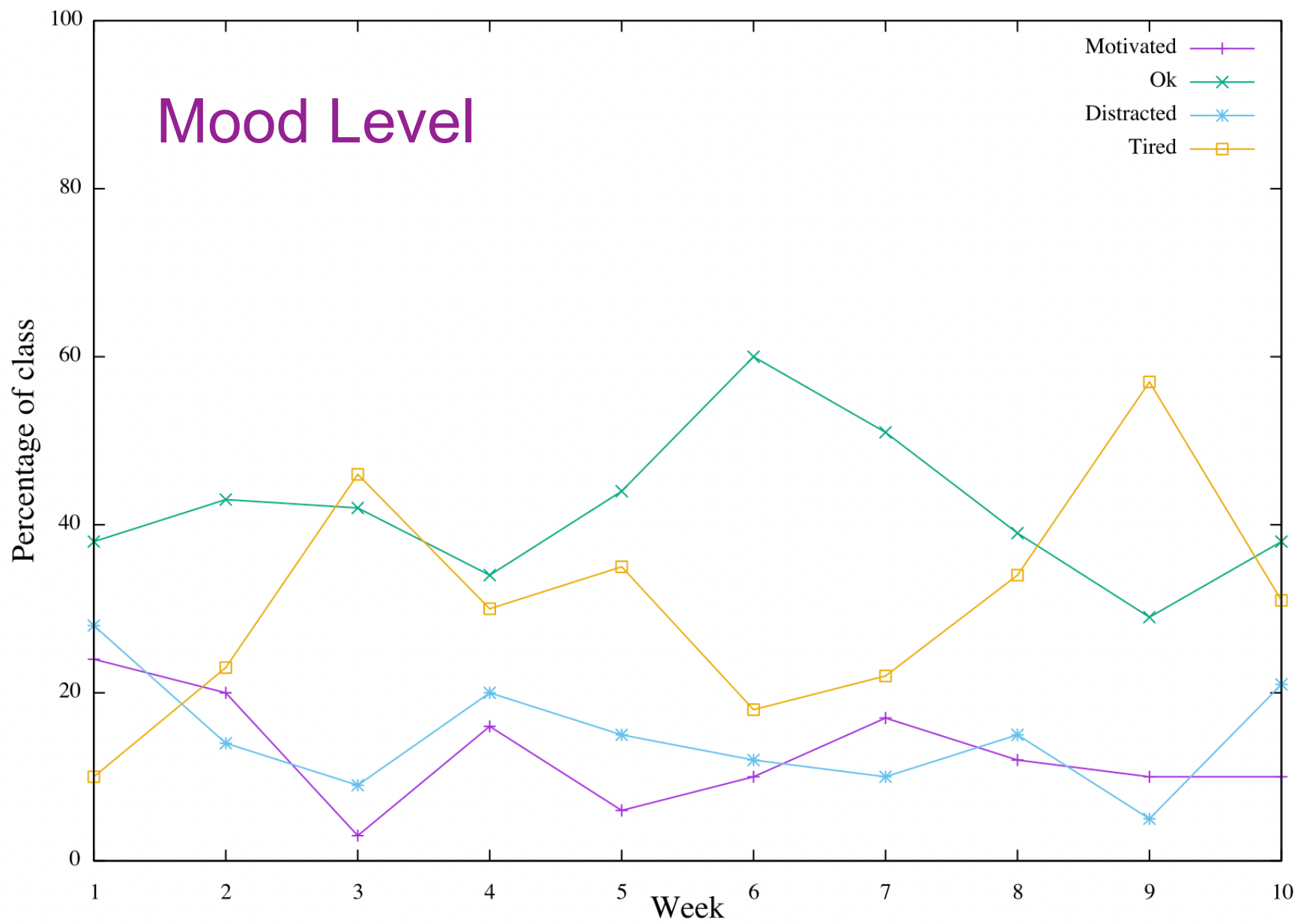




Sel'kov model of glycolysis

Strogatz, Ex. 7.3.2, page 207, course notes Ch. 5, page 42.

Sel'Kov, Self oscillations in glycolysis. A simple kinetic model.
Euro. J. Biochem. 4:79 (1968)



Let $x = [\text{ADP}] = \text{product}$
 $y = [\text{ATP}] = \text{reactant}$

The model is:

$$dx/dt = -x + a y + x^2 y$$

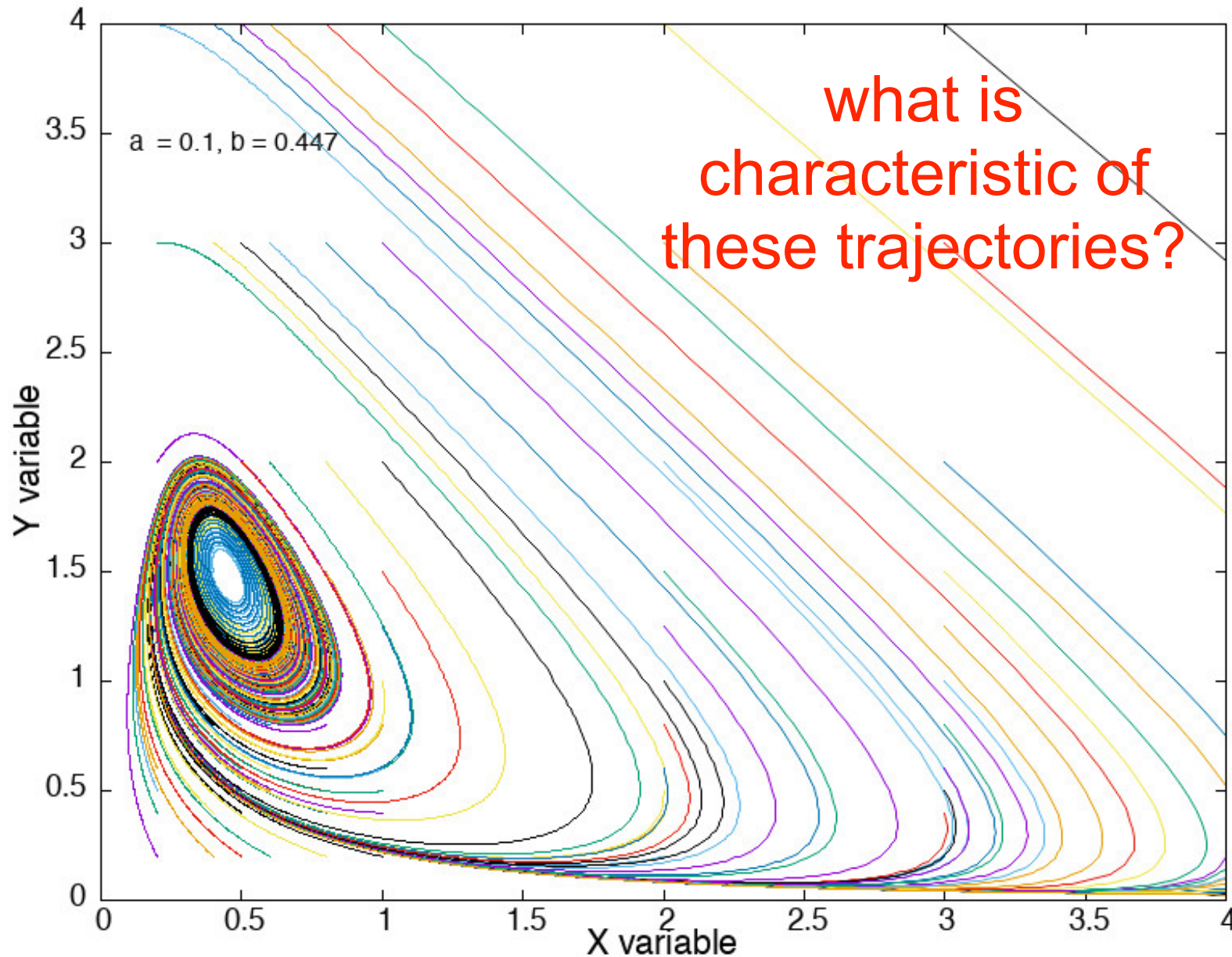
$$dy/dt = b - a y - x^2 y$$

with $a, b > 0$.

Try $a = 0.1$, $b = 0.447$
Fixed point at $(0.447, 1.49)$

Sel'kov model of glycolysis
(Lecture 7)

what is
characteristic of
these trajectories?



Trajectories cannot intersect, so in 1D and 2D they are squeezed between nearby trajectories; once they enter a region, they cannot leave (e.g., a trapping region)

So, a limit cycle in 2D must be periodic

But in 3D (and higher) trajectories can “escape” into the third dimension, and pass around each other.

A limit cycle in a 3D system can lose this periodicity, and become chaotic.

