Continuous modelling by ODEs

Biological moduli as ODEs: scalar equations

Computational Biology

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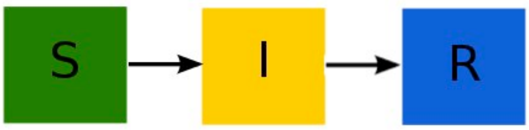
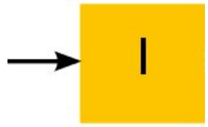
Epidemic model SIR

Epidemic model for the spread of an infectious disease (e.g *influenza* or covid19)



1. Identify important quantities (dependent variables) to keep track of: S = susceptible; I = infected; R = recovered;
2. Identify the independent variables such of time, space, age, and so on: t = time;
3. Quantify the transactions and/or interactions between these classes.

Simplified epidemic model I (infected)



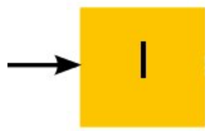
1. The dependent variable is the number of infected individuals I.
2. The independent variable is time t.
3. Assume that
   - E is the average number of people someone infected is exposed per unit time (typically a day);
   - p is the probability each exposure becoming an infection.

Then, if t represents the actual time (e.g. day)

$$I(t+1) = I(t) + \underbrace{pE}_{r} I(t) = (1+r)I(t),$$

where r represents the rate of infection.

Simplified epidemic model I (infected)



Let Δt denote a time period (e.g. a fraction of a day). Then

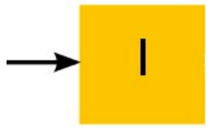
$$I(t+\Delta t) = I(t) + \Delta t r I(t) \Rightarrow \frac{I(t+\Delta t) - I(t)}{\Delta t} = rI(t).$$

Since r is constant, taking the limit as $\Delta t \longrightarrow 0$, we have

$$\frac{dI}{dt}(t) = rI(t).$$

Note: The growth rate is proportional to the number of infected individuals.

Discrete and continuous models



Discrete-time model $(t = n\Delta t)$

$$I_{n+1} = (1 + r\Delta t)I_n \overset{?}{\Rightarrow} I_n = I_0 (1 + r\Delta t)^n = I_0 \left(1 + \frac{rt}{n}\right)^n, \quad n \geqslant 1.$$

Continuous-time model (ODE)

$$\frac{dI}{dt}(t) = rI(t) \overset{?}{\Rightarrow} I(t) = I(0)e^{rt}.$$

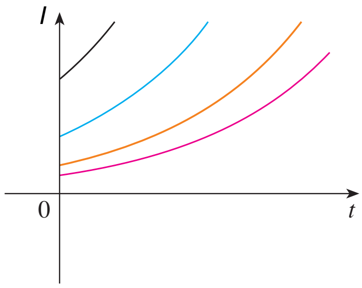


Figure: $I(t) = Ce^{rt}$, with $r > 0$, $t \geqslant 0$, for different values of C.

Ordinary differential equations (ODEs)

- Consider x the concentration of a substrate X (e.g. mRNA, protein, small molecule, metabolite, any reagent). A first order ODE for the unknown function $x(t)$

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

  and has the following interpretation
  - dx/dt describes the rate of change of the quantity x over time
  - $f(t, x(t))$ describes all source of changes in $x(t)$
- If the independent variable is time, the ODE is also called dynamic system.
- If f does not depend explicitly on t, the ODE is called autonomous.
- To solve a differential equation means to use local information ("What happens next?") to deduce long time behaviour ("What happens in the future?").

What does the ODE tell us?

