BEBI5009 Homework3
Due 04/12/2018(Thur) before midnight

1. **3.7.9 Non-cooperative multi-site binding.**

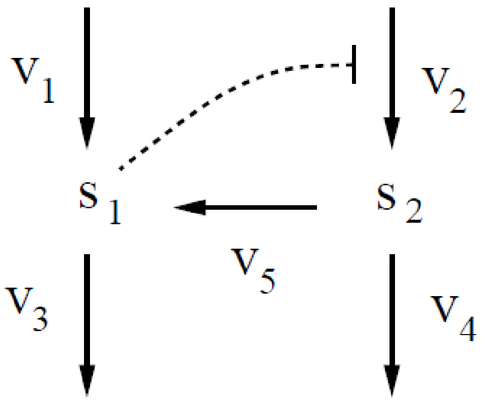
A protein with multiple binding sites that are independent (no cooperativity) cannot exhibit a sigmoidal binding curve, even when the binding sites have distinct affinities. Consider a protein with two ligand binding sites of different affinities. Show that in this case the fractional saturation is simply the sum of two hyperbolic relations:

$$Y = \frac{[X]/K_1}{2(1+[X]/K_1)} + \frac{[X]/K_2}{2(1+[X]/K_2)}$$

where K_1 and K_2 are the dissociation constants for the two sites. Plot this relation for various values of K_1 and K_2 to confirm that it describes a hyperbolic binding curve.

2. **4.8.7 Nullcline analysis.**

Consider the network below.



Suppose the reaction rates are given by

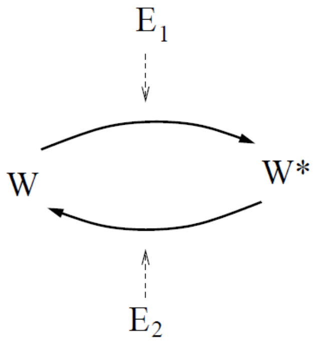
$$v_1 = V \qquad v_2 = f(s_1) \qquad v_3 = k_3 s_1$$

$$v_4 = k_4 s_2 \qquad v_5 = k_5 s_2$$

Suppose that the parameters V, k_3, k_4, and k_5 are positive constants, and that f(s1) takes positive values and is a decreasing function of s1 (i.e. as the values of s1 increase, the values of f(s1) decrease). By sketching the <u>nullclines and direction fields</u> and demonstrate that this system cannot exhibit bistability. Please also sketch a few <u>trajectories starting from different initial conditions</u> in the S_1-S_2 phase plane.

3. **6.8.6 Ultrasensitivity.**

Consider the network below.



$$W + E_1 \underset{d_1}{\overset{a_1}{\rightleftharpoons}} WE_1 \xrightarrow{k_1} W^* + E_1 \tag{6.1}$$

$$W^* + E_2 \underset{d_2}{\overset{a_2}{\rightleftharpoons}} W^*E_2 \xrightarrow{k_2} W + E_2,$$

$$\frac{k_1 E_{1T}}{k_2 E_{2T}} = \frac{w^*(w + K_1)}{w(w^* + K_2)} = \frac{w^*(1 - w^* + K_1)}{(1 - w^*)(w^* + K_2)}, \tag{6.2}$$

where E_{1T} and E_{2T} are the total enzyme concentrations and

$$K_1 = \frac{1}{W_T}\frac{d_1 + k_1}{a_1}, \qquad K_2 = \frac{1}{W_T}\frac{d_2 + k_2}{a_2}.$$

Derive equation (6.2) in Section 6.2.1, as follows. Begin by writing the steady-state conditions for each of the four species in network (6.1). Use the steady-state conditions for the complexes WE_1 and W^*E_2 to write the steady-state concentration $[WE_1]$ in terms of $[W]^{ss}$, E_{1T} , and the rate constants. Likewise, write $[W^*E_2]^{ss}$ in terms of $[W^*]^{ss}$, E_{2T} , and the rate constants. Finally, use the steady-state condition $k_1[WE_1] = k2[W^*E_2]$ and the approximation $W_T = [W] + [W^*]$ to derive equation (6.2).

Please interpret the meaning of equation 6.2 as in figure 6.7.