

Overview:

(P.1)

We have been looking at a model for enzyme catalyzed reactions governed by



After some simplifying assumptions, we obtained the following system of differential equations:

$$\frac{dx}{dt} = a - k_1 xy + k_{-1}(C - y),$$

$$\frac{dy}{dt} = -k_1 xy + (k_{-1} + k_2)(C - y),$$

where $x = [S]$ is the concentration of substrate; $y = [E]$ is the concentration of free enzyme; $z = C - y = [ES]$ is the concentration of enzyme-substrate complex and a is the inflow rate of substrate.

We found that the system had an equilibrium at

$$x^* = \frac{(k_{-1} + k_2)a}{(k_2 C - a)k_1}, \quad y^* = \frac{k_2 C - a}{k_2}$$

This equilibrium is only positive if $a < k_2 C$.

We also linearized about this equilibrium and found that the eigenvalues of this system were given by

$$\lambda = \frac{-T \pm \sqrt{T^2 - 4k_1(k_2c - a)}}{2},$$

where

$$T = \frac{k_1}{k_2}(k_2c - a) + \frac{(k_2 + k_1)a}{k_2c - a} + k_1 + k_2 > 0.$$

In particular, $\text{Re}(\lambda) < 0$ for both eigenvalues, regardless of the value of T . This means that the equilibrium is stable (at least when it is positive). Note that we could not easily determine if this equilibrium was a node or a spiral.

We now want to draw the phase portrait for this system, but we don't really have enough information yet.

To finish the phase portrait, we will also find the nullclines of the system. Nullclines are places where at least one of the derivatives $\frac{dx}{dt}$ and $\frac{dy}{dt}$ are zero. These are places where the solution curves are either vertical or horizontal. We can find these curves by setting $\dot{x}=0$ and $\dot{y}=0$. We obtain

$$\dot{x}=0 = a - k_1xy + k_{-1}(C - y)$$

$$\Rightarrow (k_1x + k_{-1})y = a + k_{-1}C$$

$$\Rightarrow y_x = \frac{a + k_{-1}C}{k_1x + k_{-1}} \leftarrow x\text{-nullcline}$$

$$\dot{y}=0 = -k_1xy + (k_{-1} + k_2)C - (k_{-1} + k_2)y$$

$$\Rightarrow (k_1x + k_{-1} + k_2)y = (k_{-1} + k_2)C$$

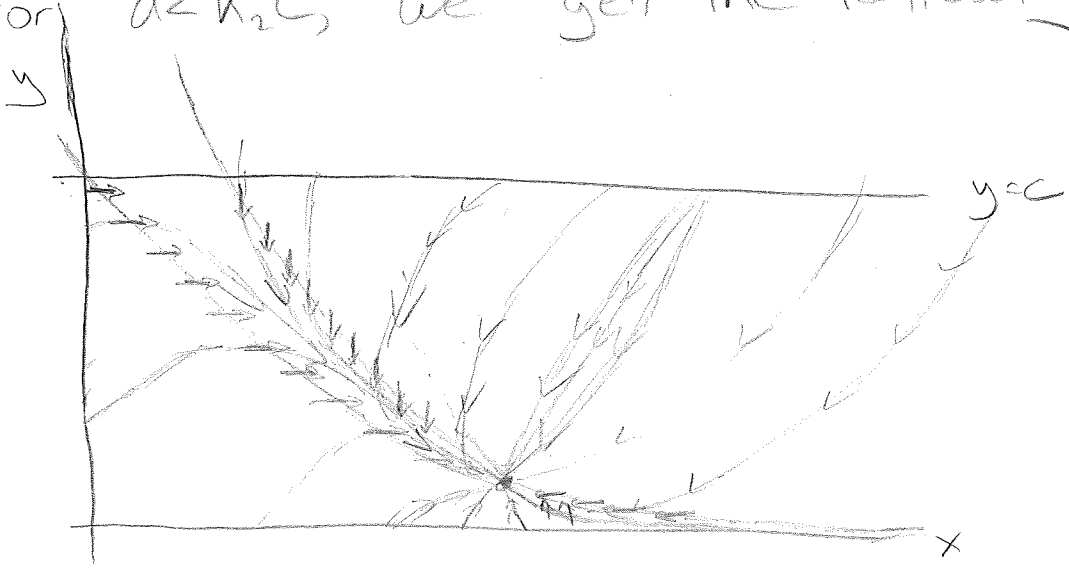
$$\Rightarrow y_y = \frac{(k_{-1} + k_2)C}{k_1x + k_{-1} + k_2} \leftarrow y\text{-nullcline}$$

Here, y_x represents the x -nullcline (where $\frac{dx}{dt}=0$) and y_y represents the y -nullcline (where $\frac{dy}{dt}=0$).

