Inference in infectious disease systems practicals

Contents

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Structure of this workshop

In these notes, R commands to be entered into the console are shown in grey boxes e.g.

```
seq(0, 1, length = 11)
```

and the corresponding outputs look like:

```
##  [1] 0.0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1.0
```

Tasks

Task 1

All **tasks** will be denoted in panel boxes like this one. In the HTML version, all solutions can be toggled by hitting the **Show Solution** buttons. In the PDF version solutions are given in the Appendix and are linked via the **Show Solution** buttons.

Show: Solution on P159

Part I

Introduction to R

Chapter 1

Getting Started in R

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R—available at https://cran.r-project.org/—is a comprehensive statistical programming language. It can be thought of as an open-source, freely available implementation of the S language. R is an **interpreted language**, and so can be used interactively, without having to compile the code into an executable file.

Although R is a functional programming language in its own right, its popularity is in large part due to its fantastic capabilities as a statistical package. However, R is much more than that. R has amazing graphical capabilities; can integrate with other languages, such as C and Python; can use scripts and be run in batch mode; and can even be used to produce **reproducible** documents, presentations and interactive webpages. Even better than that, R is completely **free** and **open-source**!

To top it off, R is also **multi-platform**, and so can be used on Windows, Mac and Linux operating systems. R is supported by a wide user base, and is extended by a large number of additional packages, and even provides the capabilities to create your own. Whilst R provides its own development environment, we will use a fantastic IDE[1] provided by RStudio. This is free to download, provides some neat features, and crucially, operates the same way on all operating systems!

All of the instructions in these practicals will assume that you are using RStudio.

1.1 Installing R and RStudio

If you want to download R for your own computer, first go to http://cran.r-project.org, and follow the instructions in the box called 'Download and Install R'. **You only need to install the `base` package**. During installation, selecting the default options should be sufficient.

Once you have installed R, you can install the **free desktop** version of RStudio from https://www.rstudio.com/products/rstudio/download/. Again, selecting the default options during installation should be sufficient.

Important

You will also have to install some additional R packages in order to complete the materials in this workshop. Details on how to install packages can be found at the end of this Chapter here. I would suggest you read through all these notes before installing the packages, but this box is here to remind you to do this. A full list of which packages to install can also be found here.

[1] Integrated Desktop Environment

1.2 What is R?

R is an **object-orientated** programming language. This means that you create objects, and give them names. You can then **do things** to those objects: you can perform calculations, statistical tests, make tables or draw plots. Objects can be single numbers, characters, vectors of numbers, matrices, multi-dimensional arrays, lists containing different objects and so on.

1.3 RStudio

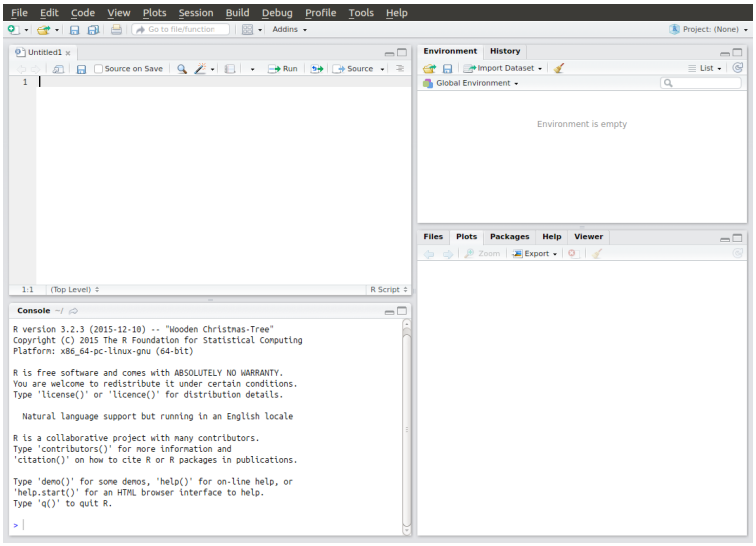


Figure 1.1: RStudio window

After loading, the RStudio window should look something like Figure 1.1. It consists of:

- **Script pane** (top-left): this is essentially RStudio's built-in text editor. It has all the usual features one would expect: syntax highlighting, automatic indentation, bracket matching, line highlighting and numbering and so on. You can open any type of text file in here, not just R scripts. (You might have to go to *File > New File > R Script* to open a new R script if you don't have one already open.)
- **Console pane** (bottom-left): This is where you run R commands and view outputs.
- **Workspace/history pane** (top-right): this shows a list of all of the objects and variables that you create during a session or a history of all of the commands that have been sent to the command window during the session.
- **Plot/help pane** (bottom-right): this shows any plots that you create or any help files that you access.

You can alter the size of the various panes by clicking and dragging the grey bar in between each window to suit your needs. You can also change their arrangement by going to *Tools > Global Options*, and then selecting the *Pane Layout* option.

1.4 Setting up an R session

It is worthwhile getting into a workflow when using R. General guidelines I would suggest are:

- Use a different folder for each new project / assignment. This helps to keep all data / script / output files in one self-contained place.
- Set the **Working Directory** for R at the outset of each session to be the folder you've specified for the particular assignment you're working on. This can be done in RStudio by going to *Session > Set Working Directory > Choose Directory*. This sets the default search path to this folder.
- Always use **script files** to keep a record of your work, so that it can be reproduced at a later date.

We will explore the **console** and **script** panes below, dealing with the other panes as and when they arise.

1.5 Console Pane

The console pane provides a direct interface with R, and looks similar to command line R (in Linux and Macs), and the console pane in R for Windows. You enter commands via the standard prompt **>**. For example, type the following into the console pane:

```
10 + 5 * 3
```

```
## [1] 25
```

You can see here that R has returned a value of 25, illustrating one of R's key features: that it can be used as an overgrown calculator, simply by entering commands into the prompt. R supports lots of basic mathematical operators, such as those found in Table 1.1.

Table 1.1: Basic mathematical operators

Symbol	Meaning
`+`	addition
`-`	subtraction
`*`	multiplication
`/`	division
`^`	to the power
`%%`	the remainder of an integer division (modulo)
`%/%`	integer division

Meanwhile, Table 1.2 has some other ones you might need. (**Note**: these are functions: just replace e.g. `x` with a number.)

Table 1.2: Other useful mathematical functions

Function	Meaning
`log(x)`	$\log_e(x)$ (or $\ln(x)$)
`exp(x)`	e^x
`log(x, n)`	$\log_n(x)$
`log10(x)`	$\log_{10}(x)$
`sqrt(x)`	$\sqrt{x}$
`factorial(x)`	$x!$
`choose(n, x)`	binomial coefficients: $\frac{n!}{x!(n-x)!}$
`gamma(x)`	$\Gamma(x)$ for continuous x or $(x-1)!$ for integer x
`lgamma(x)`	natural log of $\Gamma(x)$

Function	Meaning
`floor(x)`	greatest integer $< x$
`ceiling(x)`	smallest integer $> x$
`trunc(x)`	closest integer to x between x and 0 e.g. `trunc(1.5) = 1`, `trunc(-1.5) = -1` `trunc` is like `floor` for positive values and like `ceiling` for negative values
`round(x, digits = 0)`	round the value of x to an integer
`signif(x, digits = 6)`	round x to 6 significant figures
`cos(x)`	cosine of x in radians
`sin(x)`	sine of x in radians
`tan(x)`	tangent of x in radians
`acos(x)`, `asin(x)`, `atan(x)`	inverse trigonometric transformations of real or complex numbers
`acosh(x)`, `asinh(x)`, `atanh(x)`	inverse hyperbolic trigonometric transformations on real or complex numbers
`abs(x)`	the absolute value of x, ignoring the minus sign if there is one

R retains a **history** of all the commands you have used in a particular session. You can scroll back through these using the up (↑) and down (↓) arrows whilst in the console pane. (You can even save the history—though we will discuss a *much* better option in the next section.)

One important thing to note is that unlike a language like C, R does not require the semicolon (`;`) symbol to denote the end of each command. A carriage return is sufficient. A semicolon can be used to allow multiple commands to be written on the same line if required. For example,

```
10 + 5 * 3; sin(10)
```

```
## [1] 25
## [1] -0.5440211
```

is equivalent to

```
10 + 5 * 3
sin(10)
```

```
## [1] 25
## [1] -0.5440211
```

One thing to note is that if a command is incomplete, then R will change the `>` prompt for a `+` prompt. For example, typing `10 + 5 *` into the console pane will result in the `+` prompt appearing, telling you that the previous line is incomplete i.e.

```
> 10 + 5 *
+ 3
```

```
## [1] 25
```

You must either complete the line or hit the `Esc` key to cancel the command.

1.6 Script pane and R scripts

The console window is the engine room of R, and one can interact directly with it. One key advantage to R is that it *records* all of the commands that you enter into the console (known as the command *history*). It is possible to save the command history, or run back through it using the arrow keys. However, a much better approach is to use the **script pane** to write an R script that contains all the commands necessary for a particular project. In fact, one might argue that this is probably one of the most important features of R relative to a point-and-click statistical package such as SPSS.

Put simply, ***R scripts are just text files that contain commands to run in R***. They are **vitally important** for the following reasons:

- They keep a systematic record of your analysis, which enables you to **reproduce** your work at a later date. Scripts can be passed to collaborators or other users to enable them to **replicate** your work.
- This record means that you do not have to rely on your memory to figure out **what** you did.
- R scripts allow you to **comment** your code, which means that you also won't forget **why** you did it.
- In more advanced settings, R scripts can also be run in **batch** mode, which means that you can run scripts remotely on a server somewhere without having to be sat in front of a computer manually entering commands.
- Although programs like SPSS allow **outputs** to be saved, R scripts contain **inputs**, which are much more useful, since it is easier to generate the outputs from the inputs than it is to reconstruct the likely inputs from the outputs.
- In fact, R scripts can be combined with a markup language called 'markdown' to generate fully reproducible documents, containing both inputs and outputs. It does this using the fantastic `knitr` and `rmarkdown` packages. (In fact these notes were written using `rmarkdown` and a package called `bookdown`.)

Some comments:

- RStudio comes with its own text editor, but if you are not using RStudio, then there are plenty of others available.
- R is case-sensitive. If something doesn't work, it's often because you have failed to capitalise, or capitalised where you shouldn't have. **NEVER, EVER, EVER** use Word to edit your R scripts! Word often tries to correct your grammar and is an absolute nightmare for writing code. If you don't like RStudio's editor, then lots of lightweight and free text editors exist that you can use. By all means use Word for writing up the work[2], but ***please***, ***NEVER*** use it for writing code!

In RStudio, you can open a new script in R using: *File > New File > R Script*.

Type the following into the **script file**:

```
## calculate the hypotenuse from a right-angled triangle
## with the two other sides equal to 3 and 4
sqrt(3^2 + 4^2)
```

Notice that nothing has happened. All you've done is write some commands into a text window. However, if you highlight these lines and then hit the `Run` button in the top right-hand corner of the script pane (or, in Windows certainly, press `Ctrl-Enter`), then RStudio runs these lines in the console pane. (Alternatively, you can manually copy-and-paste these lines into the console window.) This should return:

```
## [1] 5
```

[2] although `rmarkdown` provides a powerful alternative

Note

Notice that the # symbol in the input code denotes a **comment**, such that any text after the # is ignored (up to the end of the current line). I have used a double hash here ##, though this is simply because I've written this practical using R Markdown and it seems to typeset better. This is not absolutely necessary though, since anything after the first # is ignored.

Comments are ***vital*** in code to ensure **reproducibility** and **readability**. You should ensure that all code is commented, so that both you and anyone else who wants to use your code is able to decipher it. Even if no one else is going to look at your code, it is still worthwhile to comment it. What seems obvious to you as you write a piece of code, often becomes confusing when you return to it in six months time and can't remember what you did or why you did it...

It is conventional to save R script files using the suffix '.R', though remember that they are simply **text files**, and can be viewed in any text editor. Make sure you have set up a folder to store the code for this practical in, and have changed the **working directory** to this folder (see the setup section), and then save this script file as something like `IntroToR.R`.

Important

Make sure you save your script file regularly to prevent data loss!

1.6.1 Notes on legibility

NOTE: that I use spaces within the code to make it clearer. R does not require this, but again I think it is good practice to think about how to make your code legible. Different coders have different preferences, but personally I prefer `plot(Worm.density ~ Vegetation, data = worms)` over `plot(Worm.density~Vegetation,data=worms)`. As Hadley Wickham says: "Good coding style is like correct punctuation: you can manage without it, butitsuremakesthingseasiertoread."

Note that different coders prefer different styles—there is no universal agreement, and you will notice that different lecturers on this course have slightly different styles. However, it's worth getting into the habit of writing your code neatly and with legibility in mind. A guide that is similar to my own is the `tidyverse` guide here. (Note that unlike e.g. Python, R does not require specific indentation. Instead it uses curly brackets to group lines of code together. However, indentation is still key for legibility.)

I tend to use script files to keep a record of all commands that need to be reproduced, but I often enter commands directly into the console window when I'm testing or visualising things. Try to keep redundant code out of your script files and try to make sure the code is legible and commented.

1.7 R packages

R has hundreds of add-on **packages** that provide functionality for a wide range of techniques. These repositories are growing all of the time; some packages become redundant and are removed, others are updated, some are superceded or incorporated into others, and completely new ones appear regularly. A key part of becoming proficient with R is learning how to install and update packages.

Note

R packages can be thought of in a similar way to Matlab toolboxes or Python libraries.

The principal R package repository can be found on CRAN (the Comprehensive R Archive Network). Another popular repository, predominantly aimed at bioinformatics packages, is Bioconductor, though installation of packages through Bioconductor is more difficult than through CRAN, so we will focus on the latter only here.

Some packages are included as part of R's base package. To load a package, you can use the `library()` or `require()` functions, passing the name of the required package. For example, to load the `tidyr` package, type:

```
library(tidyr)
```

If this doesn't return any error, then the package is loaded and you are now able to use any function in `tidyr` in your R code. R packages must contain help files and documentation in order to be included on CRAN. For example, the documentation for the `tidyr` package can be found here, through the *Reference Manual* link, plus some vignettes through the *Vignettes* link.

1.7.1 Installing packages from CRAN

If the package you want is not installed, then you will need to install it. To install a package that is hosted on CRAN, you can use the `install.packages()` function. For example, to install `tidyr` you can type:

```
install.packages("tidyr")
```

This will ask that you select a mirror repository—choosing one close-to-home is a good idea. It might also ask you to set up a local R library in your user directory. This is a good idea, so I would just accept the default if it asks.

If it installs without any errors, then you can load the library using `library(tidyr)` as above.

> **Note**
>
> You only have to install a package **once** (unless you update R). You have to **load** the library once during each **session**. I prefer to enter all my calls to `library()` at the top of my script file, so I can quickly see which packages are required for my script to run.

1.7.2 Installing from a local file

You can also install a package from a local ZIP file if required (though this is required much less often). For example, from the CRAN website, click on the *Packages* link, find the correct package and simply download a suitable Windows / Mac binary file as appropriate, or the 'Package Source' file (if you are on Linux, or if you have the appropriate compiler tools installed). See Figure 1.2 for an example of where these can be found for the `tidyr` package.

Once you have downloaded one of these, you can install using:

```
install.packages("PATH/TO/PACKAGENAME", repos = NULL)
```

where `PATH/TO/PACKAGENAME` is the path to the package source file (be careful to get the path in the correct format—Windows users might have to use `\` instead of `/`). The `repos = NULL` argument tells R to look for the file locally, and not online.

Figure 1.2: Location of source / binary files for 'tidyr'

1.7.3 Installing archived versions of a package

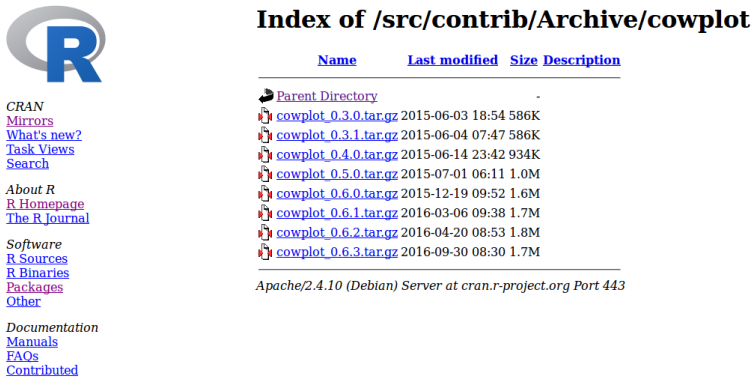
Sometimes R packages are not updated as quickly as R itself, and occasionally you might need to install an older version of a package. A really useful package is called `devtools`. This provides functions to install R packages directly from CRAN archives, which can be found by going to https://cran.r-project.org/, and clicking on the *Packages* link followed by the *Archived* link. This provides a list of older versions of a package, which can be installed using the `install_version()` function in `devtools` (as detailed below).

For example, I once had an issue with a package called `cowplot`, that didn't exist for my version of R, and returned the following error message (**don't run the code now**):

```
install.packages("cowplot")
```

```
Installing package into '/home/tj/R/x86_64-pc-linux-gnu-library/3.2'
(as 'lib' is unspecified)
Warning in install.packages :
  package 'cowplot' is not available (for R version 3.2.3)
```

I solved this by finding an older version of the package on CRAN (by clicking on *Packages* then *Archived*):



I noted the version number, and then used `install_version()` from the `devtools` package as follows (**don't run the code now**):

```
library(devtools)
install_version("cowplot", version = "0.6.3", repos = "https://cran.r-project.org/")
```

These can also be installed manually from source as in the previous section.

1.7.4 Installing development packages

In order to upload a package to CRAN, the package must pass a series of tests. The versions you find on CRAN are the **stable** versions (i.e. they have passed these tests and work well with the current version of R). However, developers often keep the latest **development** version of their package on an online repository such as GitHub. Development packages usually contain the most up-to-date functions, but are likely to contain more bugs—use them at your own risk! In addition, some packages simply aren't available on CRAN—there is no requirement to add them to this repository.

For example, to install the development version of the `gganimate` package from GitHub, locate the source code on e.g. GitHub; in this case it can be found at https://github.com/dgrtwo/gganimate. Then the package can be installed using `devtools` as follows (**don't run the code now**):

```
install_github("dgrtwo/gganimate")
```

Note the syntax `DEVELOPER/PACKAGENAME`—this can be found from the address of the repository e.g. https://github.com/dgrtwo/gganimate. For CRAN packages, the source code URL is usually listed on the package page. For example, Figure 1.2 shows that the GitHub page for `tidyr` is at https://github.com/tidyverse/tidyr.

1.7.5 Packages to install for this module

The packages you need to install for this module are listed below. Some are installed automatically by R, but have been listed here for completeness. (Please let me know if you come across any that aren't listed here.)

- deSolve
- earlyR
- MCMCpack
- outbreaks
- SimInf
- SimBIID
- utils
- tidyverse
- incidence
- patchwork
- tsiR
- chron

Many of these packages depend on other packages, but R should install all dependencies automatically. These should all be available via CRAN, and so can be installed using e.g.

```
install.packages("deSolve")
```

If you're on a Windows computer then you'll need to do some additional work to use `SimInf` and `SimBIID` (macOS and Linux users should be fine).

- Download Rtools from https://cran.r-project.org/bin/windows/Rtools/
  - Click on the appropriate version of RTools on the left.
  - For RTools 4.4 (the most up to date version) click on the link `Rtools44_installer`. It's in the third paragraph down in the second section.
  - Once it's downloaded install it using all of the default settings.
  - This might take a couple of minutes, but click Finish when it's done.

Chapter 2

Fundamentals of R

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2.1 Variables in R

R makes use of symbolic variables, i.e. words or letters that can be used to represent or store other values or objects. We will use the assignment operator <- to 'assign' a value (or object) to a given word (or letter). Run the following commands to see how this works (don't worry about the comments, these are for your understanding):

```
## assign to x the value 5
x <- 5

## print the value assigned to the
## variable x to the screen
x
```

```
## [1] 5
```

```
## we can also assign text to a variable
y <- "Hello There"

## print y
y
```

```
## [1] "Hello There"
```

```
## we can re-assign variables
y <- sqrt(10)

## or assign a variable in terms
## of other variables
ziggy <- x + y

## print variable "ziggy"
ziggy
```

```
## [1] 8.162278
```

You will notice that as we create each of these variables, they begin to appear in the **environment** pane in the top right-hand side of the RStudio window. This shows the current R **workspace**, which is a collection of objects that R stores in memory. We can remove objects from the workspace using the `rm()` function e.g.

```
## remove the variables x and y
rm(x, y)
```

Notice that `x` and `y` have now disappeared from the workspace. The variable `ziggy` still contains the correct answer though (these are not ***relative*** objects, such as the macros assigned in a program like Excel).

```
ziggy
```

```
## [1] 8.162278
```

Another way of visualising the working directory is to use the `ls()` function, which lists all objects currently in the workspace e.g.

```
ls()
```

```
## [1] "ziggy"
```

> Note
>
> Names of variables can be chosen quite freely in R. They can be built from letters, digits and other characters, such as `_`. They can't, however, start with a digit or a `.` followed by a digit. Names are **case sensitive** and so `height` is a different variable from `Height`. Try to choose **informative** variable names where possible (`height` is more informative than `x` when talking about heights for example).
>
> **Don't use spaces in variable names**. Underscores are much safer[a]. Try to avoid using long words (since you will have to type them out each time you want to access the corresponding elements—although RStudio does have *autocomplete* functionality). Often I will try to convert as much to lower case as possible. If you do need to include multiple words try to use an underscore `_` (e.g. `child_heights`), or some people prefer to use something like CamelCase (e.g. `childHeights` or `ChildHeights`). Use whatever you prefer but try to be **consistent**.
>
> [a] some people also use dots, e.g. `child.heights`, but in general I would avoid this, since dots are often used when working with functions of specific classes such as `print.lm()`

2.2 Functions in R

Next we need to understand how to do more complicated things in R. For this we need functions. This section illustrates how R's inbuilt functions work. Most commands that are used in R require the use of functions. These are very similar to mathematical functions (such as `log(x)`), in that they require both the name of the function (i.e. `log`) and some **arguments** (i.e. `x`). However a lot of functions in R have multiple arguments which can be of completely different types.

The format is that a function name is followed by a set of parentheses containing the arguments. For example, if we type `seq(0, 3, 0.5)`, the function name is `seq` and the specified arguments are `0`, `3` and `0.5`. `seq()` is an inbuilt R function that generates sequences of numbers, and we're going to continue to use it to illustrate how functions work. Try typing in the command:

```
seq(0, 3, 0.5)
```

```
## [1] 0.0 0.5 1.0 1.5 2.0 2.5 3.0
```

You can see that this function produces a sequence that starts at 0, ends at 3 and has steps of 0.5. Spaces before the parentheses or between the arguments are not important when writing functions so `seq(0,3,0.5)` will work just as well as `seq (0, 3, 0.5)`. However, as stated earlier, I think spaces in sensible places can make the code much more legible i.e. `seq(0, 3, 0.5)` is better than either of the previous options.

All functions in R have **defaults** for the majority of their arguments (some functions have dozens of arguments, and having default values avoids you having to specify them all every time you use the function). For example, the `seq()` function has the following four main arguments (in this order):

Argument	Description
`from, to`	the starting and (maximal) end values of the sequence. Of length 1 unless just `from` is supplied as an unnamed argument.
`by`	number: increment of the sequence.
`length.out`	desired length of the sequence. A non-negative number, which for seq and seq.int will be rounded up if fractional.
`along.with`	take the length from the length of this argument.

When we write `seq(0, 3, 0.5)` R assumes that the first argument corresponds to `from`, the second argument corresponds to `to` and the third argument corresponds to `by`. This is known as **positional matching**. This means that `seq(0, 3, 0.5)` will produce a vector consisting of the sequence of numbers starting at 0, ending at 3 by adding 0.5 each time. If we write `seq(10, 0, 0.5)`, then R will attempt to create a sequence starting at 10, ending at 0 by adding 0.5 each time.

Task 2

Try typing `seq(10, 0, 0.5)`. R returns an error. Why?

Show: Solution on P159

The other type of matching is called **named matching** and this would allow you to write `seq(from = 0, to = 3, by = 0.5)` or `seq(to = 3, from = 0, by = 0.5)` as equivalent function commands (i.e. the **order** of the arguments **doesn't matter** if using *named* matching).

Using named matching also allows us to access the other argument: `length.out` if we wanted to use it, though you should recognise that you cannot, in general, use all four arguments in this case to specify a vector. (Why not, do you think?)

In fact, this command needs three arguments to work, and it doesn't matter which three of the four arguments you use. To find out what arguments a function can take and what they mean use the `?FUNCTION` syntax (where you replace `FUNCTION` with whichever function you're interested in e.g. `?seq` or `?atan`). This will open the internal R help file for the function. The **Help** section of these notes contains detailed information on these help files.

Being able to access these internal help files will be of particular help for all of the statistical functions we will want to use which generally have many arguments.

Task 3

Use the R function `seq()` to create the following sequences:

1. 2, 4, 6, ..., 30.
2. A sequence of 14 numbers starting at -2.5 and ending at 15.34.
3. A sequence of 7 numbers starting at 0, increasing in increments of 0.04.
4. A sequence starting at 101, ending at -20, in decrements of 11.

Show: Solution on P159

2.2.1 Nesting functions

A useful feature of R is its ability to **nest** functions. This can help make the code more concise and avoids the need to create lots of temporary variables. Nonetheless, if used too extensively then this can render code difficult to interpret, so a balance is necessary. For example,

```
exp(sqrt(10))
```

```
## [1] 23.62434
```

This is a simple nested function, since `sqrt(10)` produces a single number, which is then used as an argument to the `exp()` function. Mathematically, this gives $e^{\sqrt{10}}$. We could have also done this in two steps, but this would have involved creating a temporary variable to store the result of the sum:

```
x <- sqrt(10)
exp(x)
```

```
## [1] 23.62434
```

To understand nested functions, think about evaluating the **inner** functions first, seeing what they output and then how that slots into the next function. We will see more examples of this later.

2.3 Help files

It is a requirement of R packages that any function made available to an end user as part of a package must be documented in a **help file**. As such, the `?` command is simply a way to get more information on any given function. For example, if you wanted to know more about how to use the `hist` function (this function is used for plotting histograms), then you could type:

```
?hist
```

This will produce something like Figure 2.1 to appear in the in the bottom-right pane.

This new window contains all of the information you need to understand how to use the `hist()` function. Although these help files can seem daunting at first, once you get used to them they will provide the route for your continued exploration of R. Help files provide all of the details that the author of the command

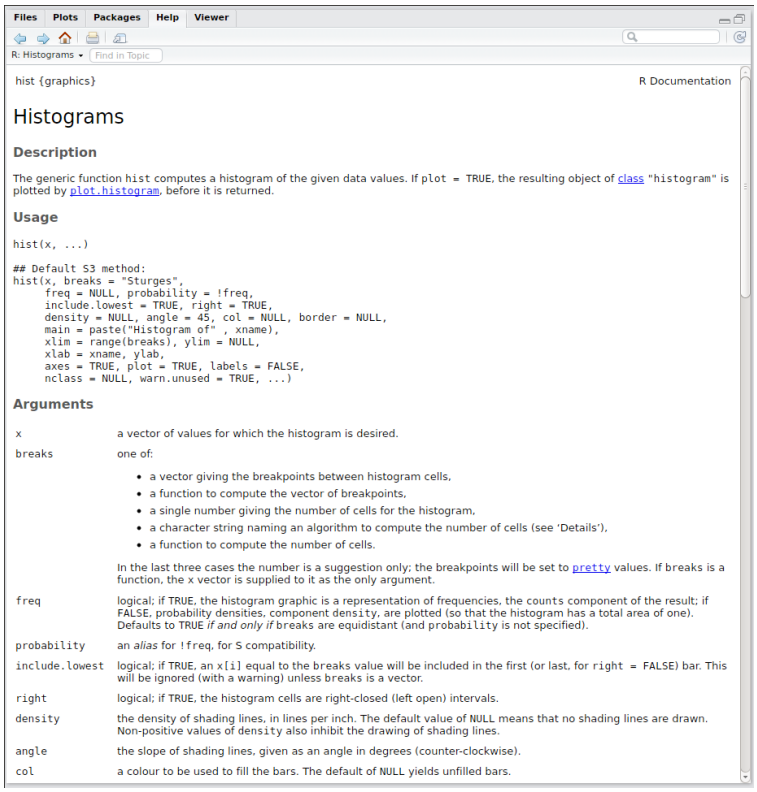

Figure 2.1: Help file for the 'hist()' function

saw fit to include. They all aim to be comprehensive but some authors assume that you are more familiar with what's going on than others. Most help files will have the following sections:

Table 2.2: General structure of R helpfiles

Section	Description
Usage:	This will show you the minimum required arguments and also what the default value are for each of the optional arguments. In this case only **x** is a required argument and all of the others are optional.
Arguments:	This gives an explanation of what each argument does and what sort of data type it should be. In this case the argument **x** needs to be a numerical vector.
Details:	This section tells you what the function should do along with any subtleties in its usage or clarifications.
Value:	This tells you what actually happens when you run the function and specifically what sort of R object the function produces. In this case it produces a special **histogram** object (which is actually just a normal list with certain specific components).
References:	This gives you some selected text books that the author feels explains the theory behind the function in greater detail.
See Also:	This should be a list of other R commands that are related to the current function. They might be of more use to you, or their help files might be better written and clarify what you're trying to do.
Examples:	This should be a set of R commands that you can copy-and-paste into either a script file or the console pane. These should give you a practical example of how to use the function in several different settings.

If you're really stuck, there is an international community of R users who regularly post questions and answers on advanced topics on sites like StackOverFlow. I tend to succeed mostly by Googling the problem. For example, Googling 'R importing data' finds me this rather excellent tutorial: http://www.r-tutor.com/r-introduction/data-frame/data-import.

2.4 Objects in R

R defines various types of object (and allows you to define your own if you so wish). We will explore the most common object types below.

2.4.1 Vectors

Vectors are fundamental R objects. In fact, we have already seen them at work in earlier examples. For instance, notice that if we type the number `10` into the command prompt, the output when R prints this to the screen is prefixed with a `[1]`:

```
10
```

```
## [1] 10
```

This shows that the output is a **vector**. (The `[1]` in the output shows that the object is of one **dimension**. Confusingly, the `1` corresponds to the element of the vector that is first printed to the screen—so here `10` is element `1` of the vector. The fact that it has one dimension can be seen by the fact that there is only one number in the square brackets. A 2-dimensional object like a matrix, would have e.g. `[1, ]`, as we will see later.) If we had a long vector, e.g.

```
seq(1, 100, by = 2)
```

```
##  [1]  1  3  5  7  9 11 13 15 17 19 21 23 25 27 29 31 33 35 37 39 41 43 45 47 49
## [26] 51 53 55 57 59 61 63 65 67 69 71 73 75 77 79 81 83 85 87 89 91 93 95 97 99
```

then when we print to the screen the vector is split up, and we can see that the first element is `1`, and the twenty-sixth element is `51` etc.

The `ziggy` variable we created earlier is also a vector of length 1:

```
ziggy
```

```
## [1] 8.162278
```

Note that vectors do not have to be numerical in value e.g.

```
"somewords"
```

```
## [1] "somewords"
```

is also a vector of length 1. R distinguishes between different 'types' of vector, with the four main types being:

- `numeric` where each element is a number (either integer or decimal);
- `character` where each element is a word or letter;
- `factor` where each element is a word or letter, but with some additional "grouping" information;
- `logical` where each element is either `TRUE` or `FALSE`.

In this section we will look at several different commands which produce vectors and then see how we can manipulate these objects in R.

2.4.1.1 Creating vectors

Probably the most common ways of creating vectors are to use the `c()`, `seq()` and `:` commands. Of these, `:` creates integer sequences, `seq()` creates structured sequences (only useful for numeric vectors), and `c()` is short-hand for *concatenate*, and it binds together all of the elements that you put inside the brackets to make a single vector.

Run the following commands to see how we can create different types of vectors:

```
1:5
6:2
```

```
## [1] 1 2 3 4 5
## [1] 6 5 4 3 2
```

Notice that brackets can be important, for example, note the differences below.

```
-4:1
-(4:1)
```

```
## [1] -4 -3 -2 -1  0  1
## [1] -4 -3 -2 -1
```

The first line above creates an integer sequence from -4 to 1, and the second creates one from -4 to -1. The `seq()` command we saw earlier, and here are some more examples:

```
seq(0, 1, by = 0.1)
seq(0, 1, length = 6)
seq(10, 5, by = -0.5)
```

```
##  [1] 0.0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1.0
## [1] 0.0 0.2 0.4 0.6 0.8 1.0
##  [1] 10.0  9.5  9.0  8.5  8.0  7.5  7.0  6.5  6.0  5.5  5.0
```

The `c()` function is very useful for concatenating non-sequential numbers or vectors of other data types e.g.

```
c(1, 3, 5, 7)
c(0.1, -6, 1, 0)
c("bob", "sam", "ted")
```

```
## [1] 1 3 5 7
## [1]  0.1 -6.0  1.0  0.0
## [1] "bob" "sam" "ted"
```

> **Note**
>
> Notice that we needed to use double-quotes to signify `character` types e.g. `c("bob", "sam", "ted")`. Note that R does not distinguish between single or double-quotes, so `c('bob', 'sam', 'ted')` would have worked equally well.

If you forget the quotes (e.g. `c(bob, sam, ted)`) then R would instead have looked for three **objects** called `bob`, `sam` and `ted` and tried to concatenate these together. If these objects do not exist, then R will return an error:

```
c(bob, sam, ted)
```

```
## Error in eval(expr, envir, enclos): object 'bob' not found
```

To this end, it is worth noting that we can also use `c()` to concatenate objects that are of the same type together. For example:

```
c(1, -6, ziggy)
```

```
## [1]  1.000000 -6.000000  8.162278
```

```
c(ziggy, seq(3, 6, length = 5))
```

```
## [1] 8.162278 3.000000 3.750000 4.500000 5.250000 6.000000
```

(In the example above we have used **nested** functions to make the code more concise.) If we try to concatenate objects of a different type, R will either return an error, or it will convert one of the objects into the same class as the other. For example,

```
c(c("bob", "sam", "ted"), ziggy)
```

```
## [1] "bob"              "sam"              "ted"              "8.16227766016838"
```

(Here we use **nested** `c()` functions to first create a `character` vector out of the strings `"bob"`, `"sam"` and `"ted"`, and then to concatenate this with the object `ziggy`.) Notice that the concatenated vector is a `character` vector (notice the **double-quotes** around `"8.16227766016838"`), indicating that R has converted the elements of `ziggy` into `characters` in order to concatenate them with a `character` vector.

> **Note**
>
> R will always convert to the most complex object type: so a combination of `character` and `numeric` values will be converted to a `character`.

Notice that R has not changed the value of the object `ziggy`—if we print `ziggy` to the screen we can see it is still a `numeric` vector:

```
ziggy
```

```
## [1] 8.162278
```

Rather, it created a copy of `ziggy` which it converted into a `character` before concatenating. In order to change the value of an object permanently, we need to reassign the object. For example, the function `as.character()` will convert a `numeric` vector into a `character` vector without changing the object e.g.

```
as.character(ziggy)
```

```
## [1] "8.16227766016838"
```

```
ziggy
```

```
## [1] 8.162278
```

To reassign it we can pass the output of the function and overwrite the original object using the assignment operator `<-` e.g.

```
ziggy <- as.character(ziggy)
ziggy
```

```
## [1] "8.16227766016838"
```

We can see that now the object `ziggy` has been changed to a `character` permanently.

You can also create "empty" vectors of specific lengths by using e.g. `numeric()`, `character()`, `logical()` functions. For example, to create an empty vectors of length 10 say, then you can use e.g.

```
y <- numeric(10)
y
```

```
##  [1] 0 0 0 0 0 0 0 0 0 0
```

```
y <- character(10)
y
```

```
##  [1] "" "" "" "" "" "" "" "" "" ""
```

```
y <- logical(10)
y
```

```
##  [1] FALSE FALSE FALSE FALSE FALSE FALSE FALSE FALSE FALSE FALSE
```

Note that these are not "empty" specifically, rather they have been filled with identical default values, however these are useful functions for creating objects that you can "fill-in" later on.

Task 4

Use the various vector creation commands to create the following sequences:

1. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11.
2. 2, 4, 6, 8, 10, … , 50.
3. All of the odd numbers from 17 through to 33.
4. The letters of the days of the week (i.e. M, T, W, T, F, S, S).

Show: Solution on P159

2.4.1.2 Subsetting and re-arranging vectors

If we only want to get at certain elements of a vector then we need to be able to subset the vector. In R, square brackets `[]` are used to get subsets of a vector.

Important

In R, objects are **indexed** such that the **first** element is element `1` (unlike C or Python for example, which indexes relative to `0`). In R the first element of `x` is `x[1]`, whereas in Python it would be `x[0]`.

Note also that in Python the command `x[-1]` would extract the **last** element of the vector `x`, whereas in R the `-` is used to **remove** elements; hence `x[-1]` would ***remove*** the **first** element of `x`.

Task 5

Copy the following commands into your script file and then run them in order to see how this works. Annotate each line using comments to describe what it is doing.

```
x <- 1:5
x[3]
x[c(2, 3, 4)]
x[1] <- 17
x[-3]
w <- x[-3]
y <- c(1, 5, 2, 4, 7)
y[-c(3, 5)]
y[c(1, 4, 5)]
i <- 1:3
y[i]
z <- c(9, 10, 11)
y[i] <- z
```

Show: Solution on P160

Task 6

Can you work out what the following functions do?

1. `order(y)`
2. `rev(y)`
3. `sort(y)`

Can you work out a way to sort `y` into decreasing order?

Show: Solution on P161

2.4.1.3 Element-wise (or vectorised) operations

R performs most operations on vectors **element-wise** , meaning that it performs each calculation on each element of a vector or array **independently** of the other elements. This can make for very fast manipulation of large data sets.

Aside

R is a **high-level** language, meaning that it is built on **low-level** languages, in this case C and Fortran. In C, if we wish to apply a function to each element of an array, we need to write a loop. In R there are so-called **vectorised** functions, that will apply a function to each element of a vector or array. We will cover loops in R later on, but generally they are much slower than the equivalent loops in C or Fortran. The source code for vectorised functions are often written in C or Fortran and hence run much faster than writing a loop in native R code. In addition they make the code more concise. For simple functions the difference in run time is often too small to really notice, but for more complex or large-scale functions the difference in run time can be large. To this end, R also offers various ways of using C code within R functions. But that is beyond the scope of this workshop…

Task 7

Copy the following commands into your script file and then run them in order to see how this works. Annotate each line using comments to describe what it is doing.

```
y <- 1:10
y^2
log(y)
exp(y)
x <- c(5, 4, 3, 2, 1, 5, 4, 3, 2, 1)
x + y
x * y
z <- c(-1, 2.2, 10)
z + y
z * y
```

Show: Solution on P161

If you add or multiply vectors of different lengths then R automatically repeats the smaller vector to make it bigger. This generates a warning if the length of the smaller vector is not a divisor of the length of the longer vector. Division and subtraction work in the same way e.g.

```
c(1:6) * c(1:2)
```

```
## [1]  1  4  3  8  5 12
```

```
c(1:3) * c(1:2)
```

```
## Warning in c(1:3) * c(1:2): longer object length is not a multiple of shorter
## object length
```

```
## [1] 1 4 3
```

This is a useful property if the shorter vector is of length 1, in which case R multiplies each element of the longer vector by the scalar e.g.

```
c(1:3) * 2
```

```
## [1] 2 4 6
```

Important

You must be **very careful** with this. I only use this feature when multiplying a vector by a scalar; otherwise I will always generate vectors of the same length, since I think this makes explicit what you are trying to achieve. Hence instead of writing `c(1:6) * c(1:2)`, I would write `c(1:6) * rep(1:2, 3)`. (I personally would rather that R did not allow elementwise operations on vectors that are of different lengths, unless one of the lengths is one. However, it does, and so one should be careful…)

R will also perform **matrix multiplication** (e.g. dot products) on vectors, and this is described in a later section.

2.4.1.4 Logical vectors and conditional subsetting

Vectors can be created according to logical criteria using the following comparison operators:

Table 2.3: Logical operators

Operator	Definition
`!=`	not equal
`<`	less than
`<=`	less than or equal to
`>`	greater than
`>=`	greater than or equal to
`==`	logical equals
`|`	logical OR
`&`	logical AND
`!`	logical NOT

Task 8

Copy the following commands into your script file and then run them in order to see how this works. Annotate each line using comments to describe what it is doing.

```
x <- 1:10
y <- c(5, 4, 3, 2, 1, 5, 4, 3, 2, 1)
x < 4
x[x < 4]
y[x < 4]
y > 1 & y <= 4
y[y > 1 & y <= 4]
z <- y[y != 3]
```

Show: Solution on P162

Finally there are many commands that are specifically aimed at vectors or sets of data. The following is a small selection for reference purposes:

Table 2.4: Common R functions

Function	Description
`length(x)`	returns the length of vector `x` (i.e. the number of elements in `x`)
`names(x)`	get or set names of `x` (i.e. we can give names to the individual elements of `x` as well as just having them numbered)
`min(x)`	returns the smallest value in `x`
`max(x)`	returns the largest value in `x`
`median(x)`	returns the median of `x`
`range(x)`	returns a vector with the smallest and largest values in `x`
`sum(x)`	returns the sum of values in `x`
`mean(x)`	returns the mean of values in `x`
`sd(x)`	returns the standard deviation of `x`
`var(x)`	returns the variance of `x`
`diff(x)`	returns a vector with all of the differences between subsequent values of `x`. This vector is of length 1 less than the length of `x`
`summary(x)`	returns different types of summary output depending on the type of variable stored in `x`

Task 9

Now that we know about **elementwise** operations, try to understand the nested function `sum(sqrt(log(seq(1, 10, by = 0.5))))`. To help with this, try to write this out in a series of steps and figure out what is returned at each stage of the nesting, and how this is passed to the next function.

Show: Solution on P163

2.4.1.5 Factors

We have seen that we can create `character` vectors. These are collections of strings, but with no further information. For example, if I try to summarise a character vector, R returns no useful information:

```
x <- c("bob", "sam", "ted")
summary(x)
```

```
##    Length     Class      Mode
##         3 character character
```

A `factor` is simply a character vector with some additional "grouping" information attached. For example,

```
x <- factor(c("bob", "sam", "ted"))
x
```

```
## [1] bob sam ted
## Levels: bob sam ted
```

```
summary(x)
```

```
## bob sam ted
##   1   1   1
```

Now the `x` object has grouped together all elements of the vector that share the same name (called the `levels` of the factor), and the `summary()` function tells us how many entries there are for each level. The `levels()` function will return the levels of a factor:

```
levels(x)
```

```
## [1] "bob" "sam" "ted"
```

R coerces `characters` to `factors` in **lexicographical order**. If you wish to set specific `levels`, then you can add a `levels` argument to the `factor()` function.

Task 10

Copy the following commands into your script file and then run them in order to see how this works. Annotate each line using comments to describe what it is doing.

```
y <- c(5, 4, 3, 2, 10, 5, 4, 3, 2, 1)
factor(y)
factor(y, levels = 1:10)
y <- as.character(c(5, 4, 3, 2, 10, 5, 4, 3, 2, 1))
factor(y)
factor(y, levels = sort(unique(as.numeric(y))))
y <- c("low", "mid", "mid", "high", "low")
factor(y)
factor(y, levels = c("low", "mid", "high"))
```

Show: Solution on P164

`factor` objects are incredibly useful when working with data, since they essentially code up **categorical** variables, though care must be taken when manipulating them. We explore the use `factor` objects in more detail in a later section and care must be taken when converting between factors and other types.

2.4.2 Conversions between object types

Before we progress to other objects, we should have a brief aside to talk about conversion between types. So far we have introduced `numeric` vectors, which store numerical values (note that R makes no distinction between `integer` or `double` types, like C or Python do). We have also seen `character` types, which store strings, and `factor` types that store strings with additional grouping information attached. We have also seen `logical` types, which simply store `TRUE` or `FALSE` values.

It is possible to convert between these different forms, using an `as.TYPE()` function (where `TYPE` is replaced with the correct type of interest). For example, we can easily convert numbers to characters:

```
x <- c(0, 1, 3, 10, 0, 4)
x
```

```
## [1]  0  1  3 10  0  4
```

```
as.character(x)
```

```
## [1] "0"  "1"  "3"  "10" "0"  "4"
```

(Notice the double-quotes around the elements of the converted vectors.) They can also easily be converted into factors (if you want to set the levels of the factor specifically, then you can use the `factor()` function as described earlier):

```
factor(x)
```

```
## [1] 0  1  3  10 0  4
## Levels: 0 1 3 4 10
```

We can also convert numbers to logical strings, in which case R converts `0` values to `FALSE` and anything else to `TRUE`. Hence,

```
as.logical(x)
```

```
## [1] FALSE  TRUE  TRUE  TRUE FALSE  TRUE
```

Conversions of `logical` vectors to `numeric` vectors results in `TRUE` values becoming `1` and `FALSE` values becoming `0`.

R can also convert characters to numbers, but only if the conversion makes sense. For example,

```
y <- c("10", "2", "8")
y
```

```
## [1] "10" "2"  "8"
```

```
as.numeric(y)
```

```
## [1] 10  2  8
```

If the conversion doesn't make sense, then R will return a **missing value** (`NA`) and print a warning:

```
y <- c("10", "2", "bob")
as.numeric(y)
```

```
## Warning: NAs introduced by coercion
```

```
## [1] 10  2 NA
```

Factors are tricky little blighters! Superficially they can look like `numeric` types when printed to the screen, but in fact they are named **groups**, and as such if we convert a `factor` to a `numeric`, then R converts according to the **level** of the factor:

```
y <- factor(c("10", "2", "8"))
y
```

```
## [1] 10 2  8
## Levels: 10 2 8
```

```
as.numeric(y)
```

```
## [1] 1 2 3
```

Notice that this returns 1, 2, 3 rather than 10, 2, 8.

If a `factor` holds a numerical value you wish to convert directly, then you must convert the factor to a `character` first (for which you can often use nested functions to do) e.g.

```
y <- factor(c("10", "2", "8"))
as.numeric(y)
```

```
## [1] 1 2 3
```

```
as.numeric(as.character(y))
```

```
## [1] 10  2  8
```

Conversions to `character` types are straightforward in any case, using `as.character()`. Conversions of `characters` or `factors` to `logical` types will produce missing values (`NA`).

2.4.3 Matrices

Matrices are another way of storing data in R. They can be thought of as 2D versions of vectors; a single structured group of numbers or words arranged in both rows and columns. Each element of the matrix is numbered according to the row and column it is in (starting from the top-left corner). The size of the matrix is given as two numbers which specify the number of rows and columns it has. The size is referred to as the **dimension** of the matrix.

The simplest way of creating a matrix in R is to use the `matrix()` function.

Task 11

Copy the following commands into your script file and then run them in order to see how this works. Annotate each line using comments to describe what it is doing.

```
matrix(1:4, 2, 2)
matrix(1:4, 2, 2, byrow = TRUE)
matrix(0, 3, 4)
```

Show: Solution on P164

Like vectors, matrices can also contain `character` values e.g.

```
matrix(letters[1:9], 3, 3)
```

```
##      [,1] [,2] [,3]
## [1,] "a"  "d"  "g"
## [2,] "b"  "e"  "h"
## [3,] "c"  "f"  "i"
```

Note

All elements of a `matrix` must be of the same type. You can have a `numeric` matrix, or a `character` matrix, but not a mixture. If you try to specify a mixture then R will convert all entries to the most complex type, which can lead to unexpected consequences unless you are careful!

2.4.3.1 Subsetting matrices

Getting access to elements of a matrix follows on naturally from getting access to elements of a vector. In the case of a matrix though you must specify both the row and column of the element that you want, using the format `[ROW, COL]`.

Task 12

Copy the following commands into your script file and then run them in order to see how this works. Annotate each line using comments to describe what it is doing.

```
vals <- c(1, 2, 3, 4, 5, 0.5, 2, 6, 0, 1, 1, 0)
mat <- matrix(vals, 4, 3)
mat[2, 3]
mat[1, ]
mat[, 3]
mat[-2, ]
mat[c(1, 3), c(2, 3)]
```

Show: Solution on P165

2.4.3.2 Creating matrices

As well as using the `matrix()` function, we can also create matrices by binding together several vectors (or other matrices). We use two commands here: `cbind()` and `rbind()`.

Task 13

Copy the following commands into your script file and then run them in order to see how this works. Annotate each line using comments to describe what it is doing.

```
x1 <- 1:3
x2 <- c(7, 5, 6)
x3 <- c(12, 19, 25)
cbind(x1, x2, x3)
rbind(x1, x2, x3)
```

Show: Solution on P165

Some useful commands for matrices are listed in Table 2.5.

Table 2.5: Useful `matrix` commands in R

Function	Example	Description
`matrix()`	`matrix(0, 3, 4)`	Creates a (3×4) matrix filled with zeros
`dim()`	`dim(mat)`	Returns the dimensions of a matrix `mat` in the form (rows $\times$ columns)
`t()`	`t(mat)`	Transpose a matrix `mat`
`rownames()`	`rownames(mat)`	Returns or sets a vector of row names for a matrix `mat`
`colnames()`	`colnames(mat)`	Returns or sets a vector of column names for a matrix `mat`
`cbind()`	`cbind(v1, v2)`	Binds vectors or matrices together by column
`rbind()`	`rbind(v1, v2)`	Binds vectors or matrices together by row

2.4.3.3 Elementwise operations

Elementwise operations also work similarly to vectors, though even more care must be taken when the vectors have different lengths.

Task 14

Copy the following commands into your script file and then run them in order to see how this works. Annotate each line using comments to describe what it is doing.

```
x <- matrix(1:9, 3, 3)
x
x * 2
x * c(1:3)
```

Show: Solution on P166

2.4.3.4 Matrix multiplication

Another key aspect of matrix manipulation that is required for many algorithms is **matrix multiplication**. R does this by using the `%*%` syntax. Note the differences between **matrix multiplication** and **elementwise multiplication**:

```
x <- matrix(1:9, 3, 3)

## matrix multiplication
x %*% x
```

```
##      [,1] [,2] [,3]
## [1,]   30   66  102
## [2,]   36   81  126
## [3,]   42   96  150
```

```
## elementwise multiplication
x * x
```

```
##      [,1] [,2] [,3]
## [1,]    1   16   49
## [2,]    4   25   64
## [3,]    9   36   81
```

Matrix multiplication also works with vectors. In this case the vector will be promoted to either a row or column matrix to make the two arguments conformable. If two vectors are of the same length, it will return the inner (or dot) product (as a matrix). Compare the following (taking note of the comments):

```
## setup a vector of length 3
x <- 1:3

## conduct elementwise multiplication
x * x
```

```
## [1] 1 4 9
```

```
## return matrix multiplication of (1 x 3) and (3 x 1) matrix
t(x) %*% x
```

```
##      [,1]
## [1,]   14
```

```
## matrix multiplication of (3 x 1) and (1 x 3) matrix
x %*% t(x)
```

```
##      [,1] [,2] [,3]
## [1,]    1    2    3
## [2,]    2    4    6
## [3,]    3    6    9
```

```
## create new vector
y <- 5:6

## return matrix multiplication of (3 x 1) and (1 x 2) matrix
x %*% t(y)
```

```
##      [,1] [,2]
## [1,]    5    6
## [2,]   10   12
## [3,]   15   18
```

```
## set up some new matrices
x <- matrix(1:6, 3, 2)
y <- matrix(1:8, 2, 4)

## return matrix multiplication of (3 x 2) and (2 x 4) matrix
x %*% y
```

```
##      [,1] [,2] [,3] [,4]
## [1,]    9   19   29   39
## [2,]   12   26   40   54
## [3,]   15   33   51   69
```

2.4.4 Lists

An R list is an object consisting of an ordered collection of objects known as its components (or elements). There is no particular need for the components to be of the same type (unlike vectors), and, for example, a list could consist of a numeric vector, a logical value, a matrix, a complex vector, a character array, and so on.

The following command creates a list object called `simpsons`, with four components: the first two are character strings, the third is an integer, and the fourth component is a numerical vector. Try creating a list as follows:

```
simpsons <- list(
    father = "Homer",
    mother = "Marge",
    no_children = 3,
    child_ages = c(10, 8, 1)
)
```

The components of a list are always numbered and may always be referred to as such. Thus with `simpsons` above, its components may be individually referred to as `simpsons[[1]]`, `simpsons[[2]]`, `simpsons[[3]]` and `simpsons[[4]]`. Since `simpsons[[4]]` is a ***vector***, we can access the elements of the vector using the `[]` notation (i.e. `simpsons[[4]][1]` is its first element).

The command `length(simpsons)` gives the number of components it has, in this case four.

The components of lists may also be named (here the names are `father`, `mother`, `no_children` and `child_ages`) and in this case the component may be referred to either by giving the component name as a character string in place of the number in double square brackets i.e. `simpsons[["father"]]` (note the double-quotes), or, more conveniently, by giving an expression of the form `simpsons$father` (note no double-quotes, since `father` is an object contained within `simpsons`).

This means that the following will all return the first component of the list `simpsons`:

```
simpsons[[1]]
```

```
## [1] "Homer"
```

```
simpsons[["father"]]
```

```
## [1] "Homer"
```

```
simpsons$father
```

```
## [1] "Homer"
```

The command `names(simpsons)` will return a vector of the component names of the list `simpsons`:

```
names(simpsons)
```

```
## [1] "father"      "mother"      "no_children" "child_ages"
```

Note the strange double square bracket notation. We can also subset a list using single square brackets, though the returned object is different. For example, typing

```
simpsons[1]
```

```
## $father
## [1] "Homer"
```

```
is.list(simpsons[1])
```

```
## [1] TRUE
```

returns a `list` object, of length 1, where the first element of the list is called `father` and is a `character` vector. Using double square brackets returns the `character` vector itself i.e.

```
simpsons[[1]]
```

```
## [1] "Homer"
```

```
is.list(simpsons[[1]])
```

```
## [1] FALSE
```

Sometimes we might wish to extract certain components of a list, but keep a list structure, for example

```
simpsons[c(1, 3)]
```

```
## $father
## [1] "Homer"
##
## $no_children
## [1] 3
```

produces a `list` of length 2, containing two components: the first is a `character` vector called `father`, and the second is a `numeric` vector called `no_children`.

Lists can be useful ways of collecting together a wide range of different bits of information that are all related. R naturally uses lists in a variety of situations but most commonly they are produced as a result of a function call. (In fact most custom classes in R are essentially lists, but with specific methods associated with that class e.g. `plot` or `summary` functions for example).

2.4.5 Data frames

A `data.frame` object is a special type of list where all of the components are in some sense the same size. The simplest form of `data.frame` consists of a list of vectors all of the same length, but not necessarily of the same type (`numeric`, `character` or `logical`). In this case a `data.frame` object may be regarded as a matrix with columns for each vector. It can be displayed in a matrix layout, and the data in its rows and columns extracted using the matrix subsetting notation (`[ROWS, COLS]`). (However, because it is also a special type of `list`, we can also extract columns by using the `DFNAME$COLNAME` notation, where `DFNAME` is the name of the `data.frame` of interest, and `COLNAME` is the name of a specific column. The `[[]]` notation also works for `data.frame` objects.)

The important difference (to R at least) between a `matrix` object and a `data.frame` object that only contains `numeric` vectors, is that R thinks of the matrix as a single object, but it thinks of the `data.frame` as several connected, but distinct objects. (To the user it can be hard to distinguish between objects, and the commands `is.matrix()`, `is.list()` and `is.data.frame()` will return `TRUE` or `FALSE` depending on whether an object is a `matrix`, a `list` or `data.frame` respectively.)

Note

`data.frames` are very important for statistical analysis, as they frequently fit the form of available data. They are so important in fact that a lot of statistical functions actually expect this.

2.5 Reading in data

Most data are stored in e.g. Excel files. Although some packages allow Excel files to be read directly into R, it is (in my opinion) much better practice to save the data as a **text file**, since this strips out unnecessary formatting and results in smaller file that can be universally used by any end user. Excel also has lots of other problems; see e.g. here for various examples.

Aside

You can save Excel spreadsheets as comma-separated text files using e.g. *File > Save As > ...*, then from the 'Save as type' options choose 'CSV (comma separated)'. There is no need to add a suffix, because Excel will automatically add `.csv` to your file name.

`.csv` files can be read into R directly as `data.frame` objects, using the `read.csv()` function.

A `.csv` file is simply a text file where each element is separated by a comma (the delimiter). This can be easily viewed and manipulated in any text editor (such as Notepad). Many R users prefer to use 'Text – Tab delimited' data files. In this case each entry is delimited by a tab. In fact, one can use any delimiter one prefers, but I often prefer commas, which are so common they have their own suffix! If you choose the tab-delimited route, you have to be **extra careful** about spaces between words in your spreadsheet, and to read the data file into R you should use `read.table()` instead of `read.csv()` (where you can explicitly specify the delimiter as an argument to the function). This is similarly true if using `.csv` files: one must be careful not to include entries with commas in them.

Note: `read.csv()` might fail if there are any spaces between words within data cells. If this happens, replace all these spaces by underscores `_` before saving the spreadsheet in Excel.

In fact, it is good practice to store your data in a much simpler way than many people are used to. Generally, try to avoid spaces between words at all in your data, even in column headers. Underscores are much safer. Try to avoid using long words (since you will have to type them out each time you want to access the corresponding elements), and often I will try to convert as much to lower case as possible (since R is case sensitive, so it speeds up your typing).

2.5.1 Example: sexual reproduction in fruitflies

These are data from Partridge and Farquhar (1981), when at the time the paper was published the cost of increased reproduction in terms of reduced longevity had been shown for female fruitflies, but not for males. The authors set up an experiment that used a factorial design to assess whether increased sexual activity affected the lifespan of male fruitflies.

The flies used were an outbred stock. Sexual activity was manipulated by supplying individual males with one or eight receptive virgin females per day. The longevity of these males was compared with that of two control types. The first control consisted of two sets of individual males kept with one or eight newly inseminated females. Newly inseminated females will not usually remate for at least two days, and thus served as a control for any effect of competition with the male for food or space. The second control was a set of individual males kept with no females. There were 25 males in each of the five groups, which were treated identically in number of anaesthetisations (using CO_2) and provision of fresh food medium.

The data should have the following columns:

- **partners**: number of companions (0, 1 or 8).
- **partner type**: type of companion (inseminated female; virgin female; control (when 'partners = 0')).
- **longevity**: lifespan, in days.
- **thorax**: length of thorax, in mm.

The file `ff.csv` contains the data from this experiment. Download this data set to your working directory. (You can view this file in a text editor if you so wish.) We can load this into R using the `read.csv()` function, here storing the resulting `data.frame` as an R object called `ff`:

```
ff <- read.csv("ff.csv")
```

> **Note**
>
> If R can't find the file, check it's in the working directory, or pass the full path to `read.csv()`.

```
head(ff)
```

```
##   partners partner.type longevity thorax
## 1        8  Inseminated        35   0.64
## 2        8  Inseminated        37   0.68
## 3        8  Inseminated        49   0.68
## 4        8  Inseminated        46   0.72
## 5        8  Inseminated        63   0.72
## 6        8  Inseminated        39   0.76
```

```
summary(ff)
```

```
##     partners   partner.type         longevity        thorax
##  Min.   :0.0   Length:125         Min.   :16.00   Min.   :0.640
##  1st Qu.:1.0   Class :character   1st Qu.:46.00   1st Qu.:0.760
##  Median :1.0   Mode  :character   Median :58.00   Median :0.840
##  Mean   :3.6                      Mean   :57.44   Mean   :0.821
##  3rd Qu.:8.0                      3rd Qu.:70.00   3rd Qu.:0.880
##  Max.   :8.0                      Max.   :97.00   Max.   :0.940
```

Looking at the data we can see a number of things:

- Since the original data had spaces in the column names, these spaces have been replaced by dots.
- Columns that can be converted into numbers in sensible ways are stored as such (e.g. the `thorax` column). You can tell this because the `summary()` function returns numerical summaries.
- Columns that can't be easily converted are stored as `character` columns (e.g. the `type` column). You can tell this because the `summary()` function returns no useful summaries for these columns except to say they are `character` columns[1].

These defaults can be useful sometimes for finding errors. For example, if a column of numbers contains a typo that prevents an entry from being converted to a number, then the whole column will be read in as a `character()`. Thus if you spot this you can often track down the typo and correct it. Please see the section on converting between types for further details on how to manually convert between types.

Important

It is a good idea to always check and read-in data to ensure each column is in the correct format before progressing any further with your analysis. A common error is that often categorical variables are coded as numbers. For example, a data set might contain numbers `0` or `1` to denote e.g. died/survived. In this case R will read the column in as a `numeric`, when it should be a `factor`. In this case you would want to manually convert your column to a `factor` before proceeding.

Task 15

Convert the `partners` column of the `ff` data frame into a `factor`. Do the same for `partner.type`. Produce a summary on the revised `ff` object. [**Hint**: you can do this by overwriting the relevant columns in `ff`.] What do you notice about the summary?

Show: Solution on P166

Objects saved as an `.rds` file can be read in and assigned to objects using the `readRDS()` function e.g.

```
## save worms data frame as an .rds file
saveRDS(ff, "ff.rds")

## read in as a new object
ff1 <- readRDS("ff.rds")
```

Here the new `ff1` object is identical to the original `ff` object. I often read in `.csv` files, clean them up into the correct formats, and then save as an `.rds` file for further analysis. Since the `.rds` file stores R objects directly, then reading in the `.rds` file means I don't have to do all the cleaning up again. For large data sets, the resulting `.rds` file can often be a much smaller file size than the original text file.

Alternative approaches can be found in other packages, and indeed a good package is `readr`, which is part of the `tidyverse` suite of packages—see here for a useful cheat sheet. Some other options can be found here.

Once we have data read in as a `data.frame` object, we can do all sorts of useful things with them, so-much-so that most of the rest of the module will be built around using these objects. As a little example, consider the ease with which we can produce a mean thorax length for control flies with just a short piece of code:

[1] note that in versions of R before R 4.0.0 these columns would have been automatically converted to `factor` columns. Whilst this is often a useful thing to do, it is much better now that R does not do this automatically and instead forces you to do this explicitly in your code so that it is documented.

```
## calculate mean thorax length for control flies
mean(ff$thorax[ff$partner.type == "Control"])
```

```
## [1] 0.836
```

We will see many more complex examples in coming practicals.

2.6 Saving outputs

R allows you to save various things, with regards to inputs we can save:

- the full history of all commands used in the current session—via `savehistory()`. This creates text files with '.Rhistory' suffixes.
- Individual script files (as text files with '.R' suffixes). We've already seen these.