- Example:

$$\frac{dx}{dt} = t - 3x \Rightarrow \begin{cases} dt/dt &= 1 \\ dx/dt &= t - 3x \end{cases}$$

  The vector field in the plane $\mathbb{R}^2$ is determined by a vector function

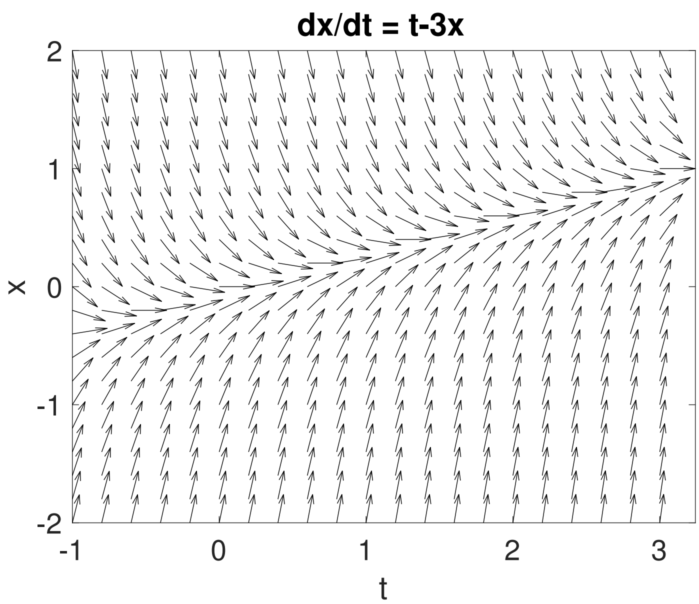
$$\vec{F}(t,x) = \begin{pmatrix} 1 \\ t - 3x \end{pmatrix}.$$

- Matlab code to visualize this field

```
% define the mesh
[t, x]=meshgrid(-1:0.2:3,-2:0.2:2);
% compute the vector field
dt = ones(size(t));
dx = t - 3*x;
% normalize the vector field
L = sqrt(dt.^2 + dx.^2);
% display the vector field
quiver(t, x, dt./L, dx./L, 'k'), axis tight;
```

Vector field

Exercise 2.1: Implement the previous Matlab code and obtain the following plot.



Vector field

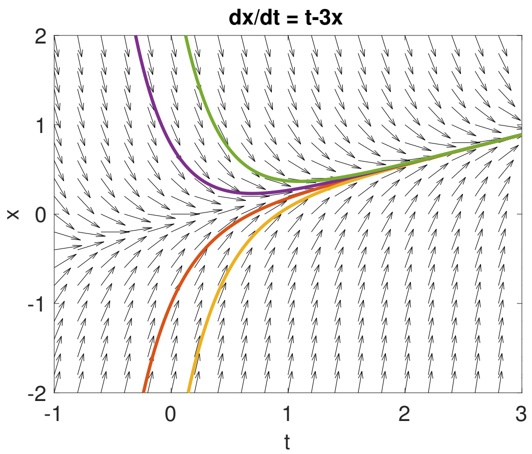
Exercise 2.2: Using https://www.wolframalpha.com/ show that the solution of

$$\frac{dx}{dt} = t - 3x$$

is giving by

$$x(t) = Ce^{-3t} + \frac{t}{3} - \frac{1}{9}.$$

and obtain the following plot (try with $C = -3, -1, 1, 3$).



Vector field

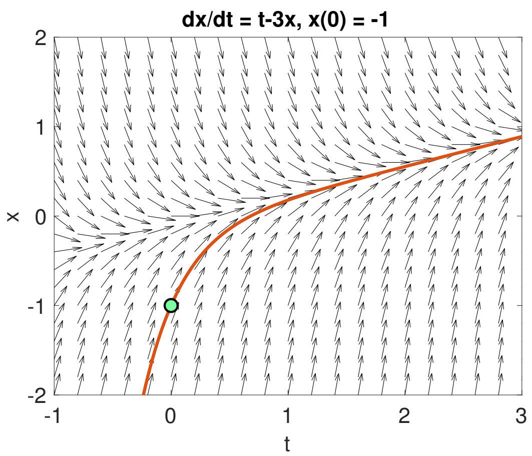
Exercise 2.3: Show that the solution of

$$\frac{dx}{dt} = t - 3x, \qquad x(0) = x_0,$$

is giving by

$$x(t) = \left(x_0 + \frac{1}{9}\right) e^{-3t} + \frac{t}{3} - \frac{1}{9}.$$

and obtain the following plot.



