PREPARED BY
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Linear Dynamics II

Analytic solution of $\ddot{x} = -\alpha x$

$$\dot{\vec{x}} = \begin{pmatrix} 0 & -\alpha \\ 1 & 0 \end{pmatrix} \vec{x} = V^{-1} \begin{pmatrix} i\sqrt{\alpha} & 0 \\ 0 & -i\sqrt{\alpha} \end{pmatrix} V \vec{x}$$

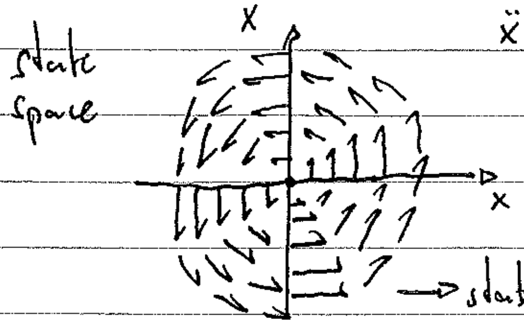
or $\dot{\vec{y}} = V\dot{\vec{x}} = \begin{pmatrix} i\sqrt{\alpha} & 0 \\ 0 & -i\sqrt{\alpha} \end{pmatrix} \vec{y} \Rightarrow$ $y_1(t) = Ae^{i\sqrt{\alpha}t}$
$y_2(t) = Be^{-i\sqrt{\alpha}t}$

and $x_1(t) = v_1 y_1(t) + v_2 y_2(t)$; $x_2(t) = v_3 y_1(t) + v_4 y_2(t)$

when dust settles : $x(t) = x_0 \cos(\sqrt{\alpha} t)$

$\dot{x}(t) = x_0 \sqrt{\alpha} \sin \sqrt{\alpha} t$

$\ddot{x}(t) = -x_0 \alpha \cos\sqrt{\alpha} t = -\alpha x(t)$ check ✓

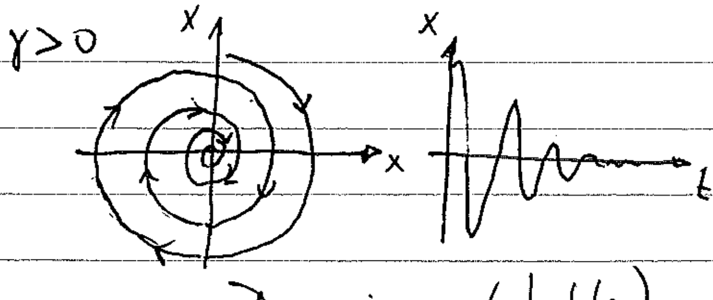


the base of each arrow is at $\begin{pmatrix} \dot{x} \\ x \end{pmatrix}$ and it points in direction of $\frac{d\vec{x}}{dt}$

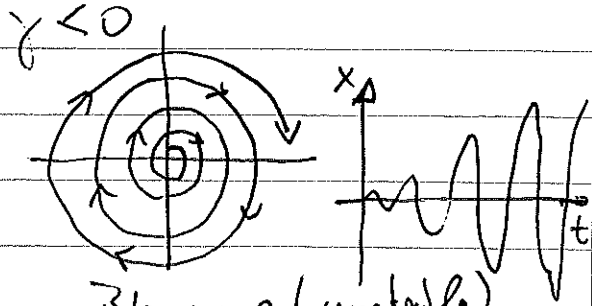
What if acceleration $\ddot{x}$ also depends on speed? $\ddot{x} = -\gamma \dot{x} - \alpha x$

$$\Rightarrow \dot{\vec{x}} = \begin{pmatrix} -\gamma \dot{x} - \alpha x \\ \dot{x} \end{pmatrix} = \begin{pmatrix} -\gamma & -\alpha \\ 1 & 0 \end{pmatrix} \vec{x} \Rightarrow \lambda_{1/2} = \frac{-\gamma \pm \sqrt{\gamma^2 - 4\alpha}}{2}$$

→ solution $x(t) = Ae^{-\frac{\gamma}{2}t} \cos \omega t$ with $\omega = \sqrt{\alpha - \frac{\gamma^2}{4}}$



Damping (stable)



Blow-up (unstable)