With regards to outputs we can save:

- the current R workspace—via `save.image()`. This creates a **binary** file with a '.RData' suffix. This can be reloaded into R using the `load()` function, and includes all objects in the current workspace.
- A selection of objects—via the `save()` function. Here we can extract subsets of objects and save them. For example, `save(x, y, file = "practical1.RData")` will save only the objects `x` and `y` into a file called "practical1.RData". Alternatively a character vector of objects can be supplied e.g. `save(list = c("x", "y"), file = "practical1.RData")` will do the same thing as the previous command.
- A single object can be saved using `saveRDS()`. This saves into a binary file with a suffix '.rds'. This is really useful for saving single objects, often cleaned `data.frame` objects, which can be loaded into R without having to recreate from scratch again. For example, `saveRDS(x, "x.rds")` would save the `x` object into a file called "x.rds". This can be loaded into a new session via the `readRDS()` function. Another useful feature is that `readRDS()` can be used to pass the contents of a .rds file directly into an object of your choice e.g. `y <- readRDS("x.rds")` will create a new object called `y`, that contains the contents of the file "x.rds".

Part II

Programming

Chapter 3

Programming—Practical 1

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3.1 Getting started

Start a new RStudio session, set your current working directory, open a new R Script and save this (blank) script to a file with an appropriate name.

Use this script file to edit and keep copies of the code you write in this practical: you may find it useful be able to look back later.

3.2 Predicting the behaviour of for loops

We will use R to generate some data in the form of vectors and use these data to form some looping constructs. Predicting what code will do and testing your predictions by running the code should help cement your understanding of for loops.

Type the following code into your script. Remember that code after `#` is a comment and will be ignored by the R interpreter (you do not have to type these comments in for yourself, but you might want to if you think you will need to refer to them later).

```
a <- 1:10           # Assign the integers 1 to 10 in order to the vector a
print(a)            # Print a to the screen
b <- sample(a)      # Set b to be a with elements shuffled into random order
print(b)            # Print b to the screen
```

Run the code a few times either by sourcing it or by highlighting it in the script then pressing the run button in RStudio.

You should note that:

- The first line creates a new vector `a` with the elements 1 to 10 in order.
- The second line prints the vector `a` to the screen.
- The third line uses a built-in R function to sample (all of) the elements of the vector `a` without replacement (i.e. to permute the elements into a random order), and assigns the result to the vector `b`.
- The fourth line prints the vector `b`.

You should also note that the code gives a different result each time you run it, since repeating the `sample` command leads to `b` being set to a new permutation of `a`.

Task 16

Write down what you expect the output of the following code to be before verifying your answer by entering the code into your script and running it.

```
for (i in 1:10) {
    print(paste(i, a[i]))
}
```

Show: Solution on P166

Task 17

Write down what you expect the output of the following code to be before verifying your answer by entering the code into your script and running it.

```
for (i in 10:1) {
    print(paste(i, b[i]))
}
```

Show: Solution on P167

Task 18

Write down what you expect the output of the following code to be before verifying your answer by entering the code into your script and running it.

```
for (i in a) {
    print(paste(i, b[i]))
}
```

Show: Solution on P167

Task 19

Write down what you expect the output of the following code to be before verifying your answer by entering the code into your script and running it.

```
for (i in sample(a)) {
    print(paste(i, b[i]))
}
```

Show: Solution on P167

3.3 Writing a `for` loop

Adapt the code from the lecture to use a `for` loop to do the following:

Task 20

Print the 12 times table using a `for` loop, i.e. produce output of the form

- 1 times 12 is 12
- 2 times 12 is 24
- ...
- 12 times 12 is 144

Show: Solution on P168

3.4 Writing a `while` loop

Repeat the previous task using a `while` loop.

Task 21

Print the 12 times table using a `while` loop, i.e. produce output of the form

- 1 times 12 is 12
- 2 times 12 is 24
- ...
- 12 times 12 is 144

Show: Solution on P168

3.5 Using loops to do more complex calculations

3.5.1 A loop for which the number of iterations is known in advance

Enter the following code to your script and check you understand the output.

```
p <- 4
print(2^p)
p <- 5
print(p^3)
```

Now write code to answer the following question.

Task 22

What is the sum of the first 15 powers of 2 (i.e. $2^1 + 2^2 + \ldots 2^{15}$)?

Show: Solution on P169

3.5.2 A loop for which the number of iterations is not known in advance

Write code to answer the following question.

Task 23

What is the smallest power of 2 that is greater than 1,000,000?

Show: Solution on P169

3.6 Writing simple functions

Type the following code into your script and run it. Before you run it, think about whether you expect any output.

```
sayHello <- function() {
    print("Hello")
}
```

Type the following at the command prompt, but before you do so, predict what will happen.

```
sayHello()
```

Now type the following code into your script.

```
sayHelloWithArg <- function(whoTo) {
    print(paste("Hello", whoTo))
}
```

Task 24

Now type each of the following instructions into the command prompt. Before typing each line, predict what will happen.

```
sayHelloWithArg()
sayHelloWithArg
sayHelloWithArg("nik")
sayHello("nik")
sayHelloWithArg(nik)
sayHelloWithArg(whoto="nik")
sayHelloWithArg(whoTo="nik")
```

Show: Solution on P169

3.7 Predicting the behaviour of a function

For now, do not type in the following code, but instead just read it.

```
cat <- 2
canary <- 4
buster <- function(cat, canary) {
  cat <- cat*2
  canary <- canary*3
  return(cat + canary)
}
ghost <- buster(canary, -cat)
```

Task 25

Think carefully about what you expect the values of `cat`, `canary` and `ghost` to be after this code is executed and write down your answer. Now execute the code and test your prediction.

Show: Solution on P170

3.8 Return values from functions

The code in the box below does the following.

- Defines a function `mySum` that returns the sum of a vector.
- Creates a vector `x` containing 100 uniform random numbers between 0 and 1.
- Finds their sum using `mySum`.
- Finds their sum using the built-in R function `sum`.
- Prints out a comparison of the two values.

Type the code into your script and make sure you are happy with how it works.

```
mySum <- function(toSum) { # my function to sum elements of a vector
  retVal <- 0
  for(i in 1:length(toSum)) {
    retVal <- retVal + toSum[i]
  }
  return(retVal)
}

a <- runif(100)      # generate 100 uniform random numbers
myWay <- mySum(a)    # calculate sum using our mySum() function
rWay <- sum(a)       # calculate sum using built-in sum() function
print(paste("My answer", myWay, "... R answer", rWay))
```

Task 26

Use the function `mySum` as a base to write a new function `mySumAndMean`.

The new function should calculate the sum and the mean of whatever vector it receives as an input. It should return a vector: the first element of the output vector should be the sum, the second the mean. You might find the built-in function `mean` helpful to test your code.

Show: Solution on P170

3.9 Additional tasks for those with programming experience

The following tasks are mainly aimed at those of you who already have experience in programming.

3.9.1 Extended example one: Monte Carlo simulation

[Note this task is optional, and you should do it only if you have time]

When I was younger, I sometimes collected Panini football stickers.

The basic idea is very simple: you collect numbered stickers to stick into an album, continuing to buy stickers until you have the full set. The problem is that you don't know which stickers you are going to get until you open a packet. Each packet contains a random sample of the available stickers, and packets are sealed at the time of purchase. This means that as you get closer and closer to completing the album, it becomes more and more unlikely that any new packet will contain any stickers you need for your album.

At the time, it was a matter of significant regret for me that I never did complete the album for the Mexico '86 World Cup. That album required a total of 427 stickers.

Now, better trained in mathematics and computing, I wondered how many stickers I might have had to buy to be successful in my quest to complete the album?

We are going to write a simple "Monte Carlo" simulation to understand this. Monte Carlo simulations rely on random sampling to obtain an estimate of a random variable. You will be writing Monte Carlo simulations of stochastic epidemic models later in the course, so this is good practice.

We remove some of the complexity by considering a slightly simpler situation, in which stickers come in packets of one.

Note the built-in R function `sample` that was introduced earlier can in fact be called in other ways. Type the following into the command line and run it a few times

```
sample(1:200,3)
```

You should see that—when it is called with two arguments—the built-in R function `sample` no longer merely shuffles the whole of the vector that is its first argument, but instead randomly samples the number of elements given by the second argument from that vector (again without replacement). The above corresponds to randomly choosing a three numbers from the list of integers between 1 and 200.

Furthermore, note the behaviour of the built-in R function `rep` by typing the following in at the command line

```
rep(TRUE,4)
```

You should see that this line of code creates a vector of length 4 where all four elements are the logical value `TRUE`.

One way of writing a simulation of a single attempt to collect the entire album would be something like the code that follows. **However, this code contains a deliberate mistake.**

Task 27

Enter the code into your script, find the mistake, fix it, and run the code.

```
totStickers <- 427
gotSticker <- rep(FALSE,totStickers)
numLeft <- totStickers
numStickersBought <- 0
while(numLeft > 0) {
  numStickersBought <- numStickersBought + 1
  thisSticker <- sample(1:totStickers, 1)
  if(gotSticker[thisSticker] == TRUE) {
    gotSticker[thisSticker] <- TRUE
    numLeft <- numLeft - 1
    print(paste('got', thisSticker, 'still need', numLeft))
  }
}
print(paste('bought', numStickersBought))
```

Show: Solution on P170

Each time you run the fixed version of the code should lead to a different result. You can get an estimate of the average number of stickers that is required to complete the album by running the code lots of times, and averaging the result.

Task 28

Add a for loop around the code above to run 100 simulations of collecting an entire album, storing the number of stickers required in each simulation in a vector. Apply the function built-in R function `mean` to the vector to estimate the average number of stickers that must be bought to complete the album.

Show: Solution on P171

The expected value (i.e. mean) number of stickers that is required to complete an album of 427 stickers is in fact $427 \times H_{427}$, where H_{427} is the 427^{th} Harmonic number (the mathematics of this is explained in the info box below if you are interested).

It turns out that $H_{427} \approx 6.635$, and so the estimated mean is about 2,800 or so. This is a lot of stickers! The requisite number would be reduced in practice, because you are able swap duplicate stickers with your friends, as well as send off to Panini on a special form for a maximum of 50 stickers towards the end, but nevertheless, this simulation has explained my disappointment as a 9-year-old child!

Show: Relating sticker collecting to the harmonic numbers on P217

3.9.2 Extended example two: the logistic map

[Note this task is optional, and you should do it only if you have time]

The logistic map is a simple population model in discrete-time, and relates the size of a population in generation $n+1$ to its size in generation n. It is one of the simplest models that shows "chaotic" behaviour.

One way of writing the logistic map is via the following recurrence

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

where x_n is the population size in year n, measured as a fraction of the carrying capacity, and r is the intrinsic rate of increase (a growth rate).

Task 29

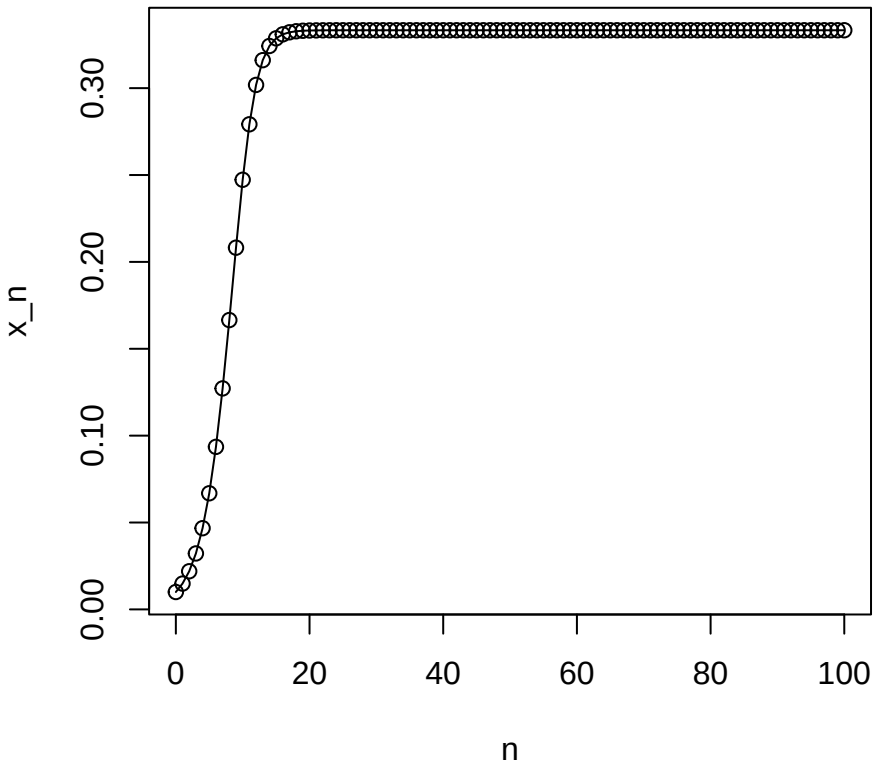
What do you think is the purpose of the following function?

```
logisticValues <- function(r, N, x0) {
  retVal <- numeric(N)
  thisX <- x0
  for(i in 1:N) {
    thisX <- r * thisX * (1 - thisX)
    retVal[i] <- thisX
  }
  return(retVal)
}
```

Show: Solution on P172

Copy the function `logisticValues` into your script file. Also include the following code that uses the function to plot a graph.

```
r <- 1.5        # growth rate
N <- 100        # max generation
x0 <- 0.01      # initial value
xn <- logisticValues(r, N, x0)  # next N starting at x0
plot(0:N, c(x0, xn), type = 'o', xlab = 'n', ylab = 'x_n')  # plot
```



This code shows the behaviour of the logistic map with $r = 1.5$ for 100 generations. Note the slightly clunky way of making sure the initial point is returned.

Task 30

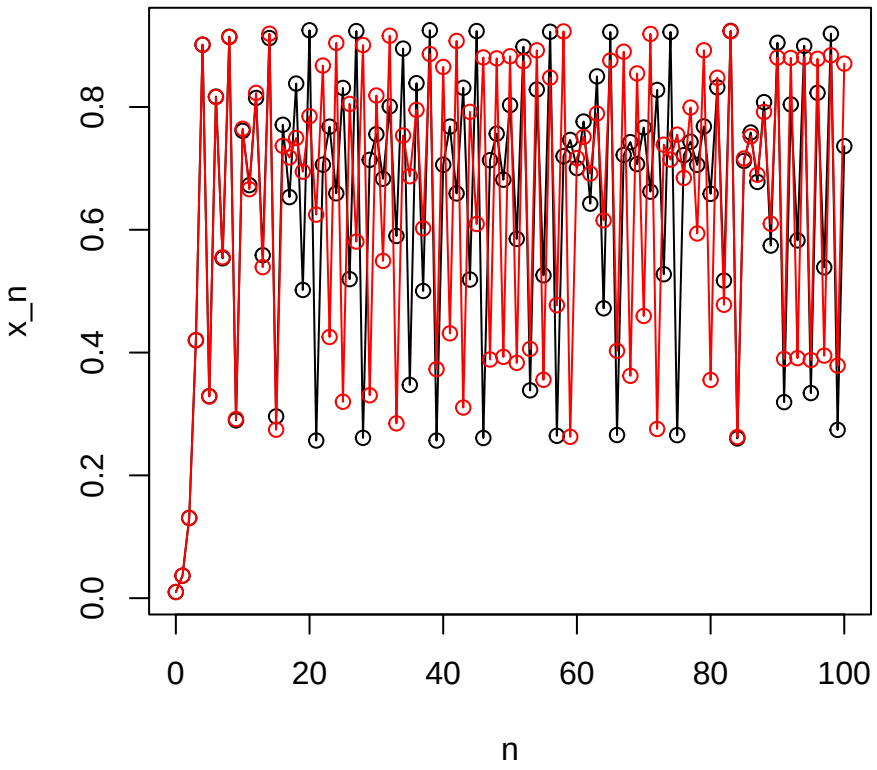
Try running the code for different values of r. What does the graph show you?

Good values of r to try would be $r = 0.5$, $r = 1.5$, $r = 2.5$, $r = 3.1$, $r = 3.5$, $r = 3.7$. You should also test the behaviour for different initial conditions: suitable values would be $x_0 = 0.01$ and $x_0 = 0.1$.

Show: Solution on P172

You should note that in the case $r = 3.7$, the pattern of successive population sizes appears to be fairly random. It also depends on the initial value of x_0. The following code confirms this (note the first five lines are almost exactly as they were before): include this code in your script to check this.

```
r <- 3.7              # growth rate
N <- 100              # max generation
x0 <- 0.01            # initial value
xn <- logisticValues(r, N, x0)    # next N starting at x0
plot(0:N, c(x0, xn), type = 'o', xlab = 'n', ylab = 'x_n') # plot
x0 <- 0.01001         # different initial value
xn <- logisticValues(r, N, x0)    # next N starting there
lines(0:N, c(x0, xn), type = 'o', col = 'red') # overlay on plot
```



Notice that, despite starting very close together, the trajectories diverge over time. “Sensitive dependence on initial conditions” is characteristic of deterministic chaos.

Task 31

What do you think the following code does?

Test your understanding by typing the function in and running it by issuing an appropriate call to the function at the command prompt.

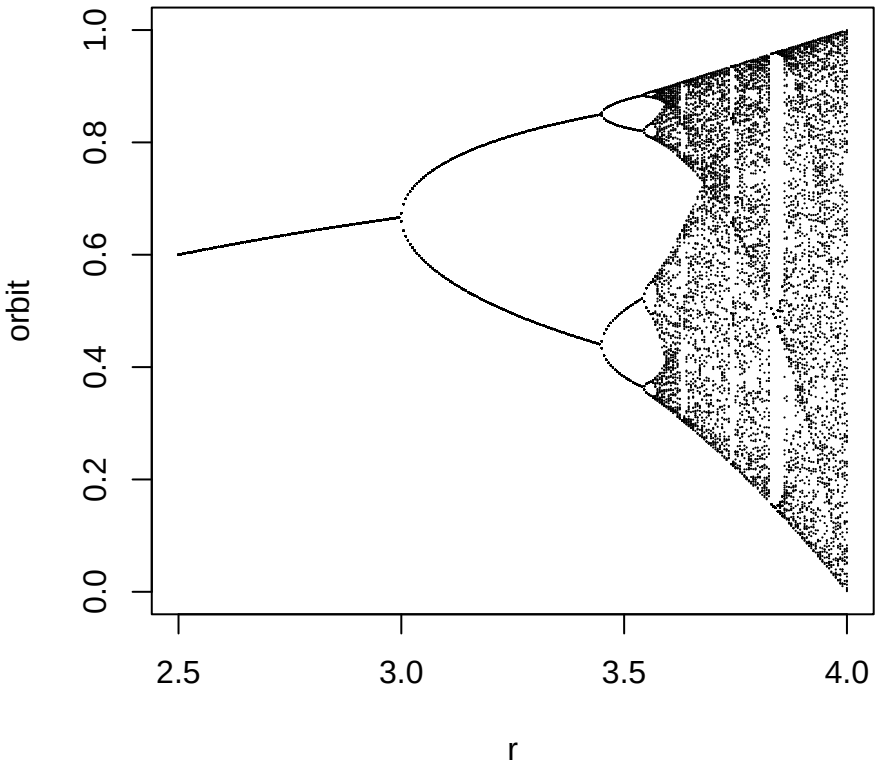
```
logisticValuesAfterBurnIn <- function(r, N, M, x0) {
  retVal <- numeric(M)
  thisX <- x0
  for(i in 1:N) {
    thisX <- r * thisX * (1 - thisX)
  }
  for(i in 1:M) {
    thisX <- r * thisX * (1 - thisX)
    retVal[i] <- thisX
  }
  return(retVal)
}
```

Show: Solution on P172

Enter the following code and run it.

```
rVals <- seq(2.5, 4, by = 0.005)
plot(c(2.5, 4), c(0, 1), type = 'n', xlab = 'r', ylab = 'orbit')
```

```
for(r in rVals) {
  N <- 1000
  M <- 100
  xn <- logisticValuesAfterBurnIn(r, N, M, 0.01)
  points(rep(r, M), xn, pch = 19, cex = 0.01)
}
```



Question 32

Do you understand what the plot—a so-called "bifurcation diagram"—is showing?

Show: Answer on P172

A very readable introduction to deterministic chaos in biology is given by May (1976). That article is widely available online and comes highly recommended.

Chapter 4

Programming—Practical 2

Matt Castle (mdc31@cam.ac.uk)

4.1 Random variables

A random variable can be thought of as the outcome of an experiment or a measurement i.e. something that can change each time you look at it.

Examples:

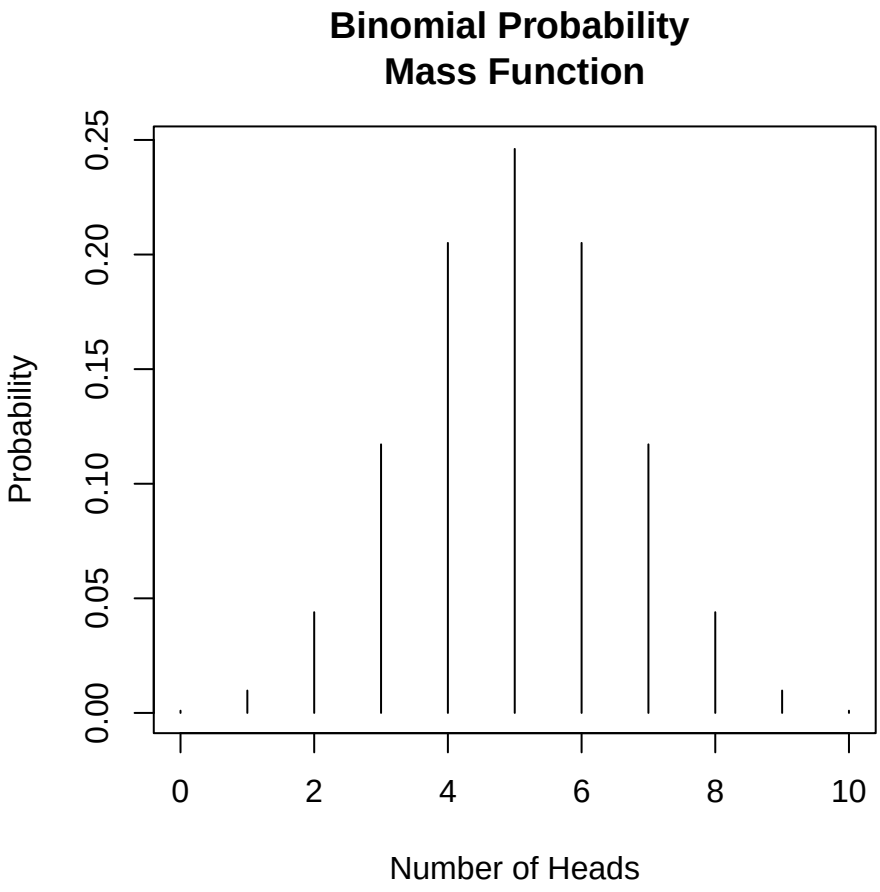
- The number of heads you obtain when tossing a coin 10 times
- The number of emails you received in one hour
- The lifetime of a light-bulb
- The length of time an individual is infected for before recovering

4.2 Probability distributions

A probability distribution will tell us the probability of a random variable taking a specific value.

A binomial distribution will be able to give us the probability of obtaining x heads if we toss a coin 10 times (where x is any number).

```
plot(
  x = 0:10,
  y = dbinom(0:10, 10, prob = 0.5),
  type = "h",
  main = "Binomial Probability \nMass Function",
  xlab = "Number of Heads",
  ylab = "Probability"
)
```

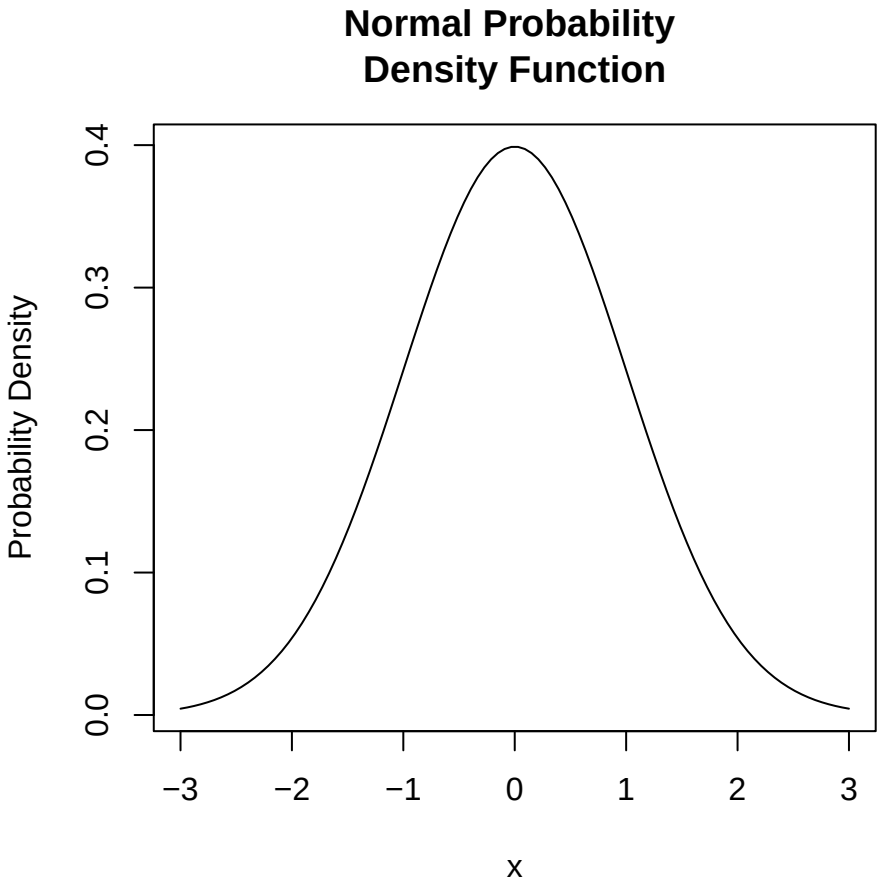


This is an example of a discrete random variables, and so the distribution is called **probability mass function**.

For continuous random variables we can only calculate the probability of being in an interval.

A normal distribution gives us the probability of measurement errors, x, being a certain size.

```
plot(
  x = seq(-3, 3, length = 100),
  y = dnorm(seq(-3, 3, length = 100), mean = 0, sd = 1),
  type = "l",
  main = "Normal Probability \nDensity Function",
  xlab = "x",
  ylab = "Probability Density"
)
```



This is an example of a continuous random variable, and so the distribution is called a **probability density function**.

4.3 Using probability distributions in R—types

R has a large number of inbuilt probability distributions.

Discrete distributions:

- Binomial
- Geometric
- Poisson
- Negative Binomial
- Hypergeometric
- Multinomial

Continuous distributions:

- Normal
- Uniform
- T (T-test)
- F (F-test)
- Exponential

- Cauchy
- Beta
- Gamma
- Weibull
- Chi-squared
- Logistic

R deals with them all in essentially the same way. Each inbuilt distribution in R is referred to by its abbreviation.

- Binomial: `binom`
- Poisson: `pois`
- Geometric: `geom`
- Normal: `norm`
- Uniform: `unif`
- Exponential: `exp`
- ...

Each inbuilt distribution in R has the same four generic functions associated with it.

For a distribution with abbreviation `dist`:

- `ddist()`: density/mass function
- `pdist()`: cumulative density/mass function
- `rdist()`: random number generator function
- `qdist()`: quantile function

4.3.1 `ddist()`

For a distribution type `dist`, the function `ddist(x,...)` returns:

- The probability $P(X = x)$ (for discrete variables) or
- The probability density at x (for continuous variables)

This can be used to calculate actual probabilities for discrete distributions.

4.3.1.1 `dbinom()`—discrete distribution

Consider a binomial distribution with 10 trials, each with a probability of success of 0.5. The R function `dbinom()` describes the distribution of the probability of success.

It takes the following arguments:

- `x`: the number of successful trials
- `size`: the total number of trials
- `prob`: the probability of success

```
dbinom(4, 10, 0.5)
```

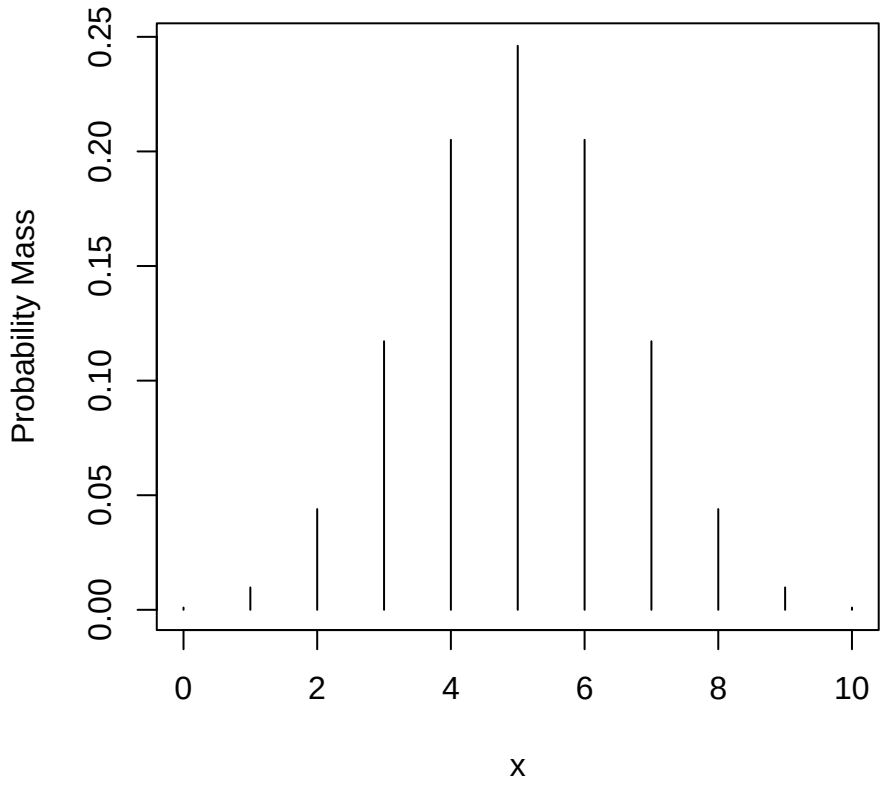
```
## [1] 0.2050781
```

Or to plot the distribution itself.

```r
dbinom(0:10, 10, 0.5)
```

```
##  [1] 0.0009765625 0.0097656250 0.0439453125 0.1171875000 0.2050781250
##  [6] 0.2460937500 0.2050781250 0.1171875000 0.0439453125 0.0097656250
## [11] 0.0009765625
```

```r
plot(0:10, dbinom(0:10, 10, 0.5), type = "h", xlab = "x", ylab = "Probability Mass")
```



4.3.1.2 `dnorm()`—continuous distribution

Consider a normal distribution with mean 0 and standard deviation 1.

The R function `dnorm()` gives the probability density at a given value of x.

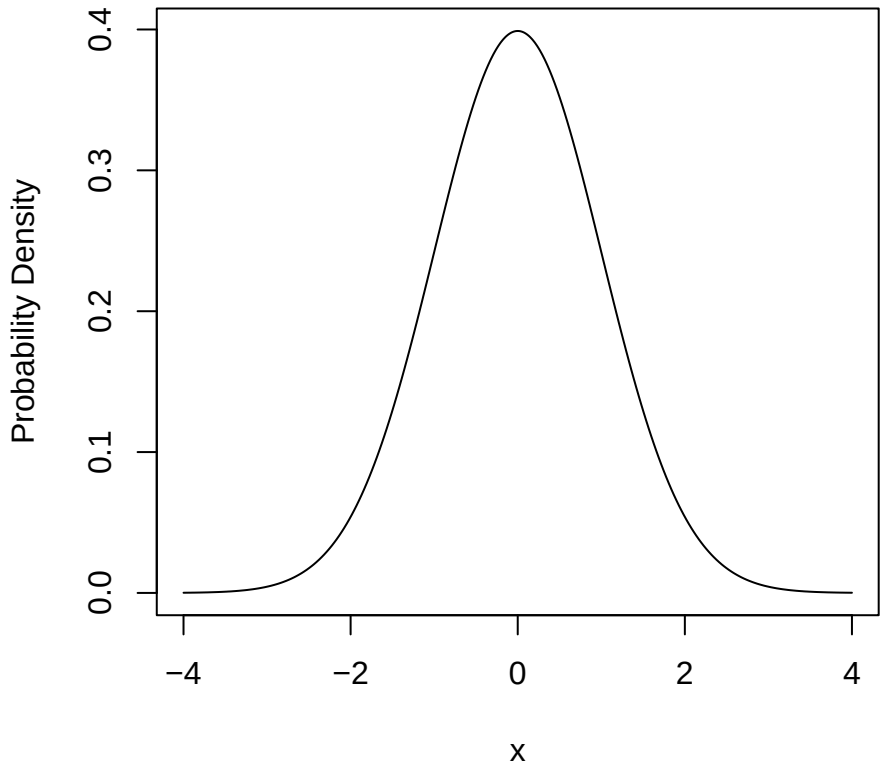
It takes the following arguments:

- `x`
- `mean`
- `sd`: standard deviation

The function `dnorm(x, mean, sd)` isn't useful in itself but is useful for plotting.

With a continuous distribution we have to choose the x coordinates close enough together to approximate a smooth curve.

```r
x <- seq(-4, 4, 0.01)
plot(x, dnorm(x, 0, 1), type = "l", xlab = "x", ylab = "Probability Density")
```



4.3.2 `pdist()`

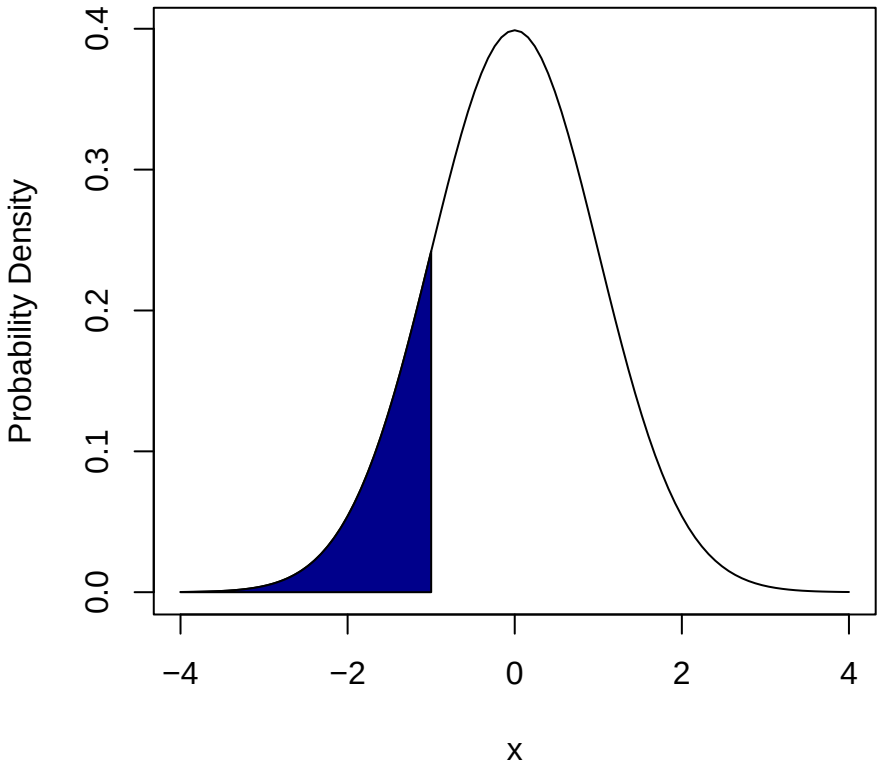
For a distribution dist `pdist(x, ...)` returns the probability $P(X \leq x)$ (which in a continuous function is an actual probability).

4.3.2.1 `pnorm()`—probability calculations

If we want to find the probability of having a value below -1 from a normal distribution we use `pnorm()`.

```r
pnorm(-1, 0, 1)
```

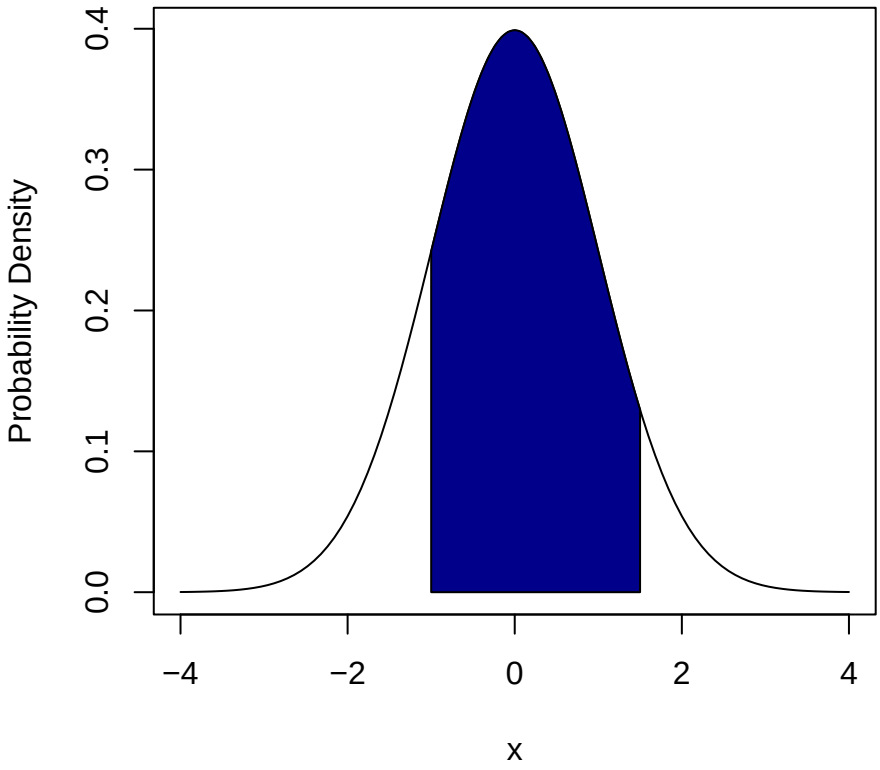
```
## [1] 0.1586553
```



If we want to find the probability of having a value between -1 and 1.5 from a normal distribution we use `pnorm()`.

```
pnorm(1.5, 0, 1) - pnorm(-1, 0, 1)
```

```
## [1] 0.7745375
```



4.3.3 `rdist()`

For a distribution dist `rdist()` returns n random numbers drawn from that distribution.

This function is of great use when trying to run stochastic models. The ability to draw random numbers from many different types of distribution is incredibly useful.

4.3.3.1 `rnorm()`—normal distribution

Consider a normal distribution with mean and standard deviation.

The R function `rnorm()` returns random numbers drawn from this distribution.

It takes the following arguments:

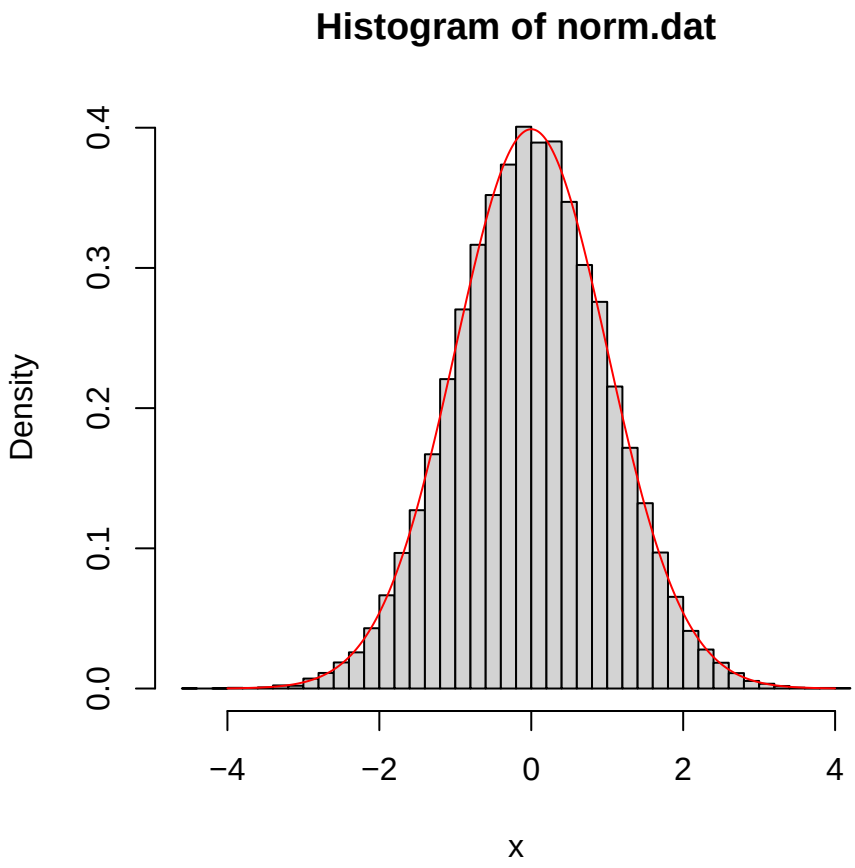
- `n`: number of random numbers to return
- `mean`
- `sd`: standard deviation

```
norm.dat <- rnorm(5, 0, 1)
print(norm.dat)
```

```
## [1]  0.01876372  0.05699356  1.68764807  0.55455829 -0.03203064
```

Consider a normal distribution with mean 0 and variable 1. We will draw thousands of random numbers from this distribution and plot a histogram of them. This should then look like the theoretical normal distribution curve we produce with `dnorm()`.

```
norm.dat <- rnorm(50000, 0, 1)
hist(norm.dat, prob = TRUE, breaks = 50, xlab = "x")
x <- seq(-4, 4, 0.01)
lines(x, dnorm(x, 0, 1), col = "red")
```



4.4 Example—using probabilities for simulation

Consider tossing a biased coin. There are two outcomes: Heads or Tails.

$P(H) = \frac{1}{3}$ & $P(T) = \frac{2}{3}$

How can we use probability distributions in R to simulate this?

4.4.1 Binomial distribution

Using the binomial distribution:

- 1 observation
- 1 trial
- Probability of success (H) is $\frac{1}{3}$

```
rbinom(
  1,  # number of observations
  1,  # number of binomial trials
  1/3 # binomial probability of success
)
```

```
## [1] 1
```

`rbinom()` returns the number of successes from our 1 observation of tossing a biased coin once.

- 0: $\frac{2}{3}$ of the time
- 1: $\frac{1}{3}$ of the time

We can check this by getting R to do many observations at once…

```
rbinom(15, 1, 1/3)
```

```
##  [1] 1 1 1 1 0 1 1 0 1 0 0 0 0 1 0
```

4.4.2 Uniform distribution

Using the uniform distribution:

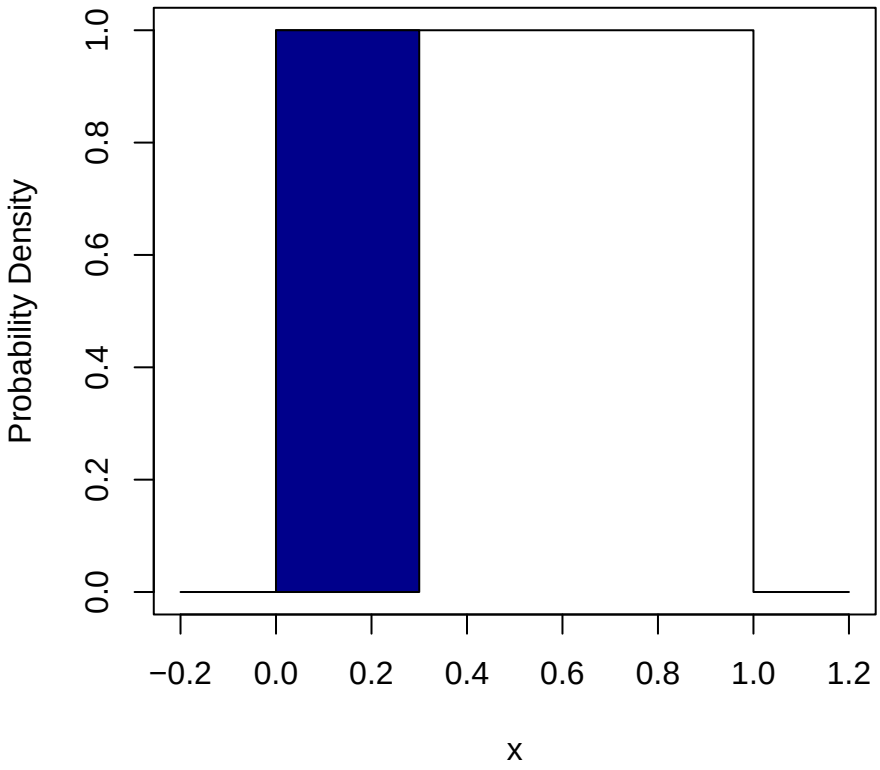
Generate single number uniformly between 0 and 1.

```
rand <- runif(
  1,  # number of observation
  0,  # minimum
  1   # maximum
)
if (rand < 1/3) {
    print("Heads")
} else {
    print("Tails")
}
```

```
## [1] "Heads"
```

```
print(rand) # confirm by printing rand
```

```
## [1] 0.1627777
```



The shaded area corresponds to the probability of drawing Heads.

4.5 Example—multiple choices

Consider tossing a very thick biased coin. There are three outcomes: Heads, Tails, or edge.

- $P(H) = \frac{3}{10}$
- $P(T) = \frac{6}{10}$
- $P(E) = \frac{1}{10}$

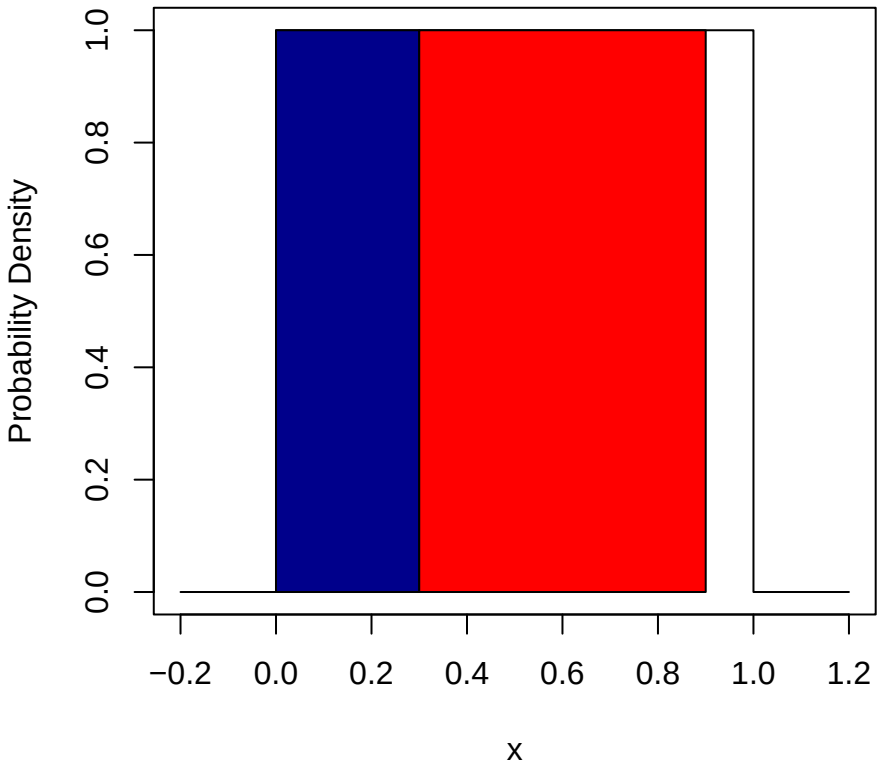
How can we use probability distributions in R to simulate this?

```
rand <- runif(1, 0, 1)
if (rand < 3/10) {
    print("Heads")
} else if (rand < 9/10) {
    print("Tails")
} else {
    print("Edge")
}
```

```
## [1] "Tails"
```

```
print(rand) # confirm by printing rand
```

```
## [1] 0.607971
```



The blue shaded area corresponds to the probability of drawing Heads. The red shaded area corresponds to the probability of drawing Tails. The unshaded area corresponds to the probability of drawing Edge.

Task 33

Consider a regular six-sided die. How could we simulate a single throw of a die in R?

- What are the possible outcomes?
- Use `runif()`.
- Use (lots of) `if else` statements.

Show: Solution on P173

4.6 Example—using R to model a death process stochastically

Consider a population of animals. Every year each animal has a fixed probability of dying (depressing I know!), independently of each other and how old they are. There are no new animals born.

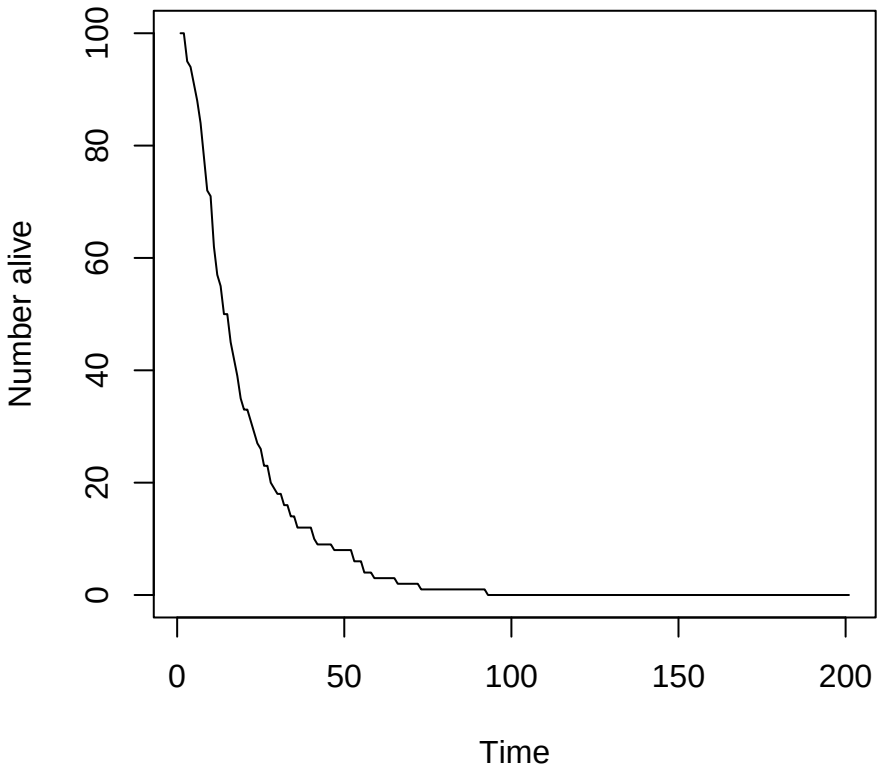
How could we model this?

- Need a program that keeps track of number of live animals.
- At each time step, we need to 'roll a die' to see if each live animal survives.
- We update the numbers of live animals and keep going until everything dies!

This is easy to do in R.

```r
nAlive <- 100                          # current number of live animals
max.time <- 200                        # keep going for up to 200 steps
nAliveStore <- numeric(max.time+1)     # vector to store how many were alive at each step
nAliveStore[1] <- nAlive               # store how many were alive at the start
for (iTim in 1:max.time) {             # loop over all time steps
    pr <- runif(nAlive, 0, 1)          # probability of dying for all currently live animals
    died <- which(pr < 0.05)           # find out which animals have died
    nDead <- length(died)              # count up how many animals have died
    nAlive <- nAlive - nDead           # update the number of currently living animals
    nAliveStore[iTim + 1] <- nAlive # store the number of living animals
    if (nAlive <= 0) {break}           # stop process when all animals are dead
}

plot(nAliveStore, type = "l", xlab = "Time", ylab = "Number alive")
```



Part III

Dynamic models

Chapter 5

Dynamic models—Practical

Katy Gaythorpe (k.gaythorpe@imperial.ac.uk)

This practical introduces the `deSolve` package in R.

5.1 A bit of theory

5.1.1 Rationale:

We have discussed the solutions of two differential equations using the fact that we were able to solve them analytically:

$$\frac{dN}{dt} = rN \rightarrow N(t) = N_0 e^{rt}$$
$$\frac{dN}{dt} = rN\left(1 - \frac{N}{K}\right) \rightarrow N(t) = \frac{K}{1 + \frac{K-N_0}{N_0}e^{rt}}$$

However, most differential equations cannot be solved analytically. For example, with the predation model presented in Dynamic Models Lecture 2, we cannot obtain a mathematical formula giving the number of bacteria (prey) $N(t)$ and amoeba (predators) $P(t)$ as functions of the parameters and initial conditions. Instead we have to resort to numerical methods to obtain approximate values of $N(t)$ and $P(t)$ for any given set of parameter values. Since this is the case for the vast majority of differential equations of interest in science, such numerical methods have been developed for many years and the advent of computers have made them increasingly popular. Throughout this course we will be using a ready-made package in R called `deSolve` which can solve numerically virtually any system of ordinary differential equations (ODE).

> **Note**
>
> In earlier versions of R, the package was called `odesolve` but worked in the same way.

5.1.2 A few notes on Euler's method

Although we will be using `deSolve` as a black box, for your information here is a very basic introduction to how differential equation solvers work. The general principle was devised by Swiss mathematician Leonhard

Euler (1707–1783). Among many other things, Euler also came up with the fascinating formula $e^{-i\pi} + 1 = 0$, but that's another story.

Here I illustrate the method with a single differential equation, but it can easily be extended to any number. Consider the logistic growth model with an arbitrary choice of parameter values: $dN/dt = 0.5N(1 - N/100)$ and initial condition $N(0) = 1$.

The trick is then to 'discretise' this equation, i.e. replace the infinitesimal variations of the differential equation by small 'discrete' variations. Remember the formal definition of the derivative of a function:

$$\frac{dN}{dt} = \lim_{\delta t \to 0} \frac{N(t + \delta t) - N(t)}{\delta t}$$

We then approximate the variations during a small time step δt as follows:

$$\frac{N(t + \delta t) - N(t)}{\delta t} \approx 0.5N(t) \left(1 - \frac{N(t)}{100}\right)$$

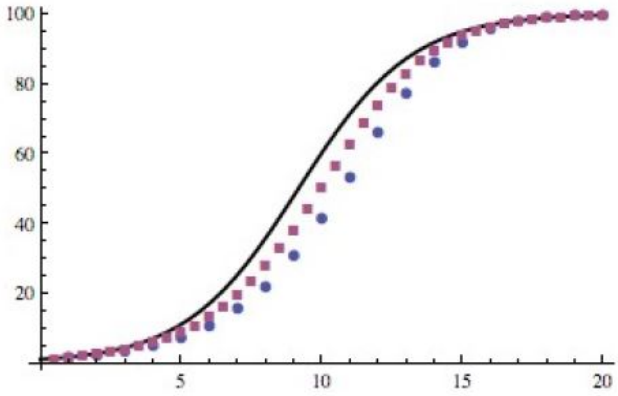
So, if we know the value of $N(t)$ at a given time t, we can estimate the value at the next time point:

$$N(t + \delta t) \approx N(t) + 0.5N(t) \left(1 - \frac{N(t)}{100}\right) \delta t$$

If you know the initial density, say $N(0) = 1$, and you choose $\delta t = 0.1$, then you can iteratively calculate approximate values of $N(0.1) \approx 1.0495$, $N(0.2) \approx 1.1014$, etc. which eventually enables you to reconstruct the numerical solution $N(t)$.

The only problem is that $N(0.2)$ is estimated based on an approximate value of $N(0.1)$, and so on. So, as you iterate the process, you accumulate errors and you run the risk of seeing your 'numerical solution' drift away from the true solution.

Of course, the smaller δt, the more accurate the discretisation. See the graph below, where the solid curve is the true solution of the above differential equation (which, in this case, can be solved analytically) and the dots are two 'discretised solutions', using $\delta t = 1$ (discs) and $\delta t = 0.5$ (squares):



So, that's basically what `deSolve` or any other software does to generate 'numerical solutions' of differential equations. They actually use more sophisticated algorithms (but based on the same 'discretisation' principle) in order to reduce the potential 'drift' from the (unknown) true solution. Different algorithms will perform better on different classes of models, but they are not 100% accurate. One of the most popular class of algorithms for the kind of ODEs used in population dynamics was designed by German mathematicians Runge & Kutta almost 100 years ago.

5.2 The return of the logistic model

5.2.1 Load the `deSolve` package

But enough theory for now. Let's shut the bonnet and sit behind the wheel! We'll start by re-visiting the logistic growth model to get you acquainted with `deSolve`.

Launch RStudio. The first thing to do is check whether the `deSolve` package is already installed, as it does not come with the R base. In RStudio, click on the "Packages" tab in the bottom-right window to see the list of R packages installed on your computer (those with a checked box are not only installed on the computer but currently loaded in your R session so that you can use them). If `deSolve` is not in the list, click on Install Packages, this opens a window asking you which package you which to install: type `deSolve` and click on Install (you may be asked first to choose a "Mirror": find the mirror closest to where you are currently located, and select it). This will download the package from the internet, which means your computer needs to be connected. You only need to do that once on any computer.

Note: Instead of using RStudio's interface, you can type the following instructions in the console: `library()` will open a window with the list of installed packages. If `deSolve` is not there, close the window, return to the R console and type: `install.packages('deSolve')`.

Once a package is installed on a computer, you still need to tell R to load the package into the memory every time you start a new session. In RStudio you can do that by checking the box of the package in the Packages window, but if you need to use the package in a script file, it is safer to type the command `library(deSolve)`.

We're now ready to start. Open a new script file for this practical code, write some comments (starting with a `#`) that will remind you what's in this file next time you open it, and type the first instruction:

```
library(deSolve)
```

REMEMBER TO SAVE YOUR FILE REGULARLY

5.2.2 Define the model

First, we must define a function `logistic_dyn()` that returns the value of the derivative dN/dt, in this case $rN(1 - N/K)$, given the values of r, K and N. This function will be used by the differential equation solver to generate the numerical solution $N(t)$, so we have to follow specific rules set by the authors of the `deSolve` package:

- The function that defined the derivative must take three arguments:
  - time,
  - a vector containing the values of the variables (in this case a single variable N), and
  - a vector of parameter values (in this case two parameters r and K).
- The function must return a list containing the value(s) of the derivative(s).

Note that the name of the function, `logistic_dyn`, is arbitrary; you may call it anything you like. Type the following code in your script file:

```
#This function calculates dN/dt for the logistic model

logistic_dyn <- function(t, N, par){
    #rename the parameters
```

```
    r <- par[1]
    K <- par[2]
    #calculate the derivative
    dN <- r*N*(1-N/K)
    #last instruction: return a list
    return(list(dN))
}
```

Note that before calculating the derivative, I defined a few local variables r, K and dN (which only 'exist' inside the function, so they do not appear in the Workspace) for convenience. A shorter version of the function, without local variables, would be:

```
logistic_dyn <- function(t, N, par) {
    list(par[1]*N*(1-N/par[2]))
}
```

but you'll probably agree that it is less easy to read for a human being. The only case when you should favour the latter version is when speed (or memory) is an issue.

Next, create three variables:

- a vector of parameter values (2 values in the order specified in `logistic_dyn`: r first and K second):

  ```
  logistic_par <- c(1, 100)
  ```

- a vector of time steps at which we want values of N (note that `deSolve` automatically computes many intermediate time steps as explained in the preamble):

  ```
  logistic_t <- seq(0, 20, 0.1)
  ```

- the initial state of the system (in this case just the value of N_0):

  ```
  logistic_init <- 1
  ```

We can then feed all that into a function called `lsoda()`, which is the only function from the `deSolve` package that we're going to use, and store the result into a variable:

```
logistic_sol <- lsoda(logistic_init, logistic_t, logistic_dyn, logistic_par)
```

Save your file and run all your code so far (click on Source in the top right corner of the script window). In the Workspace window, you should now see the variables you've defined under Values, or your new function `logistic_dyn`, under Functions. To visualise the contents of the function, click on its name in the Workspace window, or type `fix(logistic_dyn)` in the Console: this opens a separate window that you must remember to close before you can re-gain access to the command line. You can also look at the contents of the matrix `logistic_sol` in the same way: the first column is your `logistic_t` vector (i.e. the time steps) and the second column contains the corresponding values of $N(t)$.

5.2.3 Version with named parameters

A feature of R that can make your life a bit easier when using `lsoda()` is the ability to name the elements of a vector. When we defined `logistic_par` earlier, we had to remember that the first element must be r

and the second one K. Not too bad with only two parameters, but it can be more of an issue with higher numbers of variables and parameters, as we'll see next in the next part.

Here is an alternative version of the function `logistic_dyn` which assumes that the third argument, `param`, is a vector whose elements are named r and K:

```
# Calculate the derivative dN/dt using a named vector as its third argument
named_logistic_dyn <- function(t,N,par) {
    # Tell R to use the names of the elements of par (r and K)
    with(as.list(par),{
        return(list(r*N*(1-N/K)))
    })
}
```

The syntax is a bit complicated because we have to tell R that r and K (which are undefined symbols) will actually be defined within `par`. That's the role of the `with(x,{...})` statement. A further complication is that `with(x,{...})` only works with a named list as its first argument, not a named vector, which is why we wrote `with(as.list(par),{...})`. As a result, every instruction that comes inside `{ }` in the second argument of `with(x,{...})` can make use of the names of the elements of `par`.

Once the function `named_logistic_dyn` has been defined, it can only be used with a named vector as a third argument. So, in our case, we must define a new vector:

```
named_logistic_par <- c(r=1, K=100)
```

Then you can use `lsoda` as follows:

```
named_logistic_sol <- lsoda(logistic_init,
                            logistic_t,
                            named_logistic_dyn,
                            named_logistic_par)
```

This will give you exactly the same result as `logistic_sol` above. So, with this method, you don't need to remember the order of the parameters in the function that calculated the derivative, but you need to remember their names.

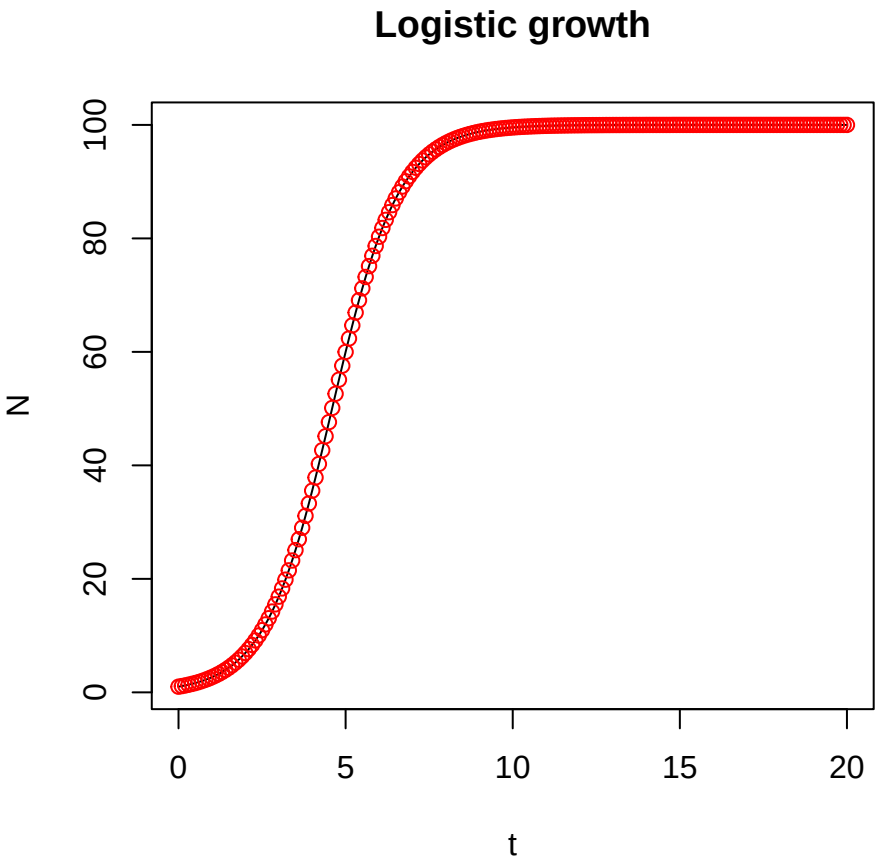
5.2.4 Plot the dynamics

The next step is to plot the dynamics of $N(t)$ using the contents of `logistic_sol`:

```
plot(logistic_sol[,1], logistic_sol[,2], type='l',
     main='Logistic growth', xlab='t', ylab='N')

# Just to check, you can superimpose the graph of the
# analytical solution of the logistic growth model

points(logistic_t,1/(0.01+0.99*exp(-logistic_t)),col='red')
```



Task 34

Now plot a few more graphs with different parameter values (re-define `logistic_par`) or different initial values (`logistic_int`).

