

UNIVERSITY OF LEEDS

PROJECT IN STATISTICS

MATH5004M

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# Epidemic Modelling

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# Abstract

The outbreak of an infectious disease can have a catastrophic effect on infrastructure, economies and most importantly human life. In such situations, modelling how an epidemic is expected to evolve can be an important tool. Applying mathematical and statistical models can help policy makers by illustrating the predicted effect that changes in procedure, or the introduction of new control measures can have.

By introducing and investigating the mathematical theory behind both deterministic and random models, this report aims to highlight the important part epidemic modelling can play in the real world.

# Contents

<b>1</b>	<b>Introduction</b>	<b>1</b>
<b>2</b>	<b>Defining an Epidemic</b>	<b>3</b>
2.1	Terminology . . . . .	3
2.2	The base reproduction ratio . . . . .	4
2.3	Different values for $r_0$ . . . . .	6
2.3.1	The case $r_0 < 1$ . . . . .	6
2.3.2	The case $r_0 = 1$ . . . . .	7
2.3.3	The case $r_0 > 1$ . . . . .	7
2.4	Vaccination . . . . .	9
<b>3</b>	<b>The Simple Deterministic Epidemic</b>	<b>10</b>
3.1	Introduction . . . . .	10
3.2	Modelling the simple epidemic deterministically . . . . .	11
3.3	Solving the simple epidemic differential equation . . . . .	11
3.3.1	The general solution . . . . .	11
3.3.2	An example . . . . .	12
3.4	The epidemic curve . . . . .	13
3.5	Time to full infection . . . . .	17
3.5.1	Comparison of $T$ and $T'$ . . . . .	18
3.6	The simple epidemic with interacting groups . . . . .	20
3.6.1	The general model . . . . .	20
3.6.2	Investigating the values for $c$ . . . . .	21
3.6.3	Adaptation to model vector transmission . . . . .	24
<b>4</b>	<b>The General Deterministic Epidemic</b>	<b>28</b>
4.1	Introduction . . . . .	28
4.2	Modelling the general epidemic . . . . .	28

4.3	A threshold for the general epidemic . . . . .	29
4.4	Investigating the behavior of the general epidemic . . . . .	29
4.4.1	Relating $x$ and $z$ . . . . .	29
4.4.2	Bounds on the evolution of an epidemic through time . . . . .	30
4.4.3	The Kermack-McKendrick approximation . . . . .	31
4.4.4	The Kendall parameterisation . . . . .	35
4.4.5	Numerical Solution . . . . .	42
<b>5</b>	<b>Introduction to Stochastic Modelling</b>	<b>45</b>
5.1	Stochastic processes . . . . .	45
5.2	Poisson processes . . . . .	46
5.3	Markov processes . . . . .	48
5.3.1	Birth and death processes . . . . .	49
<b>6</b>	<b>The Simple Stochastic Epidemic</b>	<b>51</b>
6.1	Modelling the simple epidemic stochastically . . . . .	51
6.2	Modelling the epidemic as a Poisson process . . . . .	52
6.2.1	Time to full infection . . . . .	52
6.3	Modelling the epidemic as a Markov process . . . . .	53
6.4	Time to full infection . . . . .	54
6.4.1	Numerical example of finding the time to full infection . . . . .	54
6.4.2	Finding the density for the numerical example . . . . .	55
6.4.3	Comparison of times to full infection . . . . .	56
6.5	Deriving Kolmogorov equations for the epidemic . . . . .	58
6.6	The Laplace transform . . . . .	59
6.6.1	Properties of the Laplace transform . . . . .	60
6.6.2	Applying the Laplace transform to the model . . . . .	60
6.6.3	Applying the Laplace transform to an example . . . . .	61
6.7	Probability generating functions . . . . .	63
6.7.1	Properties of probability generation functions . . . . .	64
6.7.2	Application to the state probabilities . . . . .	65
6.8	Numerical solution . . . . .	67
<b>7</b>	<b>The General Stochastic Epidemic</b>	<b>72</b>
7.1	Modelling the general epidemic stochastically . . . . .	72
7.2	Investigating the general stochastic epidemic . . . . .	73
7.3	Probability generating functions . . . . .	73

7.3.1	Bivariate probability generating functions . . . . .	73
7.3.2	Application to the general epidemic . . . . .	75
7.4	Numerical solution . . . . .	77
<b>8</b>	<b>Epidemic Modelling In Reality</b>	<b>83</b>
8.1	Measles . . . . .	83
8.1.1	The general deterministic model . . . . .	85
8.1.2	Vaccinating in the general deterministic model . . . . .	88
8.1.3	Increasing the removal rate parameter . . . . .	89
8.1.4	Adapting the model to include inhomogeneous mixing . . . . .	89
8.1.5	Adapting the model to include a latent period . . . . .	91
8.2	Disease spread in care homes . . . . .	94
8.2.1	Modelling an outbreak stochastically . . . . .	94
8.2.2	The influence of the removal rate parameter . . . . .	96
<b>9</b>	<b>Discussion</b>	<b>100</b>

# Chapter 1

## Introduction

Epidemic modelling is a key tool used by medical professionals in their fight to prevent and control infectious diseases across the world. Recent well publicised outbreaks such as swine flu in 2009, see The Independent (2010) article reporting on the cost of the outbreak, and the 2014 Ebola epidemic, see the BBC Ebola page (2015), have brought how these professionals deal with such situations under the global spotlight.

A wide range of methods are employed by epidemiologists and medical experts with the aim of managing such outbreaks. These include education, quarantining and vaccination and are discussed further by Webber (2005, p32). However, without being able to model how a disease has behaved in the past and may behave in the future, it is hard to quantify what effect these measures will have. This kind of disease modelling has a strong mathematical background, and is still a topic of mathematical research to the present day.

Drawing on a variety of books, journals and papers published over the last century, this report aims to provide an introduction into the methodology of modelling infectious diseases at a University MMath level, and to explore some of the interesting mathematical results that arise in the process.

Chapter 2 provides an overview of the terminology used in the report and an introduction to modelling using an overly simplistic method of looking at diseases.

This initial model is then developed into a dynamical system in Chapters 3 and 4, where an epidemic is modelled deterministically. This method uses techniques from statistics and applied mathematics to gain an insight into how a disease would behave if it was fully determined by its initial state.

Chapters 4 to 7 introduce stochastic processes, discussing and demonstrating how they can be used in the context of epidemic modelling. Modelling disease spread as a stochastic process provides the opportunity to introduce randomness into the model which cannot be

expressed deterministically. How the stochastic model compares to the deterministic model of the previous chapters is also investigated and discussed.

Throughout this report, mathematical results of interest that arise from the theory are investigated, and expanded upon if they are stated in literature. Finally, Chapter 8 implements some of the tools developed throughout the report, exploring how the models and theory developed in previous chapters can be applied to real world data.

# Chapter 2

## Defining an Epidemic

Before beginning to model and investigate epidemics, an overview of the disease processes and terms used in relation to epidemic modelling is needed.

### 2.1 Terminology

Consider a disease spreading through members of a population. Disease can be spread through a variety of different methods including direct physical contact, dust particles carrying the disease and vector-borne transmission. Vector-borne transmission is the case where an intermediary such as a mosquito or rat transfers the disease between two population members. In most cases examined here, only direct contact between population members will be considered as a possible method of transmission. ‘Direct contact’ is defined as when two population members are close enough for a disease to be transmitted between them, be that through the air or by direct contact of skin, saliva or blood.

In general, each member of a population can be in one of the following three states:

- susceptible to the disease,  $X$ ,
- infected with the disease,  $Y$ ,
- removed from the disease after the infection period,  $Z$ .

A population member is classed as removed when they are not, and cannot in the future, be infected with the disease. This can occur in cases of immunity, vaccination or death. The number of susceptibles, infectives and removals in each state are denoted by  $x, y$  and  $z$  respectively. In a homogeneous population it is assumed that any specific member has the same chance of



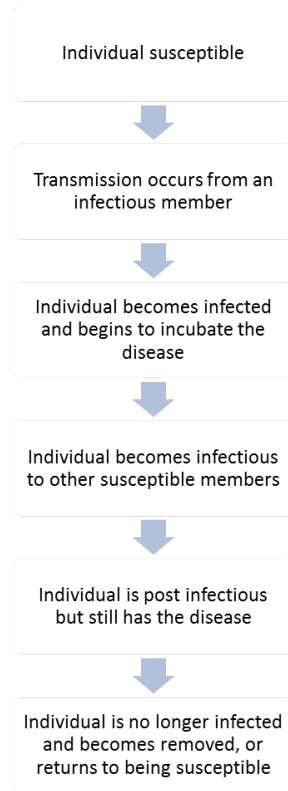


Figure 2.1: The general infection process.

having a direct contact with any other individual and hence each member has equal chance of catching the disease.

The infection rate parameter per individual per unit time is denoted by  $\beta$ , which describes the rate at which the disease is spread by contacts between susceptible and infective members. In a population with number of susceptibles equal to  $x$ ,  $\beta$  is defined to be such that one infected individual will transmit disease to  $\beta x$  susceptibles in one unit of time. The infection rate parameter is clearly greater than zero for any situation where disease is being spread.

Different diseases behave in different ways over time, but as a general reference point, a susceptible member of a population will follow the disease experience shown in 2.1.

## 2.2 The base reproduction ratio

An epidemic is defined by Gerstman (2013) to be a ‘term applied to any health-related condition that occurs in excess of normal expectancy’. However to define this mathematically is slightly more complicated.

One basic way to do this is to use the base reproduction ratio,  $r_0$ , as discussed by Brauer and Castillo-Chavez (2013). This constant is defined as the average number of susceptible members of a homogeneous population that an infective person will pass the disease onto in their infective period. For example consider Figure 2.2. This shows one example of a disease spreading in a closed population beginning with one infective member and six susceptible members.

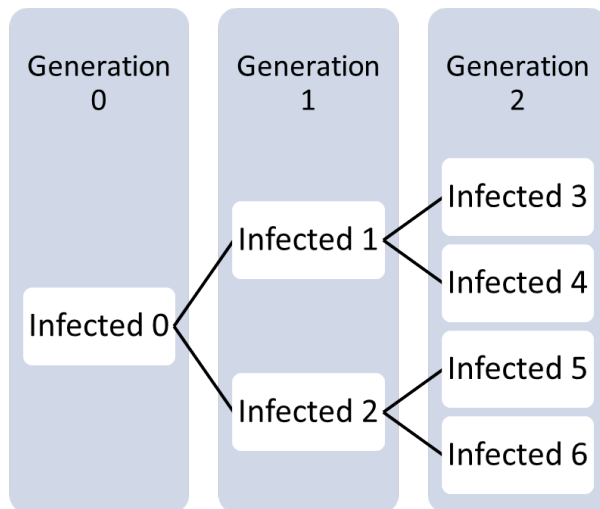


Figure 2.2: A tree diagram showing one example of how infection can spread through a population.

In this example, the incubation and post infectious illness periods for all members both have length 0, and each member becomes removed once they have completed their infected period. In this case ‘infected’ and ‘infectious’ can be used interchangeably, but note this is not always the case. It has been assumed that during their infective period, each infective member passes the illness on to exactly  $r_0 = 2$  susceptible members.

For simplicity it has also been assumed that the infective period of these two newly infected members starts immediately once the previous generation has ended, with all infectious periods being equal to one generation.

In the example it is clear to see that for  $r_0 = 2$ , the disease would spread through the whole population of susceptibles quickly, infecting  $2^n$  new susceptibles at generation  $n$ . Furthermore the total number of infected members over time forms a geometric sum. By generation  $n$  there will have been a total of

$$1 + 2 + 2^2 + \dots + 2^n = \frac{1 - 2^{n+1}}{1 - 2} = 2^{n+1} - 1$$

population members infected.

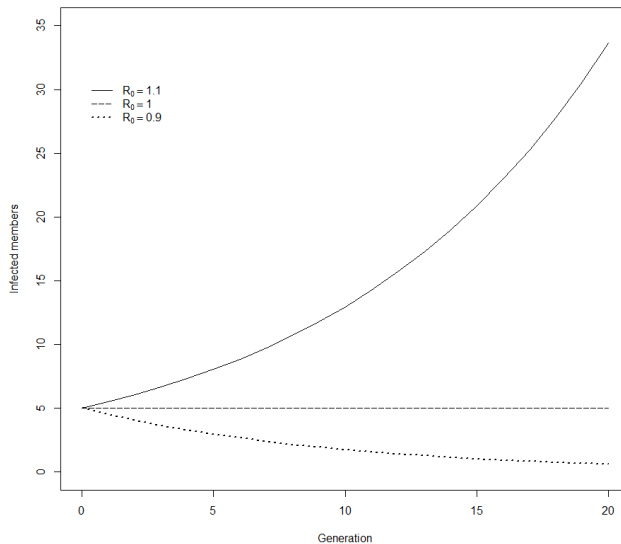


Figure 2.3: Infected members at each generation with  $y_0 = 5$ .

More generally, starting with  $y_0$  infectives and base reproduction ratio  $r_0$ , the disease would infect  $y_0(r_0)^n$  at each generation, causing the the geometric sum representing the total people infected by the disease up to generation  $n$  to become

$$y_0 + y_0 r_0 + y_0 r_0^2 + \dots + y_0 r_0^n = y_0 \left( \frac{1 - r_0^{n+1}}{1 - r_0} \right). \quad (2.1)$$

## 2.3 Different values for $r_0$

Equation (2.1) can now be used to investigate how disease spreads for different values of the base reproduction ratio. Examples of each of the three cases,  $r_0 < 1$ ,  $r_0 = 1$  and  $r_0 > 1$  are illustrated up to generation 20 in Figure 2.3. This shows the number of infectives at each generation. These three cases assume that at generation 0 there are  $y_0 = 5$  infective members within a large population susceptible to catching the disease, with the continued assumption from Section 2.2 that each infective period lasts one generation.

### 2.3.1 The case $r_0 < 1$

When  $r_0 < 1$ , equation (2.1) converges to  $\frac{y_0}{1 - r_0}$  as  $n \rightarrow \infty$ , where  $y_0$  is the initial number of infectives at generation 0. Hence an arbitrary population of susceptibles of size  $x$  would not all become infected providing  $x > \frac{y_0}{1 - r_0}$ . This suggests the disease would eventually die out without any medical intervention. This makes intuitive sense as if each infected individual on average

passed the disease on to less than one susceptible member in their infective period, the disease would become less common with each passing generation, and would eventually disappear from the population.

This is shown in Figure 2.3, plotted using the R code

```
tt=c(0:20) #time steps of 1 between 0 and 20
#new infections at each generation
I0=5
r0=1.1 #setting r0=1.1
y = I0*(r0^tt)
plot(tt, y, type="l", xlab="Generation",
ylab="Infected members",ylim=c(0,35), lty=1)
r0=0.9 #setting r0=0.9
y2= I0*(r0^tt)
points(tt,y2, type="l",lty=3,lwd=2)
r0=1 #setting r0=1
y3= I0*(r0^tt)
points(tt,y3, type="l",lty=5)
legend(0,31,c(expression(R[0]==1.1),expression(R[0]==1),
expression(R[0]==0.9)),lty=c(1,5,3),bty="n",lwd=c(1,1,2))
```

The dotted line representing the number of infected people when  $r_0 = 0.9$  is tending towards zero, implying the disease is infecting less people with each passing generation. By using the infinite geometric sum it can be seen that on average, a total of  $\frac{5}{1 - 0.9} = 50$  members would become infected over the lifetime of this disease. This is illustrated in Figure 2.4, where the plotted line seems to tend towards 50 as expected.

### 2.3.2 The case $r_0 = 1$

When  $r_0 = 1$ , on average, each infected member passes the disease onto one susceptible member before becoming removed, so the disease infects the same amount of people at each generation. For the line representing  $r_0 = 1$  in Figure 2.3, it is clear that the level of infected members of the population stays constant at the original level of five infectives. This phenomenon, where a disease is continually prevalent in a certain region, is called an endemic; see Merrill (2010). Endemics of infectious disease are quite common and can be specific to groups such as towns or age ranges. One example of an endemic is influenza, as it follows a seasonal pattern which is relatively consistent from year to year with most infections in winter.

