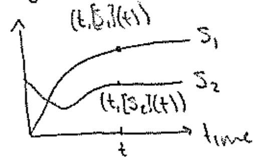
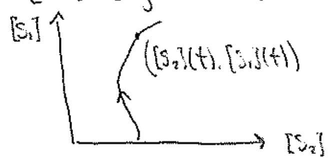
Chapter 4 - Dynamics and Stability

We've been visualizing simulations as time series

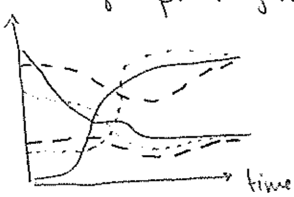


Alternatively, plot $[S_2]$ against $[S_1]$.

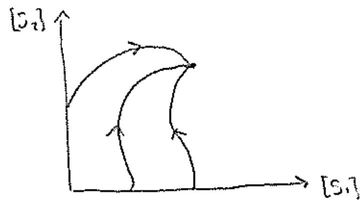


← phase-plane

one advantage: plotting multiple simulations

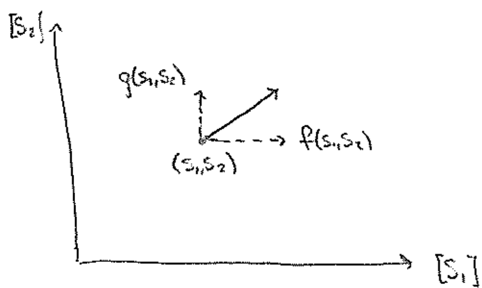


time-domain



phase-plane

How to generate the curves (trajectories) in the phase plane?

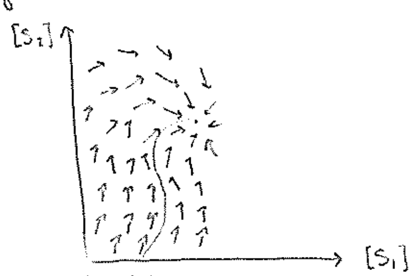


model:

$$\frac{d}{dt} s_1(t) = f(s_1(t), s_2(t))$$

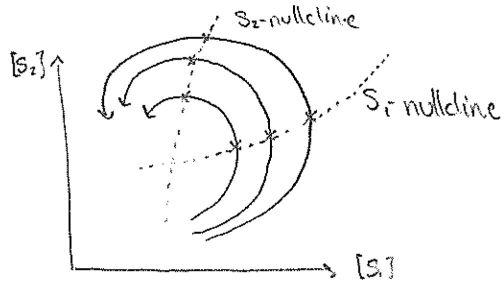
$$\frac{d}{dt} s_2(t) = g(s_1(t), s_2(t))$$

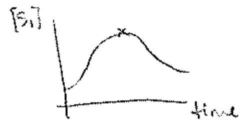
appending these arrows to a collection of points yields a direction field



(See pictures in text.)

A key feature of a <u>phase portrait</u>: the set of points where trajectories "turn around" i.e. reach maximum or minimum values in one species





These "turning points" occur where either

$$\frac{d}{dt}S_1(t) = 0 \quad (S_1\text{-nullcline})$$

$$\frac{d}{dt}S_2(t) = 0 \quad (S_2\text{-nullcline})$$

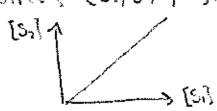
Here, S_1-nullcline is the curve $0 = f(s_1, s_2)$.

$$\xrightarrow{K_0} S_1 \xrightarrow{K_1} S_2 \xrightarrow{K_2}$$

$$\frac{d}{dt}s_1(t) = K_0 - K_1 s_1(t), \quad \frac{d}{dt}s_2(t) = K_1 s_1(t) - K_2 s_2(t)$$

