Notes on ODEs for modelling workshop

Thursday, May 23, 2019 5:30 PM

Topic Order:

1. Rate law → 1st order reaction: Chemical decay
2. Euler's method → Compare w/ analytical solution
3. Runge-Kutta method
4. Explain $L + R \rightleftharpoons LR$
5. Use solver to build bistable system
   - system behavior with time
   - analysis of system behavior

Law of Mass action:

Rate of chem. reaction ∝ Product of molecules

E.g.: $A \xrightarrow{k} B$

$A + B \xrightarrow{k} C$

Enzyme-catalyzed reactions:

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

Michaelis-Menten: $V_0 = \frac{dP}{dt} = \frac{V_{max} S}{K_M + S}$, $V_{max} = k_2 E_{Total}$, $K_M = \frac{k_{-1} + k_2}{k_1}$

First Order Chemical Reaction

↓

Decay → $A \xrightarrow{k} B$

$\therefore \frac{dA}{dt} = -k[A] = -\frac{d[B]}{dt}$

$\Rightarrow \frac{dA}{[A]} = -k \cdot dt \Rightarrow \int \frac{dA}{A} = \int -k\,dt$

$\Rightarrow \ln(A) = -kt + C$

$\Rightarrow A = e^{-kt} \cdot e^{C}$

If $t = 0$,

$A(0) = e^{0} \cdot e^{C} \Rightarrow A(0) = e^{C}$

$\boxed{A(t) = A_0 \cdot e^{-kt}}$

$t_{1/2} = \frac{\ln(2)}{k}$ (half-life)

Euler's Method:

$\frac{df}{dt} = g$

Taylor's expansion: $f(t) = \sum_{n=0}^{\infty} \frac{f^{(n)}(t_0)}{n!}(t - t_0)^n$

$f(t) = f(t_0) + f'(t_0) \cdot \Delta t + \frac{f''(t_0)}{2}\Delta t^2 \ldots$

$\Rightarrow \Delta f \sim \frac{df}{dt}\Delta t = g\,\Delta t$

Runge-Kutta Method:

$k_1 = f(x) \cdot \Delta t$ at Δt

$k_2 = f(x + 0.5k_1)\Delta t$ at $\Delta t/2$

$k_3 = f(x + 0.5k_2)\Delta t$ at $\Delta t/2$

$k_4 = f(x + k_3)\Delta t$ at Δt

$df = \frac{1}{6}(k_1 + 2k_2 + 2k_3 + k_4)$

Ligand-receptor binding

$L + R \underset{k_2}{\overset{k_1}{\rightleftharpoons}} LR$

$\frac{dL}{dt} = -k_1 \cdot L \cdot R + k_2 \cdot LR$

$\frac{dR}{dt} = -k_1 \cdot L \cdot R + k_2 \cdot LR$

$\frac{dLR}{dt} = k_1 \cdot L \cdot R - k_2 \cdot LR$

At steady state:

$k_1 \cdot L \cdot R = k_2 \cdot LR$

$\Rightarrow \frac{k_2}{k_1} = k_D = \frac{L \cdot R}{LR}$

Xenopus oocyte maturation:

- All or none process.
- Experiment: oocyte placed in progesterone (submaximal)

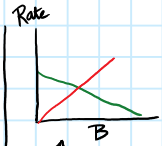
$\swarrow$ G2 $\searrow$ Metaphase Meiosis II

Rate balance plots?

Ferrell and Xiong; Chaos (2001)

$A \underset{k_2}{\overset{k_1}{\rightleftharpoons}} B$; $A + B = T$

$\frac{dB}{dt} = \underbrace{k_1(T - B)}_{\text{Forward}} - \underbrace{k_2 B}_{\text{Back}}$



Add Stimulus:

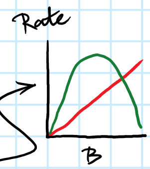
$A \underset{k_2}{\overset{S k_1}{\rightleftharpoons}} B$

$\frac{dB}{dt} = k_1 S(T - B) - k_2 B$

Linear feedback:

$A \underset{k_2}{\overset{S k_1}{\rightleftharpoons}} B$, k_f

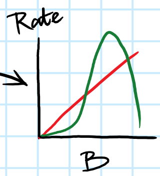
$\frac{dB}{dt} = (k_1 S + k_f B)(T - B) - k_2 B$



Ultrasensitive feedback:

$A \underset{k_2}{\overset{S k_1}{\rightleftharpoons}} B$

$\frac{dB}{dt} = \left(k_1 S + \frac{k_f B^n}{B^n + K_M^n}\right) A - k_2 B$



Hill function - How?

$P, S \rightleftharpoons B$ (complex)

$3P + S \underset{k_2}{\overset{k_1}{\rightleftharpoons}} B$

dPS

$\Rightarrow k_1 P^3 (T - B) = k_2 B$

$\Rightarrow k_1 P^3 T - k_1 P^3 B = k_2 B$

$\Rightarrow \frac{k_1 P^3 T}{k_2 + P^3} = B$

$\Rightarrow \frac{B}{T} = f_B = \frac{k_1 P^3}{k_2 + P^3}$

fraction of bound stuff

Michaelis-Menten derivation:

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

$\frac{dP}{dt} = k_2 ES$ $\qquad \frac{dES}{dt} = k_1 E \cdot S - k_{-1} ES - k_2 ES$

$k_1 \cdot E \cdot S = ES(k_{-1} + k_2) \Rightarrow E \cdot S = K_M ES$

$S \cdot E_T - S \cdot ES = K_M ES \Rightarrow S \cdot E_T = ES(K_M + S)$

$\Rightarrow ES = \frac{S \cdot E_T}{K_M + S}$ $\quad \boxed{\frac{dP}{dt} = \frac{k_2 E_T \cdot S}{K_M + S}}$

$k_4 = f(x + k_3)\,\Delta t$ at Δt

$df = \frac{1}{6}\left(k_1 + 2k_2 + 2k_3 + k_4\right)$