1D has monotonic trajectories

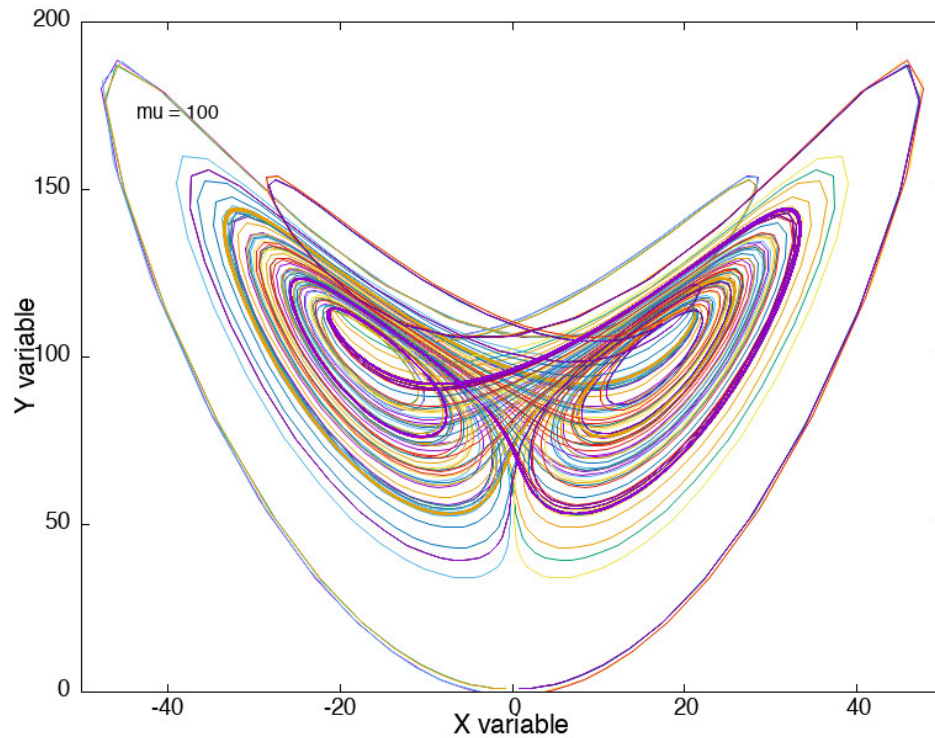
2D linear has the tau-delta plot scheme, and allows spirals,

2D non-linear also allows limit cycles.

3D allows chaotic motion.

Even in chaotic motion, there is structure, it is not random. A strange attractor exists in a bounded region (cp a limit cycle in its trapping region)

Biology is not described by straight lines and regular shapes (circles, spheres, etc)



```
// *****  
// The trio of functions to return the time derivatives at a given time.  
//  
// These are the Lorenz equations from page 319 of Strogatz.  
  
double f1(const double a[6], double x, double y, double z)  
{  
    return 10.0*(y - x);  
}  
  
double f2(const double a[6], double x, double y, double z)  
{  
    return a[0]*x - y - x*z;  
}  
  
double f3(const double a[6], double x, double y, double z)  
{  
    return x*y - 2.6667*z;  
}
```

How is this contained in these?

If we want to understand biology,
we have to go beyond simple curves and functions.

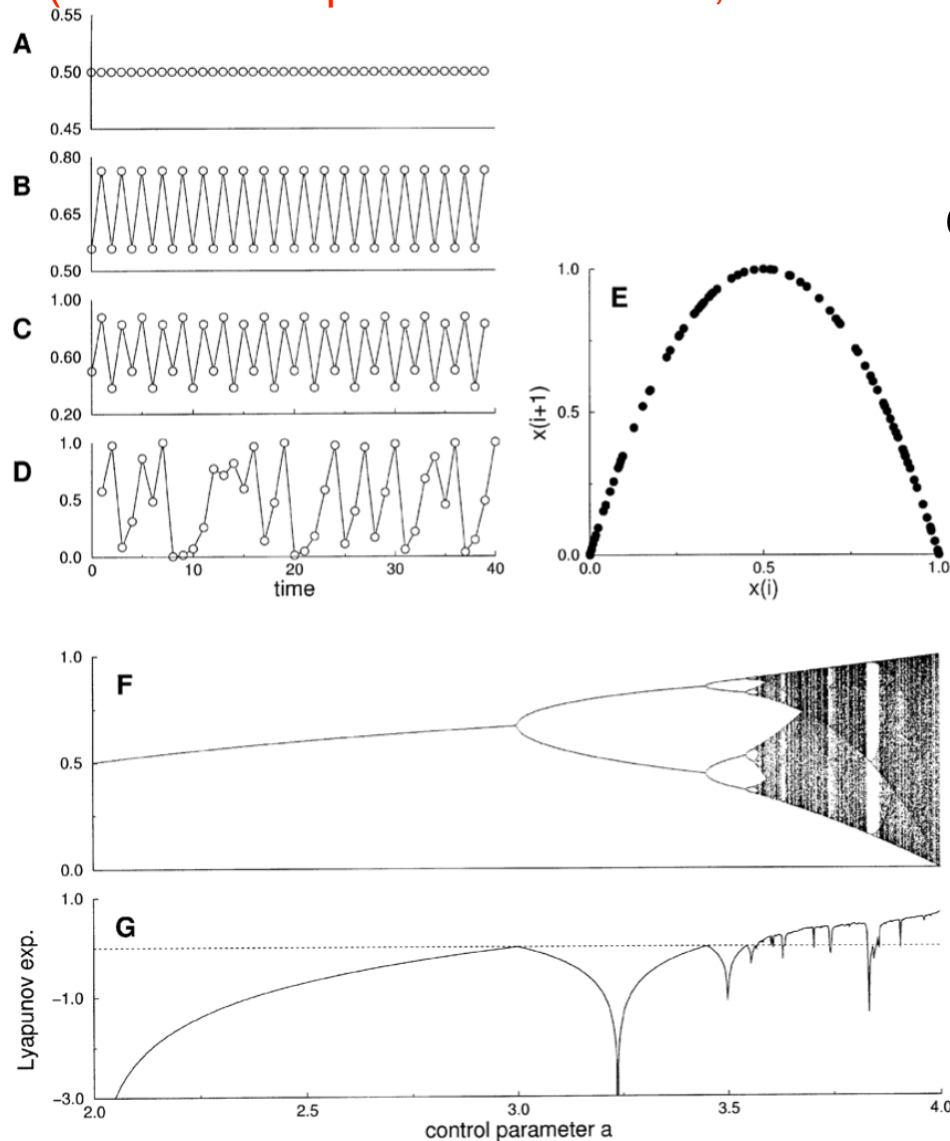


Fig. 1. The logistic equation $x_{i+1} = ax_i(1-x_i)$ with different values of bifurcation parameter a . Subsequent iterations x_i for increasing a give rise to the period-doubling route to chaos. (A) $a = 2.0$ (period-1 orbit), (B) $a = 3.1$ (period-2), (C) $a = 3.5$ (period-4), and (D) $a = 4.0$ (chaotic trajectory). When a is increased from 2 to 4, the system undergoes period-doubling bifurcations, i.e., the system switches to higher periodicities at certain parameter values. The right side (E) shows a plot

Review

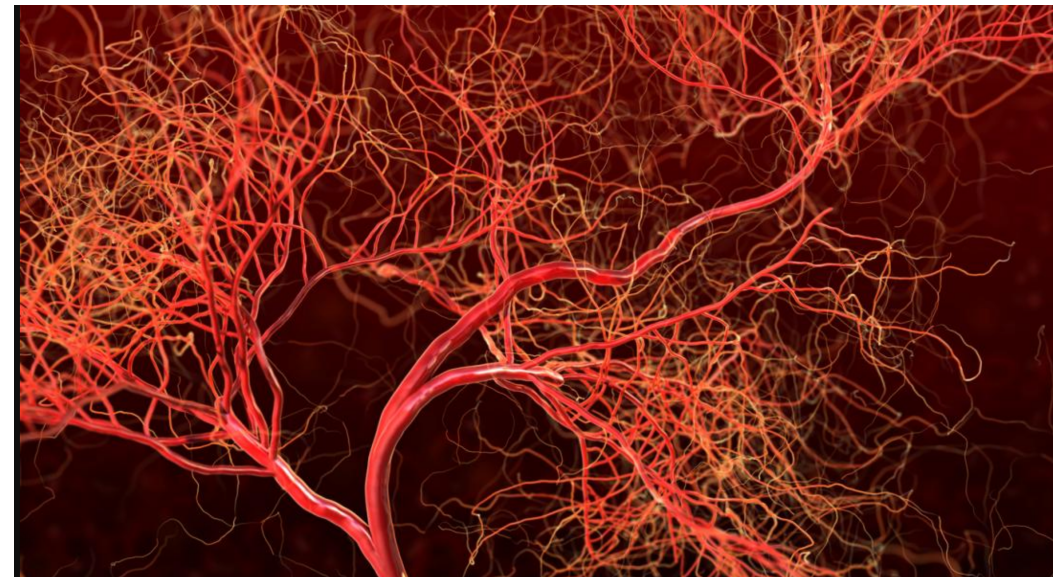
Chaos in the cardiovascular system: an update