### 2.3.3 The case $r_0 > 1$

When  $r_0 > 1$  an infective member, on average, passes the disease on to more than one person in their infective period. This means, as shown in Figure 2.3, that the number of infectives

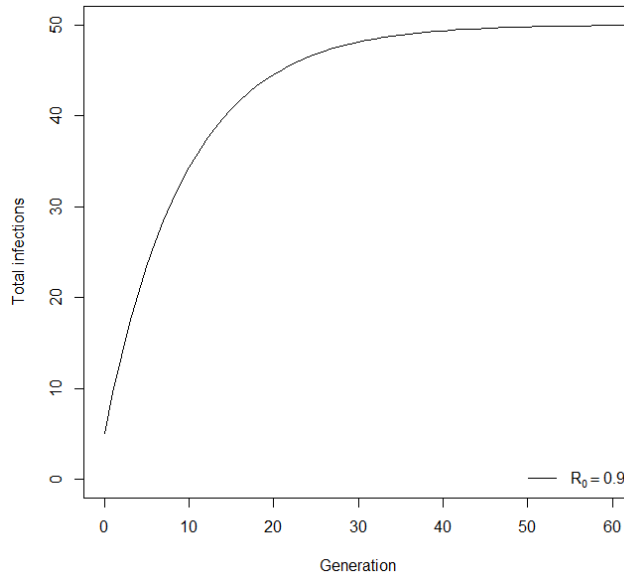


Figure 2.4: Total infections over the course of the disease for  $r_0 = 0.9$ .

Infection	$r_0$
Diphtheria	6-7
Measles	12-18
Mumps	4-7
Rubella	6-7
Smallpox	5-7
Polio	5-7

grows exponentially and is called an epidemic. This is the type of behaviour investigated in the following chapters.

Fine (1993) gives estimates for the base reproduction ratio of different diseases. They are given in the table above, but note these are just estimates and the value of  $r_0$  for the same disease in different populations or places can vary.

The impact of an epidemic is determined by these base reproduction ratios and the consequences of catching the specific disease. A highly infectious disease that does little to no damage to the infectious members before recovery would provoke little government reaction compared to a disease with a much smaller value of  $r_0$  that kills every member that becomes infected.

## 2.4 Vaccination

In an ideal world, scientists, epidemiologists and medical professionals could make use of  $r_0$  to control and stop an epidemic disease. Rather than vaccinating every population member to eradicate an infectious disease in the state of epidemic, vaccinating a suitable proportion of population members to cause the value of  $r_0$  to fall below unity would be sufficient to cause the disease to die out, as discussed in Section 2.3.1. Taking the vaccination time as  $t = 0$ , to give an initial susceptible population of size  $x_0$ , this equates to vaccinating a proportion,  $\alpha$  of susceptibles, such that

$$\alpha > 1 - \frac{1}{r_0}.$$

This gives a new base reproduction ratio,  $r_0^{new}$ , since the population of susceptibles would now be smaller, and equal to  $(1 - \alpha)x_0$ .

This gives

$$r_0^{new} = (1 - \alpha)r_0 < \frac{r_0}{r_0} = 1,$$

meaning the disease would die out regardless of the number of infectives  $y_0$ . For arbitrarily quick disease die out time, the vaccinators would need only to choose  $\alpha$  sufficiently close to one. This would cause the value of  $r_0^{new}$  to fall towards zero, which would mean no spread of the disease whatsoever. In practical terms, taking  $\alpha = 1$  equates to vaccinating the whole population which, assuming a fully effective vaccine, would certainly stop the spread of disease.

Consider a fully susceptible population with initial size  $x_0$  with one infective member. If the initial infective individual makes  $\beta x_0$  transmissions of the disease per unit time, and if the infectious period lasts  $t$  time units,  $r_0$  can be calculated as

$$r_0 = \beta x_0 t.$$

This method of calculating the vaccination proportion makes use of the assumptions mentioned throughout this chapter. These assumptions coupled with the fact that details such as  $x_0$ ,  $t$ ,  $\beta$  and hence  $r_0$  are hard to gauge in the fast moving nature of real world epidemics make this way of thinking about epidemic spread difficult to put into practice.

Heffernan *et al.* (2005) discuss the usefulness of  $r_0$ , noting that while in some simple cases  $r_0$  can be used when investigating a disease in real time, it is not until after a disease has run its course that  $r_0$  can be calculated with a great deal of certainty. Instead  $r_0 = 1$  is usually used as a threshold value, with further investigation into an epidemic required when  $r_0 > 1$ . In the following chapters more succinct ways of describing how a disease spreads will be investigated by using more involved mathematical models.

# Chapter 3

## The Simple Deterministic Epidemic

### 3.1 Introduction

In reality, diseases do not last exactly one generation for every person before removal, they are much more fluid than this, so the basic introductory investigation in Chapter 2 is not an ideal way to model an epidemic. When considering epidemic populations on a large scale, the law of large numbers implies that statistical variation due to the randomness of disease transmission has much less impact on the overall result. In such cases the spread of an epidemic can be approximated by deterministic methods, which model the disease flow between groups much like a dynamical system in applied mathematics.

The simplest of deterministic models, discussed by Bailey (1957, p20) and Daley and Gani (1999, p20), contains population members in one of two states, susceptible and infective only, and does not consider removals from the population. Since each member can only transition from susceptible to infective, it seems eventually the whole population would become infected.

Let the real valued continuous variable  $x(t)$  denote the number of susceptibles from a population of size  $n$  at time  $t$ , and let the real valued continuous variable  $y(t)$  represent the number of infectives from the same population at that time. For a closed population with no births or deaths over the inspected time period, it is the case that

$$x(t) + y(t) = n, \tag{3.1}$$

and once more it is assumed that this closed population mixes homogeneously and that the infection and infective period are equal.

Even though this is a simple model of an epidemic, it could be an acceptable approximation for some diseases in reality; for example, highly infectious but non-serious diseases where infectives will remain in contact with susceptibles for the course of the disease, such as the common cold considered over a period of a few days.

## 3.2 Modelling the simple epidemic deterministically

Recall from Section 2.1 that an infected individual will infect  $\beta x$  susceptibles in one unit time. Thus the rate per unit time at which  $y$  infectives will spread the disease through the population is

$$\frac{dy}{dt} = \beta xy = \beta(n - y)y. \quad (3.2)$$

It is intuitive to think that the rate of spread of disease is proportional to both the number of infective and susceptible members of a population. If there are many susceptible members in a population it will be easier for disease to spread, and similarly there will be more disease transmissions if there are more infective members to pass the disease on. Since this is a closed population, differentiating both sides of equation (3.1) with respect to  $t$  gives the result

$$\frac{dy}{dt} = -\frac{dx}{dt}.$$

That is, the rate that people are becoming infected is equal to the rate at which people are leaving the susceptible class. This makes intuitive sense as there are only two classes which are disjoint and contain the whole population between them.

## 3.3 Solving the simple epidemic differential equation

### 3.3.1 The general solution

Equation (3.2) can now be rewritten as

$$\frac{dy}{y(n - y)} = \beta dt$$

which, after splitting up the left hand side by partial fractions gives

$$\frac{1}{n} \left( \frac{1}{y} + \frac{1}{n - y} \right) dy = \beta dt$$

which is a differential equation that can be solved by separation of variables. Thus, the equation becomes

$$\int \left( \frac{1}{y} + \frac{1}{n - y} \right) dy = \int \beta n dt.$$

Integrating both sides gives

$$\ln(y) - \ln(n - y) = \beta nt + c$$

where  $c$  is a constant of integration. This simplifies to

$$\ln \left( \frac{y}{n - y} \right) = \beta nt + c.$$



Taking exponentials of both sides and writing  $A = e^c$  gives

$$\frac{y}{n-y} = e^{\beta nt+c} = Ae^{\beta nt},$$

which implies

$$y(t) = \frac{nAe^{\beta nt}}{1 + Ae^{\beta nt}}. \quad (3.3)$$

In the most general case an epidemic starts with  $y_0 \geq 0$  infectives at  $t = 0$ . Substituting this initial condition into equation (3.3) gives

$$y_0 = \frac{nA}{1 + A},$$

and after rearrangement for  $A$  becomes

$$A = \frac{y_0}{n - y_0}.$$

Finally, the value for  $A$  can be substituted back into equation (3.3) to give the exact solution;

$$\begin{aligned} y(t) &= \frac{\frac{ny_0}{n-y_0}e^{\beta nt}}{1 + \frac{y_0}{n-y_0}e^{\beta nt}} \\ &= \frac{ny_0e^{\beta nt}}{(n-y_0) + y_0e^{\beta nt}}. \end{aligned}$$

After multiplying the numerator and denominator through by  $e^{-\beta nt}$ , this finally becomes

$$y(t) = \frac{ny_0}{y_0 + (n-y_0)e^{-\beta nt}}. \quad (3.4)$$

### 3.3.2 An example

As an example, consider a population of size  $n = 100$  with infection rate parameter  $\beta = 0.01$ , and five original infectives,  $y_0 = 5$ . The value of  $\beta$  is chosen to be  $\frac{1}{n} = 0.01$  as in Daley and Gani (1999, p22) so that  $\beta n = 1$ . This gives the solution

$$y(t) = \frac{500}{5 + 95e^{-t}}$$

which is illustrated by the solid line in Figure 3.1. Figure 3.1 also shows the behaviour of  $y(t)$  for  $\beta = 0.02$  and  $\beta = 0.005$  to show the effect of changing the infection rate parameter.

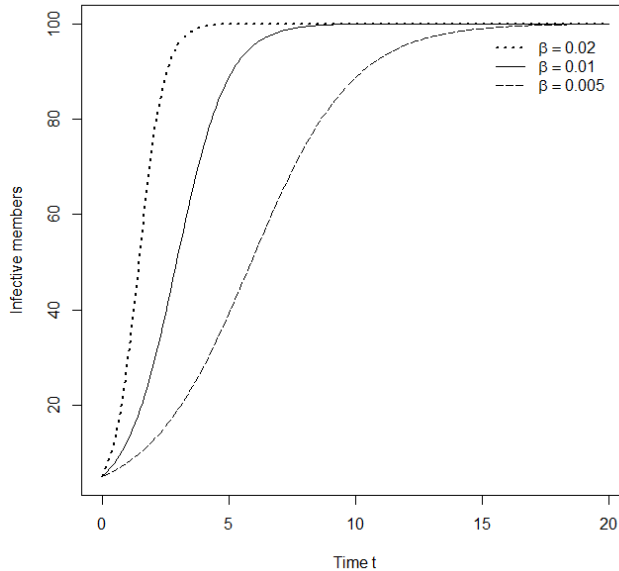


Figure 3.1: The simple epidemic model showing  $y(t)$  for different values of  $\beta$ , with  $n = 100$  and  $y_0 = 5$ .

In a population of only infectives and susceptibles, it would be expected that eventually, all members would become infective. This can be seen in Figure 3.1; regardless of the value of  $\beta$ , the number of infectives is tending towards the population limit of 100. This can be seen mathematically by taking the limit as  $t$  tends to infinity in equation (3.4), giving

$$\lim_{t \rightarrow \infty} y(t) = \lim_{t \rightarrow \infty} \frac{ny_0}{y_0 + (n - y_0)e^{-\beta nt}} = n$$

since

$$\lim_{t \rightarrow \infty} e^{-\beta nt} = 0.$$

Hence this example gives  $y \rightarrow 100$ .

In the simple epidemic solution,  $\beta$  controls how quickly the total number of infectives converges to the population limit, with larger values of  $\beta$  meaning more infectious contacts per unit time, causing the total number of infectives to rise more quickly.

### 3.4 The epidemic curve

Sometimes epidemiologists are more interested in the plot of  $\frac{dy}{dt}$  against  $t$ , as the rate of occurrence of new cases better describes an epidemical situation rather than the total number of infected people over the lifetime of the disease given by  $y(t)$ . This plot of  $\frac{dy}{dt}$  is called the epidemic curve and can be found by substituting the solution for  $y(t)$  back into equation (3.2).

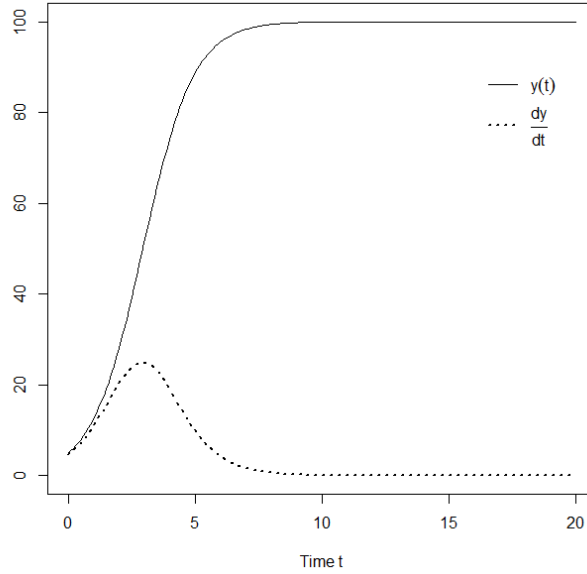


Figure 3.2: Plots of the number of infectives  $y(t)$  and the epidemic curve  $\frac{dy}{dt}$  plotted against time  $t$ , with  $n = 100$ ,  $y_0 = 5$  and  $\beta = 0.01$ .

The epidemic curve is given by

$$\begin{aligned}
 \frac{dy}{dt} &= \beta(n - y)y \\
 &= \beta \left( n - \frac{ny_0}{y_0 + (n - y_0)e^{-\beta nt}} \right) \left( \frac{ny_0}{y_0 + (n - y_0)e^{-\beta nt}} \right) \\
 &= \beta \left( \frac{ny_0 + n(n - y_0)e^{-\beta nt} - ny_0}{y_0 + (n - y_0)e^{-\beta nt}} \right) \left( \frac{ny_0}{y_0 + (n - y_0)e^{-\beta nt}} \right) \\
 &= \frac{\beta y_0 n^2 (n - y_0) e^{-\beta nt}}{(y_0 + (n - y_0) e^{-\beta nt})^2}.
 \end{aligned} \tag{3.5}$$

The evolution of the epidemic curve through time is shown by the dotted line in Figure 3.2.

One point of interest is the time  $t = t^*$ , when the rate of new infectives is maximal, which is the turning point of the epidemic curve in Figure 3.2. This found by setting the time differential of the epidemic curve equation equal to zero at  $t = t^*$  and solving for  $t^*$ , that is solving

$$\frac{d}{dt} \left( \frac{dy}{dt} \right) = 0$$

for  $t = t^*$ . For ease of notation when performing this calculation, the constant terms can be

written as  $a = \beta y_0 n^2 (n - y_0)$  and  $b = n - y_0$ . This gives

$$\frac{dy}{dt} = \frac{\beta y_0 n^2 (n - y_0) e^{-\beta n t}}{(y_0 + (n - y_0) e^{-\beta n t})^2} = \frac{a e^{-\beta n t}}{(y_0 + b e^{-\beta n t})^2},$$

which can be written as

$$\frac{dy}{dt} = a e^{-\beta n t} (y_0 + b e^{-\beta n t})^{-2}.$$

Differentiating using the product rule gives

$$\frac{d^2 y}{dt^2} = -\beta a n e^{-\beta n t} (y_0 + b e^{-\beta n t})^{-2} + 2\beta a b n e^{-2\beta n t} (y_0 + b e^{-\beta n t})^{-3}.$$

Setting this equal to zero at  $t = t^*$  and multiplying through by  $(y_0 + b e^{-\beta n t})^3$  gives

$$\begin{aligned} 0 &= 2\beta a b n e^{-2\beta n t^*} - \beta a n e^{-\beta n t^*} (y_0 + b e^{-\beta n t^*}) \\ &= \beta a n e^{-\beta n t^*} (2b e^{-\beta n t^*} - y_0 - b e^{-\beta n t^*}) \\ &= \beta a n e^{-\beta n t^*} (b e^{-\beta n t^*} - y_0). \end{aligned} \tag{3.6}$$

Notice that neither the infection rate parameter  $\beta$ , the initial number of infectives  $y_0$ , nor the population size  $n$  would equal 0 in an epidemic of any interest. Hence equation (3.6) gives

$$\begin{aligned} e^{-\beta n t^*} &= \frac{y_0}{b} \\ &= \frac{y_0}{n - y_0} \end{aligned}$$

by noting that  $b = n - y_0$ . Finally taking logarithms of both sides and dividing through by  $-\beta n$  gives

$$t^* = -\frac{1}{\beta n} \ln \left( \frac{y_0}{n - y_0} \right) = \frac{1}{\beta n} \ln \left( \frac{n - y_0}{y_0} \right) \tag{3.7}$$

since  $-\ln(a) = \ln(\frac{1}{a})$ . Figure 3.3 shows the maximum of the epidemic curve for the example in Section 3.3.2.

For this example, equation (3.7) gives

$$t^* = \frac{1}{n} \ln \left( \frac{n - y_0}{y_0} \right) = 2.944$$

which corresponds to the vertical line in Figure 3.3.

