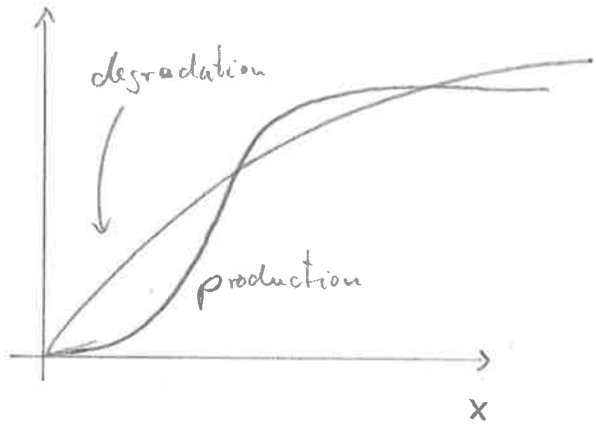
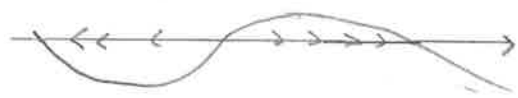
Dynamical systems cont'd

bistability

- common phenomenon in transcriptional networks

$$\frac{dx}{dt} = \frac{x^n}{1+x^n} - \frac{ax}{b+x}$$

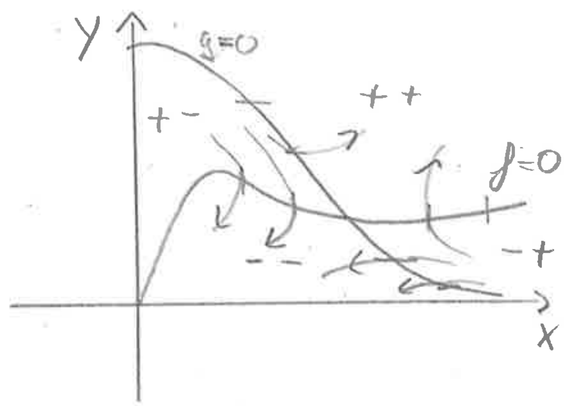




- two stable fixpoints, one unstable one
- the stable high fix point can be lost in a bifurcation.

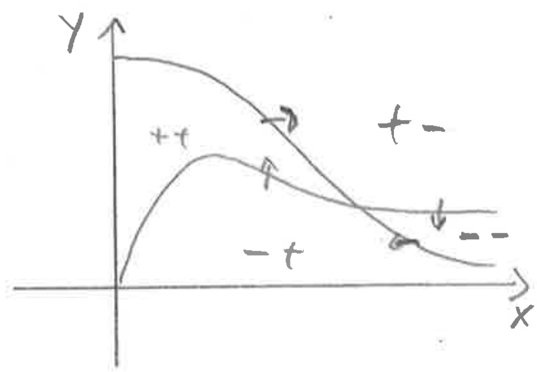
2-d systems

$$\frac{dx}{dt} = f(x,y) \qquad \frac{dy}{dt} = g(x,y)$$



- fix point is the intersection of null clines
- trajectories are fully defined by initial condition (x, y)

$\Rightarrow$ trajectories can't cross



Linear stability analysis

dynamics in the vicinity of a fixpoint

$$\delta x = x - x_f \quad , \quad \delta y = y - y_f$$

$$\frac{d\,\delta x}{dt} = f(x_f, y_f) + \left.\frac{\partial f}{\partial x}\right|_{x_f, y_f} \delta x_f + \left.\frac{\partial f}{\partial y}\right|_{x_f y_f} \delta y_f + \mathcal{O}(\delta x^2, \delta y^2)$$

$$\frac{d\,\delta\vec{x}}{dt} = \begin{pmatrix} f_x & f_y \\ g_x & g_y \end{pmatrix} \delta\vec{x} + \cdots$$

- for small $\delta\vec{x}$, ignore δx^2

$\Rightarrow$ linear equation

$\Rightarrow$ exactly solvable

Linear ODE systems

$$\frac{d\vec{x}}{dt} = \begin{pmatrix} a & b \\ c & d \end{pmatrix} \vec{x}$$

① determine eigenvalues: $\det(M - \lambda I) = 0$

$$\Rightarrow (a-\lambda)(d-\lambda) - bc = 0$$

$$\lambda_{1/2} = \frac{a+d \pm \sqrt{(a-d)^2 + 4bc}}{2}$$

- right eigenvectors

$$M\vec{x} = \lambda_{1/2}\,\vec{x} \quad \Rightarrow \quad ax + by = \lambda_1 x$$

$$\Rightarrow \quad y = \frac{\lambda_1 - a}{b}\,x$$

$$\Rightarrow \quad \vec{v}_{1/2} = c_{1/2}\begin{pmatrix} \frac{\lambda_{1/2} - a}{b} \\ 1 \end{pmatrix}$$

