Modelling in Biology - deterministic dynamical systems

Biomedical Engineering Year 3 Notes

2020-2021

1 Linear models of order 1

1.1 A deterministic, continuous, linear model of order 1

$$\dot{x}(t) = \frac{dx(t)}{dt} = kx(t) \tag{1}$$

- For $k > 0$, Equation (1) is known as "Malthusian population growth" and k denotes the growth rate per cell
- The Malthusian population growth model is based on the assumption that the increase in population size during a (small) time interval is proportional to the population size. This is only a valid assumption if resources (such as nutrients or space) are available in unlimited quantity, i.e., that there is no competition for resources in the population.

1.2 Analytical solution of first order linear ODEs

Given $x(0) = x_0$, the solution of Equation (1) is

$$x(t) = x_0 e^{kt} \tag{2}$$

1.3 Numerical solutions of ODEs: the Euler algorithm

A discretised version of Equation (1) with discretisation step h is

$$\frac{x(t+h) - x(t)}{h} \approx kx(t) \longrightarrow x(t+h) \approx x(t) + hkx(t) \tag{3}$$

If h is small, then the recursive algorithm described by Equation (3) and initiated with $x(0) = x_0$ will agree well with the analytical solution $x(t) = x_0 e^{kt}$.

1.4 Analytical solution of first order linear difference equations

$x(t+h) = x(t) + hkx(t)$ can be looked at as a linear difference equation by taking $h = 1$. For ease of notation we define x_t as $x(t)$, and get

$$x_{t+1} = (1+k)x_t = \alpha x_t \tag{4}$$

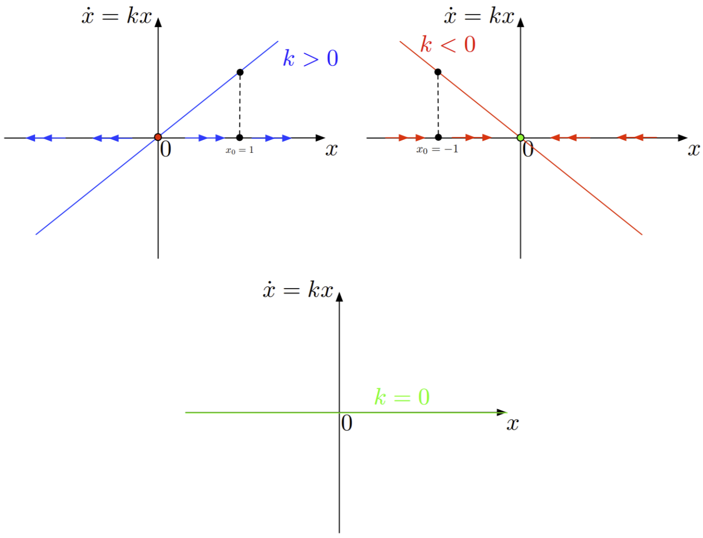
The non-zero solution of Equation (4) is

$$x_t = x_0 \alpha^t \tag{5}$$

Discrete-time models are useful to model processes which occur at specific (discrete) time instants. An example for which a discrete-time model can be useful is cell population growth.

1.5 Phase line analysis for a linear ODE of order 1

- The phase plane (a.k.a. phase space) is a representation that eliminates time as an explicit variable. Instead $\dot{x}$ is plotted against x.
- It is very useful for obtaining a qualitative understanding of the long-term or asymptotic behaviour of nonlinear ODE models (for which, typically, analytical solutions cannot be found).

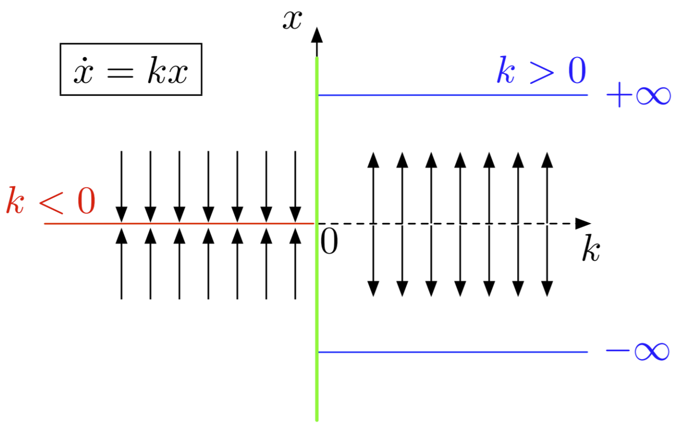


For the phase line analysis, we consider 3 possible cases for k: $k > 0$, $k < 0$ and $k = 0$.

