Homework problems on steady-state as function of input: hyperbolic, sigmoidal, adaptation.

(1) Consider this reaction:

$$A \underset{1}{\overset{s}{\rightleftarrows}} B$$

which describes for example a phosphorylation of A into B with rate constant s, and a reverse de-phosphorylation with rate constant 1.

One may think of s as the concentration of an enzyme that drives the reaction forward.

(a) Write equations for this reaction (assuming mass action kinetics; for example $da/dt = -sa + b$).

(b) Observe that $a(t) + b(t)$ is constant. From now on, assume that $a(0)$=1 and $b(0)$=0. What is the constant, then?

(c) (Still assuming $a(0)$=1 and $b(0)$=0.) Use the conservation law from (b) to eliminate a and write just one equation for b.

(d) Find the steady state $b(\infty)$ of this equation for b and think of it as a function of s. Answer this: is $b(\infty)$ a hyperbolic or sigmoidal function of s?

(e) Find the solution $b(t)$ (this is just to practice ODE's).

(2) Consider this reaction:

$$A \underset{1}{\overset{s}{\rightleftarrows}} B \underset{1}{\overset{s}{\rightleftarrows}} C$$

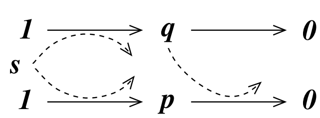
which describes for example a phosphorylation of A into B, and then of B into C, with rate constant s, and reverse de-phosphorylations with rate constant 1.

(a) Write equations for this reaction (assuming mass action kinetics).

(b) Find a conservation law, assuming that $a(0)$=1 and $b(0)$=$c(0)$=0, and, using this law, eliminate b and write a system of equations for just a and c.

(c) Find the steady state $(a(\infty), c(\infty))$ of this equation for a, c and think of $c(\infty)$ as a function of s. Answer this: is $c(\infty)$ a hyperbolic or sigmoidal function of s?

(3) Consider this reaction:



where the dashed lines mean that s and q do not get consumed in the corresponding reactions (they both behave as enzymes). There are also constants k_i for each of the rates (not shown).

Make sure that you understand then why these are the reasonable mass-action equations to describe the system:

$$\frac{dp}{dt} = k_1 s - k_2 pq$$
$$\frac{dq}{dt} = k_3 s - k_4 q$$

(or one could have used, instead, a more complicated Michaelis-Menten model).

(a) Find the steady state, written as a function of s.

(b) Note that $p(\infty)$ (though not $q(\infty)$) is independent of s.

This is an example of *adaptation*, meaning that the system transiently responds to a “signal” s (assumed a constant), but, after a while, it returns to some “default” value which is independent of the stimulus s (and hence the system is ready to react to other signals).[1]

(c) Graph (using for instance JOde) the plot of $p(t)$ versus t, assuming that k_1=k_2=2 and k_3=k_4=1, and $p(0)$=$q(0)$=0, for each of the following three values of s: $s = 0.5, 3, 20$.

You should see that $p(t) \to 1$ as $t \to \infty$ (which should be consistent to your answer to part (b)) but that the system initially reacts quite differently (in terms of “overshoot”) for different values of s.

[1] We’ll discuss in class some examples of such adaptation behavior, such as in chemotaxis.