Enzyme kinetics

In our previous discussions, we determined that (under the Law of Mass Action) the model

$$E + S \rightarrow P + E$$

does not fit empirical data very well. Michaelis and Menton developed the model

$$\mathrm{E} + \mathrm{S} \underset{k_1^-}{\overset{\mathrm{k}_1^+}{\rightleftharpoons}} \mathrm{C} \xrightarrow{k_2} \mathrm{P} + \mathrm{E}$$

which fits experimental results much better. By performing equilibrium analysis, we concluded that the rate of the reaction is

$$V = \frac{dp}{dt} = \frac{V_{max} \cdot [S]}{K_D + [S]}$$

However, this still assumed that $\frac{d}{dt}[S] \approx 0$...which is a problem. If we assume that enzymes are primarily occupied with binding substrate, then instead we can set $\frac{d}{dt}[C] \approx 0$...that is, the concentration of the substrate/enzyme complex remains more or less consistent. From this, we can derive the following.

$$\frac{dc}{dt} = k_1^+[S][E] - (k_1^- + k_2)[C]$$

Since $\frac{dc}{dt} \approx 0$, we have

$$k_1^+[S][E] = (k_1^- + k_2)[C]$$

$$[C] = \frac{k_1^+}{k_1^- + k_2}[S][E]$$

We are interested in

$$V = \frac{dp}{dt} = k_2[C]$$

in terms of $[S]$.

$$[C] = \frac{k_1^+}{k_1^- + k_2}[S](e_0 - [C]) = \frac{e_0[S]}{\frac{k_1^+}{k_1^- + k_2} + [S]} = \frac{e_0[S]}{K_M + [S]}$$

Therefore,

$$V = \frac{dp}{dt} = k_2 \frac{e_0[S]}{K_M + [S]} = \frac{V_{max} \cdot [S]}{K_M + [S]}$$

Inhibition

- competitive
- allosteric

You can distinguish these two by changing the substrate concentration and observing the maximum reaction velocity (rate).

Competitive inhibition

$$\mathrm{E} + \mathrm{S} \underset{k_1^-}{\overset{\mathrm{k}_1^+}{\rightleftharpoons}} \mathrm{C}_1 \xrightarrow{k_2} \mathrm{P} + \mathrm{E}$$

$$\mathrm{E} + \mathrm{I} \underset{k_3^-}{\overset{\mathrm{k}_3^+}{\rightleftharpoons}} \mathrm{C}_2$$

Let's assume $\frac{dc_1}{dt} \approx 0$ and $\frac{dc_2}{dt} \approx 0$.

$$[C_1] = \frac{k_i e_0 [S]}{K_M[I] + k_i[S] + K_m k_i}$$

$$[C_2] = \frac{K_m e_0 [I]}{K_M[I] + k_i[S] + K_m k_i}$$

$$k_i = \frac{k_3^-}{k_3^+} \qquad \text{(dissociation constant of inhibitor)}$$

$$k_m = \frac{k_2 + k_1^-}{k_1^+}$$

$$V = \frac{dp}{dt} = k_2[C_1]\frac{k_2 e_0 [S] k_i}{k_m[I] + k_i[S] + k_m k_i} = \frac{[S]V_{max}}{[S] + k_m\left(1 + \frac{[I]}{k_i}\right)}$$

$$V = \frac{V_{max} \cdot [S]}{[S] + k_m\left(1 + \frac{[I]}{k_i}\right)}$$

If we saturate with substrate, we will still get maximum velocity eventually.

Allosteric inhibition

$$V = \frac{V_{max}}{1 + \frac{i}{k_i}} \cdot \frac{[S]}{k_m + [S]}$$

In allosteric inhibition, the maximum velocity is reduced.