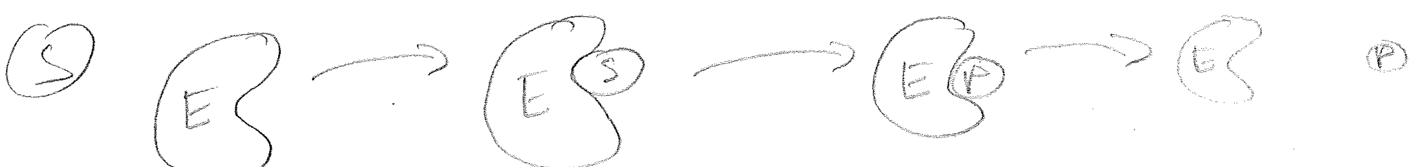
Overview:

Last week we started talking about a model for chemical reactions. In particular, we are modeling a reaction where molecule S (the substrate) turns into molecule P (the product). This reaction can be written as $S \xrightarrow{K} P$, where K is the rate constant of the reaction. Unfortunately, for most useful biochemical reactions, K is very small, so the reaction is far too slow to be practical. To speed things up, we catalyze the reaction with an enzyme E. One possible mechanism for an enzyme is the following:



The substrate attaches itself to the enzyme and is held in a conformation that makes it very easy to change into the product. Afterwards, the product detaches from the enzyme. We can write this as

$$E + S \underset{K_{-1}}{\overset{K_1}{\rightleftharpoons}} ES \xrightarrow{K_2} E + P$$

(The backwards arrow with rate K_{-1} indicates that it is possible for the substrate to detach from the enzyme before turning into product. In principle, every reaction is reversible, so we should include the reverse reaction $E + P \xrightarrow{K_{-2}} ES$ as well, but we will assume that we pump P out fast enough for this not to matter. In practice, K_{-1} is often large enough to be important while K_{-2} is not.)

We have further assumed that each reaction is governed by the "Law of mass action". That is, the rate of each reaction is proportional to the concentration of the reactants.

If we let

$x = [S]$ = concentration of substrate

$y = [E]$ = concentration of enzyme

$z = [ES]$ = concentration of enzyme-substrate complex, then we have

$$\begin{cases} \dfrac{dx}{dt} = a - K_1 x y + K_{-1} z \\[2ex] \dfrac{dy}{dt} = -K_1 x y + K_{-1} z + K_2 z \\[2ex] \dfrac{dz}{dt} = K_1 x y - K_{-1} z - K_2 z \end{cases}$$

where a is the rate at which we pump in substrate. Since $\frac{dy}{dt} + \frac{dz}{dt} = 0$, $y + z = c$ = constant, so we can ignore the third equation and just use $z = c - y$. We therefore have

$$\begin{cases} \dfrac{dx}{dt} = a - K_1 x y + K_{-1}(c - y), \\[2ex] \dfrac{dy}{dt} = -K_1 x y + (K_{-1} + K_2)(c - y). \end{cases}$$

This is a nonlinear (note the xy terms) system of two differential equations. To analyze it, we should find any equilibria and then linearize about them.

To find equilibria, we set

$$0 = a - K_1 xy + K_{-1}(c-y)$$

$$0 = -K_1 xy + (K_{-1} + K_2)(c-y).$$

If we subtract these two, we get

$$0 = a - K_2(c-y)$$

$$\Rightarrow a = K_2(c-y)$$

$$\Rightarrow \frac{a}{K_2} = c - y$$

$$\Rightarrow \boxed{y = c - \frac{a}{K_2}} = \frac{K_2 c - a}{K_2}$$

we therefore have

$$0 = a - K_1 x\left(c - \frac{a}{K_2}\right) + K_{-1}\cdot\left(\frac{a}{K_2}\right)$$

$$\Rightarrow K_1 x(K_2 c - a) = K_2 a + K_{-1} a$$

$$\Rightarrow \boxed{x = \frac{K_2 a + K_{-1} a}{K_1(K_2 c - a)}}$$

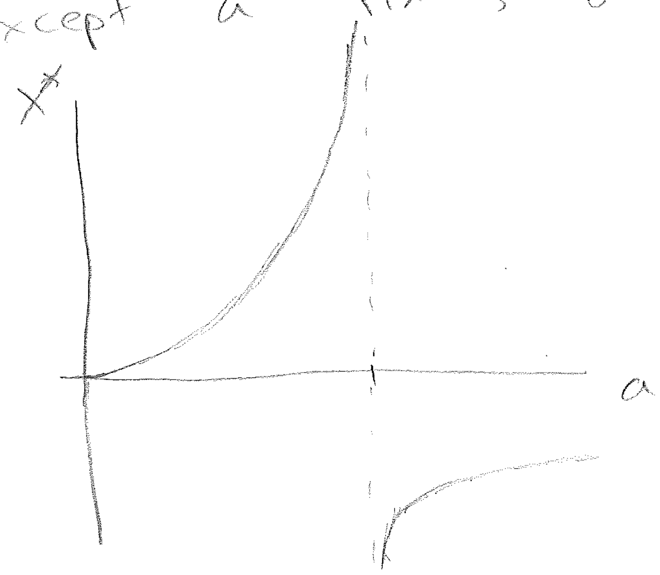
We therefore have an equilibrium at

$$\boxed{x^* = \frac{K_2 a + K_{-1} a}{K_1(K_2 c - a)}, \quad y^* = \frac{K_2 c - a}{K_2}}$$