5.3 The revenge of the amoeba

5.3.1 Code the model

We'll follow the template described in the previous section, starting with the core function that calculates dN/dt and dP/dt. The only difference is that we now have 2 variables, so the function must return a list of two derivatives. There are 5 parameters, so you must be extra careful with the order in which you store them in the vector. To be safe, we'll enter them in alphabetical order:

```
# Definition of the predation model
predation_dyn <- function(t,var,par) {
    a <- par[1]
    b <- par[2]
    d <- par[3]
    K <- par[4]
    r <- par[5]
    N <- var[1]
    P <- var[2]
```

```
    # Derivatives
    dN <- r*N*(1-N/K)-a*N*P
    dP <- -d*P+b*N*P
    return(list(c(dN,dP)))
}

# Parameter values, initial variables values and the vector of time values:
predation_par <- c(a=0.02, b=0.01, d=0.3, K=100, r=1)
predation_init <- c(N=100, P=1)
predation_t <- seq(0,40,0.2)

# Numerical solution
predation_sol <- lsoda(predation_init,
                       predation_t,
                       predation_dyn,
                       predation_par)
```

The resulting matrix has 3 columns: `predation_sol[,1]` contains the time points, `predation_sol[,2]` the values of N and `predation_sol[,3]` the values of P.

Once again, we only defined the local variables a, b, d, etc. to make it easier to read the code and spot any mistakes. But we could write a more concise version using only `par[1]`, `par[2]`, etc. instead. Alternatively, you could use `with(as.list(c(par,var)),{ ... })` as we saw above.

5.3.2 Plot some graphs

Since we have two variables in this model, we can generate more diverse graphs. You should now be getting familiar with plotting instructions, so I'll let you work out how to produce the following graphs.

Task 35

Plot $N(t)$ and $P(t)$ against time, together on a graph, using `plot()`, `lines()` and `legend()`.

Show: Solution on P173

Task 36

Plot N and P in the phase plane. Use the notes from Lecture 2 to find the equations of the nullclines, and draw them using `abline()`. Finally add the equilibrium points.

Show: Solution on P175

5.3.3 Discussion and further investigations

Task 37

The model has three equilibrium points, determined by the values of the parameters. In the example above, the dynamics converged to the equilibrium point where the prey and predator coexist.

1. Do you think it would be possible to reach another equilibrium point from different initial conditions?
2. What do the dynamics look like if we start from $N(0) = 1$ and $P(0) = 100$?

Show: Solution on P176

Question 38

Is that what you expected from a biological point of view?

Show: Answer on P177

Question 39

What limitations of the model does this suggest?

Show: Answer on P177

Task 40

Observe the effects of changing values of b and d on the equilibrium points and the dynamics. What happens if $d > bK$?

Show: Solution on P177

Task 41

Change the values of b and d simultaneously so that the ratio b/d remains contant. What do you notice?

Show: Solution on P178

Part IV

Epidemic models

Chapter 6

Epidemic models—Practical 1

Katy Gaythorpe (k.gaythorpe@imperial.ac.uk)

6.1 The basic SIR model

Task 42

Write down the equations of a frequency-dependent SIR model with no births or deaths and transmission rate β and recovery rate γ.

Show: Solution on P179

Task 43

Show that for this model the population size remains constant, i.e. that $dN/dt = 0$.

Show: Solution on P179

6.2 Coding the model

We'll follow the template for `deSolve` that we used in the previous practical, starting with the core function that calculates dS/dt, dI/dt and dR/dt. Open R, create a new text files and type in:

```
# SIR Epidemic model - Practical 1
library(deSolve)

SIR_dyn <- function(t,var,par) {
    # Rename the variables and parameters
    S <- var[1]
    I <- var[2]
    R <- var[3]
    N <- S+I+R
    beta <- par[1]
```

```
    gamma <- par[2]

    # Derivatives
    dS <- -beta*S*I/N
    dI <- beta*S*I/N-gamma*I
    dR <- gamma*I

    # Return the 3 values
    list(c(dS,dI,dR))
}
```

REMEMBER TO SAVE YOUR FILE REGULARLY

Note that in this model, the total number of individuals $S + I + R$ remains constant, so we would actually only need to define 2 variables (say S and I) and calculate 2 derivatives. I've included the 3 variables for clarity only. Then define parameter values, initial variables values and the vector of time values:

```
beta <- 1
gamma <- 0.25
SIR_par <- c(beta,gamma)
SIR_init <- c(99,1,0)
SIR_t <- seq(0,30,by=0.1)

# The numerical solution is given by
SIR_sol <- lsoda(SIR_init,
                 SIR_t,
                 SIR_dyn,
                 SIR_par)
```

If you like, you can relabel your variables so that they are easier to use:

```
TIME <- SIR_sol[,1]
S <- SIR_sol[,2]
I <- SIR_sol[,3]
R <- SIR_sol[,4]
N <- S + I + R
```

Note

You cannot label time as `time` in lower case letters because it is an inbuilt function in R.

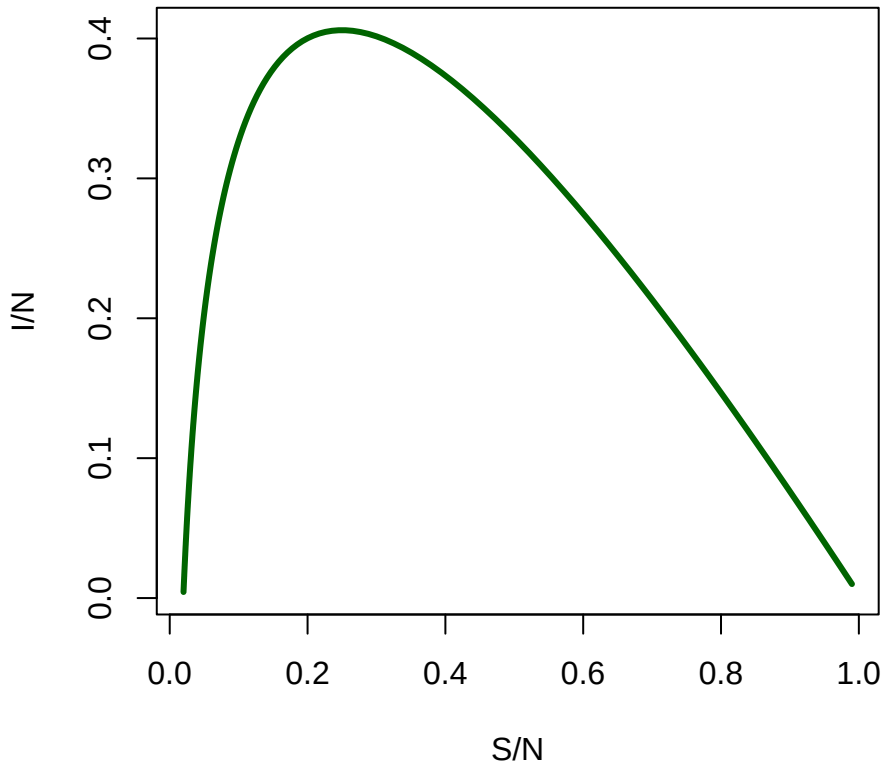
Task 44

Plot $S(t)$, $I(t)$ and $R(t)$ together on a graph, using the commands `plot()`, `lines()` and `legend()`.

Show: Solution on P180

You don't have to always plot things against time, it can also be useful to plot variables against each other. Try plotting S against I:

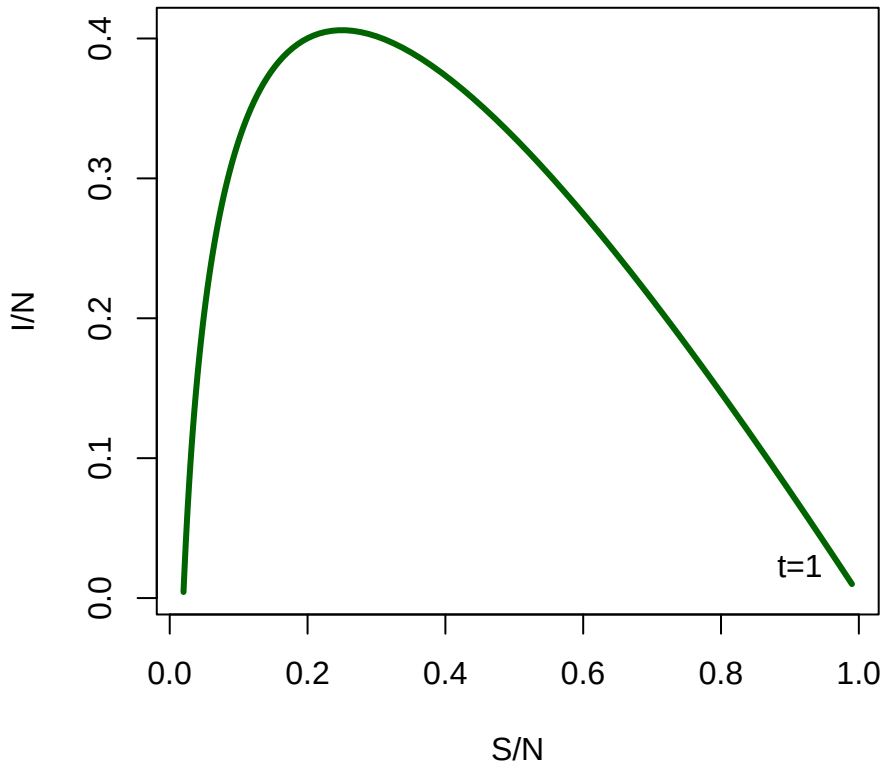
```
plot(S/N, I/N, type = "l", lwd = 3, col = "darkgreen")
```



It can be difficult to read this graph at first. Find where TIME $= 1$ (at the start $S/N \approx 1$ and $I \approx 0$) and label it on the graph.

```
index <- which(TIME == 1)

text(S[index]/N[index],I[index]/N[index],"t=1",pos=2)
```



Task 45

Also label $t = 2$, $t = 5$, $t = 10$ and $t = 15$. What is happening to time in this plot?

Show: Solution on P180

6.3 Some properties of the model

An important question is when does the epidemic reach its peak? A common misconception based on graphs similar to the one above is "$I(t)$ reaches its maximum when $S(t) = R(t)$".

By now you know that "$I(t)$ reaches its maximum when $dI/dt = 0$".

Task 46

- Given that $dI/dt = \beta SI/N - \gamma I$, when I is maximum we get $S/N = \gamma/\beta$.
- Check this relationship using the graph of S/N plotted against I/N. You might want to use `which.max()` which gives the position of the largest element in a vector.

Tip

You can use `abline` to mark on the plot where I/N reaches its maximum.

```
abline(v=S[which.max(I)]/N[which.max(I)], col ="black")
```

Next, let's look at the effects of β and γ on the dynamics of the system. In practice, β is usually not known before an epidemic, so its estimated in the early stages of an epidemic using the average infectious period $(1/\gamma)$ and R_0. Instead of calculating and plotting a series of dynamics manually, we'll use a loop to plot 6 graphs in a single window.

Task 47

Disease	R_0	Infectious period, $1/\gamma$ (days)	β	Peak size	Peak time	Epidemic size
Flu (H1N1p)	1.2	1				
Flu	1.5	1				
SARS	2.0	28				
Smallpox	5.0	5				
Measles	17.0	7				
Pertussis	17.0	14				

Fill in the blanks and execute the following instructions:

```
# set up a 2 by 3 grid for the plots:
par(mfrow=c(2,3), xaxs='i', yaxs='i')
# define the parameters:
infperiod <- c(1,1,28,5,7,14)
Rzero <- c(1.2,1.5,2,5,17,17)
for (i in 1:6) {
    gamma = signif(1/infperiod[i],2)
    beta = signif(Rzero[i]*gamma,2)
    SIR_par <- c(beta,gamma)
    SIR_sol<-lsoda(SIR_init,
                   SIR_t,
                   SIR_dyn,
                   SIR_par)
    plot(....., ylim=c(0,1),type="l", main=paste0("beta = ",beta,"gamma = ",gamma))
    lines(.....) # I(t)
    lines(.....) # R(t)
}
par(mfrow = c(1, 1))
```

Show: Solution on P181

For each combination of parameter values, write down β and read off the approximate values of the height and time of the epidemic peak and the final epidemic size (the total number of individuals that were infected). (**Hint:** you may have to extend the time period!)

You can also use the functions `max()` and `which.max()`.

Remember from the lecture that $R_0 = \beta/\gamma$, therefore $\beta = \gamma R_0$.

Task 48

Which of the last 3 quantities appear linked to R_0?

Show: Solution on P182

Note:

It can be shown mathematically that the epidemic size and the height of the epidemic peak are functions of R_0 only, although this requires some clever manipulation of the ODEs (see Appendix at the end of this practical if you're interested).

The time to the epidemic peak cannot be directly expressed from the equations, but it is linked to the initial rate of spread of the epidemic. The variations in the number of infected individuals are given by:

$$dI/dt = I(\beta S/N - \gamma)$$

At the very beginning of the outbreak, $I(t) \ll S(t) \approx N$. So we can approximate the ODE above as $dI/dt = (\beta - \gamma)I$, which can be solved as:

$$I(t) = I_0 \exp(\beta - \gamma)t$$

So the number of infected individuals initially follows an exponential growth with rate

$$\beta N - \gamma = \gamma(R_0 - 1)$$

Task 49

Plot $\log(I(t))$ for t in $[0, 4]$ for the same parameter combinations above and check that the initial gradient is equal to $\beta - \gamma$.

Tip

You can use `abline` again, this time to impose a straight line ($y = bx + c$).

Show: Solution on P183

Task 50

What dynamics do you expect with $R_0 = 1$? Plot the graph for $\beta = 1$, $\gamma = 1$. Why does $I(t)$ decrease?

Show: Solution on P184

Task 51

Explore the behaviour of the system around $R_0 \approx 1$ using the loop you wrote before. Try changing $0.9 < R_0 < 1.1$ and altering the initial number of individuals infected.

Show: Solution on P184

6.4 Calculating the infectious period

Question 52

If the recovery rate of a disease is $\gamma = 0.2$ days^{-1}, what is the average infectious period?

Show: Answer on P185

- For a given constant recovery rate of $\gamma = 0.2$ days^{-1} we can plot the proportion of individuals still infected over time.

```
# set up a vector of times:
x=seq(0,30,0.1)

# define the recovery rate, gamma:
gamma=0.2

# define the exponential function:
fx=exp(-gamma*x)

# plot:
plot(x,fx,type="l")
```

- We can also calculate the average infectious period using the function defined above.

```
print(sum(fx*x)/sum(fx))
```

Task 53

How do your two answers compare?

Show: Solution on P186

6.5 Optional section—extending SIR to other compartments

As we saw in the lecture, the SIR framework is only a crude representation of the real natural history of a disease. Think of another formulation and see how the results compare to a standard SIR model. Some suggestions:

- Include loss of immunity, so that Recovered individuals become Susceptible again after a certain period of time.
- Include a latent state post-infection but before an individual becomes infectious (this type of model is often called an $SEIR$ model, where E stands for the Exposed class).
- Include treatment in the model, allowing Infected individuals to recover more quickly.
- Sketch a diagram of your model, showing the compartments and the flows between them.
- Write down the equations that govern your model
- Write a function, such as `SEIR_dyn()` that calculates the derivatives of your model for use with `lsoda()`.

- Plot the epidemic curve, $I(t)$. How does this compare to an equivalent SIR model?

Show: Solution on P186

6.6 Appendix—Epidemic peak and final epidemic size

Although it is not possible to solve the differential equations of the SIR system analytically to obtain expressions for $S(t)$, $I(t)$ and $R(t)$, we can obtain an implicit solution in the (S, I) phase plane. In other words, we can obtain a mathematical relationship between the values of S and I at any time point. The trick is to re-write the system

$$\frac{dS}{dt} = -\beta SI/N$$
$$\frac{dI}{dt} = \beta SI/N - \gamma I$$

as a single differential equation for I as a function of S. Under certain mathematical conditions that we won't discuss here, the variations of I with respect to S can conveniently be written as:

$$\frac{dI}{dS} = \frac{dI/dt}{dS/dt} = \frac{\beta SI/N - \gamma I}{-\beta SI/N} = \frac{\gamma N}{\beta S} - 1$$

Using the integration rules from the maths lectures, we can actually solve this ODE:

So, given the initial conditions, we can deduce the value of $I(t)$ from the value of $S(t)$ at any time point. How is that helpful? First consider the question of the height of the epidemic peak. We know that $I(t)$ reaches its maximum when $S(t) = \gamma/\beta$. Hence the height of the epidemic peak:

$$I_{\max} = I_0 + \frac{\gamma}{\beta}\log\frac{\gamma}{\beta S_0} + S_0 - \frac{\gamma}{\beta}$$

Assuming that $I(0) \ll S(0) \approx N$, then we can write $R_0 \approx \beta S(0)/\gamma$, hence:

$$I_{\max}/N \approx 1 - (1 + \log R_0)/R_0$$

You can check it on the graphs from section 2 above. Next, the final epidemic size is given by the final value of $S(0) - S(t)$, i.e. taking $t \to \infty$. Under the same assumptions as above, and letting $x = S(0) - S(\infty)$ be the proportion of the N population that gets infected over the whole epidemic, we get the following equation: $x + \log(1 - x)$, which can only be solved numerically.

R does not have a built-in numerical solver for nonlinear equation, but it has a function called `optimize()` that searches for the minimum of a numerical function. The trick is to notice that solving an equation of the form $f(x) = 0$ is equivalent to finding the minimum of $f^2(x)$, the square of $f(x)$. If you're not convinced, sketch a graph of an arbitrary function that crosses the x-axis, then sketch the square of that function.

We can therefore estimate the epidemic size for any value of R0 using the following code:

```
my_fun <- function(x,R0) {
    (x+log(1-x)/R0)^2
}
optimize(my_fun, c(0,1), R0=2)
```

where the three arguments of `optimize` are:

- the function to minimize with respect to its first argument (in this case x),
- the interval over which to search for a solution
- the numerical values of any other argument of `my_fun` (in this case R_0).

We'll see more about `optimize()` next week, so I wont give any more detail here.

Chapter 7

Epidemic models—Practical 2

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7.1 Outline

In this practical we will:

- Code and run a model with vaccination.
- Investigate the critical vaccination threshold.
- Code and run a two-population model and investigate targeted vaccination.

7.2 Vaccination at birth

Consider a vaccine that confers complete protection against infection for life that is administered at birth. You will need to adapt your SIR model from practical 1 to include births, deaths and a permanent vaccination campaign where a proportion $p \leq 1$ of all newborns are immunized.

Task 54

Sketch out the model. **Hint:** You don't necessarily have to include a vaccinated compartment as you could include vaccinated people in the 'recovered' compartment.

Show: Solution on P187

Task 55

Write down the modified equations.

Show: Solution on P188

Task 56

Adapt your SIR model with births and deaths to include vaccination and run the model with parameters $\beta = 2$, $\gamma = 0.5$, $\mu = 1/70$, $p = 0$ and initial conditions $S(t = 0) = 999$, $I(t = 0) = 1$ and $R(t = 0) = 0$.

Show: Solution on P188

Task 57

What's the critical vaccination threshold for these parameters, p_{vac}?

Show: Solution on P189

Task 58

Investigate increasing the proportion of vaccinated newborns from 0 to 1. What happens to the number of infected individuals when p crosses the critical vaccination threshold?

Show: Solution on P190

Question 59

Why do you still get an initial epidemic?

Show: Answer on P191

Task 60

Plot a horizontal line to indicate $1/R_0$. Notice what happens to the number of susceptible when $p = 0.75$. What about when $p = 0.7$?

Show: Solution on P192

Task 61

Modify your model to include a one-off vaccination campaign at the start so that there is no initial epidemic.

Show: Solution on P193

Question 62

What does this tell you about vaccination at birth programmes used in isolation?

Show: Answer on P197

7.3 Targeted Vaccination

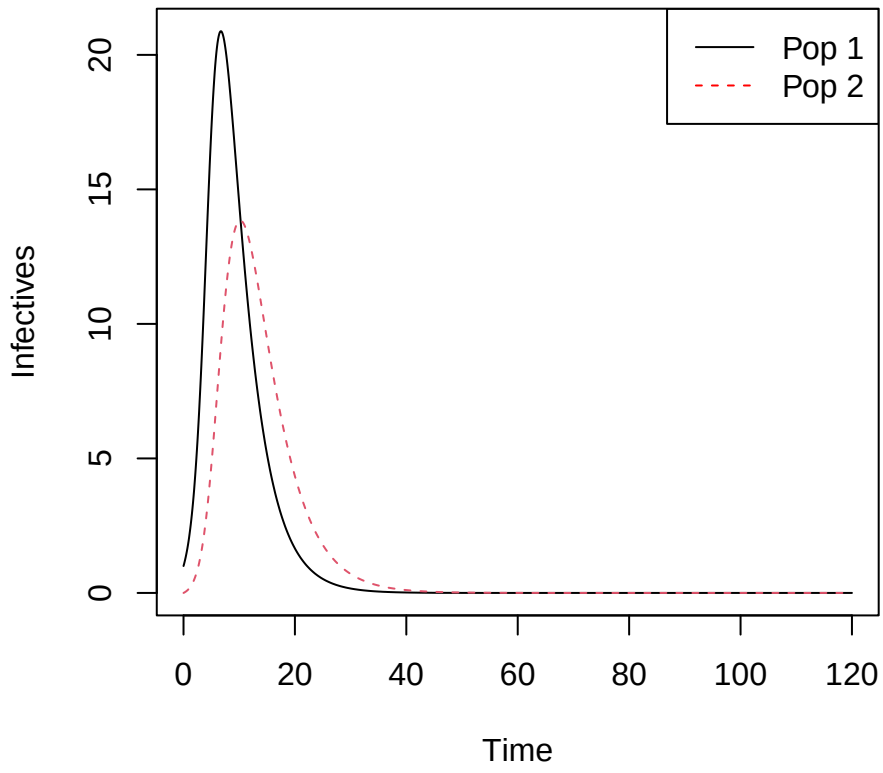
Now we will consider vaccination in a population with two age groups. We assume that the epidemic dynamics are much faster than demographic changes, so the impact of births and deaths is negligible. Firstly, code up a two-population model. You can base it on the code from the earlier SIR practical.

```
# This proposed version uses some helpful features of the R language to simplify the code:
# "with" allows us to bring named members of a vector into the local namespace
# here we use to avoid having to specifically rename the elements of par
# We use the matrix/vector functionality to avoid writing down individual equations for
# each group. We don't need to do this it would just be longer to write out each equation in
# turn. You should try this as an excercise and check your new function gives the same dynamics!

TwoPopSIR <- function(t,states,par) {

  with(as.list(c(states, par)), {

        pops<-matrix(states[1:(npops*nstates)],
        nrow=nstates,ncol=npops,byrow=T)

        S=pops[1,]
        I=pops[2,]
        R=pops[3,]

        N=colSums(pops)

        newinfections = colSums(beta*(I/N) %*% t(S))
        dS <- -newinfections
        dI <- newinfections - gamma*I
        dR <- gamma*I
        return(list(c(dS,dI,dR)))
    })
}
```

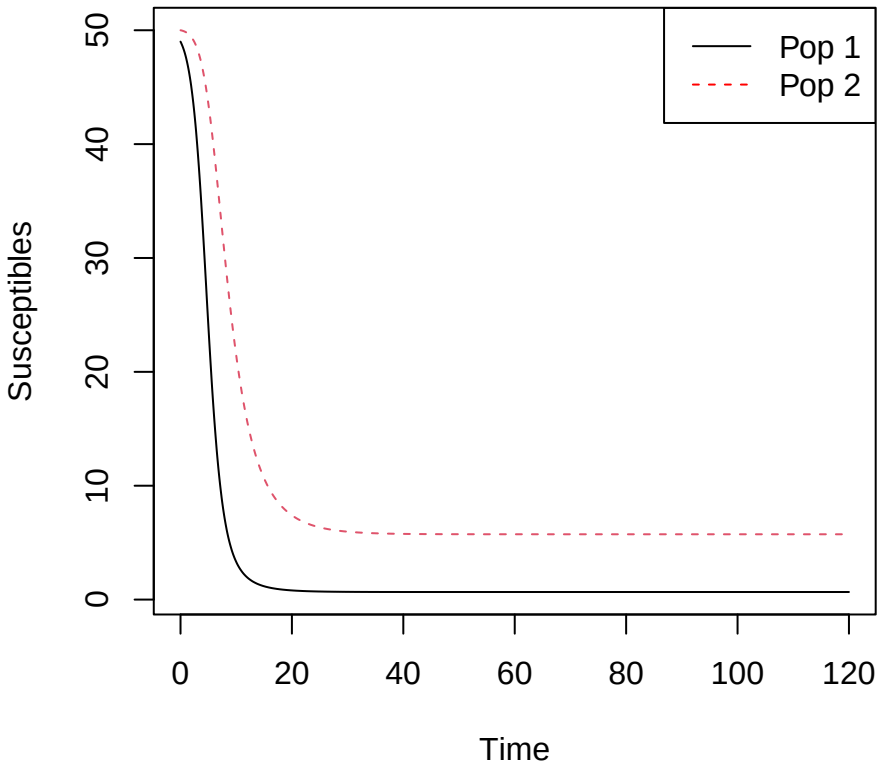
Run the model with initial conditions `init <- c(49,50,1,0,0,0)` and parameters $\gamma = \frac{1}{4}$ and $\beta = \begin{pmatrix} 1 & 0.1 \\ 0.1 & 0.5 \end{pmatrix}$.

```
# states are recorded in order (S1,S2,I1,I2,R1,R2)
# so we have 1 infected in patch 1 for initial condition, 50 individuals in both patches

TwoPop.init<-c(49,50,1,0,0,0)

# Note we have been lazy here and have written the function
# to use the "beta" matrix from the global workspace. This is bad programming form
# but again avoids messing about converting the matrix to and from vectors...

beta = matrix(c(1,0.1,0.1,0.5),2,2)

# As transmission parameters coded in beta above, one other parameter (named for use with with above).
TwoPop.par<-c(gamma=1/4.0,nstates=3,npops=2)

TwoPop.t<-seq(0,120,0.1)
```

```
TwoPop.sol <- lsoda(TwoPop.init,TwoPop.t,TwoPopSIR,TwoPop.par)

matplot(TwoPop.sol[,1],TwoPop.sol[,c(4,5)],type='l',xlab='Time',ylab='Infectives')
legend('topright',c('Pop 1','Pop 2'),col=c('black','red'),lty=c(1,2))
```




```
matplot(TwoPop.sol[,1],TwoPop.sol[,c(2,3)],type='l',xlab='Time',ylab='Susceptibles')
legend('topright',c('Pop 1','Pop 2'),col=c('black','red'),lty=c(1,2))
```



Note that the epidemic peak occurs later, and is lower, for group 2.

Task 63

Write down the next generation matrix for these parameters and calculate R_0.

Show: Solution on P197

Task 64

What is the critical vaccination threshold for this disease?

Show: Solution on P197

Let's assume that a proportion p_1 of group 1 and a proportion p_2 of group 2 are vaccinated at the start of the model. The initial conditions are:

```
p1=0.8
p2=0.8
init <- c(49*(1-p1),50*(1-p2),1,0,49*p1,50*p2)
```

Task 65

By changing the initial conditions, explore the dynamics with random vaccination, where $p_1 = p_2$.

Show: Solution on P198

Task 66

Using the formula from the lecture, plot the total proportion of the population that needs to be vaccinated to prevent an epidemic $\frac{(p1+p2)}{2}$ for different values of p_1.

Show: Solution on P199

Chapter 8

Epidemic models—Practical 3

Matt Castle (mdc31@cam.ac.uk) and Andrew Conlan (ajkc2@cam.ac.uk)

8.1 Stochastic models

Aim: To explore the effects of stochasticity on simple SI and SIR models and contrast their behaviour with previous deterministic results.

Goals:

By the end of this practical participants should be able to achieve the following:

- Code up a simple stochastic SI model in R using the `SimInf` package.
- Code up a simple stochastic SIR model in R using the `SimInf` package.
- Run both single and multiple realisations and visualise the results.
- Explore extensions to both SI and SIR models:
  - Expand the SI model to include additional transitions.
  - Understand the impact of R0 values on stochastic extinction.

Background: This practical follows on from the Stochastic Epidemic Models Lecture and echoes the content presented there.

8.2 Coding a simple SI model

We will first implement a slight modification to the code that has been presented to you in the previous Stochastic Epidemic Lecture. The key difference between the code presented in the lecture and the code shown here is that we are putting the code into a function (called `StocSI.dyn`) rather than just running a series of commands.

- Open Rstudio.
- Open a new blank script file.
- Save it as `Stock_SI.R`.

In the script window type the following commands:

```
library(SimInf)

create.StocSI <- function(N, I0, beta, f_time) {

    initial_state <- data.frame(S = N-I0 , I = I0)
    compartments <- c("S", "I")
    transitions <- c("S -> beta*S*I/(S+I) -> I")
    tspan <- seq(from = 1, to = f_time, by = 1)

    model <- mparse(transitions = transitions, compartments = compartments,
        gdata = c(beta = beta), u0 = initial_state, tspan = tspan)

    return(model)
}
```

Make sure you save your file and that your working directory is the same as the folder you have saved this into (Choose from menu Session > Set Working Directory > To Source File Location).

This code creates a function that creates a single stochastic SI model. We'll dissect/explain the code in the next section.

Open a new blank script file.

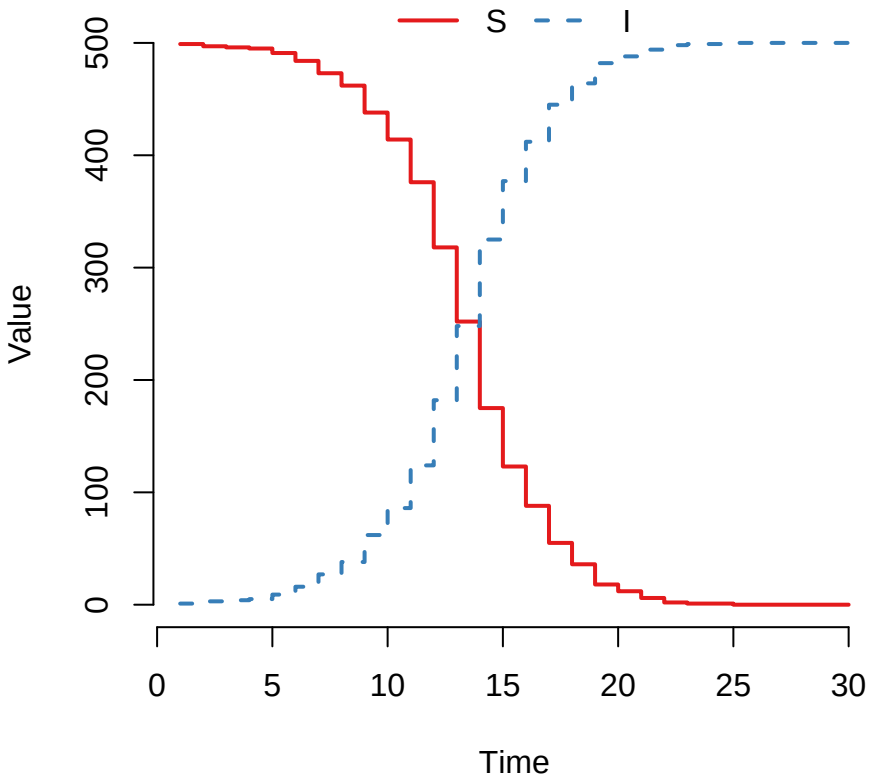
Save it as `Epi_P3.R`

We'll use this script to record all of the steps in this practical (unless otherwise indicated).

In the script window type the following commands and then run (select and press run button in RStudio):

```
source('Stoch_SI.R')
SImodel <- create.StocSI(500, 1, 0.5, 30)
out <- run(model = SImodel)
plot(out)
```

You should see a graph that looks similar to this:



Here we can see the two trajectories for an SI epidemic. The susceptible curve (red) starts at 499 and stochastically decreases down whilst the infected curve (blue) starts at 1 and mirrors the S curve increasing stochastically.

8.3 Dissecting the stochastic SI code

The function we have just created is a wrapper that takes the basic parameters that define the SI model for a particular population and creates a R object that the `SimInf` package can use to simulate the model. Our function `create.StocSI` takes four inputs:

- Total population size: `N`
- Initial number of infected: `I0`
- Infection rate: `beta`
- Time to simulate for: `f_time`

Inside the function we combine this information to create four R objects that when passed to the `SimInf` function `mparse`. The output from the `mparse` function is returned as the output to our `create.StocSI` function.

Here we will break down what we have just written and explain what is required for the `mparse` function.

Note

The `SimInf` package includes its own function that defines SIR, $SEIR$ and SIS models (of which the SI model is a special case). The `mparse` function can define any generic compartmental model so it is worth learning about.

The `mparse` function requires that you specify the following information:

- the list of all compartments of the system
- the initial states (or compartments) of the system
- the events (or transitions) of the system
- the values of any parameters
- the time points where the value of each state is to be recorded for each simulation

An SI model is described by the following system of *differential* equations:

$$\frac{dS}{dt} = -\beta\frac{SI}{N} \tag{8.1}$$

$$\frac{dI}{dt} = \beta\frac{SI}{N} \tag{8.2}$$

And from these equations we can derive a transition diagram from the system:

$$S \to \beta\frac{SI}{N} \to I$$

- From this diagram we can see that there are two states for this system: susceptible and infected (S & I). We define all of the compartments of the model using a vector:

```
compartments <- c("S","I")
```

- In order to begin the simulation, we need to specify the initial values of each compartment. We specify these using a data frame with a single row and column for each compartment specified above:

```
initial_state <- data.frame(S = N-I0, I = I0)
```

  where `N` (the total population number) and `I0` (the initial number of infected) have been specified by the user.

- There is one event (or transition): infection.

```
transitions <- c("S -> beta*S*I/(S+I) -> I")
```

  where the effect is to move one susceptible into the infected compartment at a rate $\beta\frac{SI}{N}$ where $N = S + I$ and beta must be specified by the user. The syntax we use here should be self-explanatory (hopefully) but the idea is that we have the following syntax "A $\to$ rate $\to$ B" where A is the name of the starting compartment, B is the name of the ending compartment and rate explains how to calculate the rate.

- We must tell algorithm how long we want it to run for before stopping and at what points we wish to record the value of the compartments. We use the user specified variable `f_time` to specify a sequence of daily output values up to a maximum value of `f_time`.

```
tspan <- seq(from = 1, to = f_time, by = 1)
```

> **Note**
>
> `SimInf` was designed to work with real epidemiological data and as such the minimum output timestep size is 1 (corresponding to 1 day).

- The `mparse` function takes the arguments we've just created, processes (*'parses'*) them into a low-level computer language and compiles the resulting program into machine code. This machine code is considerably (orders of magnitude) faster than the equivalent R code. We assign the output of this function to the object `SImodel` (an object in R is a special data type that combines functions with data).
- Objects can be used as arguments to functions in the same way as normal data types. In this case we can use the `run()` function to run a stochastic simulation of the `SImodel`:

```
out <- run(model = SImodel, threads = 1)
```

  The threads argument is optional here, but this argument would allow us to parallelise our code (if our setup allows it).

- The run function implements (and runs) the stochastic simulation algorithm for any stochastic model defined by the `mparse` function and returns a new object which contains the output of the simulation (which we've called out).
- The `SimInf` package provides a special plot function for this output

```
plot(out)
```

This explains the code you've produced so far, but there are limitations. We would like to plot multiple stochastic realisations onto a single plot and investigate their aggregated properties. To do this we will need to modify our code somewhat.

8.4 Performing multiple simulations

Let's update our `create.StocSI` function in the (`Stoch_SI.R` file) to create a model with multiple copies of the same population. This is the simplest possible meta-population model where there is no interaction between patches, and a neat hack to run multiple replicate simulations at the same time.

Edit `Stoch_SI.R` to update the definition of the `create.StocSI` as follows:

```
create.StocSI <- function(N, I0, beta, f_time, reps = 1) {

    initial_state <- data.frame(S = rep(N-I0, reps) , I = rep(I0, reps))
    compartments <- c("S", "I")
    transitions <- c("S -> beta*S*I/(S+I) -> I")
    tspan <- seq(from = 1, to = f_time, by = 1)

    model <- mparse(transitions = transitions, compartments = compartments,
        gdata = c(beta = beta), u0 = initial_state, tspan = tspan)
    return(model)
}
```

The only two things we've changed here are:

1. We've created a new argument call `reps` which we're using to specify the number of simulations that we want the code to run.

2. We've changed how we specify the `initial_state` dataframe. This is now a dataframe that has `reps` number of rows and 2 columns. The first column contains the starting number of susceptible individuals in each of our simulations, and the second column contains the number of initial infected individuals.

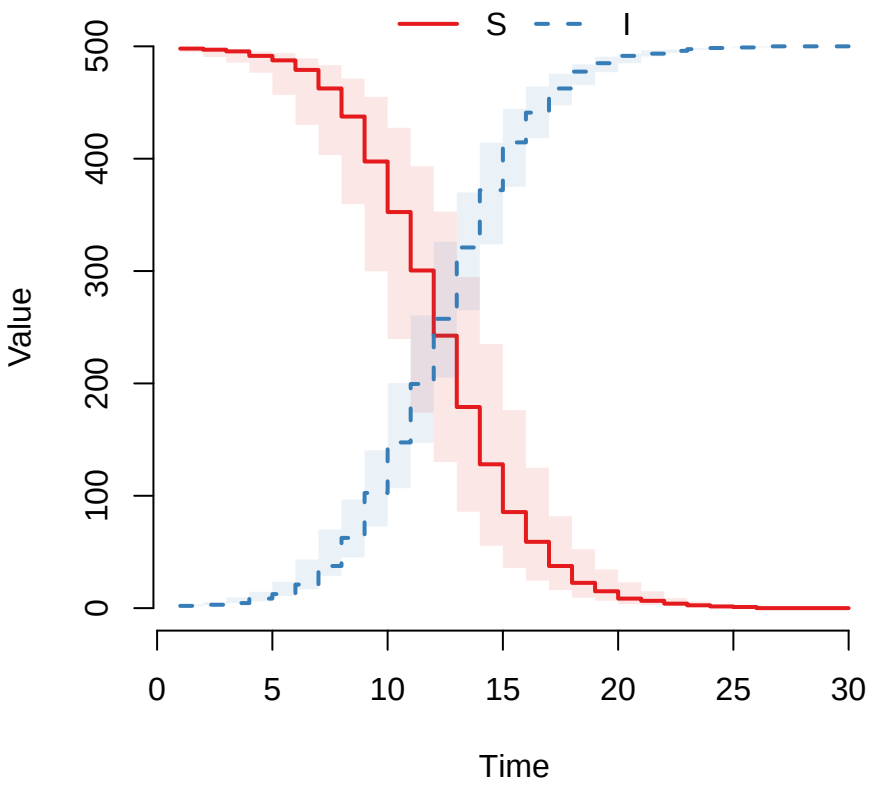
Again, remember to **save** your file.

> **Note**
>
> We have added a new argument to `create.StocSI` which has a default value `reps = 1`. By adding the argument in this way we ensure that any code we wrote earlier assuming only one replicate would still work with no modifications.

Type in the following code into `Epi_P3.R` and run:

```
#Multiple replicates
source('Stoch_SI.R')
SImodel <- create.StocSI(500, 1, 0.5, 30, 20)
out <- run(model = SImodel)
plot(out)
```

This should produce a plot that looks similar to the following:



By default the plot command will always:

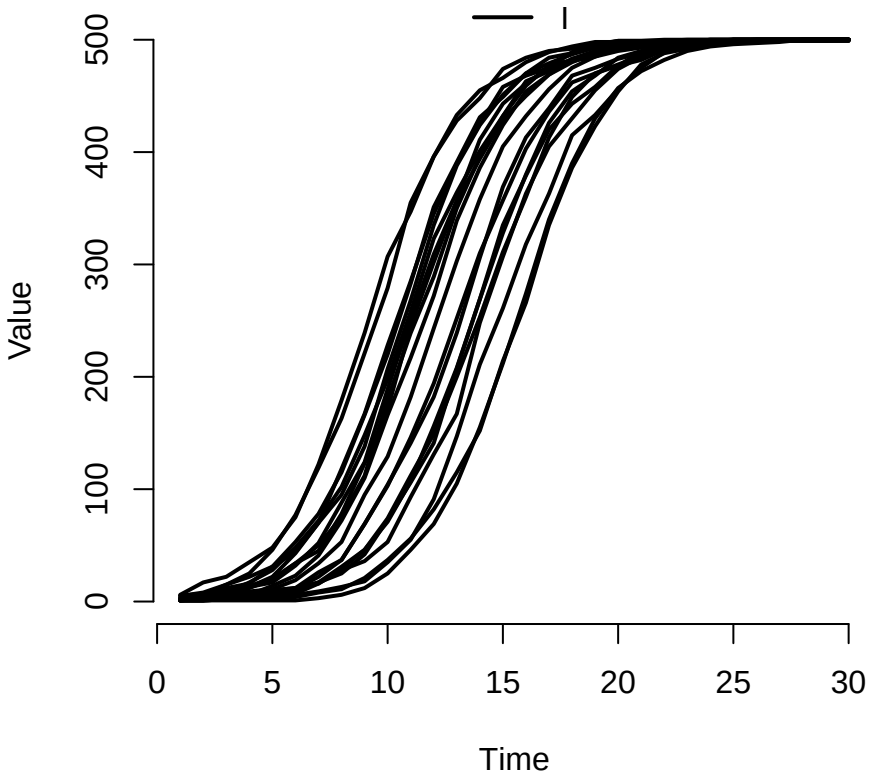
1. plot the curves for all states on the same graph (so we can see both S and I curves here)
2. use a step function to plot the curves (which is why it's a bit, um, step-y)

3. show the average and interquartile range as a transparent envelope when multiple simulations have been run.

If we want to actually see individual realisations, we need to use some of the other arguments to the plot function. **Try typing this in:**

```
plot(out , 'I', range = FALSE , type = 'l')
```

This should produce a plot that look similar to the following:



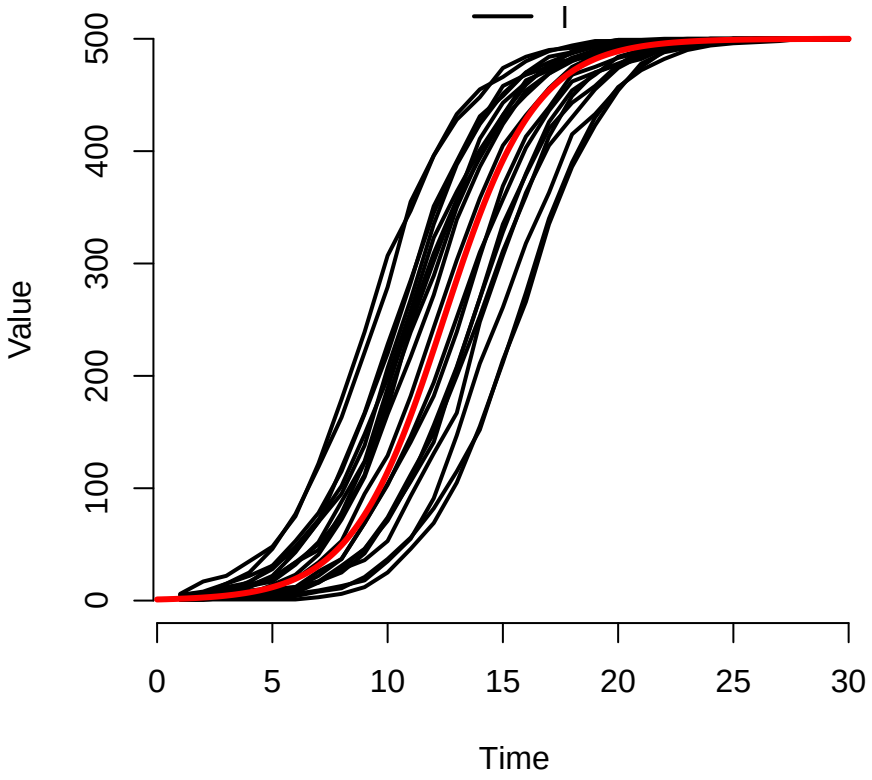
- the second argument is a character vector specifying which compartments we want to see. Here we've asked to only see the curves for the infected I compartment
- the named argument `range` is used to specify the shaded quantile on the plot. By specifying `FALSE`, we've turned it off and forced R to plot the individual trajectories instead. If we'd specified a numeric value between 0 and 1 then we would see the equivalent shaded range plotted instead (i.e. `range = 0.5` corresponds to plotting the interquartile range and `range = 0.95` corresponds to plotting the wider 95% quantiles)
- we can use the standard `type` argument from the base R plot function to specify the type of curve we want. The default is `type = 's'` for steps, but here we're asking for the smoother `type = 'l'` lines option.

8.4.1 Adding the deterministic solution curve

Download an R script file called `Det_SI.R`. It contains the code for a deterministic SI model based upon the code you encountered in the first epidemic models practical. It is specifically designed to use the same parameters as have been used in the stochastic SI code written above and will add a deterministic trajectory to your plot.

Type in the following:

```
# adding a deterministic trajectory
source('Det_SI.R')
det.sol <- DetSI.dyn(500, 1, 0.5, 30)

det.t <- det.sol[,1]
det.I <- det.sol[,3]

lines(det.t, det.I, lwd=3 , col='red')
```



8.5 Exploring the effects of stochasticity

Task 67

Modify the above code to explore the effects of different initial conditions ($I_0 = 1, 5, 10, 50, 100$) on the stochastic replicates. Keep the total population size constant ($N = 500$).

Qualitatively what effect does this have on the variability between replicates?

Show: Solution on P201

Task 68

Now vary the population size ($N = 50, 500, 5000$) with $I_0 = 1$.

Qualitatively what effect does this have on the variability between replicates?

Show: Solution on P201

Task 69

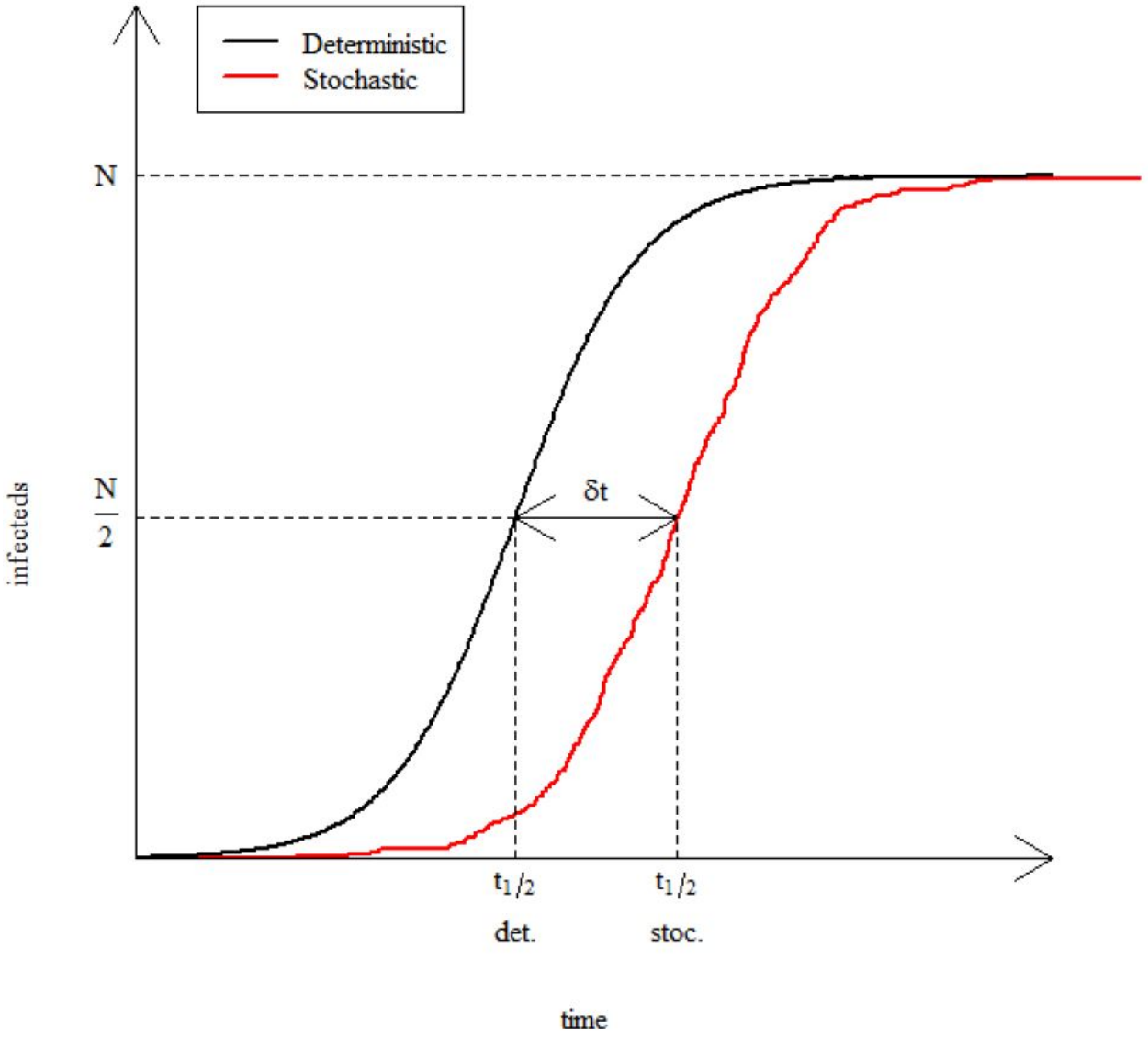
Now vary the infection rate ($\beta = 0.1, 0.5, 1$).

Qualitatively what effect does this have on the variability between replicates?

Show: Solution on P202

8.6 The delay time

Graphical exploration of model output is a good way to orientate yourself and understand the qualitative impact of changing parameters, but in practice we do need to explore various summary statistics. In this section we will compare the time it takes for a stochastic epidemic to infect half of the total population, $t_{\frac{1}{2}}$, with the time a deterministic epidemic takes. This difference is the delay time, δt (see the figure below).



We will repeat this for many stochastic replicates and plot a distribution of the delay times.

8.6.1 The deterministic half-time

The deterministic model predicts a constant value of $t_{\frac{1}{2}}$ given by the expression:

$$t_{\frac{1}{2}} = -\frac{1}{\beta} \ln\left(\frac{I_0}{N - I_0}\right)$$

(This can be derived exactly from the analytic solution to the system of differential equations for the SI system. This isn't going to be possible for more complex models.)

8.6.2 The stochastic half-time

We must now construct a function that calculates the value of $t_{\frac{1}{2}}$ for a set of stochastic simulations and the corresponding delay times:

Open a new script file and save as `Half_time.R` with the following content:

```
# Deterministic Halftime Function
det_halftime <- function(N, I0, beta) {

    # calculate deterministic half life
    return((-1/beta)*log(I0/(N-I0)))
}

# Stochastic Halftime Function
stoc_halftime <- function(model) {

    no_runs = n_nodes(model)
    N = sum(model@u0[,1])

    # create storage vector for stochastic half lives
    thalf <- numeric(no_runs)

    # loop over number of replicates
    for (iSim in 1:no_runs) {
        # extract the infected time series for each simulation
        output <- trajectory(out, "I", iSim)

        # find the first time when the infected population is at least half the total population
        ind <- min(which(output$I>=(N/2)))
        thalf[iSim] <- output$time[ind]
    }

    return(thalf)
}
```

The function `det_halftime` takes three arguments:

- The total host population `N`
- The initial number of infected `I0`
- The infection rate `beta`

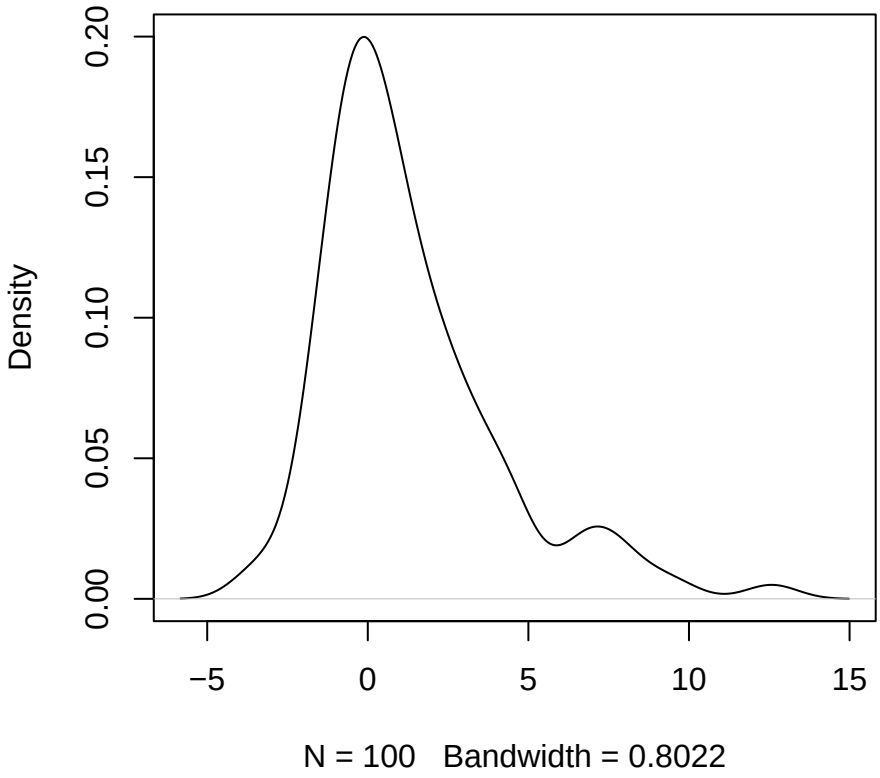
and returns the deterministic value of the time to half-height.

The function `stoc_halftime` takes a SimInf model object as its input and returns a vector with the time to half height of each model simulation (to nearest day).

We then plot a probability density plot for these delay times using the in-built function `density`.

```
source('Half_time.R')
SImodel <- create.StocSI(500, 1, 0.5, 30, 100)
out <- run(model = SImodel)

delay_times <- stoc_halftime(out) - det_halftime(500, 1, 0.5)

plot(density(delay_times), main = '')
```

`density` produces smoothed estimates of the frequency distributions of a set of samples (essentially a smooth line through the top of a histogram). This will produce a figure similar to the one below:



Task 70

Can the distribution of delay-times be used to quantify the appropriateness of the deterministic approximation for a given set of parameters? In particular, in what limits will the deterministic model produce useful predictions for the time-scale of an SI epidemic? You may wish to revisit the impact of changing the host-population size N, initial number of infectives I_0 and infection rate. Produce plots to justify your reasoning and discuss them with a demonstrator.

8.7 Coding a simple SIR model

Using the results from the earlier section on SI models as a starting point we will construct a stochastic SIR model. The deterministic SIR model equations are given by

$$\frac{dS}{dt} = -\beta \frac{SI}{N}$$

$$\frac{dI}{dt} = \beta \frac{SI}{N} - \mu I$$

$$\frac{dR}{dt} = \mu I$$

Task 71

1. Using these equations construct a transition diagram for the system
2. What are the states/compartments for this system?
3. What are the transitions events and what are the rates associated with each event?
4. What is the initial state of the system (i.e. how many individuals should be in each compartment initially)?

Open a new script in RStudio.

Task 72

Using the functions developed in the previous sections as a template construct a `create.StocSIR` function that takes five arguments:

- `N`: the total population size
- `I0`: the initial number of infected individuals
- `beta`: the infection rate
- `mu`: the recovery rate
- `f_time`: the time the simulation will run for (daily steps)
- `reps`: the number of replicate simulations to run

The skeleton function below can serve as a starting point.

```
create.StocSIR <- function(N, I0, beta, mu, f_time, reps = 1) {
    initial_state <-
    compartments <-
    transitions <-
    tspan <-

    model <- mparse(transitions = transitions,
                    compartments = compartments,
                    gdata = c(beta = beta, mu = mu),
                    u0 = initial_state,
                    tspan = tspan)

    return(model)
}
```

Hint

To specify multiple transitions in the `SimInf` algorithm you will need a transitions vector with two elements to it like this:

```
transitions <- c('S -> ?? -> I', 'I -> ?? -> R')
```

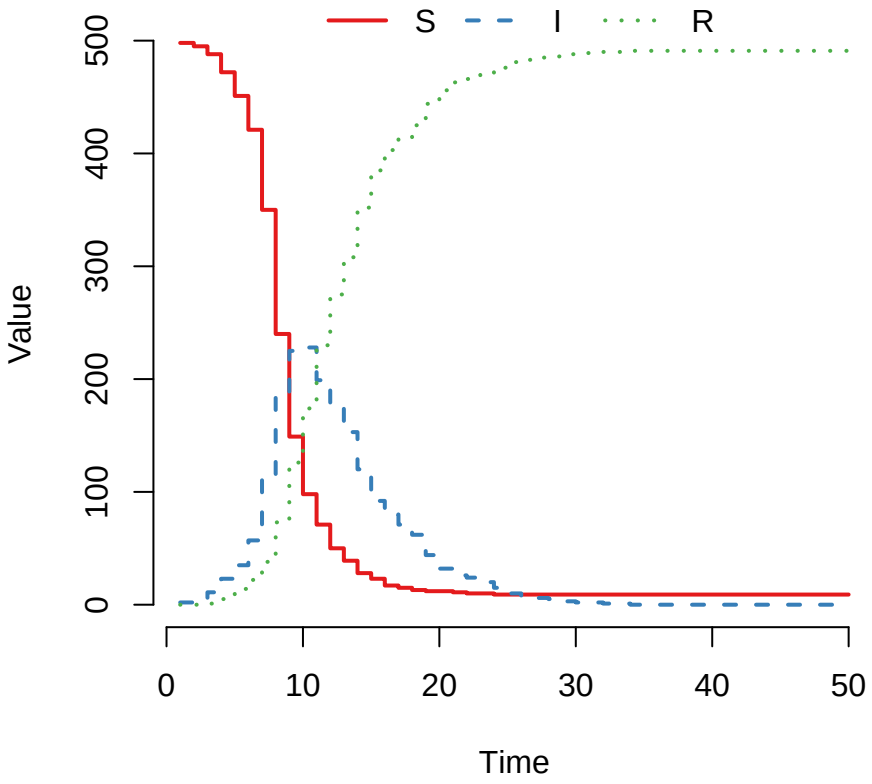
where I have deliberately replaced the relevant transition rates with `??`. You will need to replace the `??` with the correct rate equations.

Using your function run the following code:

```
SIRmodel <- create.StocSIR(500, 1, 1, 0.25, 50)
out <- run(model = SIRmodel)
plot(out)
```

Show: Solution on P203

This should produce a graph that looks like this:



However, some of you will see a very different graph. (If you do get something like this plot then try re-running the model and plotting it several times until you see something different.)

Question 73

Why might this be the case?

Show: Answer on P204

Task 74

Use this function to plot 20 replicates of the infection curves (use the code in the previous SI section as a guide).

Show: Solution on P204

Task 75

Load the R script called `Det_SIR.R` and adapting your code from the previous section make a plot that overlays the deterministic solution with the output of the stochastic model.

Show: Solution on P204

8.8 SIS Extension: Adding Recovery from Infection

Consider a system where individuals recover from infection with a fixed rate α and return to the susceptible class. This SIS system is described by the following system of equations:

$$\frac{dS}{dt} = \alpha I - \beta \frac{SI}{N}$$
$$\frac{dI}{dt} = \beta \frac{SI}{N} - \alpha I$$

Task 76

1. Draw the transition diagram for this system.
2. For each transition write down the rate at which it occurs.
3. What are the parameters required for this model?
4. Write a new function `create.StocSIS` based upon the `create.StocSI` function and add to the `Stoch_SI.R` file and repeat the above analysis. Use these initial values for the parameters:

- $\alpha = 0.1$
- $\beta = 0.5$

Show: Solution on P205

8.9 SIS Extension: Adding host demography

Consider an SI model with host demography. The system has constant birth rate Λ into the susceptible class and fixed per capita mortality rate μ from both the susceptible and infectious classes and is governed by the following equations:

$$\frac{dS}{dt} = \Lambda - \beta \frac{SI}{N} - \mu S$$

$$\frac{dI}{dt} = \beta \frac{SI}{N} - \mu I$$

Task 77

Repeat the previous steps for this model and create a `create.StocSI_demo` function in `Stoch_SI.R` and then explore its dynamics.

Hint

To specify a birth (or death) event then we use the `@` symbol to represent the "empty" compartment from which births appear (or to which deaths end up). So a birth event into the susceptible compartment would have the following transition string:

```
@ -> ?? -> S
```

Use these initial values for the parameters:

- $\mu = 0.1$
- $\beta = 0.5$
- $\lambda = 100$

Show: Solution on P207

8.10 SIR Extension: The final epidemic size

In order to further explore the effects of stochasticity in the SIR model we are going to explore the how the final size of an epidemic varies between realisations.

- What is the final size of an epidemic?
- What does it mean?
- Which state variable do we need to consider in order to calculate the final epidemic size?

For stochastic simulations the final epidemic size will vary between realisations of the epidemic which will mean that we need to think about a *distribution* of final epidemic sizes.

Task 78

Write code to calculate the final epidemic size from a `SimInf` output object. Use $\beta = 1$ and $\mu = 0.25$ as before, running the outbreak for 50 days.