- The $k < 0$ case has only one "unstable" fixed point $x^* = 0$. This is because $x = 0$, it stays at 0, however if perturbed either way, it will accelerate towards negative or positive infinity.
- The $k < 0$ has a single "asymptotically stable" fixed point $x^* = 0$. An asymptotically stable fixed point is both:
  - **Stable**: any slight perturbation from the fixed point will cause the solution to still remain in the vicinity of the fixed point.
  - **Attractive**: In the long-term, as $t \longrightarrow \infty$, the solution comes back to the fixed point.
- The $k = 0$ case ensures that $x = 0$, wherever you start.

1.6 Bifurcation diagram for a linear ODE of order 1

A **bifurcation diagram** shows how the long term / asymptotic behaviour of a system varies when a parameter is varied. In this case the parameter we can vary is k.



1.7 Stochastic differential equations (SDEs) of order 1

A stochastic version of the Malthusian growth model, known as the Langevin Equation is:

$$\frac{dx}{dt} = kx + \eta \tag{6}$$

Where η is a random variable that represents some uncertainties or stochastic effects perturbing the system.

In the absence of other knowledge about the statistics of the random variable η, η is generally assumed to have a Gaussian or normal probability distribution.

SDEs such as the Langevin Equation are typically solved numerically through discretisation using the Euler algorithm. The discretised version is:

$$x(t + \Delta t) = [1 + k\Delta t]x(t) + (\sigma\sqrt{\Delta t})\text{randn} \tag{7}$$

where randn is a function that provides a random number sampled from a Gaussian distribution of mean 0 and variance 1.

Each "run" of the simulation is called a "realisation" of the stochastic process.

2 Nonlinear ODE models of order 1

A general first order nonlinear ODE model is of the form $\dot{x} = f(x)$ where $x \in \mathbb{R}$ and f is a function from $\mathbb{R}$ to $\mathbb{R}$ as well as a "smooth" function. ($\mathbb{R}$ is the set of Real numbers, a function is smooth if it is continuously differentiable at lease 2 times).

Finding the analytical solution, $x(t, x_0)$, is in general no longer possible, unless a closed form solution can be obtained for $\int \frac{1}{f(x)} dx = \int dt$.

In general, the asymptotic stability analysis of nonlinear models of order 1 is performed using phase line and bifurcation diagrams.

2.1 Non-Malthusian population growth: the logistic equation

The non-Malthusian population growth model takes into account the "competition for resources". The net growth rate or reproduction rate per individual (or per cell) decreases as the population increases due to this competition for resources. The equation for Non-Malthusian population growth is:

$$\dot{x} = rx(1 - \frac{x}{k}) \tag{8}$$

Equation (8) is known as the Logistic equation, and k is called the "carrying capacity" of the environment.

The growth rate in Equation (8), $r(1 - \frac{x}{k})$, is non-constant, and decreases as the number of individuals in the population increases.

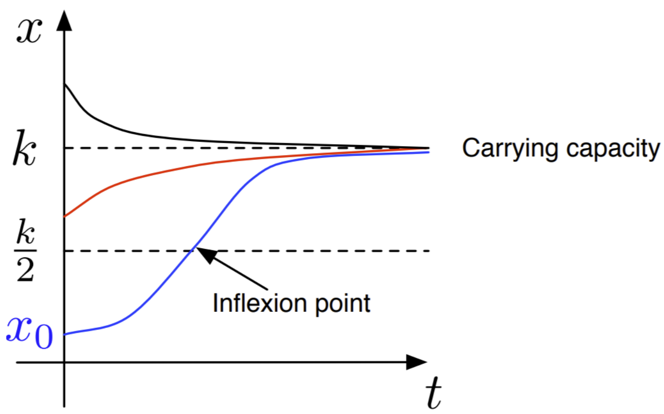
Equation (8) can also be written as $x = rx - \frac{rx^2}{k}$ where rx is the "growth rate" and $-\frac{rx^2}{k}$ is the "death rate".

