7 Modeling biochemical reactions

In biochemistry 2+ species, or reactants can react if they come together & collide. Or, 1 species can degrade.

More is needed, though: right orientation, enough energy, etc.

Ex: $CH_4 + 2O_2 \longrightarrow CO_2 + 2H_2O$ (burning of methane)

$H^+ + OH^- \longrightarrow H_2O$

unfolded protein $\longrightarrow$ folded protein

$2SO_2 + O_2 \rightleftharpoons 2SO_3$

$O_3 \longrightarrow O_2 + O$

$2O_3 \longrightarrow 3O_2$

Classification of reactions

$A \longrightarrow P$ uni-molecular

$A + B \longrightarrow P$ bi-molecular

$A + B + C \longrightarrow P$ tri-molecular.

By the law of mass-action kinetics, a reaction rate is proportional to the prob. of collision of reactants involved.

Assume this prob. is proportional to concentration of each reactant.

[2]

Ex: $A \xrightarrow{k} P$ $\quad \frac{d[P]}{dt} = k[A]$ where $[\cdot]$ denotes concentration.

$A + B \xrightarrow{k} P$ $\quad \frac{d[P]}{dt} = k[A][B]$

$A + B \underset{k_2}{\overset{k_1}{\rightleftharpoons}} P$ $\quad \frac{d[P]}{dt} = k_1[A][B] - k_2[P]$

Enzymes: Proteins that catalyze reactions (up to 10^{12}-fold!)

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

E = enzyme
S = substrate
ES = enzyme-substrate complex
P = product

$$\frac{d[ES]}{dt} = k_1[E][S] - (k_2 + k_3)[ES]$$

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

$E_0 = [E] + [ES]$ $\quad E_0$ = initial enzyme concentration.

Assumptions:
- E_0 is constant
- Enzyme-substrate complex reaches steady-state much earlier than product does, so $\frac{d[ES]}{dt} \approx 0$.

$$\Rightarrow \frac{d[ES]}{dt} = k_1[E][S] - (k_2 + k_3)[ES] = 0$$

$$\Rightarrow [E] = \frac{(k_2 + k_3)[ES]}{k_1[S]}$$

Plug this into $E_0 = [E] + [ES]$

$$\Rightarrow [ES] = \frac{E_0[S]}{\frac{k_2+k_3}{k_1} + [S]}$$

$f([S])$

Plug into $\frac{d[P]}{dt} = k_3[ES] \Rightarrow$ $\boxed{\frac{d[P]}{dt} = \frac{V_{max}\cdot[S]}{K_m + [S]}}$ "Michaelis-Menten equation"

where $V_{max} = k_3 E_0$

$K_m = \frac{k_2+k_3}{k_1}$

Remarks:

- $f([S])$ is an increasing function.
- $\lim_{[S]\to\infty} f([S]) = V_{max}$ (this is biologically, the maximum reaction rate)
- $f(K_m) = \frac{V_{max}}{2}$
- Since $V_{max} = k_3 E_0 > 0$, the reaction rate is a linear increasing function of E_0 (double E_0, reaction rate doubles)

Another assumption: Substrate concentration is conserved: $S_0 = [S] + [ES] + [P]$.

Also, usually $E_0 \ll S_0$, so $[ES] \ll [S]$ & $[P]$

$\Rightarrow S_0 \approx [S] + [P]$.

Assuming equality, $[S] = -[P] \Rightarrow \frac{d[S]}{dt} = -\frac{d[P]}{dt} = \frac{-V_{max}\cdot[S]}{K_m + [S]}$

Usually, V_{max}, K_m, S_0 are known quantities. Can solve for rest.

Multi-molecule binding

Some enzymes react with ≥ 2 substrate molecules.

Assume all binding sides on enzyme are identical, independent.

$$E + nS \underset{k_2}{\overset{k_1}{\rightleftharpoons}} ES_n \xrightarrow{k_3} P + E$$

By mass-action kinetics: $\frac{d[ES_n]}{dt} = k_1[E][S]^n - (k_2 + k_3)[ES_n]$

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

Assume $[ES_n]$ → steady-state quicker than $[P]$, $[S]$, $[E]$.

$$\left(\text{set } \frac{d[ES_n]}{dt} = 0\right) \Rightarrow [E] = \frac{(k_2 + k_3)[ES_n]}{k_1[S]^n} \quad \text{and} \quad E_0 = [E] + [ES_n]$$

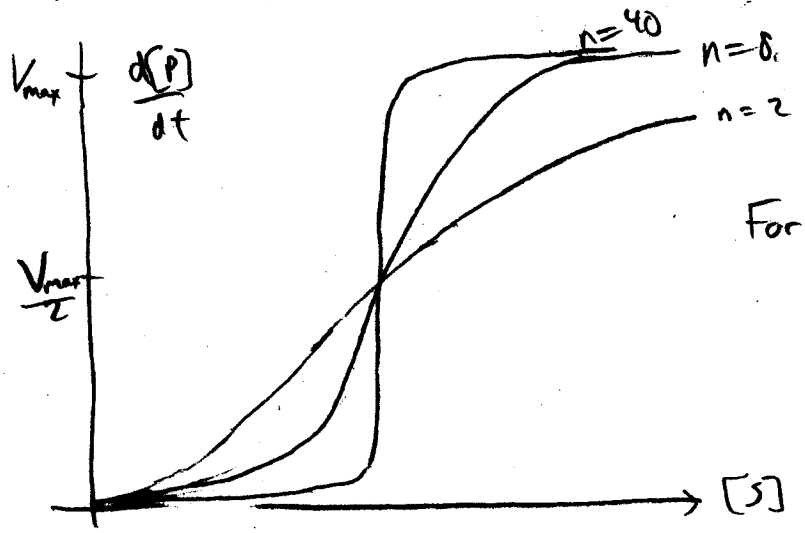
$$\Rightarrow [ES_n] = \frac{E_0[S]^n}{\frac{k_2 + k_3}{k_1} + [S]^n} \quad \text{and} \quad \boxed{\frac{d[P]}{dt} = \underbrace{\frac{V_{max}[S]^n}{K_m + [S]^n}}_{f([S])}}$$

"Hill equation", Hill coefficient n

Remarks:

- $f([S])$ is strictly increasing
- $\lim_{[S]\to\infty} f([S]) = V_{max}$
- $f(K_m^{1/n}) = \frac{V_{max}}{2}$
- Since $V_{max} = k_3 E_0$, the reaction rate is linear in E_0.
- $n=1$ is just the Michaelis-Menden function.

Hill functions



For $n \gg 1$, these are called "sigmoidal curves"

Again, usually $E_0 \ll S_0$ $\Rightarrow$ assume $S_0 = [S] + [P]$

$$\Rightarrow \frac{d[S]}{dt} = -\frac{V_{max}[S]^n}{K_m + [S]^n}$$