SIR models of epidemics

Level 1 module in "Modelling course in population and evolutionary biology"

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1 Introduction

1.1 Description of the model

A major assumption of many mathematical models of epidemics is that the population can be divided into a set of distinct compartments. These compartments are defined with respect to disease status. The simplest model, which was described by Kermack and McKendrick in 1927[a], consists of three compartments: susceptible (S), infected (I), recovered (R)[b].

Susceptible Individuals that are susceptible have, in the case of the basic SIR model, never been infected, and they are able to catch the disease. Once they have it, they move into the Infected compartment.

Infected Infected individuals can spread the disease to susceptible individuals. The time they spend in the infected compartment is the infectious period, after which they enter the recovered compartment.

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[a]Kermack, W. and McKendrick, A., 1927. A contribution to the mathematical theory of epidemics. Proc. R. Soc. London A 115, 700-721.

[b]We will later discuss some possible modifications and extensions to this simple scheme.

Recovered Individuals in the recovered compartment are assumed to be immune for life.

The SIR model is easily written using ordinary differential equations (ODEs), which implies a deterministic model (no randomness is involved, the same starting conditions give the same output), with continuous time (as opposed to discrete time). Analogous to the principles of reaction kinetics, we assume that encounters between infected and susceptible individuals occur at a rate proportional to their respective numbers in the population. The rate of new infections can thus be defined as βSI, where β is a parameter for infectivity. Infected individuals are assumed to recover with a constant probability at any time, which translates into a constant per capita recovery rate that we denote with r, and thus an overall rate of recovery rI. Based on these assumptions we can draw the scheme of the model:
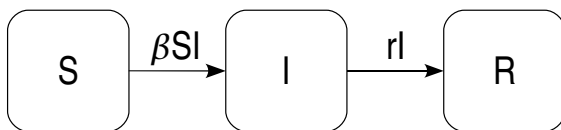

Figure 1: Scheme of the basic SIR model. Boxes represent compartments, and arrows indicate flux between the compartments.

The scheme can also be translated into a set of differential equations:

$$\begin{aligned} \frac{\mathrm{d}S}{\mathrm{d}t} &= -\beta SI \\ \frac{\mathrm{d}I}{\mathrm{d}t} &= \beta SI - rI \\ \frac{\mathrm{d}R}{\mathrm{d}t} &= rI \end{aligned} \tag{1}$$

Using this model, we will consider a mild, short-lived epidemic, e.g. influenza, in a closed population. *Closed* means that there is no immigration or emigration. Moreover, given the time scale of influenza epidemics, we will not consider demographic turnover (birth or death), and all infections are assumed to end with recovery. The size of the population $(S + I + R)$ is therefore constant and equal to the initial population size, which we denote with the parameter N.

Let us now consider a population which is naive with respect to the disease we are considering. What happens if a single infected individual is introduced into such a population? Is there going to be an epidemic? How many people will be infected? We will answer these questions by implementing and simulating the model in R.

1.2 Tips to develop the SIR model

Let us now implement the model in R, using the `lsoda` command in the `deSolve` package to numerically solve differential equations. The syntax should be like this (look at the R script

available on the web page of the module for a full and commented version):

```
library("deSolve")

 parms <- c(beta=1e-3, r=1e-1)
 inits <- c(S=499, I=1, R=0)
 dt    <- seq(0,100,0.1)

SIR <- function(t, x, parms){
  with(as.list(c(parms,x)),{
    dS <- - beta*S*I
    dI <- + beta*S*I - r*I
    dR <- r*I
    der <- c(dS, dI,dR)
    list(der)  # the output must be returned
  }) # end of 'with'

}  # end of function definition
simulation <- as.data.frame(lsoda(inits, dt, SIR, parms=parms))
```

The R script **start.R** provided on the web page will also help you to plot the results as in Fig. 2. Run the model with the preset parameters. Now take some time to think about the interpretation of the simulation. What is the population size with these settings? What is the time frame of the simulation? Is it possible to tell? What defines the time scale? Would you expect to get such a smooth curve in a real life epidemic?

Explore the model: play around with initial conditions and parameters and see what happens in the simulations (a more systematic analysis will be performed later). Observe the effect of each parameter and the possible courses of simulated epidemics. Is it possible to simulate a sustained epidemic in this model?