The maximum value of the epidemic curve can be found by substituting the value for  $t^*$  back into equation (3.5). Since

$$e^{-\beta n t^*} = e^{-\beta n \left( \frac{1}{\beta n} \ln \left( \frac{n - y_0}{y_0} \right) \right)} = e^{-\ln \left( \frac{n - y_0}{y_0} \right)} = e^{\ln \left( \frac{y_0}{n - y_0} \right)} = \frac{y_0}{n - y_0},$$

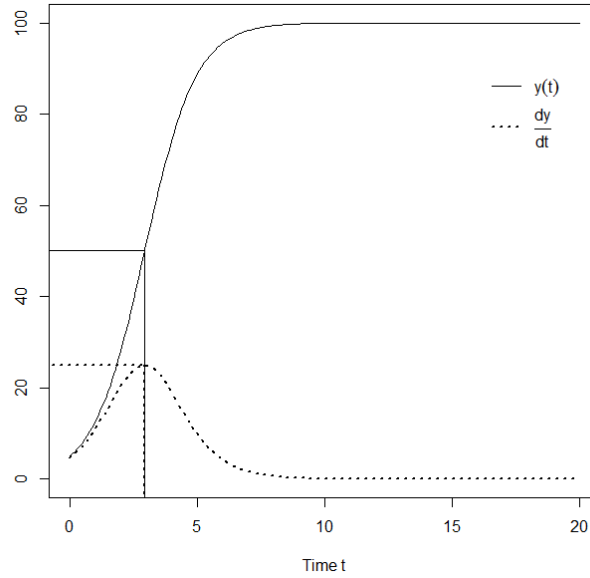


Figure 3.3: Illustrating the maximum of the epidemic curve at  $t^* = 2.944$  on the plots of  $y(t)$  and  $\frac{dy}{dt}$  against time, with  $n = 100$ ,  $\beta = 0.01$  and  $y_0 = 5$ .

at  $t = t^*$ , equation (3.5) reduces to

$$\left. \frac{dy}{dt} \right|_{t=t^*} = \frac{\beta y_0 n^2 (n - y_0) e^{-\beta n t^*}}{(y_0 + (n - y_0) e^{-\beta n t^*})^2} = \frac{\beta y_0^2 n^2}{(2y_0)^2} = \frac{\beta n^2}{4}.$$

In the example,  $\frac{\beta n^2}{4} = 25$ , which corresponds to the point where the dotted horizontal line meets the  $y$  axis in Figure 3.3, and is the maximum rate per unit time at which susceptibles population members are becoming infective.

Substituting  $t = t^*$  in the original differential equation solution given in equation (3.4), gives

$$y(t^*) = \frac{n y_0}{y_0 + (n - y_0) e^{-\beta n t^*}} = \frac{n y_0}{2 y_0} = \frac{n}{2}. \quad (3.8)$$

This implies the rate of change of infectious members is maximal at the time when half of the population is infectious and half is susceptible. This reinforces the point made in Section 3.1 that the rate of change of infectives is proportional to both the number of infectives and the number of susceptibles. In the example used in this chapter,  $\frac{1}{2}n = 50$ . Therefore when there are fifty infectious and susceptible members present in the population, the rate of change of infectives is maximised at twenty five per unit time.

### 3.5 Time to full infection

Section 3.3.2 shows that the whole population only becomes fully infected as  $t \rightarrow \infty$ . For the simple epidemic in reality, no further action can occur once all susceptibles become infected, however when modelling this deterministically the population is not fully infected unless  $t \rightarrow \infty$ .

Daley and Gani (1999, p21) suggest defining the ‘end’ of an epidemic to be the time  $T' = \inf\{t : y(t) > n - 1\}$ . That is, the first time the number of infectives is within one of the total population value. In this report the time to full infection,  $T$ , will be defined as  $\inf\{t : y(t) \geq n - \frac{1}{2}\}$ , so that the total number of infectious members, rounded to the nearest whole number, is equal to  $n$ .

The number of infectives  $y(t)$  found in Section 3.4 is a positive increasing function of time  $t$ , since for  $\Delta t > 0$ ,

$$\begin{aligned} y(t + \Delta t) &= \frac{ny_0}{y_0 + (n - y_0)e^{-\beta n(t + \Delta t)}} \\ &= \frac{ny_0}{y_0 + (n - y_0)e^{-\beta nt}e^{-\beta n\Delta t}} \\ &> \frac{ny_0}{y_0 + (n - y_0)e^{-\beta nt}} \\ &= y(t) \end{aligned}$$

as  $\beta$ ,  $n$  and  $\Delta t$  are all greater than zero, and therefore  $e^{-\beta n\Delta t} < 1$ . Equivalently, the fact that  $y(t)$  is an increasing function of time  $t$  can also be deduced directly by the fact that  $\frac{dy}{dt} > 0$  for all  $t$ . Therefore  $T$ , the smallest time  $t$  such that  $y(t) \geq n - \frac{1}{2}$  can be found by solving the equation

$$y(T) = \frac{ny_0}{y_0 + (n - y_0)e^{-\beta nT}} = n - \frac{1}{2}.$$

Multiplying both sides by  $\frac{y_0 + (n - y_0)e^{-\beta nT}}{n - \frac{1}{2}}$ , and subtracting  $y_0$  gives

$$\frac{ny_0}{n - \frac{1}{2}} - y_0 = (n - y_0)e^{-\beta nT}$$

so that

$$\frac{y_0}{2(n - \frac{1}{2})} = (n - y_0)e^{-\beta nT}.$$

Finally, rearranging for  $T$  gives

$$T = \frac{1}{\beta n} \ln \left( \frac{2(n - \frac{1}{2})(n - y_0)}{y_0} \right).$$

For example, if five people with influenza entered a closed hotel complex of 95 susceptible people, with  $\beta = 0.01$  and the unit of time being days, it would take

$$T = \frac{1}{\beta n} \ln \left( \frac{2(n - \frac{1}{2})(n - y_0)}{y_0} \right) = 8.24$$

days for every member of the hotel to be infected using the definition of the end of an epidemic given in this section and assuming homogeneous mixing between the whole population.

### 3.5.1 Comparison of $T$ and $T'$

By exactly the same working, but using the Daley and Gani (1999, p21) definition of the end time  $T'$  of an epidemic, the time to full infection is found to be

$$T' = \frac{1}{\beta n} \ln \left( \frac{(n - 1)(n - y_0)}{y_0} \right).$$

Substituting in the example values  $\beta = 0.01$ ,  $n = 100$  and  $y_0 = 5$ , gives

$$T' = \frac{1}{\beta n} \ln \left( \frac{(n - 1)(n - y_0)}{y_0} \right) = 7.54,$$

a quicker time to full infection.

This is illustrated in Figure 3.4, which shows the value of  $T$  and  $T'$  for changing  $n$ . The plots imply that, with  $\beta = 0.01$  and  $y_0 = 5$ , the  $T'$  definition of the end of an epidemic will lead to a shorter epidemic than the definition used in this report.

Note that for small population sizes, the time to full infection becomes negative. Intuitively for  $T$ , this should occur when  $n - \frac{1}{2} < y_0$  as for  $n - \frac{1}{2} = y_0$ , the epidemic is immediately defined as finished, so  $T = 0$ . This can be proved by conditioning  $T \geq 0$ . This implies

$$\frac{1}{\beta n} \ln \left( \frac{2(n - \frac{1}{2})(n - y_0)}{y_0} \right) \geq 0,$$

which means

$$\frac{2(n - \frac{1}{2})(n - y_0)}{y_0} \geq 1$$

and so

$$(n - \frac{1}{2})(n - y_0) \geq \frac{y_0}{2}.$$

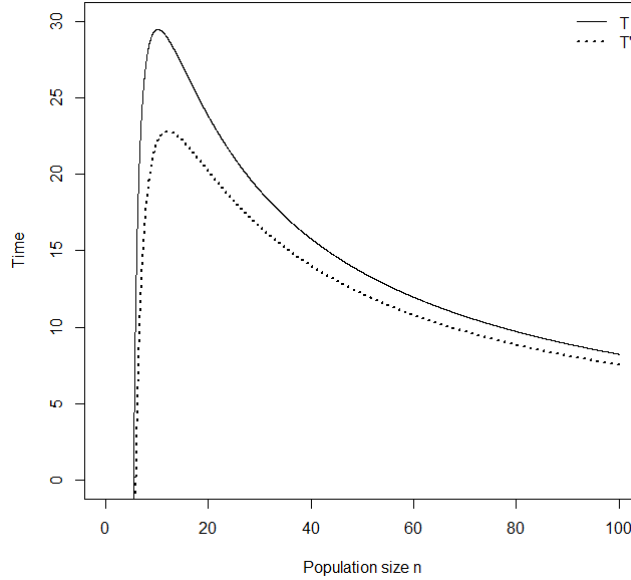


Figure 3.4: Plotting the values of  $T$  and  $T'$  for changing  $n$ , with  $\beta = 0.01$  and  $y_0 = 5$ .

After rearrangement this leaves the result

$$n - \frac{1}{2} \geq y_0,$$

with  $T = 0$  in the case of equality.

By exactly the same reasoning it can be shown that conditioning  $T' \geq 0$  gives  $n - 1 \geq y_0$ . As shown in Figure 3.4,  $T = 0$  for a slightly smaller population size than  $T'$ , which is to be expected as  $T'$  defines an epidemic to be finished for a slightly smaller number of infectives than  $T$ .

Through all values of  $n$ ,  $T > T'$  is always the case providing  $\beta$  and  $y_0$  are preserved between the two definitions since

$$\begin{aligned} T - T' &= \frac{1}{\beta n} \left[ \ln \left( \frac{2(n - \frac{1}{2})(n - y_0)}{y_0} \right) - \ln \left( \frac{(n - 1)(n - y_0)}{y_0} \right) \right] \\ &= \frac{1}{\beta n} \ln \left( \frac{2(n - \frac{1}{2})(n - y_0)}{(n - 1)(n - y_0)} \right) \\ &= \frac{1}{\beta n} \ln \left( \frac{2n - 1}{n - 1} \right). \end{aligned}$$

In an epidemic of interest,  $n$  will always be at least two, therefore  $\frac{2n-1}{n-1} > 1$  and since the logarithm is an increasing function,

$$\ln \left( \frac{2n - 1}{n - 1} \right) > \ln(1) = 0.$$



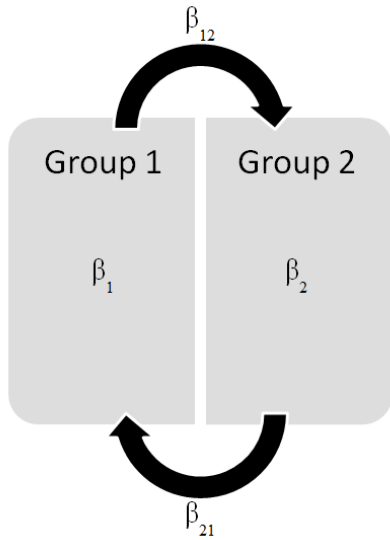


Figure 3.5: Illustrating the interacting group process for two groups, where  $\beta_i$  is the infection rate within group  $i$ , and  $\beta_{ij}$  the infection rate from group  $i$  to group  $j$ .

This means

$$T - T' = \frac{1}{\beta n} \ln \left( \frac{2n - 1}{n - 1} \right) > 0$$

and consequently  $T > T'$ .

## 3.6 The simple epidemic with interacting groups

### 3.6.1 The general model

In reality diseases may spread differently between locations or communities, whilst still spreading in the population as a whole.

For example, imagine the spread of disease in two neighbouring countries. Each is affected by the disease spread internally within each country, and externally by members of each country crossing the border into the other. In this case, a country can be thought of as a separate group, group 1 of 2 say, with its own internal number of infectives  $x_1$ , susceptibles  $y_1$ , and infection parameter,  $\beta_1$ . The spread of disease from group 1 to group 2 can then be denoted by a separate infection parameter  $\beta_{12}$  and similarly the infection rate parameter from group 2 to group 1 is denoted by  $\beta_{21}$ .

This is illustrated in Figure 3.5, reproduced from Daley and Gani (1999, p23). More generally, if there are  $m$  different communities, let the number of susceptibles and infectives

for the  $i^{\text{th}}$  community, of total size  $n_i$ , be denoted by  $x_i$  and  $y_i$  respectively, for  $i = 1, \dots, m$ . Additionally, let  $\beta_i$  be the internal infection rate in community  $i$  per unit time, and  $\beta_{ji}$  be the external infection rate from community  $j$  to community  $i$  per unit time.

Then, as in Section 3.2, the rate of change of infectives within group  $i$  is  $\beta_i x_i y_i$ . However, in the interacting groups model, this is augmented with external groups causing infections in group  $i$ . This will happen at a rate  $\beta_{ji} x_i y_j$  for every other group  $j$ , such that  $j \neq i$ . Therefore altogether there will be an external rate of infection in group  $i$  of  $\sum_{j \neq i} \beta_{ji} x_i y_j$ .

Under the homogeneous mixing assumption this leads to a system of  $m$  differential equations, first proposed by Rushton and Mautner (1955), of the form

$$\frac{dy_i}{dt} = \beta_i x_i y_i + \sum_{j \neq i} \beta_{ji} x_i y_j \quad (3.9)$$

for  $i = 1, \dots, m$ .

Note that for one group,  $m = 1$ , there is only one differential equation,

$$\frac{dy_1}{dt} = \beta_1 x_1 y_1,$$

which is as expected as this is just the general case of the simple epidemic, solved in Section 3.3.

Assumptions as to the structure of the interacting groups can be made to greatly simplify the model. Assuming a common internal infection rate parameter such that  $\beta_j = \beta$  for all  $j$ , and a common external rate as some proportion  $c$  of this internal rate so  $\beta_{ij} = c\beta$ , leads to the simplification

$$\begin{aligned} \frac{dy_i}{dt} &= \beta x_i y_i + c\beta \sum_{j \neq i} x_i y_j \\ &= \beta x_i \left( y_i + c \sum_{j \neq i} y_j \right). \end{aligned}$$

These assumptions can be sometimes justified as it is expected that the infection rate parameter between and inside different groups respectively should be quite close, especially when the groups have fairly similar conditions, such as neighbouring countries. It also provides cases where the solution to the differential equation can be derived exactly.

### 3.6.2 Investigating the values for $c$

For  $c = 1$ , the internal and external infection rate parameters for all groups are equal, meaning there is essentially just one big group, the whole population of size  $N = \sum_{i=1}^m n_i$ , with  $\sum_{i=1}^m y_i(t)$

infectives at time  $t$ . Adapting the solution to the simple epidemic given in equation (3.4) for this case gives

$$y(t) = \frac{N \sum_{i=1}^m y_{i:0}}{\sum_{i=1}^m y_{i:0} + (N - \sum_{i=1}^m y_{i:0})e^{-\beta N t}}.$$

where  $y(t)$  is the total number of infectives in the whole system at time  $t$  and  $y_{i:0}$  is the initial number of infective members of group  $i$ . Therefore the case  $c = 1$  can just be considered as in Section 3.3 and does not need to be considered in the interacting groups model.

For  $c = 0$ , there is no external interaction between groups, and hence equation (3.9) becomes a set of  $m$  independent differential equations of the form

$$\frac{dy_i}{dt} = \beta x_i y_i$$

for  $i = 1, \dots, m$ . This is a system of  $m$  independent simple epidemics, each which can be solved in the same way as in Section 3.3. This type of isolation between groups could occur, for example, between a set of mixing countries if border crossings were forbidden for a period of time to stop a common disease passing further between countries. Each country would have an independent model, and the set as a whole would have a total population of  $\sum_{i=1}^m n_i$ , with  $\sum_{i=1}^m y_i(t)$  infectives at time  $t$ , governed by the solution given in Section 3.3,

$$y_i(t) = \frac{n_i y_{i:0}}{y_{i:0} + (n_i - y_{i:0})e^{-\beta n_i t}}.$$

for  $i = 1, \dots, m$ .