Malthus Law

Figure: Thomas Malthus (1776–1834).

Malthus Law: the rate of change is proportional to the number of individuals of the population

$$\frac{dx}{dt} = rx,$$

where the (relative) rate r is (typically) the difference between the birth and mortality rates.

Solving the Malthus Law

Exercise 2.4: Show that the solution of the Malthus Law is

$$x(t) = x_0 e^{rt}, \qquad x_0 \in \mathbb{R}.$$

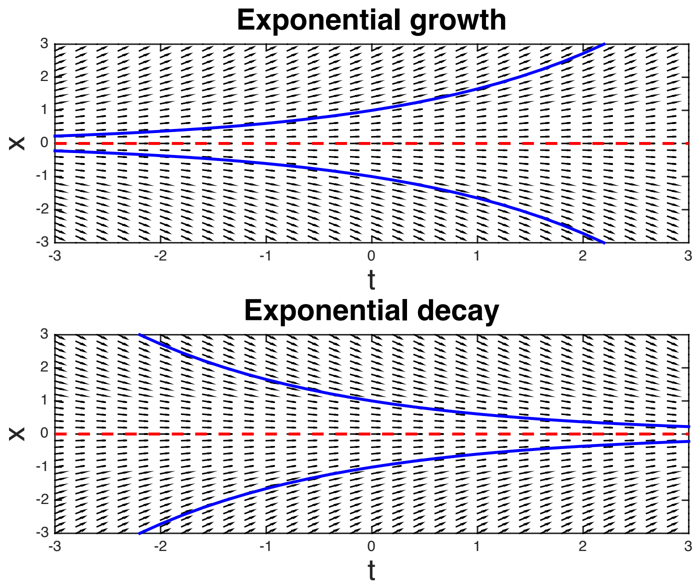
Solution: Solving by separation of variables

1. Separate the variables
$$\frac{dx}{dt} = rx \quad \Rightarrow \quad \frac{dx}{x} = rdt;$$
2. Integrate both sides
$$\int \frac{dx}{x} = \int rdt \quad \Rightarrow \quad \ln|x| = rt + c, \ \ c \in \mathbb{R}$$
3. Take the exponential
$$x(t) = Ce^{rt}, \quad C = \pm e^{c}.$$
4. Use initial condition $x(0) = x_0$ to conclude that $C = x_0$
$$x(t) = x_0 e^{rt}. \quad \square$$

Malthus Law

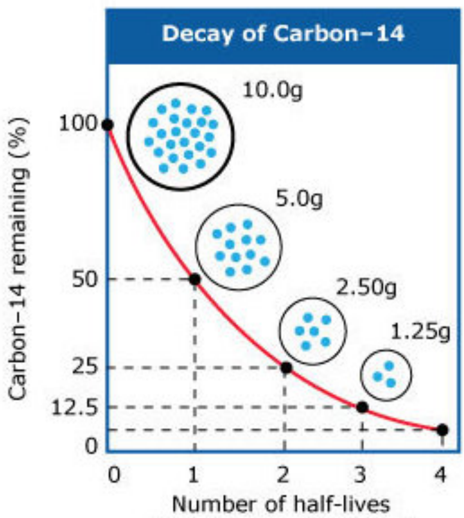
$$x(t) = x_0 e^{rt}$$

- The characteristic evolution of the Malthus law is exponential and depends on the sign of r
- $r > 0$: exponential growth; $r < 0$: exponential decay.



Radioactive decay: the $^{14}C-$method

Exercise 2.5: The $^{14}C-$method is used to estimate the age of archeological objects. It is known that living objects accumulate the radioactive $^{14}C-$isotope during their lifetime, to a certain concentration c_0. If the organism dies, then the radioactive ^{14}C decays with a life-time $T_{1/2} = 5730 \pm 40$ years.