- left eigenvectors

$$M^T\vec{x} = \lambda_{1/2}\,\vec{x} \quad \Rightarrow \quad \vec{w}_{1/2} = \begin{pmatrix} \frac{\lambda_{1/2} - a}{d} \\ 1 \end{pmatrix}.$$

- normalize such that left & right evecs are orthonormal

$$\vec{v}_i\,\vec{w}_j = \delta_{ij}$$

- expand $\vec{x}$ in right eigenmodes & substitute

$$\vec{x} = a_1(t)\,\vec{v}_1 + a_2(t)\,\vec{v}_2$$

$$a_i(t) = a_i^0\, e^{\lambda_i t}$$

- $a_i^0 = \vec{w}_i\,\vec{x}(0)$

- real eigenvalues: $(a-d)^2 + 4bc > 0$
  - → behavior depends on whether $\lambda_1, \lambda_2 < 0$, $\lambda_2 < 0 < \lambda_1$, $0 < \lambda_1, \lambda_2$
  - → stable if $\lambda_1, \lambda_2 < 0$

- complex eigenvalues: $(a-d)^2 + 4bc < 0$
  - → stable if $a+d < 0$ ⇒ negative real part
  - → unstable otherwise (necessary for sustained oscillations)
  - ⇒ spirals

$$\lambda_{1/2} = \lambda \pm i\omega \Rightarrow \text{dynamics} \sim e^{\lambda t \pm i\omega t}$$

$$e^{i\omega t} = \cos \omega t + i \sin \omega t$$

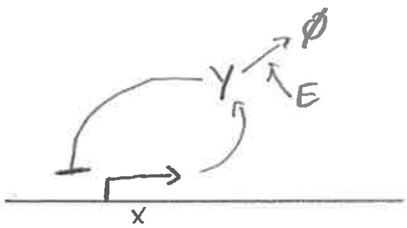
⇒ real & imaginary part oscillate

⇒ physical solution in the real part

Example

$$\frac{dx}{dt} = \frac{a}{1+y^n} - x \qquad y \text{ represses } x$$

$$\frac{dy}{dt} = x - \frac{by}{1+y} \qquad y \text{ is produced from } x \text{, degraded enzymatically}$$



Jac:

$$\begin{pmatrix} -1 & -\frac{a n y_s^{n-1}}{(1+y_s^n)^2} \\ 1 & -\frac{b}{1+y_s} + \frac{b y_s}{(1+y_s)^2} \end{pmatrix} = \begin{pmatrix} -1 & -\frac{n x_s^2}{y_s} \\ 1 & \frac{x_s}{y_s}\left(-1 + \frac{x_s}{b}\right) \end{pmatrix}$$

using fixpoint conditions

$a = 4,\ b = 3,\ n = 3$

$\Rightarrow\ x_s = 1.6\ldots \quad y_s = 1.14\ldots \qquad \lambda_{1/2} = -0.86 \pm 2.58i$

$\underline{n=1}$ $\quad y_s = \frac{a}{b} \quad x_s = \frac{ab}{a+b} \quad \Rightarrow \begin{pmatrix} -1 & -\frac{ab^3}{(a+b)^2} \\ 1 & -\frac{b^3}{(a+b)^2} \end{pmatrix}$

$$\lambda_{1/2} = \underbrace{-\frac{1}{2} - \frac{b^3}{2(a+b)^2}}_{\text{always negative}} \pm \sqrt{\ldots}$$

always negative $\Rightarrow$ never unstable

How do we make things oscillate?

- delayed negative feedback
- easiest with an explicit time delay τ

$$\frac{dy}{dt} = \frac{a}{1+y^n(t-\tau)} - \frac{b\,y(t)}{1+y(t)}$$

- in reality, delay isn't exact, but distributed

$\Rightarrow$ causes relaxation

- several intermediates and strong non-linearities necessary.

$\Rightarrow$ exercise

Dimensions & units

- quantities have units (time, concentrations, etc)
- equations relate quantities with different units
- coefficients in equations translate units
- we have already seen that answers can be "guessed" based on dimensions
- units are chosen, anything interesting can't depend on this choice

$\Rightarrow$ one can eliminate parameters through choice of 'natural' units

$$\frac{dx}{dt} = \frac{a_1}{a_2 + x^n} - a_3 x$$

$$a_3 = \frac{1}{\text{time}} \qquad a_1 = \frac{\text{conc}^{n+1}}{\text{time}} \qquad a_2 = \text{conc}^n$$

$$\Rightarrow \quad X = \frac{x}{\sqrt[n]{a_2}} \qquad \tau = t a_3 \qquad c = \frac{a_1}{a_3} a_2^{-\frac{n+1}{n}}$$

$$\Rightarrow \quad \frac{dX}{d\tau} = \frac{1}{a_3 \sqrt[n]{a_2}} \frac{dx}{dt} = \frac{a_1}{a_3 \sqrt[n]{a_2}} \frac{1}{a_2 + a_2 X^n} - X = \frac{c}{1 + X^n} - X$$