To find a range for the constant  $c$ , recall that from Chapter 2, an epidemic occurs when infectious members pass the disease on to more than one susceptible member on average in their infectious period. In the continuous time deterministic setting being considered here, this corresponds to the constraint that the rate of change of infectives at  $t = 0$  must be positive, also stated by Bailey (1957, p23). That is,

$$\left. \frac{dy}{dt} \right|_{t=0} > 0.$$

This fact implies for an epidemic to start in each group, it must be the case that

$$\beta x_{i:0} y_{i:0} + c \beta x_{i:0} \sum_{j \neq i} y_{j:0} > 0$$

which, after rearrangement, gives

$$c > \frac{-y_{i:0}}{\sum_{j \neq i} y_{j:0}}.$$

To gain a crude bound on this expression, first note that  $1 \leq y_{i:0} \leq n_i \leq \max(n_j)$  for  $j = 1, \dots, m$ . Therefore,  $-y_{i:0} \geq -\max(n_j)$  for all  $j$  and

$$\frac{1}{\sum_{j \neq i} y_{j:0}} \geq \frac{1}{\sum_{j \neq i} \max(n_j)} = \frac{1}{(m-1) \max(n_j)}.$$

Combining these two ideas together gives

$$c \geq \frac{-\max(n_j)}{\max(n_j)(m-1)} = \frac{-1}{m-1}.$$

Now, note that  $m = 0$  means there are no groups and hence no population to consider, so this case can be discounted. Furthermore, the case of  $m = 1$  considered in Section 3.6.1 was just the case of the simple epidemic solved in Section 3.3, and hence there would be no need to consider this in the interacting groups model, since there is only one group. Then, for  $m \geq 2$ ,  $f(m) = \frac{-1}{m-1}$  is a monotone increasing function of  $m$ , as implied by Figure 3.6 and proved mathematically by taking

$$\begin{aligned} \frac{-1}{(m+1)-1} - \frac{-1}{m-1} &= \frac{-1}{m} + \frac{1}{m-1} \\ &= \frac{1}{m(m-1)} > 0 \end{aligned}$$

for  $m \geq 2$ . Therefore  $f(m)$  is smallest on the interval  $[2, \infty)$  at  $m=2$ . This leads to the constraint that for an epidemic to begin between two or more groups in the simple interacting group model, it must be the case that

$$c > -1.$$

If each group size  $n_i = n$  for all  $i$ , and all initial values  $y_{i0}$  are the same,  $y_{i:0} = y_0$ , then from the assumptions made, each group has exactly the same size, infection rates, and initial conditions. Due to the lack of randomness in deterministic models, this means that every group evolves identically through time according to

$$\frac{dy_i}{dt} = \beta x_i y_i + \beta c x_i \sum_{j \neq i} y_j.$$

But, because they evolve identically for all  $i$ ,  $x_i = x_j = x$  and  $y_i = y_j = y$  for all  $t$ , which leads to the equation

$$\frac{dy}{dt} = \beta xy + \beta xyc(m-1) = \beta(1 + c(m-1))xy.$$

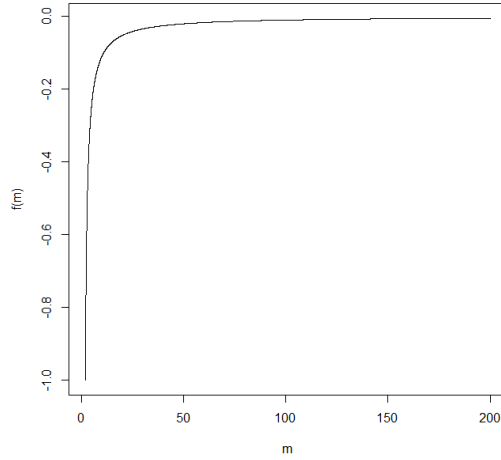


Figure 3.6: Illustrating the monotonic increasing nature of the function  $f(m) = \frac{-1}{m-1}$  when plotted against  $m$  for  $m \geq 2$ .

Therefore the number of infectives for any group evolves through time according to the equation

$$y(t) = \frac{ny_0}{y_0 + (n - y_0)e^{-\beta(1+c(m-1))nt}}.$$

### 3.6.3 Adaptation to model vector transmission

The interacting group model can also be used to gain an initial idea of how a disease transmitted to humans by an intermediary vector such as a mammal can behave over a short period of time relative to the life of a mammal, so that the two population sizes remain constant.

Consider a disease where the group of mammals can infect each other, and humans, with the disease, however humans cannot infect mammals or each other. One example of such a disease is Rabies, which can be passed between all living mammals through the transfer of saliva, and passed to humans when bitten by an infected mammal.

By taking humans as group 1 and other mammals as group 2, this equates to taking  $\beta_1 = 0$  and  $\beta_{12} = 0$  to give the relationship as shown in Figure 3.7.

This simplifies the system of equations (3.9) to

$$\frac{dy_1}{dt} = \beta_{21}x_1y_2 \tag{3.10}$$

$$\frac{dy_2}{dt} = \beta_2x_2y_2. \tag{3.11}$$

Equation (3.11), governing the number of mammal infectives, evolves independently of how the human infectives evolve. Hence it is just the case of a simple epidemic, and gives the solution

$$y_2(t) = \frac{n_2y_{2:0}}{y_{2:0} + (n_2 - y_{2:0})e^{-\beta_2n_2t}}$$

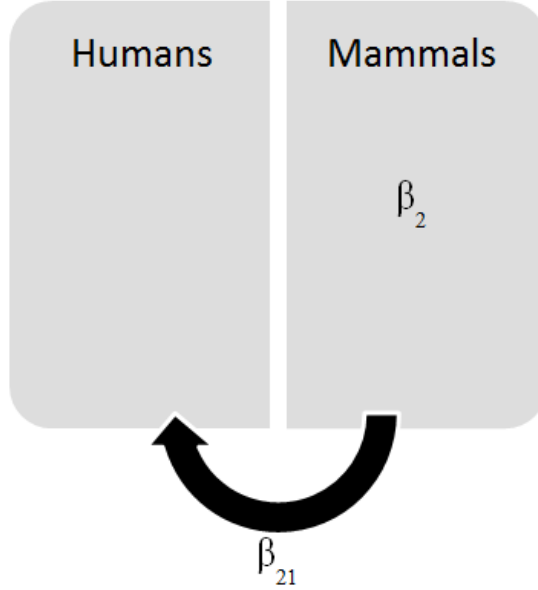


Figure 3.7: Interacting group model representing mosquito caused human infection.

where  $y_{2:0}$  is the number of infective mammals at time 0. This solution for  $y_2$  can be substituted into equation (3.10) to eliminate the dependence on  $y_2$ , changing

$$\frac{dy_1}{dt} = \beta_{21}(n_1 - y_1)y_2,$$

into

$$\int \frac{dy_1}{\beta_{21}(n_1 - y_1)} = \int \frac{n_2 y_{2:0} dt}{y_{2:0} + (n_2 - y_{2:0})e^{-\beta_2 n_2 t}}.$$

Dealing with the left-hand side first gives

$$\int \frac{dy_1}{\beta_{21}(n_1 - y_1)} = -\frac{1}{\beta_{21}} \ln(n_1 - y_1) + c_1$$

with  $c_1$  being the constant of integration. The fact that

$$\begin{aligned} \frac{d}{dt} \left( \frac{1}{\beta_2 n_2 y_{2:0}} \ln(y_{2:0} e^{\beta_2 n_2 t} + (n_2 - y_{2:0})) \right) &= \frac{1}{\beta_2 n_2 y_{2:0}} \cdot \frac{\beta_2 n_2 y_{2:0} e^{\beta_2 n_2 t}}{y_{2:0} e^{\beta_2 n_2 t} + (n_2 - y_{2:0})} \\ &= \frac{1}{y_{2:0} + (n_2 - y_{2:0})e^{-\beta_2 n_2 t}} \end{aligned}$$

can be used to integrate the right hand side. This gives

$$n_2 y_{2:0} \int \frac{dt}{y_{2:0} + (n_2 - y_{2:0})e^{-\beta_2 n_2 t}} = \frac{1}{\beta_2} \ln(y_{2:0} e^{\beta_2 n_2 t} + (n_2 - y_{2:0})) + c_2$$

where  $c_2$  is a constant of integration.

Now, combining these two results and redefining the constant term gives

$$\ln(n_1 - y_1) = -\frac{\beta_{21}}{\beta_2} \ln(y_{2:0}e^{\beta_2 n_2 t} + (n_2 - y_{2:0})) + c_3$$

which after rearrangement for  $y_1$  and setting  $A = e^{c_3}$  becomes

$$y_1(t) = n_1 - A(y_{2:0}e^{\beta_2 n_2 t} + (n_2 - y_{2:0}))^{-\frac{\beta_{21}}{\beta_2}}.$$

Imposing the initial condition of  $y_1(0) = y_{1:0}$  at  $t = 0$  leads to

$$\begin{aligned} y_{1:0} &= n_1 - A(y_{2:0} + (n_2 - y_{2:0}))^{-\frac{\beta_{21}}{\beta_2}} \\ &= n_1 - A n_2^{-\frac{\beta_{21}}{\beta_2}}. \end{aligned}$$

Upon rearrangement for  $A$  this gives

$$A = \frac{n_1 - y_{1:0}}{n_2^{-\frac{\beta_{21}}{\beta_2}}}$$

leading to the exact solution

$$y_1(t) = n_1 - \frac{n_1 - y_{1:0}}{n_2^{-\frac{\beta_{21}}{\beta_2}}} (y_{2:0}e^{\beta_2 n_2 t} + (n_2 - y_{2:0}))^{-\frac{\beta_{21}}{\beta_2}}.$$

For the solution to be bounded as  $t \rightarrow \infty$  the condition  $\beta_{21} > 0$  must be imposed. This forces  $\frac{-\beta_{21}}{\beta_2} < 0$ , since  $\beta_2 > 0$  by definition, and hence

$$(y_{2:0}e^{\beta_2 n_2 t} + (n_2 - y_{2:0}))^{-\frac{\beta_{21}}{\beta_2}} \rightarrow 0$$

as  $t \rightarrow \infty$ .

Two examples of the system are shown in Figure 3.8. Both plots have  $n_1 = n_2 = 100$ ,  $y_{1:0} = 0$ ,  $y_{2:0} = 5$ , and  $\beta_2 = 0.05$ , with Figure 3.8 (top) showing the evolution of  $y(t)$  with  $\beta_{21} = 0.01$  and Figure 3.8 (bottom) showing the case with  $\beta_{21} = 0.7$ . Small population sizes like this could be used to model an outbreak of rabies in a large dog kennel with human staff that could become infected by the dogs.

From Figure 3.8 it can be seen that increasing the rate at which the dogs infect humans does not affect how quickly the mammals become fully infected, as the curve representing  $y_2$  is the same in both plots. This is because, as mentioned earlier, the mammal epidemic evolves independently of the human epidemic. However, it does affect how quickly the human population becomes infected, with a higher mammal to human infection rate leading to a quicker time for humans to become fully infected, which makes intuitive sense.

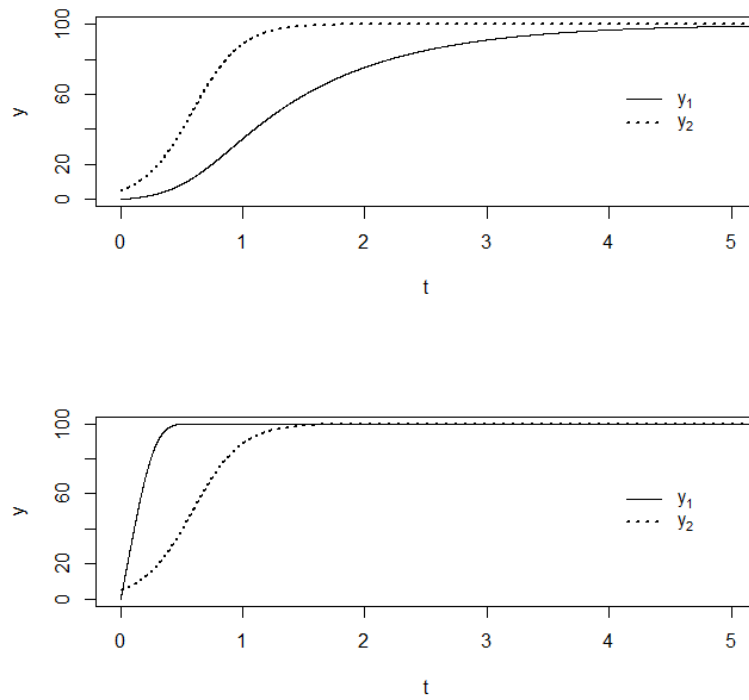


Figure 3.8: Number of infective members of each group in the interacting group model with  $n_1 = n_2 = 100$ ,  $y_{1:0} = y_{2:0} = 5$ ,  $\beta_2 = 0.05$ ,  $\beta_{21} = 0.01$  (top) and  $\beta_{21} = 0.7$  (bottom).



# Chapter 4

## The General Deterministic Epidemic

### 4.1 Introduction

Over longer periods of time, it is unrealistic to assume that every infective member stays in that state until the epidemic has finished. It is reasonable to think that some of these infective members may recover and gain immunity from the disease, be isolated from susceptibles due to their illness, or in the worst case, die from the illness.

While in reality these three cases have extremely different outcomes, when modelling epidemics deterministically they can all be considered to be part of one class of removals, as these members are no longer infective or susceptible to becoming infective again. In keeping with the definitions from Section 3.1, let  $z(t)$  represent the number of removals from the disease over the course of the epidemic, meaning that the fixed total population size is  $n = x(t) + y(t) + z(t)$ . A population member can then transition from susceptible to infectious in the same way as in Chapter 3. However once in the infective state, infectious members can leave to the removed state, at removal rate  $\gamma$  per infective member per unit time.

### 4.2 Modelling the general epidemic

As in Section 3.2, a set of differential equations to model the behaviour of this system can be derived, originally proposed by Kermack and McKendrick.

The transition from susceptible to infective is made under conditions identical to the simple epidemic. Hence, again with infection parameter rate  $\beta$ , the rate of change of susceptibles is

$$\frac{dx}{dt} = -\beta xy. \tag{4.1}$$

As in Chapter 3, the rate of susceptibles becoming infective is still  $\beta xy$ . However it is

now possible for infectious members to become removed. As stated in Section 4.1, members are becoming removed with rate  $\gamma$  per infective per unit time, and so for  $y$  infectives, the rate of infectives leaving the infectious class is  $\gamma y$ . Combining these two results gives

$$\frac{dy}{dt} = \beta xy - \gamma y. \quad (4.2)$$

Members are joining the removed class from the susceptible class at rate  $\gamma$  per infective, and once a member is removed, they remain removed. This leads to the third and final differential equation

$$\frac{dz}{dt} = \gamma y. \quad (4.3)$$

As removals take place as the epidemic evolves and not before, initially at  $t = 0$ ,  $x(0) = x_0$ ,  $y(0) = y_0$  and  $z(0) = 0$ .

### 4.3 A threshold for the general epidemic

As mentioned in Section 3.6, the condition for an epidemic to begin is

$$\left. \frac{dy}{dt} \right|_{t=0} > 0.$$

Recalling equation (3.2), for the simple epidemic

$$\frac{dy}{dt} = \beta xy,$$

which is always non-negative since  $\beta > 0$ ,  $x(t) \geq 0$  and  $y(t) \geq 0$ . However for the general epidemic, and specifically equation (4.2) this is not always the case.

For  $\left. \frac{dy}{dt} \right|_{t=0} > 0$  to be satisfied in equation (4.2), it is required that

$$x_0 > \frac{\gamma}{\beta} = \rho$$

where  $\rho$  is defined as the relative removal rate for ease of future notation; see Bailey (1957, p22). This means that for an epidemic to occur, the initial number of susceptibles in a population must be over the threshold amount of  $\rho$ .

## 4.4 Investigating the behavior of the general epidemic

### 4.4.1 Relating $x$ and $z$

Notice that equation (4.1) can be written as

$$\frac{1}{x} \frac{dx}{dt} = -\beta y \quad (4.4)$$

and that equation (4.3) can be written as

$$\frac{1}{\gamma} \frac{dz}{dt} = y. \quad (4.5)$$

Now substituting the equation for  $y$  in equation (4.5) into equation (4.4) gives

$$\frac{1}{x} \frac{dx}{dt} = -\frac{\beta}{\gamma} \frac{dz}{dt} = -\frac{1}{\rho} \frac{dz}{dt}.$$

After multiplying through by  $dt$  and integrating this becomes

$$\ln x = -\frac{z}{\rho} + c$$

where  $c$  is a constant of integration. Finally, taking exponents of both sides and writing  $A = e^c$  gives the general solution

$$x(t) = Ae^{-\frac{z(t)}{\rho}}. \quad (4.6)$$

The particular solution for equation (4.6) can be found in this case by recalling the initial conditions  $x(0) = x_0$  and  $z(0) = 0$ . Substituting in these values gives

$$x_0 = A$$

and hence

$$x(t) = x_0 e^{-\frac{z(t)}{\rho}}. \quad (4.7)$$

#### 4.4.2 Bounds on the evolution of an epidemic through time

To begin to look at how the equations evolve through time, the differential equations, and hence their solutions can be bounded.