Claus D. Wagner, Pontus B. Persson*

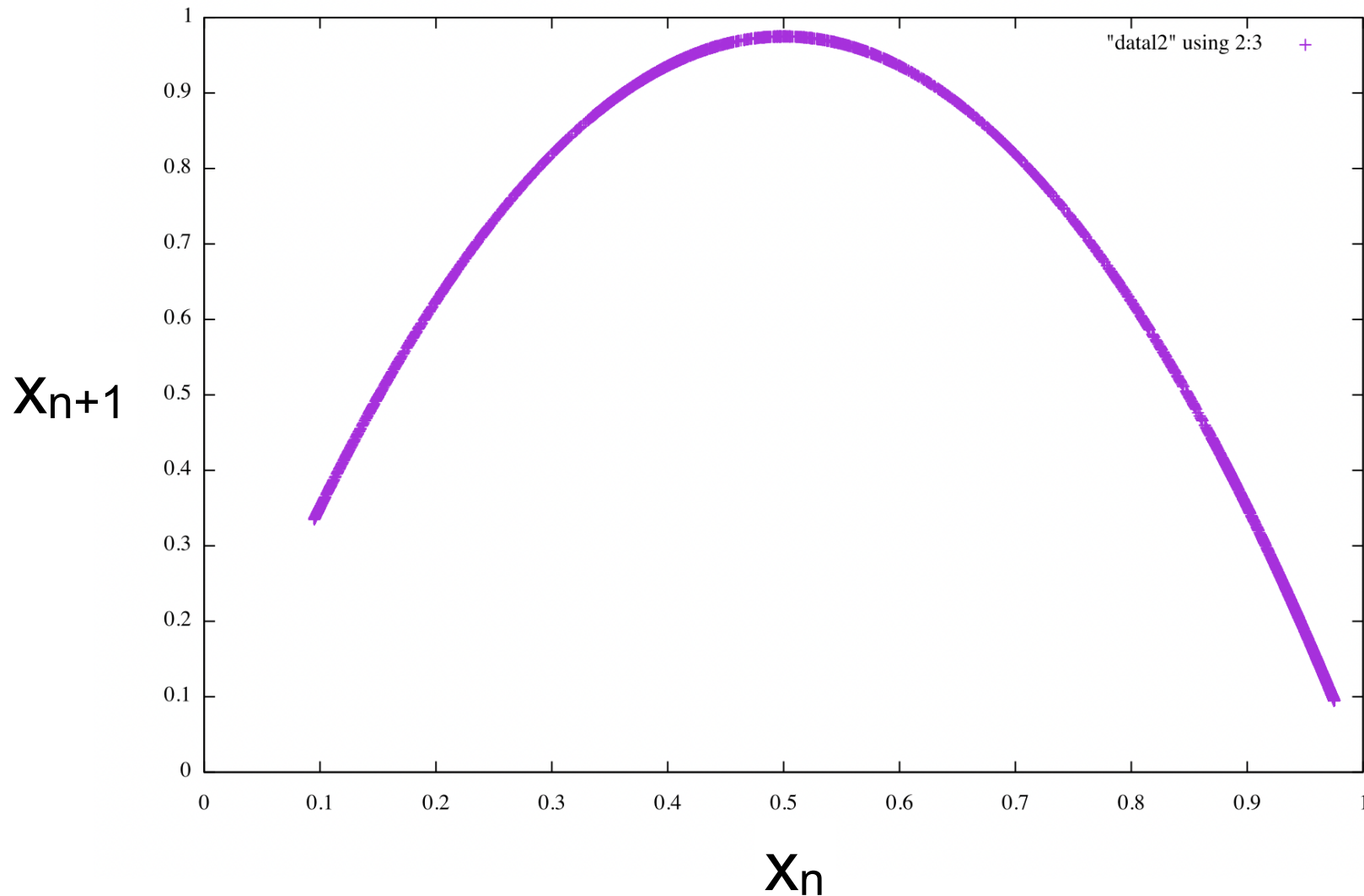
[Clinical Trial](#) > [Neuroimage](#). 2003 Nov;20(3):1765-74. doi: 10.1016/s1053-8119(03)00380-x.

Is the brain cortex a fractal?

[Valerij G Kiselev](#)¹, [Klaus R Hahn](#), [Dorothee P Auer](#)



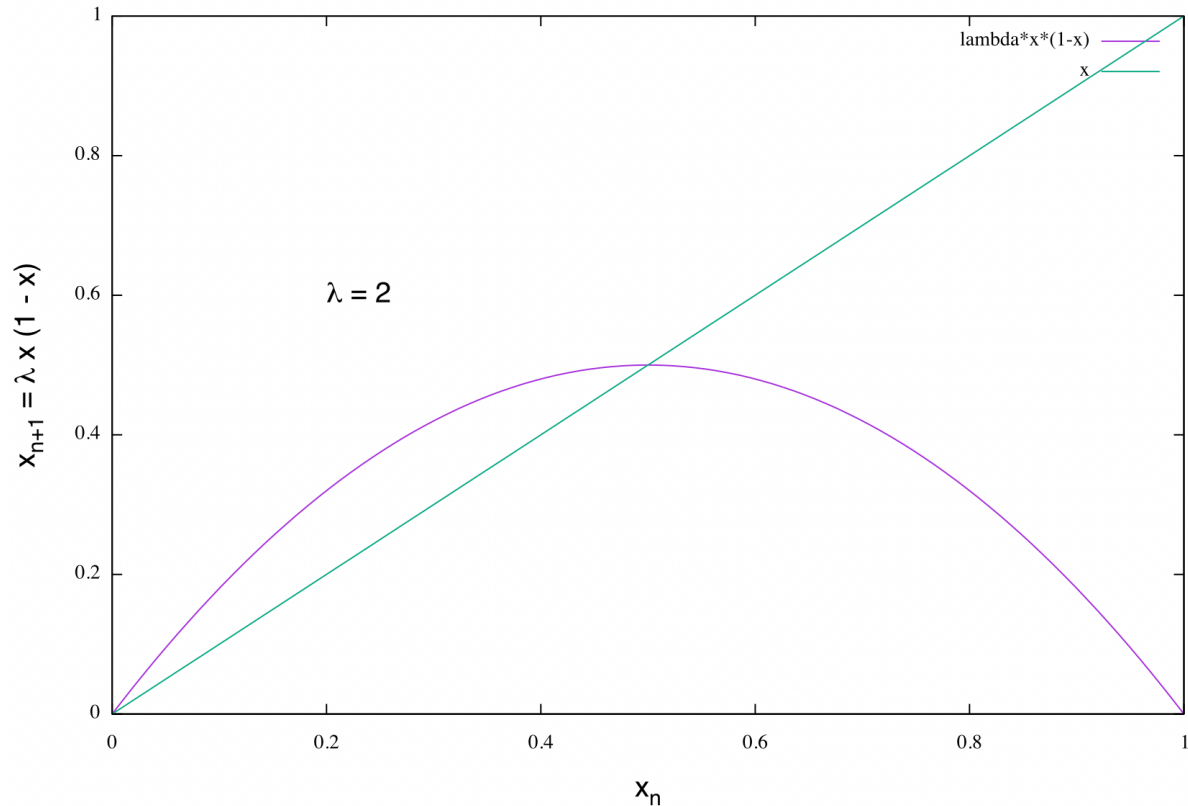
Return map for logistic map with $r = 3.9$, 5000 points ignoring first 1500



Why this shape? to prevent the iterates from leaving $(0,1)$, the solutions are bounded.

Iterating the discrete logistic map

$$x_{n+1} = \lambda x_n (1 - x_n)$$

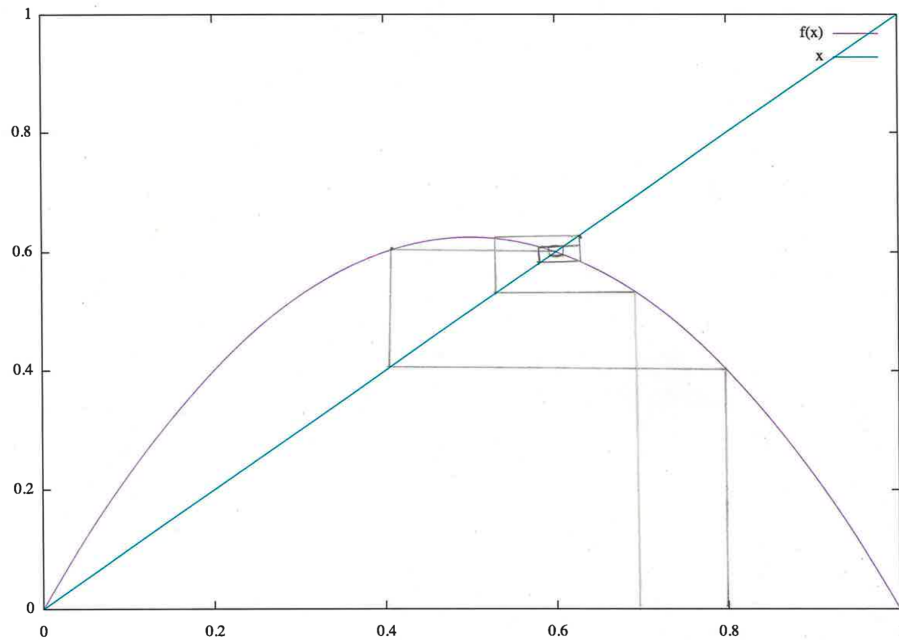


For a given value of λ in the range $(0, 4)$, pick a (random) starting value x_0 , in the range $(0, 1)$, and apply the above map to get x_1 . Repeat N times.

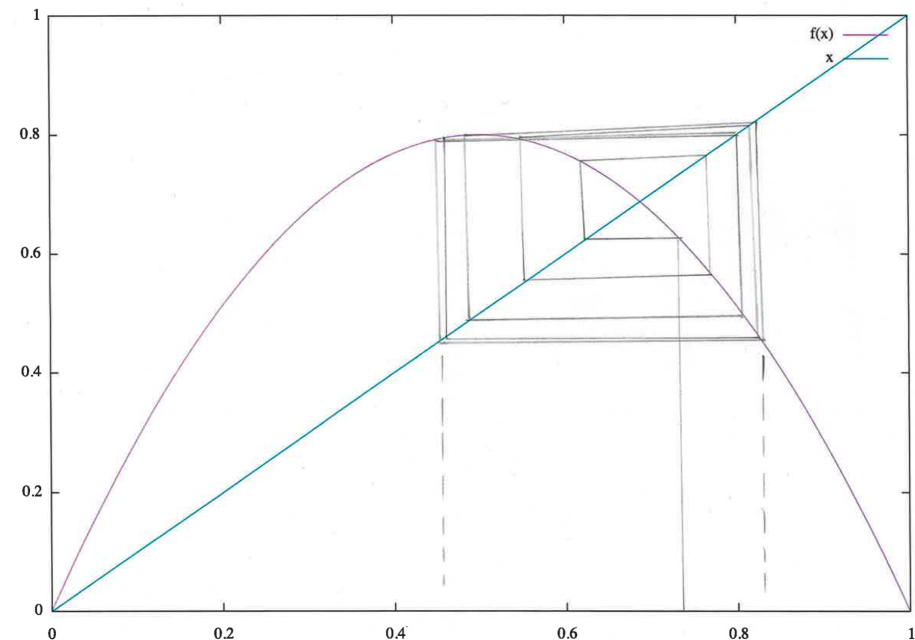
If there is a stable fixed point(s), the points will approach it.

