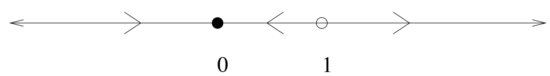
Systems Biology, Homework # 4
Mathematical Analysis

Due Sunday March 6th 11:59 pm

1. Phase analysis can be applied to systems of a single dimension. The phase portrait of a one-dimensional system lies on a *phase line*. For example, the phase portrait of the system

$$\frac{dx(t)}{dt} = x^2(t) - x(t) = x(t)(x(t) - 1),$$

is shown below, with the open circle indicating an unstable steady state, the closed circle indicating a stable steady state, and the arrows indicating the direction of motion.



   (a) Sketch the phase line for the differential equation

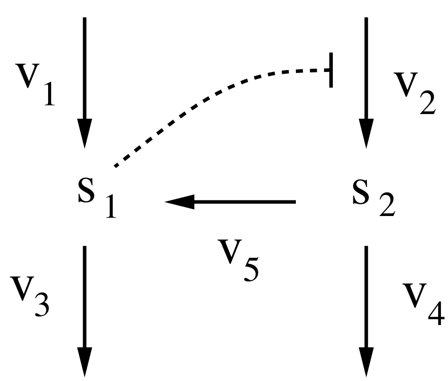
$$\frac{d}{dt}V(t) \quad = \quad V^3(t) - V(t)$$

   (b) Consider the simple model

$$\frac{d}{dt}s(t) = k - \frac{V_{\max}s}{K_M + s}$$

   in which species s is produced at a fixed rate and consumed via Michaelis-Menten kinetics. Sketch a phase line for this system. Verify that the steady state is stable for any non-negative parameter values, provided $V_{\max} > k$.

2. Consider the network:



Take all reaction rates as mass action (with rate constants as specified), except for the inhibited reaction, which has rate

$$\frac{k_2}{1+s_1^2}.$$

(a) Find general equations for the s_1- and s_2-nullclines.

(b) Fix the parameters as $k_1 = 1$ mM/min, $k_3 = 1$/min, $k_2 = 20$ mM/min, $k_4 = 1$/min, $k_5 = 2$/min. Draw, by hand, a sketch of the system's phase portrait. On your phase portrait, label the four regions of the phase space in which the trajectories increase/decrease in concentrations s_1 and s_2. (This can be accomplished by determining the direction of motion along each nullcline, on each side of the equilibrium).

3. Turn in the problem that we did in class:

$$\frac{ds_1}{dt} = V_0 - k_1 s_1$$
$$\frac{ds_2}{dt} = k_1 s_1 - \frac{V_2 s_2}{K_M + s_2}$$

(a) Identify the steady state

(b) Construct the system Jacobian at the steady by taking partial derivatives and evaluating

(c) Compute the eigenvalues of the Jacobian (Hint: if there are zeros off the diagonal, then the eigenvalues are just the diagonal elements! (Can also use matlab if you're not sure)

(d) Check the sign of their real parts and determine stability

4. **Sensitivity analysis: reversible reaction.** Consider the reversible reaction

$$A \underset{k_2}{\overset{k_1}{\rightleftharpoons}} A^*$$

with mass-action rate constants as shown. Let T be the total concentration of A and A^*.

(a) Solve for the steady-state concentration of A^* and verify (just explain in words) that an increase in k_1 leads to an increase in $[A^*]^{ss}$.

(b) Use parametric sensitivity analysis to determine whether the steady state concentration of A^* is more sensitive to a 1% increase in T or a 1% increase in k_1. Does the answer depend on the values of the parameters?