Archeologists found a piece of wood in the Nile delta which showed a concentration of 75% of c_0. Estimate the age of this piece of wood. Could Tutankhamen have been sitting in a boat made from the same tree as the one from which this piece of wood came? Consider $T_{1/2} = 5760$ years.

Solving ODEs: Matlab

- Apart from simple cases (like Maltus law) there is little chance to find explicit solutions of an ODE or of a system of ODEs. How to proceed then?
- Use a simulator to numerically integrate the ODEs (e.g. Matlab, astandard software in all engineering fields)
- Example: use the Matlab function ode45 to solve the initial value problem (IVP)

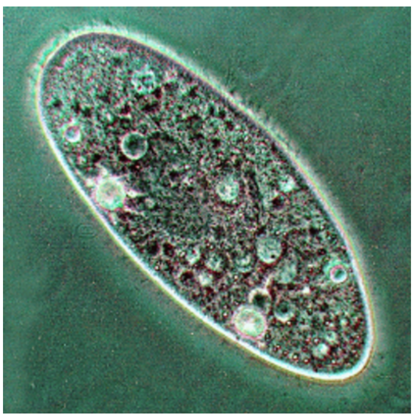
$$\begin{cases} \frac{dx}{dt} & = t - 3x, \qquad t \in (0, 3], \\ x(0) & = -1. \end{cases}$$

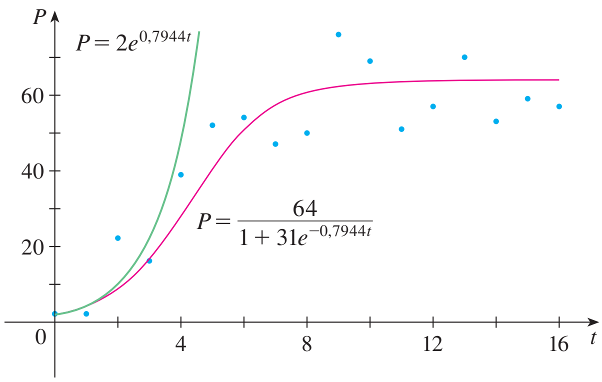
```
% Matlab code to solve an IVP with ode45
f = @(t,x) t - 3*x;    % function for the ODE
tint = [0 3];          % time interval
x0   = -1;             % initial condition
[t, x] = ode45(f, tint, x0);
plot(t, x)             % plot the solution
```

Logistic model

In may cases, exponential growth is not an appropriate model. Many populations start to grow exponentially but the population level starts to stabilize when it approaches its carrying capacity K.

Exemple: *Paramecium aurelia* is a single-celled organism that abounds in standing water tanks. It was studied by Gregory Gause in 1932.





Logistic model

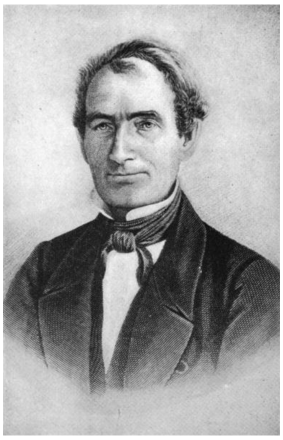


Figure: Pierre François Verhulst (1804–1849).

Verhulst Law considers the logistic equation

$$\frac{dx}{dt} = rx\left(1 - \frac{x}{K}\right)$$

that may be written, in an equivalent way, by

$$\frac{dx}{dt} = r_1 x\,(K - x)\,, \qquad r_1 = \frac{r}{K}.$$

Logistic/Verhulst model

$$\frac{dx}{dt} = rx\left(1 - \frac{x}{K}\right) = rx - \frac{r}{K}x^2$$

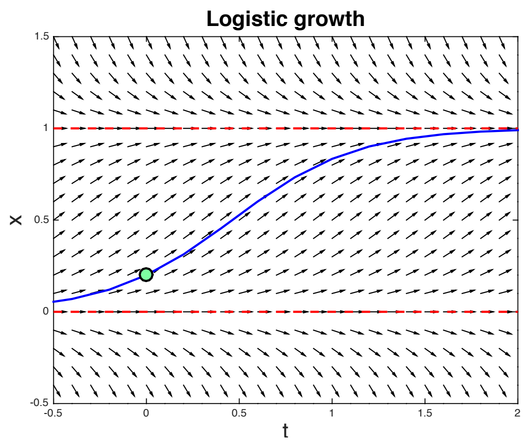
The added term $-r/Kx^2$ can be understood as a competition term from individuals of the same species.

