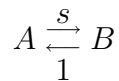


Homework problems on steady-state as function of input: hyperbolic, sigmoidal, adaptation.

(1) Consider this reaction:



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 $da/dt = -sa + b$).

$$\begin{aligned}\frac{da}{dt} &= -sa + b \\ \frac{db}{dt} &= sa - b\end{aligned}$$

(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?

$$a(t) + b(t) = 1$$

(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 .

$$\frac{db}{dt} = s(1 - b) - b$$

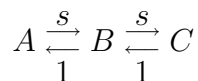
(d) Find the steady state $b(\infty)$ of this equation for b and think of it as a function of s . Answer this: is $b(\infty)$ a hyperbolic or sigmoidal function of s ?

$$b = \frac{s}{1+s}, \text{ hyperbolic.}$$

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

$$b(t) = e^{-(1+s)t} \left(b(0) - \frac{s}{1+s} \right) + \frac{s}{1+s}$$

(2) Consider this reaction:



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).

$$\begin{aligned}\frac{da}{dt} &= -sa + b \\ \frac{db}{dt} &= sa - b + c - sb \\ \frac{dc}{dt} &= sb - c\end{aligned}$$

(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 .

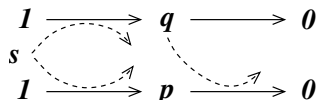
$a + b + c = 1$, so:

$$\begin{aligned}\frac{da}{dt} &= -sa + (1 - a - c) \\ \frac{dc}{dt} &= s(1 - a - c) - c\end{aligned}$$

(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 ?

We solve $-sa + (1 - a - c) = 0, s(1 - a - c) - c = 0$ for a and c , and get $a = 1/(s + s^2 + 1)$ $c = s^2/(s + s^2 + 1)$. The plot of c vs t is sigmoidal.

(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:

$$\begin{aligned}\frac{dp}{dt} &= k_1s - k_2pq \\ \frac{dq}{dt} &= k_3s - k_4q\end{aligned}$$

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

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

We solve the equations $k_1s - k_2pq = 0$ and $k_3s - k_4q$ and get $p = \frac{k_1k_4}{k_2k_3}, q = \frac{k_3}{k_4}s$

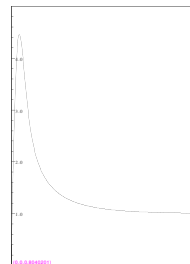
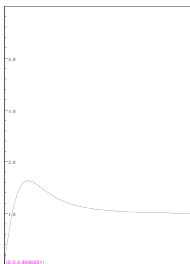
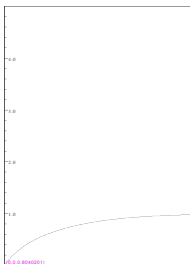
(b) Note that $p(\infty)$ (though not $q(\infty)$) is independent of s .

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 $p(t) \rightarrow 1$ as $t \rightarrow \infty$ (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 .

The graphs are as follows, for $s = 0.5, 3, 20$ respectively:



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