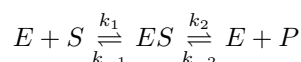


Deriving Michaelis-Menten Kinetics

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Ok, so the basic idea behind Michaelis-Menten enzyme kinetics is this: An excess supply of substrate combines with a finite amount of enzyme and forms product in two steps. The first step is relatively fast and reversible while the second step is slow. This looks like:



Because we are assuming that there is always a lot of substrate around, and that generally the concentration of any product that is made is negligible, we can ignore the reverse reaction in the second step (k_{-2}). Then, the rate of formation of product (P') is just a function of $[ES]$, given by the mass action relation

$$P' = k_2[ES]$$

Note that this is particularly true at the beginning of the reaction when there is very little product, so we call it P'_0 , the initial rate. Since it's hard to measure $[ES]$, we want to get rid of it. We make the assumption that $[ES]$ is constant (i.e. that it changes much more slowly than $[S]$ or $[P]$). Also we introduce $[E_{total}] = [E] + [ES]$, the total amount of enzyme, both free and occupied by substrate. Then we have our rate equation for the steady state of $[ES]$:

$$\begin{aligned} \text{Formation rate:} & \quad k_1[E][S] \\ \text{Breakdown rate:} & \quad (k_{-1} + k_2)[ES] \end{aligned}$$

Equating these (since it's steady state) we get

$$k_1[E][S] = (k_{-1} + k_2)[ES]$$

and inserting the total enzyme concentration, this is

$$k_1([E_{total}] - [ES])[S] = (k_{-1} + k_2)[ES]$$

Now we solve for $[ES]$:

$$[S][E_{total}] - [S][ES] = \frac{(k_{-1} + k_2)}{k_1}[ES]$$

$$\frac{[S][E_{total}]}{[ES]} - [S] = \frac{(k_{-1} + k_2)}{k_1}$$

$$[ES] = \frac{[E_{total}][S]}{\frac{(k_{-1} + k_2)}{k_1} + [S]}$$

We substitute our expression for $[ES]$ into the expression for P' (in this case defining the initial rate of reaction):

$$P'_0 = \frac{k_2[E_{total}][S]}{\frac{(k_{-1} + k_2)}{k_1} + [S]}$$

and since we know that the maximum rate of product formation P'_{max} occurs when all of the enzyme is completely occupied by substrate (in other words $[ES] = [E_{total}]$), we can use the expression for P' again, but this time at the max rate:

$$P'_{max} = k_2[E_{total}]$$

Putting this into the expression for P'_0 gives

$$P'_0 = \frac{P'_{max}[S]}{\frac{(k_{-1}+k_2)}{k_1} + [S]}$$

and introducing the 'Michaelis constant' $K_m = \frac{(k_{-1}+k_2)}{k_1}$ gives the best-known form of the M-M equation, which states that:

$$P'_0 = \frac{P'_{max}[S]}{K_m + [S]}$$

which gives the rate of product formation (at the start of the reaction, and throughout the reaction if the concentration of product is negligible with respect to concentration of substrate) as a function of substrate concentration and the enzyme-specific constants K_m and P'_{max} .

References

- [1] Lehninger Principles of Biochemistry 3rd ed. Nelson & Cox, eds. 2000. Worth Publishers. pp. 257-261