In addition, we know that, as long as we start with the physically reasonable initial conditions $x(0) \geq 0$ and $0 \leq y(0) \leq C$, then we will have $x(t) > 0$ and $0 \leq y(t) < C$ for all time. The region $[0, \infty) \times [0, C]$ is called a trapping region, because any solution that reaches it is trapped inside.

Finally, it is useful to note that if the x -nullcline and y -nullcline cross, there must be an equilibrium at the intersection point (because both $\frac{dx}{dt} = 0$ and $\frac{dy}{dt} = 0$). This means that y_x and y_y intersect once in the first quadrant if $a < k_2 C$ and not at all if $a \geq k_2 C$.

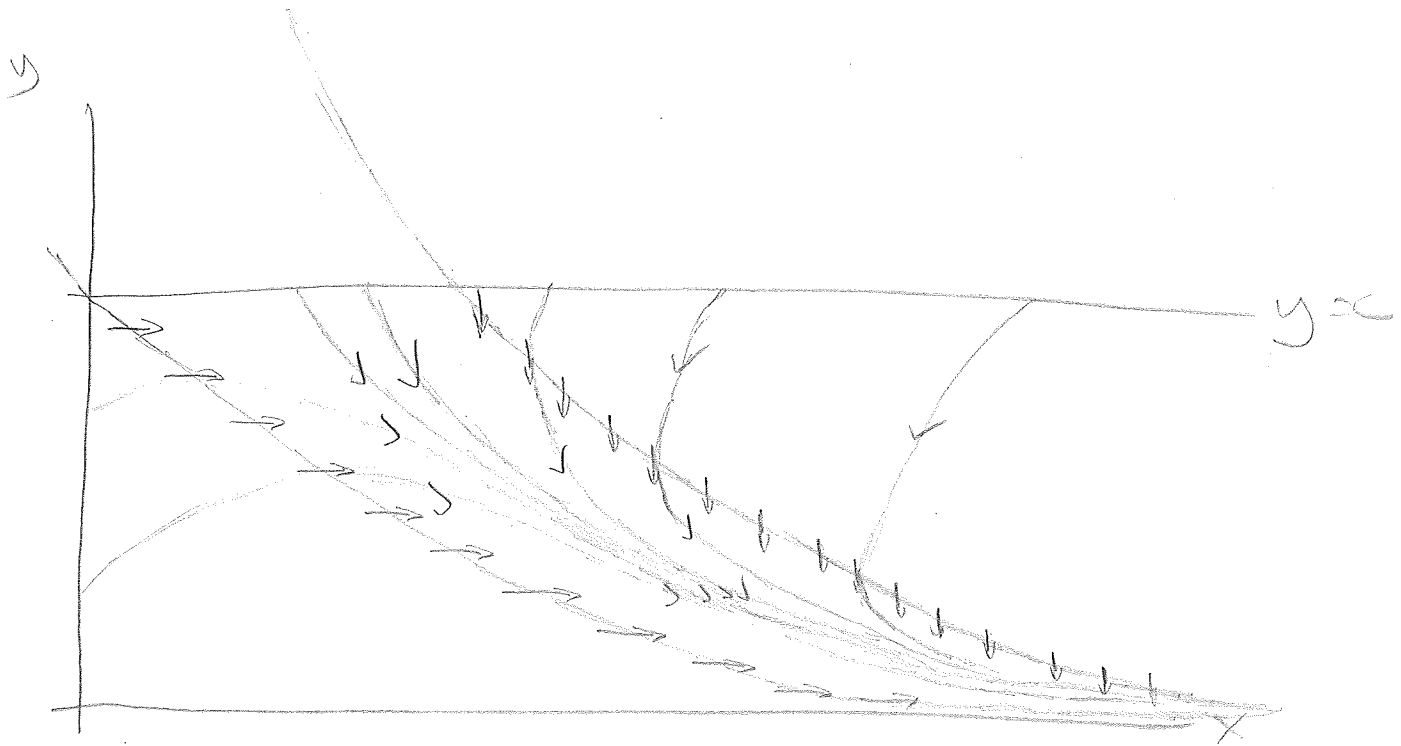
For $a < k_2 C$, we get the following phase plane:



The arrows can be filled out by continuity: We know that x is increasing at $x=0$, so it must still be increasing at the upper portion of the y -nullcline. Similarly, y is decreasing at $y=C$, so it must still be decreasing at the upper portion of the x -nullcline.

We can also see that the bands between the two nullclines are trapping regions. If a solution reaches either nullcline, it will stay between them forever. This actually tells us that our equilibrium is a stable node, not a stable spiral, because a spiral would require solutions to leave these bands.