2.2 Analytical solution of non-Malthusian population growth

In this particular case and rather exceptionally, a closed form solution to Equation (8) can be found:

$$x(t) = \frac{k}{1 + \frac{1}{C}e^{-rt}}, \; C = \frac{x_0}{k - x_0} \tag{9}$$

The solution indicates that x tends to k as time goes to infinity, which is why k is called the "carrying capacity". k represents the final population size that the resources present in the environment can sustainably carry in the long-term.



2.3 Stability analysis of the logistic equation

The fixed points are the points at which the derivative of x, $\dot{x}$, is equal to 0. Because $\dot{x} = f(x)$, we can say that a fixed point x^* must satisfy $f(x^*) = 0$.

- Equation (8) has 2 fixed points, $x^* = 0$ and $x^* = k$.
- $x^* = 0$ is an unstable fixed point

- $x^* = k$ is an asymptotically stable (stable and attractive) fixed point
- Between 0 and k, $\dot{x} > 0$ which means x is increasing.
- If x is bigger than k, $\dot{x} < 0$ which means x is decreasing.

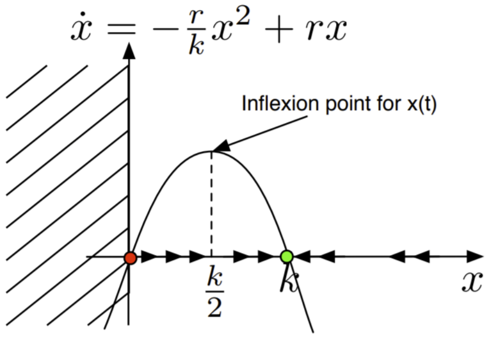


Figure 1: Phase plane of logistic equation

2.4 Stability analysis of general nonlinear ODE models of order 1

- Global stability analysis (only for models of order 1)
  - Find the fixed points $\{x^* : f(x^*) = 0\}$ and plot them on the phase line in the phase space $\dot{x}$ vs x.
  - Find the flow between the fixed points and indicate them on the phase line.
  - Conclude what the stability of the fixed point(s) is.
  - Find the long-term behaviour of the system, i.e., its attractors. Note that positive and negative infinity can be attractors. The long term behaviour is typically dependent on the initial conditions.
- Local/linear stability analysis (possible for all orders)
  - Find the fixed points.
  - Linearise the dynamics around each fixed point.
  - Study the stability of the corresponding linear systems (eig(A)).
  - Link together the local stability information around each fixed point to establish a complete picture of the attractors.

2.4.1 Linearising the dynamics around fixed points

- Consider a point x that is very closed to a fixed point x^*. This means we can express x as $x^* + \xi$ where ξ is very small
- Based on this we have $\frac{dx}{dt} = \frac{d\xi}{dt} = f(x^* + \xi)$
- We apply the Taylor Series Expansion, neglecting the terms of very small magnitude, to obtain $f(x^* + \xi) = f(x^*) + \frac{df}{dx}|_{x=x^*}\xi$
- However, by definition $f(x^*) = 0$, therefore

$$\frac{d\xi}{dt} \approx \left.\frac{df}{dx}\right|_{x=x^*} \xi \tag{10}$$

- Solving Equation (10) gives

$$\xi(t) \approx \xi_0 e^{\frac{df}{dx}|_{x=x^*} t} \tag{11}$$

- To perform the local stability analysis, we examine whether $\frac{df}{dx}|_{x=x^*}$, the derivative of f evaluated at the fixed point in question, is greater than or smaller than 0
  - If $\frac{df}{dx}|_{x=x^*} > 0$, this means that $\dot{\xi}\xi > 0$ and the magnitude of ξ tends to increase, meaning that x^* is an **unstable** fixed point.
  - If $\frac{df}{dx}|_{x=x^*} < 0$, this means that $\dot{\xi}\xi < 0$ and the magnitude of ξ tends to decrease, meaning that x^* is a **locally asymptotically stable** fixed point (locally stable and attractive).
- If $\frac{df}{dx}|_{x=x^*} = 0$, x^* is marginally stable and we cannot deduce the stability around that point using linear stability analysis. This is a consequence of the Hartman-Grobman Theorem (also called the linearisation theorem).