2 Exercises

2.1 Basic exercises

A key parameter in epidemiology is the *basic reproductive ratio*, R_0. It is defined as the average number of secondary cases transmitted by a single infected individual that is placed into a fully susceptible population. In other words, R_0 tells us about the initial rate of spread of the disease. Hence, if $R_0 > 1$, there will be an epidemic, and if $R_0 < 1$, the introduced infecteds will recover (or die) without being able to replace themselves by new infections. In this model, it is pretty easy to derive R_0. The disease-free state corresponds to: S=N, I=0, R=0. If one infected individual appears in the population, there will be an epidemic if and only if $\mathrm{d}I/\mathrm{d}t > 0$. By
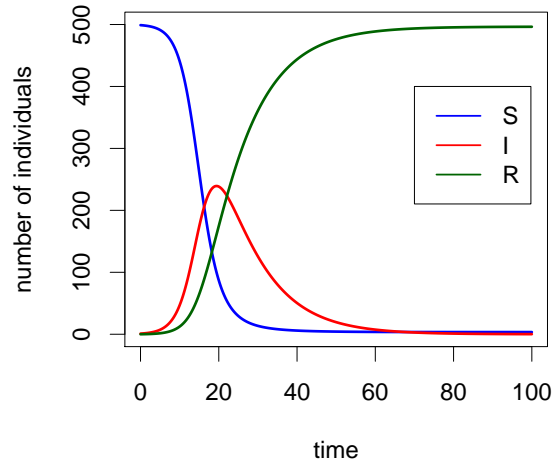
Figure 2: An epidemic simulated in the SIR model

replacing S with N in Equation 1, this yields $\beta\,N/r > 1$. That is:

$$R_0 = \frac{\beta\,N}{r} \tag{2}$$

Eb1. Check this formula by simulating the model for different sets of parameters. Fix N, and vary β and r. Choose your values such as to have combinations with both $R_0 > 1$ and $R_0 < 1$, as predicted by Equation 2. Because it is the ratio of the two parameters that matters, it is better to use a geometric, rather than an arithmetic sequence for the parameter values. Run the model for each parameter combination (R hint: use a loop structure, e.g. `for`, iterated over a pre-defined vector of parameter values; you will need two embedded loops for the two parameters), and check and record whether there has been an epidemic or not. For this, you can compare the initial and maximum number of infecteds: was there growth above the initial level? You can perform a simple "automated" test to verify the key role of R_0. For each parameter combination, record a logical value whether the maximum number of infecteds was above the initial, and another logical value whether R_0 was above 1. Store these values in two vectors and then check the identity of the two vectors with a single command. R-hint: Using the equality operator `==` compares two matrices of equal size element by element, and yields a logical matrix of the same size as a result. In contrast, the function `identical()` checks the identity of two objects (e.g. two matrices) and returns a single logical value.

Eb2. Vaccination can prevent the infection of an individual. In addition, it can also protect a population from epidemics, even if not all individuals are vaccinated (this is the concept of *herd immunity*). Based on the concept of R_0, can you think of an intuitive explanation for this phenomenon?

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Implement vaccination in the model, and determine the proportion of a population which should be vaccinated in order to prevent the initial spread of the disease. In this model, vaccination is equivalent to removal (or transfer to the Recovered compartment): a vaccinated individual cannot infect or be infected. Assume that vaccination happens before the emergence of the disease (affecting the initial conditions, but not the structure of the model). Choose different proportions of vaccinated people, and run the model. Check whether the disease spreads, and try to determine the threshold vaccination coverage. Repeat this for different values of β. How does the vaccination threshold depend on the infectivity of the disease? Try to derive the threshold analytically (drawing on R_0), and compare the analytical result to your simulations.

Eb3. Phase portraits (or phase diagrams) provide a powerful tool to visualize the dynamics of ODE systems[c]. R's graphical capabilities make the drawing of phase portraits very simple. In the starting script, the time course of a simulation was shown by plotting the variables of the system (i.e., their time series) against time, from the data frame generated by numerical integration. A trajectory (and the coordinate system of a 2D phase portrait) can simply be drawn by plotting the time series of one variable against the time series of another. Notice that the basic SIR model can be reduced to a two-dimensional system, because the variable for recovered individuals does not appear in the equations of the other two variables[d]. The reduced (S,I) system is thus the following:

$$\begin{aligned} \frac{\mathrm{d}S}{\mathrm{d}t} &= -\beta\,S\,I \\ \frac{\mathrm{d}I}{\mathrm{d}t} &= \beta\,S\,I - r\,I \end{aligned} \tag{3}$$

and can be plotted in a 2D S-I phase diagram without loss of information. For a fixed set of parameters, draw a phase portrait with trajectories corresponding to different initial conditions[e]. You can add arrows to the plot to indicate direction (see `help(arrows)`); use the (S,I) values of the simulation for proper positioning. Observe how the course of the epidemic depends on the initial conditions. Draw trajectories for different values of N. For each simulation, identify the maximum value of I, and draw the point on the phase diagram. R-hint: if a table (data frame) `TBL` contains two columns, A and B, then `max(TBL$A)`, finds the maximum value in column A, but just this value. With `TBL[TBL$A==max(TBL$A),]`, you can select the whole line at which A is maximal (i.e., the line with both `max(A)` and the corresponding value of B). It is possible to determine analytically the value of S for which the epidemic reaches its peak. Using R_0, we find $S_{I\,is\,max} = r/\beta$. Plot these values on your phase diagram, and compare them to the points you obtained previously. Interpret the result. In particular, what happens when $S_0 \leq \frac{r}{\beta}$?

