Mathematical modelling in biology

Giacomo Fantoni
telegram: @GiacomoFantoni

Github: https://github.com/giacThePhantom/mathematical-modelling-in-biology

October 24, 2022

Contents

Chapter 1

Introduction to ordinary differential equations

1.1 General concepts and methods

1.1.1 First order differential equations

A first order differential equation is written in normal form as:

$$y'(t) = f(t, y(t))$$

Where f is a function of variables t and y.

1.1.1.1 Autonomous differential equations

In the case that f does not depend on the variable t the equation is said to be autonomous: the law that regulates how $y(t)$ changes does not depend on time.

1.1.1.2 Solution of a differential equation

The solution of a differential equation if a function $y(t)$. To check whether $y(t)$ is a solution it is sufficient to compute its derivative and check that it is equal to the right hand side of the equation. So a solution if a function $y : I \to \mathbb{R}$ where I is an interval of $\mathbb{R}$ sich that $y'(t) = f(t, y(y)) \forall t \in I$.

1.1.1.3 Cauchy problems

A differential equation has infinite solutions as a function has infinite primitives. In order to predict the future evolution of a quantity it is necessary to know, besides the law regulating its dynamics or differential equation, an initial condition. An initial value problem or Cauchy problem is constituted by a differential equation and an initial condition:

$$\begin{cases} y'(t) = f(t, y(t)) \\ y(t_0) = y_0 \end{cases}$$

A solution to an initial value problem is a function defined on an interval I that contains the point t_0 such that for every $t \in I, y'(t) = f(t, y(t)))$ and also it is true that $y(t_0) = y_0$.

1.1.2 Direction fields

It is usually difficult or impossible to find exact solutions of differential equations. Because of this it is necessary to settle for something less complete. Direction fields allow to perform a graphical study of the qualitative behaviour of the solutions. The idea sit that according to the equation $y' = f(t, y)$ if a solution satisfies $y(t_0) = y_0$, the slope of the graph of $y(t)$ calculated at t_0, which is by definition $y'(t_0)$ must be equal to $f(t_0, y_0)$. Consequently, if in every (t_0, y_0) a small segment of slop $f(t_0, y_0)$ is traced the slope of a solution that goes through that point is indicated.

1.1.2.1 Draying a direction field

Many point $(\bar{t}, \bar{y})$ in a Cartesian plane are chosen an in each of them a small segment of slope $f(\bar{t}, \bar{y})$ are drawn. In this way the field of direction of $y' = f(t, y)$ can be built. Then a solution can be drawn making sure it is at all point tangent to the direction field.

1.1.2.2 Autonomous equations

Autonomous equations are a class of differential equations in which the right hand side does not depend on t:

$$y' = g(y)$$

This means that the law that regulates the dynamics of the y variable does not change over time. In particular if $y(t)$ is a solution, also $y(t - t_0)$ is a solution for all t_0. Graphically a solution can be moved horizontally and reach another one. Considering direction fields, each column in it will be equal to all the others, so it is sufficient to draw them at a given t and repeat them for all the values of t.

1.1.3 Equilibria

Given the autonomous differential equation $y' = f(y(t))$ the points $\bar{y}$ such that $f(\bar{y}) = 0$ are said to be equilibria because if $y(0) = \bar{y}$ then $y(t) = \bar{y}$ for every t. Since solutions cannot cross each other if $f(y_0) > 0$ then $f(y(t)) > 0$ for every t and then $y'(t) = f(y(t)) > 0$ or $y(t)$ is an increasing function. The same happens in the case of $f(y_0) < 0$.

1.2 Solution through separation of variables

The separation of variables is a technique that allows to find an explicit expression for the exact solutions of a class of equations.

1.2.1 Equations in which the right hand-side does not depend on y

In the case of an equation where the right-had side does not depend on y, it can be written as:

$$y' = f(t)$$

In this case the derivative of $y(t)$ is explicitly assigend. Solutions are all the primitives of f, so:

$$y(t) = \int f(t)dt$$

1.2.2 Separable equations

Separable equations are equations of the form:

$$y' = f(t)g(y)$$

They can be solved through the following steps:

1. The derivative y' is written using the Leibniz notation:

$$\frac{dy}{dt} = f(t)g(y)$$

2. Then dt gets multiplied as if it were a number:

$$\frac{dy}{g(y)} = f(t)dt$$

3. The integral is then applied to each of the members:

$$\int \frac{dy}{g(y)} = \int f(t)dt$$

4. Then the last equality is interrogated: a primitive $H(y)$ of $\frac{1}{g(y)}$ and $F(t)$ of $f(t)$ are chosen, such that for each t:

$$H(y(t)) = F(t) + C$$

   Is true, where C is a constant and $y(t)$ is the value of the solution at time t.