Since  $y(t) \leq n$  implies  $-y(t) \geq -n$ , equation (4.4) can be bounded by

$$\frac{dx}{dt} = -\beta xy \geq -\beta xn.$$

Therefore

$$x(t) \geq Ae^{-\beta nt}$$

which, when applying the initial conditions of  $x(0) = x_0 > 0$  at  $t = 0$ , gives a bound on  $x(t)$  to be

$$x(t) \geq x_0 e^{-\beta nt} > 0. \quad (4.8)$$

Furthermore,  $\frac{dx}{dt}$  is negative for all  $t$ , and therefore  $x(t)$  is a strictly decreasing function that is bounded below, so will converge to some finite value  $x_\infty$ , say.

This implies  $z(t) \geq 0$  cannot diverge to infinity, as this would cause  $x(t)$  in equation (4.7) to tend to zero, which has been shown in equation (4.8) to not be the case. Moreover, because  $x(t)$  converges to a finite value,  $z(t)$  must also converge to some finite value  $z_\infty$ , related to  $x_\infty$  by the limit of equation (4.7),

$$x_\infty = x_0 e^{-\frac{z_\infty}{\rho}}. \quad (4.9)$$

Finally, it is still required that the total population has size  $n$  regardless of time. Considering  $x(t) + y(t) + z(t) = n$  as  $t \rightarrow \infty$  implies that  $y(t)$  must also converge to a finite limit, denoted  $y_\infty$ , as otherwise the constraint would not hold. Furthermore, it must be the case that  $y_\infty = 0$ , otherwise  $\frac{dz}{dt}$  would not tend to zero as  $t$  increases, which is required to have a finite  $z_\infty$ .

### 4.4.3 The Kermack-McKendrick approximation

Recalling that  $x(t) + y(t) + z(t) = n$ , substituting equation (4.7) into equation (4.3) gives

$$\begin{aligned} \frac{dz}{dt} &= \gamma y \\ &= \gamma(n - z - x) \end{aligned} \quad (4.10)$$

$$= \gamma(n - z - x_0 e^{-\frac{z}{\rho}}). \quad (4.11)$$

This differential equation cannot be solved in its current form, however Kermack and McKendrick (1927) proposed an approximation to the exponential term which gives an integrable equation, elaborated on by Daley and Gani (1999, p30).

Recalling the Maclaurin expansion of the exponential function

$$e^x = \sum_{n=0}^{\infty} \frac{x^n}{n!},$$

equation (4.11) can be approximated by

$$\begin{aligned} \frac{dz}{dt} &\approx \gamma \left( n - z - x_0 \left( 1 - \frac{z}{\rho} + \frac{z^2}{2\rho^2} \right) \right) \\ &= \gamma \left( n - x_0 + \left( \frac{x_0}{\rho} - 1 \right) z - \frac{x_0}{2\rho^2} z^2 \right) \\ &= \gamma \left( y_0 + \left( \frac{x_0}{\rho} - 1 \right) z - \frac{x_0}{2\rho^2} z^2 \right). \end{aligned} \quad (4.12)$$

Figure 4.1 shows how increasing the number of terms in the expansion of  $e^{-\frac{z}{\rho}}$  affects the approximation. The left hand side plot shows the approximation to  $\frac{dz}{dt}$  with just the first,

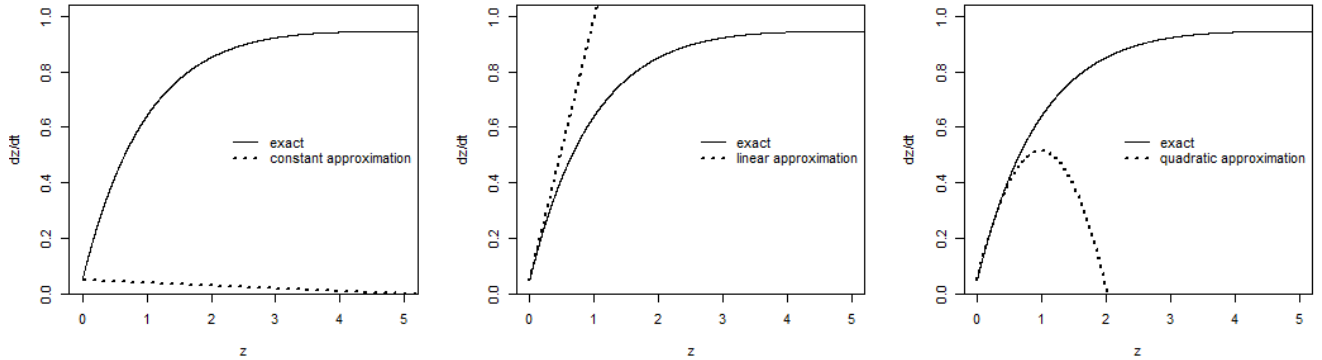


Figure 4.1:  $\frac{dz}{dt}$  with  $n = 100$ ,  $\beta = 0.01$ ,  $\gamma = 0.01$  and  $y_0 = 5$  for changing  $z$  plotted with a constant exponential approximation (left), a linear exponential approximation (centre) and a quadratic exponential approximation (right).

constant, term of the exponential expansion; the central plot shows the exponential function approximated by  $1 - \frac{z}{\rho}$ , and finally the right hand side plot shows the expansion up to second order used in equation (4.12).

From the graph, it is clear the approximations are only useful for small  $z$ , therefore when performing the expansion to derive equation (4.12), it is assumed that  $\frac{z}{\rho}$  is small, since  $\rho$  is constant. Although the second order term in the exponential expansion is usually taken to be small with respect to the first order term, and hence ignored, here it is needed since, as seen in equation (4.12), the first order term may also be small. This occurs for  $x_0$  close to the threshold  $\rho$ , so the second order term is required to keep a stable approximation at this point.

Equation (4.12) can then be written as

$$\frac{dz}{y_0 + \left(\frac{x_0}{\rho} - 1\right)z - \frac{x_0}{2\rho^2}z^2} = \gamma dt, \tag{4.13}$$

which can be solved by integrating both sides. The right hand side can be easily integrated to give

$$\int \gamma dt = \gamma t + d_1,$$

where  $d_1$  is a constant of integration.

The left hand side of equation (4.13) can be solved using the standard integral given in Bronshtein and Semendyayev (1973, p415),

$$\int \frac{dz}{Z} = \frac{-2}{\sqrt{-\Delta}} \tanh^{-1} \left( \frac{2az + b}{\sqrt{-\Delta}} \right)$$

where  $Z = az^2 + bz + c$  and  $\Delta = 4ac - b^2 < 0$ .

Writing

$$a = -\frac{x_0}{2\rho^2}, b = \frac{x_0}{\rho} - 1, c = y_0$$

gives the integral form consistent with the left hand side of equation (4.13) and the fact that

$$\Delta = 4ac - b^2 = -\frac{2x_0y_0}{\rho^2} - \left(\frac{x_0}{\rho} - 1\right)^2 < 0$$

shows the standard result can now be implemented. By letting

$$\alpha = \sqrt{-\Delta} = \sqrt{\frac{2x_0y_0}{\rho^2} + \left(\frac{x_0}{\rho} - 1\right)^2},$$

equation (4.13) can be written as

$$\frac{-2}{\alpha} \tanh^{-1} \left( \frac{2az + b}{\alpha} \right) = \gamma t + d_2$$

where  $d_2$  is a new constant of integration. Multiplying through by  $-\frac{1}{2}\alpha$  and redefining the constant term gives

$$\tanh^{-1} \left( \frac{2az + b}{\alpha} \right) = -\frac{1}{2}\alpha\gamma t + d_3$$

and rearranging for  $z(t)$  gives

$$z(t) = \frac{1}{2a} \left( \alpha \tanh \left( -\frac{1}{2}\alpha\gamma t + d_3 \right) - b \right). \quad (4.14)$$

By recalling the initial condition  $z = 0$  at  $t = 0$ , the constant term is found to be  $d_3 = \tanh^{-1} \left( \frac{b}{\alpha} \right)$ . Using this fact, and re-substituting in for  $a$  and  $b$  gives

$$\begin{aligned} z &= \frac{-\rho^2}{x_0} \left( -\left(\frac{x_0}{\rho} - 1\right) + \alpha \tanh \left( -\frac{1}{2}\alpha\gamma t + d_3 \right) \right) \\ &= \frac{\rho^2}{x_0} \left( \frac{x_0}{\rho} - 1 - \alpha \tanh \left( -\frac{1}{2}\alpha\gamma t + d_3 \right) \right). \end{aligned}$$

Finally, by using the exponential definition of  $\tanh$ , it is seen that

$$-\tanh(x) = -\left( \frac{e^x - e^{-x}}{e^x + e^{-x}} \right) = \frac{e^{-x} - e^{-(-x)}}{e^{-x} + e^{-(-x)}} = \tanh(-x).$$

so,  $\tanh$  is an odd function. This then gives the final approximation of

$$z = \frac{\rho^2}{x_0} \left( \frac{x_0}{\rho} - 1 + \alpha \tanh \left( \frac{1}{2}\alpha\gamma t - d_3 \right) \right), \quad (4.15)$$

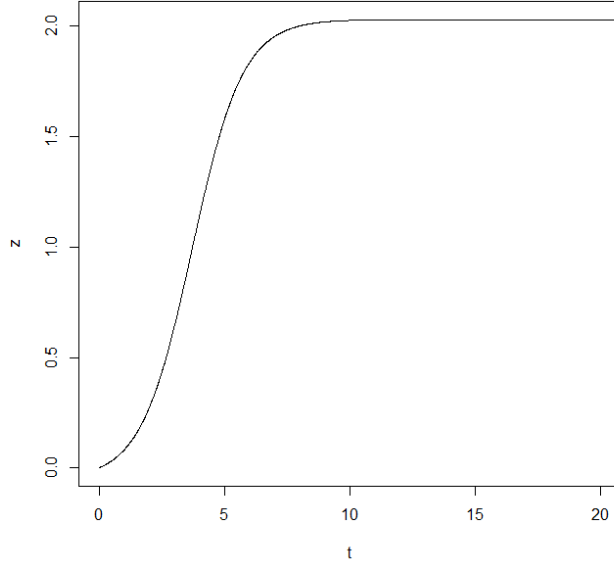


Figure 4.2: Plot of the approximation of  $z$  through time with  $n = 100$ ,  $\beta = 0.01$ ,  $\gamma = 0.01$  and  $y_0 = 5$ .

where

$$\alpha = \sqrt{\frac{2x_0y_0}{\rho^2} + \left(\frac{x_0}{\rho} - 1\right)^2},$$

and

$$d_3 = \tanh^{-1}\left(\frac{\frac{x_0}{\rho} - 1}{\alpha}\right).$$

This agrees with the result given in Daley and Gani (1999, p30).

An example of the evolution of  $z(t)$  through time can be seen in Figure 4.2 in the case where  $n = 100$ ,  $\beta = 0.01$ ,  $\gamma = 0.01$  and  $y_0 = 5$ . Figure 4.2 reinforces the result in Section 4.4.2, which states that  $z(t)$  has some limiting value in this approximation,  $\hat{z}_\infty$ , which in this example seems to be close to two.

This can be more closely analysed by looking at the behaviour of equation (4.15) as  $t \rightarrow \infty$ . To do this, because  $t$  is contained in the  $\tanh(x)$  expression, it would first make sense to understand how  $\tanh$  behaves asymptotically. The plot of  $\tanh(x)$  given in Figure 4.3 seems to tend to one as  $x \rightarrow \infty$ . This can be seen explicitly by taking the limit of the exponential definition of  $\tanh(x)$  as  $x$  tends to infinity,

$$\lim_{x \rightarrow \infty} \tanh(x) = \lim_{x \rightarrow \infty} \left( \frac{e^x - e^{-x}}{e^x + e^{-x}} \right) = \lim_{x \rightarrow \infty} \left( \frac{1 - e^{-2x}}{1 + e^{-2x}} \right) = 1.$$

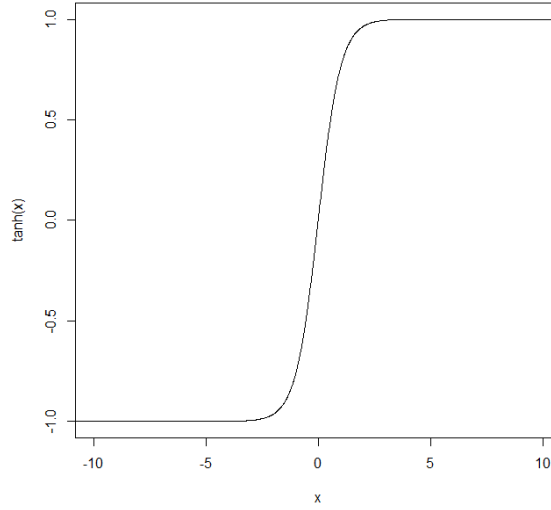


Figure 4.3: A plot of  $\tanh(x)$  against  $x$ .

Therefore, since  $\alpha$ ,  $\gamma$  and  $d_3$  are all constants, with  $\alpha \geq 0$  and  $\gamma \geq 0$ ,

$$\lim_{t \rightarrow \infty} \tanh\left(\frac{1}{2}\alpha\gamma t - d_3\right) = 1$$

and hence

$$\begin{aligned} \hat{z}_\infty &= \lim_{t \rightarrow \infty} \frac{\rho^2}{x_0} \left( \frac{x_0}{\rho} - 1 + \alpha \tanh\left(\frac{1}{2}\alpha\gamma t - d_3\right) \right) \\ &= \frac{\rho^2}{x_0} \left( \frac{x_0}{\rho} - 1 + \alpha \right). \end{aligned}$$

For the example illustrated in Figure 4.2,

$$\hat{z}_\infty = \frac{\rho^2}{x_0} \left( \frac{x_0}{\rho} - 1 + \alpha \right) = 2.031.$$

Using the earlier specified example, the approximation states there will be two removals from the disease over the course of the epidemic. This asymptote is added to the plot of  $z(t)$  against  $t$  as the dashed line in Figure 4.4.

#### 4.4.4 The Kendall parameterisation

As an alternative to the Taylor series approximation of Kermack and McKendrick (1927) proposed in Section 4.4.3, Kendall (1956) proposed that, by allowing  $\beta$  to vary as a specific function



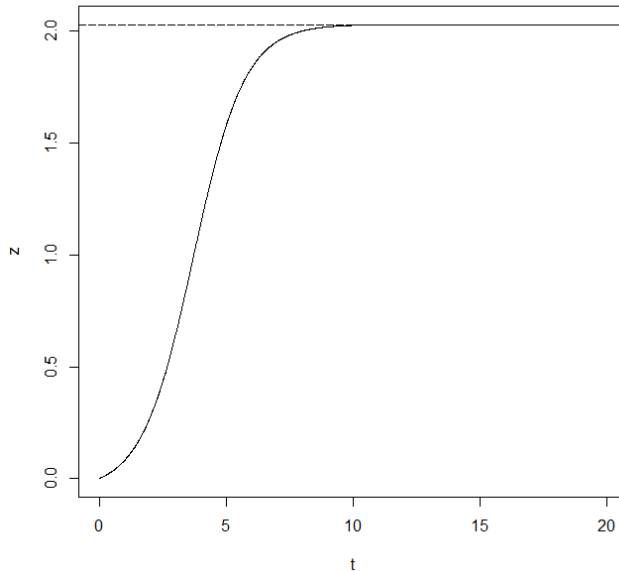


Figure 4.4: Plot of  $z(t)$  against time  $t$  with  $n = 100$ ,  $\beta = 0.01$ ,  $\gamma = 0.01$  and  $y_0 = 5$ .

of  $z$  rather than a constant as previously assumed, equation (4.11) holds exactly for small  $z$ . Specifically Kendall stated that taking

$$\beta(z) = \frac{2\beta}{\left(1 - \frac{z}{\rho}\right) + \left(1 - \frac{z}{\rho}\right)^{-1}}$$

led to equation (4.12), with the added constraint that  $z$  is small, specifically  $z < \rho$ , otherwise the infection rate parameter would become negative.

Conveniently, taking  $\beta$  in this form leads to an exact version of the approximation in Section 4.4.3. The proof that this occurs, omitted by Bailey (1957, p24), is shown below.