Fixed points are stable when the magnitude of their slope is less than 1.

When is a fixed point in a discrete map stable?



$r = 2.5$



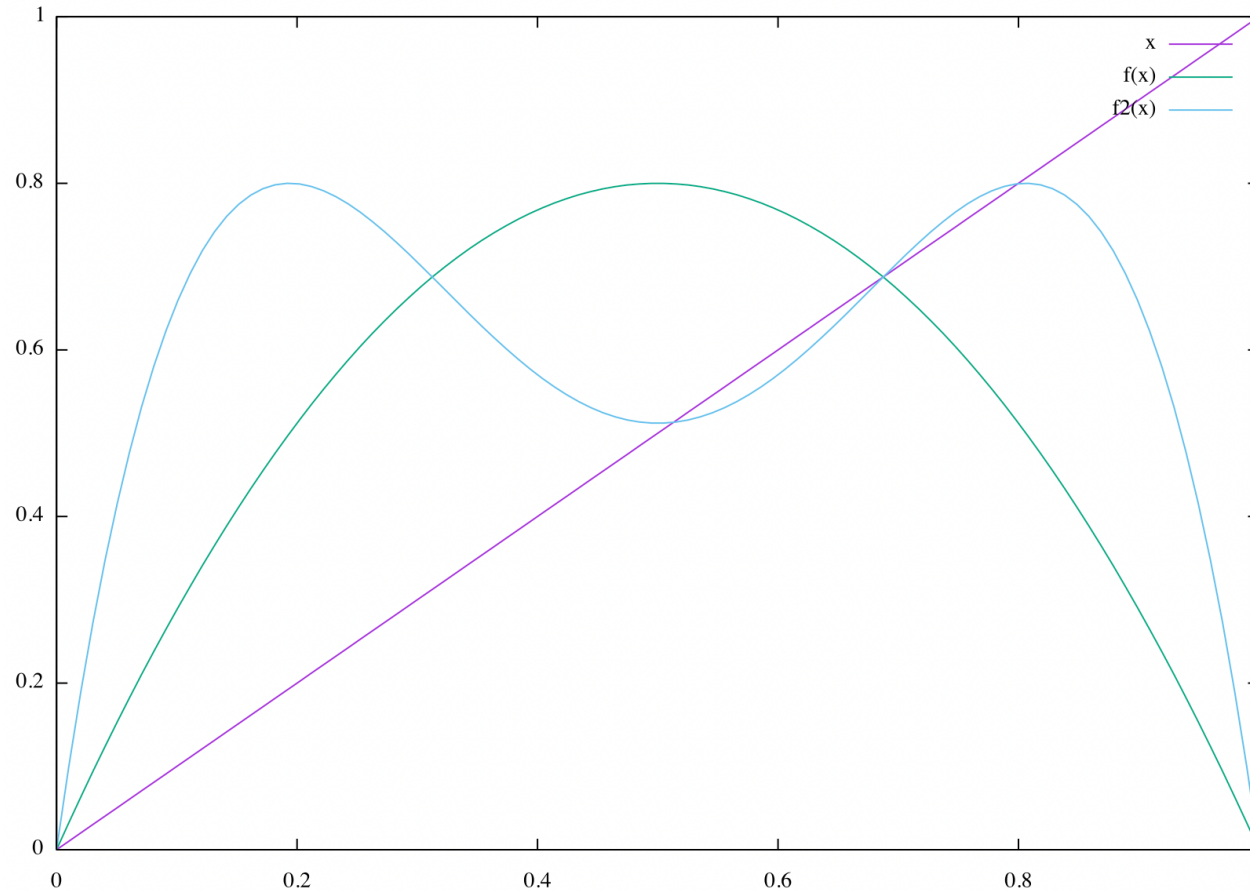
$r = 3.2$

Cobweb plot

Choose an x_n , go vertically to $x_{n+1} = f(x_n)$, then horizontally to x_{n+1} (diagonal), then vertically again to $f(x_{n+1})$, etc.

Either you spiral closer to the fixed point (stable left), or you don't (two stable points, right). **how do we know?**

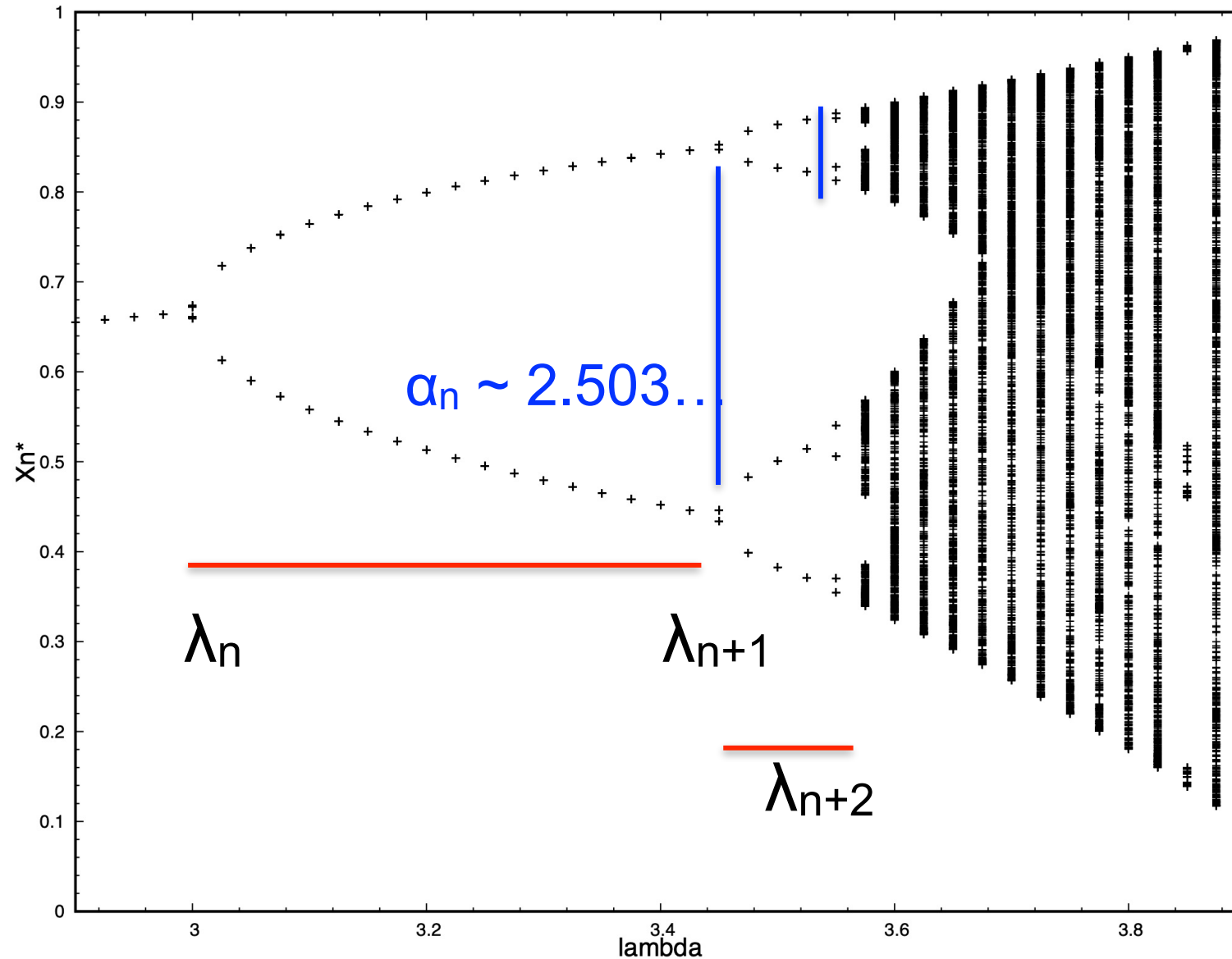
When a fixed point of $f(x)$ becomes unstable, new ones appear for $f(f(x))$, etc.



$x_{n+1} = \lambda x_n (1 - x_n) = f(x)$, but $f(x^*)$ is now unstable

$f2(x) = f(f(x))$ has two stable fixed points

the period doubling route to chaos: $x_{n+1} = \lambda x_n (1 - x_n)$



$$\delta_n = \frac{\lambda_{n+1} - \lambda_n}{\lambda_{n+2} - \lambda_{n+1}} \sim 4.6692\dots$$

as λ increases by smaller increments,
system becomes more complex,
eventually chaotic

Feigenbaum numbers

$$\delta_n = \frac{\lambda_{n+1} - \lambda_n}{\lambda_{n+2} - \lambda_{n+1}} \sim 4.6692\dots$$

$$\alpha_n \sim 2.503\dots$$

δ tells you that to reach the next splitting you must increase the control parameter by about 1/5 of its previous increment.

Splittings get closer together!

α gives the ratio of the separation of the new fixed points.

Period Doubling is a means by which continuous equations can contain chaotic motion.