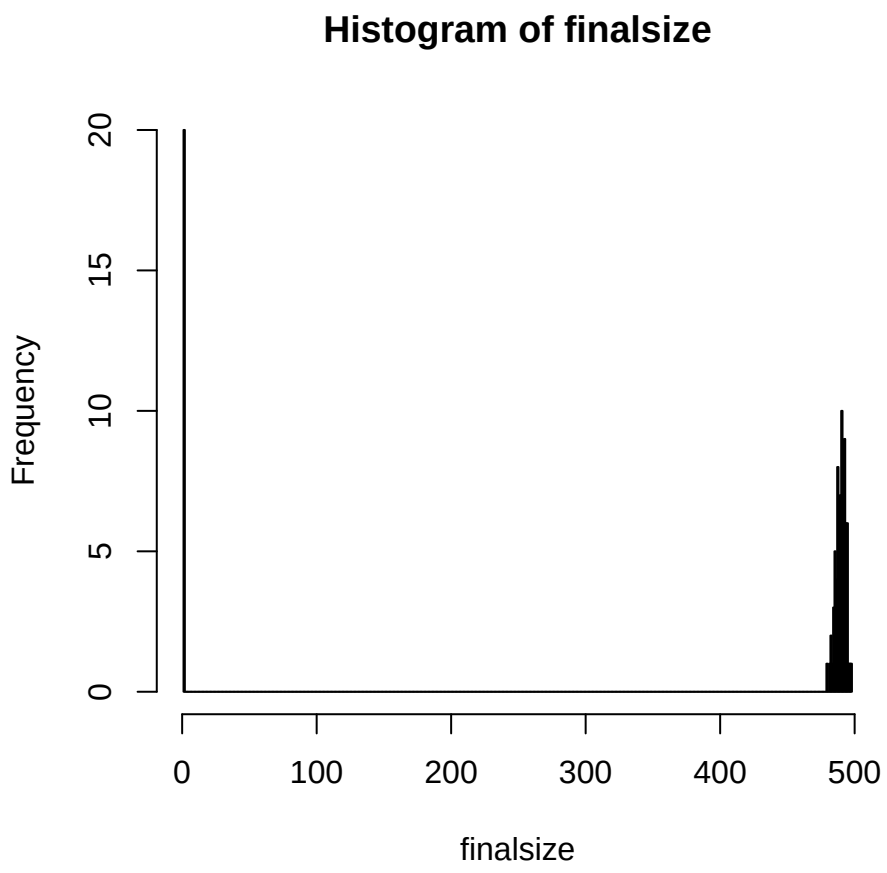
Hint

- What value should the final time for the simulations be set to (roughly)?
- As we've seen before, the function `trajectory` can be used to extract the actual values of the different compartments at each time point.
- Look at the code we used in the previous practical for calculating the halftime values for a single simulation and modify that logic accordingly.

Show: Solution on P208

Task 79

Run 100 realisations, extract the final epidemic size from each one and then produce a histogram of the final sizes. It should look something similar to the figure below:



Hint

- You'll probably want to use a loop to extract the final size for each simulation
- Set the histogram to use 500 bins

Why does the histogram have a bimodal distribution?

Show: Solution on P209

Recall that the final epidemic size for the deterministic SIR model showed strong dependency on the value of the basic reproductive number, R_0.

Task 80

- Write down an expression for R_0 for this system as a function of the parameters β and μ.
- Does this help explain the bimodal result?

Show: Solution on P209

For this section, we shall vary the value of R_0 by varying the transmission rate, β, whilst keeping the recovery

rate, μ, at a fixed value.

Task 81

Explore how the final size distribution varies with R_0 by producing histograms of the final size distribution as per the above figure for values of $R_0 = 20.0, 5.0, 2.0, 1.2, 1.0, 0.9, 0.5$.

Can you always identify the two modes of the distribution?

Show: Solution on P210

8.11 SIR Extension: Stochastic extinction

One of the primary differences between the deterministic and stochastic formulations of the SIR model is that in the stochastic formulation the epidemic becomes extinct within a finite time, the so-called extinction time. The extinction time varies between realisations and in this section we are going to explore this distribution.

Question 82

Which state variable do we need to consider in order to calculate the time to epidemic extinction and what is the value of this state variable at extinction?

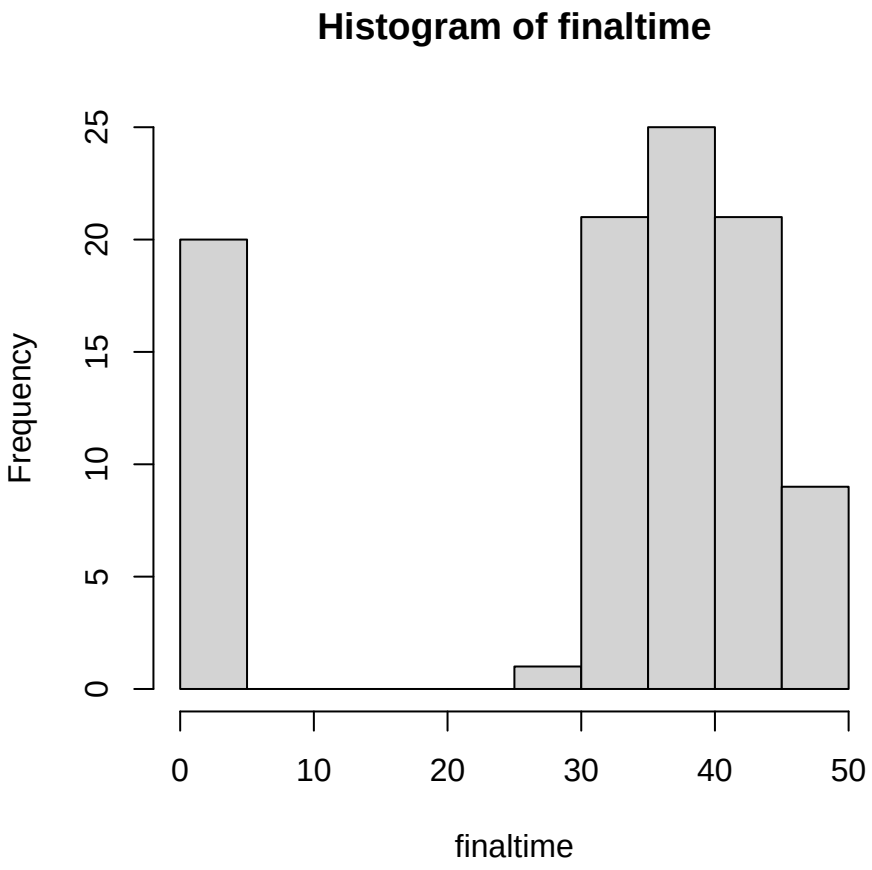
Show: Answer on P211

As with the final epidemic size, the extinction time will vary over realisations of the epidemic which will result in a distribution of extinction times, which we are now going to explore.

Task 83

Adapt your previous code to calculate the extinction time for each realisation.

- Run 100 realisations in order to produce a histogram of the time to extinction, as per the figure below:



- Explore the distribution of extinction times for several values of $R_0 = 20.0, 5.0, 2.0, 1.2, 1.0, 0.9, 0.5$.
- What do you notice about the distribution as R_0 gets close to 1?

Show: Solution on P211

Part V

Additional Materials

```
## [conflicted] Will prefer SimInf::run over any other package.
```

Chapter 9

Estimating R_0

Andrew Conlan (ajkc2@cam.ac.uk)

Aim: To compare final size and exponential growth estimators for R_0 using simulated data.

Outline:

1. Introduction: models and data sets
2. Final size method
3. Regression method
4. RECON `earlyR` method

> **Important**
>
> All required data and script files can be downloaded here. Please download this ZIP file and extract the files to your working directory.

9.1 Introduction: models and data sets

In Epidemic Practicals 1, 2 & 3 you wrote functions to numerically solve and simulate the deterministic and stochastic SIR models. For this practical we have extended these functions to add a latent class and implement the SEIR epidemic model introduced in lectures. If you have time at the end of this practical you can use these functions to simulate your own "Outfluenza" and "Biggles" data and explore the performance of the final size and linear regression methods.

However, so we all get the same results, we have provided simulated epidemics of "Outfluenza" and "Biggles" from which we will estimate R_0 using the final size, (log)-linear regression and the `earlyR` method from the **R E**pidemics **Con**sortium (RECON, https://www.repidemicsconsortium.org/).

The simulated outbreaks are provided as **line lists**, a common instrument used to collect data on individual cases during an outbreak where the date of infection (or rather the notification of a case) is recorded along with other relevant epidemiological information. For our purposes, the date of notification is sufficient to reconstruct the epidemic curve and test our different estimators of R_0.

Begin by reading in the line lists and converting the dates (stored as character strings) to date objects:

```
require(chron)
require(incidence)
# Load line lists of cases for simulated outbreaks
outfluenza1 <- read.table('Outfluenza1_cases.dat')
outfluenza1$x = as.Date(outfluenza1$x)

outfluenza2 <- read.table('Outfluenza2_cases.dat')
outfluenza2$x = as.Date(outfluenza2$x)

biggles <- read.table('biggles_cases.dat')
biggles$x = as.Date(biggles$x)
```

We are going to use the `incidence` package from RECON which has been written to simplify computing, visualising and modelling incidence of infectious disease from dated event data such as line lists.

To illustrate the key functions and concepts we will use `incidence` to construct daily incidence and cumulative incidence curves for the first outfluenza outbreak.

The main workhorse function is called `incidence` which converts a list of dates into an `incidence` object that bins cases into a given interval:

```
outfluenza1.i = incidence(outfluenza1$x,interval=1)
```

We can see a summary of the incidence object by simply typing the name of the variable:

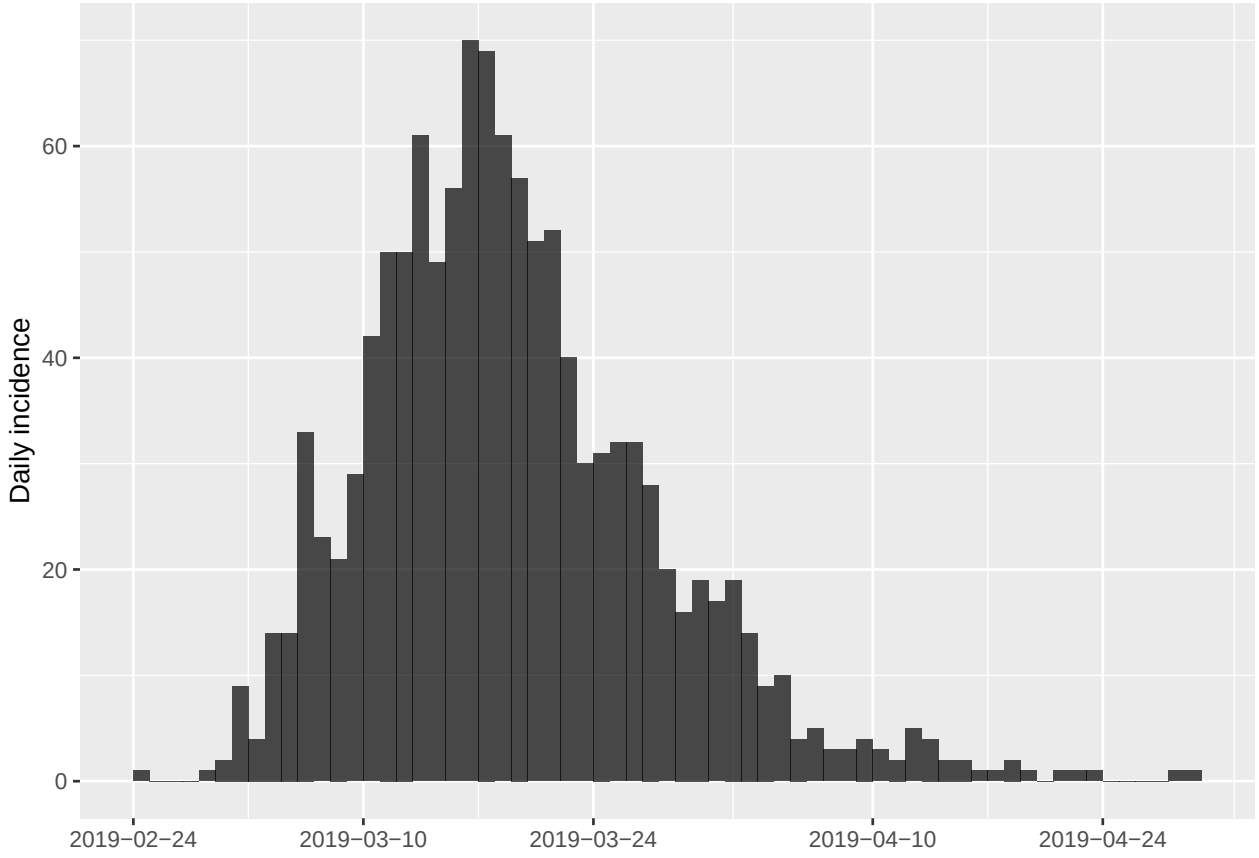
```
outfluenza1.i
```

```
## <incidence object>
## [1183 cases from days 2019-02-24 to 2019-04-29]
##
## $counts: matrix with 65 rows and 1 columns
## $n: 1183 cases in total
## $dates: 65 dates marking the left-side of bins
## $interval: 1 day
## $timespan: 65 days
## $cumulative: FALSE
```

So, the outfluenza1 outbreak consists of 1183 cases over the course of 65 days. We have chosen to bin cases on a daily interval (which is also the default so we could have simply left out this argument and will do so from now on).

The `incidence` package provides custom plot functions for `incidence` objects:

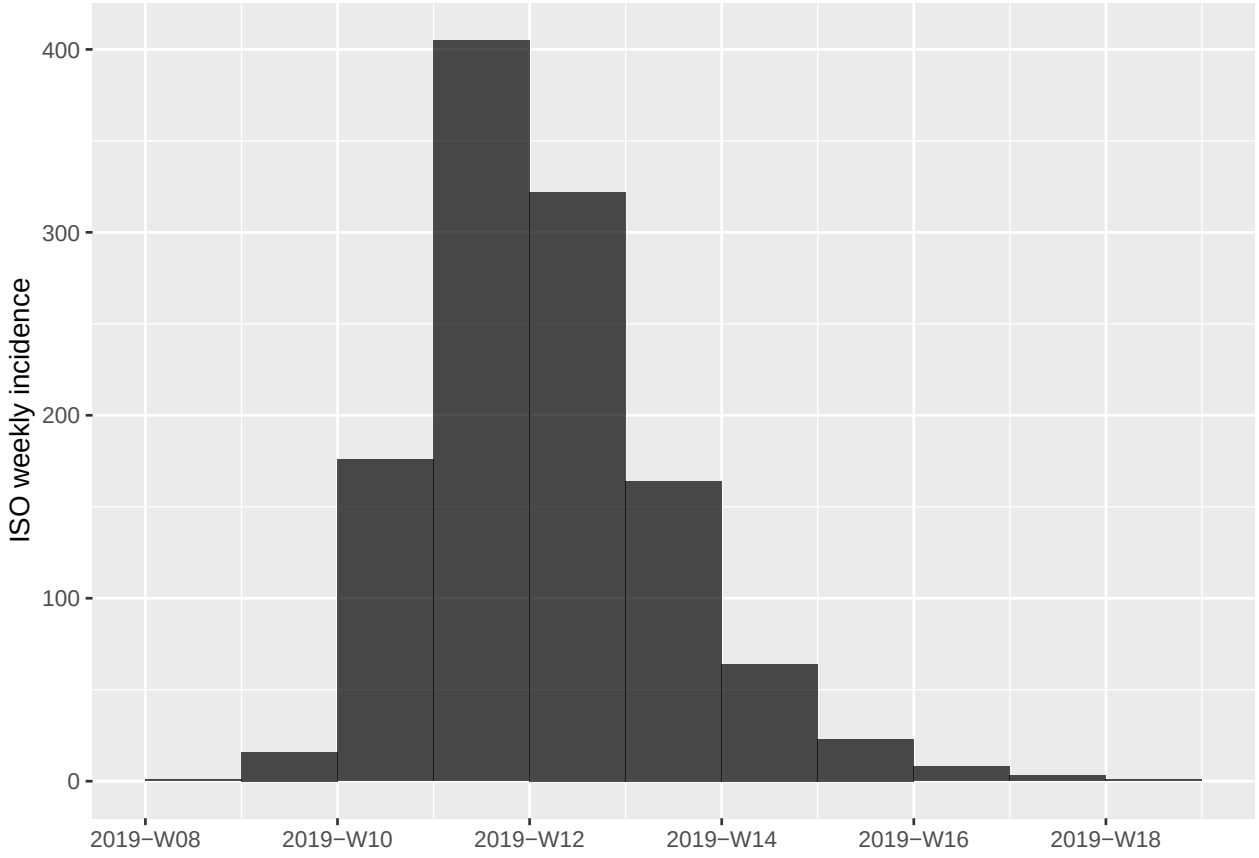
```
plot(outfluenza1.i)
```



Which should be familiar from the lectures.

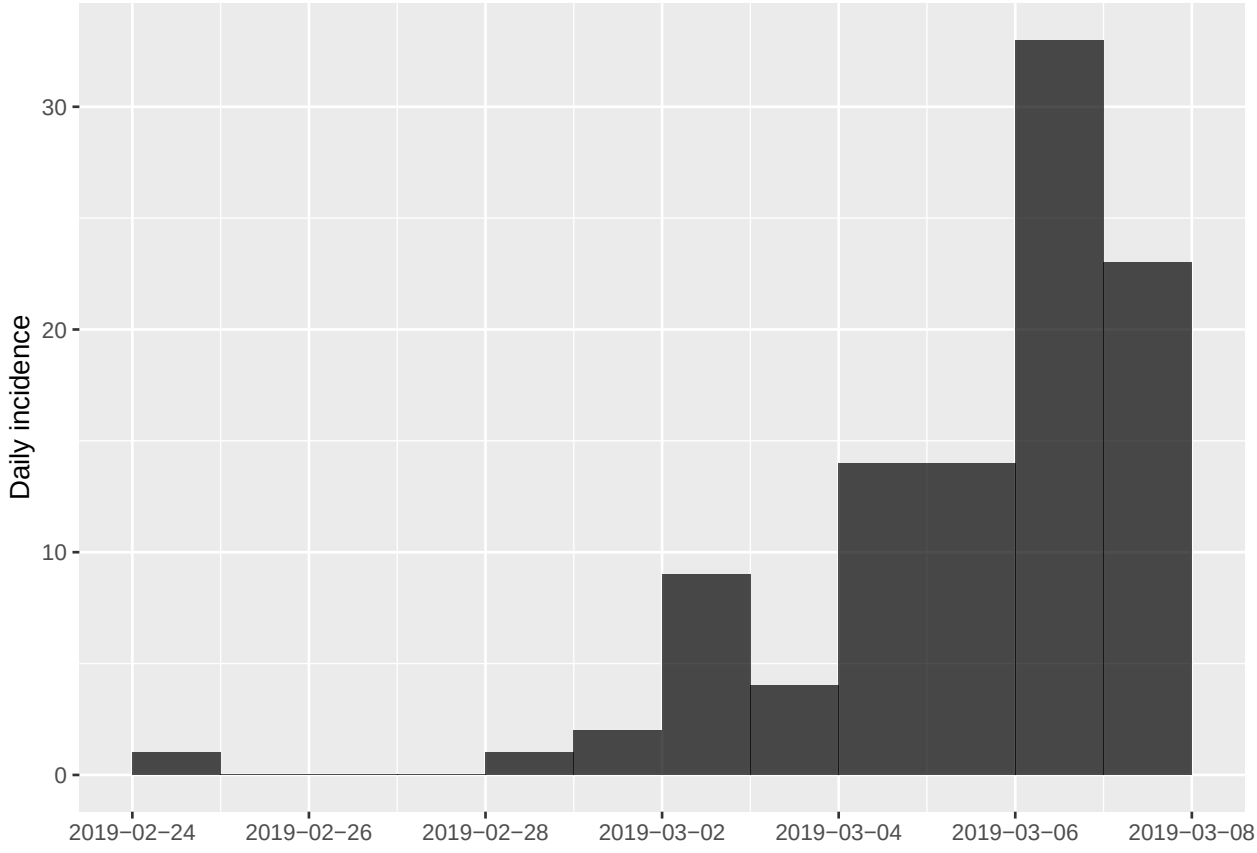
You can try experimenting with different intervals to see how this affects the shape of the epidemic curve:

```
plot(incidence(outfluenza1$x,interval=7))
```



`incidence` also allows you to subset curves between start and end dates:

```
plot(subset(outfluenza1.i,from=outfluenza1$x[1],to=outfluenza1$x[100]))
```



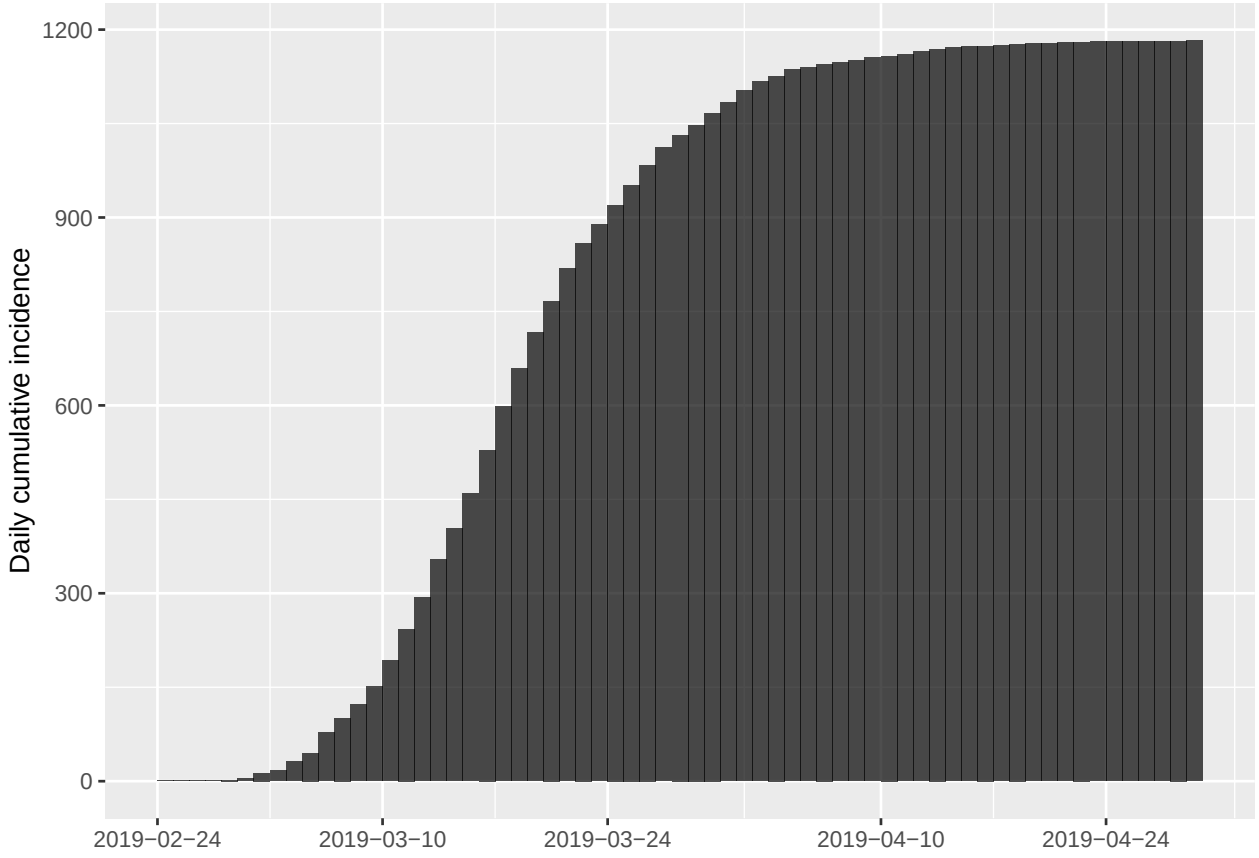
Task 84

What is the significance of choosing the dates to subset in this way?

Show: Solution on P213

The `cumulate()` function returns a the cumulative incidence curve:

```
plot(cumulate(outfluenza1.i))
```



Finally, you can convert an `incidence` object to a data frame by using the cast function `data.frame()`:

```
outfluenza1.df = data.frame(outfluenza1.i)
head(outfluenza1.df)
```

```
##        dates counts
## 1 2019-02-24      1
## 2 2019-02-25      0
## 3 2019-02-26      0
## 4 2019-02-27      0
## 5 2019-02-28      1
## 6 2019-03-01      2
```

9.2 Final size method

Final size methods for R_0 are in themselves a whole field of research. In this practical we will consider the utility of the basic deterministic "first estimate" also known as the final size formula:

$$R_0 = -\frac{\ln(1 - z_f)}{z_f} \tag{9.1}$$

where z_f is the total fraction of the population infected at the end of an epidemic in a closed population.

Task 85

Write a function `R0final` that returns the value of R_0 for a given value of z_f. Is there any restriction on the values that z_f can take for the final size equation to be valid? Your function should check that z_f takes a valid value and return a missing value (NA) when the final size equation is not defined.

Show: Solution on P214

This formula is more commonly used to predict the final size (z_f) of an epidemic once we have an independent estimate of R_0. This is less straightforward as we cannot solve equation (9.1) explicitly for z_f. We can progress by rewriting (9.1) into a problem we can solve numerically:

$$R_0 + \frac{\ln(1 - z_f)}{z_f} = 0 \tag{9.2}$$

We can find the final size (z_f) corresponding to a given value of R_0, by solving for the value(s) of z_f for which (9.2) is equal to zero. Finding the roots of a function is a common problem, so it should not surprise you that there is a R function to do the job. `uniroot` uses an numerical procedure to estimate the roots of an arbitrary function `f` within a fixed `interval=c(lower,upper)`. We can use `uniroot` to write a function that returns the predicted final size for a given value of R_0:

```
FinalSize <- function(R0) {
    return(uniroot(function(zf)
        {R0+log(1-zf)/zf},
        interval=c(.Machine$double.xmin,1.0))$root)
}
```

Check this function works by trying these test values on the R terminal:

```
FinalSize(1.2)
```

```
## [1] 0.3136976
```

```
FinalSize(1.0)
```

```
## [1] 6.103516e-05
```

```
FinalSize(0.9)
```

```
## [1] 6.103516e-05
```

The exact values may differ slightly between versions of R on different machines.

Note

Numerical methods are only accurate up to a specified precision or **tolerance**. This is fundamentally limited by the precision with which real numbers can be represented on a computer (that naturally works with integer or binary numbers). `.Machine$double.xmin` is the smallest number (or difference between two numbers) that can be stored in a given version of R. This value may change between versions and on different computer platforms (Windows, Mac OS, Linux…)

Task 86

Use the auxiliary functions of the incidence package and these new functions you have just written to estimate R_0 for the exemplar outfluenza and biggles outbreaks. (Remember the school size for all of these outbreaks was 1300 children.)

Show: Solution on P214

9.3 Regression method

In the lectures we discussed how the early phase of an epidemic can be approximately modelled by an exponential growth model:

$$I(t) = I(0)e^{\Lambda t} \tag{9.3}$$

where the exponential rate can be related to R_0 with the functional form depending on the structure of the epidemic model (in particular with respect to the distribution of latent and infectious periods). If we take logs of both sides of equation (9.3) and rearrange we get the equation of a straight line:

$$\log(I(t)) = \Lambda t + \log(I(0)) \tag{9.4}$$

with y-intercept given by the constant $\log(I(0)$ and slope Λ. So, we can therefore obtain a first approximation to R_0 simply by estimating the slope of the (logged) epidemic curve.

In principle, estimating R_0 using this method could be as straightforward as plotting the incidence or cumulative incidence curve on logarithmic graph paper and fitting a "best-fit" line, or using the Solver in Excel. We can be a little more sophisticated and use the linear regression model (`lm`) function in R. `lm()` uses a least squares method, effectively optimising the fit of the straight line to minimise the squared error between the line and the data.

As the exponential approximation is only valid early in the epidemic, including data from the full epidemic curve would bias our estimate of R_0. As discussed in the lecture we will use the first 100 cases. For a given simulation we need to select all the data-points up to the 100^{th} case. We can achieve this by sub setting the incidence object as before:

```
outflu1.sub<- data.frame(subset(outfluenza1.i,from=outfluenza1$x[1],to=outfluenza1$x[100]))
```

We fit a linear model (best straight line fit) to find the slope of the log cumulative cases as described in the lectures:

```
# Fit straight line to plot of biggles$t (time) and log of the cumulative cases (C)
outflu1.fit = lm(log(1+counts) ~ dates, data=outflu1.sub)
```

Note:

We add 1 to counts to handle any zero cases (this should not affect the estimated slope).

We can see the result of the regression by using the `summary` function:

```
summary(outflu1.fit)
```

```
##
## Call:
## lm(formula = log(1 + counts) ~ dates, data = outflu1.sub)
##
## Residuals:
##     Min      1Q  Median      3Q     Max
## -0.7081 -0.3553 -0.1211  0.3675  0.9870
##
## Coefficients:
##               Estimate Std. Error t value Pr(>|t|)
## (Intercept) -5.996e+03  7.855e+02  -7.633 1.77e-05 ***
## dates        3.340e-01  4.374e-02   7.635 1.77e-05 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.5231 on 10 degrees of freedom
## Multiple R-squared:  0.8536, Adjusted R-squared:  0.8389
## F-statistic:  58.3 on 1 and 10 DF,  p-value: 1.768e-05
```

Task 87

The `summary()` function provides a lot of detailed information on the statistical fit of the regression line – for the purpose of estimating R_0 the key value is the estimated slope highlighted in bold above. Using the expression for the SIR model presented in the lectures calculate the R_0 of outfluenza using this slope:

Show: Solution on P214

We can estimate the uncertainty in our estimate of R_0 from the uncertainty in our estimate of the slope from the linear regression. The R function `confint()` will calculate 95% confidence intervals for our regression model:

```
confint(outflu1.fit)
```

```
##                     2.5 %        97.5 %
## (Intercept) -7745.8850733 -4245.5519457
## dates           0.2365213     0.4314554
```

Task 88

Use these confidence intervals to calculate a 95% confidence interval for your estimate of R_0.

Show: Solution on P214

The incidence package has built in functions that simplify estimating the exponential growth rate. The base function is `fit` returns an `incidence_fit` object which returns details of the fit including the estimated exponential growth rate r and the confidence interval:

```
outflu1.fit2 <- fit(outfluenza1.i)
outflu1.fit2
```

```
## <incidence_fit object>
##
## $model: regression of log-incidence over time
##
## $info: list containing the following items:
##   $r (daily growth rate):
## [1] -0.0504102
##
##   $r.conf (confidence interval):
##            2.5 %      97.5 %
## [1,] -0.06954703 -0.03127338
##
##   $halving (halving time in days):
## [1] 13.75014
##
##   $halving.conf (confidence interval):
##         2.5 %   97.5 %
## [1,] 9.966597 22.16413
##
##   $pred: data.frame of incidence predictions (57 rows, 5 columns)
```

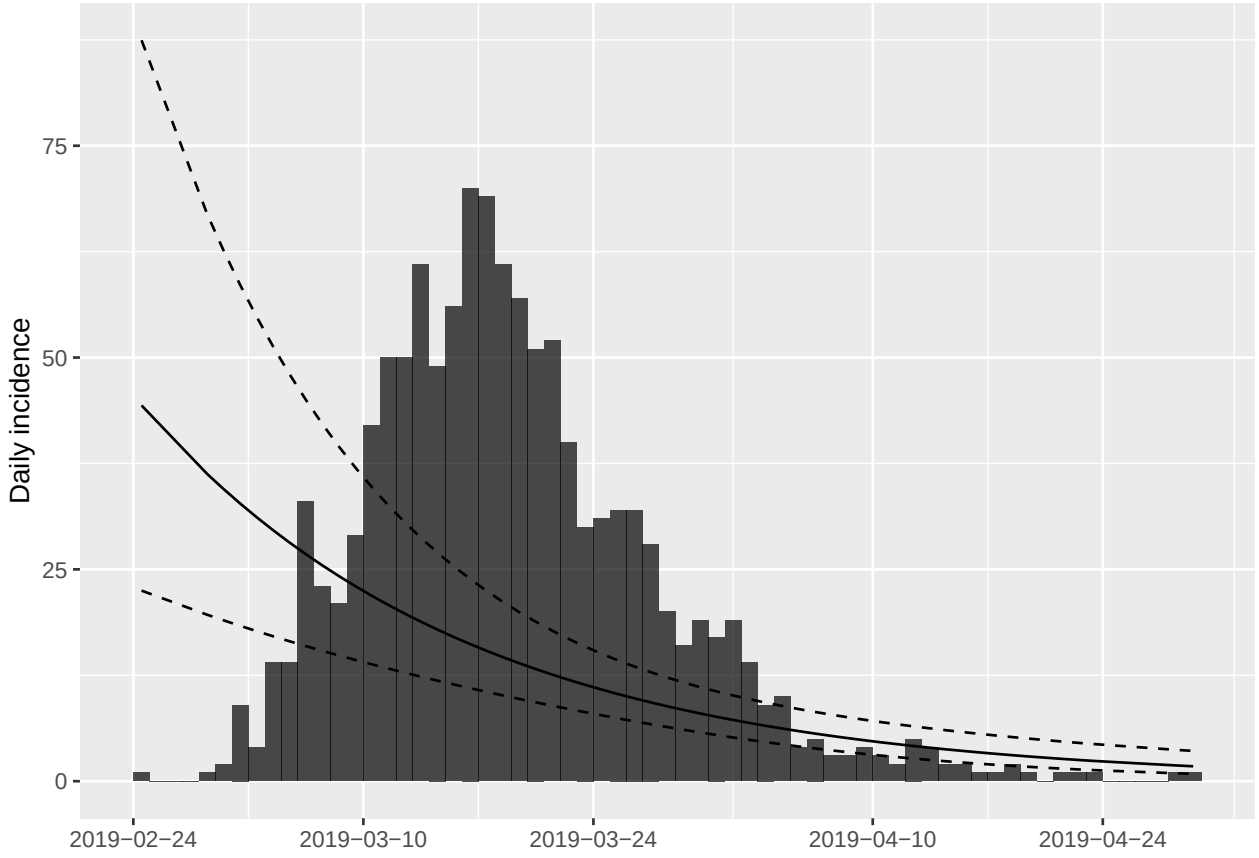
Question 89

Why does `fit` ignore dates with 0 incidence?

Show: Answer on P214

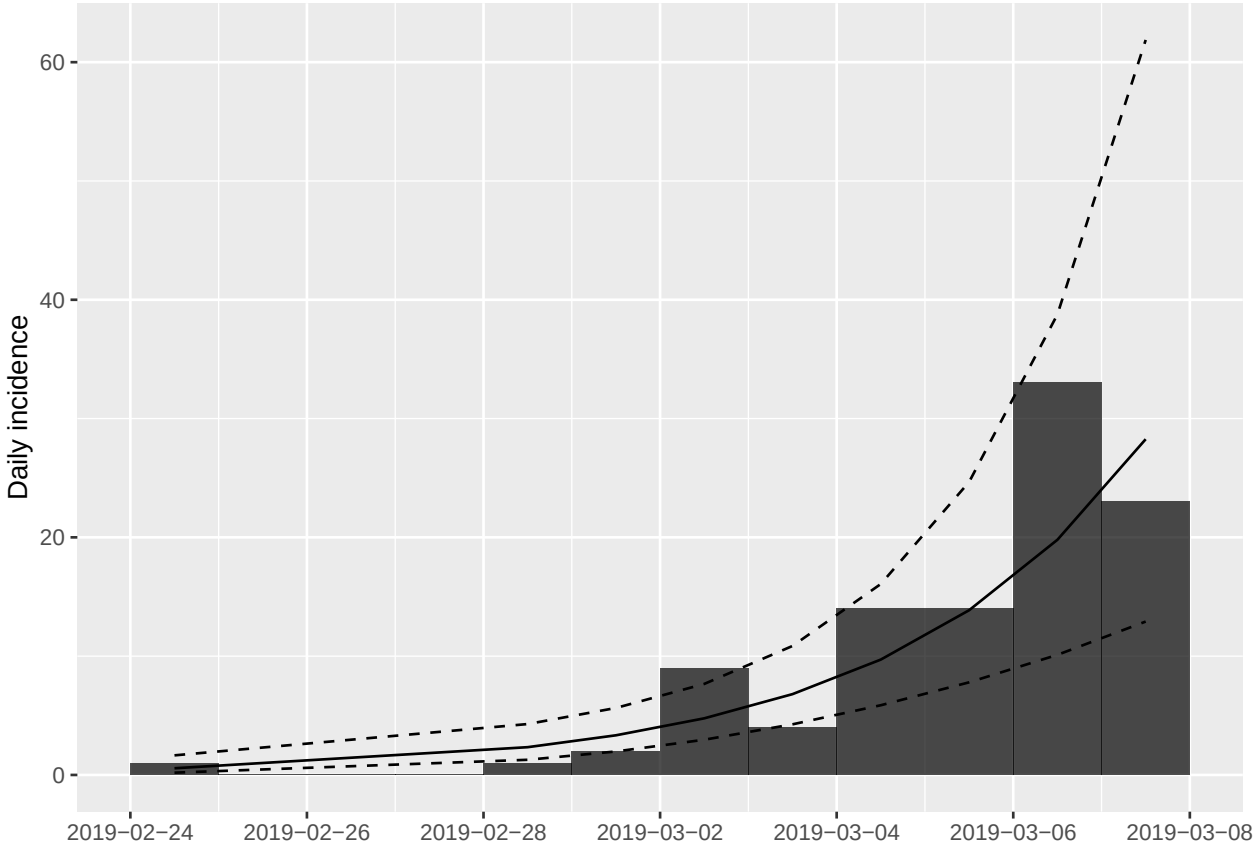
The estimated r is much lower than we obtained by our manual estimate. To see what has happened we can add the obtained fit to a plot of the incidence:

```
plot(outfluenza1.i, fit= outflu1.fit2)
```



We can use the `subset` function to limit our fit to the first 100 cases as before:

```
outflu1.sub = subset(outfluenza1.i,from=outfluenza1$x[1],to=outfluenza1$x[100])

outflu1.fit3 = fit(outflu1.sub)

plot(outflu1.sub,fit=outflu1.fit3)
```



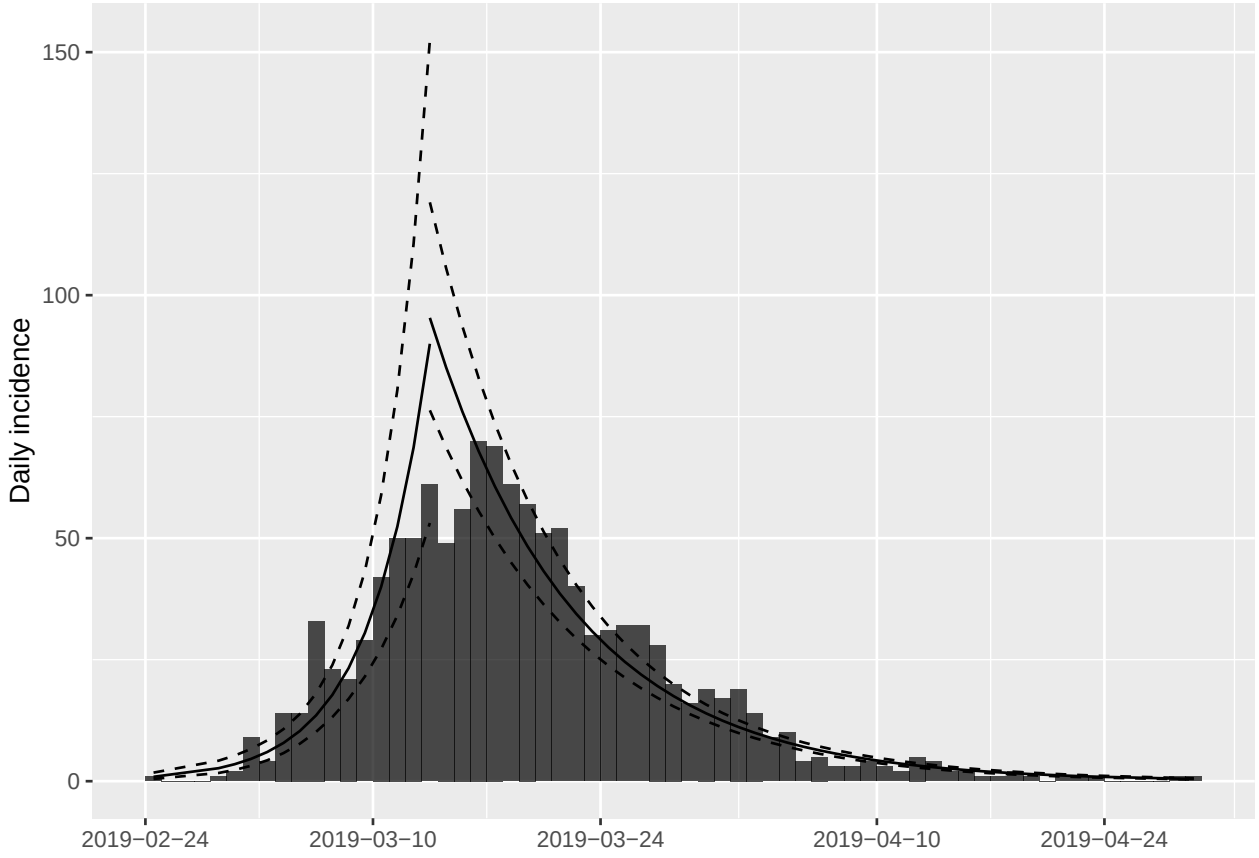
Question 90

How do the estimates from the incidence package and our manual estimate compare to each other and why (what's different)?

Show: Answer on P215

The `incidence` package provides a method for automatically sub setting the data by finding the optimum fit of two log-linear models (minimising the squared error of both):

```
outflu1.fit5 = fit_optim_split(outfluenza1.i)
plot(outfluenza1.i,fit=outflu1.fit5$fit)
```



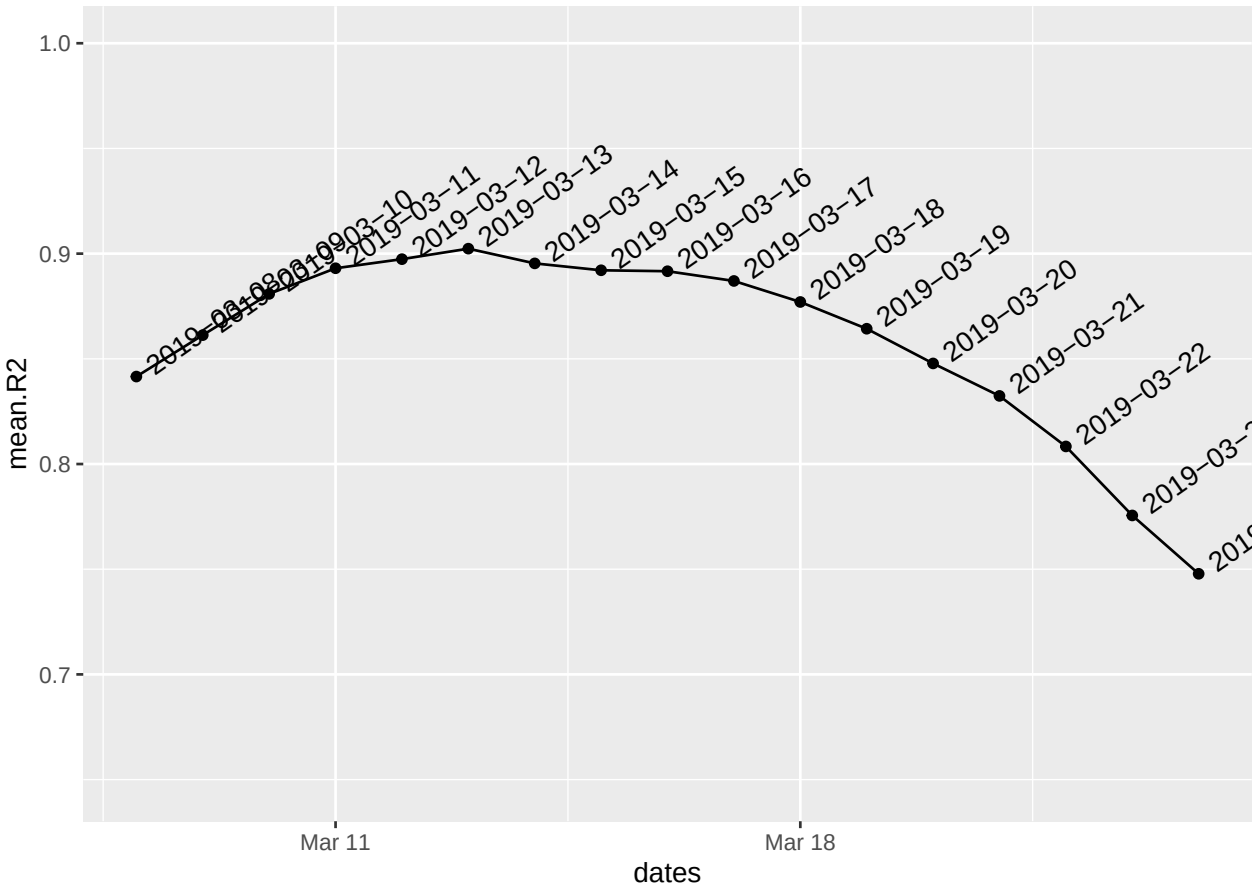
Note

The output of `fit_optim_split` now continues information on the two log-linear model fits, the first for the attack of the epidemic, the second describing the decay after the epidemic peak (which is also estimated as the **changepoint** between the two models).

Examine the output by entering into the R console:

```
outflu1.fit5
```

Which should also generate a plot of the mean r-squared error (R^2) of the two log-linear models against different dates for the changepoint:



9.4 RECON `earlyR` method

Finally we will use the `earlyR` package implementation of the Teunis and Wallinga method to estimate R_0 and compare to the other methods. The key function of the `earlyR` package is the `get_R` function that returns an estimate of R_0 when passed an incidence object and a serial interval distribution. The serial interval can be specified manually, but we will use the default gamma distribution which is parameterised by the mean (`si_mean`) and standard deviation (`si_sd`). For outfluenza, the serial interval distribution is exponentially distributed with mean equal to the variance (`si_mean = 5`, `si_sd = 5`).

```
library(earlyR)
estR = get_R(outfluenza1.i,si_mean=5,si_sd=5)
estR
```

```
##
## /// Early estimate of reproduction number (R) //
##  // class: earlyR, list
##
##  // Maximum-Likelihood estimate of R ($R_ml):
## [1] 1.001001
##
##
##  // $lambda:
##   NA 0.1812692 0.1484107 0.1215084 0.09948267 0.2627188...
```

```
##
##  // $dates:
## [1] "2019-02-24" "2019-02-25" "2019-02-26" "2019-02-27" "2019-02-28"
## [6] "2019-03-01"
## ...
##
##  // $si (serial interval):
## A discrete distribution
##   name: gamma
##   parameters:
##     shape: 1
##     scale: 5
```

Once again we have obtained a much lower estimate of R ($R_0 = 1.0$) than expected as the `earlyR` method is only valid during the exponential phase of the epidemic. If we subset again using the first 100 cases you should obtain a more consistent estimate of R_0 of 2.43.

We can calculated a boostrapped 95% confidence interval for the estimate using the `sample_R` function:

```
quantile(sample_R(estR), c(0.025, 0.975))
```

```
##     2.5%    97.5%
## 0.960961 1.046296
```

So our `earlyR` estimate of $R_0 = 2.43$ (2.0–3.0, 95% CI).

Task 91

Now we have introduced all of the methods, let's compare the estimates (and confidence intervals where possible) of R_0 for our three exemplar outbreaks. Complete the following table by adapting the code you have used in the practical.

Remember that for Outfluenza the mean serial interval is 5 days (standard deviation 5 days). For Biggles the latent period is 5 days, the exposed period is 5 days. As discussed in lectures, adding two exponentially distributed variables together gives a gamma distributed variable. So the serial interval for Biggles will be gamma distributed with a scale parameter of 10 days and a shape parameter of 2, giving a mean serial interval of 10 and standard deviation of $5\sqrt{2}$. *(Ask your instructor for more details if interested!)*

Outbreak	Regression r	Regression R_0	Final Size R_0	earlyR R_0
Outfluenza1				
Outfluenza2				
Biggles				

Task 92

Compare your estimates from the three methods of estimation. Are you surprised by the variability in estimates of R_0 that you have obtained compared to the size of the 95% confidence intervals of the estimates?

Show: Solution on P215

9.5 Appendix

You might be interested now in explore how well the final size and regression estimators perform on different stochastic replicates of the SIR or SEIR models.

`SIRmodels.R` and `SEIRmodels.R` files provide functions to allow you to generate your own simulated epidemics of Biggles and Outfluenza.

To load the functions into the R workspace using the following R code:

```
source('SIRmodels.R')
source('SEIRmodels.R')

N = 1300
```

`SIRmodels.R` provides two familiar functions:

- `DetSIR.dyn`

  Uses the internal R function `lsoda()` to numerically solve the **deterministic** SIR model given 5 parameters:

  - `N`: Population size
  - `I0`: Initial infected
  - `B`: transmission rate
  - `M`: "recovery" rate = $1/T_I$ corresponding to average infectious period of T_I
  - `f_time`: run time for numerical solution

- `create.StocSIR` defines an stochastic SIR model to use with the SimInf package and takes 6 arguments:

  - `N`: Population size
  - `I0`: Initial infected
  - `beta`: transmission rate
  - `m`: "recovery" rate = $1/T_I$ corresponding to average infectious period of T_I
  - `f_time`: run time for numerical solution
  - `reps`: number of replicates to simulate

`SEIRmodels.R` provides equivalent functions `DetSEIR.dyn` and `StocSEIR.dyn` that implement the deterministic and stochastic SEIR epidemic model respectively.

Both of these functions implementing the SEIR model take 7 parameters in the order that follows:

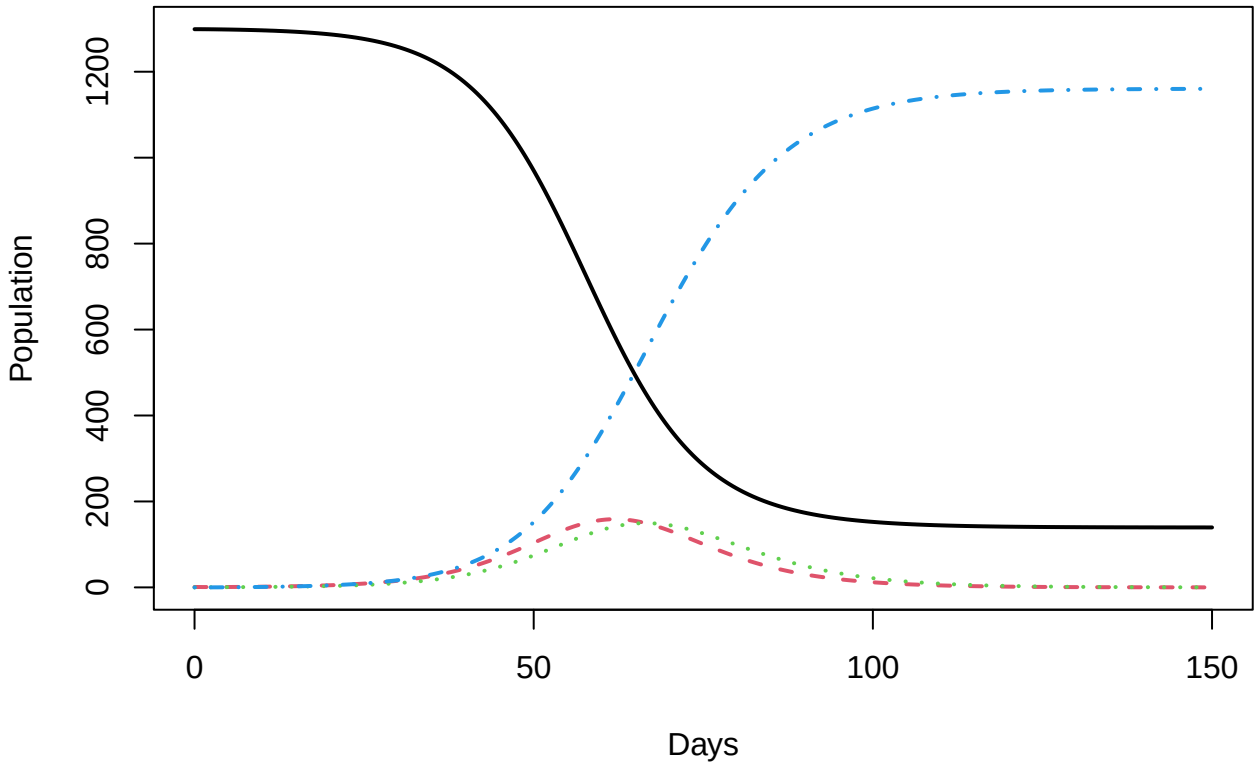
- `N`: Population size
- `I0`: Initial infected
- `E0`: Initial exposed
- `B`: transmission rate
- `G`: "progression" rate = $1/T_E$, with average exposed period of T_E
- `M`: "recovery" rate = $1/T_I$ corresponding to average infectious period of T_I
- `f_time`: run time for numerical solution

The deterministic equations for the SEIR are then:

$$\begin{aligned}\frac{dS}{dt} &= -\frac{\beta SI}{N}\\ \frac{dE}{dt} &= \frac{\beta SI}{N} - gE\\ \frac{dI}{dt} &= gE - mI\\ \frac{dR}{dt} &= mI\end{aligned}$$

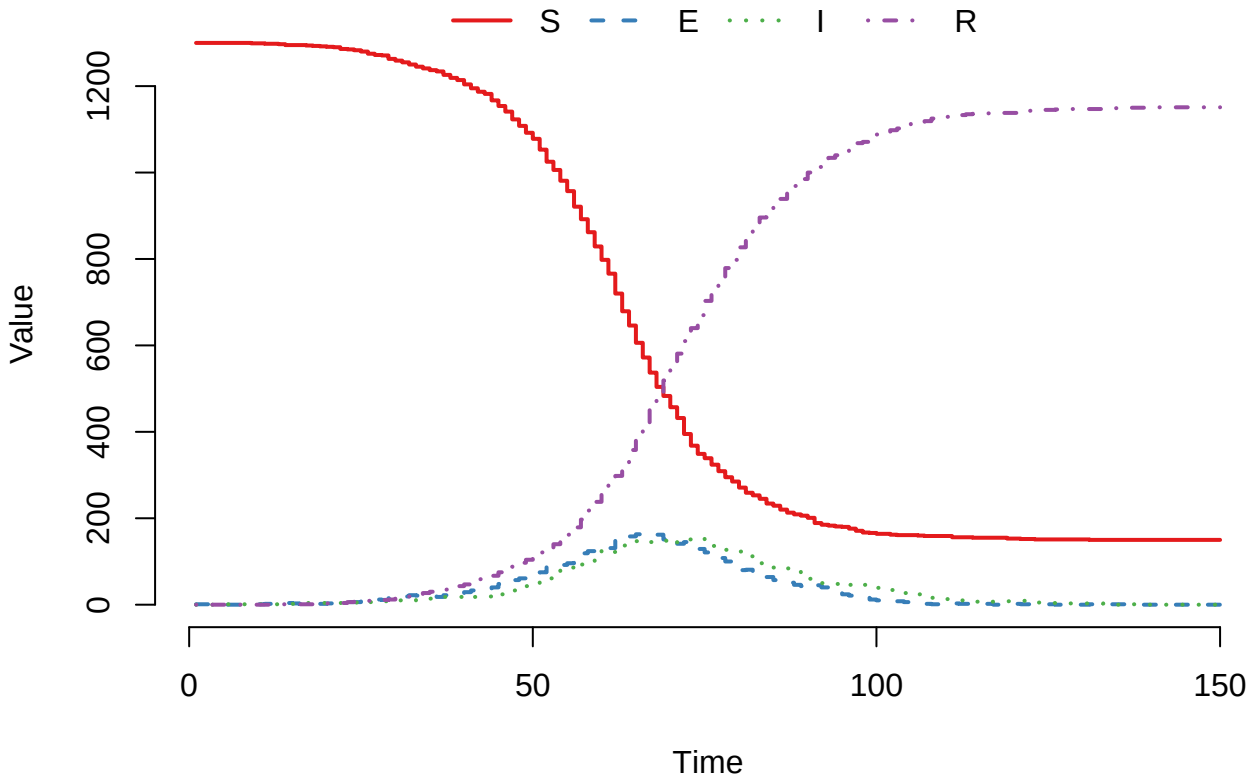
You can check this new code for the deterministic $SEIR$ model by simulating an epidemic using the Biggles parameters from the lecture and comparing to the figures in the lecture notes:

```
# Biggles Examplar Epidemic
det.sol<-DetSEIR.dyn(1300, 1,0, 0.5, 1/5.0, 1.0/5.0, 150)
matplot(det.sol[,1],det.sol[,2:5],type='l',xlab='Days',ylab='Population',lwd=2)
```



Checking the stochastic model is more difficult as the output will be different every time we run it! As a first sanity check we can compare stochastic simulations to the deterministic epidemic, checking that they (roughly) scatter evenly around the "mean" behaviour:

```
SEIRmodel <- create.StocSEIR(1300, 1, 0, 0.5, 1.0/5.0, 1/5.0, 150,1)
out <- run(model=SEIRmodel)
plot(out)
```



To simplify working with the incidence package we also provide a wrapper function `line_list()` that takes a `SimInf` object (out) as argument, along with a numeric value (node) and returns a line list of dates of cases for specified node:

```
SEIRmodel <- create.StocSEIR(1300, 1, 0, 0.5, 1.0/5.0, 1/5.0, 150,100)
out <- run(model=SEIRmodel)
line_list(out,1)
```

Chapter 10

Seasonality and Measles Epidemics

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10.1 Measles data and challenge

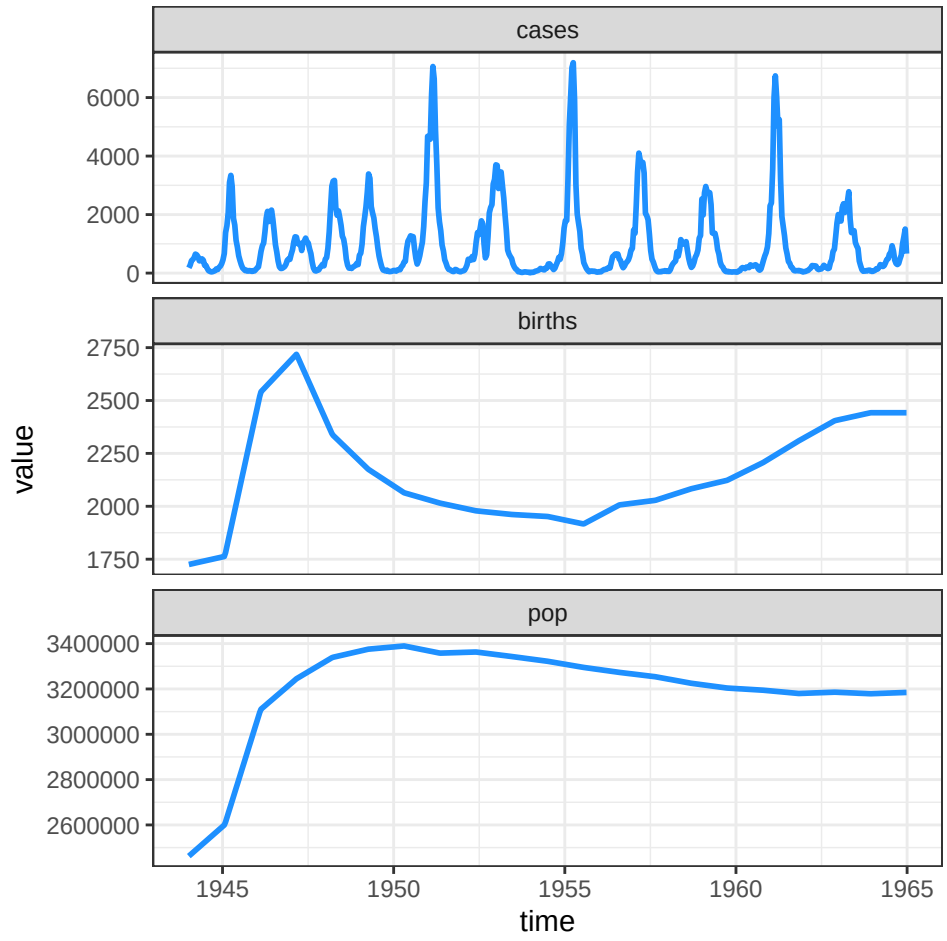
Implement a deterministic model to predict the impact of vaccination on the timing of outbreaks of measles in London. You should make the following assumptions to proceed:

- Constant population size of 3.3 million
- Birth rate of 20 per thousand per year
- Basic reproduction number $R_0 = 17$ (for sinusoidal forcing model)
- Cases can be approximately calculated from the number of infectives by multiplying by 7/5 (i.e. reporting period /average infectious period)
- The reporting rate during this period was 40%

A time-series of measles cases from London from 1950–1964 (immediately prior to the introduction of vaccination in the UK) are included as part of the `tsiR` package in R that provides historical time-series data from England and Wales along with functions to work with the so-called time-series SIR model ($TSIR$)—a discrete time chain binomial model that can be used to very successfully model and predict measles dynamics (and to a lesser extent other strongly immunizing childhood infections).