2.4.2 Linear stability analysis of the logistic equation

Differentiating Equation (8) gives $\frac{df}{dx} = r - \frac{2xr}{k}$. We know that the fixed points are $x = 0$ and $x = k$ so we just need to plug those values in:

- $\frac{df}{dx}|_{x=0} = r$, therefore as $r > 0$, the fixed point $x = 0$ is unstable
- $\frac{df}{dx}|_{x=k} = -r$, therefore as $-r < 0$, the fixed point $x = k$ is locally asymptotically stable

2.5 Non-dimensionalisation (also called "renormalisation")

The goal of non-dimensionalisation is to reduce the number of parameters appearing in the equations. This is very useful as it enables you focus parameter-dependent analyses (such as parameter sensitivity analysis and bifurcation analysis) on a fewer number of parameters. Using non-dimensionalisation, the number of parameters can always be reduced to the total number of variables (dependent + independent).

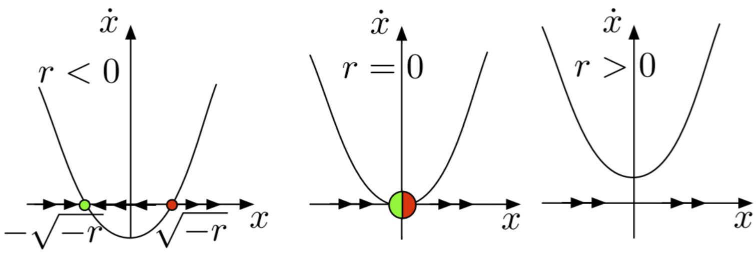
2.6 Bifurcations for nonlinear ODE models of order 1

A bifurcation occurs when a change in the parameter(s) of the model produces a qualitative (or "large") change in the long-term behaviour (of the attractors) of the system, for example:

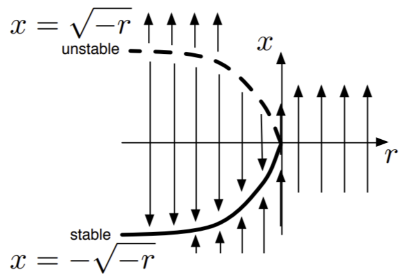
- The number of attractors (e.g., fixed points) changes
- The type of attractors changes (e.g., from fixed point to limit cycle)
- The stability of attractors (e.g., fixed points or limit cycles) changes

2.6.1 Saddle-node Bifurcation (also called Blue Sky Bifurcation)

- The saddle-node bifurcation is characterised by a **merging** and **subsequent disappearance** (or sudden creation depending how the parameter is varied) of **a stable and an unstable fixed point**.
- An example of a saddle node bifurcation is $\dot{x} = r + x^2$

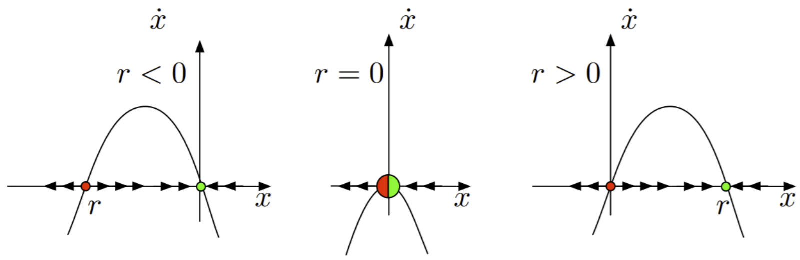


- When r is increased from negative to positive values, the two fixed points coalesce at $r = 0$ and then disappear for $r > 0$.
- The Saddle-node bifurcation diagram for $\dot{x} = r + x^2$ therefore looks like this:

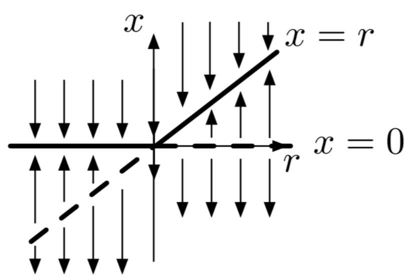


2.6.2 Transcritical Bifurcation

- The transcritical bifurcation is characterised by a **merging** and **subsequent stability reversal** of **a stable and an unstable fixed point**.
- An example of a saddle node bifurcation is $\dot{x} = x(r - x)$



