

NATIONAL TAIWAN UNIVERSITY,
GRADUATE INSTITUTE OF BIOMEDICAL ENGINEERING AND BIOINFORMATICS

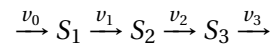
BEBI5009:
Mathematical Modeling of System Biology
Homework 2

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1 3.7.5 Michaelis-Menten kinetics: first-order approximation.

Consider the reaction chain



in which the ν_i are labels for the reaction rates (not mass-action constants). Take the rate ν_0 as fixed and presume the other reactions follow Michaelis-Menten kinetics, with

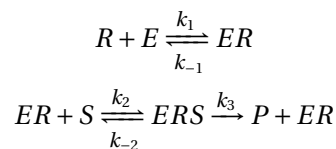
$$\nu_i = \frac{V_{max}^i s_i}{K_M^i + s_i},$$

where $s_i = [S_i]$. Take parameter values (in mM/min) $\nu_0 = 2$, $V_{max}^1 = 9$, $V_{max}^2 = 12$, $V_{max}^3 = 15$; (in mM) $K_{M1} = 1$, $K_{M2} = 0.4$, $K_{M3} = 3$.

- Simulate the system from initial conditions (in mM) $(s_1, s_2, s_3) = (0.3, 0.2, 0.1)$. Repeat with initial condition $(s_1, s_2, s_3) = (6, 4, 4)$.
- Generate an approximate model in which the rates of reactions 1, 2, and 3 follow first-order mass-action kinetics (i.e. $\nu_i = k_i s_i$, for $i = 1, 2, 3$). Choose values for the rate constants k_i that give a good approximation to the original nonlinear model. Explain your reasoning. (Hint: Exercise 3.1.2(b) provides one viable approach.)
- Simulate your simpler (mass-action based) model from the sets of initial conditions in part (a). Comment on the fit. If the approximation is better in one case than the other, explain why.

2 3.7.8 Allosteric activation

Consider an allosteric activation scheme in which an allosteric activator must be bound before an enzyme can bind substrate. This is called compulsory activation. The reaction scheme resembles a two-substrate reaction, but the enzyme-activator complex stays intact after the product dissociates:



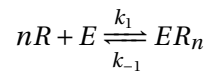
,where R is the allosteric activator (regulator).

- Apply a quasi-steady-state assumption to the two complexes ER and ERS (and use enzyme conservation) to verify that the rate law takes the form

$$v = \frac{srk_3e_T}{r \frac{k_{-2}+k_3}{k_2} + \frac{k_{-1}(k_{-2}+k_3)}{k_1k_2} + sr} = \frac{V_{max}sr}{K_1r + K_2 + rs}.$$

where r is the regulator concentration and s is the substrate concentration

- b) Next, consider the case in which catalysis can only occur after n regulator molecules have bound. Assuming the the binding involves strong cooperativity, we can approximate the regulator-binding events by:



Verify that in this case the rate law takes the form

$$v = \frac{V_{max}sr^n}{K_1r^n + K_2 + r^ns}.$$

- c) Confirm that when regulator and substrate are at very low concentration, the rate law in part (b) can be approximated as

$$v = \frac{V_{max}}{K_2} sr^n.$$