Firstly, combining equations (4.1) and (4.3) gives

$$\frac{dx}{dt} = -\beta(z) \frac{1}{\gamma} \frac{dz}{dt}$$

and integrating both sides with respect to  $t$  leads to

$$\int_{x_0}^{x(t)} \frac{du}{u} = \log x(t) - \log x_0 = -\frac{1}{\gamma} \int_{z=0}^{z(t)} \beta(w) dw.$$

Therefore

$$x(t) = x_0 e^{-\frac{1}{\gamma} \int_{z=0}^{z(t)} \beta(w) dw}.$$

Then substituting this form for  $x$  into equation (4.10) gives

$$\frac{dz}{dt} = \gamma \left( n - z - x_0 e^{-\frac{1}{\gamma} \int_0^z \beta(w) dw} \right).$$

The integral within the exponential function can be calculated as

$$\begin{aligned} -\frac{1}{\gamma} \int_0^z \beta(w) dw &= -\frac{1}{\gamma} \int_0^z \frac{2\beta dw}{\left(1 - \frac{w}{\rho}\right) + \left(1 - \frac{w}{\rho}\right)^{-1}} \\ &= -\frac{2\beta}{\gamma} \int_0^z \frac{dw}{\left(1 - \frac{w}{\rho}\right) + \left(1 - \frac{w}{\rho}\right)^{-1}}. \end{aligned}$$

After multiplying through by  $\frac{\left(1 - \frac{w}{\rho}\right)}{\left(1 - \frac{w}{\rho}\right)}$  this becomes

$$-\frac{1}{\gamma} \int_0^z \beta(w) dw = -\frac{2}{\rho} \int_0^z \frac{1 - \frac{w}{\rho}}{\left(1 - \frac{w}{\rho}\right)^2 + 1} dw.$$

This can then be solved by the substitution  $u = 1 - \frac{w}{\rho}$ , which implies that  $dw = -\rho du$  and that the limits of integration change from  $w = 0$  and  $w = z$  to  $u = 1$  and  $x = 1 - \frac{z}{\rho}$  respectively. Performing this substitution gives

$$\begin{aligned} -\frac{1}{\gamma} \int_0^z \beta(w) dw &= -\frac{2}{\rho} \int_0^z \frac{1 - \frac{w}{\rho}}{\left(1 - \frac{w}{\rho}\right)^2 + 1} dw. \\ &= 2 \int_1^{1 - \frac{z}{\rho}} \frac{u}{1 + u^2} du \\ &= 2 \left[ \frac{1}{2} \ln(1 + u^2) \right]_1^{1 - \frac{z}{\rho}} \\ &= \ln \left( 1 + \left(1 - \frac{z}{\rho}\right)^2 \right) - \ln(2) \\ &= \ln \left( 2 - \frac{2z}{\rho} + \frac{z^2}{\rho^2} \right) - \ln(2) \\ &= \ln \left( 1 - \frac{z}{\rho} + \frac{z^2}{2\rho^2} \right) \end{aligned}$$

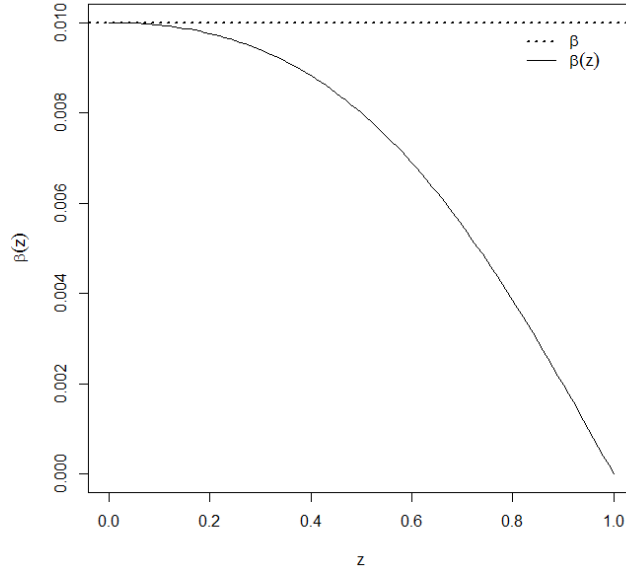


Figure 4.5: Plots of  $\beta$  and  $\beta(z)$  against  $z$  with  $\beta = 0.01$  and  $\rho = 1$ .

since  $\ln(a) - \ln(b) = \ln\left(\frac{a}{b}\right)$ . Therefore,

$$\begin{aligned}
 \frac{dz}{dt} &= \gamma \left( n - z - x_0 e^{-\frac{1}{\gamma} \int_0^z \beta(w) dw} \right) \\
 &= \gamma \left( n - z - x_0 e^{\ln\left(1 - \frac{z}{\rho} + \frac{z^2}{2\rho^2}\right)} \right) \\
 &= \gamma \left( n - z - x_0 \left( 1 - \frac{z}{\rho} + \frac{z^2}{2\rho^2} \right) \right) \\
 &= \gamma \left( n - x_0 + z \left( \frac{x_0}{\rho} - 1 \right) - \frac{z^2}{2\rho^2} \right)
 \end{aligned}$$

which is equivalent to the result derived when using the Taylor series expansion in equation (4.12). However, note that

$$\beta(0) = \frac{2\beta}{\left(1 - \frac{0}{\rho}\right) + \left(1 - \frac{0}{\rho}\right)^{-1}} = \beta$$

and Figure 4.5, reproduced from Daley and Gani (1999, p32), shows that  $\beta(z) \leq \beta$  for  $z \leq \rho$ . It follows that the infection rate parameter  $\beta$  is underestimated by  $\beta(z)$ , and so the size of the epidemic approximated in Section 4.4.3 and this section will also be underestimated. To counter this and try and find an exact solution, Kendall (1956) viewed the epidemic more generally, writing equation (4.11) as

$$\frac{1}{\gamma} \int_0^z \frac{dw}{n - w - x_0 e^{-\frac{w}{\rho}}} = t. \tag{4.16}$$

As  $t \rightarrow \infty$ ,  $z(t) \rightarrow z_\infty$  which is the unique positive root of  $g(z) = n - z - x_0 e^{\frac{-z}{\rho}}$ . This can be shown by using equation (4.9) and the fact that  $y_\infty = 0$  to give

$$\begin{aligned} g(z_\infty) &= n - z_\infty - x_0 e^{\frac{-z_\infty}{\rho}} \\ &= x_\infty + y_\infty + z_\infty - z_\infty - x_\infty \\ &= 0 \end{aligned}$$

and therefore equation (4.16) is limited by  $0 \leq z < z_\infty$ . This means the exact value of the  $z_\infty$  asymptote in Figure 4.6 (left) can be found by solving

$$g(z) = n - z - x_0 e^{\frac{-z}{\rho}} = 0$$

for  $z \geq 0$ . This cannot be solved exactly but solving by numerical methods on R with the code

```
x=c(-100000:150000)*0.001
f1=function(x) (100-x-95*exp(-x))
uniroot(f1,c(0,1000))
$root
100
```

gives  $z_\infty$ , as shown in Figures 4.6 (left) and 4.8 (top), to be 100.

This value for  $z_\infty$  is quite different to the approximation given in Section 4.4.3. Since the approximation is only appropriate for small  $z$ , the estimate  $\hat{z}_\infty$  does not necessarily correspond well to the exact value of  $z_\infty$ . This is highlighted for this example in Figure 4.6 where for small  $z$ , the values are well matched, while as  $z$  increases the exact and approximate curves for  $z(t)$  are far apart. In this case, the exact curve for  $z$  has been found using the numerical method described in the following Section 4.4.5.

Higher values for  $\gamma$ , with everything else constant, means a higher removal rate, so infective members are removed quicker, and hence infect fewer people during this time. This leads to a lower number of infected members in total, and therefore a lower number of removals. Figure 4.7 illustrates this fact, and since the total evolution of removals takes place over smaller  $z(t)$ , the approximation for the whole evolution of removals improves, however there is still a slight underestimation of the exact size of removals as noted earlier.

Figure 4.8 shows the function  $g(z)$  plotted against  $z$ . It can be seen that  $g(z) = 0$  has a second root, at  $z = z_{-\infty}$ . This second root is the first time  $g(z)$  crosses the axis in the top plot of Figure 4.8, and is shown more explicitly in the lower plot, which focuses on a smaller region of the top plot to show  $z_{-\infty}$  more clearly. Again using R to solve  $g(z) = 0$  with  $n = 100$ ,  $x_0 = 95$  and  $\rho = 1$  it is found that  $z_{-\infty} = -0.052$ .

Daley and Gani (1999, p32) suggest the deterministic epidemic can be thought of as spanning the time interval  $(-\infty, \infty)$ , beginning at  $t = -\infty$  with a total population of size

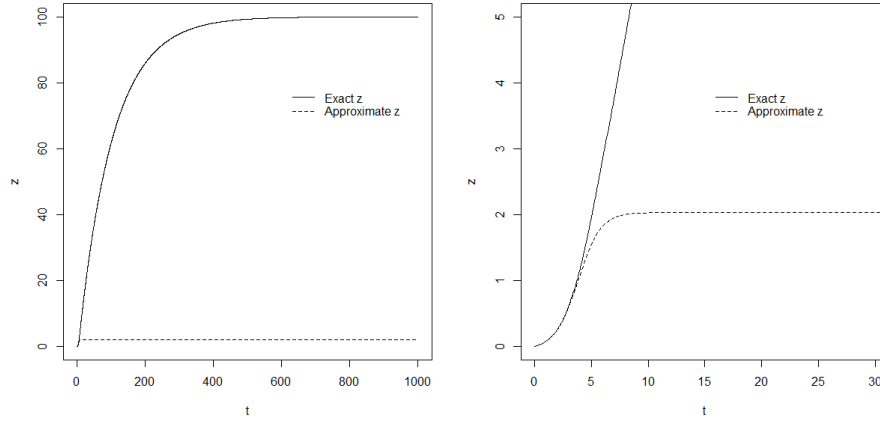


Figure 4.6: Plot of exact and approximate  $z(t)$  through time with  $n = 100$ ,  $\beta = 0.01$ ,  $\gamma = 0.01$  and  $y_0 = 5$  (left), and the same plot focused on the region of small  $z$  (right).

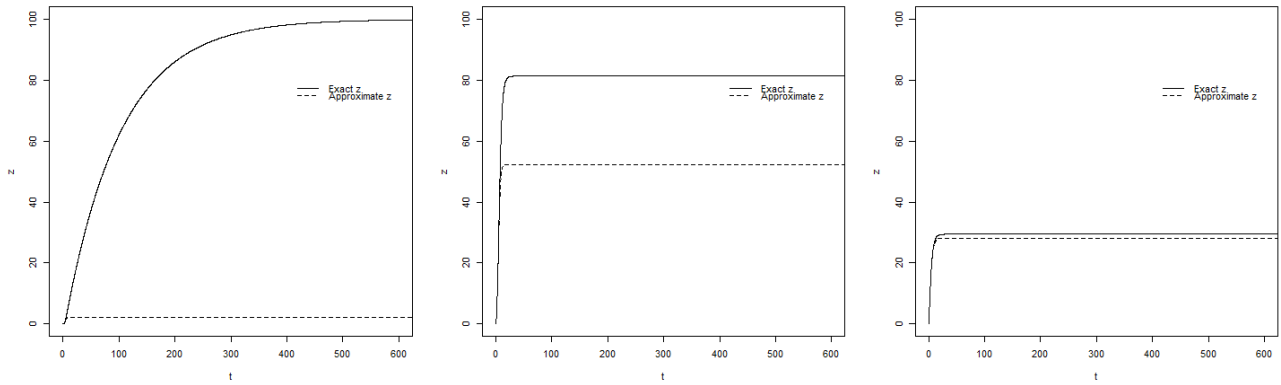


Figure 4.7: Plot of exact and approximate  $z(t)$  through time with  $n = 100$ ,  $\beta = 0.01$ ,  $y_0 = 5$  and  $\gamma = 0.01$  (left),  $\gamma = 0.5$  (centre) and  $\gamma = 0.99$  (right).

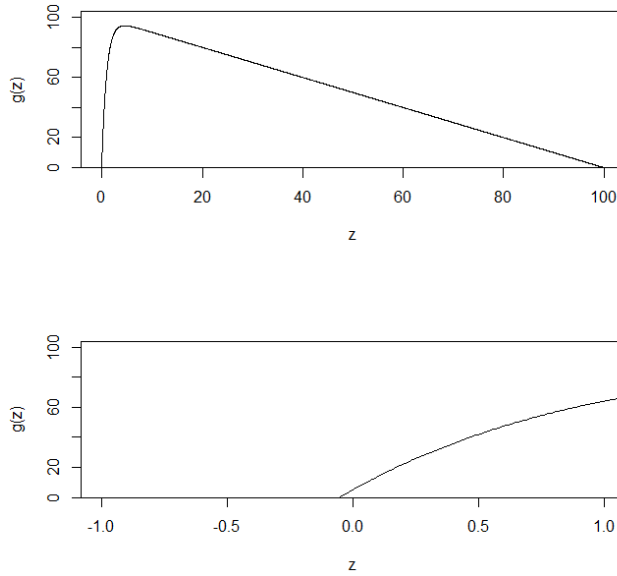


Figure 4.8: Plot of  $g(z)$  against  $z$  with  $n = 100$ ,  $y_0 = 5$  and  $\rho = 1$  (top), and the same plot magnified about  $z = 0$  (bottom)

$N = n + |z_{-\infty}|$ , with a very small number  $\epsilon$  of infectives, and  $N - \epsilon$  susceptibles. Then, from  $t = -\infty$  to  $t = 0$  there will be  $|z_{-\infty}|$  removals and the number of infectives will evolve from  $\epsilon$  to  $y_0$ . This returns the familiar initial conditions of  $x_0$  susceptibles,  $y_0$  infectives and 0 removals at  $t=0$ . Then as  $t \rightarrow \infty$  the epidemic finally evolves to  $x_\infty$  susceptibles,  $z_\infty$  removals and 0 infectives as discussed earlier.

The intensity of an epidemic is then defined by Daley and Gani (1999, p33) to be

$$i = \frac{|z_{-\infty}| + z_\infty}{N}$$

where  $0 < i \leq 1$ . The case  $i = 1$  occurs when all members of the population become infected and then removed throughout the course of the disease, as in this case  $z_\infty = n$ . This can be used to compare the strength of epidemics by examining the relative number of removals after infection.

The example used throughout this chapter with  $n = 100$ ,  $\rho = 1$  and  $y_0 = 5$  has  $z_\infty = 100 = n$  and  $z_{-\infty} = -0.052$ . Also, recall  $N = n + |z_{-\infty}|$ , so that

$$i = \frac{|z_{-\infty}| + z_\infty}{N} = \frac{|z_{-\infty}| + n}{n + |z_{-\infty}|} = 1.$$

This example gives the highest intensity possible; all population members become infected and then removed.

As a second example recall the parameters used in Figure 4.7; where  $n = 10$ ,  $\rho = 14$  and  $y_0 = 1$ . This gives  $z_\infty = 2.439$ , implying that roughly 7 population members remain uninfected after the epidemic has run its course. Furthermore,  $z_{-\infty} = -13.343$  which leads to an intensity of

$$\begin{aligned} i &= \frac{|z_{-\infty}| + z_\infty}{N} \\ &= \frac{|z_{-\infty}| + z_\infty}{n + |z_{-\infty}|} \\ &= 0.676. \end{aligned}$$

#### 4.4.5 Numerical Solution

To conclude the discussion in this chapter, the solutions to the three differential equations proposed in Section 4.2 can be approximated numerically, for small time steps  $dt$ , by the iterations

$$\begin{aligned} x_{i+1} &= x_i - (\beta x_i y_i) dt \\ y_{i+1} &= y_i + (\beta x_i y_i - \gamma y_i) dt \\ z_{i+1} &= z_i + \gamma y_i dt \end{aligned}$$

with initial conditions at  $t = 0$  of  $x_0$ ,  $y_0$  and  $z_0 = 0$ , and  $i$  referring to the time  $t = idt$  where  $dt = 0.1$  and  $i = 1, 2, \dots, 10000$ .