Exercise 2.6: Prove that the solution for the logistic model is

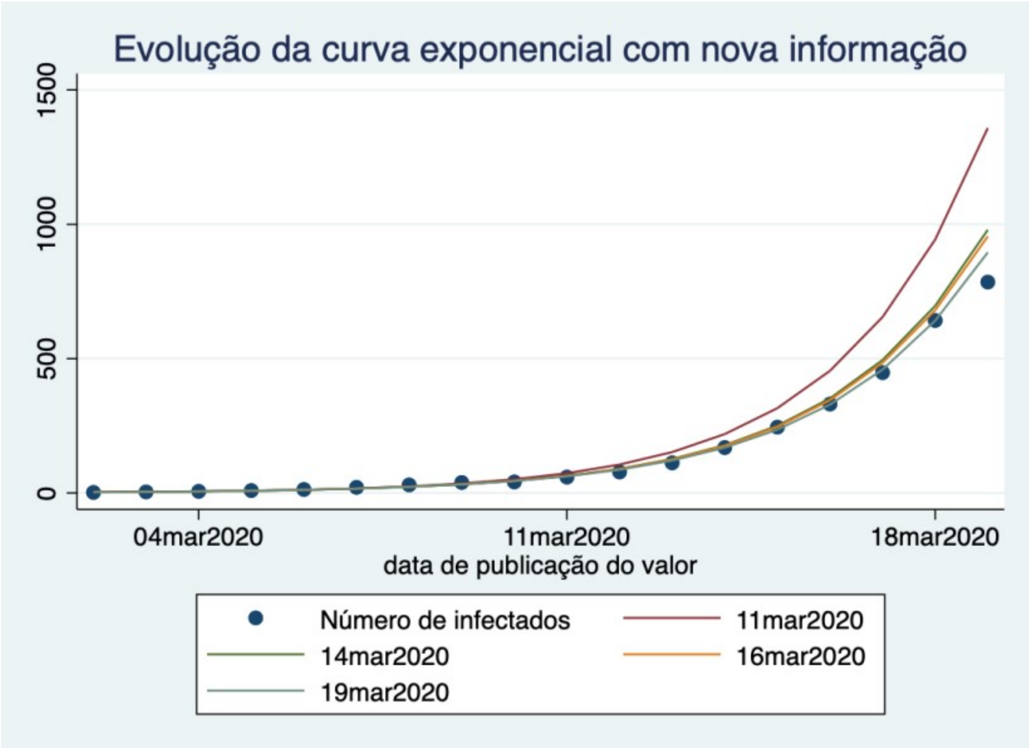
$$x(t) = \frac{K}{1 + Ce^{-rt}}, \qquad C = \frac{K - x(0)}{x(0)}.$$

Exercise 2.7: Obtain the following plot, where:

- $r = 3$ (intrinsic rate)
- $K = 1$ (carrying capacity)
- $x(0) = 0.2$



COVID-19 Portugal: exponential or logistic growth?