Optional: trajectories can also be obtained analytically by integrating $\mathrm{d}S/\mathrm{d}I$, which yields $I(t) = I(0) + \frac{r}{\beta}(\ln(S(t)) - \ln(S(0))) - S(t) + S(0)$. You can check this by plotting this

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[c]See lecture script "Ecology and Evolution II: Populations" by Sebastian Bonhoeffer.

[d]This implies that the dynamics of the susceptible and infected compartments is fully described by the 2D system, and that the dynamics of the recovered compartment can be derived from the solution of this system.

[e]R-hint: you can add further trajectories to the same plot by using `lines` instead of `plot`. Different trajectories may span different ranges over the axis: to get the axes right, initiate the coordinate system by calling an "empty" plot command, like `plot(c(xmin,xmax),c(ymin,ymax),type="n",xlab="",etc)`, where `xmin` is the smallest value of the variable on the X axis, `ymax` is the greatest value of the variable on the Y axis, etc.

function over the graphs you obtained by numerical integration.

Finally, draw trajectories with different β-r combinations that yield the same R_0 (but now keep the initial conditions constant: introduce a single infected individual into a population of fixed size, as in the beginning). Previously, we have observed that R_0 can predict the overall outcome of the epidemic. Is there a difference in the course of the epidemic depending on how the same R_0 is obtained? Check this also in a time plot.

Conclude about the key role of R_0 in epidemiology. How does it help you to predict possible compensatory effects between different parameters of the model?

2.2 Advanced/additional exercises

Ea1. Determine the total number of individuals infected during an epidemic (denoted by, e.g., I_{tot}) for different combinations of r and β. (Hint: all infecteds end up in the Recovered compartment in the current model). Calculate also R_0 for each parameter combination, and plot the total number of infections as a function of R_0. Compare the number of infections for combinations of r and β that yield the same R_0: is there a difference?

Optional reading: The relationship between R_0 and the overall magnitude of the epidemic is not trivial. We will derive a formula for s_∞, the proportion of remaining susceptibles when the epidemic is over. (This is easily linked to the total number of infections as $s_\infty = (N - I_{tot})/N$). Consider dI/dS, and separate the variables.

$$\frac{dI}{dS} = \frac{r}{\beta S} - 1$$
$$\Rightarrow \quad \int dI = \int \frac{r}{\beta} \frac{dS}{S} - dS \tag{4}$$
$$\Rightarrow \quad \frac{r}{\beta} ln(S) - S - I = C$$

where C is a constant.
Assuming that $R > 1$, and noting that $S(-\infty) = N$ and that $I(-\infty) = I(+\infty) = 0$, it can be shown that

$$\frac{r}{\beta} ln(S_\infty) = S_\infty - N + \frac{r}{\beta} ln(N)$$
$$ln(s_\infty) = R_0(s_\infty - 1) \tag{5}$$

where $s = S/N$ is the proportion of susceptibles. You can validate this result by recording s_∞ for several parameter combinations and checking the formula.

Ea2. One of the (numerous!) simplifying assumptions of the basic SIR model is life-long immunity. What happens if there is a loss of immunity, that is, if a given proportion of recovered individuals become susceptible again at rate l? Extend the model to implement this possibility. Run simulations and plot the time course of the epidemics; experiment with the new parameter. Is it possible to model a sustained epidemic in this extended model? You may try to derive R_0, or to determine by simulations whether increasing l from zero decreases or increases it (i.e. whether it makes it more or less difficult to start an epidemic when the other parameters are varied). Use the techniques learnt in the previous exercises (e.g. contour plot, phase portrait). How is the vaccination threshold affected?

Ea3. Model the treatment of infected individuals (assuming again life-long immunity). Implement a new 'Infected-Treated' (IT) compartment. Let infected individuals initiate treatment at a certain rate, and let treated individuals recover at a faster rate compared to untreated infecteds. Model the effect of more and less effective drugs. What happens if treated individuals are also less infectious than untreated infecteds?

Ea4. The development of drug resistance is a major problem in the treatment of several infectious diseases. Model the emergence of drug-resistant pathogens. Extend the previous model with compartments corresponding to individuals infected with drug-resistant pathogens, e.g. a 'Treated-Resistant' (TR) and a 'Nontreated-Resistant' (NR) compartment. Assume complete resistance, i.e. let treatment have no effect on the recovery of resistant infections. What processes can give rise to a resistant infection?

Experiment with the model. To interpret the results, you can define broad classes, e.g., total infected (containing all infected classes), total resistant (containing all resistant classes), etc. Make assumptions about the infectivity rate of wild-type (non-resistant) and drug-resistant pathogens. How can you implement a trade-off? Given your assumptions, you may try to calculate the R_0 of wild-type and resistant pathogens. Does the rate of treatment play a role?

Determine the optimal rate of treatment by simulation. Fix all other parameters and run simulations with different treatment rates. To find the "optimal rate" you will also need to define your evaluation criteria: what would you try to optimise? Then find the optimal rate(s) for one or more criteria.

Ea5. Finally, up till now we have considered short transient epidemics in a closed population. Now allow for longer time scales by implementing the birth and death of individuals. Can you get a sustained epidemic? What is now the optimal rate of treatment?