\[ \frac{ds}{dt} = -f(s) \]

Rate of reaction \( f(s) = \frac{k_1 k_2 e_0 r s}{k_1 s + k_2 r k_3 r} \]

\[ = \frac{k_2 e_0 r s}{s + k_2 r k_3 r} \]

\[ = k_m \frac{s}{s + K} \]

where \( k_m = \frac{k_2 e_0 r}{k_1} \)

\( K = \frac{k_2 r}{k_1} \)

We say \( f(s) \) saturates at the value \( k_m \)

(increases to horizontal asymptote \( y = k_m \))
\[ \frac{ds}{dt} = -km \frac{s}{s + K} \]

**Phase portrait**

<table>
<thead>
<tr>
<th>0</th>
<th>1</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>s</td>
</tr>
</tbody>
</table>

**Hints for HW2 Question 1**

**saturation function**

\[ \frac{dx}{dt} = f(x) = x - x^2 - \frac{\lambda}{x + a}, \quad x \geq 0 \]

**x**

\[ 0 = x \left( 1 - x - \frac{\lambda}{x + a} \right) \]

\[ x_0^* = 0 \]

\[ x_1^* = \frac{-B - \sqrt{B^2 - 4AC}}{2A}, \quad x_2^* = \frac{-B + \sqrt{B^2 - 4AC}}{2} \]

**0 real roots** if \( B^2 - 4AC < 0 \)

**1 real root** if \( B^2 - 4AC = 0 \)

**2 real roots** if \( B^2 - 4AC > 0 \)
When are $x_1^* > 0$, $x_2^* > 0$?

Both have same sign as $-\frac{B}{2A}$ if $4AC > 0$.

If $4AC = 0$ one of the roots is 0.

If $4AC < 0$ then $x_1^* < 0 < x_2^*$.

Vector field, phase portraits

$$\frac{dx}{dt} = f(x) = \frac{f_1(x)}{x(1-x)} - \frac{f_2(x)}{\mu \frac{x}{x+a}}$$

\[\text{Example:} \quad y(x) = x(1-x) \text{ for some } \mu, a\]
Bifurcation diagram

Equilibria \( x = 0 \) or \( 1 - x - \frac{m}{x + a} = 0 \)

\[ m = (1-x)(x+a) \]

parabola with intersections \( x = 1, x = -a \)

\( x = 0 \)

Decide stability from phase portraits

Appropriateness of quasi-static approximation in Michaelis-Menten derivation

\[
\begin{align*}
\frac{ds}{dt} &= -k_1 s (e_0 - c) + k_2 c \\
\frac{d}{dt} &= k_1 s (e_0 - c) - k_2 c - k_3 c r \\
\frac{d}{dt} &= -k_1 e_0 s + (k_1 + k_3 s) c \\
\frac{d}{dt} &= k_1 e_0 s - (k_1 + k_3 s + k_2 r) c
\end{align*}
\]
In what real situation is the quasi-static approximation $\frac{dc}{dt} = 0$ appropriate?

Rescale and write in nondimensional form.

Define $\hat{s} = \frac{s}{a}$, $\hat{c} = \frac{c}{\beta}$, $\tau = \frac{t}{\gamma}$

Then $s = a\hat{s}$, $c = \beta\hat{c}$, $\frac{d}{dt} = \frac{1}{\delta} \frac{d}{d\tau}$

and we get (Exercise)

$$
\begin{align*}
\frac{d\hat{s}}{d\tau} &= -\gamma k_1 e_0 \hat{s} + \frac{\beta \gamma}{a} (k_{-1} + k_1 a\hat{s}) \hat{c} \\
\frac{d\hat{c}}{d\tau} &= \frac{\gamma}{\beta} k_1 e_0 \hat{s} - \gamma (k_{-1} + k_2 \tau + k_1 a\hat{s}) \hat{c}
\end{align*}
$$

Now choose $a = s_0$, $\beta = e_0$, $\gamma = \frac{1}{k_1 e_0}$

and get

$$
\begin{align*}
\frac{d\hat{s}}{d\tau} &= -\hat{s} + \left(\frac{k_{-1}}{k_1 s_0} + \hat{s}\right) \hat{c} \\
\frac{e_0}{s_0} \frac{d\hat{c}}{d\tau} &= \hat{s} - \left(\frac{k_{-1} + k_2 \tau}{k_1 s_0} + \hat{s}\right) \hat{c}
\end{align*}
$$
If $0 < e_0 << s_0$ then $\frac{e_0}{s_0} \frac{dc}{dt} \approx 0$.

is an appropriate approximation, i.e. the quasi-static approximation.

I.e. if the initial enzyme concentration is much smaller than the initial substrate concentration

\[ E + S \xrightarrow{k_{i}} C \]

In this case the small amount of $E$ available gets "used up", bound in the complex $C$ and the rate of reaction cannot exceed some maximal value (horizontal asymptote)
Example 2. N Bistability and hysteresis

Tank of lactose solution and E. coli cells
There is lactose outside and inside the cells.

\[ \lambda = \text{concentration of extracellular lactose} \]
\[ \geq 0 \quad \text{outside cells} \]

\[ y(t) = \text{average concentration of intracellular lactose} \]
\[ \geq 0 \quad \text{inside cells} \]

Box model for average cell

\[ \frac{dy}{dt} = \text{Rate in} - \text{Rate out} \]
Rate out: metabolic loss
\[ \text{lactate} \xrightarrow{k} \text{glucose + galactose} \]

law of mass action: rate out = ky 
(\(k > 0\) constant)

Rate in: complicated!

positive feedback.

increase y \rightarrow \text{increase rate in} \rightarrow \text{more increase y}

rate saturates

Experimental picture

[Diagram showing the relationship between rate in, diffusion, positive feedback, and saturation]