So the S_2-nullcline is the points (s_1, s_2) such that $K_1 s_1 - K_2 s_2 = 0$, ie

$$s_1 = \frac{K_2}{K_1} s_2$$



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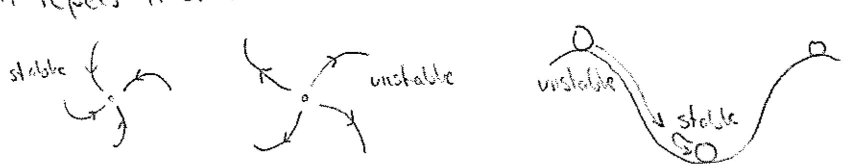
<u>direction field</u>: direction of motion at a set of grid-points
<u>nullcline</u>: "turning points" at which a concentration reaches a min/max
The intersection of both nullclines is a steady state.
(See pictures in text.)

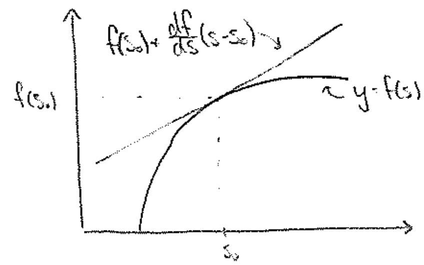
Stability

A steady state is <u>stable</u> if it attracts nearby trajectories, and is <u>unstable</u> if it repels them.



Linearization criterion for stability

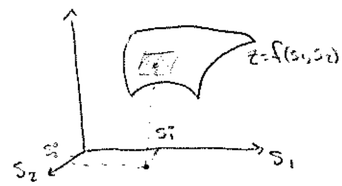
Recall, for a function $y = f(s)$, we can approximate the value of y near a given point $s = s_0$ by



Linearization:

$$f(s) \approx f(s_0) + \frac{df}{ds}\bigg|_{s=s_0} \cdot (s - s_0)$$

Likewise, for a function of two variables $f(s_1, s_2)$



$$f(s_1, s_2) \approx f(s_1^\circ, s_2^\circ) + \frac{\partial f}{\partial s_1}\bigg|_{(s_1^\circ, s_2^\circ)} (s_1 - s_1^\circ) + \frac{\partial f}{\partial s_2}\bigg|_{(s_1^\circ, s_2^\circ)} (s_2 - s_2^\circ)$$

Now, for a model:

$$\frac{d}{dt} s_1(t) = f(s_1(t), s_2(t)), \qquad \frac{d}{dt} s_2(t) = g(s_1(t), s_2(t))$$

for (s_1, s_2) near (s_1°, s_2°) we can approximate

$$\frac{d}{dt} s_1(t) \approx f(s_1^\circ, s_2^\circ) + \frac{\partial f}{\partial s_1}\bigg|_{(s_1^\circ, s_2^\circ)} (s_1(t) - s_1^\circ) + \frac{\partial f}{\partial s_2}\bigg|_{(s_1^\circ, s_2^\circ)} (s_2(t) - s_2^\circ)$$

$$\frac{d}{dt} s_2(t) \approx g(s_1^\circ, s_2^\circ) + \frac{\partial g}{\partial s_1}\bigg|_{(s_1^\circ, s_2^\circ)} (s_1(t) - s_1^\circ) + \frac{\partial g}{\partial s_2}\bigg|_{(s_1^\circ, s_2^\circ)} (s_2(t) - s_2^\circ)$$

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Eigenvalue characterization of Stability

To characterize stability directly from the model.
If (s_1°, s_2°) is a steady state.

$$\frac{d}{dt} s_1(t) = \frac{\partial f}{\partial s_1} \cdot (s_1(t) - s_1^\circ) + \frac{\partial f}{\partial s_2} \cdot (s_2(t) - s_2^\circ)$$

$$\frac{d}{dt} s_2(t) = \frac{\partial g}{\partial s_1} \cdot (s_1(t) - s_1^\circ) + \frac{\partial g}{\partial s_2} \cdot (s_2(t) - s_2^\circ)$$