- In this case, there are always two fixed points: one at $x = 0$ and another at $x = r$. At $r = 0$, there is a reversal in the stability of the fixed points
- The transcritical bifurcation diagram for $\dot{x} = x(r - x)$ therefore looks like this:

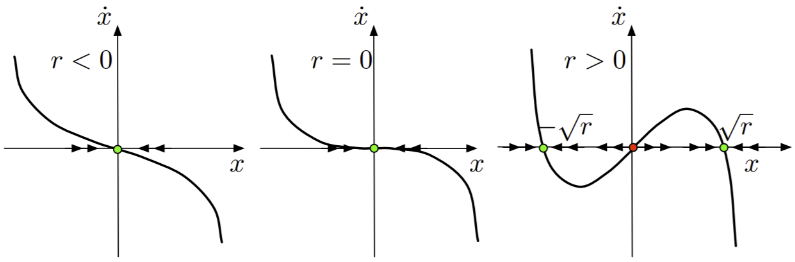


- This is the type of bifurcation we would observe for the logistic equation (8) if we considered k as a parameter that could also take negative values.

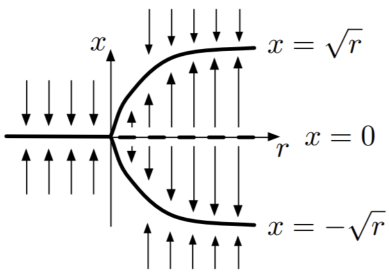
2.6.3 Pitchfork Bifurcation

- If, when changing the value of the parameter, **two new stable fixed points appear** while the **third fixed point is now unstable instead of stable**, the corresponding pitchfork bifurcation is said to be **supercritical**.

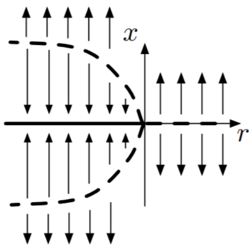
- On the contrary, if, when changing the value of the parameter, **two new unstable fixed points appear** while the **third fixed point is now stable instead of unstable**, the corresponding pitchfork bifurcation is said to be **subcritical**.
- An example of a supercritical pitchfork bifurcation is $\dot{x} = x(r - x^2)$



- In this case, there is always one fixed point at $x = 0$. Furthermore, if $r > 0$, there are 2 other fixed points at $x = \sqrt{r}$ and $x = \sqrt{-r}$.
- The (supercritical) pitchfork bifurcation diagram for $\dot{x} = x(r - x^2)$ therefore looks like this:



- An example of a subcritical pitchfork bifurcation is $\dot{x} = x(r + x^2)$
- The (subcritical) pitchfork bifurcation diagram for $\dot{x} = x(r - x^2)$ looks like this:



- The pitchfork bifurcation is common to systems that present symmetry. For example, the dynamics that we have considered here do not change under the change of variable $\tilde{x} = -x$. (Bifurcation diagram vertically symmetric).

3 Linear ODE models of order 2 and higher

The order of the model is defined as the number of dependent variables appearing in the ODE. For higher order models, it is convenient to express the state equation in the form

$$\dot{\boldsymbol{x}} = kA\boldsymbol{x} \tag{12}$$

where the dimension of $\boldsymbol{x}$, a vector, is the order of the model.

A change of variables is then used to diagonalise the matrix A.

3.1 Diagonalisation

Diagonalisation allows you to decouple the equations, and therefore to reduce the problem to finding the solution of 1st order linear ODEs (which we now know how to do). To diagonalise we:

