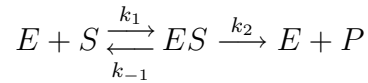# Simple MM

The enzymatic reaction is assumed to be irreversible, and the product does not bind to the enzyme.

$$E + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ES \xrightarrow{k_2} E + P$$

We can write down the following kinetic equations where we use the quasi-steady-state assumption for the enzyme-substrate complex and the assumption that the total enzyme concentration is constant over the timescale considered:

$$\frac{d[ES]}{dt} = k_1[E][S] - [ES](k_{-1} + k_2) \overset{!}{=} 0$$

$$\frac{d[P]}{dt} = k_2[ES]$$

$$[E]_0 = [E] + [ES] \overset{!}{=} \text{const}$$

We then express [ES] in terms of the other variables
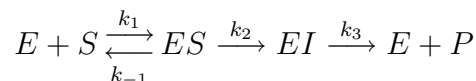
$$0 = k_1[S]([E]_0 - [ES]) - [ES](k_{-1} + k_2)$$

$$k_1[S][E]_0 = k_1[S][ES] + [ES](k_{-1} + k_2)$$

$$[S][E]_0 = [S][ES] + [ES]\underbrace{\frac{k_{-1} + k_2}{k_1}}_{K_M}$$

$$[S][E]_0 = (K_M + [S])[ES]$$

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

We can now express the (initial) reaction rate as follows

$$\frac{d[P]}{dt} = v_0 = k_2[ES] = \underbrace{k_2[E]_0}_{v_{max}} \frac{[S]}{K_M + [S]}$$

$$v_0 = \frac{v_{max}[S]}{K_M + [S]}$$

$$\frac{1}{v_0} = \frac{K_M}{v_{max}} \cdot \frac{1}{[S]} + \frac{1}{v_{max}}$$

MM with intermediate

For the less simple case with an intermediate we have

$$E + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ES \xrightarrow{k_2} EI \xrightarrow{k_3} E + P$$

We can write down the following kinetic equations where we use the quasi-steady-state assumptions for both intermediate enzyme complexes and the assumption that the total enzyme concentration is constant over the timescale considered:

$$\frac{d[P]}{dt} = k_3[EI]$$

$$\frac{d[EI]}{dt} = k_2[ES] - k_3[EI] \overset{!}{=} 0$$

$$\frac{d[ES]}{dt} = k_1[E][S] - [ES](k_{-1} + k_2) \overset{!}{=} 0$$

$$[E]_0 = [E] + [ES] + [EI] \overset{!}{=} \text{const}$$

Now again we express [ES] in terms of the other variables

$$0 = k_1[S]([E]_0 - [ES] - [EI]) - [ES](k_{-1} + k_2)$$

$$k_1[S]([E]_0 - [EI]) = k_1[S][ES] + [ES](k_{-1} + k_2)$$

$$[S]([E]_0 - [EI]) = [S][ES] + [ES]\underbrace{\frac{k_{-1} + k_2}{k_1}}_{K_M}$$

$$[S]([E]_0 - [EI]) = (K_M + [S])[ES]$$

$$[ES] = \frac{[S]([E]_0 - [EI])}{K_M + [S]}$$

This time we have another intermediate complex, for which we have to find an expression, thus we solve for [EI]:

$$0 = k_2[ES] - k_3[EI]$$

$$0 = k_2\frac{[S]([E]_0 - [EI])}{K_M + [S]} - k_3[EI]$$

$$0 = k_2\frac{[S][E]_0}{K_M + [S]} - k_2\frac{[S][EI]}{K_M + [S]} - k_3[EI]$$

$$k_2\frac{[S][E]_0}{K_M + [S]} = (k_2\frac{[S]}{K_M + [S]} + k_3)[EI]$$

$$[EI] = k_2\frac{[S][E]_0}{(K_M + [S])(k_2\frac{[S]}{K_M+[S]} + k_3)}$$

$$[EI] = k_2\frac{[S][E]_0}{k_2[S] + k_3(K_M + [S])}$$

Now we can express the (initial) reaction rate as follows

$$\frac{d[P]}{dt} = v_0 = k_3[EI] = k_3 k_2 \frac{[E]_0[S]}{k_3 K_M + [S](k_2 + k_3)}$$