Stability analysis for n-dimensional system $\frac{d\vec{x}}{dt} = f(\vec{x})$

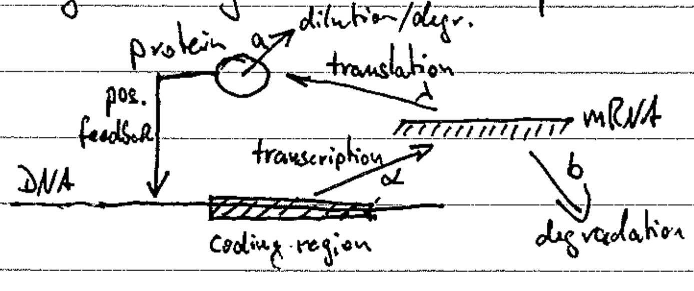
1. find steady state $\vec{x}_{st}$ such that $\left(\frac{d\vec{x}}{dt}\right)\Big|_{\vec{x}=\vec{x}_{st}} = f(\vec{x}_{st}) = 0$
2. calculate "derivative" at the steady state $A = Df\big|_{\vec{x}=\vec{x}_{st}}$
   ← called a JACOBIAN Matrix
3. compute eigenvalues of A
   → if all eigenvalues have negative real part, $\vec{x}_{st}$ is stable
   → if at least one is positive and none are zero, $\vec{x}_{st}$ is unstable
   → if at least one is zero, $\vec{x}_{st}$ can be either

for damped oscillator: $\dot{\vec{x}} = \begin{pmatrix} -\gamma\dot{x} - \alpha x \\ \dot{x} \end{pmatrix} = f(\vec{x}) \Rightarrow \vec{x}_{st} = \begin{pmatrix} 0 \\ 0 \end{pmatrix}$

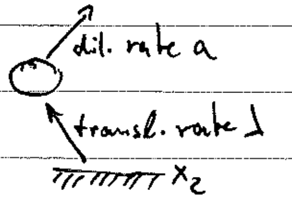
$$Df\big|_{x_{st}} = \begin{pmatrix} \frac{\partial f_1}{\partial x_1} & \frac{\partial f_1}{\partial x_2} \\ \frac{\partial f_2}{\partial x_1} & \frac{\partial f_2}{\partial x_2} \end{pmatrix} = \begin{pmatrix} -\gamma & -\alpha \\ 1 & 0 \end{pmatrix}$$ ← same matrix ⇔ is already linearized

$$\lambda_{1/2} = \frac{-\gamma \pm \sqrt{\gamma^2 - 4\alpha}}{2} \qquad \text{if } \alpha > 0 \begin{cases} \gamma > 0 & \text{damping} \rightarrow \text{stable} \\ \gamma < 0 & \text{blowup} \rightarrow \text{unstable} \end{cases}$$

Example: gene regulation with positive feedback



protein x_1



$$\frac{dx_1}{dt} = -a x_1 + \lambda x_2 \qquad \text{I}$$

max. expression rate

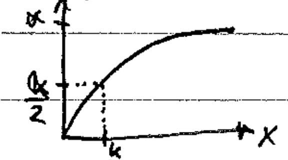
$$\frac{dx_2}{dt} = \frac{\alpha x_1}{K + x_1} - b x_2 \qquad \text{II}$$

transcription degradation

conc. "unit" / 50% activation conc.

few genes are purely constitutive (like "rate s" in previous example), mostly outside signals influence expression → Transcription factors TFs can "activate" or "repress"

usually use a Hill-type function $\frac{\alpha X}{K+X}$ for activation



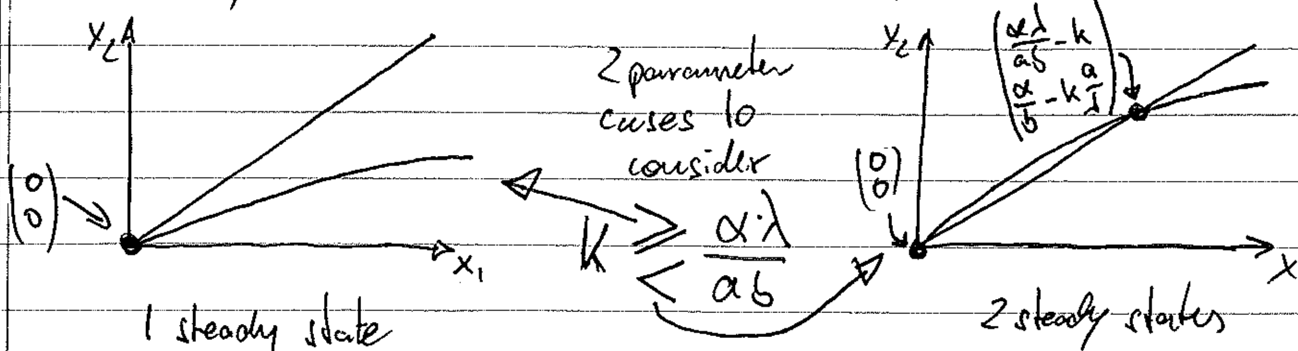
→ transcription rate increases, as TF conc increases