The `plotdata` function from the `tsiR` package provides a summary of the incidence and demographic data (birth rates and population size):

```
require(tsiR)
require(tidyverse)
require(ggplot2)
require(patchwork)
require(deSolve)

data("twentymeas")

LondonMeas <- twentymeas[["London"]]

plotdata(LondonMeas)
```



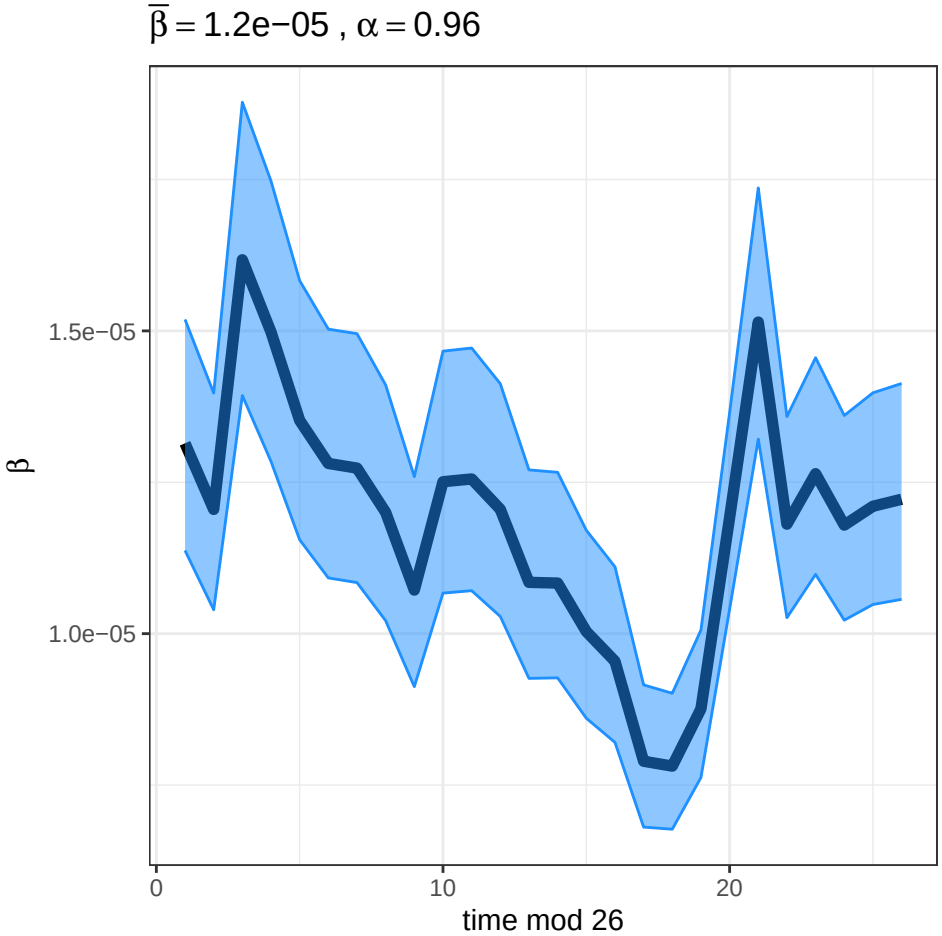
As you can see, our simplifying assumption of fixed birth and population size glosses over the "baby boom" post **WWII** that pushed the typical two-year cycle of measles epidemics into annual outbreaks and led (along with migration) to an increase in the population size. The $TSIR$ model can be used to estimate the seasonal variation in transmission rates presented in the background slides (on which we overlay the typical pattern of school terms in England and Wales calculated by the `mk_terms` function below):

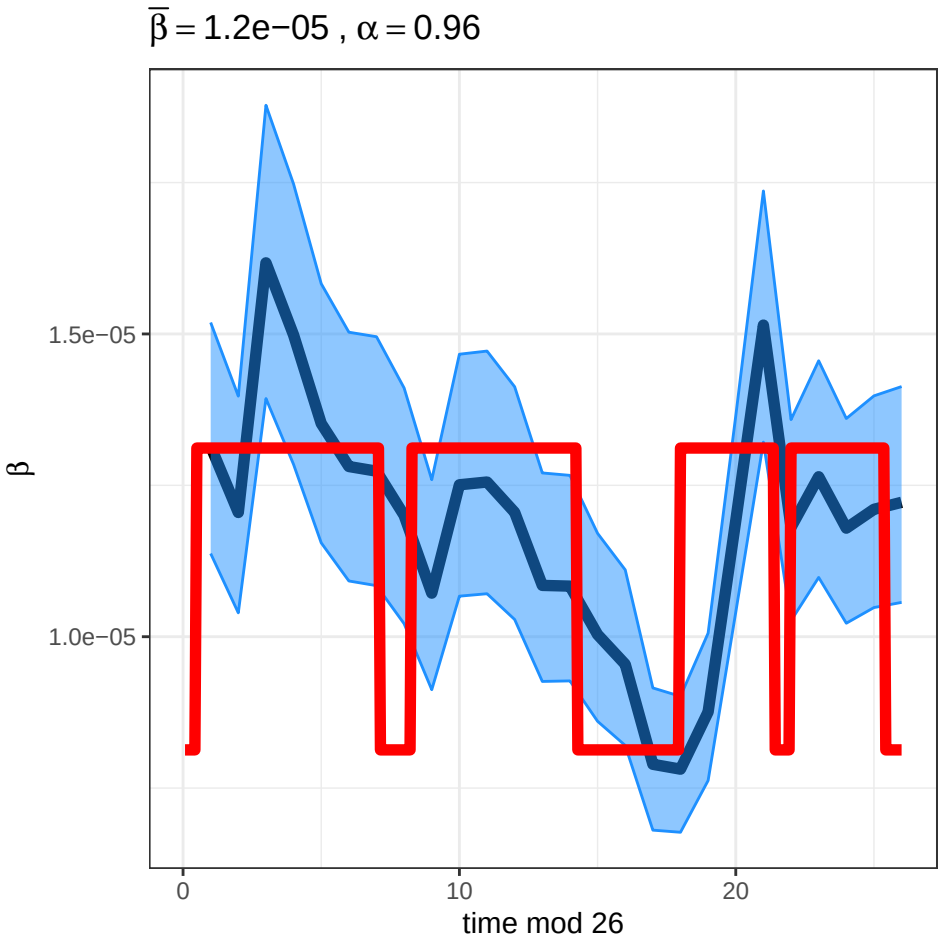
```
LondonRes <- runtsir(data=LondonMeas, IP = 2,
                     xreg = 'cumcases', regtype='gaussian',
                     alpha = NULL, sbar = NULL,
                     family = 'gaussian', link = 'identity',
                     method = 'negbin', nsim = 100)
```

```
##            alpha        mean beta         mean rho         mean sus
##         9.60e-01         1.19e-05         4.57e-01         1.14e+05
## prop. init. sus. prop. init. inf.
##         3.01e-02         6.12e-05
```

```
mk_terms <- function(beta, alpha)
{
  s = 273.0/364.0
  bh = (beta*(1 + 2*alpha*(1-s)))
  bl = (beta*(1 - 2*alpha*s))
```

```
  terms = numeric(364)

  terms[c(252:299)] = bh
  terms[c(300:307)] = bl
  terms[c(308:355)] = bh
  terms[c(356:364)] = bl
  terms[c(1:6)] = bl
  terms[c(7:99)] = bh
  terms[c(100:115)] = bl
  terms[c(116:199)] = bh
  terms[c(200:251)] = bl

  return(terms)

}

plotbeta(LondonRes) + annotate('line',x=seq(1,364,1)/14,y=mk_terms(mean(LondonRes$beta),0.21),lwd=2,col=
```

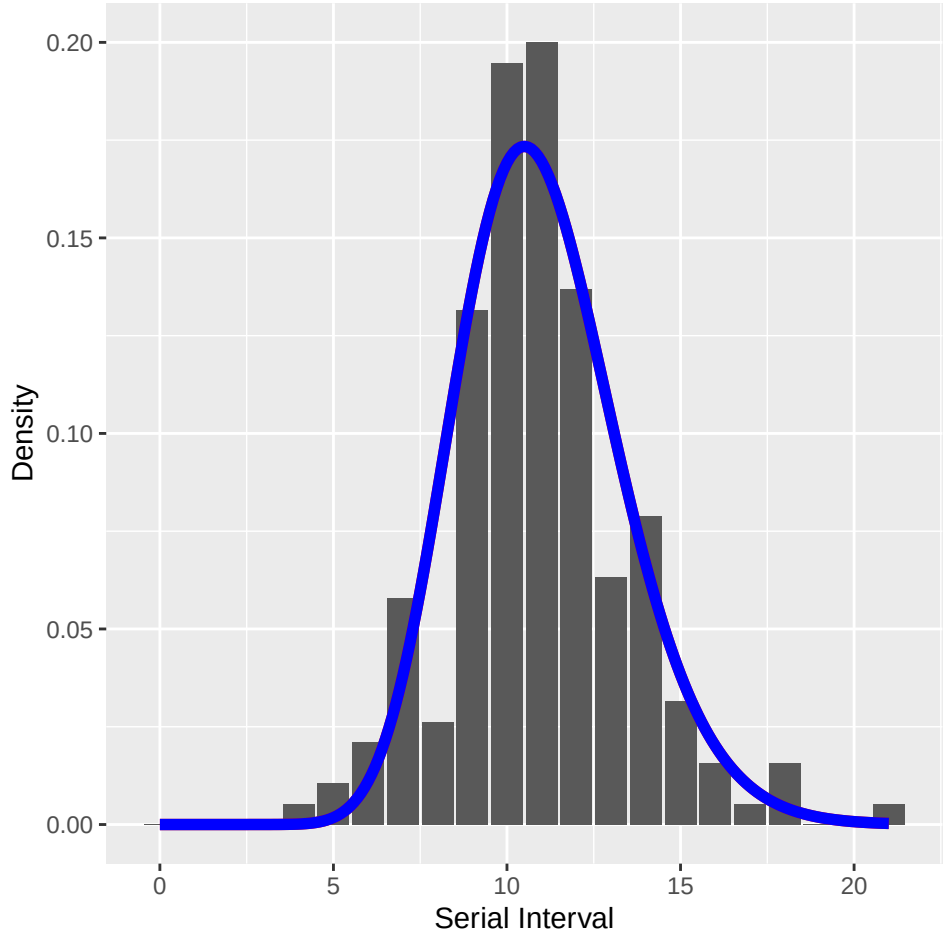




Important to note that the estimated transmission parameters from the $TSIR$ model **do not** translate directly to the transmission parameters for continuous-time (ordinary differential or stochastic) models. The qualitative pattern is informative rather than the specific estimates. (Conceptually I would consider these estimates to be closer to reproduction numbers than transmission rates as they are usually presented.). Note also that the α used in the $TSIR$ model is not an amplitude of seasonality but a correction (i.e. fudge) factor for the density dependence of the transmission term which—in some sense—can be used to adjust for artifacts arising from the discrete time approximation.

We also provided you with Hope-Simpson's estimates of the serial interval of measles and illustrated that it suggests that the latent and infectious periods of measles are less dispersed (less variable) than exponential and well described by a gamma distribution where the shape and scale parameters are approximately equal:

```
household <- as_tibble(read.csv('Materials/BYOM/Data/measles_hope_simpson.csv'))

SIR_gamma <-  tibble(interval=seq(0,21,0.1),value=dgamma(seq(0,21,0.1),22,22/11))
SEIR_gamma <- tibble(interval=seq(0,21,0.1),value=dgamma(seq(0,21,0.1),22,22/11))

ggplot(household,aes(x=interval,y=B/sum(B))) + geom_col() +
  annotate('line',x=SIR_gamma$interval,y=SIR_gamma$value,col='red',lwd=2) +
  annotate('line',x=SEIR_gamma$interval,y=SEIR_gamma$value,col='blue',lwd=2) +
  xlab('Serial Interval') + ylab('Density')
```



Show: Standard $SEIR$ (exponential) with sinusoidal forcing on P217

Show: Standard $SEIR$ (exponential) with term-time forcing on P227

Show: Gamma $SEIR$ with term-time forcing on P236

Chapter 11

Outbreak of influenza in a boarding school

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11.1 Data summary and challenge

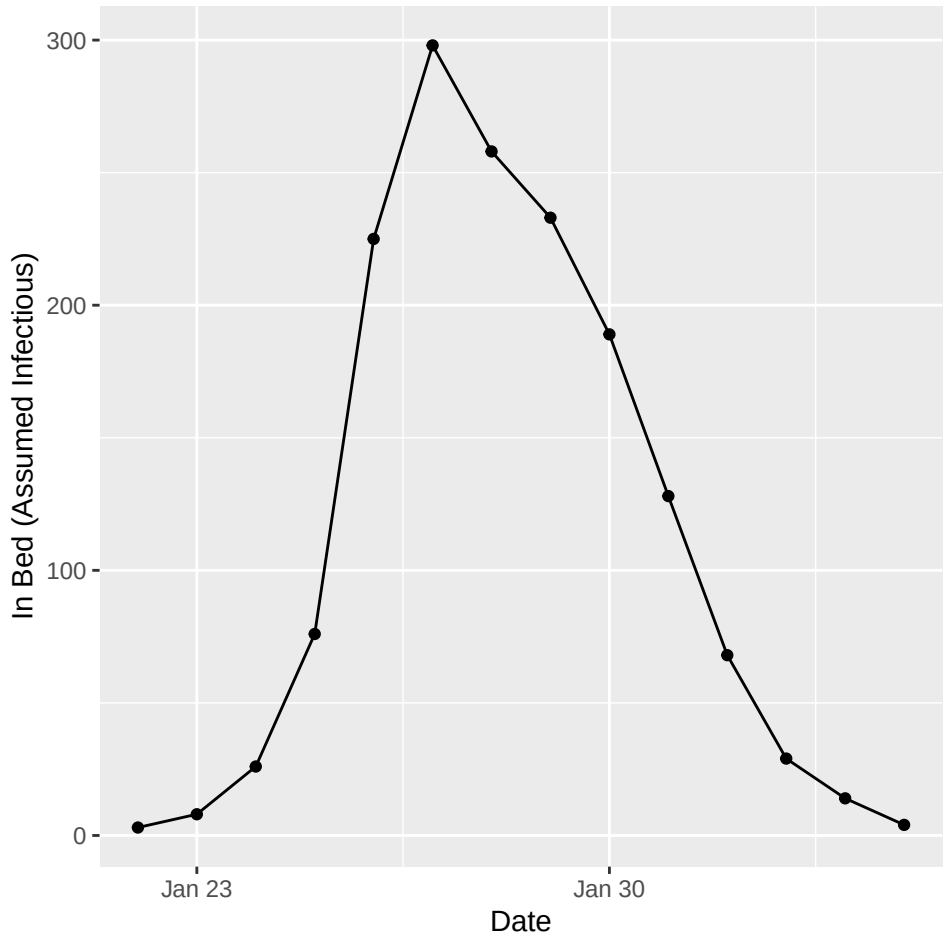
In this practical you will calibrate a transmission model to describe the outbreak of influenza in a English boarding school.

For the purposes of this practical assume that the numbers of pupils in bed measure the numbers infectious on each date. Not a great assumption as they are to an extent self-isolating, but also not terrible given the relatively short latent and (effective) infectious period for influenza (~ 1 day).

Model the likely impact on the outbreak should 80% of the boys have been vaccinated before the start of the outbreak with a vaccine with 50% (direct) protection from infection.

> **Note**
>
> For a single outbreak it is reasonable to neglect the potential for loss of immunity to reinfection so modelling vaccination in this case only amounts to changing the **initial conditions** of the model (i.e. the number susceptible and recovered when infection is introduced.) We are told to assume an exposed period of 1 hour and an infectious period of 2 days so a standard $SEIR$ compartmental model should be sufficient. You should use a deterministic model for your initial calibration and the explore how the dynamics differ for the corresponding stochastic model.

```
require(outbreaks)
require(tidyverse)
require(deSolve)

ggplot(influenza_england_1978_school,aes(x=date,y=in_bed)) + geom_point() + geom_line() + xlab('Date') +
```




```
targetI <- influenza_england_1978_school$in_bed
```

Show: Deterministic model on P245

Show: Stochastic model on P248

Part VI

Appendices

References

Hens, Niel, Ziv Shkedy, Marc Aerts, Christel Faes, Pierre Van Damme, and Philippe Beutels. 2012. *Modeling Infectious Disease Parameters Based on Serological and Social Contact Data*. Springer. https://doi.org/10.1007/978-1-4614-4072-7.

Answers

Solution 1

The answer is, of course, 42.

Return to task on P9

Solution 2

R returns an error because you've asked the `seq()` function to move from 10 to 0 by adding 0.5 each time, which it clearly can't do. The step size would have to be -0.5 in order to generate decreasing numbers.

Return to task on P25

Solution 3

```
## 1.
seq(2, 30, by = 2)
## 2.
seq(-2.5, 15.34, length.out = 14)
## 3.
seq(0, by = 0.04, length.out = 7)
## 4.
seq(101, -20, by = -11)
```

Return to task on P26

Solution 4

```
## 1.
1:11
## 1. (alternative)
seq(1, 11, by = 1)
## 2.
seq(2, 50, by = 2)
## 3.
seq(17, 33, by = 2)
## 4.
c("M", "T", "W", "T", "F", "S", "S")
```

Return to task on P31

Solution 5

```r
## generate a vector x of five elements from 1 to 5
x <- 1:5

## extract the third element of x
x[3]

## extract the 2, 3 and 4th elements of x
x[c(2, 3, 4)]

## change the first element of x to 17
x[1] <- 17

## extract all elements of x except the third
x[-3]

## extract all elements of x except the third
## and save to new object w
w <- x[-3]

## create a vector of length 5 called y with
## corresponding entries below
y <- c(1, 5, 2, 4, 7)

## extract all elements of y except the third
## and fifth
y[-c(3, 5)]

## extract elements 1, 4 and 5 from y
y[c(1, 4, 5)]

## create a vector i containing three elements:
## 1, 2 and 3
i <- 1:3

## extract elements 1, 2 and 3 from y
y[i]

## create a vector z of length 3 with elements
## 9, 10 and 11
z <- c(9, 10, 11)

## replace elements 1, 2 and 3 in y with z
y[i] <- z
```

Return to task on P32

Solution 6

```r
## 1. this sorts the vector y into increasing order.
order(y)
## 2. this reverses the order of y.
rev(y)
## 3. this sorts the vector y into increasing order.
sort(y)

## there are various ways to sort `y` into decreasing order e.g.
sort(y, decreasing = TRUE)
rev(sort(y))
order(-y)
```

Return to task on P32

Solution 7

```r
## creates a vector y containing entries
## 1, 2,  ..., 10
y <- 1:10

## squares each entry of y
y^2

## takes the natural log of each entry of y
log(y)

## takes the anti-log of each entry of y
exp(y)

## creates a vector called x containing
## entries below
x <- c(5, 4, 3, 2, 1, 5, 4, 3, 2, 1)

## adds each element of x to its corresponding
## element in y
x + y

## multiplies each element of x with its corresponding
## element in y
x * y

## creates a vector of length 3 called z
## with entries below
z <- c(-1, 2.2, 10)

## repeats z 4 times, and takes the first
## 11 entries, which it then adds to
## each corresponding entry of y
z + y

## repeats z 4 times, and takes the first
## 11 entries, which it then multiplies with
## each corresponding entry of y
z * y
```

Return to task on P33

Solution 8

```r
## create a vector x containing elements 1:10
x <- 1:10

## create a vector y containing the elements below
y <- c(5, 4, 3, 2, 1, 5, 4, 3, 2, 1)

## generate a logical vector where each
## element denotes whether x is < 4 (TRUE)
## or >= 4 (FALSE)
x < 4

## extracts all elements of x that are < 4
x[x < 4]

## extracts all elements of y where
## x < 4
y[x < 4]

## creates a logical vector where elements are TRUE
## if the element of y is > 1 AND <= 4, and FALSE
## otherwise
y > 1 & y <= 4

## extracts all elements of y that are > 1 and
## <= 4
y[y > 1 & y <= 4]

## extracts all elements of y that are not equal
## to 3 and pass them into a new vector z
z <- y[y != 3]
```

Return to task on P34

Solution 9

```r
## Here are the steps:

## 1. First create a sequence of numbers
## from 1 to 10 in increments of 0.5
## returns a vector
seq(1, 10, by = 0.5)

## 2. take the natural log of each
## element of the vector - returns a vector
log(seq(1, 10, by = 0.5))

## 3. take the square root of each logged
## element - returns a vector
sqrt(log(seq(1, 10, by = 0.5)))

## 4. sums all the elements of the
## transformed vector - returns a single
## number (a vector of length 1)
sum(sqrt(log(seq(1, 10, by = 0.5))))
```

Return to task on P35

Solution 10

```
## create a vector y containing the numbers below
y <- c(5, 4, 3, 2, 10, 5, 4, 3, 2, 1)

## visualise y as a factor
factor(y)

## visualise y as a factor but set the levels
## this means some levels will have zero
## entries
factor(y, levels = 1:10)

## create a character vector y containing the numbers
## below coded a strings
y <- as.character(c(5, 4, 3, 2, 10, 5, 4, 3, 2, 1))

## visualise y as a factor - sorts levels
## lexicographically (hence 10 coded before 2 etc.)
factor(y)

## visualise y as a factor, but set levels that would
## be equivalent to if y was numeric instead of
## a character vector
factor(y, levels = sort(unique(as.numeric(y))))

## create a character vector y containing the strings below
y <- c("low", "mid", "mid", "high", "low")

## visualise y as a factor - sorts levels
## lexicographically (so alphabetically in this case)
factor(y)

## visualise y as a factor - sorts levels
## into a more sensible ordering
factor(y, levels = c("low", "mid", "high"))
```

Return to task on P36

Solution 11

```
## creates a (2 x 2) matrix with entries
## 1:4 placed down the columns first
matrix(1:4, 2, 2)

## creates a (2 x 2) matrix with entries
## 1:4 placed across the rows first
matrix(1:4, 2, 2, byrow = TRUE)

## creates a (3 x 4) matrix filled with zeros
matrix(0, 3, 4)
```

Return to task on P38

Solution 12

```
## create a vector vals and fill with values
vals <- c(1, 2, 3, 4, 5, 0.5, 2, 6, 0, 1, 1, 0)

## create a (4 x 3) matrix and fill with entries
## from vals, filling down the columns first
mat <- matrix(vals, 4, 3)

## extract the entry of mat in the
## 2nd row and 3rd column
mat[2, 3]

## extract the first row of mat
mat[1, ]

## extract the third column of mat
mat[, 3]

## extract all rows of mat except the second
mat[-2, ]

## extract entries in the first and third row,
## and second and third column
mat[c(1, 3), c(2, 3)]
```

Return to task on P39

Solution 13

```
## create a vector x1 containing the entries 1:3
x1 <- 1:3

## create a vector x2 containing the entries below
x2 <- c(7, 5, 6)

## create a vector x3 containing the entries below
x3 <- c(12, 19, 25)

## bind x1, x2 and x3 together as columns
## to form a (3 x 3) matrix
cbind(x1, x2, x3)

## bind x1, x2 and x3 together as rows
## to form a (3 x 3) matrix
rbind(x1, x2, x3)
```

Return to task on P39

Solution 14

```
## create a (3 x 3) matrix x containing
## the numbers 1:9 down the columns
x <- matrix(1:9, 3, 3)

## print x to the screen
x

## mutliply each element of x by 2
x * 2

## multiply row 1 by 1, row 2 by 2 and row 3 by 3
x * c(1:3)
```

Return to task on P40

Solution 15

```
## convert columns to factors
ff$partners <- factor(ff$partners)
ff$partner.type <- factor(ff$partner.type)

## produce summary
summary(ff)
```

```
##  partners      partner.type   longevity         thorax
##  0:25     Control    :25    Min.   :16.00   Min.   :0.640
##  1:50     Inseminated:50    1st Qu.:46.00   1st Qu.:0.760
##  8:50     Virgin     :50    Median :58.00   Median :0.840
##                             Mean   :57.44   Mean   :0.821
##                             3rd Qu.:70.00   3rd Qu.:0.880
##                             Max.   :97.00   Max.   :0.940
```

Notice that the summary now produces counts for each level of the relevant categorical variables.

Return to task on P46

Solution 16

Prints numbers in order.

```
## [1] "1 1"
## [1] "2 2"
## [1] "3 3"
## [1] "4 4"
## [1] "5 5"
## [1] "6 6"
## [1] "7 7"
## [1] "8 8"
## [1] "9 9"
## [1] "10 10"
```

Return to task on P52

Solution 17

Prints numbers in reverse order according to whatever is in sample `b`.

```
## [1] "10 7"
## [1] "9 8"
## [1] "8 1"
## [1] "7 3"
## [1] "6 2"
## [1] "5 6"
## [1] "4 4"
## [1] "3 5"
## [1] "2 9"
## [1] "1 10"
```

Return to task on P52

Solution 18

Prints numbers in forward order according to whatever is in vector `b`.

```
## [1] "1 10"
## [1] "2 9"
## [1] "3 5"
## [1] "4 4"
## [1] "5 6"
## [1] "6 2"
## [1] "7 3"
## [1] "8 1"
## [1] "9 8"
## [1] "10 7"
```

Return to task on P52

Solution 19

Prints numbers in a random order from whatever is in vector `b`.

```
## [1] "3 5"
## [1] "10 7"
## [1] "9 8"
## [1] "6 2"
## [1] "8 1"
## [1] "2 9"
## [1] "1 10"
## [1] "5 6"
## [1] "4 4"
## [1] "7 3"
```

Return to task on P52

Solution 20

```
for (i in 1:12) {
    result <- i * 12
    print(paste(i, "times 12 is", result))
}
```

```
## [1] "1 times 12 is 12"
## [1] "2 times 12 is 24"
## [1] "3 times 12 is 36"
## [1] "4 times 12 is 48"
## [1] "5 times 12 is 60"
## [1] "6 times 12 is 72"
## [1] "7 times 12 is 84"
## [1] "8 times 12 is 96"
## [1] "9 times 12 is 108"
## [1] "10 times 12 is 120"
## [1] "11 times 12 is 132"
## [1] "12 times 12 is 144"
```

Return to task on P53

Solution 21

```
i <- 1
while(i <= 12) {
  result <- i * 12
  print(paste(i, "times 12 is", result))
  i <- i + 1
}
```

```
## [1] "1 times 12 is 12"
## [1] "2 times 12 is 24"
## [1] "3 times 12 is 36"
## [1] "4 times 12 is 48"
## [1] "5 times 12 is 60"
## [1] "6 times 12 is 72"
## [1] "7 times 12 is 84"
## [1] "8 times 12 is 96"
## [1] "9 times 12 is 108"
## [1] "10 times 12 is 120"
## [1] "11 times 12 is 132"
## [1] "12 times 12 is 144"
```

Return to task on P53

Solution 22

```
runningSum <- 0
for(i in 1:15) {
  runningSum <- runningSum + 2^i
}
print(paste("Sum is", runningSum))
```

```
## [1] "Sum is 65534"
```

Note you can do the above more efficiently using vectorised operators, e.g. `sum(2^(1:15))`.

Return to task on P53

Solution 23

```
thisIDX <- 1
thisPower <- 2^thisIDX
while(thisPower<1000000) {
  thisIDX <- thisIDX + 1
  thisPower <- 2^thisIDX
}
print(paste("2^",thisIDX,"=",thisPower,sep=""))
```

```
## [1] "2^20=1048576"
```

Return to task on P54

Solution 24

```
sayHelloWithArg()       # error, since not passed argument
```

```
## Error in sayHelloWithArg(): argument "whoTo" is missing, with no default
```

```
# echos function's code to screen (happens in general if
# type function's name without brackets)
sayHelloWithArg
```

```
## function(whoTo) {
##     print(paste("Hello", whoTo))
## }
```

```
sayHelloWithArg("nik")  # works as expected
```

```
## [1] "Hello nik"
```

```
sayHello("nik")         # error, since too many arguments for the simpler function
```

```
## Error in sayHello("nik"): unused argument ("nik")
```

```
sayHelloWithArg(nik)    # error, since variable nik is not defined
```

```
## Error in eval(expr, envir, enclos): object 'nik' not found
```

```
sayHelloWithArg(whoto="nik") # error, since argument names are case sensitive
```

```
## Error in sayHelloWithArg(whoto = "nik"): unused argument (whoto = "nik")
```

```
sayHelloWithArg(whoTo="nik") # works as expected
```

```
## [1] "Hello nik"
```

Return to task on P54

Solution 25

The line `ghost <- buster(canary, -cat)` sets `ghost` to be 2, but leaves `cat` and `canary` unchanged.

Return to task on P55

Solution 26

```
# my function to sum elements of a vector and return that and the mean
mySumAndMean <- function(toSum) {
  retVal <- 0
  for(i in 1:length(toSum)) {
    retVal <- retVal + toSum[i]
  }
  meanVal <- retVal/length(toSum) # find the mean, too
  return(c(retVal,meanVal))       # return two values by wrapping up into vector
}
```

Return to task on P56

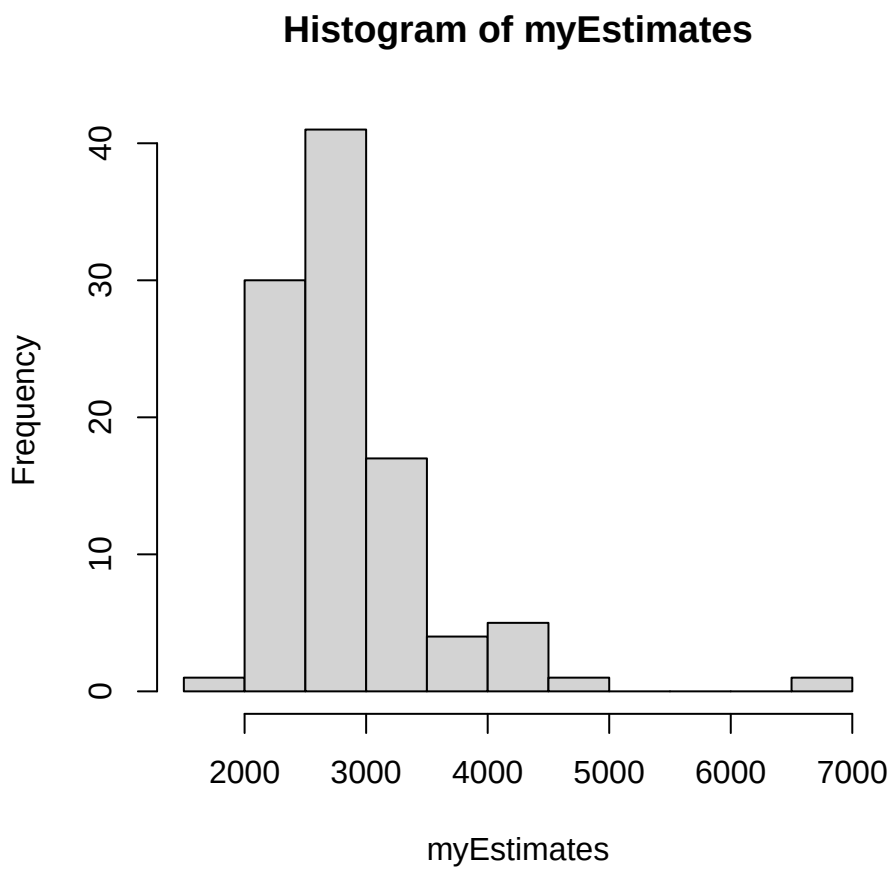
Solution 27

There is a mistake in the code on line 8. The condition in the `if` statement should be checking for `FALSE`, not `TRUE`.

Return to task on P57

Solution 28

```
myEstimates <- numeric(0)
numRuns <- 100
for(i in 1:numRuns) {
  totStickers <- 427
  gotSticker <- rep(FALSE,totStickers)
  numLeft <- totStickers
  numStickersBought <- 0
  while(numLeft > 0) {
    numStickersBought <- numStickersBought + 1
    thisSticker <- sample(1:totStickers, 1)
    if(gotSticker[thisSticker] == FALSE) {     # this is the line which had an error (fixed here)
      gotSticker[thisSticker] <- TRUE
      numLeft <- numLeft - 1
    }
  }
  myEstimates[i] <- numStickersBought
}
hist(myEstimates)
```




```
mean(myEstimates)
```

```
## [1] 2842.71
```

Return to task on P57

Solution 29

The given function returns N iterates of the logistic map starting at x_0 (note, it does not store the initial value).

Return to task on P58

Solution 30

As you change the value of r in the above code the system goes from having a single equilibrium in the long term, to oscillating between a pair of values, to oscillating between four values. By $r = 3.7$, the trajectory depends very sensitively to the initial value x_0 (as is demonstrated by the below code). This is called deterministic chaos.

Return to task on P59

Solution 31

The given code performs N iterations of the logistic map starting from x_0 but does not store them. It then calculates, stores and returns the following M iterations of the logistic map.

Return to task on P60

Answer 32

The key idea is that, for each value of r, it calculates $N = 1000$ iterations of the map, but totally ignores them. It then plots the values of the next 100 iterations (as the y-value on a graph which has the value of r as the x-ordinate). The idea behind all this is to let the system equilibriate—if it is ever going to do so. So from the bifurcation diagram you can see from this picture that there is/are:

- a single equilibrium for $2.5 < r < 3.0$
- two equilibria for $3.0 < r < 3.45$ (-ish)
- four equilibria for 3.45(-ish) $< r < 3.54$ (-ish)
- by $r \sim 3.57$, we have chaos (as seen in plots for different starting conditions above) which here corresponds to a more or less random—although lying within certain bounds—set of 100 points plotted for each r.

This is explained well on the relevant Wikipedia page

Return to task on P61

Solution 33

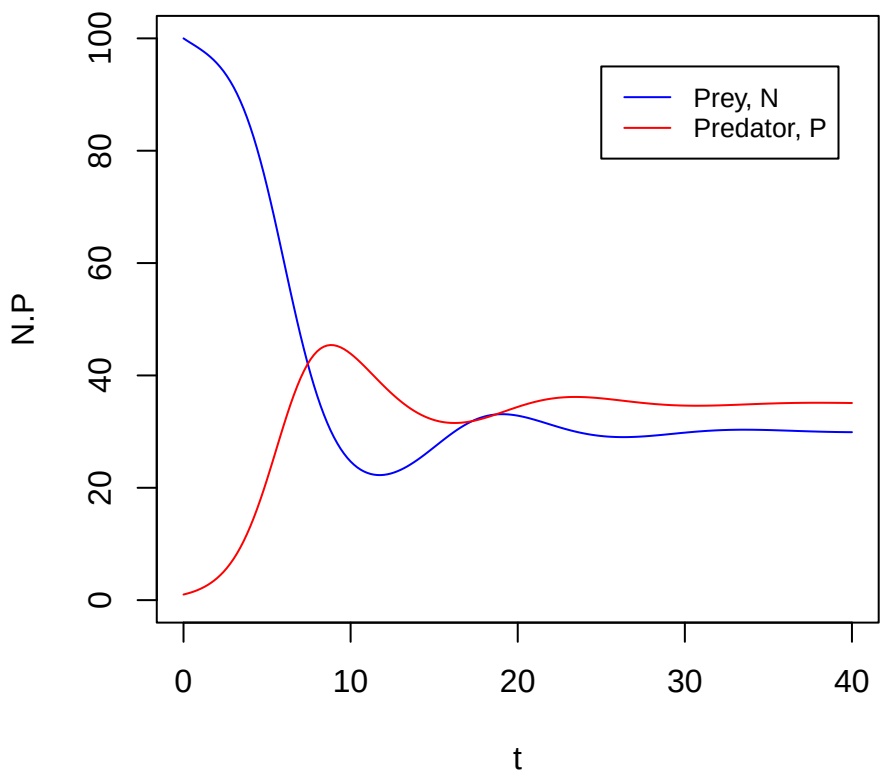
```
rand <- runif(1, 0, 1)
if (rand < 1/6) {
    print(1)
} else if (rand < 2/6) {
    print(2)
} else if (rand < 3/6) {
    print(3)
} else if (rand < 4/6) {
    print(4)
} else if (rand < 5/6) {
    print(5)
} else {
    print(6)
}
```

```
## [1] 1
```

Return to task on P74

Solution 35

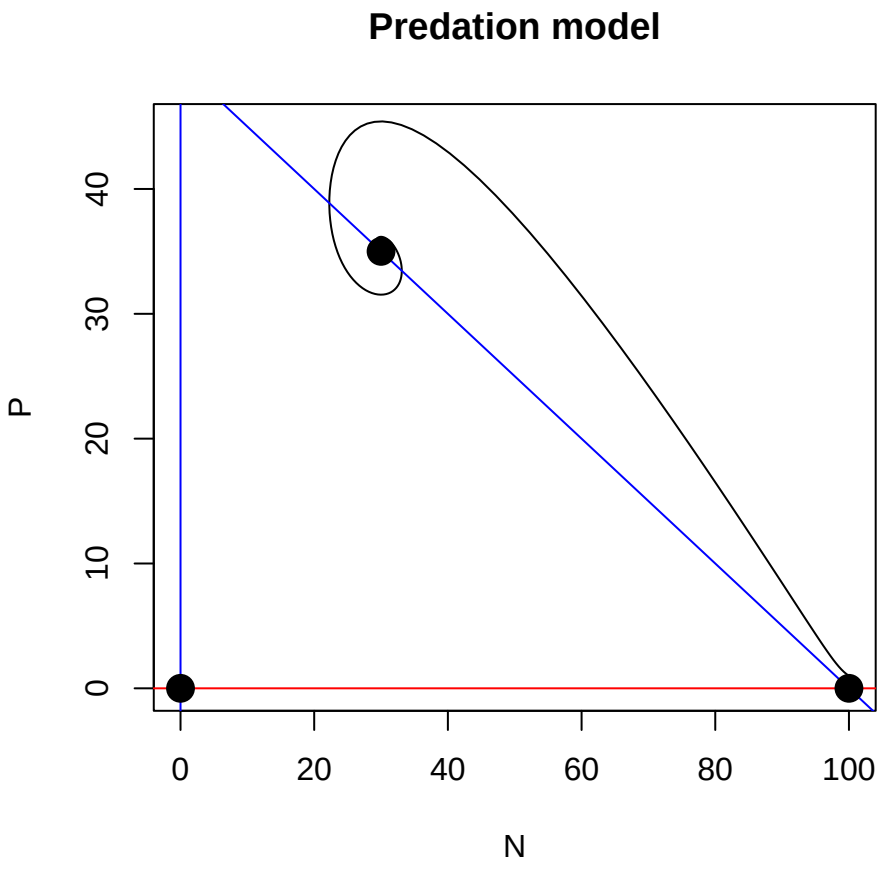
```
# plot the first line using `plot()`
plot(predation_sol[,1], predation_sol[,2], type = "l", main='Predation model',
     xlab='t', ylab='N.P', ylim = c(0, 100), col = "blue")

# plot the second line using `lines()`
lines(predation_sol[,1], predation_sol[,3], col = "red")

# add legend using `legend()`
legend(25, 95, legend=c("Prey, N", "Predator, P"),
       col=c("blue", "red"), lty=1, cex=0.8)
```



Return to task on P85

Solution 36

```
plot(predation_sol[,2], predation_sol[,3], type = "l",
     main='Predation model', xlab='N', ylab='P',
     xlim = c(0, 100), ylim = c(0, 45), col = "black")

# N = 0
abline(v = 0, col = "blue")

# P = 0
abline(h = 0, col = "red")

# P = (r/a) - (rN/Ka)
intercept = predation_par["r"]/predation_par["a"]
slope = -predation_par["r"]/(predation_par["K"]*predation_par["a"])

abline(intercept, slope, col = "blue")

# equilibrium points
points(0, 0, pch = 16, cex = 2)
points(predation_par["K"], 0, pch = 16, cex = 2)
points(
    x = predation_par["d"]/predation_par["b"],
    y = (predation_par["r"]/predation_par["a"]) -
        ((predation_par["r"]*predation_par["d"])/
            (predation_par["a"]*predation_par["b"]*predation_par["K"])),
    pch = 16,
    cex = 2
)
```

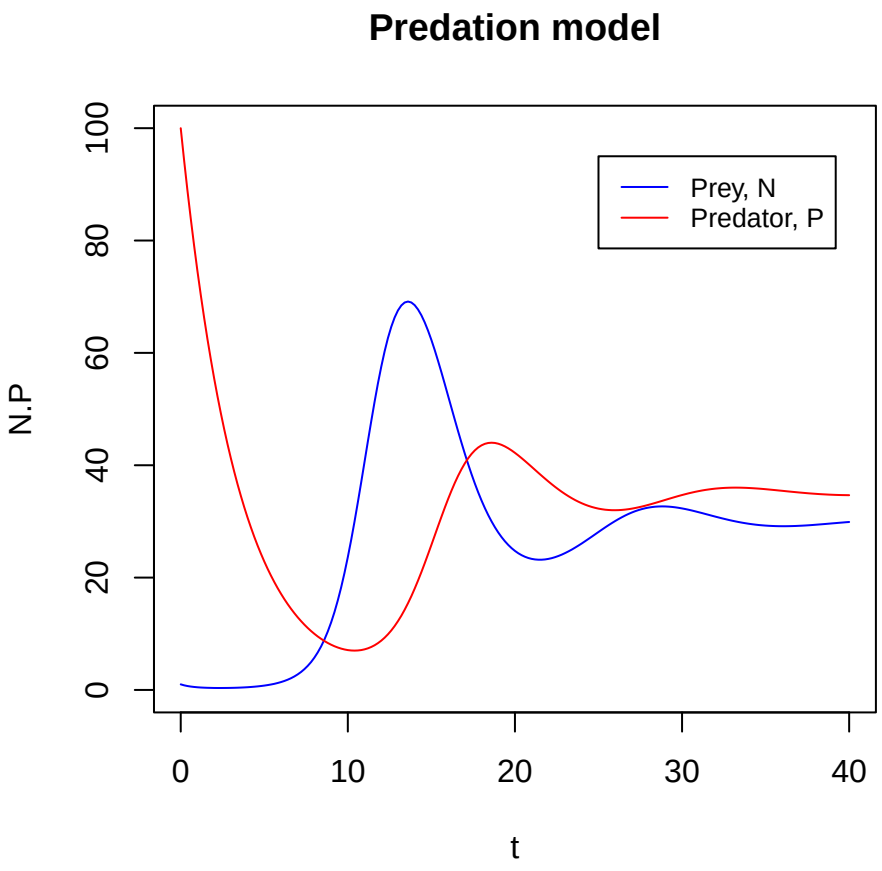


Return to task on P85

Solution 37

1. Only if you started at another equilibrium point, otherwise this equilibrium is globally stable and will attract all trajectories.

2.
```r
predation_init <- c(N=1, P=100)

# Numerical solution
predation_sol <- lsoda(predation_init,
                       predation_t,
                       predation_dyn,
                       predation_par)

# plot the first line using `plot()`
plot(predation_sol[,1], predation_sol[,2], type = "l",
     main='Predation model', xlab='t', ylab='N.P',
     ylim = c(0, 100), col = "blue")

# plot the second line using `lines()`
lines(predation_sol[,1], predation_sol[,3], col = "red")

# add legend using `legend()`
legend(25, 95, legend=c("Prey, N", "Predator, P"),
       col=c("blue", "red"), lty=1, cex=0.8)
```



Return to task on P86

Answer 38

Hopefully! No food for the predators but because this is deterministic, the populations still reach the equilibrium.

Return to task on P86

Answer 39

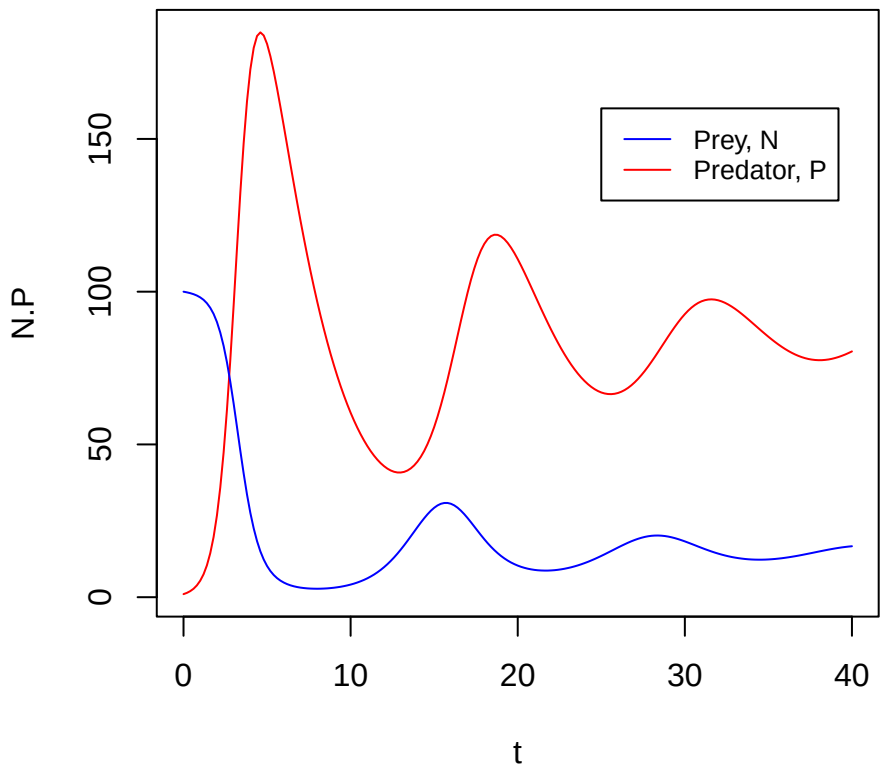
No stochastic die out.

Return to task on P86

Solution 40

In the below figure, $b = 0.02$ and $d = 0.01$. We can see that the prey population essentially dies out. This changes the stability of the equilibrium points so that the stable equilibrium is the one with both populations nead 0.

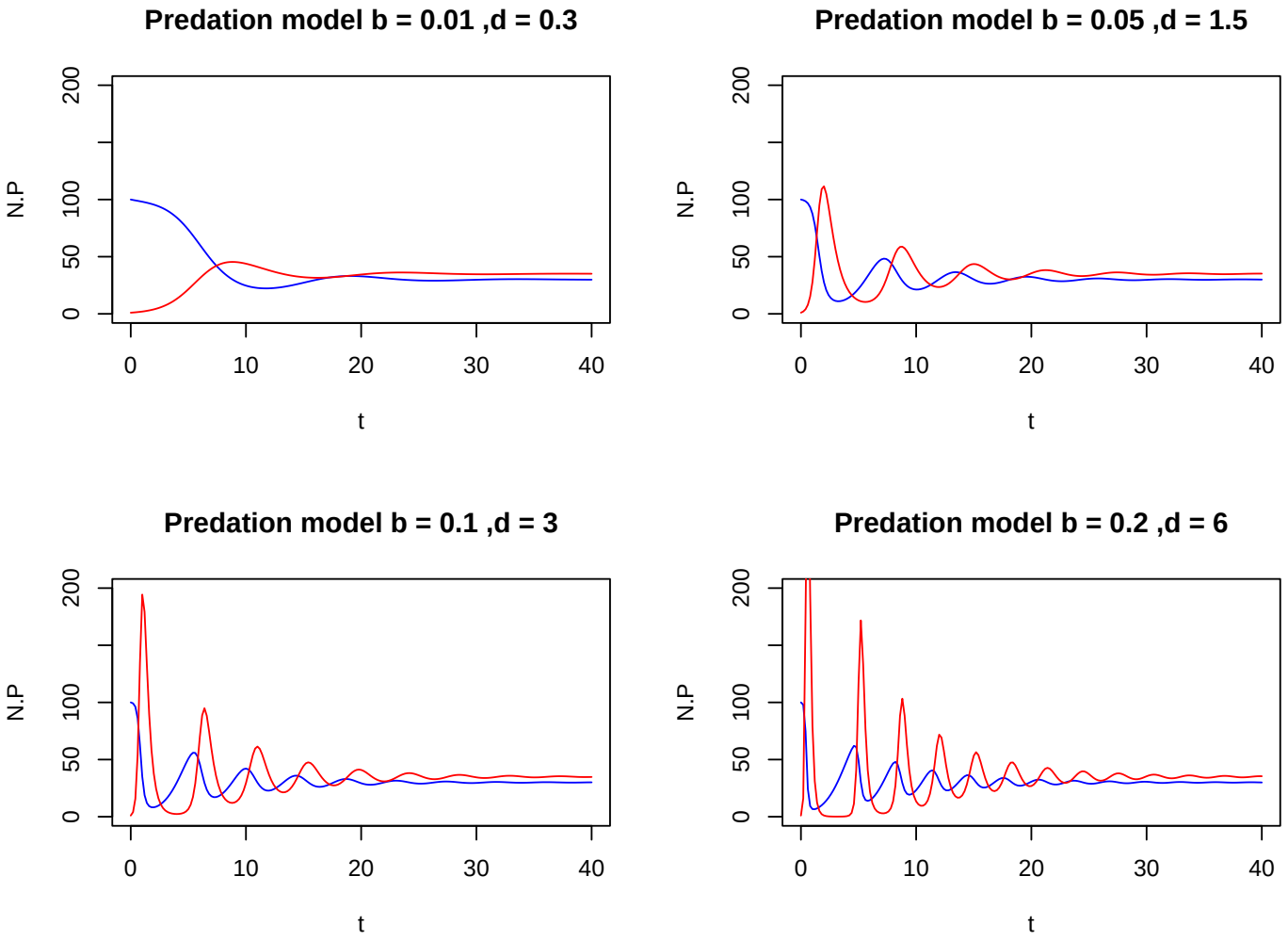
```
predation_par <- c(a=0.01, b=0.02, d=0.3, K=100, r=1)
predation_init <- c(N=100, P=1)
predation_t <- seq(0,40,0.2)

# Numerical solution
predation_sol <- lsoda(predation_init,
                       predation_t,
                       predation_dyn,
                       predation_par)

# plot the first line using `plot()`
plot(predation_sol[,1], predation_sol[,3], type = "l",
     main='Predation model', xlab='t', ylab='N.P', col = "red")

# plot the second line using `lines()`
lines(predation_sol[,1], predation_sol[,2], col = "blue")

# add legend using `legend()`
legend(25, 160, legend=c("Prey, N", "Predator, P"),
       col=c("blue", "red"), lty=1, cex=0.8)
```



Return to task on P86

Solution 41

```
par(mfrow = c(2,2))

b_vec = c(0.01, 0.05, 0.1, 0.2)
d_vec = b_vec/(0.01/0.3)

for(i in 1:4) {
    predation_par <- c(a=0.02, b=b_vec[i], d=d_vec[i], K=100, r=1)
    predation_init <- c(N=100, P=1)
    predation_t <- seq(0,40,0.2)

    # Numerical solution
    predation_sol <- lsoda(predation_init,
                           predation_t,
                           predation_dyn,
                           predation_par)

    plot(predation_sol[,1], predation_sol[,2], type = "l", col = "blue",
         main = paste("Predation model", "b =", b_vec[i], ",d =", d_vec[i]),
         xlab = "t", ylab = "N.P", ylim = c(0, 200))

    lines(predation_sol[,1], predation_sol[,3], col = "red")
}
par(mfrow = c(1, 1))
```



Similar equilibrium but it takes different times to reach it.

Return to task on P86

Solution 42

$$\begin{aligned}\frac{dS}{dt} &= \frac{-\beta SI}{N}\\ \frac{dI}{dt} &= \frac{\beta SI}{N} - \gamma I\\ \frac{dR}{dt} &= \gamma I\end{aligned}$$

Return to task on P89

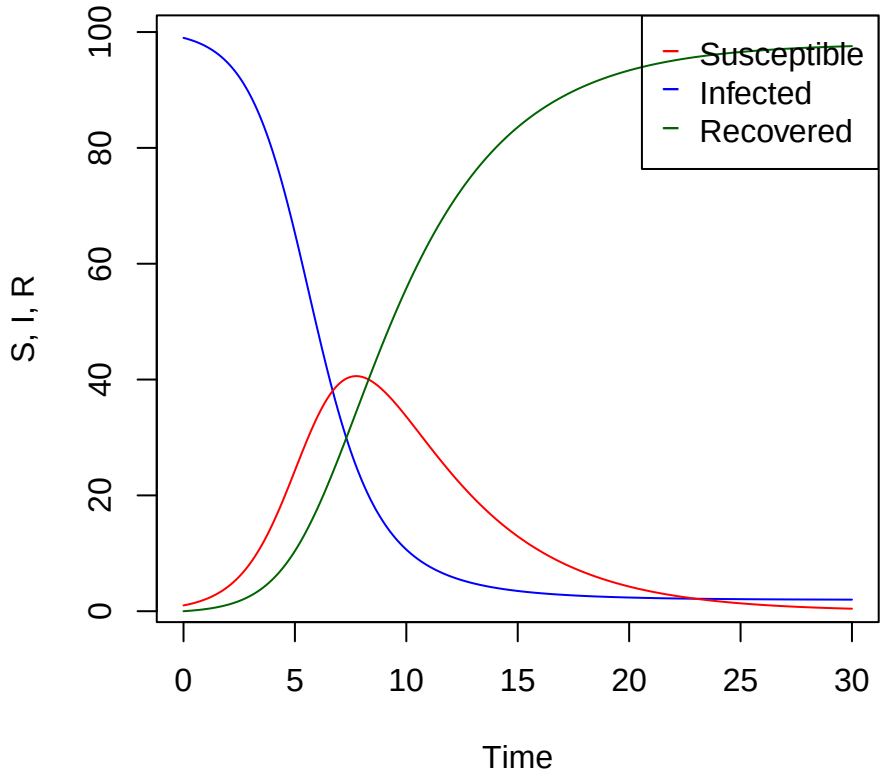
Solution 43

$$\begin{aligned}\frac{dN}{dt} &= \frac{dS}{dt} + \frac{dI}{dt} + \frac{dR}{dt}\\ &= \frac{-\beta SI}{N} + \frac{\beta SI}{N} - \gamma I + \gamma I\\ &= 0\end{aligned}$$

Return to task on P89

Solution 44

```
plot(TIME, S, col = "blue", type = "l", ylab = "S, I, R", xlab = "Time")
lines(TIME, I, col = "red")
lines(TIME, R, col = "darkgreen")

legend("topright", legend = c("Susceptible", "Infected", "Recovered"),
       col = c("red", "blue", "darkgreen"),
       pch = c("-","-", "-") )
```



Return to task on P90

Solution 45

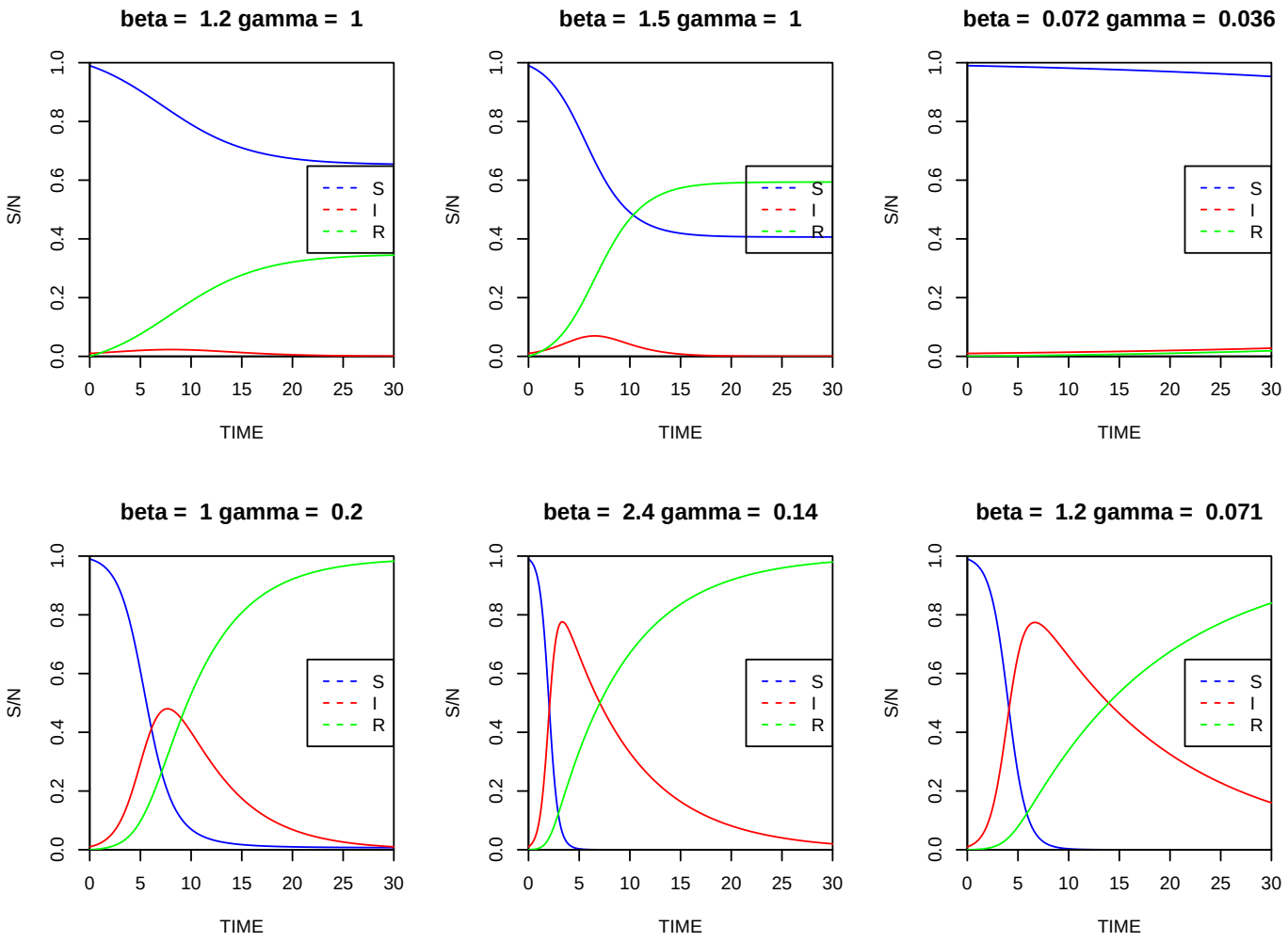
Approaching the steady state.

Return to task on P92

Solution 47

```
# set up a 2 by 3 grid for the plots:
par(mfrow=c(2,3), xaxs='i', yaxs='i')
# define the parameters:
infperiod <- c(1,1,28,5,7,14)
Rzero <- c(1.2,1.5,2,5,17,17)
SIR.t =seq(0,500, by=0.1)
for (i in 1:6) {
    gamma = signif(1/infperiod[i],2)
    beta = signif(Rzero[i]*gamma,2)
    SIR_par <- c(beta,gamma)
    SIR.sol <- lsoda(SIR_init,SIR_t,SIR_dyn,SIR_par)
    TIME <- SIR.sol[,1]
    S <- SIR.sol[,2]
    I <- SIR.sol[,3]
    R <- SIR.sol[,4]
    N <- S + I + R
    plot(TIME,S/N,col='blue', type='l', ylim=c(0,1),
         main=paste("beta = ",beta,"gamma = ",gamma))
    lines(TIME,I/N,col="red")
    lines(TIME,R/N,col="green")
    legend("right", col = c("blue","red","green"),legend = c("S","I","R"), lty = 2)
    print(paste("peak size = ",max(I/N)))
    print(paste("peak time = ",TIME[which.max(I/N)]) )
    print(paste("Epidemic size = ",max(R/N)))
}
par(mfrow = c(1, 1))
```

```
## [1] "peak size =  0.0231066389917149"
## [1] "peak time =  8.1"
## [1] "Epidemic size =  0.344611420022074"
## [1] "peak size =  0.0697227613470483"
## [1] "peak time =  6.5"
## [1] "Epidemic size =  0.593574217769393"
## [1] "peak size =  0.0278724769684512"
## [1] "peak time =  30"
## [1] "Epidemic size =  0.0189539739504256"
## [1] "peak size =  0.480101096709578"
## [1] "peak time =  7.7"
## [1] "Epidemic size =  0.982652741440976"
## [1] "peak size =  0.776354567432811"
## [1] "peak time =  3.3"
## [1] "Epidemic size =  0.979907643827461"
## [1] "peak size =  0.774111948146292"
## [1] "peak time =  6.7"
## [1] "Epidemic size =  0.840041300875431"
```



Return to task on P93

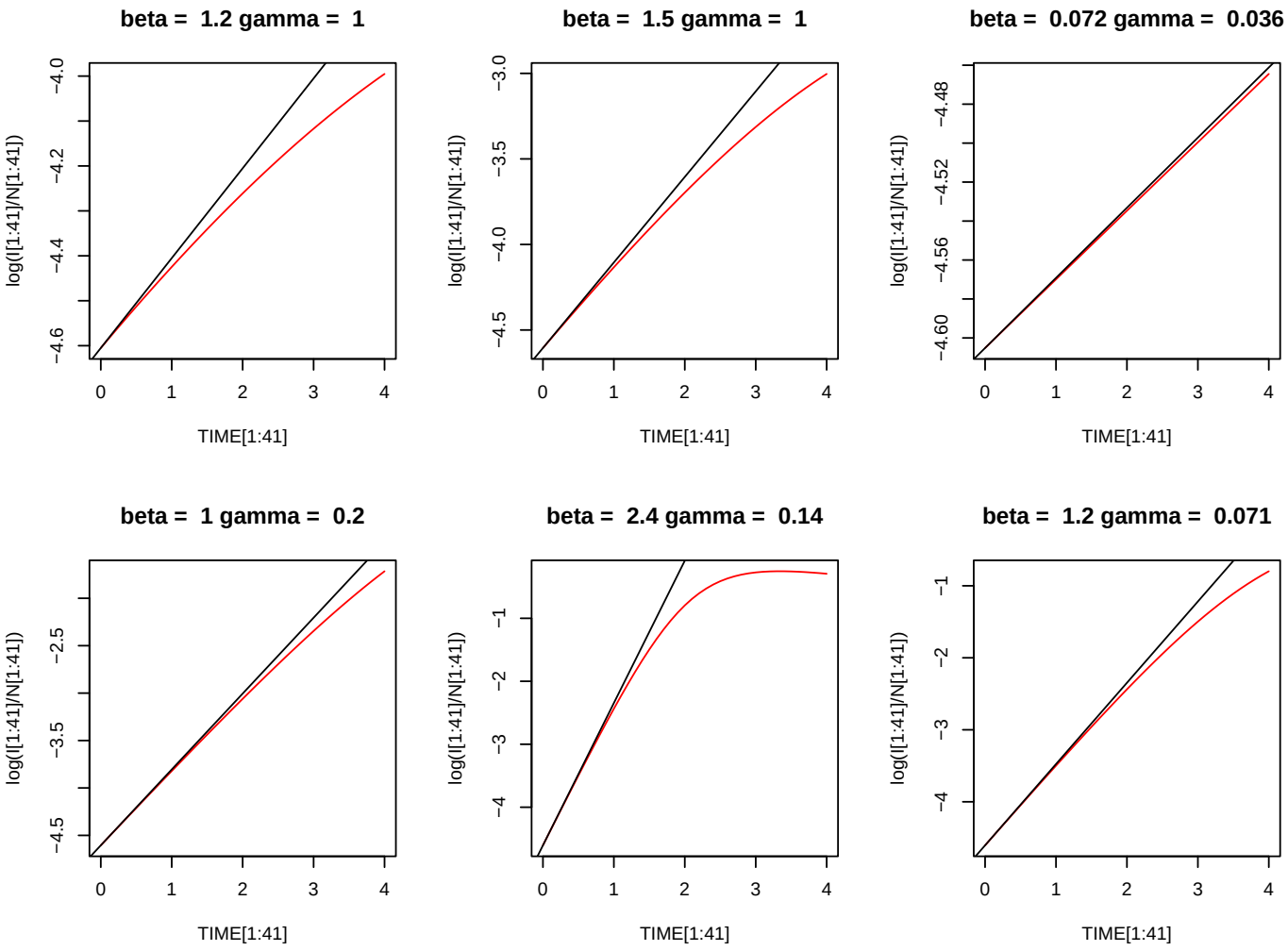
Solution 48

Peak size and epidemic size.