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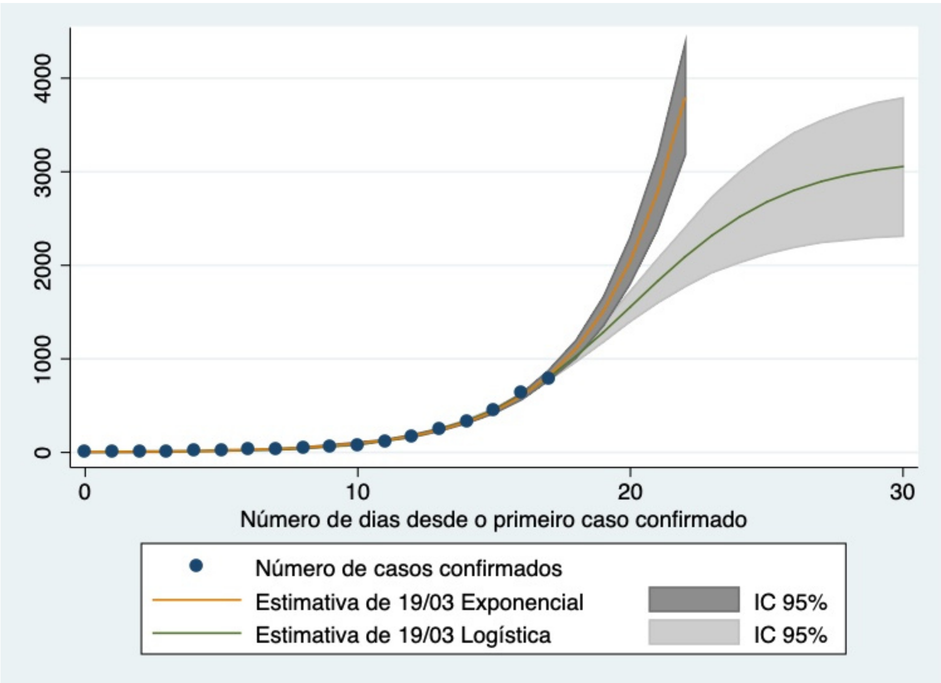
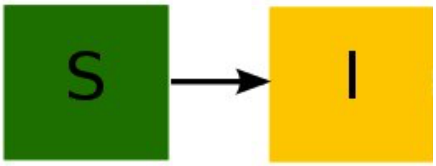


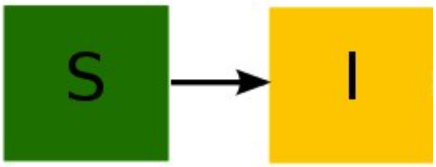
Epidemic model SI (susceptible + infected)

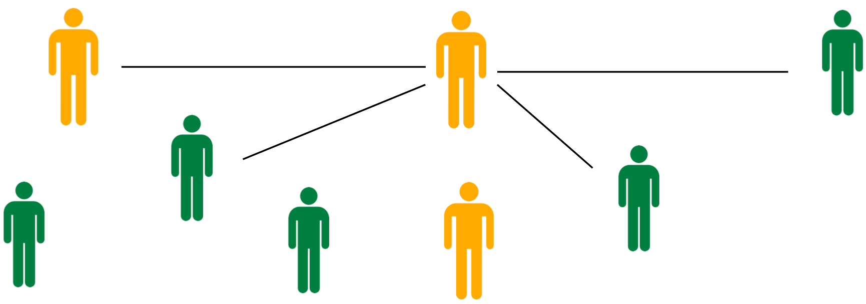
Epidemic model for the spread of an infectious disease (e.g *influenza* or covid19)



1. The dependent variables are the number of susceptible individuals S and the of infected individuals I.
2. The independent variable is time t.
3. We assume that the rate of infection is proportional to the number of contacts between susceptible and infected individuals.

