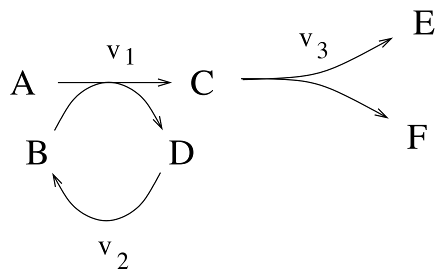
Systems Biology, Homework # 2, Part 2: Chemical Reaction Networks

Due Friday January 28th 2 pm

1. Consider the chemical reaction network in Fig. 1, with rate constants as shown.

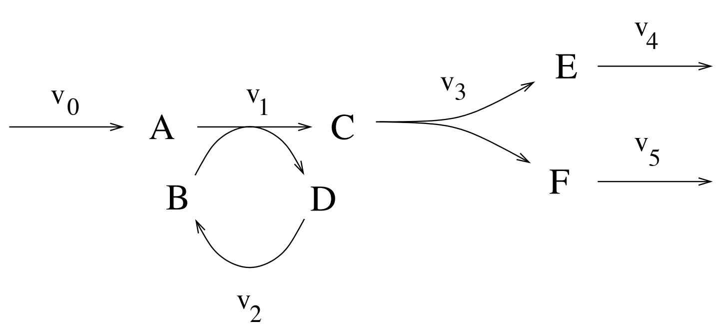


   (a) Write a set of six differential equations describing the behaviour of the concentrations of the species, starting from an arbitrary initial concentration profile.

   (b) Use conservations to reduce the system description to three differential equations and three conservation statements.

   (c) Determine the system steady state as a function of the initial concentrations. (Note, the answer is rather trivial since the system is closed). Recall that the steady state is the concentration profile (for A, B, etc.) for which all rates of change are zero. In this case, the steady state depends on the initial concentrations via the conserved quantities you identified in part (b).

   (d) Repeat (a-c) for the open system in Figure 1d. There are fewer structural conservations in this case. Note, the zeroth-order production reaction has fixed rate k_0.



   (e) Verify the steady state you obtained in (d) by simulating the open system from initial condition (in mM) ([A], [B], [C], [D], [E], [F]) $= (1, 1, \frac{1}{2}, 0, 0, 0)$. For the simulation take rate constants $k_0 = 0.5$ mM sec^{-1}, $k_1 = 3$ mM^{-1} sec^{-1}, $k_2 = 1\,\text{sec}^{-1}$, $k_3 = 4$ sec^{-1}, $k_4 = 1$ sec^{-1}, $k_5 = 5$ sec^{-1}.

   (f) Explain why is there no steady state if we choose $k_0 = 5$ mM sec^{-1}? (Hint: it depends on the conservation).

2. Consider the closed system:

$$A \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} B \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} C. \tag{1}$$

Suppose the mass action rate constants are (in sec^{-1}) $k_1 = 0.05$, $k_2 = 0.7$, $k_{-1} = 0.005$, and $k_{-2} = 0.4$.

(a) Construct a differential equation model of the system. Simulate your model with initial conditions, in mM, $A(0) = 1.5$, $B(0) = 3$, $C(0) = 2$. Plot the transient and steady state behaviour of the system. You may need to make two plots to capture all of the dynamics (i.e. two different window sizes).

(b) It should be clear from your simulation in (a) that the system dynamics occur on two different time-scales. (This is also apparent in the widely separated reaction constants.) Use a rapid equilibrium assumption to reduce your description of the system by replacing a differential equation with an algebraic condition.

(c) Run a simulation of your reduced model in (b) to compare with the simulation in part (a). Verify that the simulation of the reduced system is in good agreement with the original, except for a short initial transient. (Note, you will have to select initial conditions for the reduced system so that the total concentration agrees with (a) and the rapid equilibrium condition is satisfied.)