1 The Michaelis-Mentil Model

Image from Biostats Book

Where does this come from?

1.1 Some background

In biochemistry, Michaelis-Menten kinetics is one of the simplest and best-known models of enzyme kinetics. It is named after German biochemist Leonor Michaelis and Canadian physician Maud Menten. The reaction can be illustrated as

$$\mathrm{E} + \mathrm{S} \rightleftharpoons \mathrm{ES} \longrightarrow \mathrm{E} + \mathrm{P}$$

where E is the enzime, S is the substrate, ES is the enzyme binding to the substrate, and P is a product.

Question: How can we model this?

1.2 Building a Mathematical Model

$$\mathrm{E} + \mathrm{S} \rightleftharpoons \mathrm{ES} \longrightarrow \mathrm{E} + \mathrm{P}$$

- $\frac{d[E]}{dt}$ depends on ??
- $\frac{d[S]}{dt}$ depends on ??
- $\frac{d[ES]}{dt}$ depends on ??
- $\frac{d[P]}{dt}$ depends on ??

This leads to the following system of differential equations:

$$\mathrm{E} + \mathrm{S} \underset{\mathrm{k_r}}{\overset{\mathrm{k_f}}{\rightleftharpoons}} \mathrm{ES} \xrightarrow{\mathrm{k_{cat}}} \mathrm{E} + \mathrm{P}$$

$$\frac{d[S]}{dt} = -k_f[E][S] + k_r[ES] \tag{1}$$

$$\frac{d[E]}{dt} = -k_f[E][S] + k_r[ES] + k_{cat}[ES] \tag{2}$$

$$\frac{d[ES]}{dt} = k_f[E][S] - k_r[ES] - k_{cat}[ES] \tag{3}$$

$$\frac{d[P]}{dt} = k_{cat}[ES] \tag{4}$$

2 Simplifying the Model

Now we make some simplifications:

- If the enzyme is conserved, then $[E]+[ES] = [E]_0$ is a constant.
- In situations where $\frac{d[P]}{dt}$ is constant (3) and (4) imply that $\frac{d[ES]}{dt} = 0$. This is often used as an approximation when $\frac{d[P]}{dt}$ is nearly constant.

- From this it follows that

$$
\begin{aligned}
k_f[E][S] &= (k_r + k_{cat})[ES] \\
k_f([E]_0 - [ES])[S] &= (k_r + k_{cat})[ES] \\
([E]_0 - [ES])[S] &= \frac{k_r + k_{cat}}{k_f}[ES] \\
[E]_0[S] &= \left(\frac{k_r + k_{cat}}{k_f} + [S]\right)[ES] \\
[ES] &= \frac{[E]_0[S]}{\frac{k_r+k_{cat}}{k_f} + [S]} \\
k_{cat}[ES] &= \frac{k_{cat}[E]_0[S]}{\frac{k_r+k_{cat}}{k_f} + [S]} \\
v = \frac{d[P]}{dt} &= \frac{k_{cat}[E]_0[S]}{\frac{k_r+k_{cat}}{k_f} + [S]}
\end{aligned}
$$

- From
$$v = \frac{d[P]}{dt} = \frac{k_{cat}[E]_0[S]}{\frac{k_r+k_{cat}}{k_f} + [S]}$$
ignoring the meaning of the constants (for the moment) and focusing on the form, we now have the following sort of relationship between v and $[S]$
$$v = \frac{\alpha[S]}{\beta + [S]} \tag{5}$$
That is, the "velocity" of the reaction (rate at which the product is produced) is determined by the concentration of the substrate and constants that do not depend on v or $[S]$.