To clean up the notation introduce a change of variables:

$$x_1(t) = s_1(t) - s_1^\circ, \quad x_2(t) = s_2(t) - s_2^\circ.$$

These measure displacement from the steady state (s_1°, s_2°). Then

$$\frac{d}{dt}x_1(t) = \frac{d}{dt}s_1(t), \quad \frac{d}{dt}x_2(t) = \frac{d}{dt}s_2(t).$$

We have as our linearization

$$\frac{d}{dt}x_1(t) = \frac{\partial f}{\partial s_1}x_1(t) + \frac{\partial f}{\partial s_2}x_2(t)$$

$$\frac{d}{dt}x_2(t) = \frac{\partial g}{\partial s_1}x_1(t) + \frac{\partial g}{\partial s_2}x_2(t)$$

Define

$$a = \frac{\partial f}{\partial s_1}, \quad b = \frac{\partial f}{\partial s_2}, \quad c = \frac{\partial g}{\partial s_1}, \quad d = \frac{\partial g}{\partial s_2}$$

Then

$$\frac{d}{dt}x_1(t) = ax_1(t) + bx_2(t), \quad \frac{d}{dt}x_2(t) = cx_1(t) + dx_2(t)$$

This is a linear system of differential equations. Solutions take the form.

$$x_1(t) = C_{11}e^{\lambda_1 t} + C_{12}e^{\lambda_2 t}$$

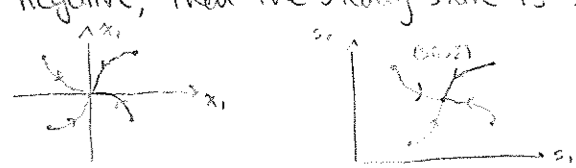
$$x_2(t) = C_{21}e^{\lambda_1 t} + C_{22}e^{\lambda_2 t}$$

The constants C_{ij} depend on the specifics of the initial condition, but the constants λ_1, λ_2 depend only on the system. λ_1, λ_2 are the eigenvalues of the matrix $\begin{bmatrix} a & b \\ c & d \end{bmatrix}$, which is called the system Jacobian. They are the roots of the quadratic equation

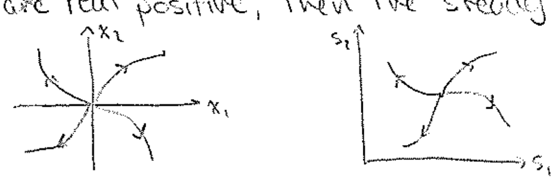
$$\lambda^2 - (a+d)\lambda + (ad - bc) = 0.$$

Observation: the behaviour of $x_1(t)$ and $x_2(t)$ depends on the nature of λ_1, λ_2.

Eg. If λ_1, λ_2 are real and negative, then the steady state is stable.



Eg. If either of λ_1, λ_2 ~~are~~ is real positive, then the steady state is unstable.



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If λ_1, λ_2 are complex, we'll have $\lambda_{1,2} = a \pm ib$. a is the real part and b is the imaginary part.

e.g. $3 + 4i$, $i = \sqrt{-1}$

real part, imaginary part

To evaluate $e^{(a+ib)t}$ we'll make use of Euler's formula:

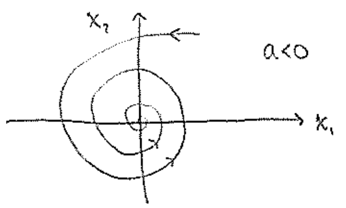
$$e^{a+ib} = e^a(\cos(b) + i\sin(b)).$$

Now

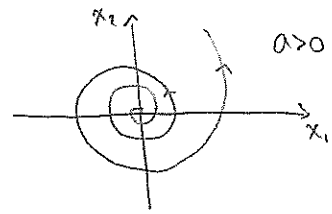
$$
\begin{aligned}
x_1(t) &= C_{11} e^{\lambda_1 t} + C_{12} e^{\lambda_2 t} \\
&= C_{11} e^{(a+ib)t} + C_{12} e^{(a-ib)t} \\
&= C_1 e^{at}(\cos(bt) + i\sin(bt)) + C_{12} e^{at}(\cos(-bt) + i\sin(bt)).
\end{aligned}
$$

The long-term behaviour is dictated by the sign of a.

