), so the mechanism is valid. Since no rate-determining step has been specified, we next choose a reactant or product of the overall reaction and generate an expression for the rate of the overall reaction with respect to the chosen species. Here we will choose the product, P, but the exact same answer would be obtained if we chose the substrate, S. The rate of the overall reaction with respect to P is equal to the sum of its rate of generation in each of the mechanistic steps as expressed in equation (4).

Expanding the summation and the continuous products leads to equation (5). The problem statement also specifies that step (3) is irreversible. This means that the rate of step (3) in the reverse direction can be set equal to zero, resulting in the rate expression given in equation (6).

$$r_{P,1} = \sum_{\substack{s=\text{all} \\ \text{steps}}} v_{P,s} \left(k_{s,f} \prod_{\substack{m=\text{all} \\ \text{reactants}}} [m]^{-v_{m,s}} - k_{s,r} \prod_{\substack{n=\text{all} \\ \text{products}}} [n]^{v_{n,s}} \right) \quad (4)$$

$$r_{P,1} = k_{3,f} [E - S] - k_{3,r} [E][P] \quad (5)$$

$$r_{P,1} = k_{3,f} [E - S] \quad (6)$$

This rate expression is not acceptable because it contains the concentration of a reactive intermediate (the enzyme-substrate complex). To eliminate this reactive intermediate concentration, the Bodenstein steady state approximation, equation (7), can be applied to each reactive intermediate. In this problem there are two reactive intermediates, E and E-S. Applying equation (7) to E and E-S yields equations (8) and (9). The rate of reaction (3) in the reverse direction was set equal to zero when generating these equations because the problem states that reaction (3) is irreversible.

$$0 = \sum_{\substack{s=\text{all} \\ \text{steps}}} v_{i,s} \left(k_{s,f} \prod_{\substack{m=\text{all} \\ \text{reactants}}} [m]^{-v_{m,s}} - k_{s,r} \prod_{\substack{n=\text{all} \\ \text{products}}} [n]^{v_{n,s}} \right) \quad i = \text{reactive intermediate} \quad (7)$$

$$0 = -k_{2,f} [E][S] + k_{2,r} [E - S] + k_{3,f} [E - S] \quad (8)$$

$$0 = k_{2,f} [E][S] - k_{2,r} [E - S] - k_{3,f} [E - S] \quad (9)$$

The two equations are identical, so they can't be solved to get expressions for the concentrations of the reactive intermediates in terms of constants and the concentrations of stable species. An additional relationship is needed, and this comes from the conservation of catalyst or enzyme as expressed in equation (10). In equation (10), E^0 denotes the total amount of enzyme in the system, expressed as its equivalent concentration (i. e. its concentration if it were added to the system and it all remained non-complexed). While neither $[E]$ nor $[E-S]$ are typically known or easily measured, E^0 is known because it can be measured at the time the enzyme is being added to the system.

$$E^0 = [E] + [E - S] \quad (10)$$

Now either equation (8) or equation (9) can be solved along with equation (10) to obtain expressions for the concentrations of the reactive intermediates in terms of constants and the concentrations of stable species. This can be done manually, or software for symbolic algebra can be used. In either case, the results are given in equations (11) and (12).

$$[E] = \frac{E^0}{1 + \frac{k_{2,f}}{k_{2,r} + k_{3,f}}[S]} \quad (11)$$

$$[E - S] = \frac{k_{2,f}E^0[S]}{k_{2,r} + k_{3,f} + k_{2,r}[S]} \quad (12)$$

Finally, substituting equation (12) into equation (6) gives the desired result, equation (13). Comparing equation (13) to equation (9.5) from the informational reading, it can be seen that the two equations are equivalent if V_{max} and K_m are defined as in equations (14) and (15). Since E^0 is a constant with a known value, its presence in the rate expression presents no problems.

$$r_{p,1} = \frac{k_{2,f}k_{3,f}E^0[S]}{k_{2,r} + k_{3,f} + k_{2,r}[S]} = \frac{k_{3,f}E^0[S]}{\frac{k_{2,r} + k_{3,f}}{k_{2,f}} + [S]} \quad (13)$$

$$V_{max} = k_{3,f}E^0 \quad (14)$$

$$K_m = \frac{k_{2,r} + k_{3,f}}{k_{2,f}} \quad (15)$$