As a increases, the x -nullcline moves higher, and the intersection is therefore pushed to the right. At $a=K_2C$, the x -nullcline moves completely above the y -nullcline and we don't have any equilibrium anymore. The corresponding phase portrait is:



Once again, the band between the two nullclines is a trapping region, so solutions that reach either nullcline will remain between them forever.

This means that, eventually, every solution will have $y_y < y(t) < y_x$. Since both y_y and y_x go to zero, we also have $y(t) \rightarrow 0$ as $t \rightarrow \infty$. This means that all of the enzyme will be bound to substrate,

so $y_\infty = 0$ and $z_\infty = C$. We will therefore produce product with rate $\frac{d[P]}{dt} = k_2 z_\infty = k_2 C$.

We therefore know that

$$\frac{d[P]}{dt} = \begin{cases} a & a \leq k_2 C, \\ k_2 C & a \geq k_2 C. \end{cases}$$

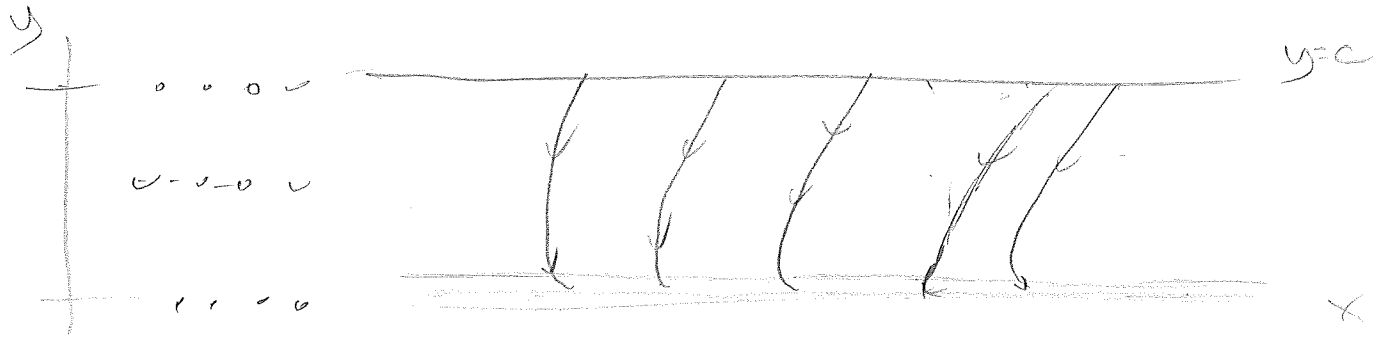
This result might seem a little surprising. (P.7)

It looks like our rate of production has very little to do with the enzyme. We would imagine that an efficient enzyme has a very large k_1 and k_2 , but k_1 didn't even appear in our final production rate! Why is that?

The main idea is that equilibrium (or infinite time, if $a \gg k_2 c$) production rates are only attained after waiting, well, infinite time. From an engineering perspective, this is impractical. If the equilibrium production rate is large (say, because a is large enough and k_2 is large) but it takes 100 years to ramp up to that production rate, we would call the process a failure.

A more useful question is "How quickly does the process reach full capacity?"

Let's imagine that we start this process with ^(P.8) a lot of substrate already in our tank, then dump in a batch of enzymes, so that $x(0) = x_0$ is very large and $y(0) = C$. This means we are in the far right of our phase portrait:



We expect y to change very rapidly until our solution reaches the nullclines, but x will only change by a few multiples of $k_2 C$, which is very small compared to x_0 . We can therefore approximate x by the constant solution $x(t) = x_0$.

This means that, until y reaches the nullclines, we have the single ode

$$\begin{aligned} \dot{y} &\approx -k_1 x_0 y + (k_{-1} + k_2)(C - y) \\ &= -(k_1 x_0 + k_{-1} + k_2)y + (k_{-1} + k_2)C \end{aligned}$$

(P.9)

This is a linear, constant coefficient ode, and we have already solved it several times.

If $y' = ay + b$, then

$$y(t) = \left(y_0 + \frac{b}{a}\right) e^{at} - \frac{b}{a}.$$

In our case, $a = -(K_1 X_0 + K_{-1} + K_2)$ and $b = (K_{-1} + K_2) C$, so we have

$$y(t) = \left(C - \frac{(K_{-1} + K_2) C}{K_1 X_0 + K_{-1} + K_2}\right) e^{-(K_1 X_0 + K_{-1} + K_2)t} + \frac{(K_{-1} + K_2) C}{K_1 X_0 + K_{-1} + K_2}$$

From this, we see that K_1 tells us how rapidly we reach the trapping region, and therefore how rapidly we reach high production.