1D Discrete iterated maps, fractals (lecture 13)

Be able to find a fixed point of an iterated map and calculate its stability from the derivative of the iteration function evaluated at the fixed point, i.e., its magnitude must be less than one.

Be able to apply a rule to construct a fractal iteratively (like the Koch curve or Cantor set), and generate a few iterations of the curve.

Then determine the fractal dimension of the curve from the box-counting method:

$$D = \lim_{\varepsilon \rightarrow 0} \frac{\ln(N(\varepsilon))}{\ln(1/\varepsilon)}$$

iterative process to construct a fractal

Break

Comme vous le savez, tous les cours font l'objet d'une évaluation approfondie chaque semestre. L'enquête d'évaluation approfondie pour votre cours BIOENG-455_SA24/25 vient d'être ouverte aux étudiant·es et restera disponible jusqu'au 12.01.2025 23:59:00.

Le rapport sera disponible une fois la période d'examen terminée, le 11 février 2025.

Les commentaires des étudiant·es vous seront plus utiles si le taux de réponse est élevé et nous vous recommandons donc, si possible, de consacrer 5 minutes au début ou à la fin d'un cours pour qu'ils et elles puissent répondre à l'enquête.

Les évaluations sont accessibles via la page d'accueil de moodle. Pour y accéder, les étudiant·es doivent :

Se connecter à moodle et rester sur la page d'accueil (tableau de bord, pas la page du cours). Cliquer sur la flèche en haut à droite de l'écran qui fera apparaître un bloc contenant la tuile intitulée "Évaluation approfondie" (veuillez noter que toutes les évaluations seront regroupées dans la tuile d'évaluation sur la page d'accueil de moodle, et non pas séparées dans chaque page moodle de cours). Les étudiant·es peuvent alors sélectionner votre cours et compléter le feedback.

Les étudiant·es peuvent également accéder aux évaluations de cours via l'application PocketCampus. Nous espérons que cela rendra les enquêtes plus accessibles et vous aidera ainsi à augmenter le taux de réponse.

Les enseignant·es pouvez accéder aux évaluations au même endroit sur la page d'accueil de moodle (Tableau de bord):

Accéder au taux de réponse pendant que l'évaluation est ouverte (Moodle - nouveau plugin). Accéder au rapport dès le 11 février 2025.

Si vous partagez les responsabilités d'enseignement pour ce cours, veuillez en informer vos collègues car, afin d'éviter que de nombreux enseignants reçoivent plusieurs courriels, seul un·e enseignant·e par cours a reçu cette notification.

In-depth evaluation of BIO 341
7 minutes

As you know, all courses receive an in-depth evaluation each semester. The in-depth evaluation survey for your course BIO-341_SA24/25 has just been opened to students and will remain available until 12.01.2025 23:59:00.

The report will be available to you once the exam period has ended, on 11 February 2025.

The student feedback will be more useful to you if the response rate is higher and so we recommend that, if possible, you dedicate 5 minutes at the beginning or end of a class for students to complete the survey.

The evaluations are accessible via the moodle. To access them, students have to:

Log onto moodle and stay on the moodle home page (dashboard, not the course page). Click on the arrow to the top right of the screen which will reveal a block that contains the entitled "In-depth evaluation" tile (please note: all evaluations will be together in the evaluation tile on the moodle home page, and not separate in each course moodle page). Students can then select your course and complete the feedback.

Students will also be able to access the course evaluations via the EPFL Campus App. We hope this will make the surveys more accessible and so help you to increase the response rate.

Teachers can access evaluations in the same location on the moodle home page. You will be able to:

Access the response rate while the evaluation is open (Moodle - nouveau plugin). Access the report from 11 February 2025.

In-depth evaluation of BIO 341
7 minutes

Topics for the exam

1D and 2D dynamical systems (nullclines, fixed points, type & stability, eigenvectors/stable/unstable manifold, draw a phase portrait)

Population models

Bifurcations, what is hysteresis?

Entrained oscillator/Kuramoto model

Fractal dimension of a set

Note. There will be no long derivations or coordinate transformations.

One-dimensional dynamical systems (autonomous)

$$dx/dt = f(x)$$

Graph 1 shows the vector field dx/dt against the coordinate x .

Fixed points (FP) are places where the vector field is zero $f(x^*) = 0$.

In a phase portrait, an FP has its stability indicated:

-  for stable
-  empty dot for unstable
-  semi-stable, the solid half on the stable side.

Linear stability analysis involves expanding the function $f(x)$ about a fixed point x^* and finding the sign of the first derivative, i.e., $df/dx(x^*)$. A FP is **unstable** if this is **positive**, and **stable** if it is **negative**. This means an FP is stable if the trajectory through it slopes down as x increases, and unstable if it slopes up. If the trajectory is horizontal at an FP, higher derivatives of the vector field must be consulted to determine stability.

Graph 2 shows the trajectories $x(t)$ as a function of time.

The slope of a trajectory at an initial point, x_0 , i.e., $t = 0$ is essential for drawing the correctly “shaped” curves $x(t)$. It requires evaluating dx/dt at $x = x_0$, and drawing the initial part of the curve with that slope. But this is just the value of the function at $x = x_0$.

Hysteresis can occur in a 1D system as a parameter changes.

This means that there is a change in the flow of the vector field as a parameter increases through a certain value (FP appears/disappears), but the inverse change doesn't happen at the same value of the parameter as it is decreased, but at a smaller value.

Main goal: relate Graph 1 to Graph 2 so you can draw trajectories knowing only dx/dt as a function of x without actually solving the equation.

Lecture 3 Gene expression model

$$dg/dt = s - r^*g + g^2 / (1 + g^2)$$



saturated growth
because of denominator

Case $s=0$:

No basal production, 1-3 FPs, $g^*=0$ always one of them.

Case $s>0$:

Again 1-3 FPs, but $g^*=0$ is not one.

Location of FPs depends on intersection of the functions:

$$f(g) = r g - s$$

$$h(g) = g^2 / (1 + g^2)$$

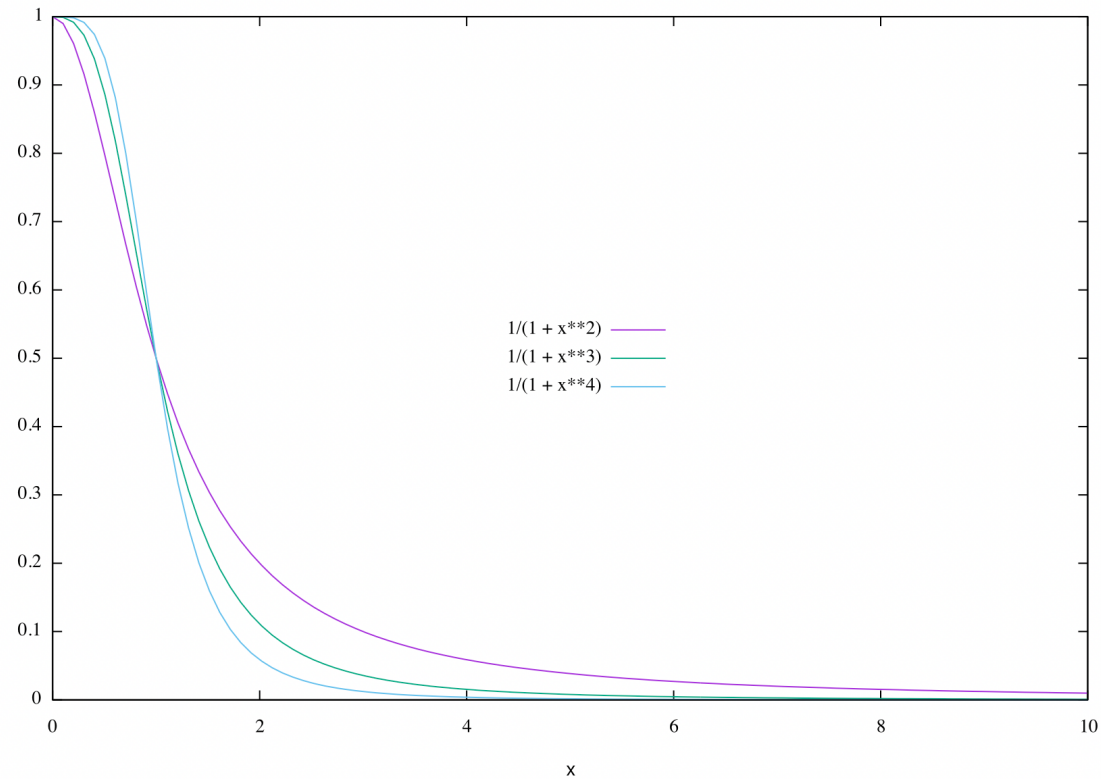
Hysteresis in r ; gene expression jumps from low g^* to high g^* and vice versa at different values of the degradation parameter r .