$$\frac{d[P]}{dt} = \underbrace{\frac{k_3 k_2}{k_2 + k_3}}_{k_{cat}} \cdot \frac{[E]_0[S]}{\underbrace{\frac{k_3}{k_2 + k_3} K_M}_{K'_M} + [S]}$$

$$v_0 = k_{cat} \frac{[S][E]_0}{K'_M + [S]}$$

MM with intermediate and backreaction

For the more general case with an intermediate and reverse reaction we have
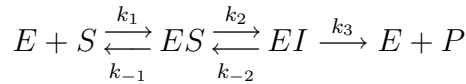
$$E + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ES \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} EI \xrightarrow{k_3} E + P$$

We can write down the following kinetic equations where we use the quasi-steady-state assumptions for both intermediate enzyme complexes and the assumption that the total enzyme concentration is constant over the timescale considered:

$$\frac{d[P]}{dt} = k_3[EI]$$

$$\frac{d[EI]}{dt} = k_2[ES] - k_{-2}[EI] - k_3[EI] \overset{!}{=} 0$$

$$\frac{d[ES]}{dt} = k_1[E][S] + k_{-2}[EI] - [ES](k_{-1} + k_2) \overset{!}{=} 0$$

$$[E]_0 = [E] + [ES] + [EI] \overset{!}{=} \text{const}$$

Now again we express [ES] in terms of the other variables

$$0 = k_1[S]([E]_0 - [ES] - [EI]) + k_{-2}[EI] - [ES](k_{-1} + k_2)$$

$$k_1[S]([E]_0 - [EI]) + k_{-2}[EI] = k_1[S][ES] + [ES](k_{-1} + k_2)$$

$$[S]([E]_0 - [EI]) + \frac{k_{-2}}{k_1}[EI] = [S][ES] + [ES] \underbrace{\frac{k_{-1} + k_2}{k_1}}_{K_M}$$

$$[S]([E]_0 - [EI]) + \frac{k_{-2}}{k_1}[EI] = (K_M + [S])[ES]$$

$$[ES] = \frac{[S]([E]_0 - [EI])}{K_M + [S]} + \frac{k_{-2}}{k_1} \frac{[EI]}{K_M + [S]}$$

Here we have to solve for [EI]:

$$0 = k_2[ES] - k_{-2}[EI] - k_3[EI]$$

$$0 = k_2\frac{[S][E]_0}{K_M + [S]} - k_2\frac{[S][EI]}{K_M + [S]} + k_2\frac{k_{-2}}{k_1}\frac{[EI]}{K_M + [S]} - k_{-2}[EI] - k_3[EI]$$

$$k_2\frac{[S][E]_0}{K_M + [S]} = (k_2\frac{[S]}{K_M + [S]} + k_2\frac{k_{-2}}{k_1}\frac{1}{K_M + [S]} + k_{-2} + k_3)[EI]$$

$$[EI] = k_2[S][E]_0\frac{1}{k_2[S] + k_2\frac{k_{-2}}{k_1} + K_M(k_{-2} + k_3) + [S](k_{-2} + k_3)}$$

Now we can express the (initial) reaction rate as follows

$$\frac{d[P]}{dt} = v_0 = k_3[EI]$$

$$v_0 = k_3 k_2 [E]_0 \cdot \frac{[S]}{K_M(k_{-2} + k_3) + [S](k_2 + k_{-2} + k_3) + k_2\frac{k_{-2}}{k_1}}$$

We can try to simplify and again get an expression that is similar to the simple Michaelis-Menten equation

$$v_0 = \underbrace{\frac{k_3 k_2}{k_2 + k_{-2} + k_3}}_{k_{cat}}[E]_0 \cdot \frac{[S]}{\underbrace{K_M \frac{k_{-2} + k_3}{k_2 + k_{-2} + k_3}}_{K'_M} + [S] + \underbrace{\frac{k_2 k_{-2}}{k_1(k_2 + k_{-2} + k_3)}}_{\gamma}}$$

$$v_0 = k_{cat}\frac{[E]_0[S]}{K'_M + [S] + \gamma}$$

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