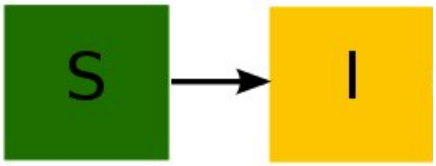
Transmission by contact





growth rate of $I = rS/N$, N = size of the population

Epidemic model SI (susceptible + infected)



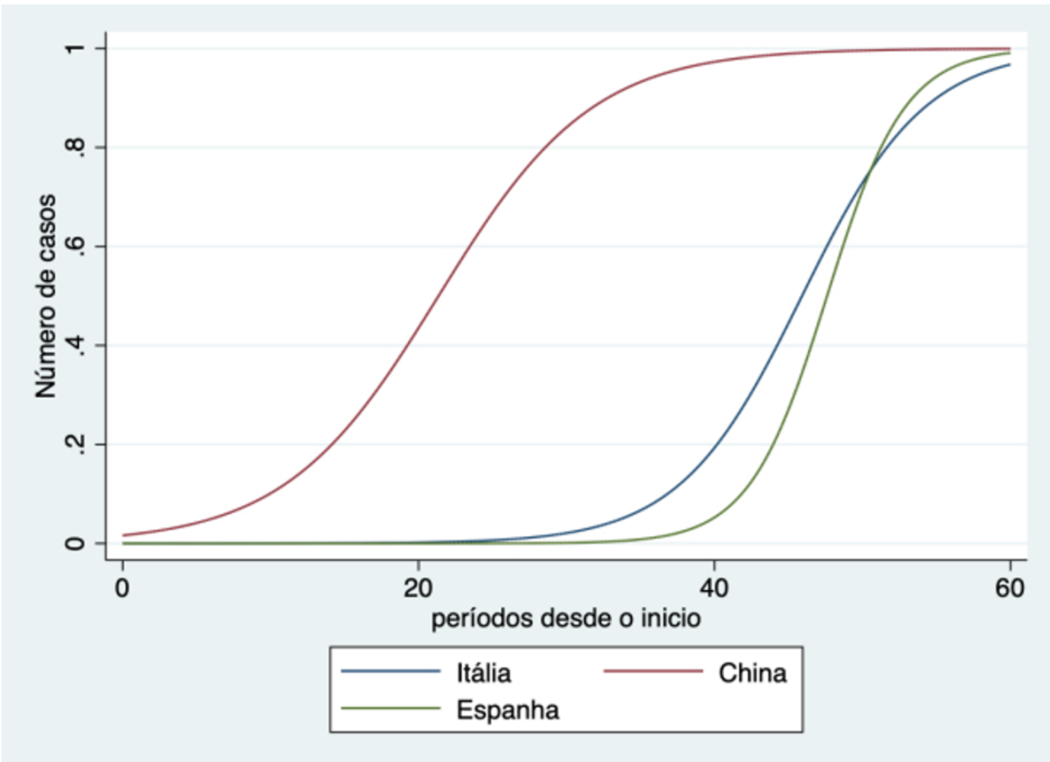
Logistic model:

$$\frac{dI}{dt} = r\left(\frac{S}{N}\right)I = rI\left(1 - \frac{I}{N}\right)$$

that is equivalent to

$$\frac{dI}{dt} = r_1 I\,(N - I)\,, \qquad r_1 = \frac{r}{N}.$$

COVID-19: normalised cumulative cases (first wave)



Leraning curves

Exercise 2.8: Psychologists interested in learning theory study learning curves. A learning curve is a graph of a function of $P(t)$, the performance of someone learning a skill as a function of the training time t.

1. What does dP/dt represents?
2. Discuss why the differential equation

$$\frac{dP}{dt} = k(M - P),$$

   where k and M are positive constants, is a reasonably model for learning. What is the meaning of k and M? What would be a reasonable initial condition for the model? Include the graph of dP/dt versus P as part of your discussion.
3. Make a qualitative sketch of solutions to the differential equation.

Homework #5: Epidemic model with recovery

Exercise 2.9: We want to describe the spreading of an infectious disease, which is transmitted at rate α if an infected individual meets a non-infected one, and from which infected individuals recover at rate μ. Let P be the proportion of infected individuals in a population.

1. Obtain the ODE that describes the dynamics of the disease.
2. Draw the phase line diagrams for $\alpha > \mu$ and $\alpha < \mu$. What follows for the qualitative behaviour? Sketch selected solutions.
3. Discuss what the two cases mean for the state of health of the population and the spreading of the disease?