The equations can be numerically iterated using the formulas above since in the limit  $dt \rightarrow 0$

$$\frac{x_{t+dt} - x_t}{dt} = -\beta x_t y_t$$

and similarly for  $y$  and  $z$ . Therefore small  $dt$ , equal to 0.1 in this case, can be used to simulate the equations numerically. These iterations were performed in R using the code

```
beta=0.01; gamma=0.01; rho=gamma/beta; x0=95; y0=5
dt=0.1
tt=c(0:10000)*dt
x=numeric(10001)
y=numeric(10001)
z=numeric(10001)
x[1]=x0
y[1]=100-x0
z[1]=0
for (i in 1:10000){
x[i+1]=x[i]-beta*x[i]*y[i]*dt
y[i+1]=y[i]+(beta*x[i]*y[i]-gamma*y[i])*dt
```

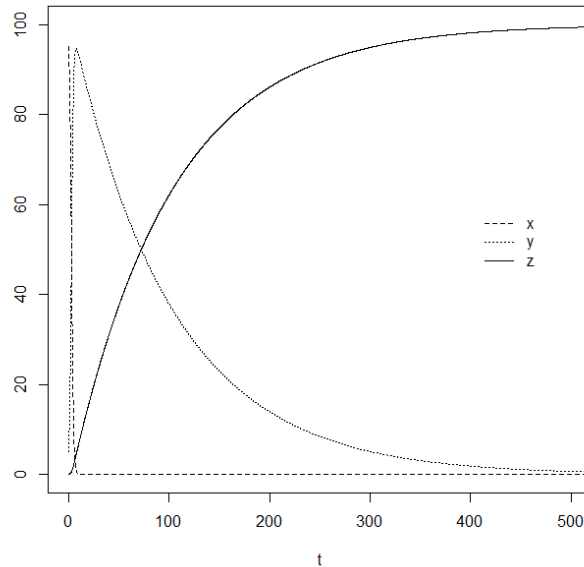


Figure 4.9: Numerical solutions to the number of susceptibles,  $x$ , infectives,  $y$ , and removals,  $z$ , for  $\beta = \gamma = 0.01$ ,  $n = 100$ ,  $y_0 = 5$ .

```

z[i+1]=z[i]+gamma*y[i]*dt
}
plot(tt,z,type="l",xlab="t",ylab="",xlim=c(0,500),ylim=c(0,100))
# shows z --> 100 as t --> infinity
points(tt,x,type="l",lty=2)
points(tt,y,type="l",lty=3)

```

Figure 4.9 illustrates how, in this example, the number of susceptibles converges to zero relatively quickly, and then the number of removals and infectives take a longer period of time to converge to  $z_\infty = 100$  and  $y_\infty = 0$ .

Figure 4.10 demonstrates how the number of susceptibles need not converge to zero. In this case, the parameters take the values  $n = 10$ ,  $y_0 = 1$ ,  $\beta = 0.05$  and  $\gamma = 0.7$ , causing  $x(t)$  to drop and converge to a value just below 8. Using the calculations at the end of Section 4.4.4, it is found that  $x_\infty = n - z_\infty = 7.561$ . Here all three solutions converge to their limiting values at roughly the same rate, in contrast to Figure 4.9.



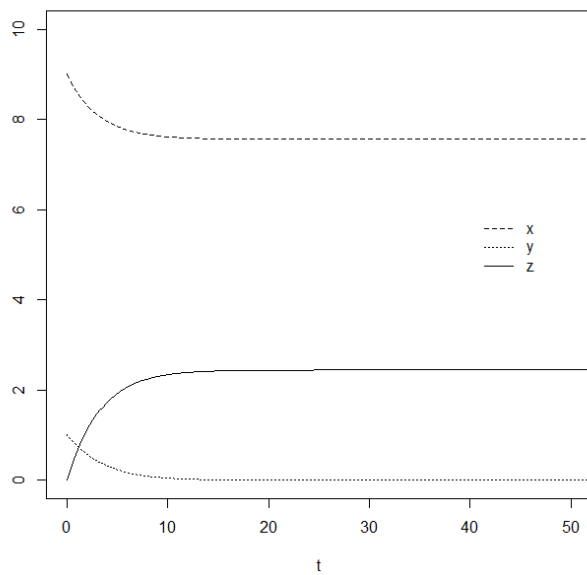


Figure 4.10: Numerical solutions to the number of susceptibles  $x(t)$ , infectives  $y(t)$  and removals  $z(t)$ , for  $\beta = 0.05$ ,  $\gamma = 0.7$ ,  $n = 10$ ,  $y_0=1$ .

# Chapter 5

## Introduction to Stochastic Modelling

As noted in Section 3.1, the spread of disease in large scale populations can be thought of as non-random and modelled deterministically. However when considering smaller population sizes, the statistical variation in the data becomes increasingly prevalent, and hence models used to investigate smaller population sizes need to take this into account.

Stochastic and Markovian processes can be used to model disease spread in this context. Variations of these models will be investigated in the following chapters, however this chapter is concerned with establishing some key points of stochastic theory that will be required to model epidemics in this way.

### 5.1 Stochastic processes

A stochastic process is a sequence of random variables which describe the evolution of some quantity in time or space. More formally, a stochastic process  $X$  is a collection of random variables  $X(t)$  for each  $t$  in some time set  $T$ . That is

$$X = \{X(t), t \in T\}.$$

Each  $X(t)$  describes the state of the process at time  $t$ , and the set of possible values that each  $X(t)$  can take is called the state space  $S$  of the stochastic process  $X$ . In general, both the time set  $T$  and the state space  $S$  can be discrete or continuous.

For a stochastic process at time  $t$ , the value of  $X(t)$  is known, since it has been observed. However, the future values are yet to occur so are unknown random variables. These future values may be influenced by the past and present values of the stochastic process.

For example, the number of susceptible members in an epidemic population can be thought of as a stochastic process  $X$ . At time  $t$ , the number of susceptibles is observed to be  $X(t)$  with

the future observations unknown as there is some probability that the disease will be transmitted or not transmitted. Hence these future observations can be treated as random variables.

## 5.2 Poisson processes

A Poisson process is an example of a continuous time stochastic process. It is a counting process which counts the number of events  $X(t)$  up to time  $t$ .

Formally,  $\{X(t), t \geq 0\}$  is a Poisson process if

1.  $X(0) = 0$  and  $X(s) \leq X(t)$  for  $s \leq t$ .
2. The process has independent and stationary increments, that is for non-overlapping intervals  $[s, s + h]$  and  $[t, t + h]$ ,  $X_{s+h} - X_s$  and  $X_{t+h} - X_t$  are independent and identically distributed.
3. Transitions occur one at a time, that is for small  $h$

$$Pr(X(t + h) - X(t) = 1) = \lambda h + o(h)$$

$$Pr(X(t + h) - X(t) > 1) = o(h)$$

$$Pr(X(t + h) - X(t) = 0) = 1 - \lambda h + o(h)$$

where  $o(h)$  is a function of small order such that  $\lim_{h \rightarrow 0} \frac{o(h)}{h} \rightarrow 0$ .

An alternative but equivalent definition, proved by Ross (1996, p231), replaces parts 2 and 3 of the above definition with the condition that the number of events occurring in any time interval of width  $h$  has a Poisson distribution with rate  $\lambda h$ . That is

$$Pr(X(t + h) - X(t) = x) = \frac{(\lambda h)^x e^{-\lambda h}}{x!}, \quad x = 0, 1, 2, \dots$$

Each increase in the value of the process can be thought of as an arrival, or birth, and since these events occur randomly, the times between these arrivals are also random. To investigate these inter-arrival times, let  $T_i$  be the time from the  $(i - 1)^{th}$  to the  $i^{th}$  observation. Considering the time  $T_1$  between zero and the first observation gives

$$\begin{aligned} F_{T_1}(t) &= Pr(T_1 \leq t) \\ &= Pr(X(t) \geq 1) \\ &= 1 - Pr(X(t) = 0) \\ &= 1 - \frac{(\lambda t)^0 e^{-\lambda t}}{0!} \\ &= 1 - e^{-\lambda t}. \end{aligned}$$

Hence the probability density function of  $T_1$  is

$$f_{T_1}(t) = \frac{d}{dt}F_{T_1}(t) = \lambda e^{-\lambda t}$$

for  $t \geq 0$ . This is the density of the exponential distribution with rate  $\lambda$ . Therefore the time between zero and the first observation is an exponential random variable with rate  $\lambda$ . Since these disjoint increments are independent and stationary, it must also be the case that each  $T_i$  is an independent exponential random variable with rate  $\lambda$ . Three independent realisations of a Poisson process with rate  $\lambda = 1$  are shown in Figure 5.1. This is done with the R code

```
T=rexp(10,1)
tt=c(0,T[1],T[1]+T[2],T[1]+T[2]+T[3],T[1]+T[2]+T[3]+T[4],
T[1]+T[2]+T[3]+T[4]+T[5],T[1]+T[2]+T[3]+T[4]+T[5]+T[6],
T[1]+T[2]+T[3]+T[4]+T[5]+T[6]+T[7],
T[1]+T[2]+T[3]+T[4]+T[5]+T[6]+T[7]+T[8],
T[1]+T[2]+T[3]+T[4]+T[5]+T[6]+T[7]+T[8]+T[9],
T[1]+T[2]+T[3]+T[4]+T[5]+T[6]+T[7]+T[8]+T[9]+T[10])
X=c(0,1,2,3,4,5,6,7,8,9,10)
plot(tt,X,type="s",xlab="Time t",ylab="X(t)")
```

In the top plot the time until the first observation  $T_1$  is 0.41, the middle plot has  $T_1 = 0.26$ , whereas in the bottom plot the value for  $T_1$  is 1.52. This highlights the randomness of the model.

The distribution of the time from zero until the  $n^{\text{th}}$  observation can be found. Let  $S_n = T_1 + \dots + T_n$ , then

$$\begin{aligned} 1 - F_{S_n}(t) &= Pr(T_1 + \dots + T_n \geq t) \\ &= Pr(X(t) \leq n). \end{aligned}$$

This is the case because if the time until the  $n^{\text{th}}$  observation is greater than or equal to  $t$ , then at most  $n$  observations can have occurred at time  $t$ . Hence

$$\begin{aligned} 1 - F_{S_n} &= \sum_{r=0}^{n-1} Pr(X(t) = r) \\ &= \sum_{r=0}^{n-1} \frac{(\lambda t)^r e^{-\lambda t}}{r!}. \end{aligned}$$

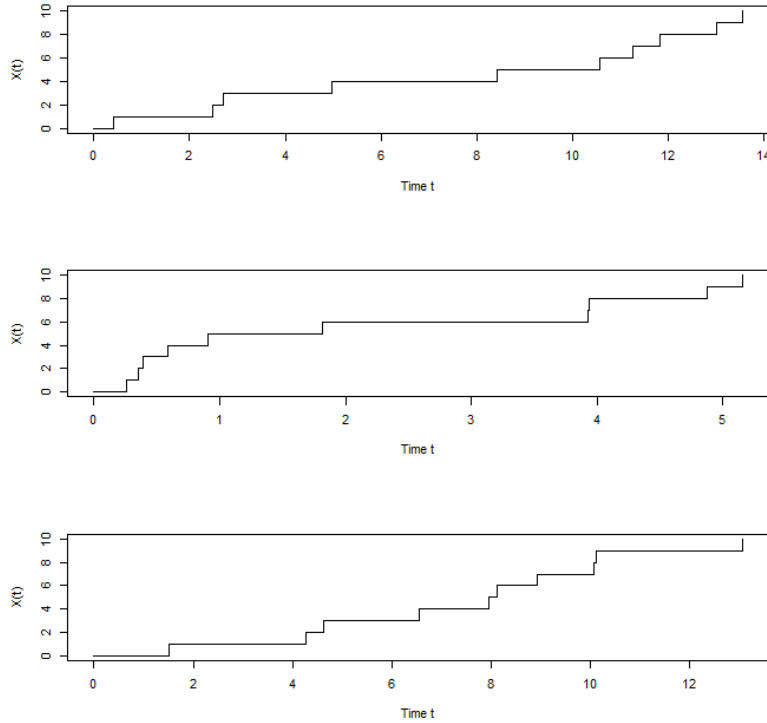


Figure 5.1: Three realisations of a Poisson process with rate  $\lambda = 1$ .

Therefore

$$\begin{aligned}
 f_{S_n}(t) &= \frac{d}{dt} F_{S_n}(t) \\
 &= \frac{d}{dt} \left( 1 - \sum_{r=0}^{n-1} \frac{(\lambda t)^r e^{-\lambda t}}{r!} \right) \\
 &= - \sum_{r=0}^{n-1} \left( \frac{r \lambda (\lambda t)^{r-1} e^{-\lambda t}}{r!} - \frac{\lambda (\lambda t)^r e^{-\lambda t}}{r!} \right) \\
 &= \frac{\lambda^n t^{n-1} e^{-\lambda t}}{(n-1)!}, \quad t \geq 0.
 \end{aligned}$$

This is the density of a gamma distribution with parameters  $n$  and  $\lambda$ , and hence  $S_n$  is a gamma distributed random variable with mean  $\frac{n}{\lambda}$  and variance  $\frac{n}{\lambda^2}$ .

### 5.3 Markov processes

A stochastic process is said to be a Markov process when it has the Markov property. In continuous time and discrete state space, Ross (1996, p231) defines a stochastic process  $\{X(t), t \geq 0\}$

to be a Markov process if for all  $h, t, u \geq 0$  with  $u \leq t$  and integers  $i, j, k$ ,

$$Pr(X(t+h) = j | X(t) = i, X(u) = k) = Pr(X(t+h) = j | X(t) = i).$$

In other words, knowledge of the process up until time  $t$  is irrelevant, as long as the value of the process at time  $t$  is known. A Poisson process is an example of this as it is just a counting process; knowing how it has evolved up until time  $t$  will have no influence on the future probabilities providing the value at time  $t$  is known.

In most epidemic models, it is assumed that the number of infectives at some future time depends only on the present number of infective members at time  $t$ , and knowing the evolution of infectives up until this time  $t$  does not change this. In this context disease spread can be modelled by a Markov process.

The conditional probabilities  $Pr(X(t+s) = j | X(t) = i)$  are known as the transition probabilities. A Markov process is said to be homogeneous when these transition probabilities depend only on  $s$ ; that is for  $s > 0$

$$Pr(X(t+h) = j | X(t) = i) = Pr(X(h) = j | X(0) = i).$$

When

$$Pr(X(t+h) = i | X(t) = i) = 1,$$

then state  $i$  is said to be an absorbing state. Once state  $i$  is reached, the process stays there with no chance of leaving.

### 5.3.1 Birth and death processes

A birth and death process is a special case of a continuous time Markov process, and builds on some of the ideas developed for Poisson processes. Consider a continuous time Markov process with discrete state space indexed by  $i = 0, 1, 2, \dots$ . In state  $i$ , births occur from a Poisson distribution with rate  $\lambda_i$  and independently deaths occur as a Poisson distribution with rate  $\mu_i$  for each state  $i = 0, 1, 2, \dots$ . This process is called a birth and death process when the only transitions possible from state  $i$  are to state  $i+1$  with rate  $\lambda_i$  or transition to state  $i-1$  at rate  $\mu_i$ . After a new birth or death has taken place, the process changes states and new transition rates can apply. Also,  $\mu_0 = 0$  and if the state space of the process has an upper limit  $n$  say, then  $\lambda_n = 0$ . This is illustrated in Figure 5.2. The transition probabilities for birth or death are then

$$\begin{aligned} Pr(X(t+h) = i+1 | X(t) = i) &= \lambda_i + o(h) \\ Pr(X(t+h) = i-1 | X(t) = i) &= \mu_i + o(h). \end{aligned}$$

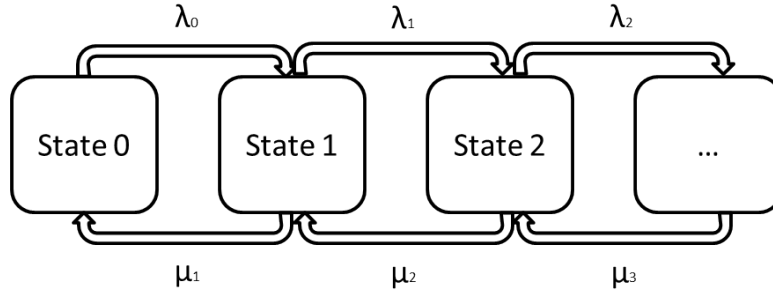


Figure 5.2: A birth and death process with birth rates  $\lambda_i$  and death rates  $\mu_i$ .

Note that since births occur independently of deaths, when in state  $i$  the time until the next birth is an exponentially distributed random variable with rate  $\lambda_i$  and the time until next death is an exponential distribution with rate  $\mu_i$ . Furthermore, since births and deaths are independent,

$$\begin{aligned}
 Pr(\text{transition before time } t) &= Pr(\text{death before } t \text{ or birth before } t) \\
 &= 1 - Pr(\text{no death before } t \text{ and no birth before } t) \\
 &= 1 - (e^{-\lambda_i t}) (e^{-\mu_i t}) \\
 &= 1 - e^{-(\lambda_i + \mu_i)t}
 \end{aligned}$$

shows that the time until the next transition from state  $i$  is a exponential random variable with rate  $\lambda_i + \mu_i$ .