1. Find the Eigenvalues, which are the solutions of $\det(A - \lambda I) = 0$
2. Find the normalised Eigenvectors, which are the solutions of $A\boldsymbol{v} = \lambda \boldsymbol{v}$ for each eigenvalue λ
3. For linear ODE models of order 2, the eigenvalues can also be easily found by noting the following properties: $\det(A) = \lambda_1\lambda_2$ and $\mathrm{trace}(A) = \lambda_1 + \lambda_2$. (The trace of a square matrix A is the sum of elements on the main diagonal (from the upper left to the lower right) of A)
4. From the eigenvectors of A, we construct a new matrix V having the eigenvectors of A as columns.
5. We then have $V^{-1}AV = \Lambda$ where Λ is a matrix with the corresponding eigenvalues as its diagonal entries and zeros everywhere else.
6. Using diagonalisation, we can therefore transform $\dot{\boldsymbol{x}} = kA\boldsymbol{x}$ into the form:
$$\frac{d\boldsymbol{x}}{dt} = k\Lambda\boldsymbol{x} \text{ where } \boldsymbol{x} = V^{-1}\boldsymbol{x} \tag{13}$$
7. Now we can solve for X_1, X_2, etc. separately. For example, for a second order system, we get something of the form:
$$\begin{pmatrix} \dot{X}_1 \\ \dot{X}_2 \end{pmatrix} = k \begin{pmatrix} \lambda_1 & 0 \\ 0 & \lambda_2 \end{pmatrix} \begin{pmatrix} X_1 \\ X_2 \end{pmatrix} \iff \begin{matrix} \dot{X}_1 = k\lambda_1 X_1 \\ \dot{X}_2 = k\lambda_2 X_2 \end{matrix} \implies \begin{matrix} X_1(t) = X_1(0)e^{k\lambda_1 t} \\ X_2(t) = X_2(0)e^{k\lambda_2 t} \end{matrix} \tag{14}$$
8. The final step is to transform back into the original coordinates using $\boldsymbol{x} = V\boldsymbol{x}$ (This means multiplying eigenvector 1 by X_1 , eigenvector 2 by X_2, etc.

3.2 General solution of linear ODE model of order 2

For a linear, second order ODE of the form shown in Equation (12), where all members of $\boldsymbol{x}$ are real numbers and A is diagonalisable, the solution is a linear combination of exponentials of the form $e^{\lambda_i t}$ where λ_i are the eigenvalues of A. Therefore, the general solution of a linear, second order ODE is of the form:

$$\boldsymbol{x}(t) = \boldsymbol{v}_1 X_1(0)e^{k\lambda_1 t} + \boldsymbol{v}_2 X_2(0)e^{k\lambda_2 t} = \mathbf{c}_1 e^{k\lambda_1 t} + \mathbf{c}_2 e^{k\lambda_2 t} \tag{15}$$

If $\lambda_\pm$ are complex conjugate numbers, i.e., $\lambda_\pm = \alpha \pm i\beta$ then the general solution is of the form

$$\boldsymbol{x}(t) = e^{\alpha t}(\mathbf{c}_+ e^{i\beta t} + \mathbf{c}_- e^{-i\beta t}) \tag{16}$$

A useful thing to bear in mind here is Euler's formula - namely $e^{\pm i\beta t} = \cos(\beta t) \pm \sin(\beta t)$

3.3 General solution for linear ODEs models of any order

The section above generalises to linear ODEs of any order. The solution is therefore of the form:

$$\boldsymbol{x}(t) = \sum_{i=1}^{n} \boldsymbol{v}_i X_i(0) e^{\lambda_i t} = \sum_{i=1}^{n} \mathbf{c}_i e^{\lambda_i t} \tag{17}$$

where λ_i are the eigenvalues of A and $\boldsymbol{v}_i$ are the corresponding eigenvectors of A.

4 Nonlinear ODE models of order 2

The general form of a nonlinear ODE model of order 2 is:

$$\dot{\boldsymbol{x}} = \boldsymbol{f}(\boldsymbol{x}) \Longleftrightarrow \begin{pmatrix} \dot{x_1} \\ \dot{x_2} \end{pmatrix} = \begin{pmatrix} f_1(x_1, x_2) \\ f_2(x_1, x_2) \end{pmatrix} \tag{18}$$

where all elements of $\boldsymbol{x}$ are real numbers, $\boldsymbol{f}$ is a function from $\mathbb{R}^2$ to $\mathbb{R}^2$ and $\boldsymbol{f}$ is a smooth function.