Notice that if we do not add new substrate (so $a=0$), then the only equilibrium is at $x^*=0$, $y^*=C$ and therefore $z^*=0$.

This should make sense. If we don't add new substrate, it is eventually all turned into product, and then all of the enzymes remain free (in the E state).

It is also worth noting that something unusual must happen when $K_2C=a$. In this case, there is no free enzyme at equilibrium, but there is infinite substrate. If we hold all parameters except a fixed, we get



To find the stability of this equilibrium, we need to find the Jacobian matrix of this system. If

$$f_1(x,y) = a - K_1 xy + K_{-1}(c-y),$$

$$f_2(x,y) = -K_1 xy + (K_{-1}+K_2)(c-y),$$

then

$$Df(x,y) = \begin{pmatrix} \frac{\partial f_1}{\partial x} & \frac{\partial f_1}{\partial y} \\ \frac{\partial f_2}{\partial x} & \frac{\partial f_2}{\partial y} \end{pmatrix} = \begin{pmatrix} -K_1 y & -K_1 x - K_{-1} \\ -K_1 y & -K_1 x - K_{-1} - K_2 \end{pmatrix}.$$

We therefore have

$$Df(x^*,y^*) = \begin{pmatrix} -K_1 \cdot \left(\frac{K_2 c - a}{K_2}\right) & -K_1 \cdot \left(\frac{(K_2+K_{-1})a}{K_1(K_2 c - a)}\right) - K_{-1} \\ -K_1 \cdot \left(\frac{K_2 c - a}{K_2}\right) & -K_1 \cdot \left(\frac{(K_2+K_{-1})a}{K_1 \cdot (K_2 c - a)}\right) - K_{-1} - K_2 \end{pmatrix}$$

This means that the eigenvalues of the linearized system satisfy:

$$\left(-\frac{K_1}{K_2}(K_2C-a)-\lambda\right)\cdot\left(-\left(\frac{(K_2+K_{-1})a}{K_2C-a}\right)-K_{-1}-K_2-\lambda\right)$$

$$-\frac{K_1}{K_2}(K_2C-a)\cdot\left(\frac{(K_2+K_{-1})a}{(K_2C-a)}+K_{-1}\right)=0$$

$$\Rightarrow \lambda^2+\underbrace{\left(\frac{K_1}{K_2}(K_2C-a)+\frac{(K_2+K_{-1})a}{K_2C-a}+K_{-1}+K_2\right)}_{T}\lambda+K_1(K_2C-a)=0$$

Notice, if $K_2C-a>0$, then $T>0$

$$\lambda=\frac{-T\pm\sqrt{T^2-4K_1(K_2C-a)}}{2}.$$

We are only interested in the case where $K_2C-a>0$, because this is the only case that gives non-negative equilibria. In this case, $T>0$, and $T^2-4K_1(K_2C-a)<T^2$. If $T^2-4K_1(K_2C-a)\leq 0$, then $Re(\lambda)=-\frac{T}{2}$, so the equilibrium is stable.

If $T^2-4K_1(K_2C-a)>0$, then $\sqrt{T^2-4K_1(K_2C-a)}<T$,

so $\frac{-T-\sqrt{T^2-4K_1(K_2C-a)}}{2}<\frac{-T+\sqrt{T^2-4K_1(K_2C-a)}}{2}<0$,

so the equilibrium is also stable.

This means that, for a low enough inflow a (or high enough concentration of enzymes c), we have a positive, stable equilibrium

$$x^* = [S]^* = \frac{(K_2 + K_{-1})\,a}{K_1(K_2 c - a)} \quad \text{and} \quad y^* = [E]^* = \frac{K_2 c - a}{K_2}.$$

Since $[ES] = z = c - y$, we have

$$[ES]^* = z^* = \frac{a}{K_2}.$$

Ultimately, we are interested in the rate at which we produce product. From the law of mass action, we have

$$\frac{d[P]}{dt} = K_2 \cdot [ES],$$

so when the system reaches equilibrium, we will have $\frac{d[P]}{dt} = K_2 \cdot [ES]^* = K_2 \cdot \frac{a}{K_2} = a.$