The solution exhibits oscillatory behaviour



$a<0$ damped oscillation spiralling to zero (stable)



$a>0$ spiralling out (unstable)

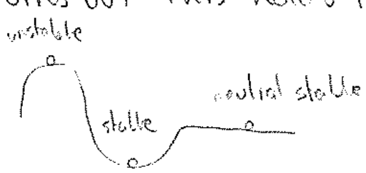
It turns out the imaginary components are zero when initial conditions are real.

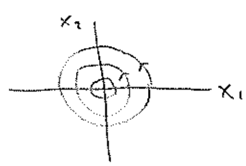
Conclusion:

$$\mathrm{Re}(\lambda_1), \mathrm{Re}(\lambda_2) < 0 \Rightarrow \text{stable}$$

$$\text{either } \mathrm{Re}(\lambda_1), \mathrm{Re}(\lambda_2) > 0 \Rightarrow \text{unstable}$$

It turns out this holds in n dimensions too.





(See pictures in text.)

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Nonlinear dynamics:

- phase plane - stability - eigenvalue criterion
- bifurcation analysis - sensitivity analysis

Continuation diagram: plot of steady state of s_1 or s_2 against a parameter value.

(See bifurcation discussion and pictures in text.)

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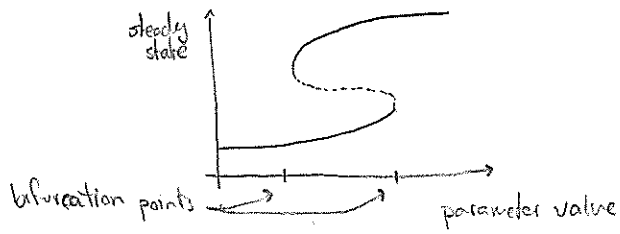
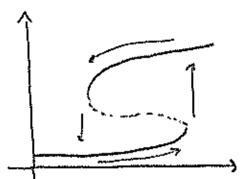
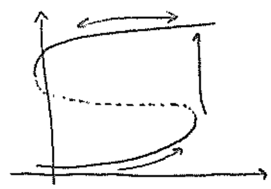
Bifurcation diagrams





hysteresis loop
hysteretic switching



irreversible switching

Parameter sensitivity analysis:

- global sensitivity analysis
- local sensitivity analysis

Eg. $\xrightarrow{v_0} S \xrightarrow{v_1}$

$$v_0 = V$$

$$v_1 = \frac{V_{max}[S]}{K_M + [S]}$$

$$s^{ss} = \frac{V K_M}{V_{max} - V}$$

$$\left.\begin{array}{l} V = 2 \text{ mM/min} \\ K_M = 1.5 \text{ mM} \\ V_{max} = 4 \text{ mM/min} \end{array}\right\} \text{nominal parameter values}$$

local parametric sensitivity coefficient for V_{max}

absolute: $$\frac{\partial s^{ss}}{\partial V_{max}} = \frac{-3}{(V_{max}-2)^2} \text{ min}$$

at $V_{max} = 4$ mM/min, this is $-3/4$ min. A more useful measure is the relative sensitivity

$$\frac{\partial s^{ss}/s^{ss}}{\partial V_{max}/V_{max}} = \frac{V_{max}}{s^{ss}} \frac{\partial s^{ss}}{\partial V_{max}} = -2.$$

This says a 1% increase in V_{max} leads to a 2% decrease in s^{ss}.