1.2.2.1 Theorem

Consider the equation $y' = f(t)g(y)$. Let $F(t)$ be a primitive of f: $F'(t) = f(t)$ and $H(y)$ a primitive of $\frac{1}{g}$, $H'(y) = \frac{1}{g(y)}$. Then:

- If $y(t)$ is a solution of $y' = f(t)g(y)$ such that $g(y(t)) \neq 0$ then there exists a constant C such that $H(y(t)) = F(t) + C$ for each t.
- If $y(t)$ satisfies $H(y(t)) = F(t) + C$ and $g(y(t)) \neq 0$ for each t or, in other words, $H(y(t)) - F(t)$ is constant, then $y(t)$ is a solution of $y' = f(t)g(y)$.

1.2.3 Linear equations

A linear differential equation is an equation in which the second member is linearly dependent on y, so that it has form:

$$y' = a(t)y + b(t)$$

1.2.3.1 Type of linear equation

- $b(t) = 0$: homogeneous.
- $b(t) \neq 0$: non-homogeneous.
- $a(t) \equiv a \wedge b(t) \equiv b$: autonomous.
- $a(t) \equiv a \wedge b(t) \equiv$ *any*: constant coefficients.

1.2.3.2 Solution of linear equations

Autonomous and homogeneous linear equations can be solved by separating variables if and only if a primitive of $a(t)$ is found following the same procedure described above. Non-homogeneous linear equations can be solved creating a new variable equal to $y(t)$ over the solution of the corresponding homogeneous equation.

1.2.4 Separable equations that cannot be solved

To be able to explicitly write the solutions of a differential equation with the method of separating variables, after making sure that the equation can be written in $y' = f(t)g(y)$. First the primitives $\int \frac{dy}{g(y)}$ and $\int f(t)dt$ need to be computed and this is not always possible. Once this is done, the solution of the equation satisfy $H(y(t)) = F(t) + C$. So, in order to be able to explicitly write the solutions $y(t)$ it must be isolable in that expression: H must be invertible.

1.3 Systems of differential equations

A system of two autonomous differential equation can be written as:

$$\begin{cases} x'(t) = f(x(t), y(t)) \\ y'(t) = g(x(t), y(t)) \end{cases}$$

1.3.1 Vector field and isoclines

An isocline is a set of point where one of the two derivatives is equal to zero. In general:

$$\{(x, y) : f(x, y) = 0\} \qquad \wedge \qquad \{(x, y) : g(x, y) = 0\}$$

After having found the isoclines the regions where the derivatives of x are y are positive or negative:

$$\{(x, y) : f(x, y) > 0\}\ \{(x, y) : f(x, y) < 0\}\ \{(x, y) : g(x, y) > 0\}\ \{(x, y) : g(x, y) < 0\}$$

It can be noted how these regions will be divided by the isoclines. At the intersections of the isoclines there are the equilibria.

1.4 Equilibria of differential equations and their stability

An equilibrium for an autonomous differential equation $y'(t) = f(y(t))$ is a point $\bar{y}$ such that $f(\bar{y}) = 0$. In particular:

- $f(y) > 0$ for $y > \bar{y}$ and $f(y) < 0$ for $y < \bar{y}$ $\bar{y}$ is repulsive: the solutions that start near $\bar{y}$ go away from it.
- $f(y) < 0$ for $y > \bar{y}$ and $f(y) > 0$ for $y < \bar{y}$ $\bar{y}$ is attractive: the solutions that start near $\bar{y}$ tend to it.

1.4.1 Stability

An equilibrium $\bar{y}$ is stable if for each $\epsilon > 0$ there exists a neighbourhood U of $\bar{y}$ such that if the starting point y_0 is in U, the distance between $y(t; y_)$ (the solution that starts from y_0 and $\bar{y}$ is below ϵ for every $t > 0$. In other words an equilibrium is stable if solutions remain arbitrarily close to $\bar{y}$ when the starting point y_0 is close enough.

1.4.2 Asympotical stability

An equilibrium $\bar{y}$ is asymptotically stable if it is stable and for each y_0 close enough to $\bar{y}$:

$$\lim_{t\to\infty} y(t, y_0) = \bar{y}$$

An asymptotically stable equilibrium is stable and attracting.

1.4.3 Unstability

An equilibrium is said to be unstable if it is not stable: a value η such that $\forall\epsilon > 0$ there exists y_0 whose distance from $\bar{y}$ is below ϵ and such that the solution $y(t)$ starting from y_0 at some time will be at a distance larger than η from $\bar{y}$.

1.4.4 Condition of stability

Given an equilibrium $\bar{y}$ of the single equation $y' = f(y)$:

- If $f'(\bar{y}) < 0$, then $\bar{y}$ is asymptotically stable.
- If $f'(\bar{y}) > 0$, then $\bar{y}$ is unstable.

This follow from the discussion on the sign of f or can be proven, allowing it to be extended to systems of equations through linearization.