What do the following curves look like?

$$\frac{dx}{dt} = \frac{1}{1+x^2}$$

$$\frac{dx}{dt} = \frac{1}{1+x^3}$$

$$\frac{dx}{dt} = \frac{1}{1+x^4}$$



$$\frac{dx}{dt} = \frac{x^2}{1+x^2}$$

$$\frac{dx}{dt} = \frac{x^3}{1+x^3}$$

???

$$\frac{dx}{dt} = \frac{x^4}{1+x^4}$$

lecture 3

Summary of $S=0$ case

We have the following fixed points:

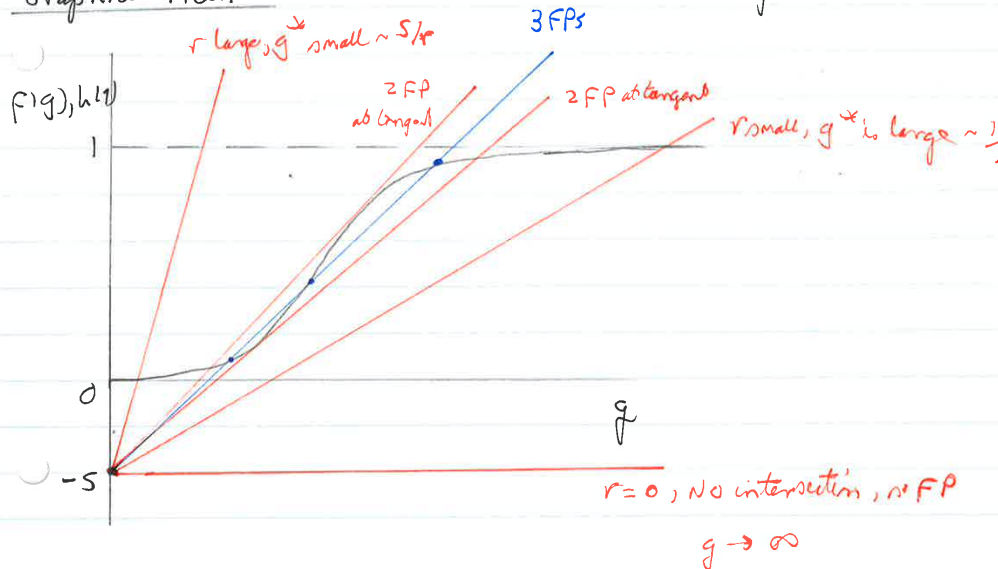
- $r=0$, only $g^*=0$ (g keeps increasing forever)
- $r < \frac{1}{2}$, $g^*=0$ and two more: $g^*=r$, $\frac{1}{1-r}-r$
- $r = \frac{1}{2}$, $g^*=0, 1$
- $r > \frac{1}{2}$, $g^*=0$ only

Consider the $S \neq 0$ case:

$$\dot{g} = S - rg + \frac{g^2}{1+g^2} = F(g) = -f(g) + 1$$

where $f(g) = rg - S$
 $h(g) = \frac{g^2}{1+g^2}$

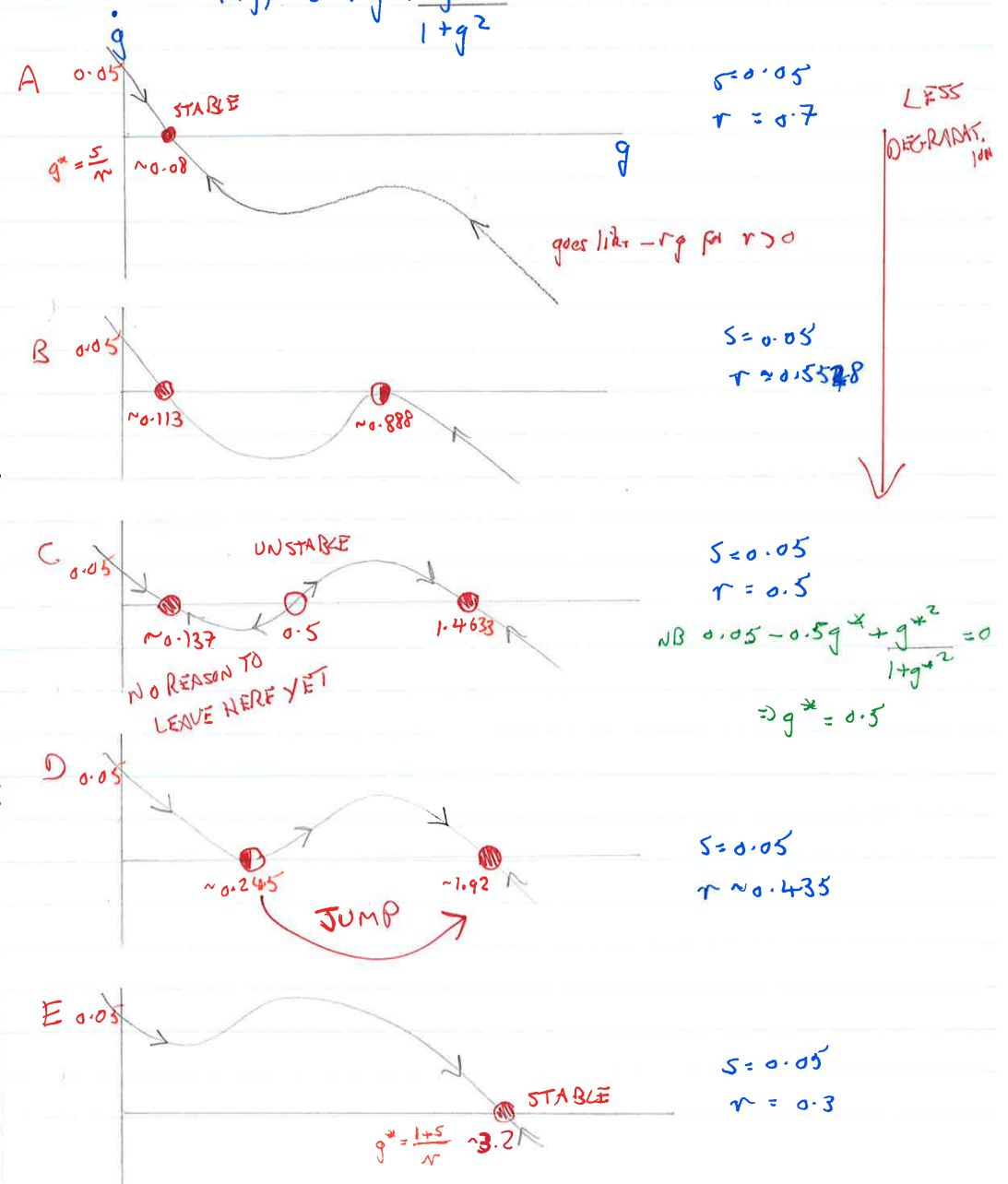
Graphical Method



BISTABILITY AND HYSTERESIS

86

$$F(g) = S - rg + \frac{g^2}{1+g^2}$$



Two-dimensional dynamical systems (autonomous)

$$dx/dt = f(x, y)$$

$$dy/dt = g(x, y)$$

Know the different terms that can occur (see lecture 6)

(exact names are less important, but knowing their effect is)

$dx/dt = a$ source term

$a x$ linear growth ($-a x$ linear degradation)

NB. linear refers to the term x appearing linearly in the ODE, but the solution is exponential growth; be clear what you mean if you describe this term.)

$ax(b - x)$ logistic growth (a = initial growth rate, b = carrying capacity)

$-xy$ competition

$+xy$ promotion or anti-competition

$x / (1 + x)$ saturated self-promotion (must go to a constant or zero as x goes to infinity)

$-xy / (1 + x)$ saturated competition (must go to a constant or zero as x goes to infinity)

The 2D **linear** system $d\mathbf{X}/dt = \mathbf{M} \mathbf{X}$ has one isolated fixed point at the origin that determines trajectories for the WHOLE phase portrait (if $\det \mathbf{M} \neq 0$).

The type of FP is determined by the trace and determinant of the matrix $\mathbf{M}$ only.

If $\det \mathbf{M} < 0$, it's a saddlepoint.

$\det \mathbf{M} = 0$, non-isolated FP.

If $\det \mathbf{M} > 0$ and ...

If $\text{Tr } \mathbf{M} < 0$, FP is stable; if $\text{Tr } \mathbf{M} > 0$, FP is unstable. In both cases:

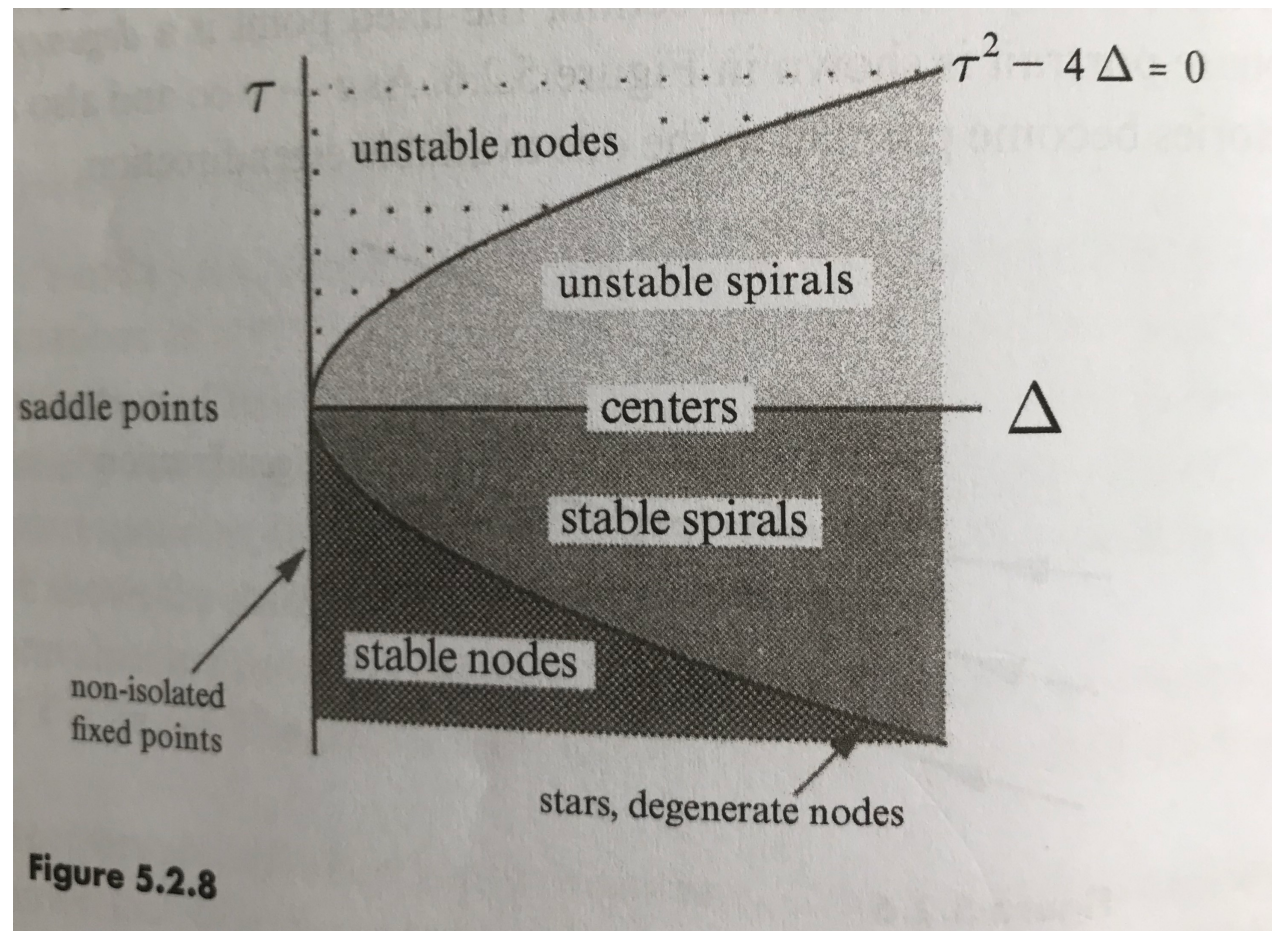
If $\tau^2 - 4\Delta < 0$, it's a spiral,