Return to task on P93

Solution 49

```
#checking initial gradient
par(mfrow=c(2,3))
# define the parameters:
infperiod <- c(1,1,28,5,7,14)
Rzero <- c(1.2,1.5,2,5,17,17)
SIR.t =seq(0,500, by=0.1)
for (i in 1:6) {
    gamma = signif(1/infperiod[i],2)
    beta = signif(Rzero[i]*gamma,2)
    SIR_par <- c(beta,gamma)
    SIR.sol <- lsoda(SIR_init,SIR_t,SIR_dyn,SIR_par)
    TIME <- SIR.sol[,1]
    S <- SIR.sol[,2]
    I <- SIR.sol[,3]
    R <- SIR.sol[,4]
    N <- S + I + R
    plot(TIME[1:41],log( I[1:41]/N[1:41] ),col='red', type='l',
         main=paste("beta = ",beta,"gamma = ",gamma))
    abline(a = log( I[1]/N[1] ), b = beta-gamma, col = "black")
}
par(mfrow=c(1,1))
```



Return to task on P94

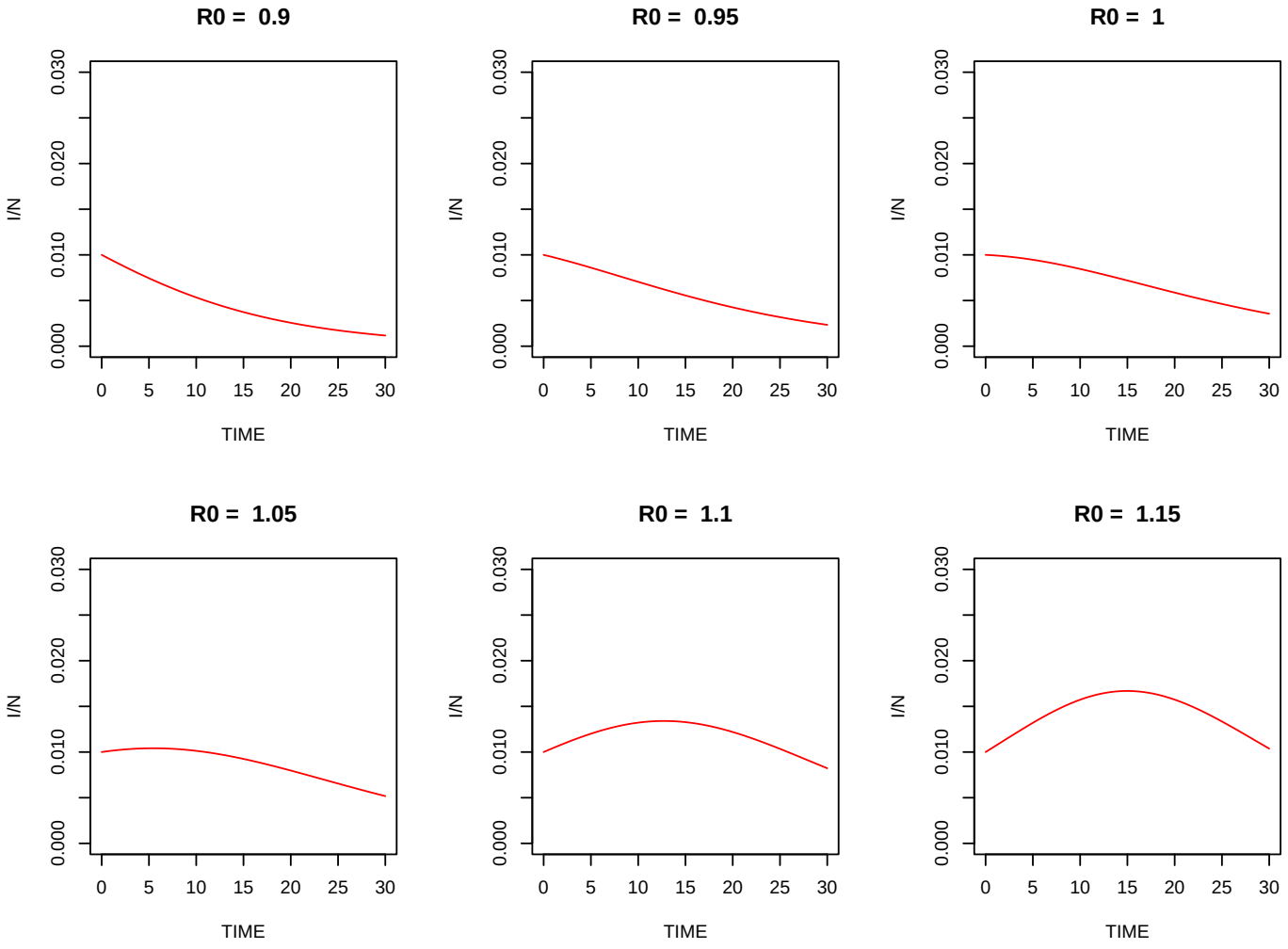
Solution 50

As our initial conditions are with 99 susceptible people, and $R_0 = 1$ this renders the **effective reproduction number** less than 1 so $I(t)$ decreases.

Return to task on P94

Solution 51

```
### looking around R0 = 1
par(mfrow=c(2,3))
# define the parameters:
SIR.init <- c(99,1,0)
infperiod <- rep(2,6)
Rzero <- c(0.9,0.95,1,1.05,1.1, 1.15)
SIR.t =seq(0,100, by=0.1)
for (i in 1:6) {
    gamma<- signif(1/infperiod[i],2)
    beta <- signif(Rzero[i]*gamma,2)
    SIR_par <- c(beta,gamma)
    SIR.sol <- lsoda(SIR_init,SIR_t,SIR_dyn,SIR_par)
    TIME <- SIR.sol[,1]
    S <- SIR.sol[,2]
    I <- SIR.sol[,3]
    R <- SIR.sol[,4]
    N <- S + I + R
    plot(TIME, I/N,col='red', type='l', ylim=c(0,0.03),
main=paste("R0 = ",Rzero[i]))
}
par(mfrow=c(1,1))
```



Return to task on P94

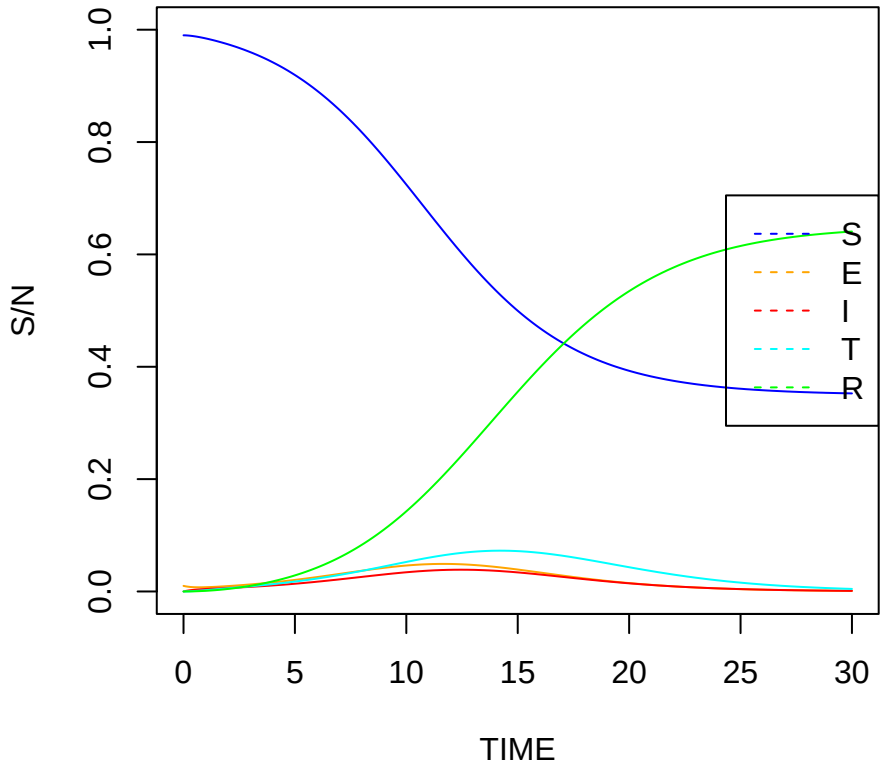
Answer 52

The average infectious period is $1/\gamma = 5$ days.

Return to task on P95

Solution 53

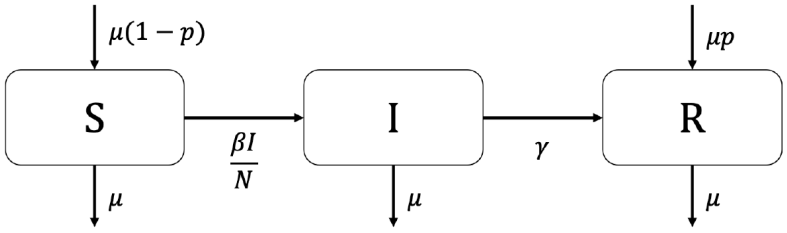
```
#### Extra exercise
# I am putting everything in at once

SEITRS.dyn <- function(t, var, par) {
    # Rename the variables and parameters
    S <- var[1]
    E <- var[2]
    I <- var[3]
    tr <- var[4]
    R <- var[5]
    N <- S + E + I + tr + R
    beta <- par[1]
    gamma <-par[2]
    epsilon <- par[3] #rate of latency loss
    tau <- par[4] #treatment rate
    omega <- par[5] #recovery rate for treated people

    # Derivatives
    dS <- -beta*S*I/N
    dE <- beta*S*I/N - epsilon*E
    dI <- epsilon*E - gamma*I - tau*I
    dT <- tau*I - omega*tr
    dR <- gamma*I + omega*tr
    # Return the 5 values
    list(c(dS, dE, dI, dT, dR))
}

beta <- 2
gamma <- 0.25
epsilon <- 1
tau <- 1
omega <- gamma*2

SEITRS.par <- c(beta,gamma,epsilon,tau,omega)
SEITRS.init <- c(99,1,0,0,0)
SEITRS.t <- seq(0,30,by=0.1)

SEITRS.sol <- lsoda(SEITRS.init,SEITRS.t,SEITRS.dyn,SEITRS.par)

TIME <- SEITRS.sol[,1]
S <- SEITRS.sol[,2]
E <- SEITRS.sol[,3]
I <- SEITRS.sol[,4]
tr <- SEITRS.sol[,5]
R <- SEITRS.sol[,6]

N <- S + E + I + tr + R

plot(TIME,S/N,col='blue', type='l', ylim=c(0,1))
lines(TIME,E/N,col="orange")
lines(TIME,I/N,col="red")
lines(TIME,tr/N,col="cyan")
lines(TIME,R/N,col="green")
legend("right", col = c("blue","orange", "red","cyan","green"), legend = c("S","E","I","T","R"), lty = 2)
```



Plenty to note on the different dynamics as you experiment with the above- one thing to examine is that we now have multiple infected states and this can make calculating R_0 more complicated as we need to use the next generation matrix approach, shown later in the course.

Return to task on P95

Solution 54



Return to task on P99

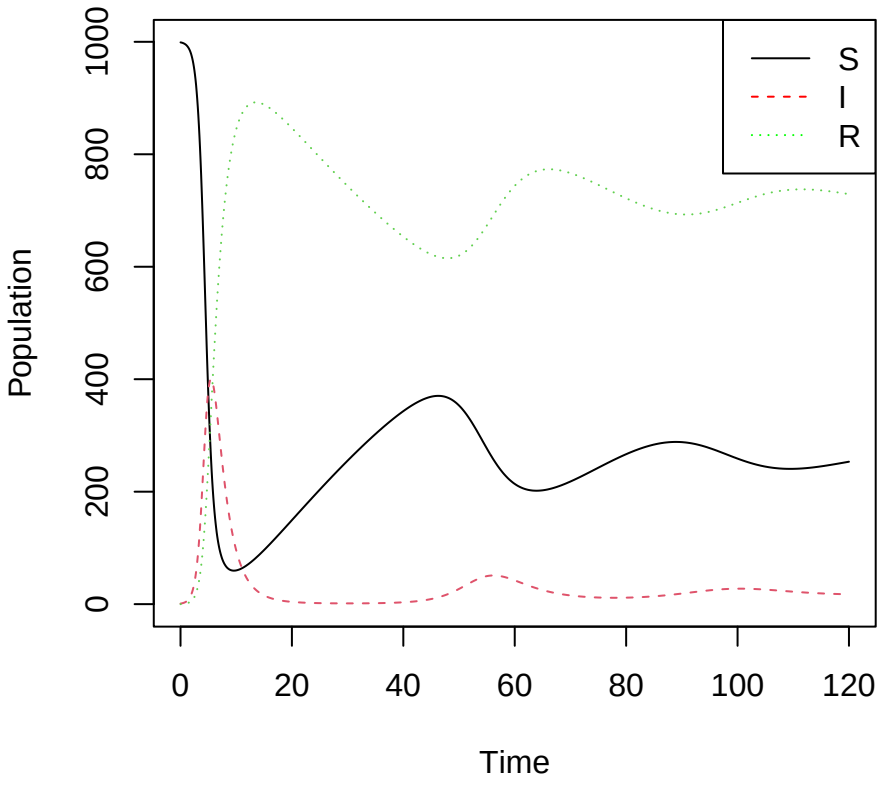
Solution 55

$$\frac{\mathrm{d}S}{\mathrm{d}t} = \mu(1-p)N - \frac{\beta SI}{N} - \mu$$
$$\frac{\mathrm{d}I}{\mathrm{d}t} = \frac{\beta SI}{N} - \gamma I - \mu$$
$$\frac{\mathrm{d}R}{\mathrm{d}t} = \mu pN + \gamma I - \mu$$

Return to task on P99

Solution 56

```
library(deSolve)

SIR.dyn <- function(t,var,par) {
    S <- var[1]
    I <- var[2]
    R <- var[3]
    N <- S+I+R
    beta <- par[1]
    gamma <- par[2]
    mu <- par[3]
    p <- par[4]

    dS <- (1-p)*mu*N - beta*S*I/N - mu*S
    dI <- beta*S*I/N - gamma*I - mu*I
    dR <- gamma*I - mu*R + p*mu*N
    return(list(c(dS,dI,dR)))
}

SIR.par<-c(beta=2,gamma=0.5,mu=1/70.0,p=0)
SIR.init<-c(S=999,I=1,R=0)
SIR.t<-seq(0,120,0.1)

det.sol <- lsoda(SIR.init,SIR.t,SIR.dyn,SIR.par)

matplot(det.sol[,1],det.sol[,2:4],type='l',xlab='Time',ylab='Population')
legend('topright',c('S','I','R'),col=c('black','red','green'),lty=c(1,2,3))
```



Return to task on P100

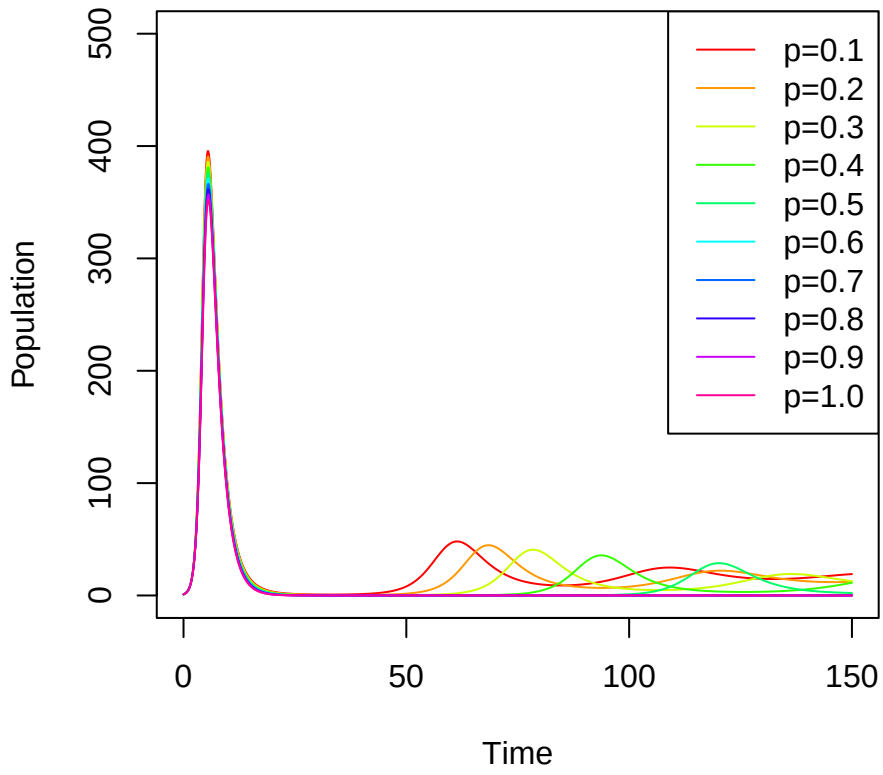
Solution 57

$p_{vac} = 1 - \frac{1}{R_0} = 1 - \frac{\gamma+\mu}{\beta} = 26/35 \simeq 0.75$

Return to task on P100

Solution 58

```
# Values of vaccination coverage to try
p_vals = seq(0.1,1.0,0.1)
# Color palette for plotting
col_vals = rainbow(length(p_vals))

# Make an empty plot
plot(0,xlim=c(0,150),ylim=c(0,500),pch=' ',xlab='Time',ylab='Population')

# Initial conditions and time points same for each solution
SIR.init<-c(S=999,I=1,R=0)
SIR.t<-seq(0,150,0.1)

for(i in 1:length(p_vals)) {
    # Change vaccination coverage
    SIR.par<-c(beta=2,gamma=0.5,mu=1/70.0,p=p_vals[i])

    det.sol <- lsoda(SIR.init,SIR.t,SIR.dyn,SIR.par)

    # plot I curve only

    lines(SIR.t,det.sol[,3],col=col_vals[i])
}

legend('topright',c('p=0.1',
                    'p=0.2',
                    'p=0.3',
                    'p=0.4',
                    'p=0.5',
                    'p=0.6',
                    'p=0.7',
                    'p=0.8',
                    'p=0.9',
                    'p=1.0'),col=col_vals,lty=1)
```



Return to task on P100

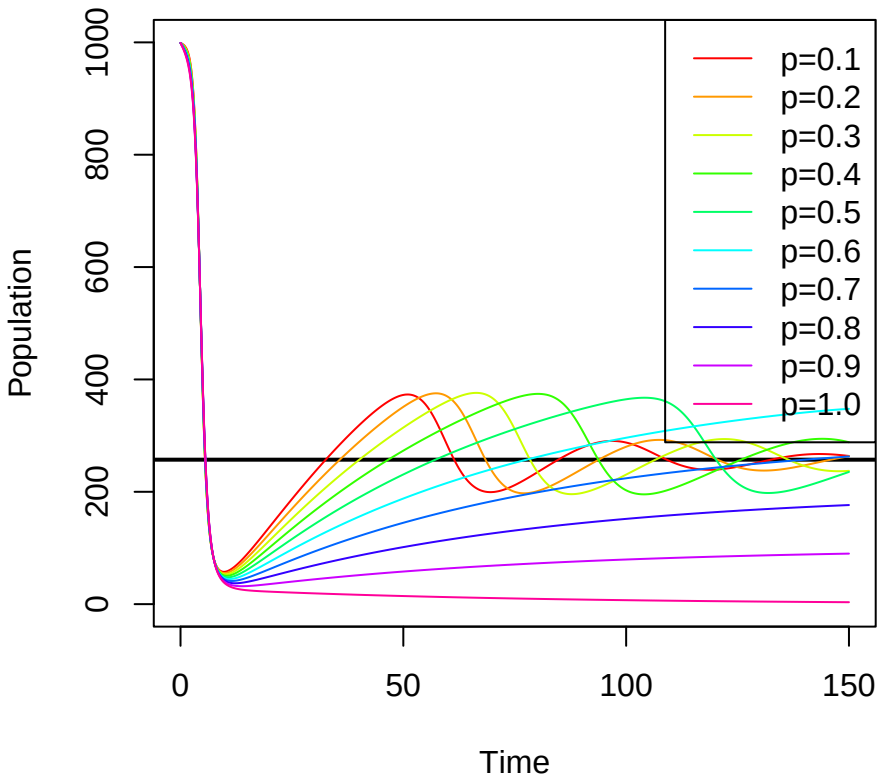
Answer 59

We can see that for $p < p_{vac}$, we have a second outbreak following the initial first outbreak. This does not occur if $p > p_{vac}$. We still get an initial epidemic in all cases because we start with an entirely susceptible population. Since we only vaccinate individuals as they are born, it takes some time for the total proportion of population vaccinated to be high enough to ensure herd immunity.

Return to task on P100

Solution 60

```
# Values of vaccination coverage to try
p_vals = seq(0.1,1.0,0.1)
# Color palette for plotting
col_vals = rainbow(length(p_vals))

# Make an empty plot
plot(0,xlim=c(0,150),ylim=c(0,1000),pch=' ',xlab='Time',ylab='Population')

# Add herd immunity threshold

abline(h=(1-26/35)*1000,col='black',lwd=2)

# Initial conditions and time points same for each solution
SIR.init<-c(S=999,I=1,R=0)
SIR.t<-seq(0,150,0.1)

for(i in 1:length(p_vals)) {
    # Change vaccination coverage
    SIR.par<-c(beta=2,gamma=0.5,mu=1/70.0,p=p_vals[i])

    det.sol <- lsoda(SIR.init,SIR.t,SIR.dyn,SIR.par)

    # plot S curve only

    lines(SIR.t,det.sol[,2],col=col_vals[i])
}

legend('topright',c('p=0.1',
                    'p=0.2',
                    'p=0.3',
                    'p=0.4',
                    'p=0.5',
                    'p=0.6',
                    'p=0.7',
                    'p=0.8',
                    'p=0.9',
                    'p=1.0'),col=col_vals,lty=1)
```



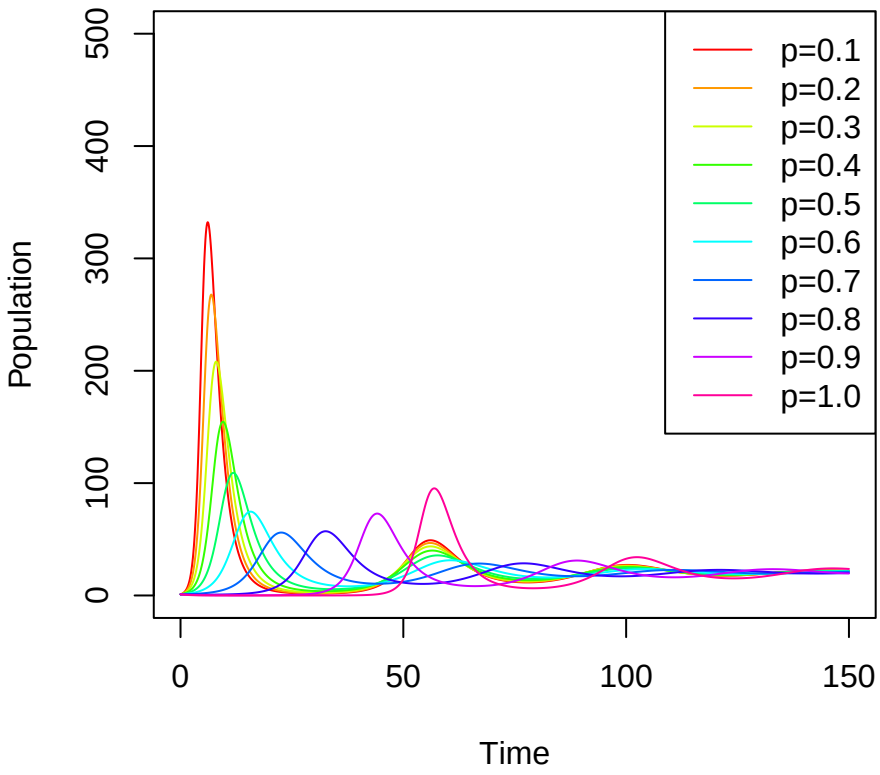
In all cases except $p = 1$, we tend towards the steady state at $\frac{1}{R_0}$ (shown in black). If $p < p_{vac}$, the proportion of susceptibles increases after the initial peak and overshoots $\frac{1}{R_0}$ before fluctuating and settling to the steady state; otherwise the number of susceptibles slowly increases to the steady state.

Return to task on P100

Solution 61

First consider one-off campaign on it's own without vaccination at birth.

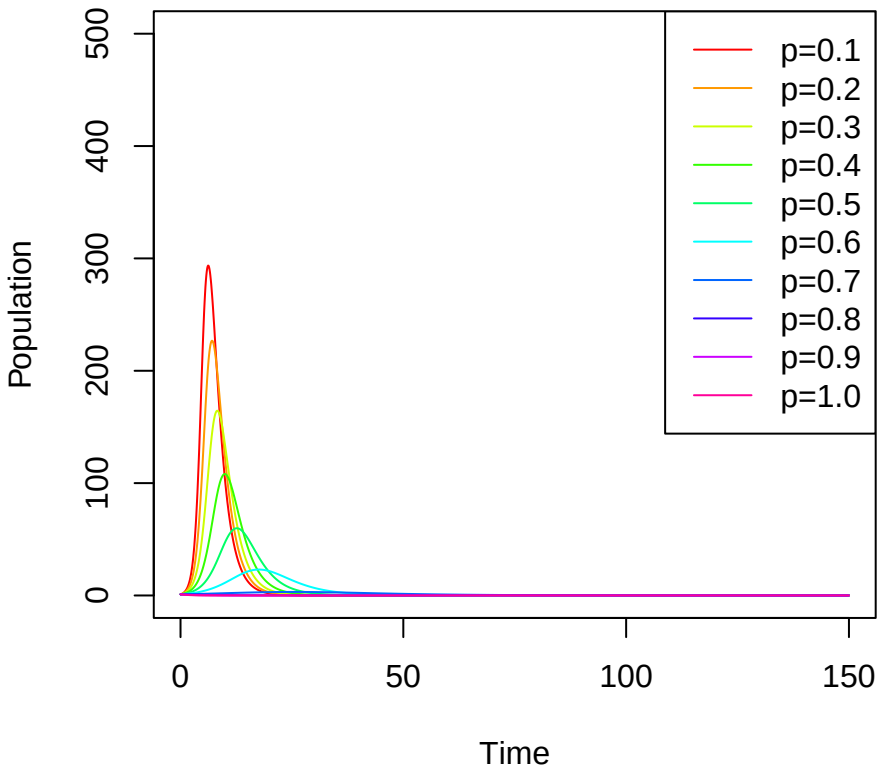
```
# Values of vaccination coverage to try
p_vals = seq(0.1,1.0,0.1)
# Color palette for plotting
col_vals = rainbow(length(p_vals))
# Vaccination at birth now 0
SIR.par<-c(beta=2,gamma=0.5,mu=1/70.0,p=0.0)

# Make an empty plot
plot(0,xlim=c(0,150),ylim=c(0,500),pch=' ',xlab='Time',ylab='Population')

# Time points same for each solution

SIR.t<-seq(0,150,0.1)

for(i in 1:length(p_vals)) {
    # Now model one-off vaccination campaign at start by modifying the initial conditions
    SIR.init<-c(S=(999)*(1-p_vals[i]),I=1,R=(999)*(p_vals[i]))

    det.sol <- lsoda(SIR.init,SIR.t,SIR.dyn,SIR.par)

    # plot I curve only
    lines(SIR.t,det.sol[,3],col=col_vals[i])
}

legend('topright',c('p=0.1',
                    'p=0.2',
                    'p=0.3',
                    'p=0.4',
                    'p=0.5',
                    'p=0.6',
                    'p=0.7',
                    'p=0.8',
                    'p=0.9',
                    'p=1.0'),col=col_vals,lty=1)
```



A single one off campaign can delay - but not prevent an epidemic. Even for $p > 0.75$, there will still be an smaller outbreak once enough births have accumulated to bring the number of susceptibles above the herd immunity threshold.

If we now consider a one-off campaign in addition to vaccination at birth at 75%:

```
# Values of vaccination coverage to try
p_vals = seq(0.1,1.0,0.1)
# Color palette for plotting
col_vals = rainbow(length(p_vals))
# Vaccination at birth now 0.75
SIR.par<-c(beta=2,gamma=0.5,mu=1/70.0,p=0.75)

# Make an empty plot
plot(0,xlim=c(0,150),ylim=c(0,500),pch=' ',xlab='Time',ylab='Population')

# Time points same for each solution

SIR.t<-seq(0,150,0.1)

for(i in 1:length(p_vals)) {
    # Now model one-off vaccination campaign at start by modifying the initial conditions
    SIR.init<-c(S=(999)*(1-p_vals[i]),I=1,R=(999)*(p_vals[i]))

    det.sol <- lsoda(SIR.init,SIR.t,SIR.dyn,SIR.par)

    # plot I curve only

    lines(SIR.t,det.sol[,3],col=col_vals[i])
}

legend('topright',c('p=0.1',
                    'p=0.2',
                    'p=0.3',
                    'p=0.4',
                    'p=0.5',
                    'p=0.6',
                    'p=0.7',
                    'p=0.8',
                    'p=0.9',
                    'p=1.0'),col=col_vals,lty=1)
```



Now we can see that increasing p for an initial campaign not only decreases the size of the initial outbreak, but for $p > p_{vac}$ for the initial campaign, there is now no outbreak.

Return to task on P100

Answer 62

This suggests that birth programmes used in isolation are insufficient to prevent outbreaks; we also need a sufficiently large proportion of the population immune to begin with.

Return to task on P100

Solution 63

$K = \frac{1}{\gamma}\beta = \begin{pmatrix} 4 & 0.4 \\ 0.4 & 2 \end{pmatrix}$

Return to task on P103

Solution 64

Using the formula for R_0 from the lectures:

$R_0 = \frac{4+2+\sqrt{(4+2)^2-4(4\times 2-0.4^2)}}{2} \simeq 4.08$

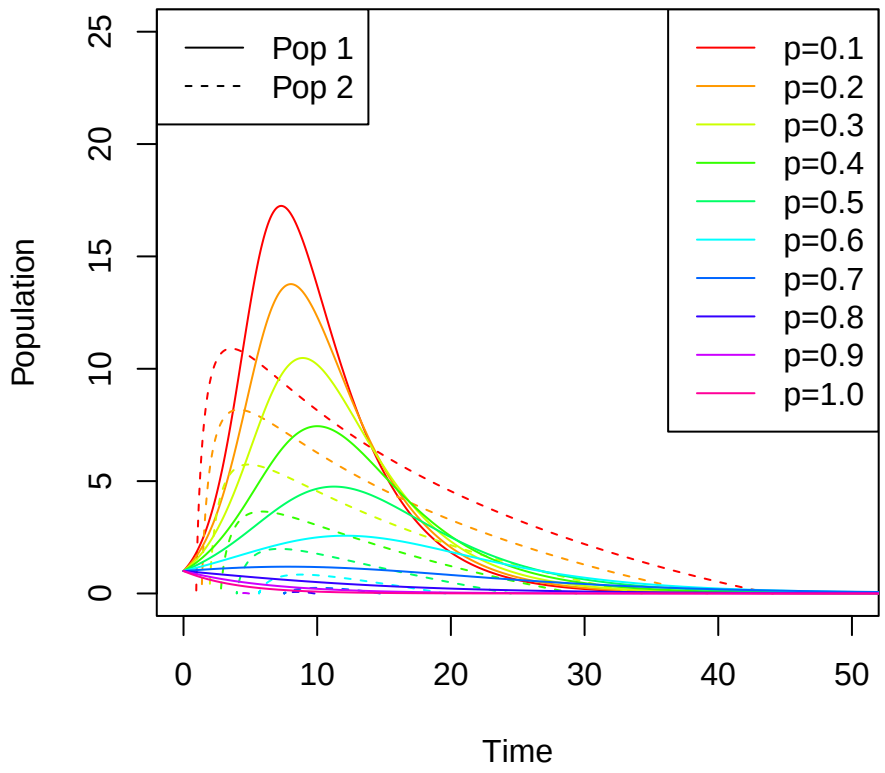
The critical vaccination threshold is

```
# Next Generation Matrix and R0

ngm = (4.0)*matrix(c(1,0.1,0.1,0.5),byrow=T,nrow=2)

R0 = max(eigen(ngm)$values)

p_critical = 1 - 1/R0
```

Return to task on P103

Solution 65

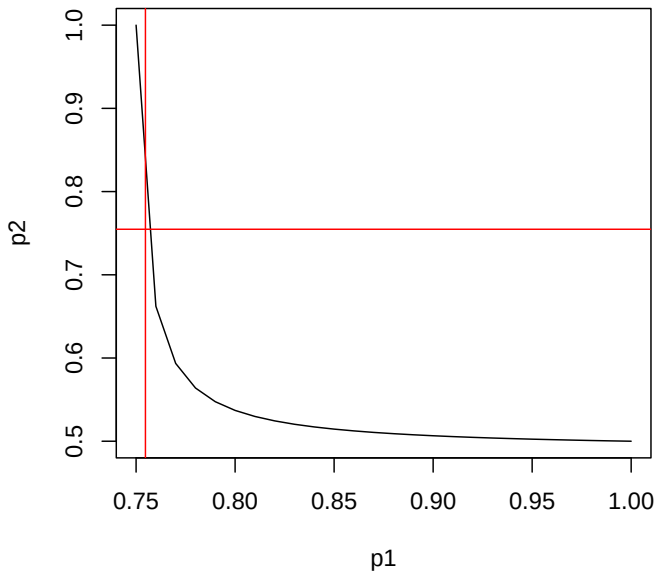
```
# Values of vaccination coverage to try
p_vals = seq(0.1,1.0,0.1)
# Color palette for plotting
col_vals = rainbow(length(p_vals))

# Make an empty plot
plot(0,xlim=c(0,50),ylim=c(0,25),pch=' ',xlab='Time',ylab='Population')

for(i in 1:length(p_vals)) {
    # Now model one-off vaccination campaign at start by modifying the initial conditions
    init <- c(49*(1-p_vals[i]),50*(1-p_vals[i]),1,0,49*p_vals[i],50*p_vals[i])

    TwoPop.sol <- lsoda(init,TwoPop.t,TwoPopSIR,TwoPop.par)

    # plot I curve only

    lines(TwoPop.sol[,1],TwoPop.sol[,4],col=col_vals[i],lty=1)
    lines(TwoPop.sol[,2],TwoPop.sol[,5],col=col_vals[i],lty=2)
}

legend('topright',c('p=0.1',
                    'p=0.2',
                    'p=0.3',
                    'p=0.4',
                    'p=0.5',
                    'p=0.6',
                    'p=0.7',
                    'p=0.8',
                    'p=0.9',
                    'p=1.0'),col=col_vals,lty=1)

legend('topleft',c('Pop 1','Pop 2'),col='black',lty=c(1,2))
```

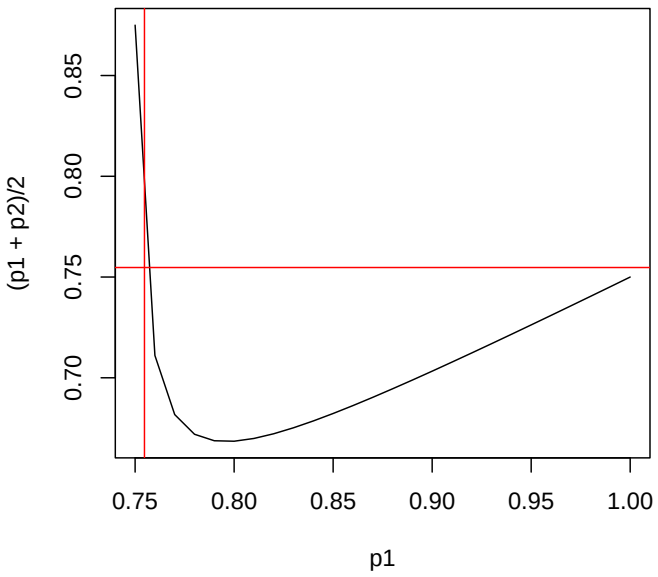


Return to task on P103

Solution 66

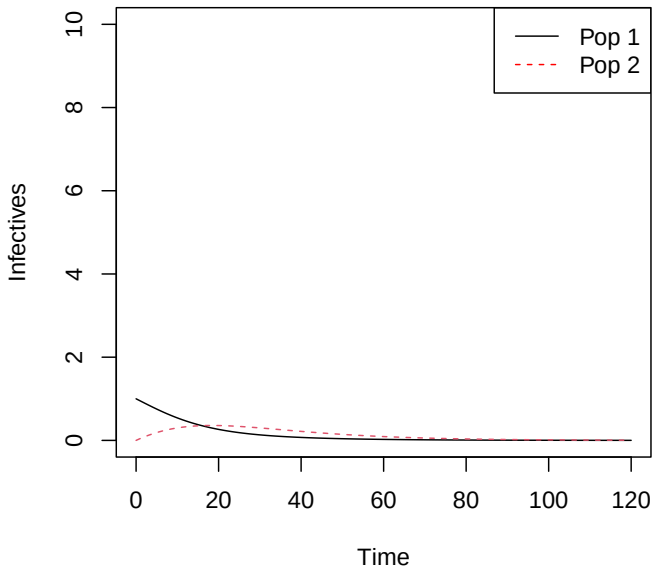
```
# Critical proportion (p2) that needs to be vaccinated given a value of p1
# Using equation from lectures

a = ngm[1,1];b = ngm[1,2]; c = ngm[2,1]; d = ngm[2,2]

# p1 must be greater than 1 - 1/a
p1 = seq(1-1/a,1,0.01)

p2 = 1 - ((1 - a*(1-p1))/(d - (a*d - b*c)*(1-p1)))

par(mfrow=c(1,2))

plot(p1,p2,type='l')
abline(v=p_critical,col='red')
abline(h=p_critical,col='red')
plot(p1,(p1+p2)/2,type='l')
abline(v=p_critical,col='red')
abline(h=p_critical,col='red')
par(mfrow=c(1,1))
```

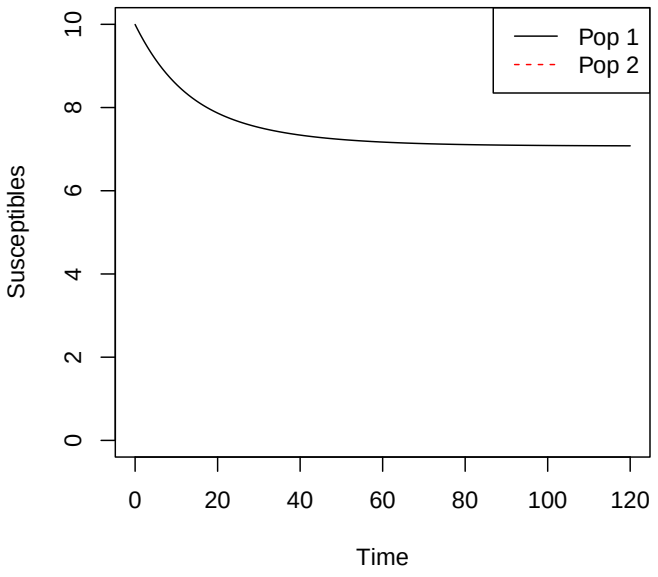




We can read off the minimum possible value of p off our graph. This gives $p \simeq 0.668$, $p_1 \simeq 0.796$ and $p_2 \simeq 0.541$. Overall, this is a lower level of vaccination than random vaccination, so may be more efficient. The optimal vaccination scenario below, not that although the number of infectives in the second population initially increase it never crosses 1.

```
p1=0.796
p2=0.541
Optimal.init<- c(49*(1-p1),50*(1-p2),1,0,49*p1,50*p2)

TwoPop.t<-seq(0,120,0.1)
# Note, at optimal coverage I[2] initially increases, but never crosses 1...

TwoPop.sol <- lsoda(Optimal.init,TwoPop.t,TwoPopSIR,TwoPop.par)

par(mfrow=c(1,2))
matplot(TwoPop.sol[,1],TwoPop.sol[,c(4,5)],type='l',xlab='Time',ylab='Infectives',ylim=c(0,10))
legend('topright',c('Pop 1','Pop 2'),col=c('black','red'),lty=c(1,2))
matplot(TwoPop.sol[,1],TwoPop.sol[,c(2,3)],type='l',xlab='Time',ylab='Susceptibles',ylim=c(0,10))
legend('topright',c('Pop 1','Pop 2'),col=c('black','red'),lty=c(1,2))
par(mfrow=c(1,1))
```



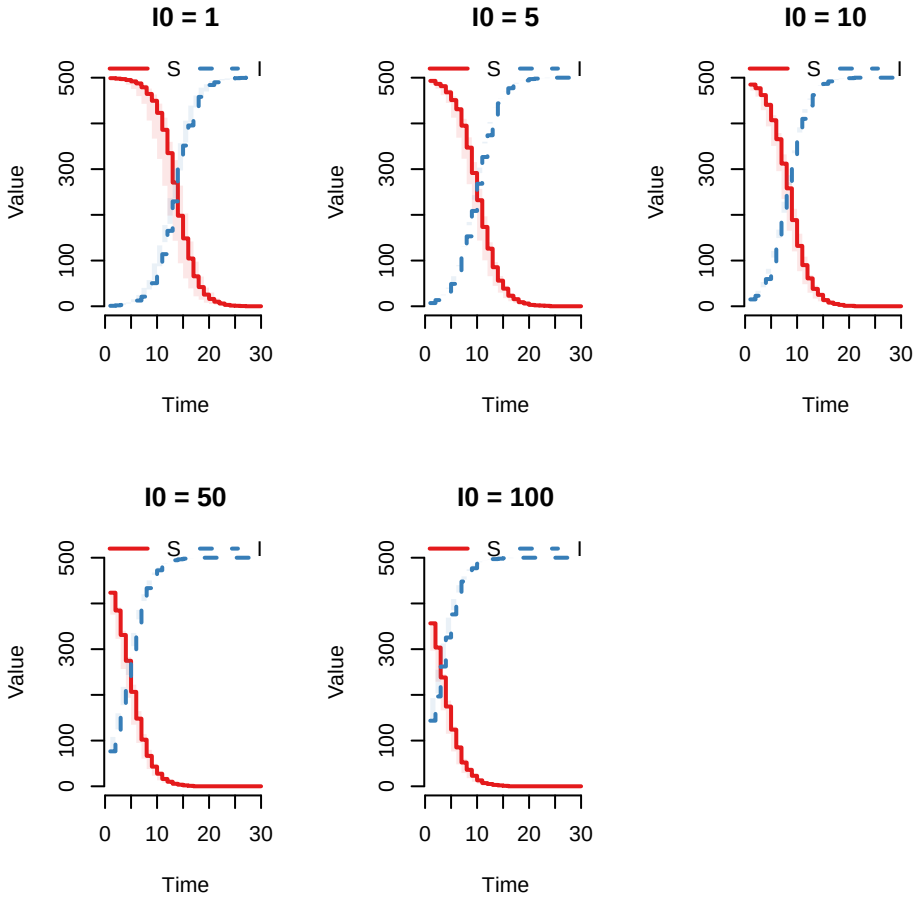


Return to task on P104

Solution 67

As the initial number of infectives increases the variability between replicates decreases.

```
ninf <- c(1, 5, 10, 50, 100)
par(mfrow = c(2, 3))
for(i in ninf) {
    SImodel <- create.StocSI(500, i, 0.5, 30, 20)
    out <- run(model = SImodel)
    plot(out, main = paste0("I0 = ", i))
}
par(mfrow = c(1, 1))
```

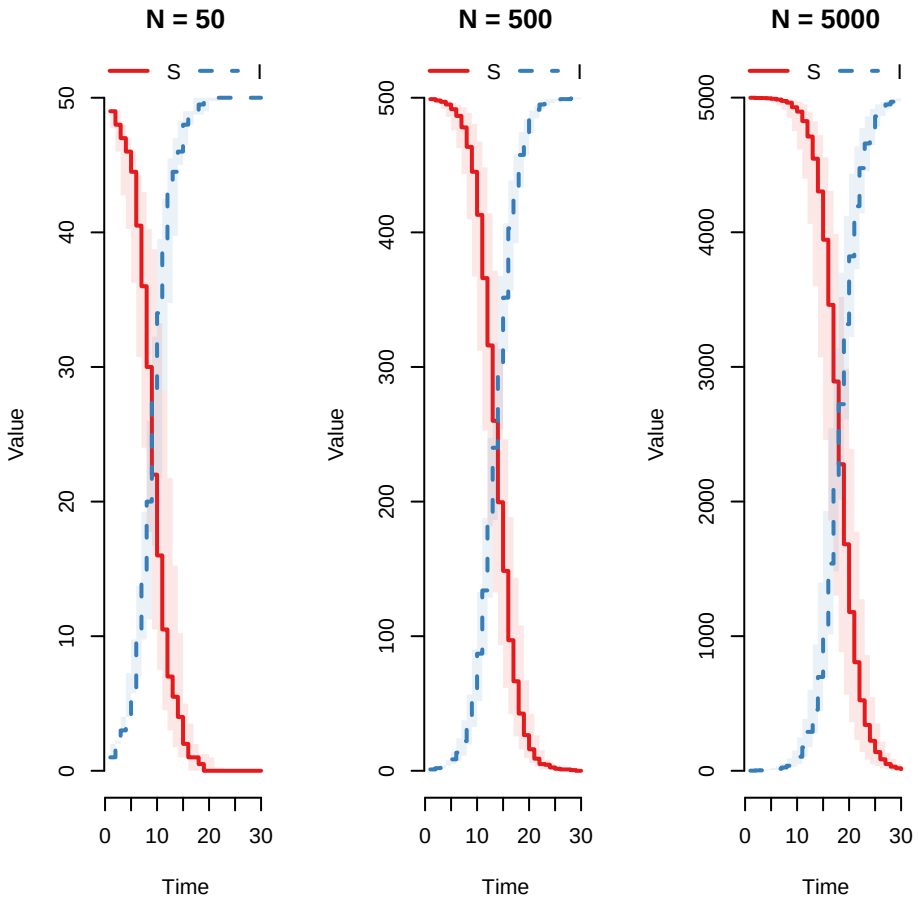


Return to task on P112

Solution 68

In contrast to varying the initial number of infectives, the host population size has little to no impact on the variability between replicates of the SI model. The relevant "large population" limit for the SI model is the number of infectives not the size of the host population.

```
npop <- c(50, 500, 5000)
par(mfrow = c(1, 3))
for(i in npop) {
    SImodel <- create.StocSI(i, 1, 0.5, 30, 20)
    out <- run(model = SImodel)
    plot(out, main = paste0("N = ", i))
}
par(mfrow = c(1, 1))
```

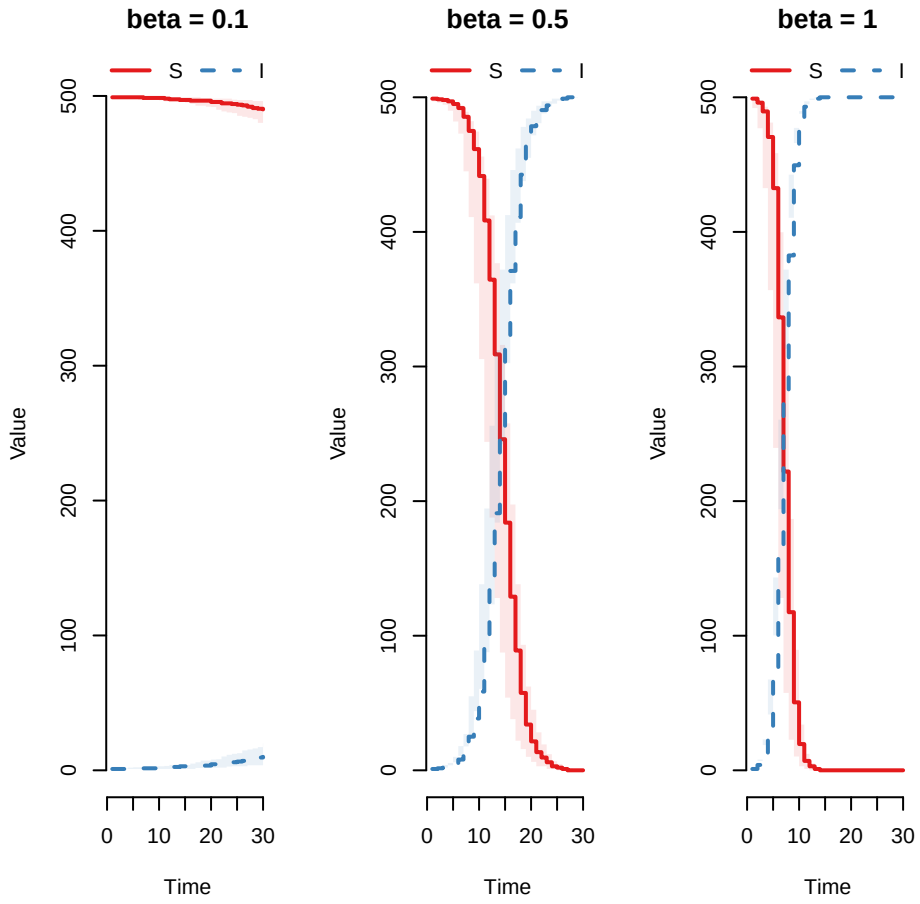


Return to task on P113

Solution 69

As discussed in lectures, increasing the transmission rate reduces the impact of stochasticity and the variability between replicates.

```
beta <- c(0.1, 0.5, 1)
par(mfrow = c(1, 3))
for(i in beta) {
    SImodel <- create.StocSI(500, 1, i, 30, 20)
    out <- run(model = SImodel)
    plot(out, main = paste0("beta = ", i))
}
par(mfrow = c(1, 1))
```



Return to task on P113

Solution 72

```
create.StocSIR <- function(N, I0, beta, mu, f_time, reps = 1) {
    initial_state <- data.frame(S = rep(N-I0, reps), I = rep(I0, reps), R = rep(0, reps))
    compartments <- c("S", "I", "R")
    transitions <- c("S -> beta*S*I/(S+I+R) -> I", "I -> mu*I -> R")
    tspan <- seq(from = 1, to = f_time, by = 1)

    model <- mparse(transitions = transitions,
                    compartments = compartments,
                    gdata = c(beta = beta, mu = mu),
                    u0 = initial_state,
                    tspan = tspan)

    return(model)
}
SIRmodel <- create.StocSIR(500, 1, 1, 0.25, 50)
out <- run(model = SIRmodel)
plot(out)
```

Return to task on P118

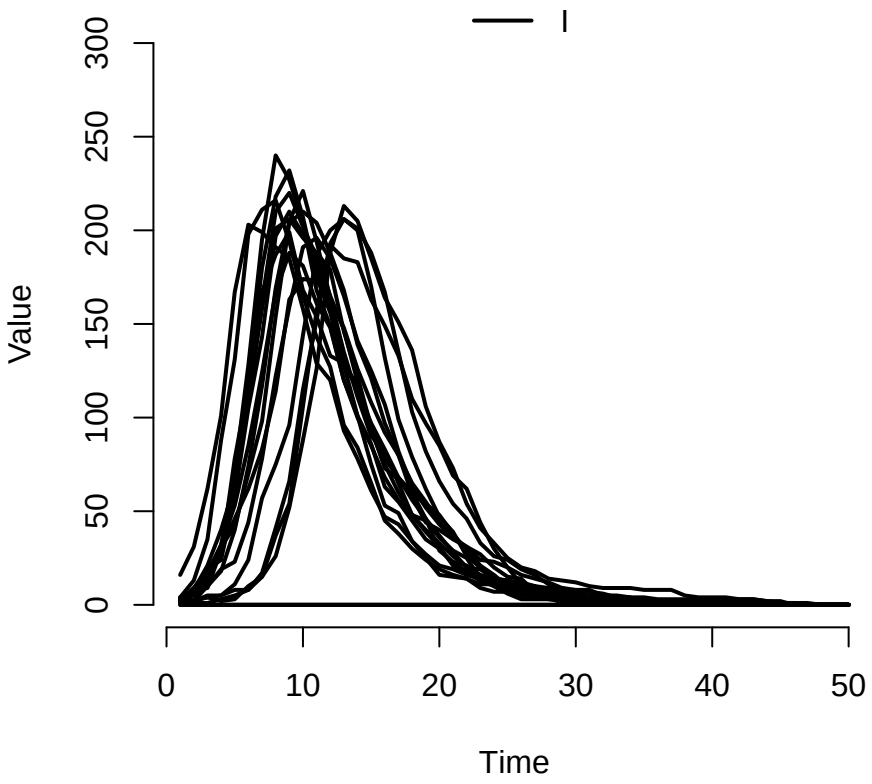
Answer 73

For some replicates the initial infected individual will recover before transmitting, the disease will go extinct and there will be no epidemic.

Return to task on P119

Solution 74

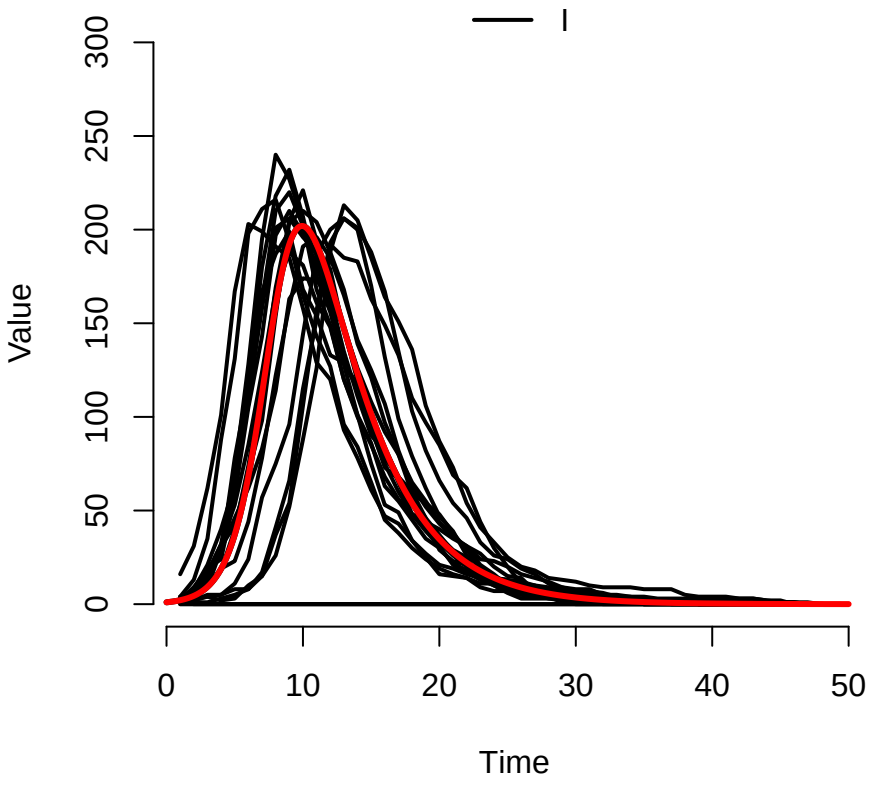
```
SIRmodel <- create.StocSIR(500, 1, 1, 0.25, 50, 20)
out <- run(model = SIRmodel)
plot(out , 'I', range=FALSE , type = 'l', ylim = c(0, 300))
```



Return to task on P119

Solution 75

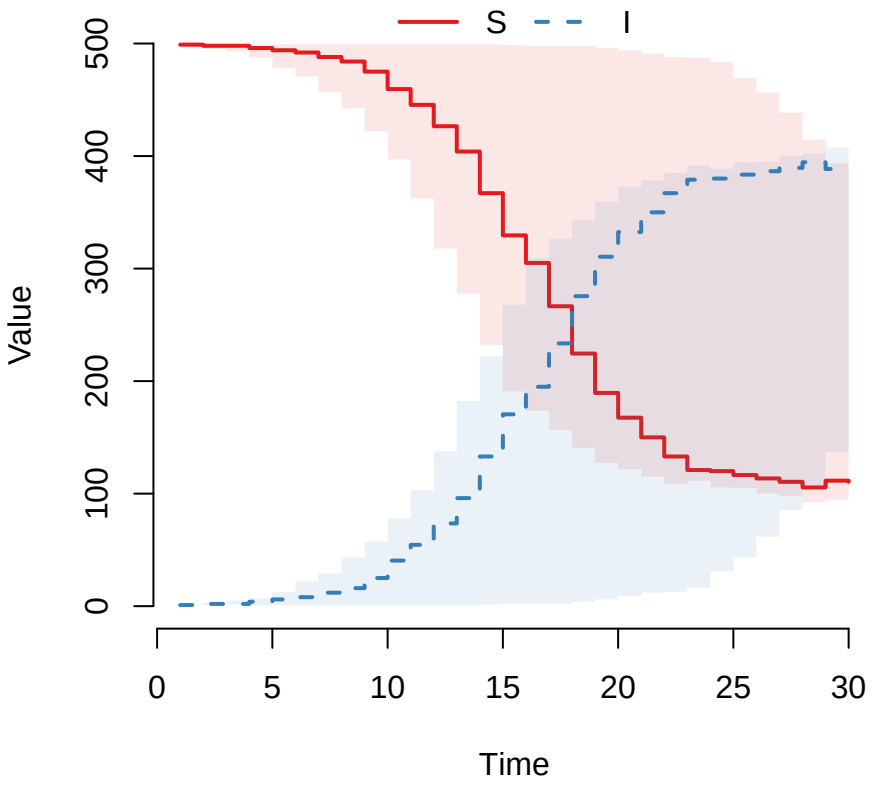
```
source('Materials/Epidemic_models/Functions/Det_SIR.R')
det.sol <- DetSIR.dyn(500, 1, 1, 0.25, 50)
det.t <- det.sol[,1]
det.I <- det.sol[,3]
lines(det.t, det.I, lwd = 3, col = 'red')
```



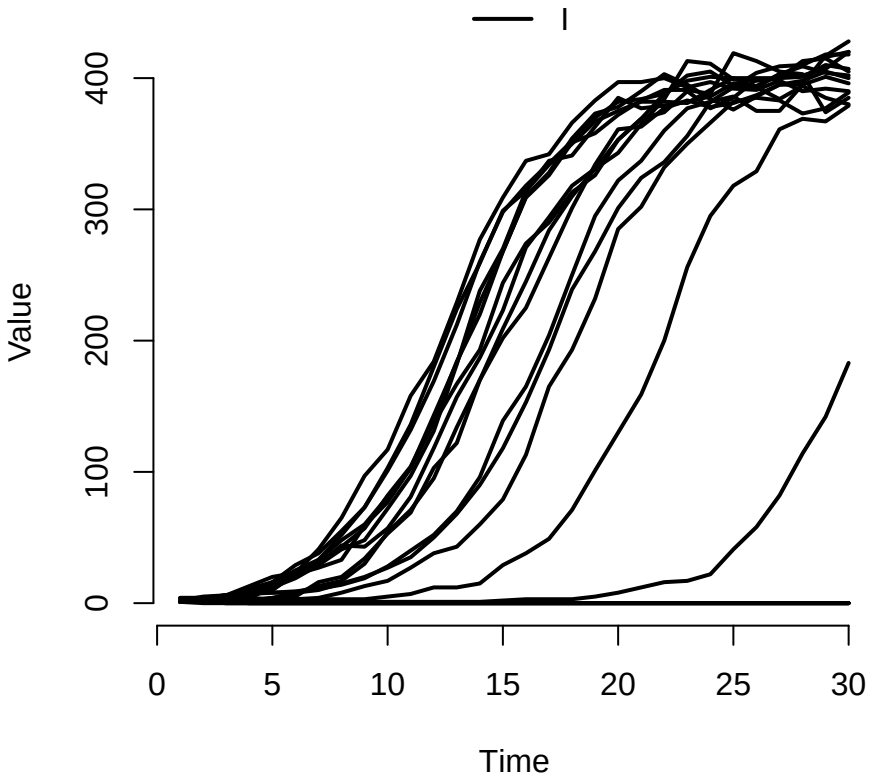
Return to task on P119

Solution 76

```
create.StocSIS <- function(N, I0, alpha, beta, f_time, reps = 1) {
    initial_state <- data.frame(S = rep(N-I0, reps), I = rep(I0, reps))
    compartments <- c("S", "I")
    transitions <- c("S -> beta*S*I/(S+I) -> I", "I -> alpha*I -> S")
    tspan <- seq(from = 1, to = f_time, by = 1)

    model <- mparse(transitions = transitions,
                    compartments = compartments,
                    gdata = c(alpha = alpha, beta = beta),
                    u0 = initial_state,
                    tspan = tspan)

    return(model)
}
SISmodel <- create.StocSIS(500, 1, 0.1, 0.5, 30, 20)
out <- run(model = SISmodel)
plot(out)
```



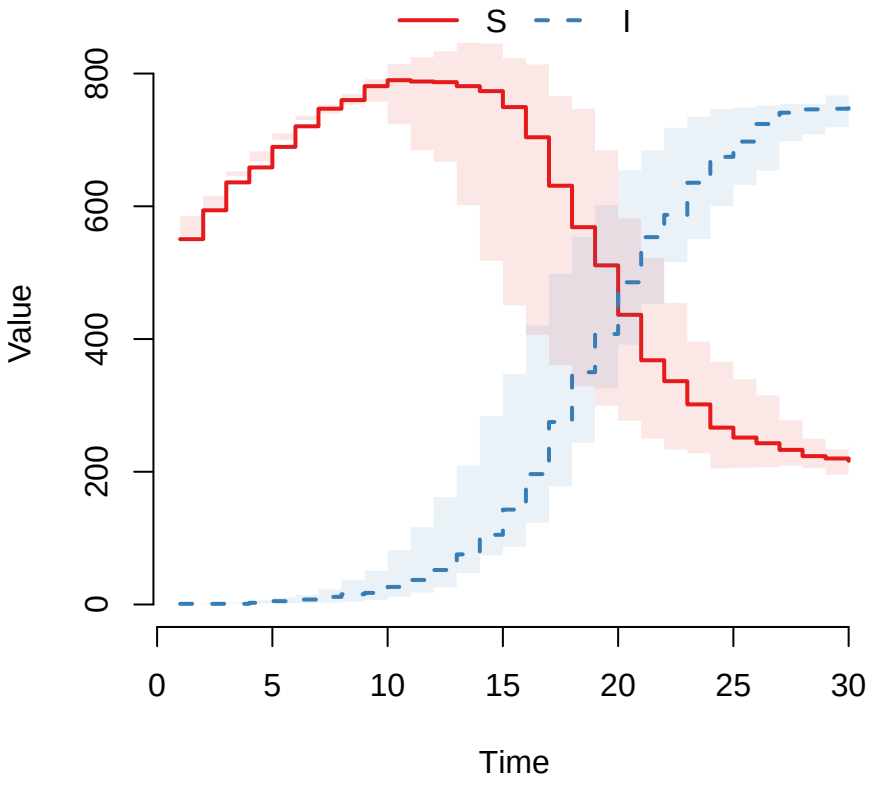

```
plot(out , 'I', range = FALSE , type = 'l')
```



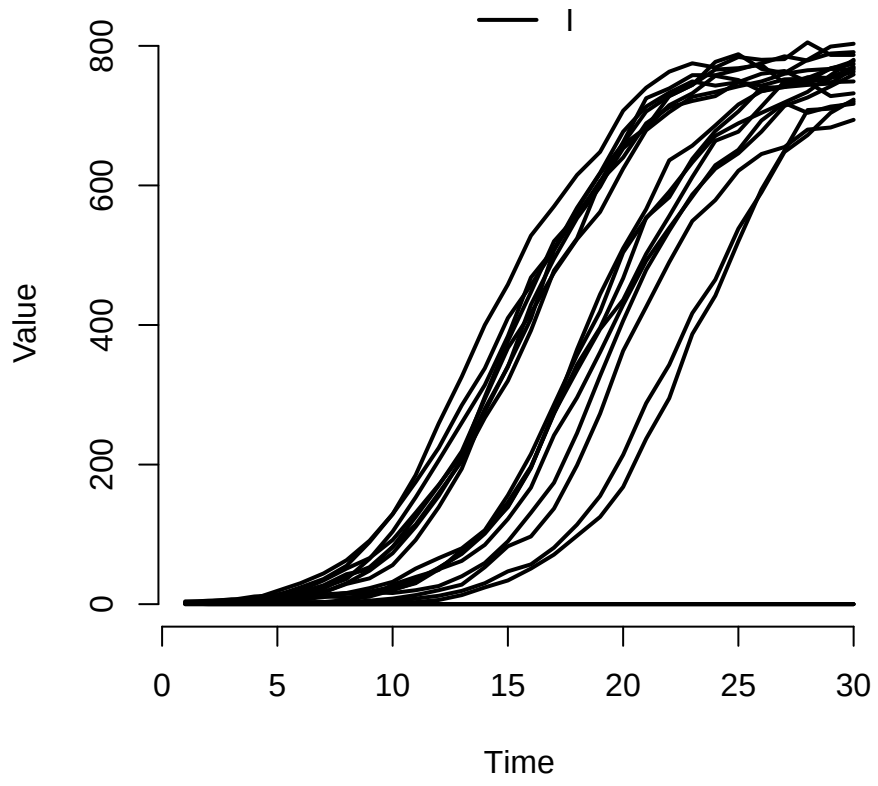
Return to task on P120

Solution 77

```
create.StocSI_demo <- function(N, I0, mu, beta, lambda, f_time, reps = 1) {
    initial_state <- data.frame(S = rep(N-I0, reps), I = rep(I0, reps))
    compartments <- c("S", "I")
    transitions <- c(
        "@ -> lambda -> S",
        "S -> beta*S*I/(S+I) -> I",
        "S -> mu*S -> @",
        "I -> mu*I -> @"
    )
    tspan <- seq(from = 1, to = f_time, by = 1)

    model <- mparse(transitions = transitions,
                    compartments = compartments,
                    gdata = c(mu = mu, beta = beta, lambda = lambda),
                    u0 = initial_state,
                    tspan = tspan)

    return(model)
}
SI_demo_model <- create.StocSI_demo(500, 1, 0.1, 0.5, 100, 30, 20)
out <- run(model = SI_demo_model)
plot(out)
```




```
plot(out, 'I', range = FALSE , type = 'l')
```



Return to task on P121

Solution 78

Here we will extract the number of removals at time $t = 50$ as an approximation of the final epidemic size.

```
## check for a single simulation
SIRmodel <- create.StocSIR(500, 1, 1, 0.25, 50)
out <- run(model = SIRmodel)

## extract states
u <- trajectory(out)

## find approximate final epidemic size
finalsize <- u$R[u$time == 50]
finalsize
```

```
## [1] 491
```

Return to task on P121

Solution 79

```
## run 100 replicates
SIRmodel <- create.StocSIR(500, 1, 1, 0.25, 50, 100)
out <- run(model = SIRmodel)

## extract states
u <- trajectory(out)

## find approximate final epidemic size for each replicate
finalsize <- rep(NA, 100)
for(i in 1:100) {
    finalsize[i] <- u$R[u$node == i & u$time == 50]
}
hist(finalsize, breaks = 500)
```

This has a bimodal distribution because as before, with a small number of initial infectious individuals there is a non-zero probability that these early infections will recover before they infect anyone else. If an epidemic does take off then the final sizes tend to cluster around the deterministic final size ($\approx N = 500$ here).

