Due 10/27/2016: before class(9:10am)
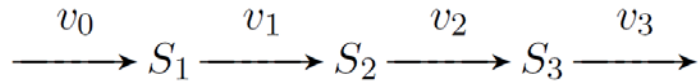
Problem sets from the textbook:

3.7.5 Michaelis-Menten kinetics: first-order approximation. Consider the reaction chain

$$\xrightarrow{\;v_0\;} S_1 \xrightarrow{\;v_1\;} S_2 \xrightarrow{\;v_2\;} S_3 \xrightarrow{\;v_3\;}$$

in which the vi are labels for the reaction rates (not mass-action constants). Take the rate v0 as fixed and presume the other reactions follow Michaelis-Menten kinetics, with

$$v_i = \frac{V_{max}^i s_i}{K_{Mi} + s_i},$$

where si = [Si]. Take parameter values (in mM/min) v0 = 2, V^1_{max} = 9, V^2_{max} = 12, V^3_{max} = 15; (in mM) KM1 = 1, KM2 = 0.4, KM3 = 3.
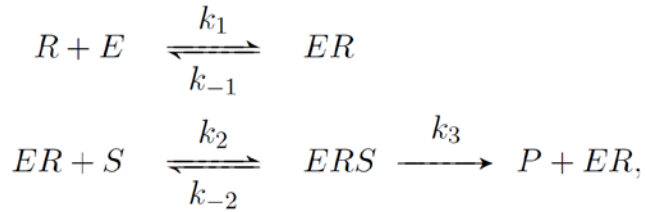
a) Simulate the system from initial conditions (in mM) (s1, s2, s3) = (0.3, 0.2, 0.1). Repeat with initial condition (s1, s2, s3) = (6, 4, 4).

b) Generate an approximate model in which the rates of reactions 1, 2, and 3 follow first-order mass-action kinetics (i.e. vi = ki*si, for i = 1, 2, 3). Choose values for the rate constants ki that give a good approximation to the original nonlinear model. Explain your reasoning. (Hint: Exercise 3.1.2(b) provides one viable approach.)

c) 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.

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:

$$R + E \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ER$$

$$ER + S \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} ERS \overset{k_3}{\longrightarrow} P + ER,$$

,where R is the allosteric activator (regulator).

a) 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

$$v = \frac{srk_3 e_T}{r\frac{k_{-2}+k_3}{k_2} + \frac{k_{-1}(k_{-2}+k_3)}{k_1 k_2} + sr} = \frac{V_{\max} sr}{K_1 r + K_2 + rs}$$

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:

$$nR + E \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ER_n$$
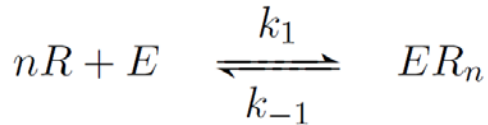
Verify that in this case the rate law takes the form

$$v = \frac{V_{\max} sr^n}{K_1 r^n + K_2 + r^n s}$$

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

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