else if $\tau^2 - 4\Delta > 0$, it's a node,

else if $\tau^2 - 4\Delta = 0$, it's a star or degenerate node.

In all cases, the stability is given by the sign of $\text{Tr } \mathbf{M}$.

If $\det \mathbf{M} > 0$ and $\text{Tr } \mathbf{M} = 0$, it's a centre, i.e., circles/ellipses.



Note for completeness (see Strogatz, Ch. 6)

The type and stability of a fixed point are determined by the trace and determinant of J evaluated at the fixed point ONLY for **saddlepoints, nodes, and spirals**. The borderline cases — centres, stars, degenerate nodes, and non-isolated fixed points — require a non-linear analysis to determine their stability.

Population models in 1D and 2D

Be aware that population models usually have:

$$dN/dt = N f(N)$$

because this ensures that the origin is a fixed point (no individuals $\Rightarrow$ no growth). Hence the axes are nullclines, and don't forget them when checking for fixed points.

Population models only exist in the first quadrant ($X, Y \geq 0$).

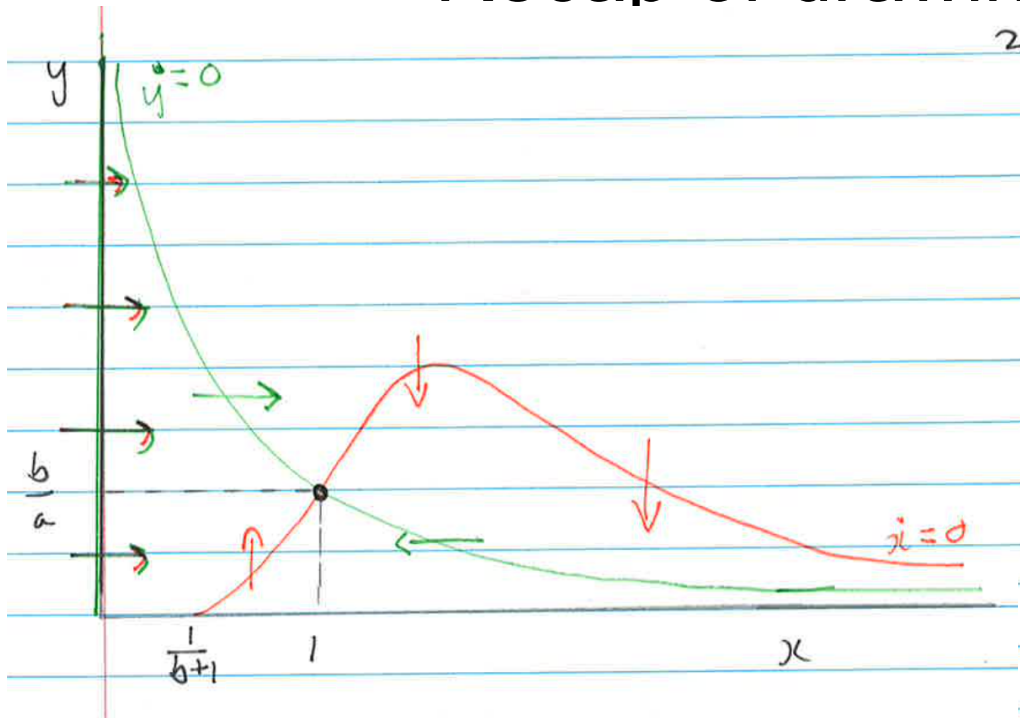
Lotka Volterra models (competing populations):

$$dx/dt = a x - b x y - c x^3$$

$$dy/dt = -e y + f x y$$

what are the terms here?

