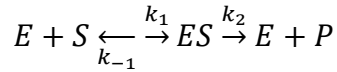


Handout 4

Michaelis-Menten enzyme kinetics



E = enzyme S = substrate P = product

Full reaction kinetics for this system:

$$\begin{aligned} \frac{d[E]}{dt} &= -k_1[E][S] + k_{-1}[ES] + k_2[ES] & \frac{d[ES]}{dt} &= k_1[E][S] - k_{-1}[ES] - k_2[ES] \\ \frac{d[S]}{dt} &= -k_1[E][S] + k_{-1}[ES] & \frac{d[P]}{dt} &= k_2[ES] \end{aligned}$$

Approach 1: quasi steady-state approximation for ES

$$\frac{d[ES]}{dt} \approx 0 = k_1[E][S] - k_{-1}[ES] - k_2[ES]$$

Using

$$[E] + [ES] = [E]_0 = \text{const} \quad \rightarrow \quad [E] = [E]_0 - [ES]$$

Substituting in above for [E] and solving for [ES],

$$\begin{aligned} [ES] &= \frac{k_1[E]_0[S]}{k_1[S] + k_{-1} + k_2} \\ &= \frac{[E]_0[S]}{[S] + (k_{-1} + k_2)/k_1} \\ &= \frac{[E]_0[S]}{[S] + K_M} \end{aligned}$$

where we have made the definition:

$$K_M \equiv \frac{k_{-1} + k_2}{k_1}$$

Now compute the rate of product formation:

$$\begin{aligned} v &= \frac{dP}{dt} \\ &= k_2[ES] \\ &= \frac{k_2[E]_0[S]}{[S] + K_M} \end{aligned}$$

Make the definition:

$$v_{\max} \equiv k_2[E]_0$$

Then the rate is given by,

$$v = v_{\max} \frac{[S]}{[S] + K_M}$$

Approach 2: rapid equilibrium approximation for $E + S \leftrightarrow ES$

Assume that substrate binding is in equilibrium with the reactants. Then,

$$\frac{[ES]}{[E][S]} = \frac{k_1}{k_{-1}}$$

Solving for $[E]$,

$$[E] = \frac{k_{-1}[ES]}{k_1[S]}$$

Combining with the mass balance equation $[E] + [ES] = [E]_0$,

$$\frac{k_{-1}[ES]}{k_1[S]} + [ES] = [E]_0$$

Solving for $[ES]$,

$$[ES] = \frac{[E]_0[S]}{[S] + \frac{k_{-1}}{k_1}}$$

If we now define

$$K_M \equiv \frac{k_{-1}}{k_1}$$

Then,

$$[ES] = \frac{[E]_0[S]}{[S] + K_M}$$

And the remainder of the derivation proceeds as before.

Therefore the quasi steady-state and equilibrium approximations lead to slightly different expressions for the Michaelis constant K_M . For reactions that are rate-limited in the formation of the product, $k_2 \ll k_{-1}$, the two approaches are roughly equivalent.