4.1 Stability analysis of nonlinear ODE models of order 2

Global stability analysis for models of order ≥ 2 is difficult seeing as the motion of the system is no longer in 1D and it may not be obvious where the trajectories will go from a given initial condition. Instead we rely on local stability analysis:

- Find the set of fixed points - these are the points $\boldsymbol{x}^*$ for which $\boldsymbol{f}(\boldsymbol{x}^*) = \mathbf{0}$.
- Linearise the dynamics around each fixed point.
- Study the stability of the corresponding linear systems.
- Draw the local flows around each fixed point.
- Try to link together the local stability information around each fixed point to establish a global picture of the attractors in the state space. Two important properties of autonomous, time-invariant, ODE models are important here:
  - **Nullclines**: these are the curves in the phase plane which correspond to individual first derivatives being equal to 0 ($\dot{x}_1 = 0$, for example). This is equivalent to the curves $f_1(x_1, x_2) = 0$, $f_2(x_1, x_2) = 0$, etc.
    * The fixed points are located at the intersection of the nullclines
    * By definition, the vector field on a nullcline always has one of its components equal to 0. This means that on a nullcline, the vector field flow can only be either horizontal or vertical (depending on which component of the vector field is equal to 0).
  - **Trajectories in the phase plane / space cannot cross**. This basically corresponds to the idea that, for these types of systems, you cannot have different pasts that lead to the same future without this future being a fixed point, or, said differently, that you cannot have different futures (or trajectories) starting from the same state (or point in the state space). This non-crossing property makes it sometimes easier to build a global picture of the attractors and their corresponding basins of attraction for models of order 2. This property is however less useful for models of order 3 or higher.

4.2 Linearisation of nonlinear ODE models of order 2

First we need to find the fixed points such that $\boldsymbol{f}(\boldsymbol{x}^*) = \boldsymbol{0}$. This is solving a system of algebraic equations

$$\begin{aligned} f_1(x_1^*, x_2^*) = 0 \\ f_2(x_1^*, x_2^*) = 0 \end{aligned} \tag{19}$$

To do this one can use MATLAB and the fsolve function. To find multiple zeros, you must initialise fsolve with various different initial guesses.

After the fixed points have been found, we linearise the dynamics around each fixed point. Using the taylor series expansion and neglecting small terms, it can be found that when considering $\dot{\boldsymbol{x}} = \boldsymbol{f}(\boldsymbol{x})$ with $\boldsymbol{x} = \boldsymbol{x}^* + \boldsymbol{\xi}$, we obtain:

$$\dot{\boldsymbol{\xi}} = J(\boldsymbol{x}^*)\boldsymbol{\xi} \tag{20}$$

where $J(\boldsymbol{x}^*)$ is the Jacobian matrix evaluated at fixed point $J(\boldsymbol{x}^*)$.

The Jacobian matrix is a constant matrix whose (i, j) element is given by:

$$J_{(i,j)}(\boldsymbol{x}^*) = \left.\frac{\partial f_i(\boldsymbol{x})}{\partial x_j}\right|_{\boldsymbol{x}=\boldsymbol{x}^*} \tag{21}$$

Finally we study the stability of (20) by diagonalising $J(\boldsymbol{x}^*)$, i.e. $\tilde{\boldsymbol{\xi}} = V^{-1}\boldsymbol{\xi}$

An important result (the Hartman-Grobman theorem) justifies the study of linearisations. It states that solutions of the nonlinear system $\dot{\boldsymbol{x}} = \boldsymbol{f}(\boldsymbol{x})$ in vicinity of the steady state $\boldsymbol{x}^*$ look "qualitatively" like the solutions of the linearised equation $\dot{\boldsymbol{\xi}} = J(\boldsymbol{x}^*)\boldsymbol{\xi}$ do in the vicinity of $\boldsymbol{\xi} = \boldsymbol{0}$.

4.2.1 Diagonalisation of the Jacobian for ODE models of order 2

The eigenvalues of a 2×2 matrix can be found from the equation:

$$\lambda_\pm = \frac{\tau \pm \sqrt{\tau^2 - 4\Delta}}{2} \tag{22}$$

where Δ is the determinant of the matrix and τ is the trace of the matrix.

Diagonalising $J(\boldsymbol{x}^*)$ gives us a general solution of the form:

$$\boldsymbol{\xi}(t) = \boldsymbol{c}_+ e^{\lambda^+ t} + \boldsymbol{c}_- e^{\lambda^- t} \tag{23}$$

where $\boldsymbol{c}_\pm$ are the eigenvectors.

See section 3.1 for why this is the case.