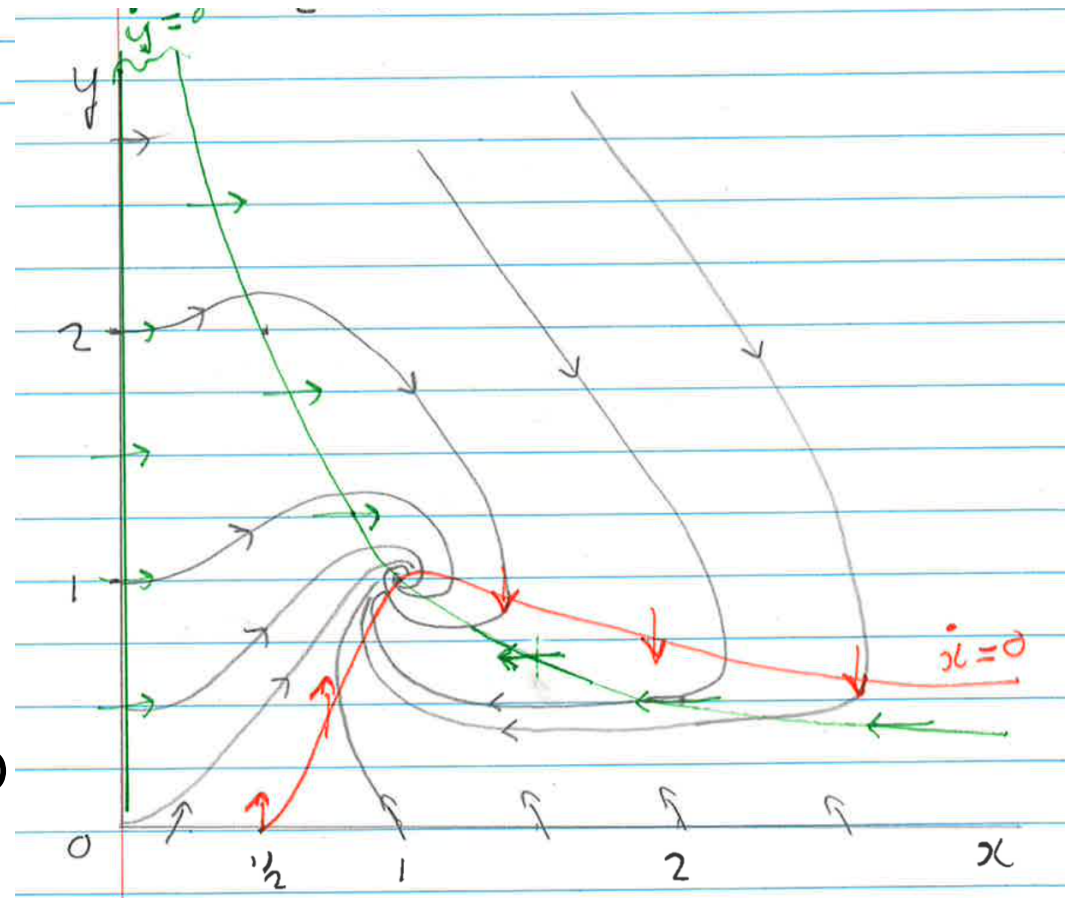
Recap of drawing a phase portrait

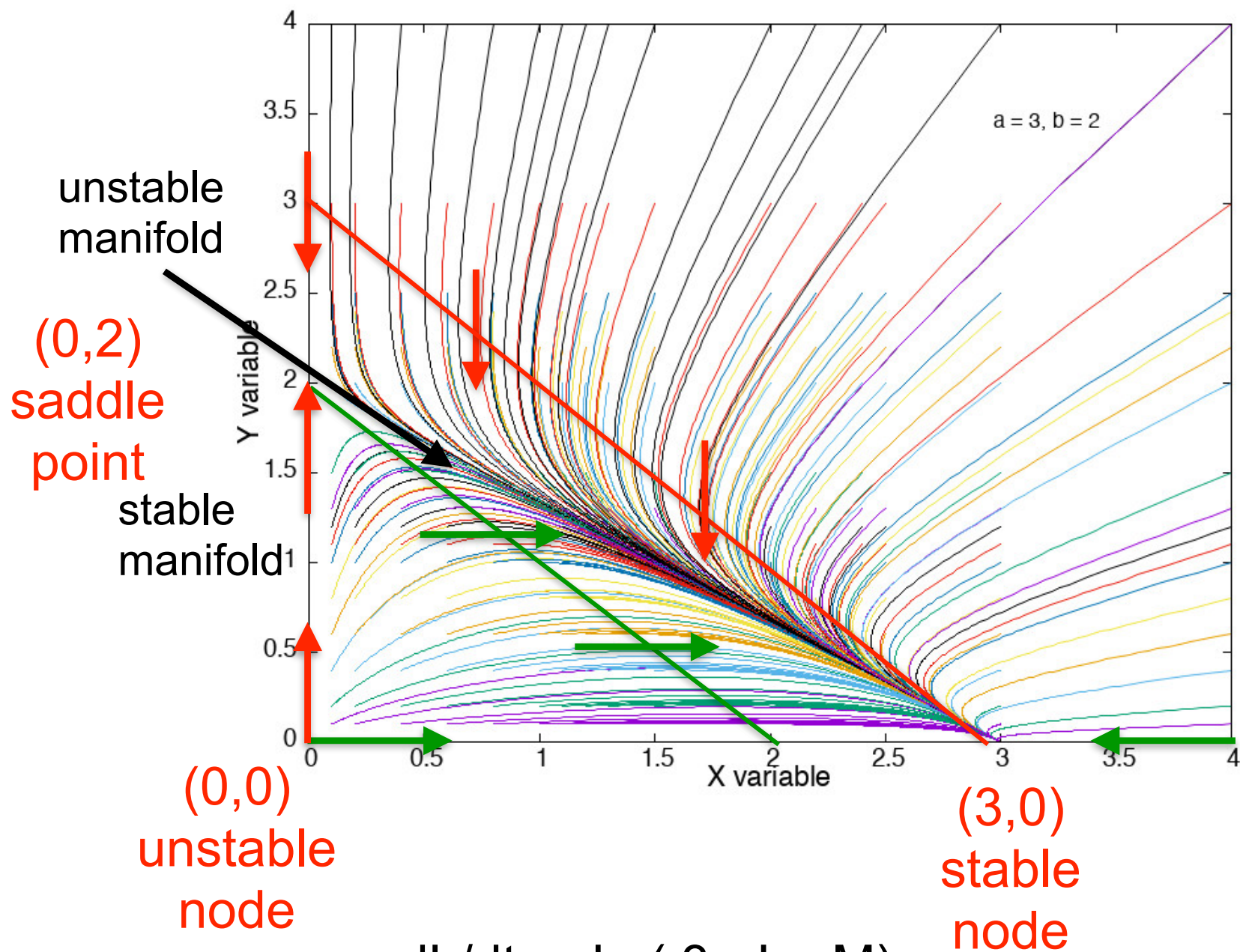


$$\frac{dx}{dt} = 1 - (b + 1)x - ax^2y$$

$$\frac{dy}{dt} = bx + ax^2y$$

- Check if 1st quadrant only
- Find nullclines (**axes!**), fixed point(s)
- Vector field on nullclines and axes
- Type/stability of FPs (esp. saddles)
- Vector field in different regions
- (esp. large x , y , near axes)
- Add trajectories with arrows smoothly crossing nullclines and NO intersections





Why unstable node
not saddlepoint?

$$\frac{dL}{dt} = L (3 - L - M)$$

$$\frac{dM}{dt} = M (2 - L - M)$$

what are the terms here?

Arrows indicate the direction of flow of the vector field.

Be able to draw/recognise how trajectories approach/leave stable/unstable nodes (slow and fast eigenvectors); meaning of stable and unstable manifolds of a saddlepoint.

Be able to draw/recognise the vector field in a phase portrait, and draw trajectories in the phase portrait that connect fixed points sensibly; know how to determine what trajectories do as they head off to infinity, i.e.,

$$dy/dx = dy/dt / dx/dt$$

Note. Trajectories must start/end on a fixed point, a boundary (typically the axes) or go to infinity.

Poincare Bendixson theorem (lecture 7)

Know the Poincare Bendixson theorem and the conditions for a limit cycle in a bounded region of the phase portrait.

A limit cycle is an isolated, closed trajectory. Limit cycles are periodic.

(NB. Centres are NOT limit cycles because they are not isolated, there are infinitely close trajectories that are also centres.)

Conditions for a limit cycle:

a stable (unstable) limit cycle exists inside a bounded region R of the phase portrait if there is a trapping region (bounded by a closed curve) along whose boundary the trajectories all pass inwards (outwards) and there is an unstable (stable) node or spiral in the trapping region.

Bifurcations in 1D and 2D (lectures 8, 9, 10)

Know the types of 1D bifurcation - Saddle-node, Transcritical, Pitchfork - super- and sub-critical; draw Graph 1 for these as the parameter changes.

Be able to draw/recognise how the fixed points/spirals/limit cycles appear/disappear as a parameter is varied in the gene expression problem (lecture 3) and a Hopf bifurcation (lecture 10).

Entrained oscillators (lecture 11)

An oscillator has an internal frequency $\omega = 2\pi / T$, where T is its period, and its state is represented by the phase angle $\theta(t)$:

$$d\theta(t)/dt = 2\pi t / T = \omega$$

An external stimulus is represented by another oscillator with a different frequency $\Omega = 2\pi / T_e$, where T_e is the period of the external stimulus. This is represented by the phase angle $\alpha(t)$:

$$d\alpha(t)/dt = 2\pi t / T_e = \Omega$$

We couple the external stimulus to the oscillator by a periodic function $f(\theta, \alpha)$ (Q. Why must it be periodic?)

$$d\theta(t)/dt = \omega + f(\theta, \alpha)$$

A simple case is: $f(\theta, \alpha) = K \sin(\alpha - \theta)$,

where $K > 0$ is the strength of the coupling, i.e., the coupling constant.

Note. $f(\theta, \alpha)$ must be periodic so $d\theta/dt$ is single valued.

If $\alpha > \theta$, i.e., the phase of the external stimulus is *ahead* of the oscillator, and the coupling “pulls” the oscillator with it, while if $\theta > \alpha$, then the coupling drags the oscillator *back* to it.

The coupled system can be written as

$$d\phi/dt = \mu - \sin(\phi)$$

and if $\mu < 1$, there are fixed points representing states where the oscillator is entrained to the external stimulus, i.e., moves at a fixed phase angle with it. If $\mu > 1$, the oscillator cannot follow the stimulus, and is said to be “drifting.”

Kuramoto model (lecture 12)

Given N oscillators all coupled all-to-all with the same coupling constant K , the equation for the phase of any one oscillator i is:

$$\frac{d\theta_i}{dt} = \omega_i + \frac{K}{N} \sum_{j=1}^N \sin(\theta_j - \theta_i)$$

We regard each oscillator as a unit vector centred on the origin whose tip is on the unit circle, and they all rotate with their own frequency and phase. The question is under what conditions do they all synchronize? i.e., have constant phase with respect to each other?

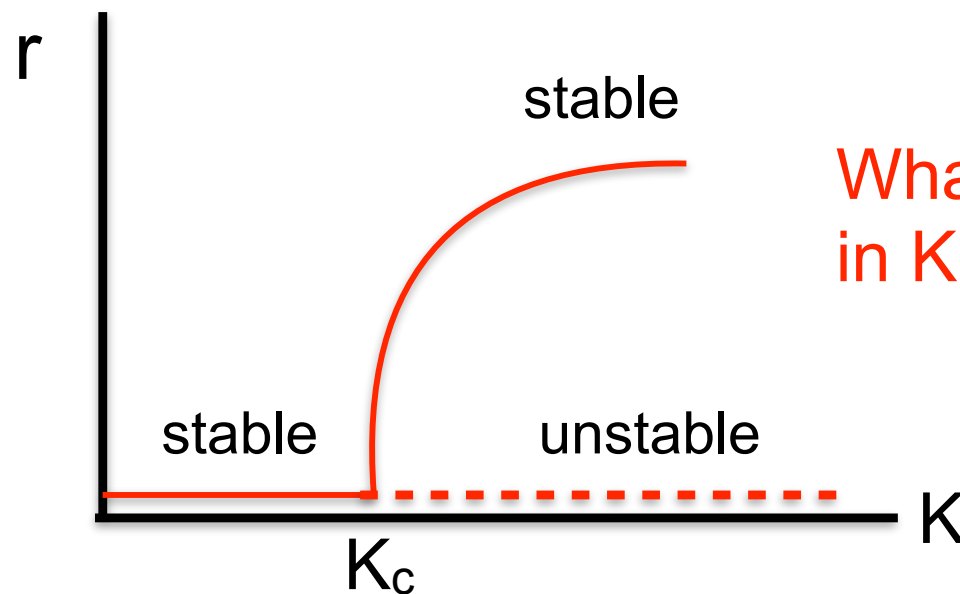
Let r = magnitude of the sum of all the phase vectors, and is a function of K and the distribution of the frequencies (taken here to be a Gaussian with mean ω_0 and standard deviation σ).

In steady-state $r = \text{constant}$ (depends on K not on θ_i), and each oscillator satisfies:

$$\frac{d\theta_i}{dt} = \omega_i - K r \sin(\theta_i)$$

i.e. all oscillators are decoupled and behave the same way. Comparing this to the entrained oscillator problem, there is a range of ω relative to r and K for which the oscillators are locked together, and a range where they drift.

Know the phase diagram in the r K plane, and the meaning of the various branches of the curves.



What does K_c depend on in Kuramoto model?



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