Mathematical Biology - Lecture 4 — biochemical kinetics
• molecular and cellular biology – frontier between the physical sciences and the life sciences

• kinetics of chemical processes: metabolism, information transmission, defence mechanisms, transport of essential substances, mechanical work

• complexity in biochemical reactions – conventional wisdom about equilibrium – Prigogine – complexity possible when far from equilibrium – metabolism
chemical kinetics

law of mass action: Guldberg, Waage and van’t Hoff

$$A + B \rightleftharpoons C + D$$

chemical affinity or reaction force: $\alpha [A]^a [B]^b$

developed a dynamical view of the chemical reaction based on chemical affinity but too complicated – so study of equilibrium conditions

at equilibrium, forward and backward reactions go at a rate such that there is no more change:

$$k_+[A][B] = k_-[C][D]$$
dynamics of chemical processes

\[ A + B \rightarrow C \]

\[ \frac{d[C]}{dt} = -\frac{d[A]}{dt} = -\frac{d[B]}{dt} = k[A][B] \]

\[ A + B \Leftrightarrow C \]

\[ \frac{d[C]}{dt} = -\frac{d[A]}{dt} = -\frac{d[B]}{dt} = k_+[A][B] - k_-[C] \]
Michaelis-Menten kinetics

Victor Henri – chemistry of enzyme reactions – Michaelis and Menten – hydrolysis of sucrose and fructose catalysed by invertase

substrate S, enzyme E, complex C, product P

\[ E + S \rightleftharpoons C \rightarrow P + E \]

forward rates: \( k_1, k_2 \)

backward rate: \( k_{-1} \)

\[
\frac{dS}{d\tau} = k_{-1}C - k_1SE; \quad \frac{dE}{d\tau} = (k_{-1} + k_2)C - k_1SE
\]

\[
\frac{dC}{d\tau} = k_1SE - (k_{-1} + k_2)C; \quad \frac{dP}{d\tau} = k_2C
\]
Michaelis-Menten kinetics

\[
\frac{d(E + C)}{d\tau} = 0; \quad E + C = E_0
\]

\(E_0\) - conservation of total amount of enzyme in free and bound state

\[
\frac{d(S + C + P)}{d\tau} = 0; \quad S + C + P = S_0
\]

\(S_0\) - conservation of substrate as itself, complex or product; enzyme is only a catalyst
Michaelis-Menten kinetics

\[ \frac{dS}{d\tau} = k_{-1}C - k_1S(E_0 - C); \quad \frac{dC}{d\tau} = k_1S(E_0 - C) - (k_{-1} + k_2)C \]

\[ S(0) = S_0; \quad E(0) = E_0; \quad C(0) = P(0) = 0 \]

Hydrolysis of benzoyl-L-arginine ethyl ester by trypsin
different time scales of the reaction and different concentrations

concentration of complex rises very fast, substrate remains unchanged concentrations of substrate and complex change at a slower time scale

Assuming \( \frac{dc}{d\tau} = 0 \), we can solve for the equilibrium concentration of complex

\[
C = \frac{k_1 SE_0}{k_1 + k_2 + k_1 S} = \frac{SE_0}{K_m + S}
\]

\[
\frac{dS}{d\tau} = -k_2 C = -\frac{V_m S}{K_m + S}, \quad V_m = k_2 E_0; \quad K_m = \frac{k_{-1} + k_2}{k_1}
\]
quasi-steady-state

saturation function: \( Y(S) = \frac{C}{E+C} = \frac{S}{K_m+S} \)

overall rate of the reaction \( \frac{dP}{d\tau} = V_m Y(S) = \frac{V_mS}{K_m+S} \) - Michaelis-Menten rate equation

in more complicated cases, we use a technique of matched asymptotic expansions

exercise in non-dimensionalising
Hill function

\[
\frac{dx}{dt} = f(x; \theta) = \frac{ax^n}{\theta^n + x^n}
\]

Reaction velocity curve sigmoidal in many cases – co-operative phenomenon

Several identical binding units – protomers and one binding site for each ligand for each protomer

dimer: \( E + S \xrightarrow[k_{-1}]{2k_1} C_1 \xrightarrow{k_3} E + P \), \( C_1 + S \xrightarrow[k_1']{2k_2'} C_2 \xrightarrow{2k_2'} C_1 + P \).
Hill function

\[
\frac{dS}{d\tau} = -2k_1 ES - k'_1 C_1 S + k_{-1} C_1 + 2k'_{-1} C_2
\]

\[
\frac{dE}{d\tau} = -2k_1 ES + k_{-1} C_1 + k_2 C_1
\]

\[
\frac{dC_1}{d\tau} = 2k_1 ES - k_2 C_1 - k'_1 C_1 S - k_{-1} C_1 + 2k'_{-1} C_2 + 2k'_2 C_2
\]

\[
\frac{dC_2}{d\tau} = k'_1 C_1 S - 2k'_{-1} C_2 - 2k'_1 C_2
\]

\[
\frac{dP}{d\tau} = k_2 C_1 + 2k'_2 C_2
\]

\[
E + C_1 + C_2 = E_0; \quad S + C_1 + 2C_2 + P = S_0
\]
Hill function

saturation function \( Y(S) = \frac{c_1+2c_2}{2(E+c_1+c_2)} = \frac{S(K_m'+S)}{K_mK_m'+2K_m'S+S^2} \)

\[
V = \frac{dP}{d\tau} = \frac{2E_0S(k_2K_m' + k_2'S)}{K_mK_m' + 2K_m'S + S^2} = V_mY(S) \text{ if } k_2 = k_2'
\]

Limiting case: Very little of the first complex present but non-negligible quantities of free enzyme and second complex

\[ K_m' \ll S \ll K_m; \quad K^2 = K_mK_m' \]

\[ V = V_mY(S) = \frac{V_mS^2}{K^2 + S^2} \]