1. Steady states?

$$\left.\begin{array}{l} \frac{dx_1}{dt}=0 \Rightarrow x_2 = \frac{a}{\lambda} x_1 \\ \frac{dx_2}{dt}=0 \Rightarrow x_2 = \frac{\alpha}{b}\frac{x_1}{K+x_1} \end{array}\right\}$$

two functions $x_2 = f(x_1)$ called <u>NULLCLINES</u>

⇒ steady state occurs at <u>intersection</u> of nullclines



⇒ a qualitative change in dynamics due to variation of parameters ⟷ called <u>BIFURCATION</u>

2. Stability?

→ Jacobian matrix $A = \begin{pmatrix} -a & \lambda \\ \frac{\alpha k}{(k+x_1)^2} & -b \end{pmatrix} \Rightarrow \lambda_{1/2} = \frac{-(a+b) \pm \sqrt{(a+b)^2 - 4(ab - \frac{\lambda\alpha}{k})}}{2}$ at $\vec{x}_{st} = (0,0)$

λ_2 positive when $-4(ab - \frac{\lambda\alpha}{k}) > 0$ or $\boxed{k < \frac{\lambda\alpha}{ab}} \Rightarrow \vec{x}_{st} = \begin{pmatrix}0\\0\end{pmatrix}$ switches from stable to unstable

For $\vec{x}_{st} = \begin{pmatrix}\frac{\alpha\lambda}{ab}-k\\ \frac{\alpha}{b}-k\frac{a}{\lambda}\end{pmatrix}$ λ_2 is positive when $-4(ab - \frac{a^2b^2}{\alpha\lambda}k) > 0$

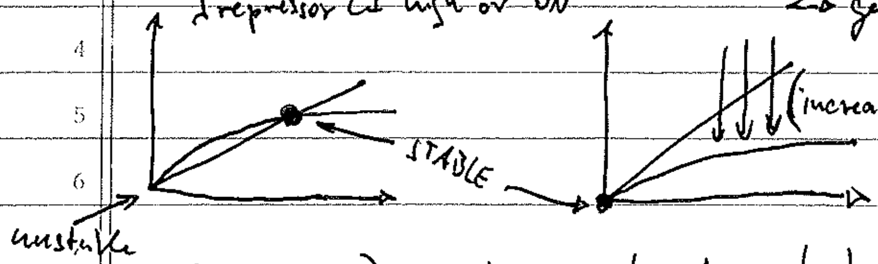
$\Rightarrow k > \frac{\lambda\alpha}{ab}$ but also $k < \frac{\lambda\alpha}{ab}$ (because otherwise $\vec{x}_{st}$ would not exist)

⇒ hence only $k = \frac{\lambda\alpha}{ab}$ can make $\vec{x}_{st}$ unstable.

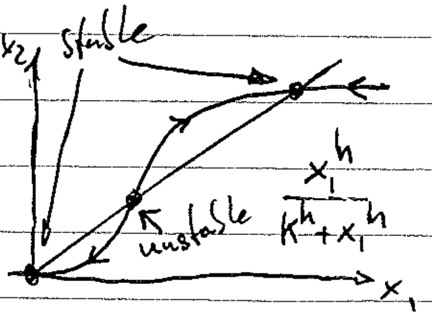
Can we use this "network" for anything? quiescence ↑ infectious spread ↑

→ genetic switch? Example: phage lambda lysogenic vs. lytic cycle

↔ gene CI controls cycle switch upon external signal (stress)

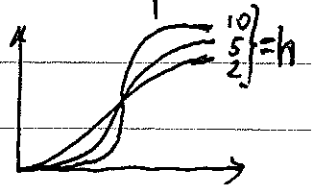


Problems: 1) switch is sluggish, not sharp
2) OFF state is unstable



Solution: make Hill function steeper:

h is a "Hill coefficient"



mechanistically increasing Hill coefficient through "cooperativity":
- one interaction (e.g. binding event) changes interaction of 2nd event

General state spaces for 2×2 matrices: $A = \begin{pmatrix} v & s \\ w & t \end{pmatrix}$

Δ = discriminant of characteristic polynomial of A

3 possibilities:

1. simple case $\Delta > 0$
   eigenvalues are real and distinct $A \xrightarrow{\text{change of basis}} \begin{pmatrix} a & 0 \\ 0 & b \end{pmatrix}$

2. complex case $\Delta < 0$
   eigenvalues are complex and conjugate $A \longrightarrow \begin{pmatrix} a & -b \\ b & a \end{pmatrix}$

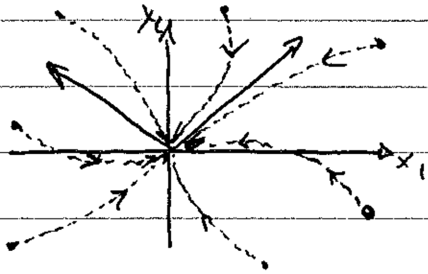
3. awkward case $\Delta = 0$
   eigenvalues are real and equal $A \longrightarrow \begin{pmatrix} a & b \\ 0 & a \end{pmatrix}$

solution of $\dot{\vec{x}} = A\vec{x}$ is $\vec{x}(t) = e^{At}\vec{x}_0$ ⇒ need matrix exp

use: $\exp A = T^{-1}\exp(TAT^{-1})T = T^{-1}\exp(D)T$

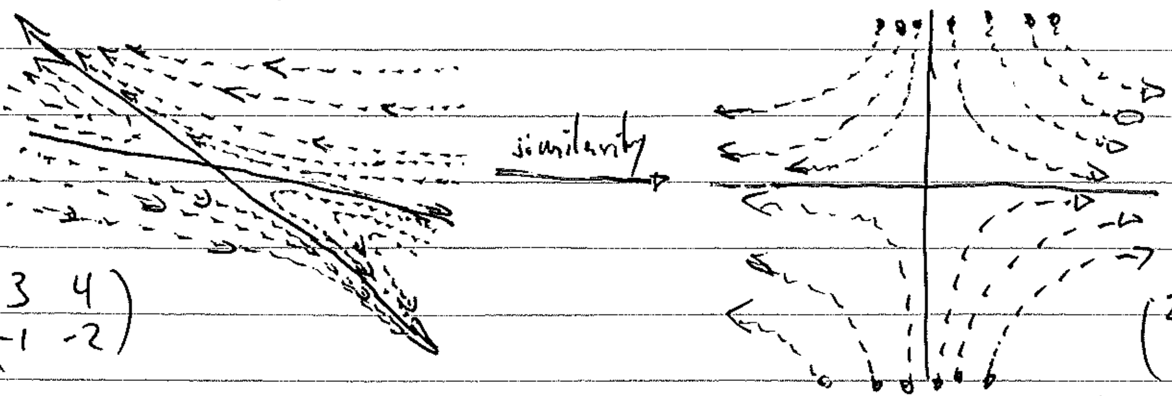
1. $\Delta > 0$ $\lambda_1, \lambda_2 < 0$ $\exp\begin{pmatrix} a & 0 \\ 0 & b \end{pmatrix} = \begin{pmatrix} \exp a & 0 \\ 0 & \exp b \end{pmatrix}$

ex: $\begin{pmatrix} -3 & 1 \\ 1 & -2 \end{pmatrix}$



stable node

$\Delta > 0$ $\lambda_1 < 0, \lambda_2 > 0$ → saddle node

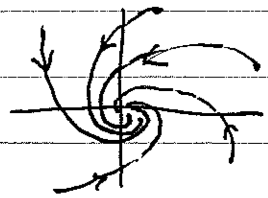


$\begin{pmatrix} 3 & 4 \\ -1 & -2 \end{pmatrix}$ $\begin{pmatrix} 2 & 0 \\ 0 & -1 \end{pmatrix}$

2. $\Delta < 0$ complex λ_1 and λ_2 $\exp\begin{pmatrix} a & -b \\ b & b \end{pmatrix} = \exp(a) \begin{pmatrix} \cos b & -\sin b \\ \sin b & \cos b \end{pmatrix}$

$\Rightarrow \lambda_{1,2} = a \pm ib$

ex: $\begin{pmatrix} -2 & -5 \\ 1 & -1 \end{pmatrix}$



stable spiral

3. $\Delta = 0$ $\lambda_1 = \lambda_2 = a$ (real) $\exp\begin{pmatrix} a & 0 \\ 0 & a \end{pmatrix} = \begin{pmatrix} \exp a & b\exp a \\ 0 & \exp a \end{pmatrix}$

can't make up its mind whether to be node or spiral

4. $\Delta < 0$, Trace $= 0$

can't make up its mind whether to be stable or unstable