1.4.4.1 Proof

Consider $u(t) = y(t) - \bar{y}$ the deviation from the equilibrium. A function can be approximated near a $\bar{y}$ with its tangent line in $\bar{y}$:

$$f(y) = f(\bar{y}) + f(\bar{y})(y - \bar{y}) + E(y) \approx a(y - \bar{y})$$

Where $a = f'(\bar{y}) \wedge f(\bar{y}) = 0$ and $E(y)$ is the error arising from using the tangent line, which is negligible when $|y - \bar{y}|$ is small. Then:

$$u'(t) = y'(t) = f(y(t)) \approx a(y(t) - \bar{y}) = au(t)$$

$u(t)$ satisfies assuming that $|u(t)|$ is close to 0 solving a simple linear equation:

$$u(t) = u(0)e^{at} = (y_0 - \bar{y})e^{at}$$

If $|y_0 - \bar{y}|$ is small and $a < 0$, $|u(t)|$ remains small for all $t > 0$ and satisfies $\lim_{t\to\infty} u(t) = 0$. So if $a < 0$, $\bar{y}$ is stable. If $a > 0$, although $|y_0 - \bar{y}|$ is small, at some point $|u(t)|$ becomes big, so $\bar{y}$ is unstable and the linear approximation cannot be valid for all $t > 0$ and the non-linear equation must be considered.

1.4.5 Linearized stability for systems of differential equations

An equilibrium for the system written in matrix form is:

$$\vec{y}'(t) = \vec{f}(\vec{y}(t))$$

To generalize the idea of linearization the deviation is considered:

$$v(t) = \begin{pmatrix} x(t) - \bar{x} \\ y(t) - \bar{y} \end{pmatrix} \; satisfying \; v'(t) = \begin{pmatrix} f(x(t), y(t)) \\ g(x(t), y(t)) \end{pmatrix}$$

The vector needs to be approximated to the right hand side. To do so the Jacobian matrix of $\vec{f}$ is built:

$$A = \begin{pmatrix} \frac{\partial f_1}{\partial y_1}(\bar{y}) & \frac{\partial f_1}{\partial y_2}(\bar{y}) & \cdots & \frac{\partial f_1}{\partial y_n}(\bar{y}) \\ \frac{\partial f_2}{\partial y_1}(\bar{y}) & \frac{\partial f_2}{\partial y_2}(\bar{y}) & \cdots & \frac{\partial f_2}{\partial y_n}(\bar{y}) \\ \vdots & \vdots & \cdots & \vdots \\ \frac{\partial f_n}{\partial y_1}(\bar{y}) & \frac{\partial f_n}{\partial y_2}(\bar{y}) & \cdots & \frac{\partial f_n}{\partial y_n}(\bar{y}) \end{pmatrix}$$

It can be shown that:

$$(f(y(t))) \sim f(\bar{y}) + A(y(t) - \bar{y}) = Av(t)$$

Higher order terms are neglected as the deviation $v(t)$ is assumed to be small. Ultimately the linearized equation is obtained:

$$v'(t) = Av(t)$$

In order to understand the stability of $\bar{y}$ the behaviour of the solutions of $v'(t) = Av(t)$ where A is the Jacobian matrix of f at $\bar{y}$ need to be analysed.

1.4.6 Linear systems

The analysis of the linear case is important because it can give a full description of the solutions or because in the nonlinear cases, local analysis in a neighbourhood of an equilibrium point resorts on linearisation to draw conditions for stability. The problem to consider is:

$$\vec{Y}'(t) = A\vec{Y}(t) \qquad \vec{Y}(0) = \vec{Y}_0$$

Where A is an $n \times n$ matrix. In such a case the origin $\vec{O}$ is an equilibrium and the solution can be expressed through:

$$e^{tA} = \sum_{k=0}^{\infty} \frac{t^k}{k!} A^k \qquad as\; \vec{Y}(t) = e^{tA}\vec{Y}_0$$

Chapter 2

Biological models based on differential equations

2.1 The bathtub

Let $Q(t)$ the quantity of a substance in the bathtub, then:

$$Q'(t) = I(t) - O(t)$$

Where:

- $I(t)$ is the input rate: the quantity that enters in the time unit.
- $O(t)$ is the output rate, the quantity that exits in the time unit.

If $I_{t,t+\delta t}$ is the quantity that enters in the interval, then $I_{t,t+\delta t} = I(t)\Delta t + o(\Delta t)$, where $o(\Delta t)$ is a higher order infinitesimal than Δt. This means that when Δt goes to i, not only $\lim\limits_{\Delta t \to 0} o(\Delta t) = 0$ and that $\lim\limits_{\Delta t \to 0} \frac{o(\Delta t)}{\Delta t} = 0$. Hence:

$$I(t) = \lim_{\Delta t \to 0} \frac{I_{t,t+\Delta t}}{\Delta t}$$

So the input rate behaves like an instantaneous velocity and is measured in $[\frac{C}{t}]$ Where $[C]$ represents the concentration. The same applies for the exit rate $O(t)$.