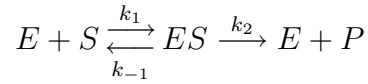


Simple MM

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



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:

$$\begin{aligned}\frac{d[ES]}{dt} &= k_1[E][S] - [ES](k_{-1} + k_2) \stackrel{!}{=} 0 \\ \frac{d[P]}{dt} &= k_2[ES] \\ [E]_0 &= [E] + [ES] \stackrel{!}{=} \text{const}\end{aligned}$$

We then express [ES] in terms of the other variables

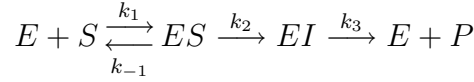
$$\begin{aligned}0 &= k_1[S]([E]_0 - [ES]) - [ES](k_{-1} + k_2) \\ k_1[S][E]_0 &= k_1[S][ES] + [ES](k_{-1} + k_2) \\ [S][E]_0 &= [S][ES] + [ES] \underbrace{\frac{(k_{-1} + k_2)}{k_{-1}}}_{K_M} \\ [S][E]_0 &= (K_M + [S])[ES] \\ [ES] &= \frac{[S][E]_0}{K_M + [S]}\end{aligned}$$

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

$$\begin{aligned}\frac{d[P]}{dt} &= v_0 = k_2[ES] = \underbrace{k_2[E]_0}_{v_{max}} \frac{[S]}{K_M + [S]} \\ v_0 &= \frac{v_{max}[S]}{K_M + [S]} \\ \frac{1}{v_0} &= \frac{K_M}{v_{max}} \cdot \frac{1}{[S]} + \frac{1}{v_{max}}\end{aligned}$$

MM with intermediate

For the less simple case with an intermediate we have



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:

$$\begin{aligned} \frac{d[P]}{dt} &= k_3[EI] \\ \frac{d[EI]}{dt} &= k_2[ES] - k_3[EI] \stackrel{!}{=} 0 \\ \frac{d[ES]}{dt} &= k_1[E][S] - [ES](k_{-1} + k_2) \stackrel{!}{=} 0 \\ [E]_0 &= [E] + [ES] + [EI] \stackrel{!}{=} \text{const} \end{aligned}$$

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

$$\begin{aligned} 0 &= k_1[S]([E]_0 - [ES] - [EI]) - [ES](k_{-1} + k_2) \\ k_1[S]([E]_0 - [EI]) &= k_1[S][ES] + [ES](k_{-1} + k_2) \\ [S]([E]_0 - [EI]) &= [S][ES] + [ES] \underbrace{\frac{(k_{-1} + k_2)}{k_{-1}}}_{K_M} \\ [S]([E]_0 - [EI]) &= (K_M + [S])[ES] \\ [ES] &= \frac{[S]([E]_0 - [EI])}{K_M + [S]} \end{aligned}$$

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

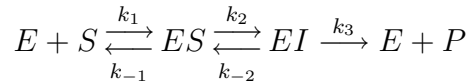
$$\begin{aligned} 0 &= k_2[ES] - k_3[EI] \\ 0 &= k_2 \frac{[S]([E]_0 - [EI])}{K_M + [S]} - k_3[EI] \\ 0 &= k_2 \frac{[S][E]_0}{K_M + [S]} - k_2 \frac{[S][EI]}{K_M + [S]} - k_3[EI] \\ k_2 \frac{[S][E]_0}{K_M + [S]} &= (k_2 \frac{[S]}{K_M + [S]} + k_3)[EI] \\ [EI] &= k_2 \frac{[S][E]_0}{(K_M + [S])(k_2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

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

$$\begin{aligned}\frac{d[P]}{dt} &= v_0 = k_3[EI] = k_3k_2 \frac{[E]_0[S]}{k_3K_M + [S](k_2 + k_3)} \\ \frac{d[P]}{dt} &= \underbrace{\frac{k_3k_2}{k_2 + k_3}}_{k_{cat}} \cdot \frac{[E]_0[S]}{\underbrace{\frac{k_3}{k_2 + k_3}K_M + [S]}_{K'_M}} \\ v_0 &= k_{cat} \frac{[S][E]_0}{K'_M + [S]}\end{aligned}$$

MM with intermediate and backreaction

For the more general case with an intermediate and reverse reaction we have



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:

$$\begin{aligned}\frac{d[P]}{dt} &= k_3[EI] \\ \frac{d[EI]}{dt} &= k_2[ES] - k_{-2}[EI] - k_3[EI] \stackrel{!}{=} 0 \\ \frac{d[ES]}{dt} &= k_1[E][S] + k_{-2}[EI] - [ES](k_{-1} + k_2) \stackrel{!}{=} 0 \\ [E]_0 &= [E] + [ES] + [EI] \stackrel{!}{=} \text{const}\end{aligned}$$

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

$$\begin{aligned}0 &= k_1[S]([E]_0 - [ES] - [EI]) + k_{-2}[EI] - [ES](k_{-1} + k_2) \\ k_1[S]([E]_0 - [EI]) + k_{-2}[EI] &= k_1[S][ES] + [ES](k_{-1} + k_2) \\ [S]([E]_0 - [EI]) + \frac{k_{-2}}{k_1}[EI] &= [S][ES] + [ES] \underbrace{\frac{(k_{-1} + k_2)}{k_{-1}}}_{K_M} \\ [S]([E]_0 - [EI]) + \frac{k_{-2}}{k_1}[EI] &= (K_M + [S])[ES] \\ [ES] &= \frac{[S]([E]_0 - [EI])}{K_M + [S]} + \frac{k_{-2}}{k_1} \frac{[EI]}{K_M + [S]}\end{aligned}$$

Here we have to solve for $[EI]$:

$$\begin{aligned}
 0 &= k_2[ES] - k_{-2}[EI] - k_3[EI] \\
 0 &= k_2 \frac{[S][E]_0}{K_M + [S]} - k_2 \frac{[S][EI]}{K_M + [S]} + k_2 \frac{k_{-2}}{k_1} \frac{[EI]}{K_M + [S]} - k_{-2}[EI] - k_3[EI] \\
 k_2 \frac{[S][E]_0}{K_M + [S]} &= (k_2 \frac{[S]}{K_M + [S]} + k_2 \frac{k_{-2}}{k_1} \frac{1}{K_M + [S]} + k_{-2} + k_3)[EI] \\
 [EI] &= k_2[S][E]_0 \frac{1}{k_2[S] + k_2 \frac{k_{-2}}{k_1} + K_M(k_{-2} + k_3) + [S](k_{-2} + k_3)}
 \end{aligned}$$

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

$$\begin{aligned}
 \frac{d[P]}{dt} &= v_0 = k_3[EI] \\
 v_0 &= k_3 k_2 [E]_0 \cdot \frac{[S]}{K_M(k_{-2} + k_3) + [S](k_2 + k_{-2} + k_3) + k_2 \frac{k_{-2}}{k_1}}
 \end{aligned}$$

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

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

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