Return to task on P122

Solution 80

$$R_0 = \frac{\beta}{\gamma} = \frac{1}{0.25} = 4.$$

From the lecture notes we have that the probability of early extinction is $P(E) \approx \frac{1}{R_0} = 0.25$. We can produce an approximation of the early extinction probabilities by counting the proportion of realisations that die out early. Based on the final size graph above, given the two very distinct modes, if we define early extinction as being any realisation with a final size < 250 say, then we can generate an estimate for $P(E)$ as:

```
PE <- sum(finalsize < 250) / length(finalsize)
PE
```

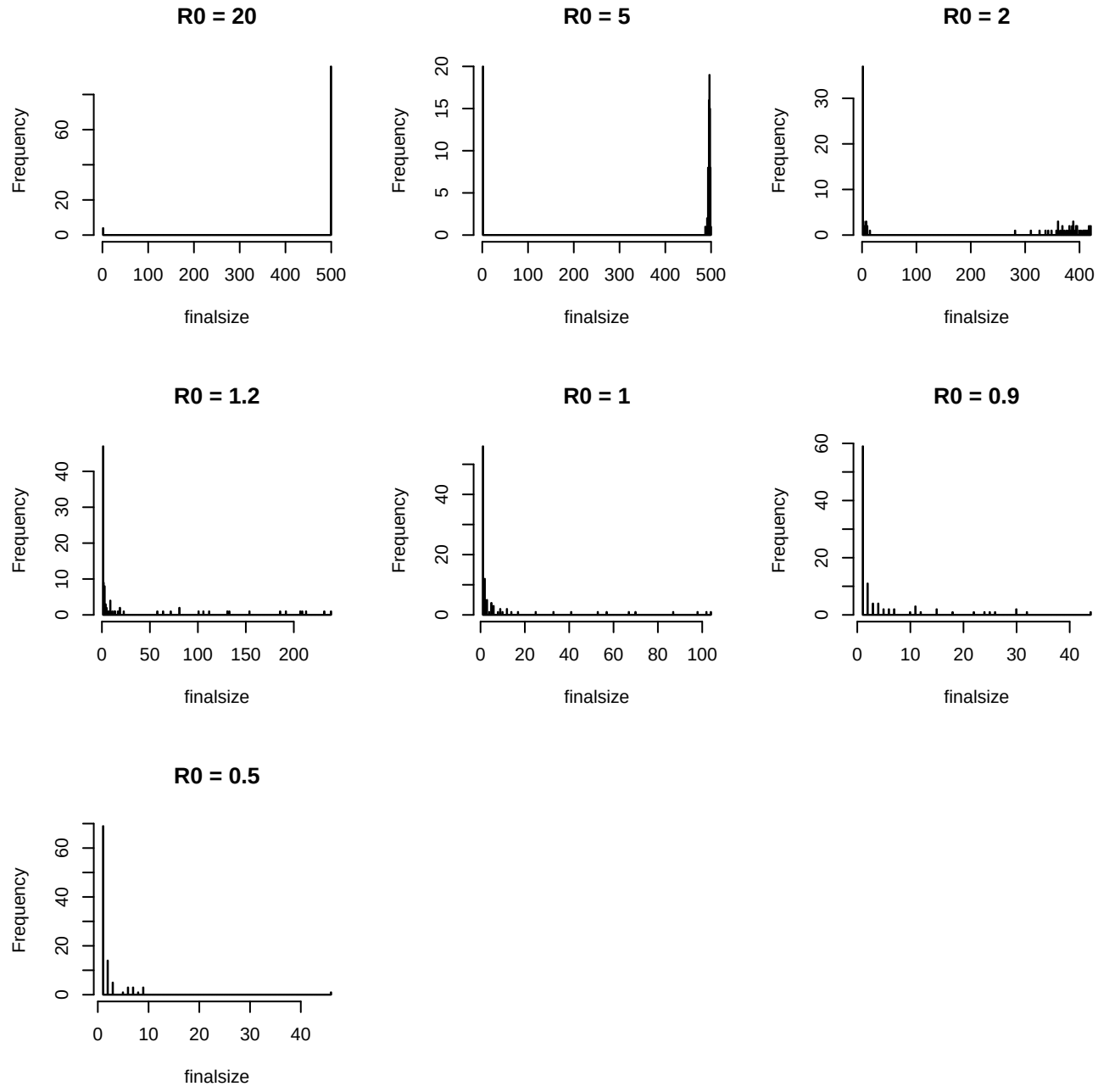
```
## [1] 0.2
```

We can see that this closely aligns to our theoretical approximation.

Return to task on P122

Solution 81

```
## set vector of R0 values
R0 <- c(20, 5, 2, 1.2, 1.0, 0.9, 0.5)

## set mu
mu <- 0.25

## set plot layout
par(mfrow = c(3, 3))

## loop over R0 values
for(i in 1:length(R0)) {

    ## calculate beta for fixed mu and R0
    beta <- R0[i] * mu

    ## set up and run model
    SIRmodel <- create.StocSIR(500, 1, beta, mu, 50, 100)
    out <- run(model = SIRmodel)

    ## extract states
    u <- trajectory(out)

    ## find final epidemic size for each replicate
    finalsize <- rep(NA, 100)
    for(j in 1:100) {
        finalsize[j] <- u$R[u$node == j & u$time == 50]
    }
    hist(finalsize, breaks = 500, main = paste0("R0 = ", R0[i]))
}
par(mfrow = c(1, 1))
```



For intermediate values of R_0 the two modes will merge together.

Return to task on P123

Answer 82

We should monitor the first time at which the number of infectious individuals, I, equals 0.

Return to task on P123

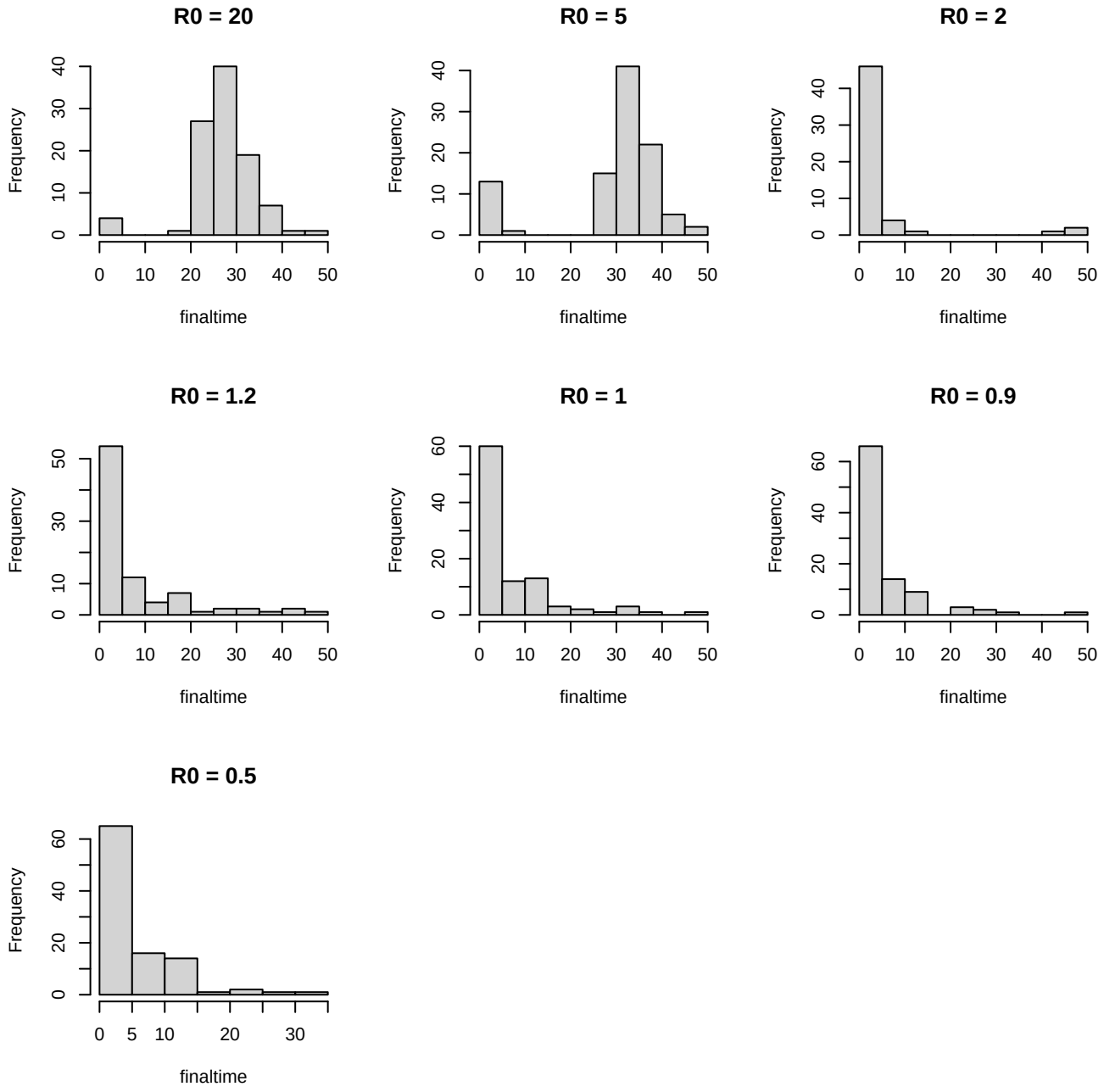
Solution 83

To generate the first figure, consider:

```r
set.seed(126)
## run 100 replicates
SIRmodel <- create.StocSIR(500, 1, 1, 0.25, 50, 100)
out <- run(model = SIRmodel)

## extract states
u <- trajectory(out)

## find extinction time for each replicate
finaltime <- rep(NA, 100)
for(i in 1:100) {
    ## note that this will return an NA if the epidemic hasn't ended
    finaltime[i] <- u$time[u$node == i & u$I == 0][1]
}
hist(finaltime)
```

To then explore how this distribution changes for different values of R_0, consider:

```r
## set vector of R0 values
R0 <- c(20, 5, 2, 1.2, 1.0, 0.9, 0.5)

## set mu
mu <- 0.25

## set plot layout
par(mfrow = c(3, 3))

## loop over R0 values
for(i in 1:length(R0)) {

    ## calculate beta for fixed mu and R0
    beta <- R0[i] * mu

    ## set up and run model
    SIRmodel <- create.StocSIR(500, 1, beta, mu, 50, 100)
    out <- run(model = SIRmodel)

    ## extract states
    u <- trajectory(out)

    ## find extinction time for each replicate
    finaltime <- rep(NA, 100)
    for(j in 1:100) {
        ## note that this will return an NA if the epidemic hasn't ended
        finaltime[j] <- u$time[u$node == j & u$I == 0][1]
    }
    hist(finaltime, main = paste0("R0 = ", R0[i]))
}
par(mfrow = c(1, 1))
```



As R_0 gets closer to one, the extinction time distribution loses the upper mode and moves far closer to zero.

Return to task on P124

Solution 84

We have limited the graph to only plot the first 100 cases. We achieved this by using the date of the 100^{th} entry of the line list (`outfluenza1$x`) to set the upper limit.

Return to task on P133

Solution 85

```
R0final <- function(zf) {
    # zf must be proportion between 0 and 1
    # Trap for division by zero(zf=0.0)
    # Trap for log(1) (-Inf)
    if(zf<=0 || zf>=1.0) {
        return(NA)
    } else {
        return(-log(1-zf)/zf)
    }
}
```

Return to task on P135

Solution 86

```
R0final(incidence(outfluenza1$x)$n/1300)
```

```
## [1] 2.646094
```

```
R0final(incidence(outfluenza2$x)$n/1300)
```

```
## [1] 2.378981
```

```
R0final(incidence(biggles$x)$n/1300)
```

```
## [1] 2.463143
```

Return to task on P136

Solution 87

$R_0 = 1 + 0.335 \times 5 = 2.67$

Return to task on P137

Solution 88

$R_0 = 2.67$ (95% CI, 2.1–3.1)

Return to task on P137

Answer 89

We are fitting a log-linear relationship and $\log(0)$ is undefined.

Return to task on P138

Answer 90

`outflu1.fit2` is clearly a poor fit to the exponential growth rate as we have not subsetted the data to the exponential phase. The point estimates from the incidence package and our manual estimate are pretty comparable, however the confidence intervals from our manual estimate are smaller (0.2–0.4 compared to 0.2–0.5) reflecting the effective **smoothing** we applied to the data by using the cumulative case counts instead of raw incidence. We could similarly smooth the time series by increasing the time interval to sum up incidence - this runs the risk of introducing **artifacts** to the data or giving us false confidence in our estimates.

Return to task on P140

Solution 92

The confidence intervals from our regression model capture the variability (scatter) in the model output around the best-fit line for this particular realisation of the epidemic model. Stochastic effects will generate far greater variability between realisations, which our linear model contains no information about. The uncertainty in the estimate of the slope will therefore typically underestimate the true variability in the epidemic model. The Likelihood function for the `earlyR` method includes more information on the variability of the serial interval derived from an epidemic model and better represents the true **uncertainty** in our estimates.

Return to task on P143

Additional information

Relating sticker collecting to the harmonic numbers

In the lecture I claimed that the example of collecting things is somehow related to the harmonic series. To see this does not require sophisticated mathematics.

If there are a total of N stickers, of which you have already collected M, the probability of a new sticker being one you "need" is $p_M = (N - M)/N$. Assuming that successive purchases are independent, the number of stickers that must be bought to get a sticker you need when you already have M stickers in your album would follow a geometric probability distribution[a]. The expected number of stickers needed to get the M^{th} sticker is therefore $\frac{1}{p_M}$.

The number of stickers that you must buy to complete the entire album is then just the expected number of stickers to get the first sticker in your album (i.e. when you have already got 0), plus the expected number required for your second sticker (i.e. when you have already got 1), ..., all the way up to the expected number to get the final sticker (i.e. when you have already got $N\check{}1$).

Therefore

$$\text{Average number of stickers required} = \frac{1}{p_0} + \frac{1}{p_1} + \cdots + \frac{1}{p_{N-1}}.$$

However (by the definition of p_M) this reduces to

$$\begin{aligned}\text{Average number of stickers required} &= \frac{N}{N} + \frac{N}{N-1} + \cdots + \frac{N}{1} \\ &= N\left(\frac{N}{N} + \frac{N}{N-1} + \cdots + \frac{1}{1}\right) \\ &= N\left(1 + \cdots + \frac{1}{N-1} + \frac{1}{N}\right) \\ &= N \times H_N\end{aligned}$$

where we reversed the order of the sum in going from line 2 to line 3, and have used the definition of the N^{th} harmonic number (see lecture slides) on line 4.

Return to P57

[a] You will be reminded of basic facts about probability distributions in a forthcoming lecture. Note the expected number is quite intuitive: as a simple example, consider rolling a dice until you get a six. The probability of getting a six is $\frac{1}{6}$: hopefully it seems reasonable that you should have to roll the dice an average of 6 times to get one. That's all that is happening here, just written in symbols.

Standard $SEIR$ (exponential) with sinusoidal forcing

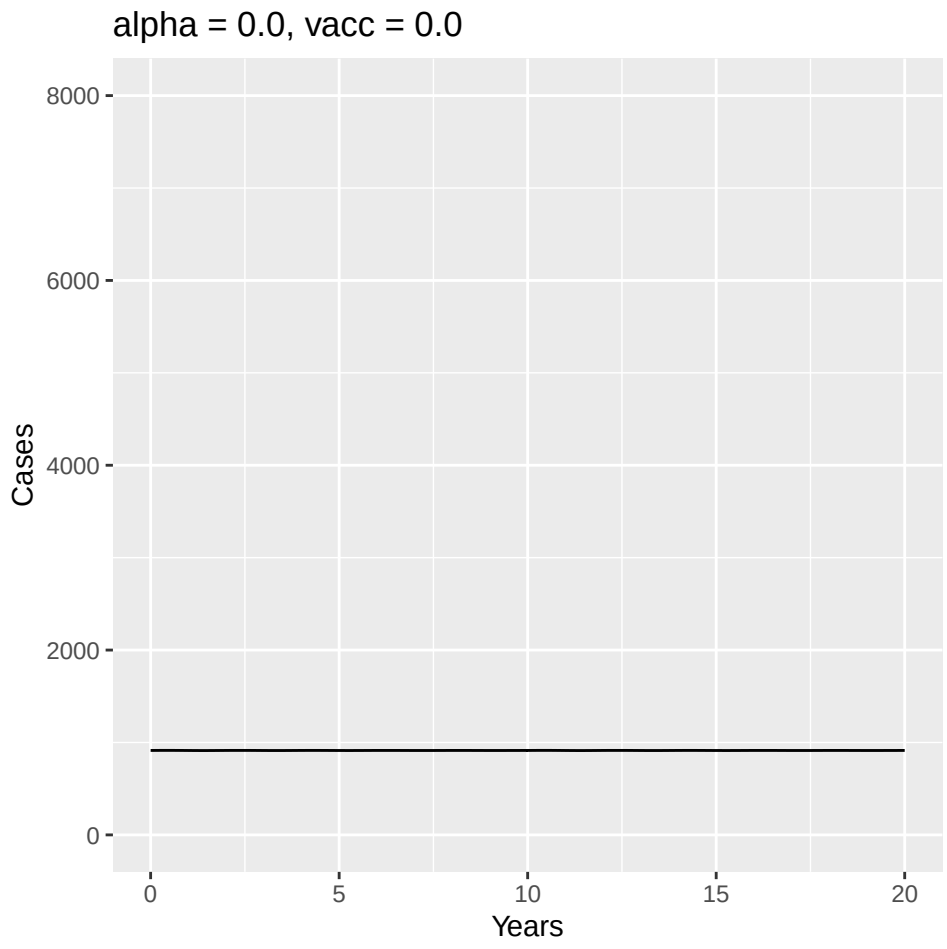
We first present an implementation of the standard $SEIR$ model—with constant rates of progression through the latent and infectious compartments—and sinusoidal forcing term. The basic template here is similar to what you have seen before in earlier practicals except that the transmission rate now depends on the time. Here we wrote a wrapper function which sets some sensible default initial conditions (the fixed points of the unforced $SEIR$ model where $\alpha = 0.0$) and then runs the model for three periods. No matter the initial model conditions the seasonally forced $SEIR$ model will **eventually** converge towards a stable dynamic behaviour (often described as an "attractor" in analogy to the fixed points of an unforced model). We can run the model for a "burn-in" period (analogous to the

same concept for MCMC convergence) to remove this “transient” behaviour. Our function solves the model for three periods. We forward-simulate the initial conditions for `burnin` years discarding the results but using the final state to set the initial conditions for a run of `prevacc` years. We then adjust the birth rate to model vaccination at birth and then run for an additional `postvacc` years, returning a tibble with the sampling times and state variables of the model:

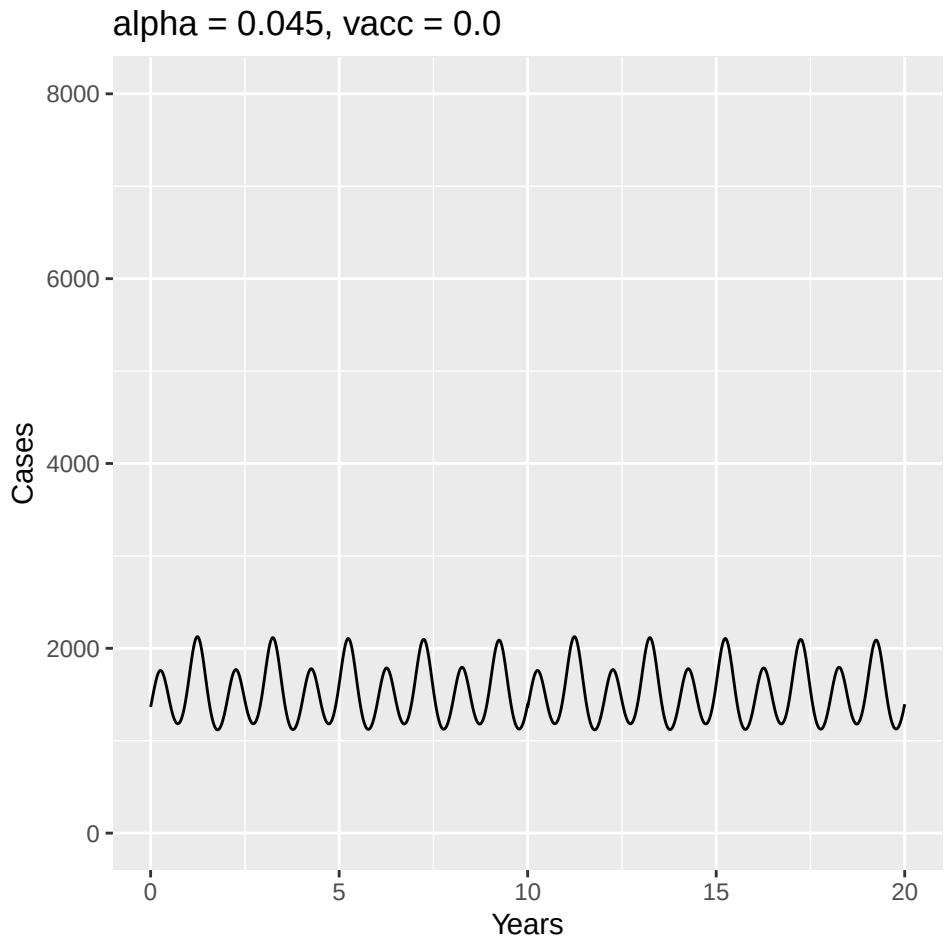
```
SEIR_exp <- function(t,y,theta) {

  beta = theta[1];
  TE = theta[2];
  TI = theta[3];
  alpha = theta[4];
  mu    = theta[5]

  I_tot=0;
  N_tot=0;

  dy_dt = numeric(4);

  N_tot = sum(y)

  lambda = (1  + alpha * cos(2*pi*t/364))*beta*y[3]/N_tot

  dy_dt[1] = mu*N_tot - (lambda  + mu) * y[1];
  dy_dt[2] =  lambda * y[1]  - (1.0/TE + mu) * y[2];
  dy_dt[3] = (1.0/TE) * y[2] - (1.0/TI + mu) * y[3];
  dy_dt[4] = (1.0/TI)*y[3] - mu*y[4];

  return(list(dy_dt))
}

det_SEIR_exp <-function(N0,R0,TE,TI,mu,alpha,burnin,prevacc,postvacc,vacc)
{

  theta = numeric(7)

  # Set initial conditions to endemic fixed points

  beta = R0/TI
  s0 = 1/R0
  e0 = (TI*mu*(mu+1/TI)/(beta/TE))*(R0-1)
  i0 = (mu/beta)*(R0-1)

  y0 = numeric(4);
  y0[1] = s0*N0;
  y0[2] = e0*N0;
  y0[3] = i0*N0;
  y0[4] = (1-s0-e0-i0)*N0;


  theta[1] = beta;
  theta[2] = TE;
  theta[3] = TI;
  theta[4] = alpha
  theta[5] = mu

  # Run for burnin years and use final state
  # as initial condition
  y<-lsoda(y0,seq(0,burnin*364,1),SEIR_exp,theta)
  y0 = y[dim(y)[1],2:5]
  # Run for prevacc years
  y<-lsoda(y0,seq(0,prevacc*364,1),SEIR_exp,theta)
  # store time (in years) and numbers in each compartment
  output <- tibble(time=y[,1]/364,S=y[,2],E=y[,3],I=y[,4],R=y[,5])
  # Reduce birth rate by vaccination proportion
  theta[5] = (1-vacc)*mu
  # Run for postvacc years
  y<-lsoda(y0,seq(0,postvacc*364,1),SEIR_exp,theta)
```

Using the suggested parameter values you should find that a seasonal forcing of $\alpha = 0.19$ gives a reasonable qualitative fit to the two year cycle of measles outbreaks seen in London after 1950:

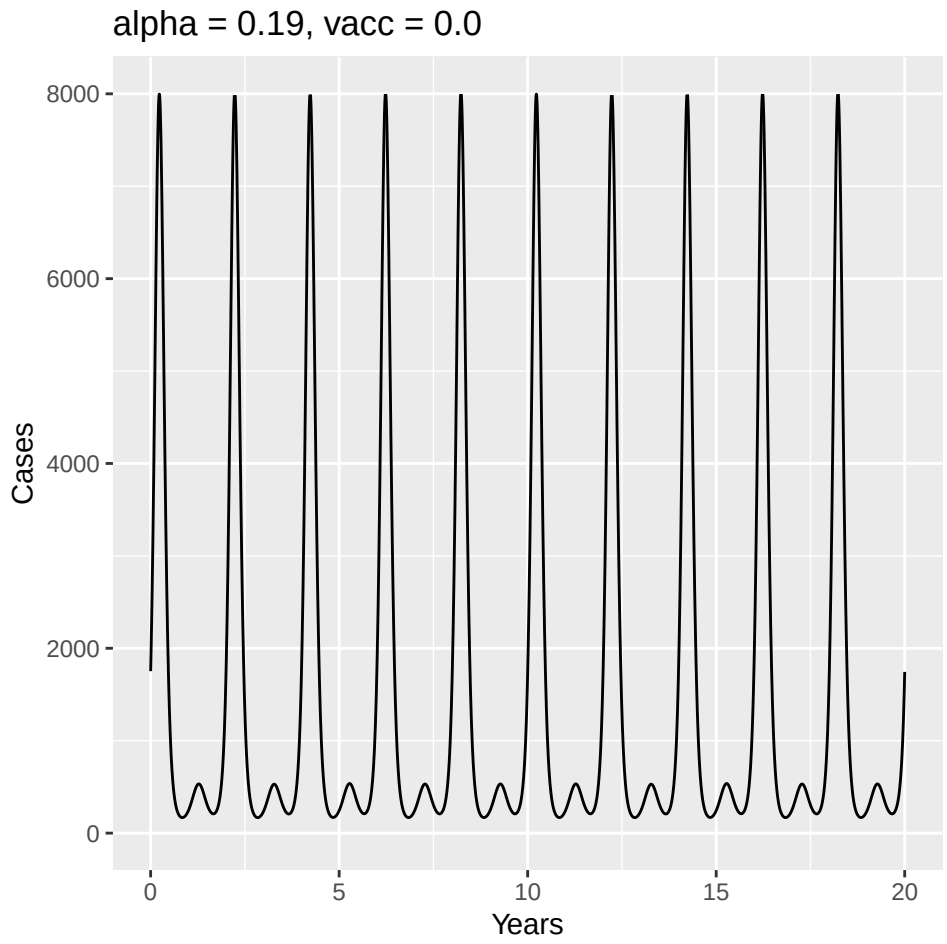
```
x<-det_SEIR_exp(3.3e6,17,8,3,20/(1000*364),0.0,50,10,10,0.0)

ggplot(x,aes(x=time,y=I*(1/0.4)*(5/7))) + geom_line() + xlab('Years') + ylab('Cases') +
  ggtitle("alpha = 0.0, vacc = 0.0") + ylim(0,8000)
```



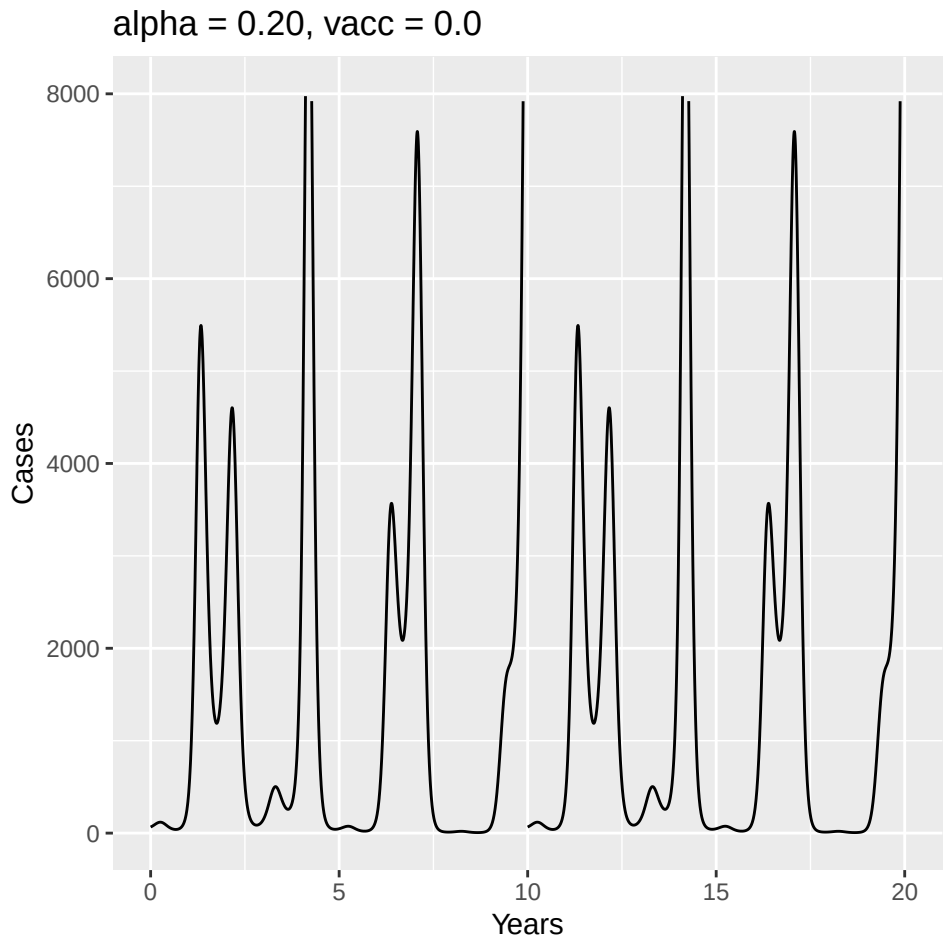

```
x<-det_SEIR_exp(3.3e6,17,8,5,20/(1000*364),0.045,50,10,10,0.0)

ggplot(x,aes(x=time,y=I*(1/0.4)*(5/7))) + geom_line() + xlab('Years') + ylab('Cases') +
  ggtitle("alpha = 0.045, vacc = 0.0") + ylim(0,8000)
```




```
x<-det_SEIR_exp(3.3e6,17,8,5,20/(1000*364),0.19,50,10,10,0.0)

ggplot(x,aes(x=time,y=I*(1/0.4)*(5/7))) + geom_line() + xlab('Years') + ylab('Cases') +
  ggtitle("alpha = 0.19, vacc = 0.0") + ylim(0,8000)
```



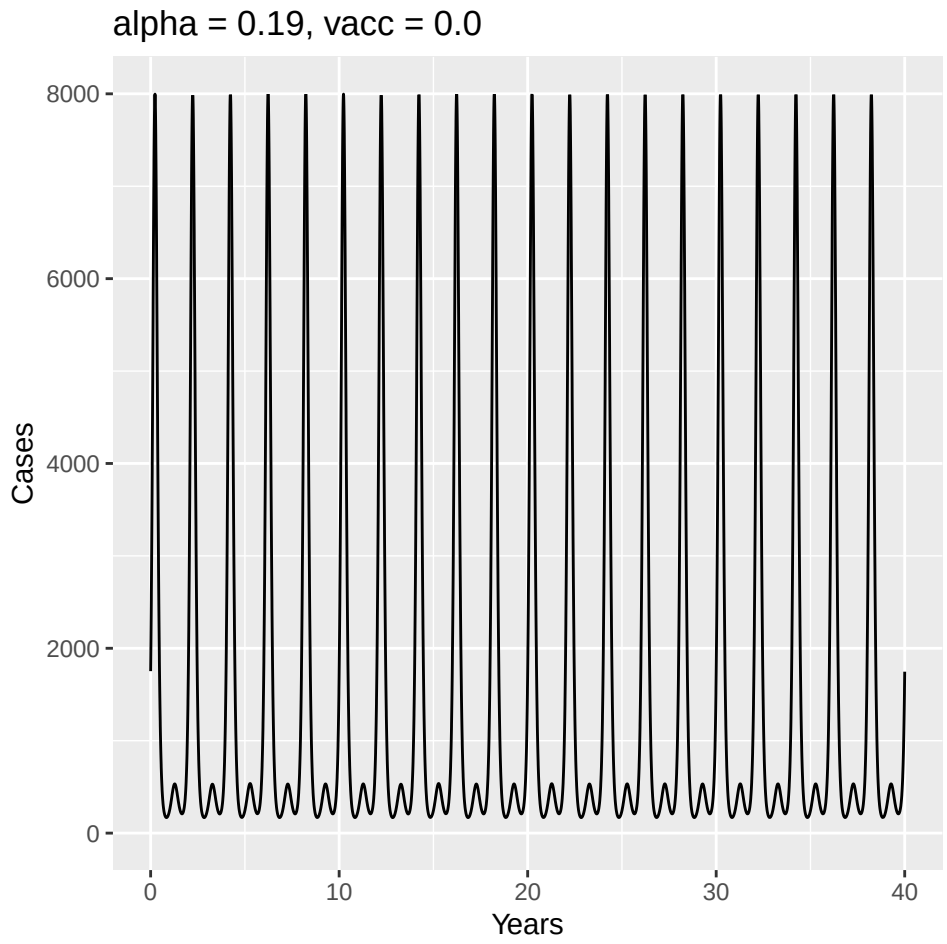

```
x<-det_SEIR_exp(3.3e6,17,8,5,20/(1000*364),0.20,50,10,10,0.0)

ggplot(x,aes(x=time,y=I*(1/0.4)*(5/7))) + geom_line() + xlab('Years') + ylab('Cases') +
  ggtitle("alpha = 0.20, vacc = 0.0") + ylim(0,8000)
```



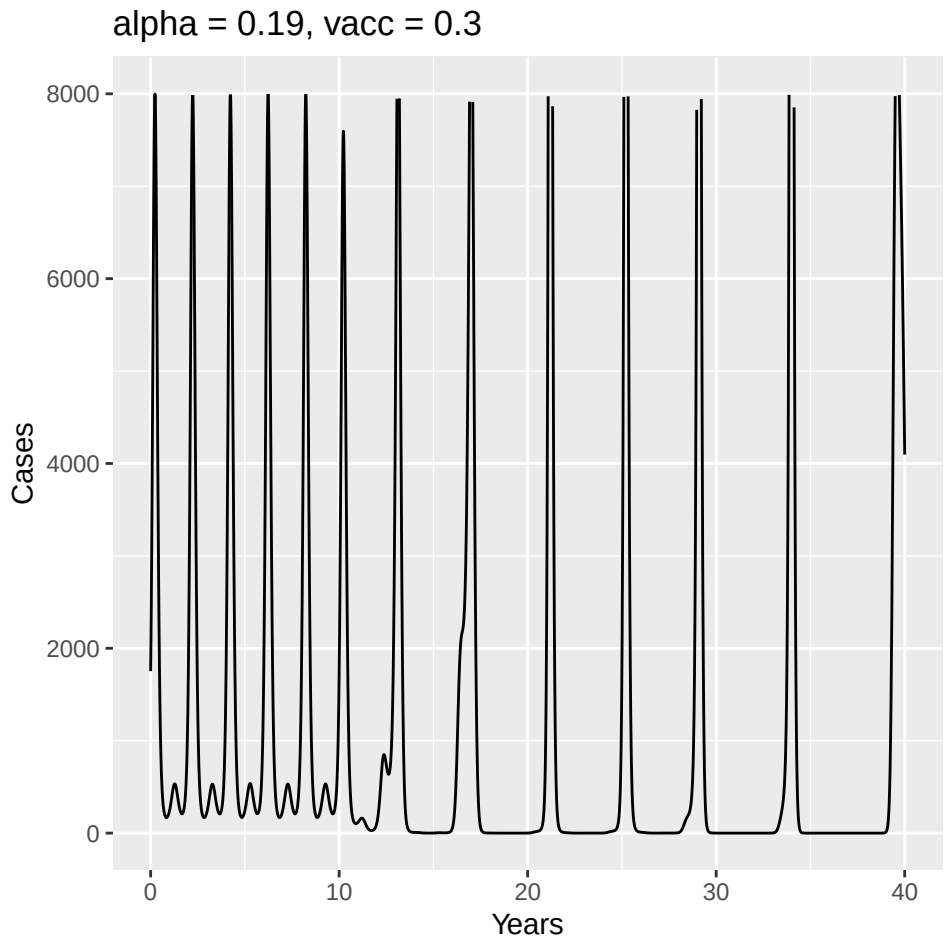
For sinusoidal forcing the bifurcation to two-yearly cycles occurs for a very small amount of seasonal forcing ($\alpha \sim 0.02$) with the amplitude of the two-year cycle increasing with increasing α before further bifurcations to three, four and irregular multiannual cycles.

If we now examine the effect of increasing vaccination coverage we see that at low coverage vaccination progressively increases the time between outbreaks—shifting cycles to 3, 4 and higher (irregular cycles). However, the incidence between outbreaks now falls to unrealistically low levels (nano-scale number of infectives!)—highlighting the likely increased importance of stochastic effects after the introduction of vaccination.

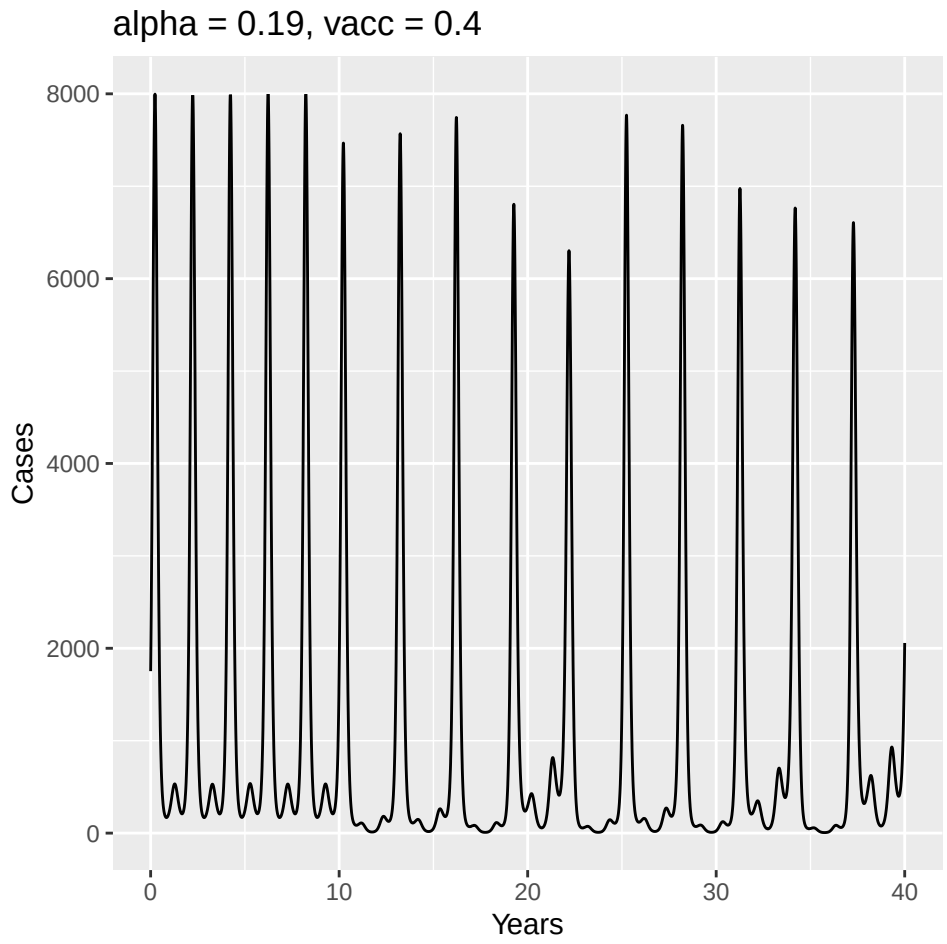
```
x<-det_SEIR_exp(3.3e6,17,8,5,20/(1000*364),0.19,50,10,30,0.0)

ggplot(x,aes(x=time,y=I*(1/0.4)*(5/7))) + geom_line() + xlab('Years') + ylab('Cases') +
  ggtitle("alpha = 0.19, vacc = 0.0") + ylim(0,8000)
```



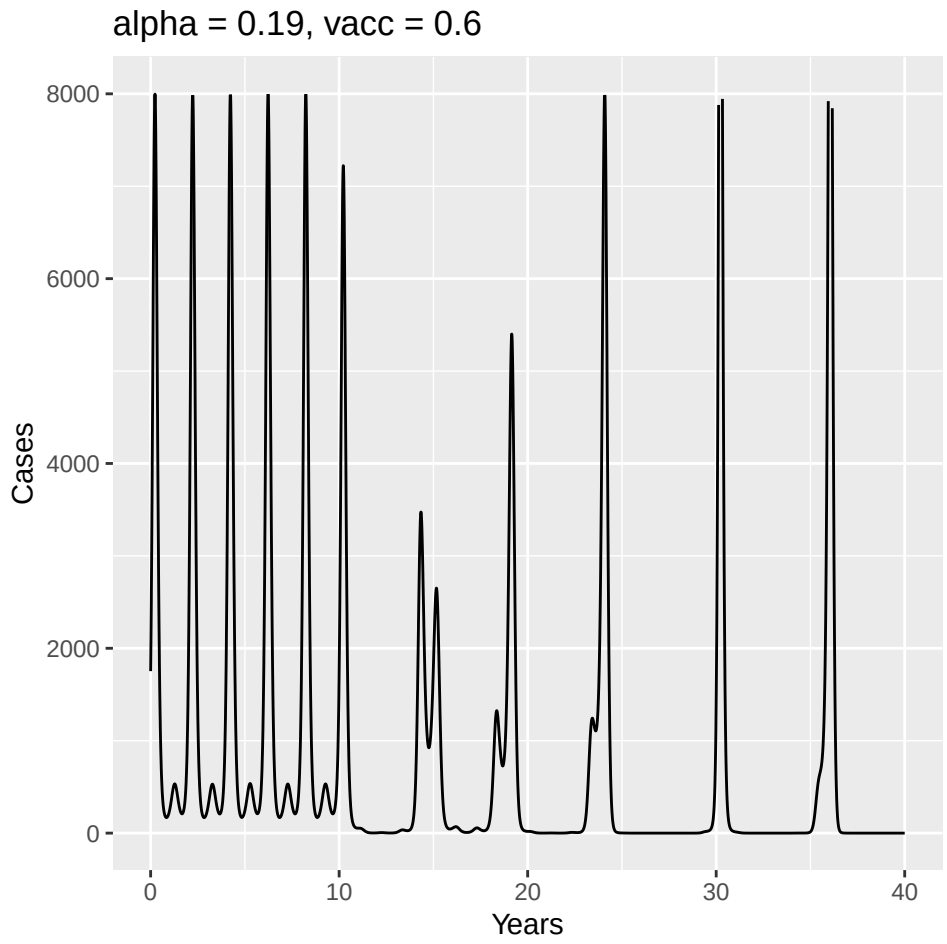

```
x<-det_SEIR_exp(3.3e6,17,8,5,20/(1000*364),0.19,50,10,30,0.3)

ggplot(x,aes(x=time,y=I*(1/0.4)*(5/7))) + geom_line() + xlab('Years') + ylab('Cases') +
  ggtitle("alpha = 0.19, vacc = 0.3") + ylim(0,8000)
```




```
x<-det_SEIR_exp(3.3e6,17,8,5,20/(1000*364),0.19,50,10,30,0.4)

ggplot(x,aes(x=time,y=I*(1/0.4)*(5/7))) + geom_line() + xlab('Years') + ylab('Cases') +
  ggtitle("alpha = 0.19, vacc = 0.4") + ylim(0,8000)
```




```
x<-det_SEIR_exp(3.3e6,17,8,5,20/(1000*364),0.19,50,10,30,0.6)

ggplot(x,aes(x=time,y=I*(1/0.4)*(5/7))) + geom_line() + xlab('Years') + ylab('Cases') +
  ggtitle("alpha = 0.19, vacc = 0.6") + ylim(0,8000)
```



These types of models can be very sensitive to both initial conditions and numerical errors meaning that more sophisticated numerical methods (such as AUTO) need to be used to map out the full range of dynamical behaviours accurately.

Return to P151

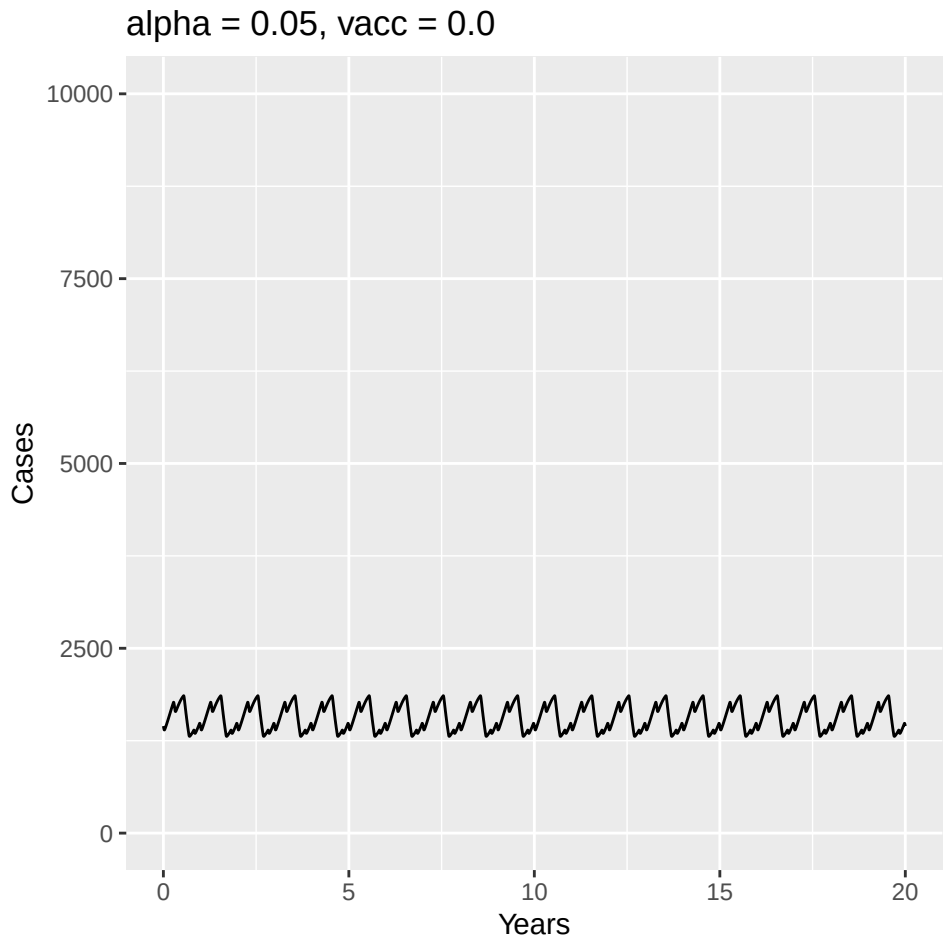
Standard $SEIR$ (exponential) with term-time forcing

We now adapt the previous code to use a term-time forcing function and run the same model scenarios:

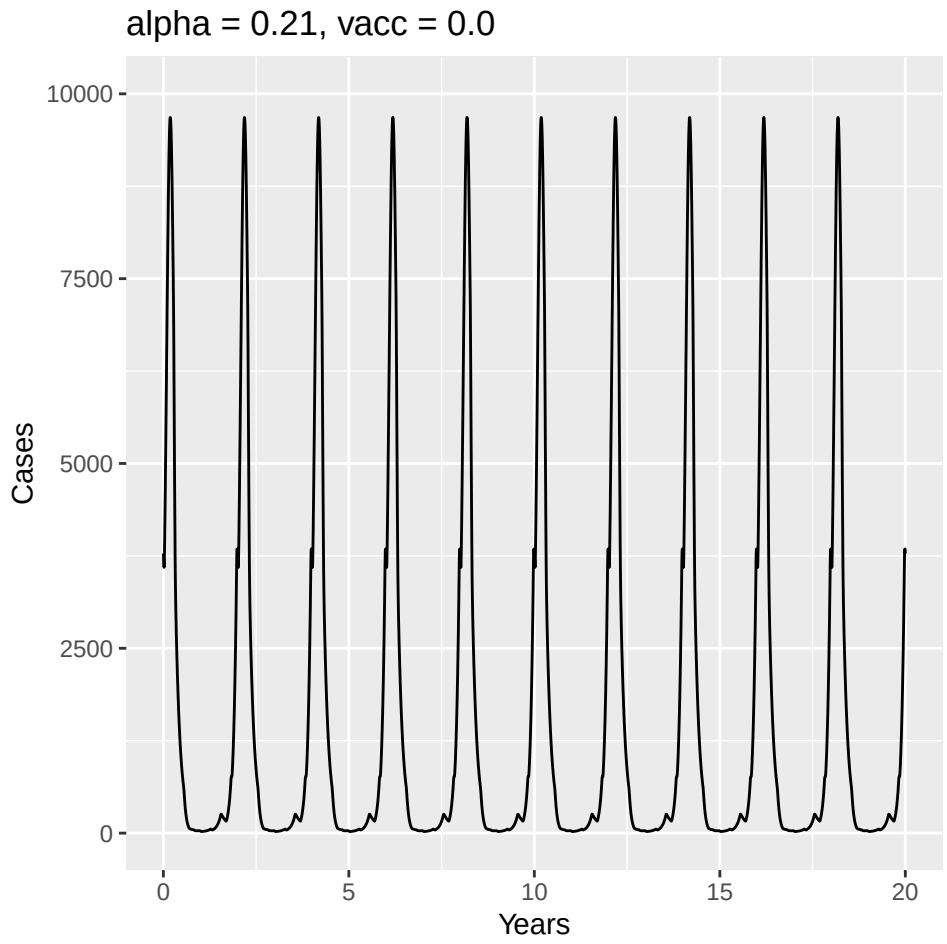
```
SEIR_exp <- function(t,y,theta) {

  beta = theta[1];
  TE = theta[2];
  TI = theta[3];
  alpha = theta[4];
  mu    = theta[5]

  I_tot=y[3];
  N_tot=0;

  dy_dt = numeric(4);

  N_tot = sum(y)

  terms = mk_terms(beta,alpha)
  lambda = terms[1 + t %% 364]*beta*I_tot/N_tot

  dy_dt[1] = mu*N_tot - (lambda  + mu) * y[1];
  dy_dt[2] =  lambda * y[1]  - (1.0/TE + mu) * y[2];
  dy_dt[3] = (1.0/TE) * y[2] - (1.0/TI + mu) * y[3];
  dy_dt[4] = (1.0/TI)*y[3] - mu*y[4];

  return(list(dy_dt))
}
```

The term-time forcing function leads to a very different (and richer) bifurcation structure. Indeed, if you tried this form of the model you likely could not find values of α that gave a reasonable match to the London time-series for the assumed parameter values. Reducing the assumed value of R_0 to 12 you can achieve a comparable fit (arguably better with respect to the qualitative shape of the attractor).