4.3 Local stability analysis for ODE models of order 2

Given a 2D Jacobian matrix evaluated at a fixed point $\boldsymbol{x}^*$, there are 6 possible options of the local behavior, which is determined by the signs of Δ, τ and $\tau^2 - 4\Delta$:

1. $\Delta > 0$ **and** $\tau > 0$ **and** $\tau^2 - 4\Delta > 0$
    - This means both eigenvalues are greater than 0
    - Exponential growth in both directions
    - "Repelling or unstable node"
2. $\Delta > 0$ **and** $\tau > 0$ **and** $\tau^2 - 4\Delta < 0$
    - This means the two eigenvalues are complex conjugates with positive real parts
    - "Unstable spiral"
3. $\Delta > 0$ **and** $\tau < 0$ **and** $\tau^2 - 4\Delta > 0$
    - This means both eigenvalues are smaller than 0
    - Exponential decay in both directions
    - "Attracting or stable node"
4. $\Delta > 0$ **and** $\tau < 0$ **and** $\tau^2 - 4\Delta < 0$
    - This means the two eigenvalues are complex conjugates with negative real parts
    - "Stable spiral"
5. $\Delta > 0$ **and** $\tau = 0$
    - This means both eigenvalues are purely imaginary
    - "Center"
6. $\Delta < 0$
    - This means one eigenvalue is smaller than 0 and the other is greater than 0
    - Exponential decay in one direction and exponential growth in the other
    - "Saddle point"

Fixed point is stable if all the eigenvalues of the Jacobian evaluated at the fixed point have negative real parts.

Once you have a local picture around all the fixed points, the global behaviour of a system of order 2 can be obtained by remembering that for models of the form $\dot{\boldsymbol{x}} = \boldsymbol{f}(\boldsymbol{x})$ trajectories do not cross. This non-crossing property makes it sometimes easier to build a global picture of the attractors and their corresponding basins of attraction for models of order 2.

4.4 Periodic behaviour and limit cycles

4.4.1 Linear oscillations and their limitations

In the case of linear ODE models of order 2, periodic oscillations can only be obtained if the system has a fixed point which is a center. Linear ODE models of order 2 with eigenvalues that are purely imaginary lead to ellipsoidal trajectories in the phase plane.

Oscillations are often useful in biological systems, however linear or "harmonic" oscillations have 2 serious limitations:

- They are fragile and non-robust to small pertubations in the model
- The oscillation characteristics (amplitude and phase) depend on the initial condition

4.4.2 Limit cycles

Limit cycles can only occur in nonlinear ODEs. A stable limit cycle is a periodic trajectory which attracts other solutions to it (at least those starting close to the limit cycle). Stable, attractive limit cycles are robust in ways that linear periodic solutions are not. In biology, periodic oscillations are typically the result of limit cycles.

- If a (small) perturbation moves the state to a different initial state away from the limit cycle, the system will return to the limit cycle by itself. In particular, if, no matter where we start, we end up on the limit cycle, then the limit cycle is a global attractor of our system. On the contrary, if the limit cycle is only attracting solutions starting in a particular region of the phase plane around it, then it is a local attractor and the corresponding region is called the basin of attraction.
- If the dynamics change a little, a limit cycle will still exist, close to the original one.

4.4.3 Hopf Bifurcation

The signature of a Hopf bifurcation is the emergence, when a parameter is varied, of a limit cycle with increasing amplitude.

This typically happens when at the critical bifurcation value, two complex conjugate eigenvalues of the Jacobian cross the imaginary axis (i.e., at the critical bifurcation value, two eigenvalues of J are purely imaginary). Note that this property of the eigenvalues of J is not enough to ensure the emergence of a limit cycle and that limit cycles can only occur for nonlinear systems.

4.4.4 Local (linear) and global stability are not equivalent for nonlinear ODE models of order 2 and higher

In particular, the stability of a fixed point in a nonlinear system can be deduced from the local stability analysis of the system linearised around this fixed only if this point is not a center (the precise formulation of this statement is known as the Hartman-Grobman theorem).

4.5 The Poincaré-Bendixson Theorem

For an ODE model of order 2, if you are able to find a region in the phase plane which does not contain any fixed point and is attractive, then this region must contain a limit cycle.

5 Nonlinear ODE models of order 3 and higher

ODE models of order 3 and higher can exhibit the same behaviour as those of order 2, with the additional options of:

- quasi-periodicity
- deterministic chaos