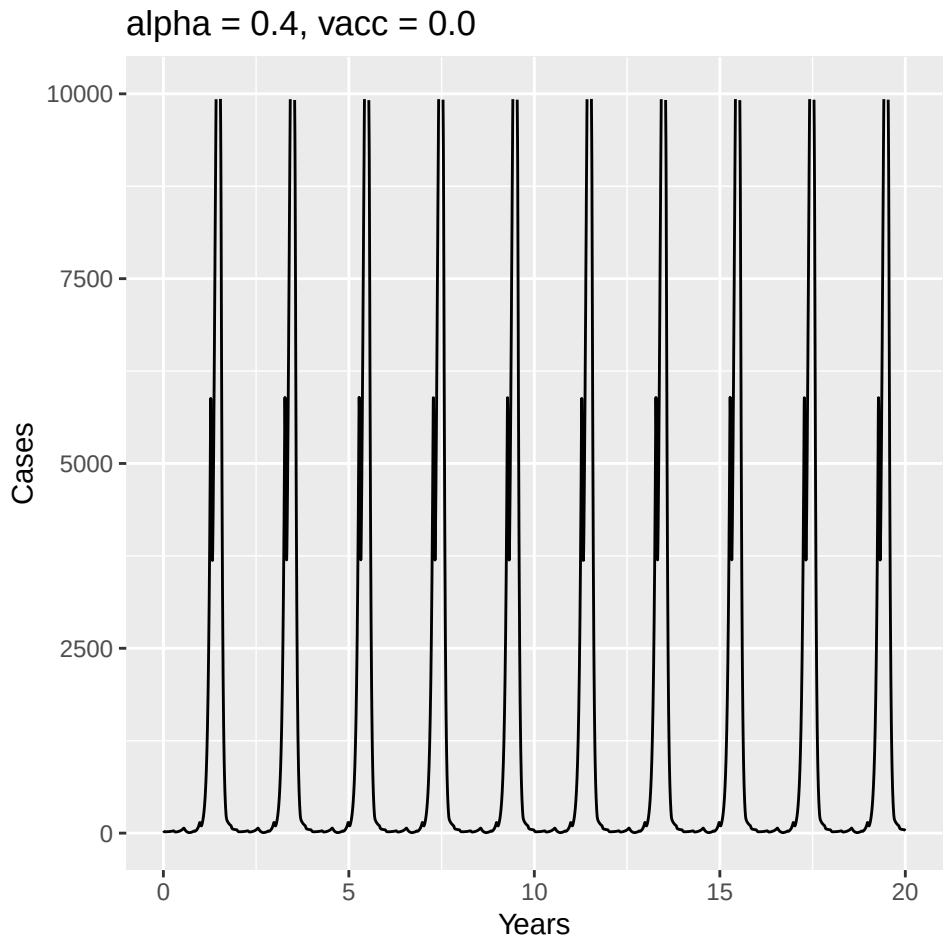
```
x<-det_SEIR_exp(3.3e6,12,8,5,20/(1000*364),0.05,50,10,10,0.0)

ggplot(x,aes(x=time,y=I*(1/0.4)*(5/7))) + geom_line() + xlab('Years') + ylab('Cases') +
  ggtitle("alpha = 0.05, vacc = 0.0") + ylim(0,10000)
```



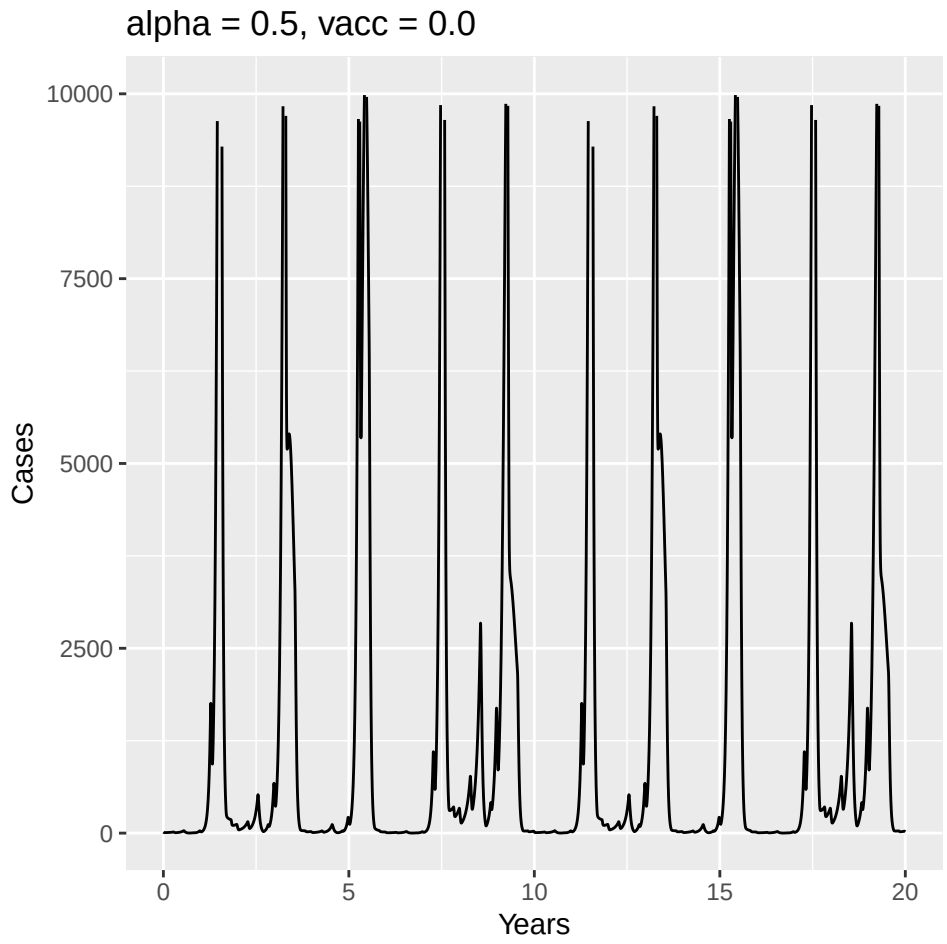

```
x<-det_SEIR_exp(3.3e6,12,8,5,20/(1000*364),0.21,50,10,10,0.0)

ggplot(x,aes(x=time,y=I*(1/0.4)*(5/7))) + geom_line() + xlab('Years') + ylab('Cases') +
  ggtitle("alpha = 0.21, vacc = 0.0") + ylim(0,10000)
```




```
x<-det_SEIR_exp(3.3e6,12,8,5,20/(1000*364),0.40,50,10,10,0.0)

ggplot(x,aes(x=time,y=I*(1/0.4)*(5/7))) + geom_line() + xlab('Years') + ylab('Cases') +
  ggtitle("alpha = 0.4, vacc = 0.0") + ylim(0,10000)
```

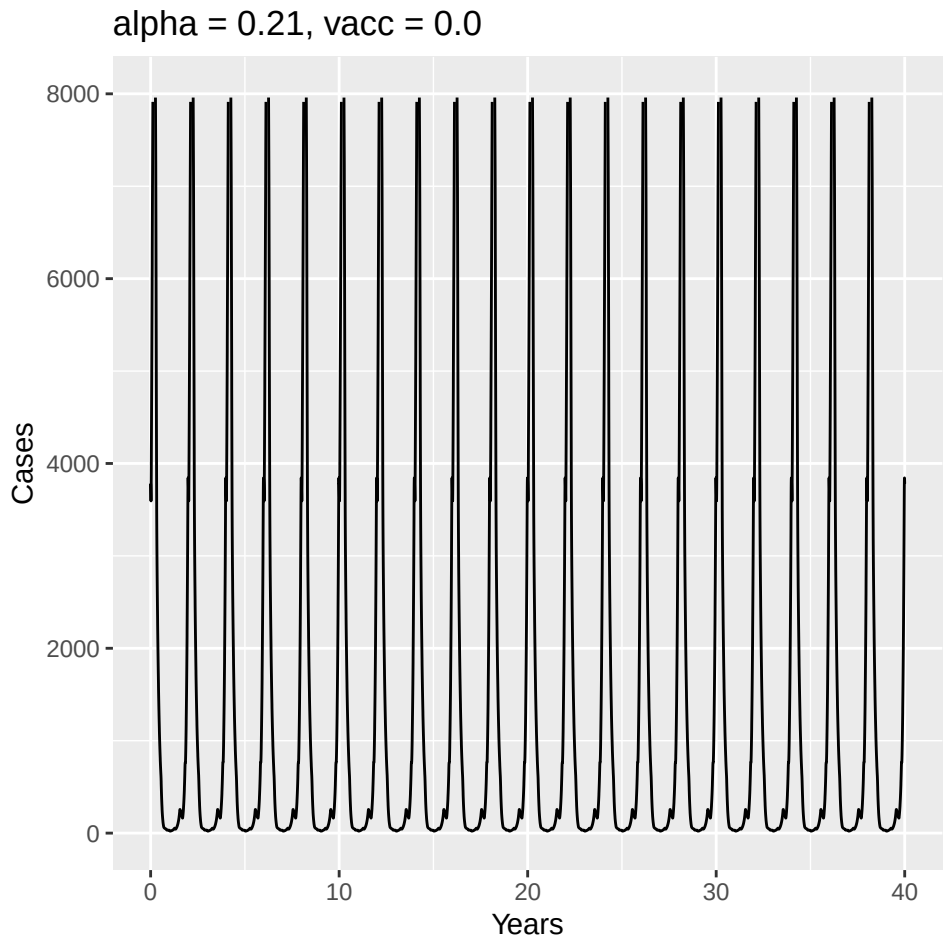



```
x<-det_SEIR_exp(3.3e6,12,8,5,20/(1000*364),0.5,50,10,10,0.0)

ggplot(x,aes(x=time,y=I*(1/0.4)*(5/7))) + geom_line() + xlab('Years') + ylab('Cases') +
  ggtitle("alpha = 0.5, vacc = 0.0") + ylim(0,10000)
```

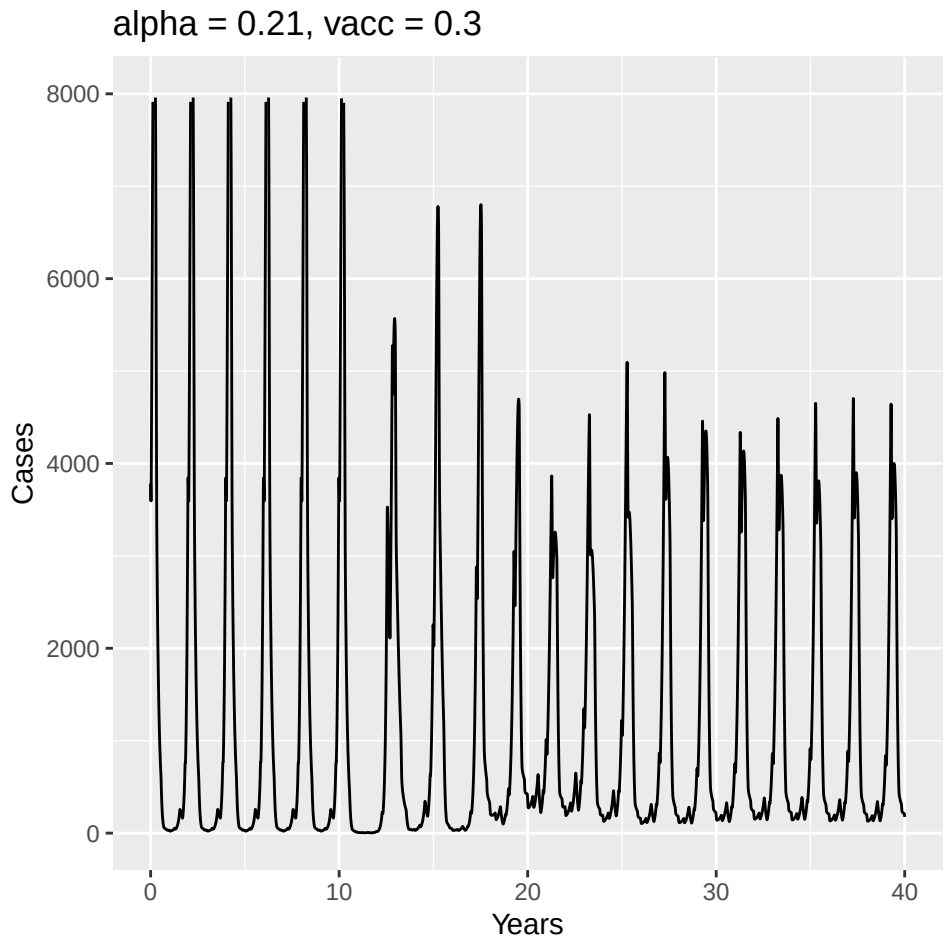


We see the same qualiative impact of vaccination as before, but note that the higher troughs in prevalence between major outbreaks predicted by the term-time forcing model mean that stable (and plausible in terms of depth of trough between outbreaks) dynamics are seen for a wider range of birth/vaccination rates:

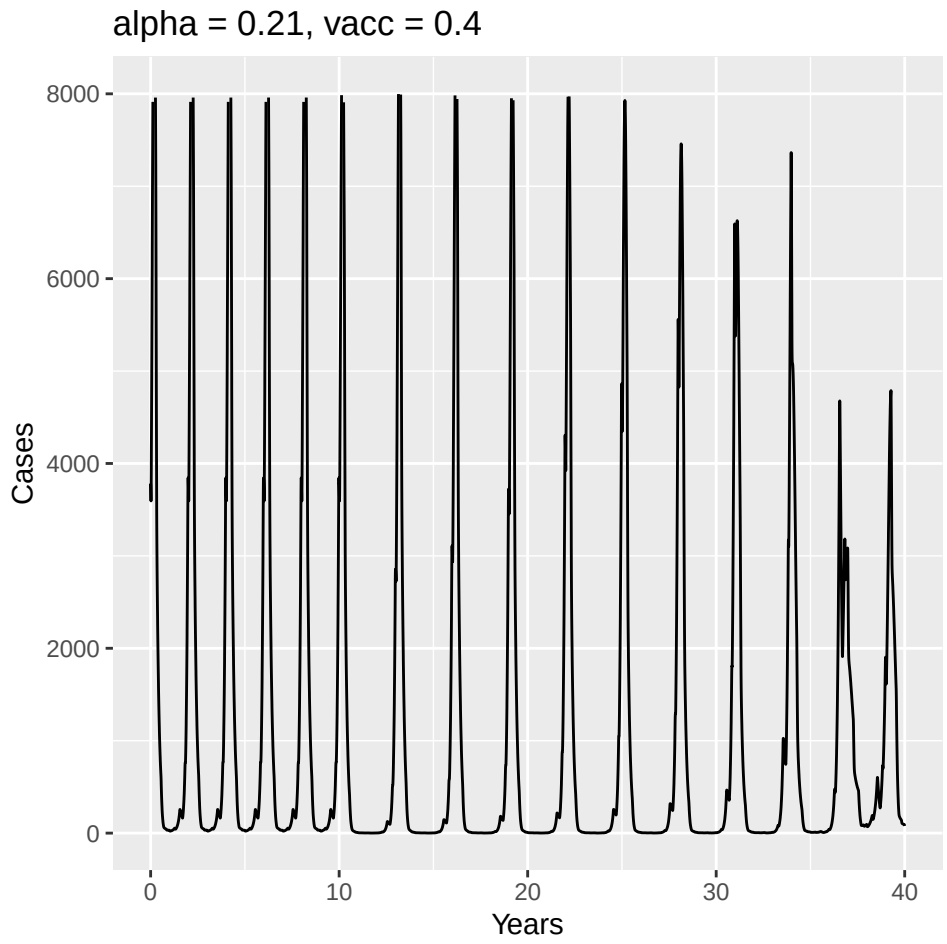
```
x<-det_SEIR_exp(3.3e6,12,8,5,20/(1000*364),0.21,50,10,30,0.0)

ggplot(x,aes(x=time,y=I*(1/0.4)*(5/7))) + geom_line() + xlab('Years') + ylab('Cases') +
  ggtitle("alpha = 0.21, vacc = 0.0") + ylim(0,8000)
```



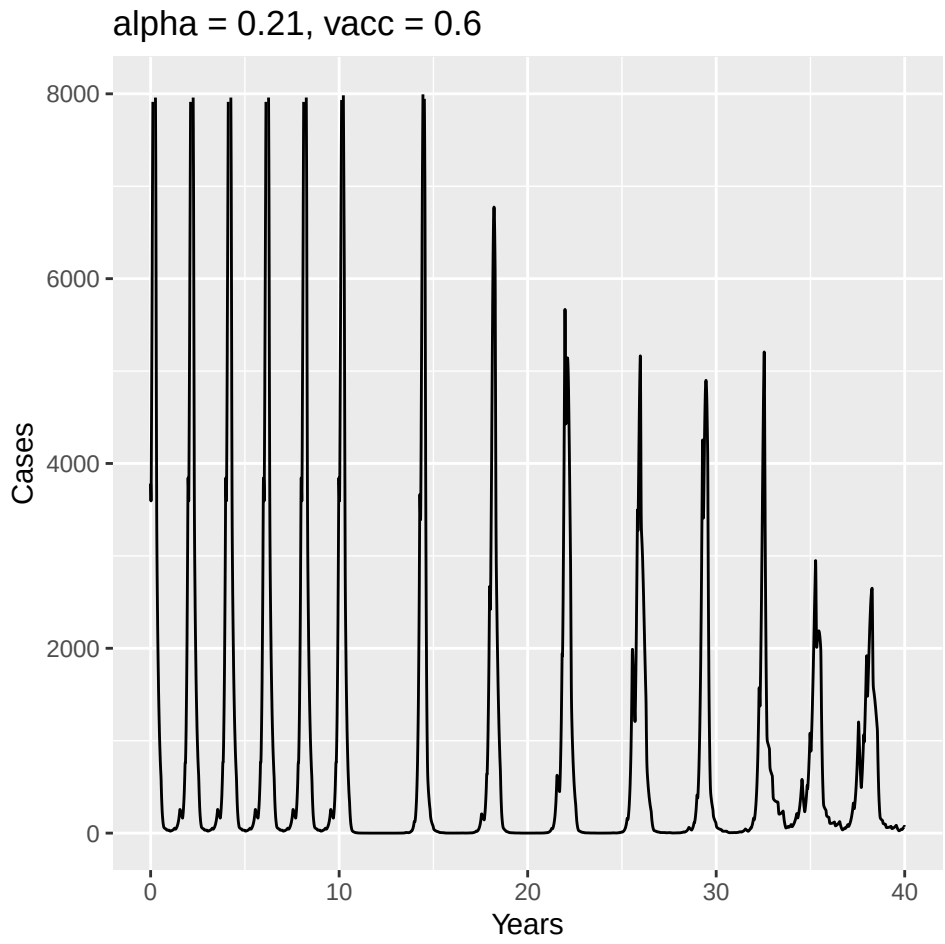

```
x<-det_SEIR_exp(3.3e6,12,8,5,20/(1000*364),0.21,50,10,30,0.3)

ggplot(x,aes(x=time,y=I*(1/0.4)*(5/7))) + geom_line() + xlab('Years') + ylab('Cases') +
  ggtitle("alpha = 0.21, vacc = 0.3") + ylim(0,8000)
```




```
x<-det_SEIR_exp(3.3e6,12,8,5,20/(1000*364),0.21,50,10,30,0.4)

ggplot(x,aes(x=time,y=I*(1/0.4)*(5/7))) + geom_line() + xlab('Years') + ylab('Cases') +
  ggtitle("alpha = 0.21, vacc = 0.4") + ylim(0,8000)
```




```
x<-det_SEIR_exp(3.3e6,12,8,5,20/(1000*364),0.21,50,10,30,0.6)

ggplot(x,aes(x=time,y=I*(1/0.4)*(5/7))) + geom_line() + xlab('Years') + ylab('Cases') +
  ggtitle("alpha = 0.21, vacc = 0.6") + ylim(0,8000)
```



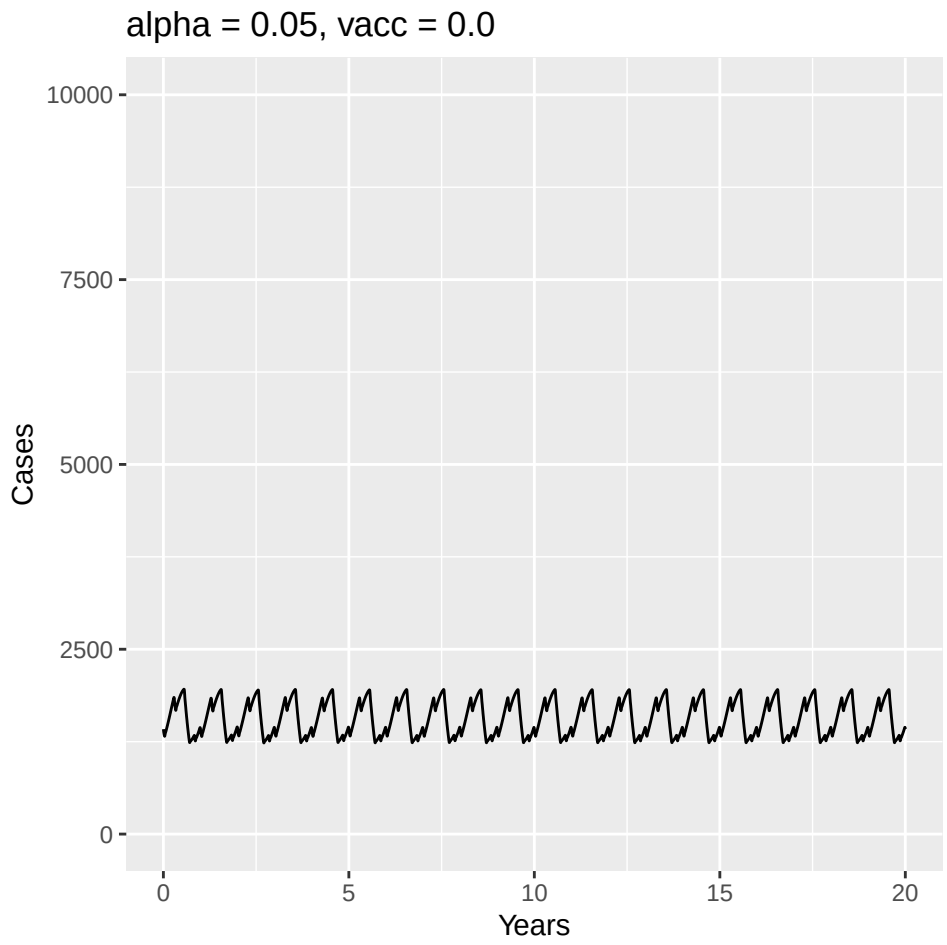
Return to P151

Gamma $SEIR$ with term-time forcing

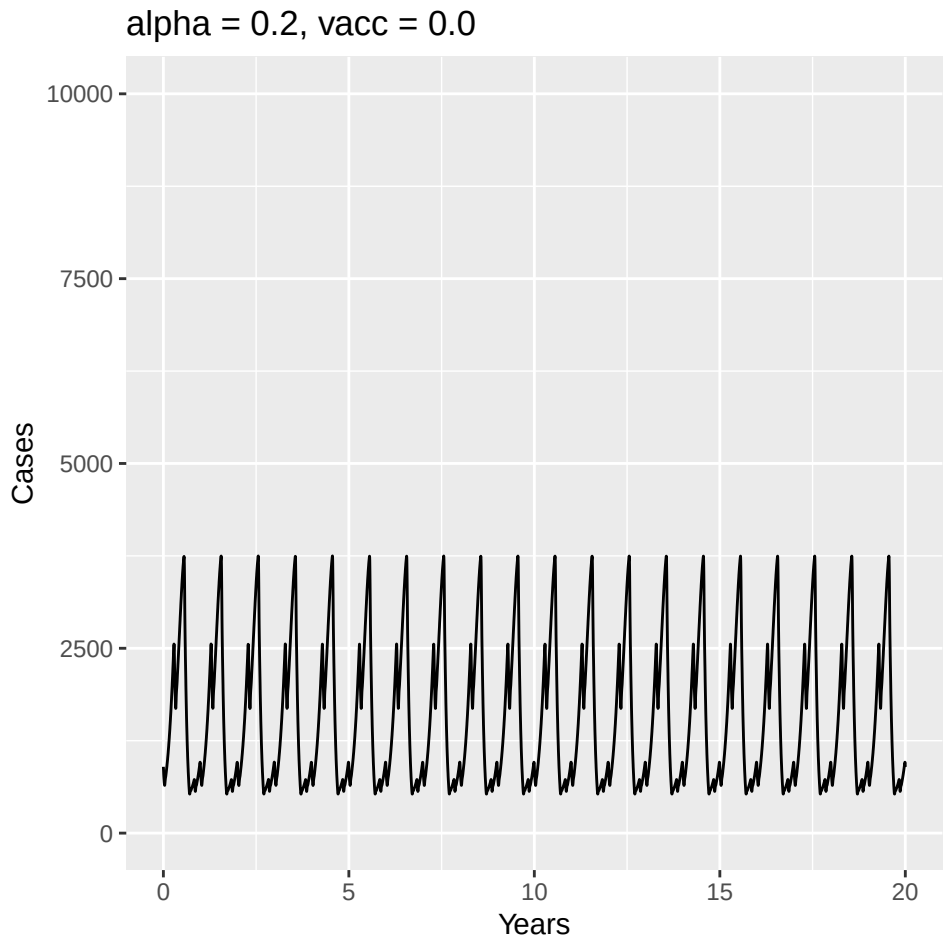
Finally, we present an implementation of the term-time forcing model with realistic (gamma) distributed latent and infectious periods. The Gamma-$SEIR$ model is much more sensitive to changes in the forcing amplitude α requiring lower amplitudes to generate the same qualitative dynamics as the (less biologically accurate) standard model with constant rates. These models are even more difficult to work with numerically and presented here purely for completeness and a cautionary note on the extent to which these model assumptions impact on the range of model parameters that will be consistent with real data. This sensitivity, and strong trade-offs between transmission rates, birth rates and distributional assumptions makes this type of model particular problematic (and therefore particularly interesting) to perform inference with.

```
SEIR_gamma <- function(t,y,theta) {

  x_i = integer(2);
  beta = theta[1];
  TE = theta[2];
  TI = theta[3];
  alpha = theta[4];
  mu    = theta[5]
  x_i[1] = theta[6];
  x_i[2] = theta[7];

  I_tot=0;
  N_tot=0;

  dy_dt = numeric(2+x_i[1]+x_i[2]);

  for(k in (1+x_i[1]+1):(1+x_i[1]+x_i[2])){I_tot = I_tot + y[k];}
  for(k in 1:(2+x_i[1]+x_i[2])){N_tot = N_tot + y[k];}

  terms = mk_terms(beta,alpha)
  lambda = terms[1 + t %% 364]*beta*I_tot/N_tot

  #Susceptibles
  dy_dt[1] = mu*N_tot - (lambda  + mu) * y[1];
  #First stage of Exposed (but not yet infectious)
  dy_dt[2] =  lambda * y[1]  - (x_i[1]/TE + mu) * y[2];

  #If shape parameter > 1 update internal exposed stages
  if(x_i[1]>1){
    for(k in 3:(1+x_i[1]))
    {dy_dt[k] = (x_i[1]/TE) * y[k-1] - (x_i[1]/TE + mu) * y[k];}
    }
  #First infectious stage
  dy_dt[(1+x_i[1]+1)] = (x_i[1]/TE)*y[(1+x_i[1])] - (x_i[2]/TI + mu)*y[(1+x_i[1]+1)];
  #If more than one infectious stage, run through internal stages
    if(x_i[2]>1)
    {
      for(k in (3+x_i[1]):(1+x_i[1]+x_i[2]))
      {dy_dt[k] = (x_i[2]/TI) * y[k-1] - (x_i[2]/TI + mu) * y[k];}
    }

    # Final absorbing recovered stage
    dy_dt[(1+x_i[1]+x_i[2]+1)] = (x_i[2]/TI)*y[(1+x_i[1]+x_i[2])] - mu*y[(1+x_i[1]+x_i[2]+1)];


  return(list(dy_dt))
}

det_SEIR_gamma <-function(N0,R0,TE,TI,shape_E,shape_I,mu,alpha,burnin,prevacc,postvacc,vacc)
{

  theta = numeric(7)

  # Use fixed points of exponential model to approximate initial conditions
  # (Need to run burn in period anyway)

  beta = R0/TI
  s0 = 1/R0
  e0 = (TI*mu*(mu+1/TI)/(beta/TE))*(R0-1)
  i0 = (mu/beta)*(R0-1)

  y0 = numeric(2+shape_E+shape_I);
```

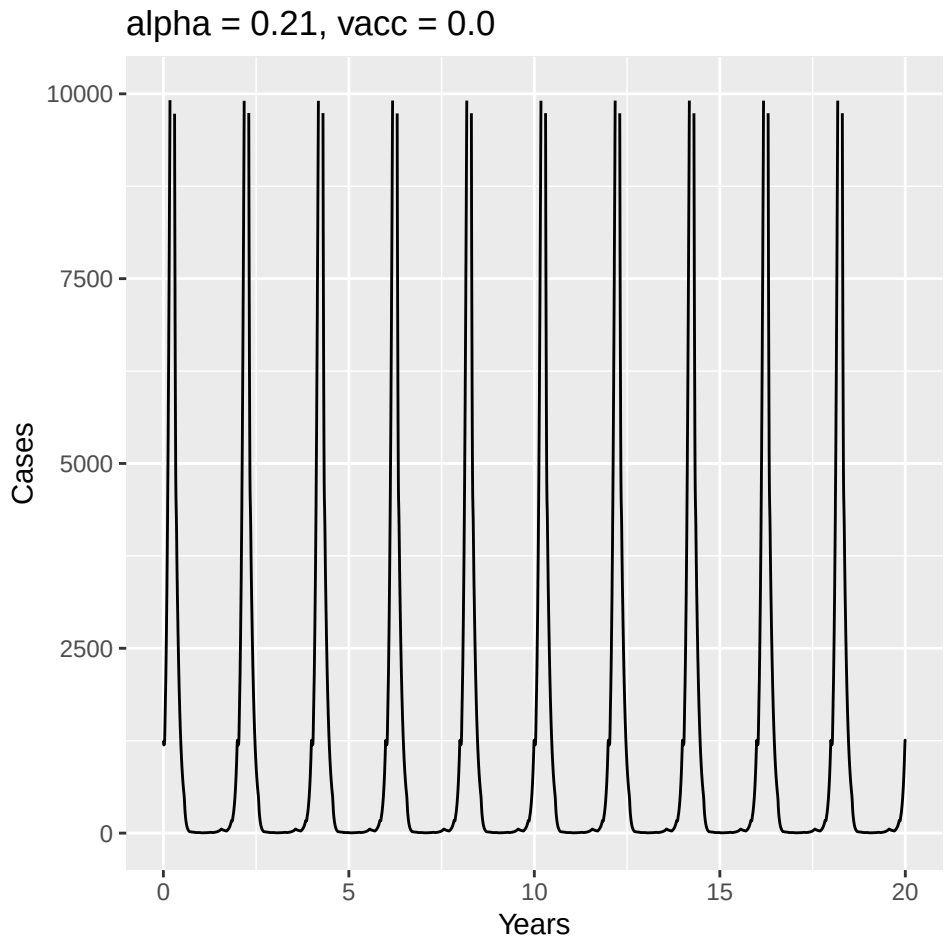
```
# The extra compartments in gamma-distributed models can cause memory problems
# Here we run the garbage collection function manually to try and head off any crashes

# gc()

x<-det_SEIR_gamma(3.3e6,12,8,5,8,5,20/(1000*364),0.05,50,10,10,0.0)

ggplot(x,aes(x=time,y=I*(1/0.4)*(5/7))) + geom_line() + xlab('Years') + ylab('Cases') +
  ggtitle("alpha = 0.05, vacc = 0.0") + ylim(0,10000)
```



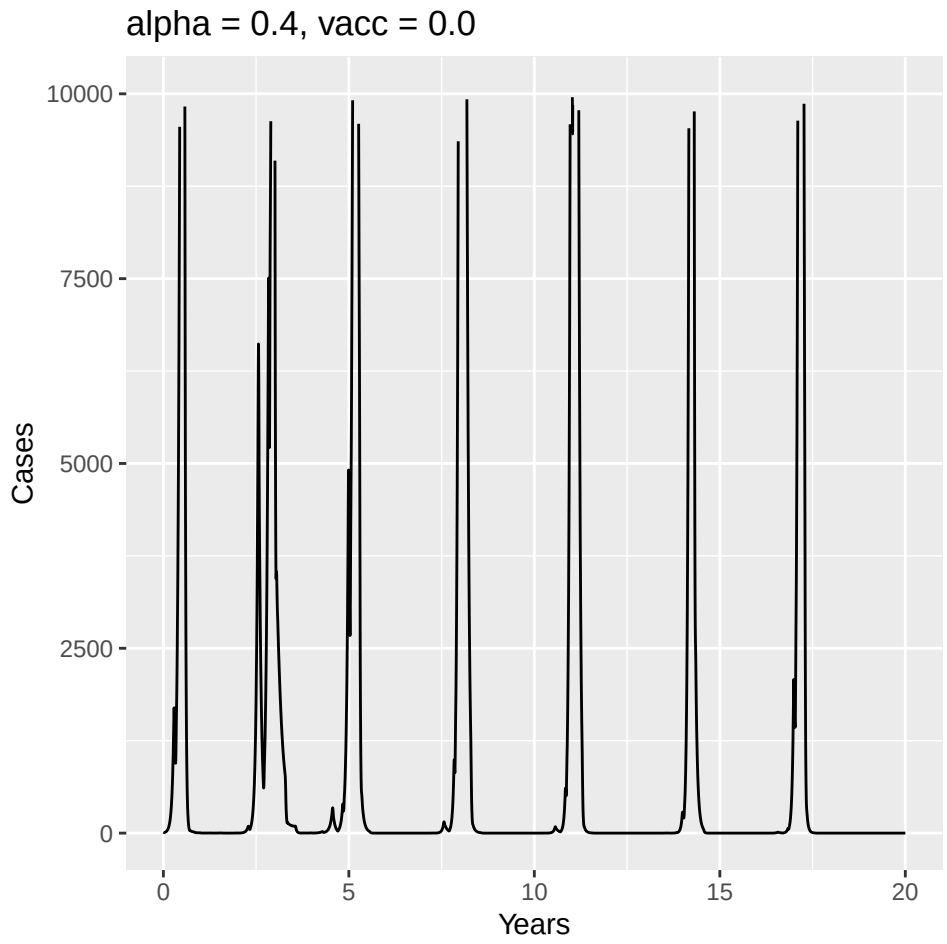

```
x<-det_SEIR_gamma(3.3e6,12,8,5,8,5,20/(1000*364),0.2,50,10,10,0.0)

# gc()

ggplot(x,aes(x=time,y=I*(1/0.4)*(5/7))) + geom_line() + xlab('Years') + ylab('Cases') +
  ggtitle("alpha = 0.2, vacc = 0.0") + ylim(0,10000)
```



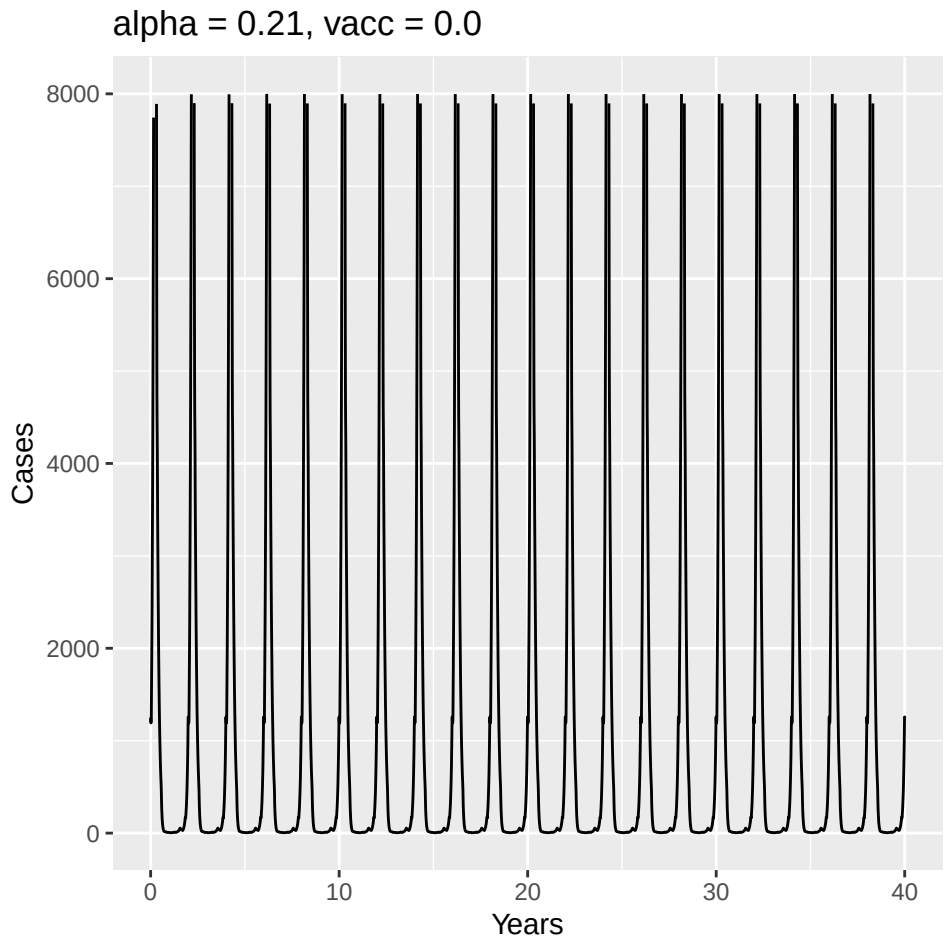

```
x<-det_SEIR_gamma(3.3e6,12,8,5,8,5,20/(1000*364),0.21,50,10,10,0.0)

# gc()

ggplot(x,aes(x=time,y=I*(1/0.4)*(5/7))) + geom_line() + xlab('Years') + ylab('Cases') +
  ggtitle("alpha = 0.21, vacc = 0.0") + ylim(0,10000)
```



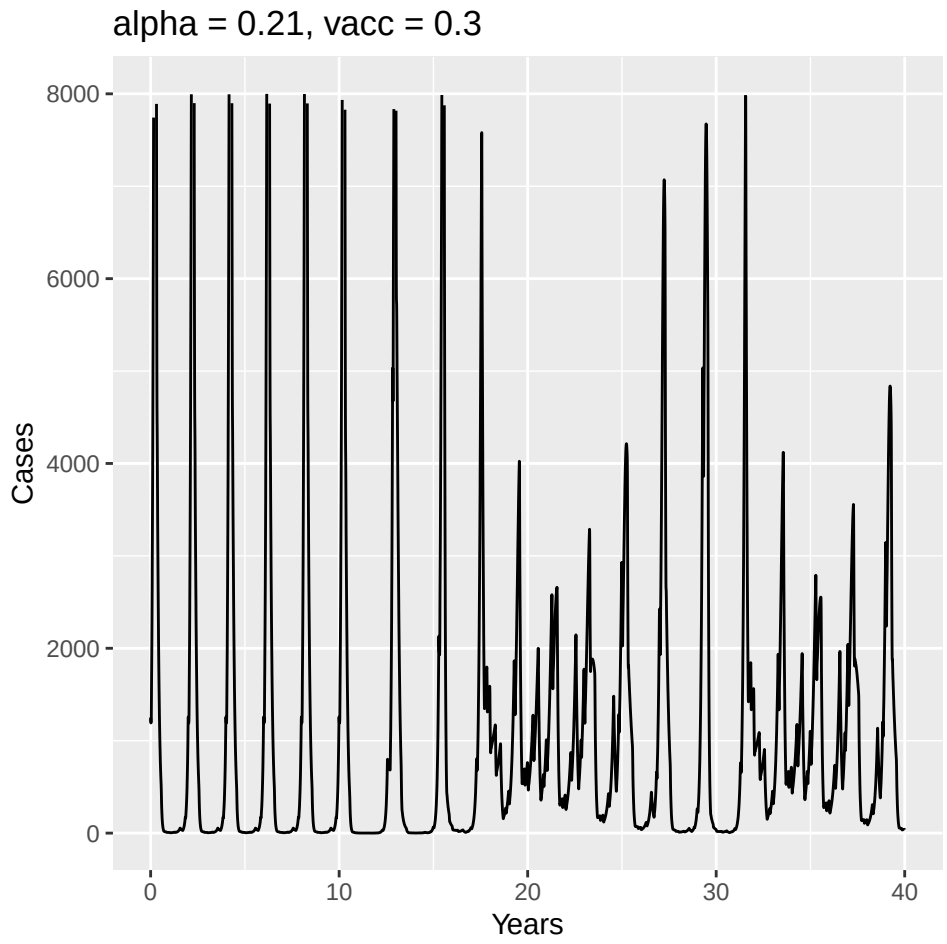

```
x<-det_SEIR_gamma(3.3e6,12,8,5,8,5,20/(1000*364),0.4,50,10,10,0.0)

# gc()

ggplot(x,aes(x=time,y=I*(1/0.4)*(5/7))) + geom_line() + xlab('Years') + ylab('Cases') +
  ggtitle("alpha = 0.4, vacc = 0.0") + ylim(0,10000)
```



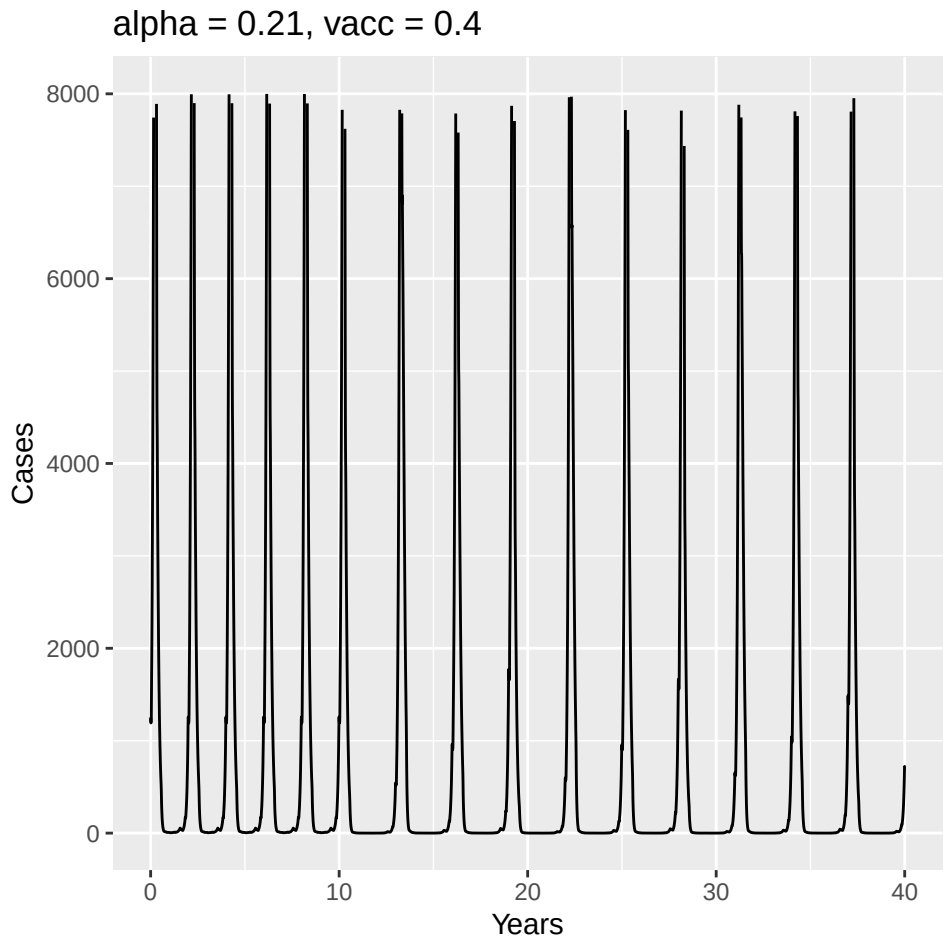

```
# gc()

x<-det_SEIR_gamma(3.3e6,12,8,5,8,5,20/(1000*364),0.21,50,10,30,0.0)

# gc()

ggplot(x,aes(x=time,y=I*(1/0.4)*(5/7))) + geom_line() + xlab('Years') + ylab('Cases') +
  ggtitle("alpha = 0.21, vacc = 0.0") + ylim(0,8000)
```



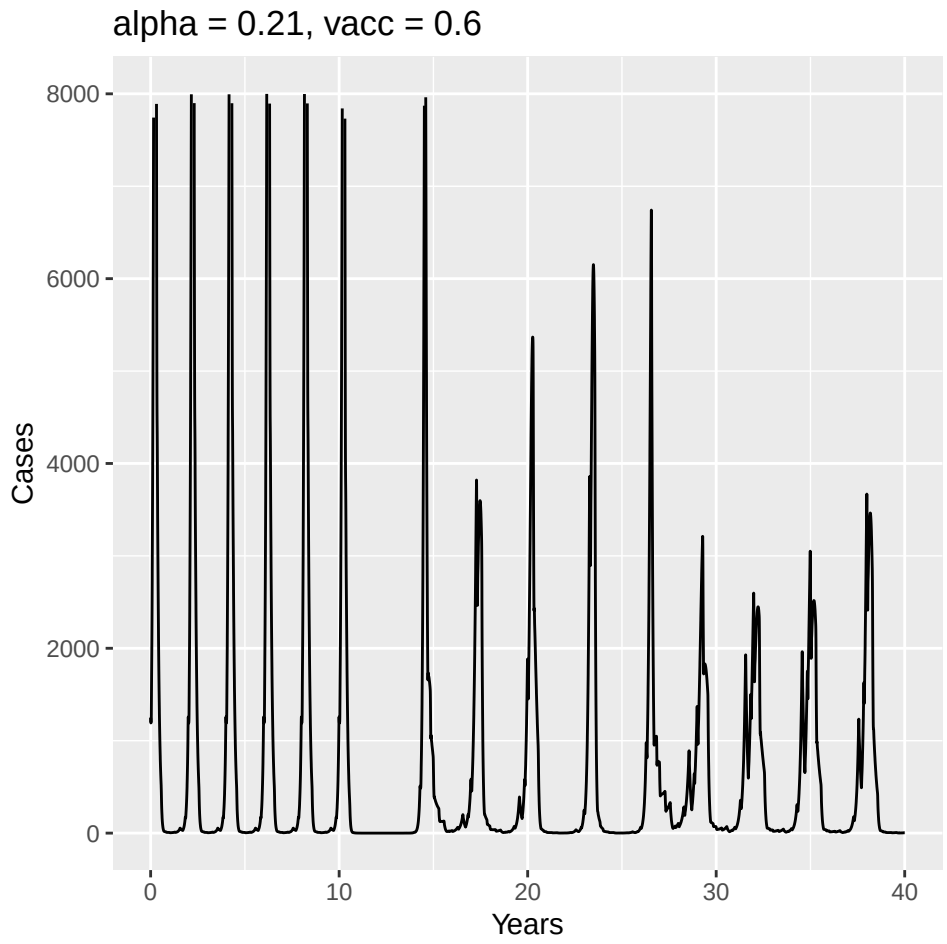

```
x<-det_SEIR_gamma(3.3e6,12,8,5,8,5,20/(1000*364),0.21,50,10,30,0.3)

# gc()

ggplot(x,aes(x=time,y=I*(1/0.4)*(5/7))) + geom_line() + xlab('Years') + ylab('Cases') +
  ggtitle("alpha = 0.21, vacc = 0.3") + ylim(0,8000)
```




```
x<-det_SEIR_gamma(3.3e6,12,8,5,8,5,20/(1000*364),0.21,50,10,30,0.4)

# gc()

ggplot(x,aes(x=time,y=I*(1/0.4)*(5/7))) + geom_line() + xlab('Years') + ylab('Cases') +
  ggtitle("alpha = 0.21, vacc = 0.4") + ylim(0,8000)
```




```
x<-det_SEIR_gamma(3.3e6,12,8,5,8,5,20/(1000*364),0.21,50,10,30,0.6)

# gc()

ggplot(x,aes(x=time,y=I*(1/0.4)*(5/7))) + geom_line() + xlab('Years') + ylab('Cases') +
  ggtitle("alpha = 0.21, vacc = 0.6") + ylim(0,8000)
```



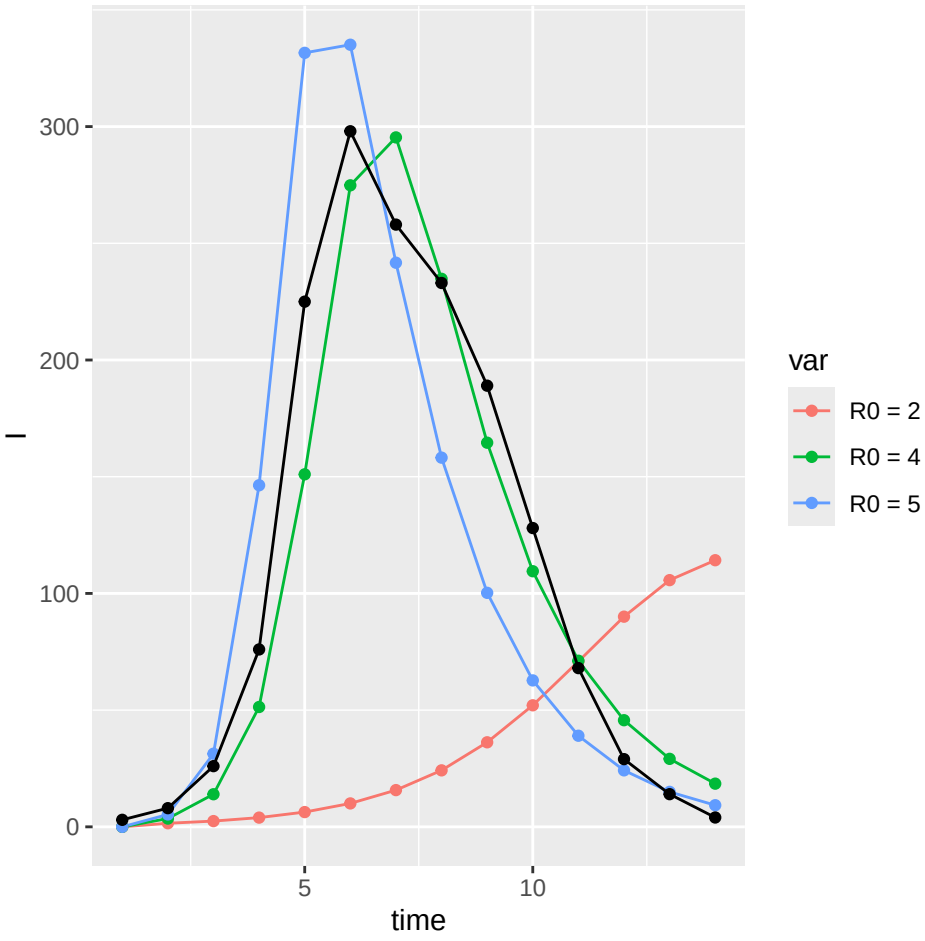
Return to P151

Deterministic model

For the standard $SEIR$ model with constant rates of progression through the exposed and infectious compartments an R_0 of ~ 4.0 gives a rough calibration to the observed data (black points and lines):

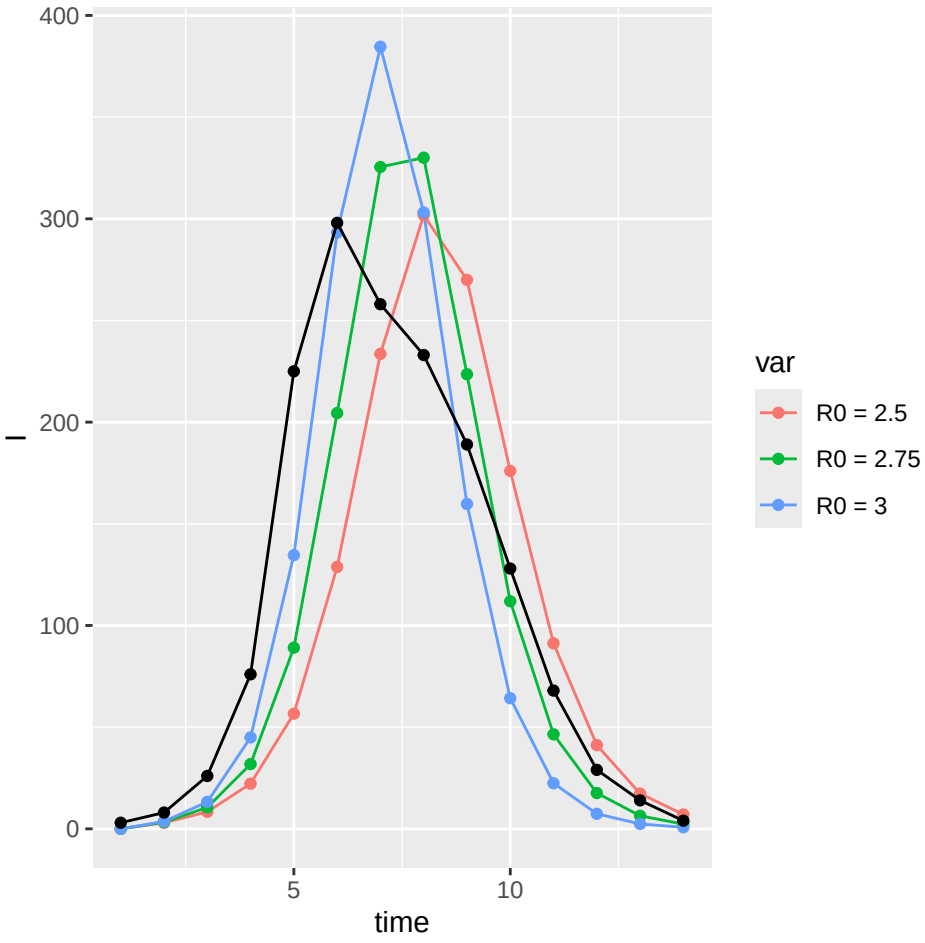
```
SEIR_gamma <- function(t,y,theta) {

  x_i = integer(2);
  beta = theta[1];
  TE = theta[2];
  TI = theta[3];
  x_i[1] = theta[4];
  x_i[2] = theta[5];

  I_tot=0;
  N_tot=0;

  dy_dt = numeric(2+x_i[1]+x_i[2]);

  for(k in (1+x_i[1]+1):(1+x_i[1]+x_i[2])){I_tot = I_tot + y[k];}
  for(k in 1:(2+x_i[1]+x_i[2])){N_tot = N_tot + y[k];}

  lambda = beta*I_tot/N_tot

  #Susceptibles
  dy_dt[1] =  - (lambda) * y[1];
  #First stage of Exposed (but not yet infectious)
  dy_dt[2] =  lambda * y[1]  - (x_i[1]/TE) * y[2];

  #If shape parameter > 1 update internal exposed stages
  if(x_i[1]>1){
    for(k in 3:(1+x_i[1]))
    {dy_dt[k] = (x_i[1]/TE) * y[k-1] - (x_i[1]/TE) * y[k];}
  }
  #First infectious stage
  dy_dt[(1+x_i[1]+1)] = (x_i[1]/TE)*y[(1+x_i[1])] - (x_i[2]/TI)*y[(1+x_i[1]+1)];
  #If more than one infectious stage, run through internal stages
  if(x_i[2]>1)
  {
    for(k in (3+x_i[1]):(1+x_i[1]+x_i[2]))
    {dy_dt[k] = (x_i[2]/TI) * y[k-1] - (x_i[2]/TI) * y[k];}
  }

  # Final absorbing recovered stage
  dy_dt[(1+x_i[1]+x_i[2]+1)] = (x_i[2]/TI)*y[(1+x_i[1]+x_i[2])];


  return(list(dy_dt))
}

det_SEIR <-function(R0,TE,TI,shape_E,shape_I,vacc)
{
  N0 = 763.0

  theta = numeric(5)

  beta = R0/TI
  s0 = (1-vacc)*(N0-1)
  e0 = 1
  i0 = 0
  r0 = vacc*(N0-1)

  y0 = numeric(2+shape_E+shape_I);
  y0[1] = s0;
  y0[2] = 1
  y0[2+shape_E+shape_I] = r0
```

```
# Standard SEIR model (exponential latent, infectious periods)

expI <- det_SEIR(2.0,0.04,2.0,1,1,0.0)
det_calibrate <- tibble(time=1:14,var='R0 = 2',I=expI[1:14])

expI <- det_SEIR(4.0,0.04,2.0,1,1,0.0)
det_calibrate <- det_calibrate %>% bind_rows(tibble(time=1:14,var='R0 = 4',I=expI[1:14]))

expI <- det_SEIR(5.0,0.04,2.0,1,1,0.0)
det_calibrate <- det_calibrate %>% bind_rows(tibble(time=1:14,var='R0 = 5',I=expI[1:14]))


ggplot(det_calibrate,aes(x=time,y=I,col=var)) + geom_line() + geom_point() +
  annotate('point',1:14,targetI[1:14]) + annotate('line',1:14,targetI[1:14])
```



This rough calibration does not hold up if we now vary the distributional assumption for the latent and infectious periods. The supplied code has implemented the $SEIR$ model with gamma distributed (strictly an Erlang distribution were the shape parameter is an integer) latent and infectious periods. If we vary the shape parameters for I and E we see that the peak prevalence and initial rate of exponential growth are very sensitive to changes in the distribution. Less dispersed distributions (i.e. higher shape parameters) have sharper epidemics with higher peak prevalence. The final size (and approximate value of R_0) on the other had are insensitive to these changes. Below we plot a set of three curves below for shape parameters = 10 illustrating that we now require a lower value of R_0 to (roughly) match the data. The fit is not as good as I deliberately picked the average infectious and latent periods to give a reasonable fit with the exponential model…

```
# Standard SEIR model (gamma 10 latent, infectious periods)

expI <- det_SEIR(2.5,0.04,2.0,10,10,0.0)
det_calibrate <- tibble(time=1:14,var='R0 = 2.5',I=expI[1:14])

expI <- det_SEIR(2.75,0.04,2.0,10,10,0.0)
det_calibrate <- det_calibrate %>% bind_rows(tibble(time=1:14,var='R0 = 2.75',I=expI[1:14]))

expI <- det_SEIR(3.0,0.04,2.0,10,10,0.0)
det_calibrate <- det_calibrate %>% bind_rows(tibble(time=1:14,var='R0 = 3',I=expI[1:14]))


ggplot(det_calibrate,aes(x=time,y=I,col=var)) + geom_line() + geom_point() +
  annotate('point',1:14,targetI[1:14]) + annotate('line',1:14,targetI[1:14])
```



In practice the latent and infectious period distributions are not identifiable purely from a single epidemic curve. As this very simple comparison demonstrates calibrating our model based on the wrong assumption can lead to a significant under or over estimate of R_0.

Return to P154

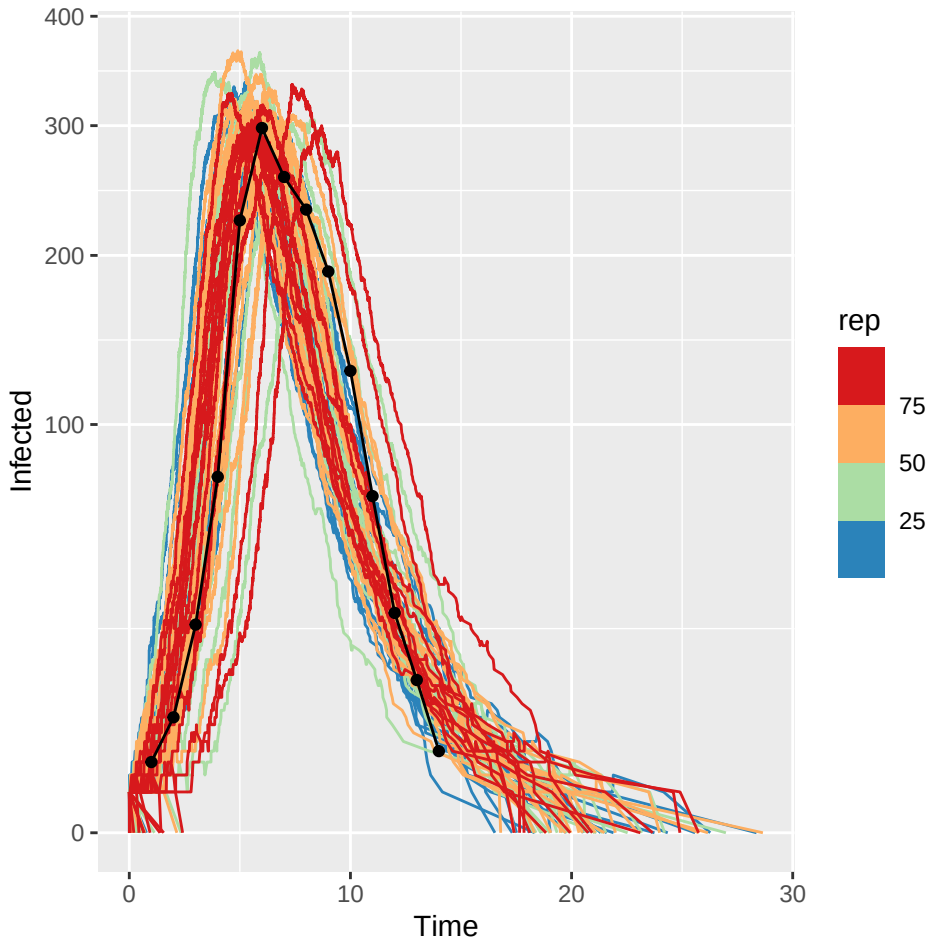
Stochastic model

The rough calibration we identified using the deterministic model mostly holds up for the stochastic model with replicates scattering around the observed numbers. Although the population is small, the transmission rate is

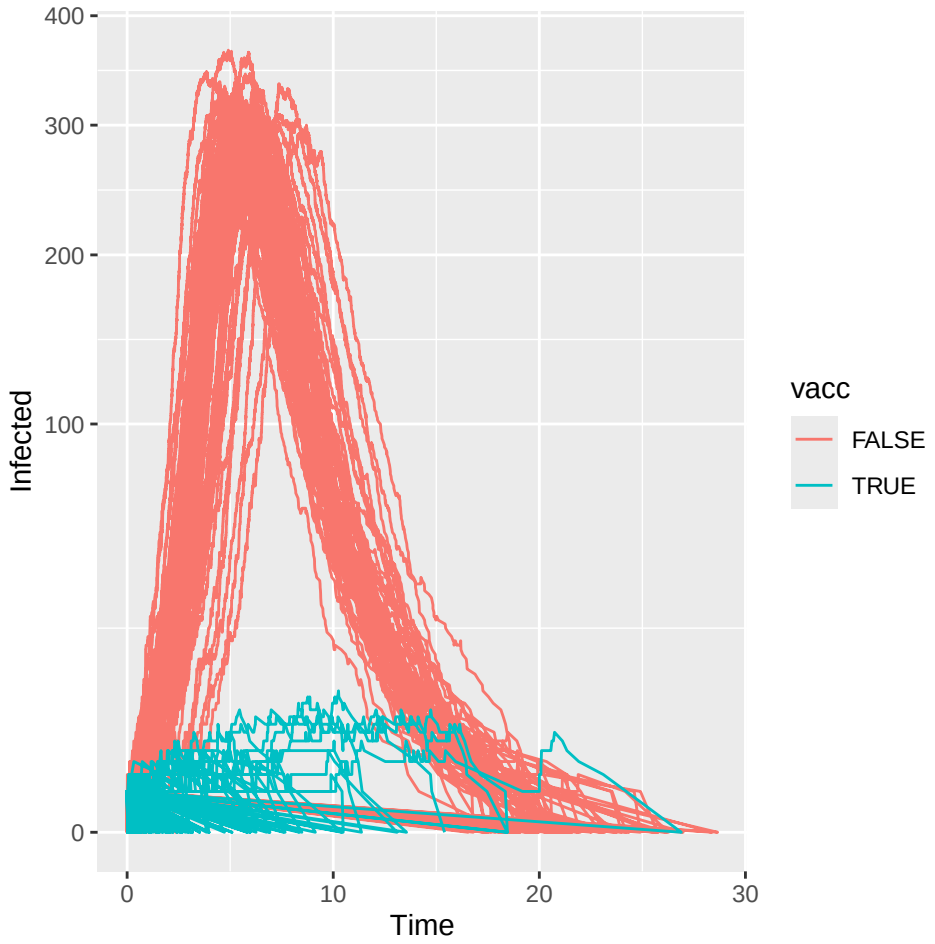
relatively high ($R_0 = 4$) so the deterministic model is a reasonable approximation for the average of the stochastic simulations. If the transmission rate was lower this would not necessarily be the case.

```
SEIR_rates <- function(state,p)
{
rate <- numeric(2)
# Probability of a transmission sum(state) = population size N
rate[1] <- p['beta']*state['S']*state['I']/sum(state)
# Probability of emergence from E to I
rate[2] <-p['sigma']*state['E']
# Probability of recovery from I to R
rate[3] <-p['gamma']*state['I']
return(rate)
}

SEIR_events <- function(state,rate)
{
    total_rate <- sum(rate)
    # Draw single random variate
    x <- runif(1)
    if(x*total_rate < rate[1])
    { # Transmission
      state['S'] = state['S'] - 1
      state['E'] = state['E'] + 1
    }else if(x*total_rate < sum(rate[1:2]))
    { # Emergence
      state['E'] = state['E'] - 1
      state['I'] = state['I'] + 1
    }else{
      # Recovery
      state['I'] = state['I'] - 1
      state['R'] = state['R'] + 1
    }
    return(state)
  }

stochastic_rep_SEIR <- function(R0,TE,TI,vacc,tmax)
{
n0 = 763.0
i0 = 1
# State Vector (One variable)
state <- c('S'=round((n0-1)*(1-vacc)),'E'=0,'I'=i0,'R'=round(vacc*(n0-i0)))
# Parameters
p = c('beta'=R0/TI,'sigma'=1/TE,'gamma'=1/TI)

# Time Variable
t <- 0.0;
# Save I and R only (I to compare to data, R to calculate final size)
# Could record all states but will be more costly in terms if memory use and run time
# so omitted here.
# Subtract off initial number vaccinated so that R counts total cumulative infections
output <- tibble(t=0,I=state['I'],R=state['R']-round(vacc*(n0-i0)))

# Calculate initial rate of events
rate_vector <- SEIR_rates(state,p)
total_rate = sum(rate_vector)
# Main Loop
repeat
{
  # Update time - sample time increment from from exponential distribution
  # with rate given by total rate
  t = t + rexp(1,total_rate)
  # Simulate the event using relative rates in rate_Vector
  state <-SEIR_events(state,rate_vector)
  # Output
```

```
out <- tibble()

for(i in 1:100) {
    out <- out %>% bind_rows(stochastic_rep_SEIR(4.0,0.04,2.0, 0.0, 30) %>% mutate(rep=i))
}

ggplot(out,aes(x=t,y=I,col=rep,group=rep)) + geom_path() + scale_y_sqrt() +
  annotate('point',1:14,targetI[1:14]) + annotate('line',1:14,targetI[1:14]) +
  scale_color_fermenter(palette = "Spectral") + xlab('Time') + ylab('Infected')
```




```
outvacc <- tibble()

for(i in 1:100) {
    outvacc <- outvacc %>% bind_rows(stochastic_rep_SEIR(4.0,0.04,2.0, 0.8, 30) %>% mutate(rep=i))
}

outagg <- (out %>% mutate(vacc=FALSE)) %>% bind_rows(outvacc %>% mutate(vacc=TRUE))

ggplot(outagg,
       aes(x=t,y=I,col=vacc)) + geom_path() + xlab('Time') + ylab('Infected') + scale_y_sqrt()
```

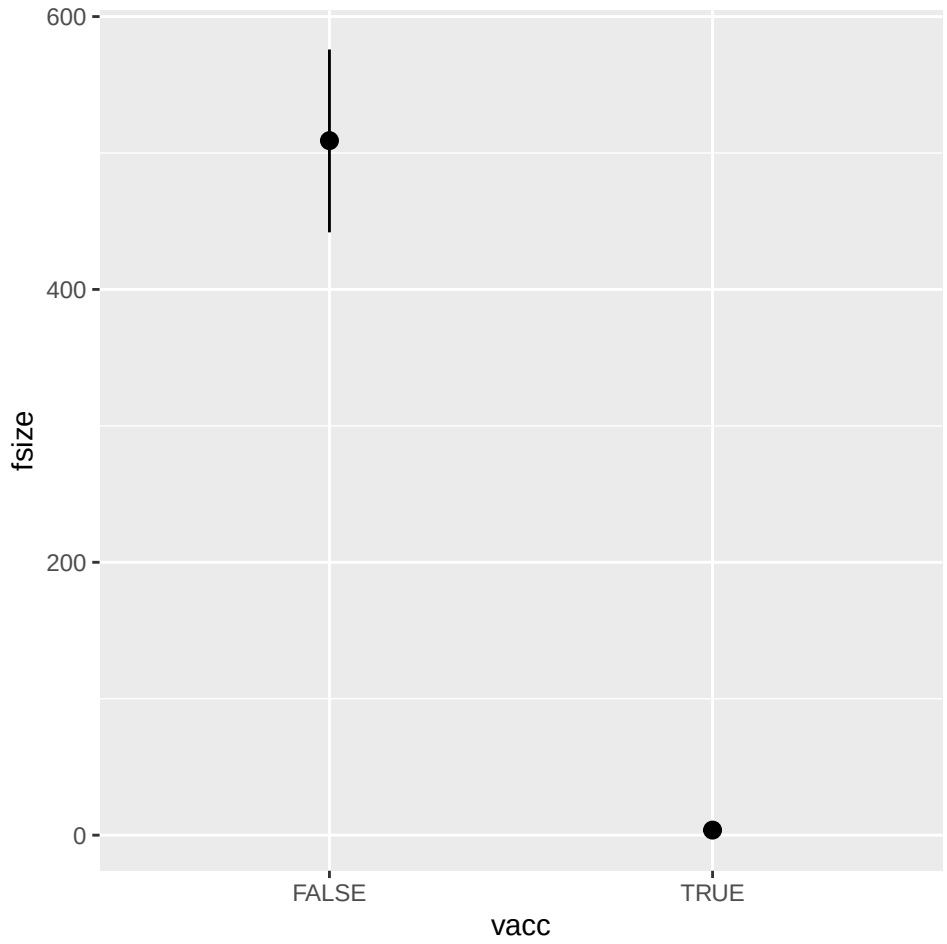


The main reason for considering a stochastic model for this question is then to quantify how vaccination changes the chances of seeing an outbreak at all. We can calculate this from our simulated scenarios by calculate the mean number of simulations that have more than one infection (mean(outbreak) in table below) or compare the final size distribution for the two scenarios.

```
outagg %>%
    group_by(rep,vacc) %>%
    summarise(outbreak=max(R)>1) %>%
    ungroup() %>%
    group_by(vacc) %>%
    summarise(mean(outbreak))
```

```
## # A tibble: 2 x 2
##   vacc  `mean(outbreak)`
##   <lgl>            <dbl>
## 1 FALSE             0.75
## 2 TRUE              0.36
```

```
ggplot(outagg %>%
        group_by(rep,vacc) %>%
        summarise(fsize=max(R)),
    aes(x=vacc,y=fsize)) +
        stat_summary(fun.data = "mean_cl_boot")
```



Return to P154