Setting  $\mu_i = 0$  and  $\lambda_i = \lambda$  for all  $i$ , gives the Poisson process considered in Section 5.2. Taking  $\mu_i = 0$  for all  $i$  is called a pure birth process and  $\lambda_i = 0$  for all  $i$  is called a pure death process.

In the context of modelling the simple epidemic stochastically, susceptibles and infectives make up the whole closed population. This means the state of one of the two random variables denoting susceptible and infective members uniquely determines the whole system.

# Chapter 6

## The Simple Stochastic Epidemic

### 6.1 Modelling the simple epidemic stochastically

In the simple stochastic model, much like the deterministic model in Chapter 3, infective and susceptible members make up the closed population, with no removals. Once a population member is infective they remain in that state.

Let number of susceptibles and infectives at time  $t$  be denoted by the discrete random variables  $X(t)$  and  $Y(t)$  respectively and let the vector  $\mathbf{U}(t) = (X(t), Y(t))$ . Here the initial conditions are  $\mathbf{U}(0) = (N, I)$  with  $I \geq 1$  and  $N \geq 1$ , otherwise the epidemic would not begin and there would be no need for further investigation. The closed population constraint imposes the result  $X(t) + Y(t) = N + I$  for all  $t$ . This is a change of notation from the deterministic model, where the population had total size  $n$ , however for the stochastic model it is more convenient to initialise the population into two explicit classes,  $N$  and  $I$ . Once more homogeneous mixing between all population members is assumed. Note that here the states  $i, j$  must be nonnegative as they are representing the size of the susceptible and infective population classes respectively.

Now  $\{\mathbf{U}(t), t \geq 0\}$  can be viewed as a multivariate stochastic process in continuous time, indexed by the state space  $\{(i, j) : i, j \in \mathbb{Z}^+, 0 \leq i \leq N, I \leq j \leq N + I\}$ . In the simple epidemic,  $i$ , denoting the number of susceptibles, decreases from  $N$  to 0 through time as more susceptible members become infective. This causes  $j$  to increase from  $I$ , the initial number of infective members, to contain the whole population,  $N + I$ . This model can be investigated using the tools developed in Chapter 5.



## 6.2 Modelling the epidemic as a Poisson process

For a very simplistic stochastic model, suppose it could be assumed that the probability at which members transition from susceptible to infective is independent of the number of infectives and susceptibles. If this is the case, then susceptible members become infected at some constant rate  $\lambda > 0$ . This is not usually assumed to be the case in an epidemic, however viewing the epidemic as a Poisson process provides a good place to start when beginning to build the stochastic epidemic model.

Due to the closed population constraint, the number of susceptibles, or alternatively the number of infectives, uniquely determines the whole system at time  $t$ . With this construction, the number of new infectives  $Y^*(t)$  is a Poisson process. The number of new infectives is defined here as the number of susceptibles that become infective, in effect not counting the initial number of infectives  $I$ . It is to satisfy the definition of a Poisson process in Section 5.2, that  $Y^*(0) = 0$ . This system has an absorbing state  $Y^*(t) = N$ , as once all the initial  $N$  susceptible population members have become infected, the epidemic is over, and no more counting can be done.

Then in a small time period  $h$ , the only possible events are one susceptible member transitions into the infective state, which occurs with probability  $\lambda h + o(h)$ , or there are no transitions, which occurs with probability  $1 - \lambda h + o(h)$ . Formally these transition probabilities are

$$Pr(\mathbf{U}(t+h) = (i-1, j+1) | \mathbf{U}(t) = (i, j)) = Pr(Y^*(t+h) = j+1 | Y^*(t) = j) = \lambda h + o(h)$$

$$Pr(\mathbf{U}(t+h) = (i, j) | \mathbf{U}(t) = (i, j)) = Pr(Y^*(t+h) = j | Y^*(t) = j) = 1 - \lambda h + o(h)$$

for  $I \leq j \leq N+I$ ,  $i = N+I-j$  and absorbing state  $Y^*(t) = N$ . This means the probability of a new infective occurring in the period  $(t, t+h)$  is  $\lambda h$  when the total number of new infectives is between 0 and  $N$ , and 0 otherwise. Therefore, from Section 5.2, the time between new infectives occurring is an exponential distribution with parameter  $\lambda$  for  $0 \leq Y^*(t) \leq N$ .

### 6.2.1 Time to full infection

Also from Section 5.2, the time to full infection is a gamma  $(N, \lambda)$  random variable, meaning the mean time to full infection would be  $\frac{N}{\lambda}$ .

For example consider a family with one infective member and three susceptible members, with constant infection rate independent of the number of infectives and susceptibles of  $\lambda = 0.5$  per unit time. The time to full infection is expected to be  $\frac{3}{0.5} = 6$ .

In comparison, the deterministic time to full infection in Section 3.3.2 with equivalent parameters, a population size  $n = 4$ ,  $y_0 = 1$  and infection rate parameter  $\beta = 0.5$  gives a time to full infection of

$$T = \frac{1}{0.5 \times 4} \ln \left( \frac{2(4 - \frac{1}{2})(4 - 1)}{1} \right) = 1.52.$$

Furthermore for a population of size 100 with  $I = 5$  and  $N = 95$ , taking  $\lambda = 0.01$  gives the same initial parameters as discussed in Section 3.5. The Poisson process time to full infection for these parameters is

$$\frac{95}{0.01} = 9500.$$

This is a huge difference from the deterministic time to full infection, derived in Section 3.5 as 8.24. This is to be expected as in the deterministic model the transitions depend on which state the system is currently in, whereas when modelling the system as a Poisson process the probability of a transition at each state is the same. This emphasises the fact that the modelling of an epidemic as a Poisson process with constant infection rate independent of the number of susceptibles and infectives is not an adequate model. This simple model is too basic to take state dependence into account, so the model needs to be refined to give a more accurate description of what is going on.

### 6.3 Modelling the epidemic as a Markov process

To improve the model suggested in Section 6.2, the infection rate parameter can be given dependence on the number of susceptibles and infectives at that time  $\lambda_{ij}$ . To give the simplest dependence on the states,  $\lambda_{ij}$  is set to be proportional to the number of infectives and susceptibles by taking  $\lambda_{ij} = \lambda ij$ . Note that this is different from the deterministic setting, where the infection rate parameter was denoted by  $\beta$  instead of  $\lambda$ .

By returning to the notation of  $\mathbf{U}(t) = (X(t), Y(t))$  for a population of size  $N + I$ , with  $\mathbf{U}(0) = (N, I)$ , the only non zero transition probabilities in some small time  $h$  are suggested by Daley and Gani (1999, p57) to be

$$\begin{aligned} Pr(\mathbf{U}(t+h) = (i-1, j+1) | \mathbf{U}(t) = (i, j)) &= \lambda hij + o(h) \\ Pr(\mathbf{U}(t+h) = (i, j) | \mathbf{U}(t) = (i, j)) &= 1 - \lambda hij + o(h) \end{aligned} \tag{6.1}$$

with absorbing state  $\mathbf{U}(t) = (0, N + I)$ . Again, since only susceptibles and infectives make up the whole closed population, the state of one of the two random variables uniquely determines the whole system as  $\mathbf{U}(t) = (X(t), N + I - X(t)) = (N + I - Y(t), Y(t))$ . Therefore the transition probability

$$Pr(\mathbf{U}(t+h) = (i-1, j+1) | \mathbf{U}(t) = (i, j)) = \lambda hij + o(h)$$

can be considered as

$$Pr(Y(t+h) = j+1 | Y(t) = j) = \lambda j(N+I-j)h + o(h)$$

and similarly

$$Pr(\mathbf{U}(t+h) = (i, j) | \mathbf{U}(t) = (i, j)) = 1 - \lambda h i j + o(h)$$

becomes

$$Pr(Y(t+h) = j | Y(t) = j) = 1 - \lambda j(N+I-j)h + o(h).$$

Therefore  $Y(t)$  can be thought of as a pure birth process because the number of infectives can only increase and  $X(t)$  can be thought of as a pure death process, since the number of susceptibles cannot increase.

## 6.4 Time to full infection

By taking  $Y(t)$  as a pure birth process with rate  $\lambda_j = \lambda j(N+I-j)$ , the time spent in state  $j$ ,  $T_j$ , is an exponential distribution with rate  $\lambda_j(N+I-j)$ . Therefore the expected time spent in state  $j$  is  $E(T_j) = \frac{1}{\lambda j(N+I-j)}$ . By combining all these expectations, the expected time to full infection is

$$T = T_I + \dots + T_{N+I} = \sum_{j=I}^{N+I} \frac{1}{\lambda j(N+I-j)}.$$

### 6.4.1 Numerical example of finding the time to full infection

For example, consider the system determined by  $\mathbf{U}(0) = (3, 1)$ . Starting with one initial infective  $j = I = 1$ , the time  $T_1$  until the transition to two infectives is an exponentially distributed random variable with rate  $\lambda_1 = \lambda(3+1-1) = 3\lambda$ . Similarly the time  $T_2$  between the first and second infections, during which there are two infectives and two susceptibles is an exponentially distributed random variable with parameter  $4\lambda$ . Finally the same reasoning gives  $T_3 \sim \exp(3\lambda)$ .

The expected time to full infection is then  $E(T_1 + T_2 + T_3)$ , since after the third transition from susceptible to infective the whole population will be infected. Since these times are independent, for  $T_1 \sim \exp(3\lambda)$ ,  $T_2 \sim \exp(4\lambda)$  and  $T_3 \sim \exp(3\lambda)$ , the expected time to full infection is found to be

$$E(T_1 + T_2 + T_3) = \frac{1}{3\lambda} + \frac{1}{4\lambda} + \frac{1}{3\lambda} = \frac{11}{12\lambda}. \quad (6.2)$$

## 6.4.2 Finding the density for the numerical example

In addition to just the expectation, the probability density function of the random variable  $T = T_1 + T_2 + T_3$  can be obtained. To do this, firstly consider the time  $T_1$  until the first transition from susceptible to infective. Since  $T_1$  is exponentially distributed with rate  $3\lambda$  it has cumulative distribution function

$$F_{T_1}(t) = Pr(T_1 \leq t) = 1 - e^{-3\lambda t}.$$

Then by considering all possible transition times  $u$  for the first transition,

$$\begin{aligned} F_{T_1+T_2}(t) &= Pr(T_1 + T_2 \leq t) = \int_0^t Pr(T_1 + T_2 \leq t | T_1 = u) f_{T_1}(u) du \\ &= \int_0^t Pr(T_2 \leq t - u) f_{T_1}(u) du \\ &= \int_0^t (1 - e^{-4\lambda(t-u)}) 3\lambda e^{-3\lambda u} du \\ &= \int_0^t 3\lambda e^{-3\lambda u} - 3\lambda e^{\lambda u} \cdot e^{-4\lambda t} du \\ &= [-e^{-3\lambda u}]_{u=0}^{u=t} - e^{-4\lambda t} [3e^{\lambda u}]_{u=0}^{u=t} \\ &= -e^{-3\lambda t} + 1 - 3e^{-3\lambda t} + 3e^{-4\lambda t} \\ &= 1 - 4e^{-3\lambda t} + 3e^{-4\lambda t}. \end{aligned}$$

Therefore the probability density of  $T_1 + T_2$  is

$$\begin{aligned} f_{T_1+T_2}(t) &= \frac{d}{dt} F_{T_1+T_2}(t) \\ &= 12\lambda e^{-3\lambda t} - 12\lambda e^{-4\lambda t}, \quad t > 0. \end{aligned}$$

Repeating this procedure including  $T_3$  will lead to the probability density of  $T = T_1 + T_2 + T_3$ . Firstly the cumulative distribution function  $F_T(t)$  is

$$\begin{aligned} Pr(T \leq t) &= \int_0^t Pr(T_1 + T_2 + T_3 \leq t | T_1 + T_2 = u) f_{T_1+T_2}(u) du \\ &= \int_0^t (1 - e^{-3\lambda(t-u)}) (12\lambda e^{-3\lambda u} - 12\lambda e^{-4\lambda u}) du \\ &= \int_0^t 12\lambda e^{-3\lambda u} - 12\lambda e^{-4\lambda u} - 12\lambda e^{-3\lambda t} + 12\lambda e^{-3\lambda t} e^{-\lambda u} du \\ &= [-4e^{-3\lambda u} + 3e^{-4\lambda u} - 12\lambda u e^{-3\lambda t} - 12e^{-3\lambda t} e^{-\lambda u}]_{u=0}^{u=t} \\ &= -4e^{-3\lambda t} + 4 + 3e^{-4\lambda t} - 3 - 12\lambda t e^{-3\lambda t} - 12e^{-4\lambda t} + 12e^{-3\lambda t} \\ &= 8e^{-3\lambda t} - 9e^{-4\lambda t} - 12\lambda t e^{-3\lambda t} + 1. \end{aligned}$$

Therefore the probability density function of  $T$  is found to be

$$\begin{aligned} f_T(t) &= \frac{d}{dt}F_T(t) = -24\lambda e^{-3\lambda t} + 36\lambda e^{-4\lambda t} - 12e^{-3\lambda t} + 36\lambda t e^{-3\lambda t} \\ &= 36\lambda e^{-4\lambda t} - 36\lambda e^{-3\lambda t} + 36\lambda^2 t e^{-3\lambda t}, \quad t > 0. \end{aligned}$$

Noting that the time  $t$  could possibly take any value greater than zero, the expected time to full infection for this example can be calculated as

$$\begin{aligned} E(T) &= \int_0^\infty t f_T(t) dt \\ &= \int_0^\infty (36\lambda t e^{-4\lambda t} - 36\lambda t e^{-3\lambda t} + 36\lambda^2 t^2 e^{-3\lambda t}) dt. \end{aligned}$$

After integrating each respective term by parts this becomes

$$E_T(t) = -\frac{4}{\lambda} + \frac{9}{4\lambda} + \frac{8}{3\lambda} = \frac{11}{12\lambda}$$

which agrees with equation (6.2).

Plots of the densities of  $f_{T_1}(t)$ ,  $f_{T_1+T_2}(t)$  and  $f_T(t)$  with  $\lambda = 0.5$  are shown in Figure 6.1. The density  $f_{T_1}(t)$  looks like an exponential distribution as expected. The subsequent densities illustrate the logical fact that each time another observation is included, the expected value increases as previous events have to be observed first. This is illustrated by more of the probability density under each of the successive density lines shifting to later times.

### 6.4.3 Comparison of times to full infection

For the example discussed in Section 6.2.1 with one initial infective and three initial susceptibles, the stochastic model gives the time to full infection to be  $\frac{11}{12 \times 0.5} = 1.83$ . This is much closer to the 1.52 time units to full infection predicted by the deterministic model than the 6.00 predicted from the Poisson model. This seems to reinforce the suggestion that forcing the infection rate to have no dependence on the number of susceptibles and infectives makes a big difference to analysis of an epidemic.

The difference between the time to full infection for the three models with three initial susceptibles and one initial infective across different infection rate parameter values is illustrated in Figure 6.2. Here, the time to full infection of all three models diverges to infinity as the infection rate parameter approaches zero value, and the time to full infection of all three models converges to zero for large infection rate parameter values. However, in between these two values, the stochastic and deterministic models are much better matched than the Poisson model, again suggesting that the stochastic model is more appropriate than the Poisson model.

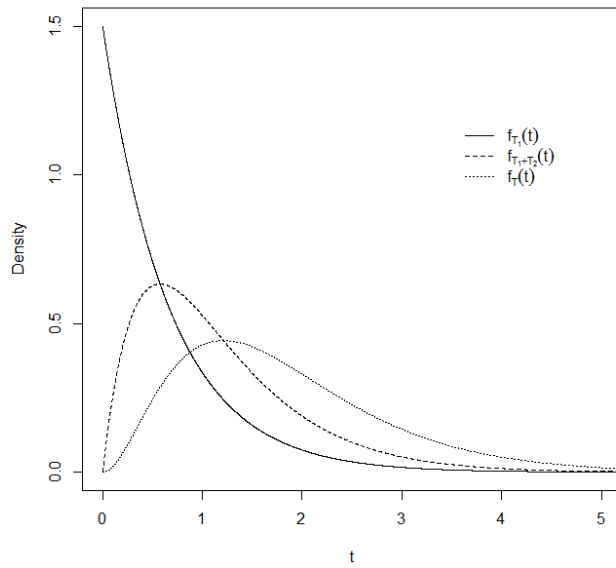


Figure 6.1: Plots of the densities of  $f_{T_1}(t)$ ,  $f_{T_1+T_2}(t)$  and  $f_T(t)$  with  $\lambda = 0.5$ .

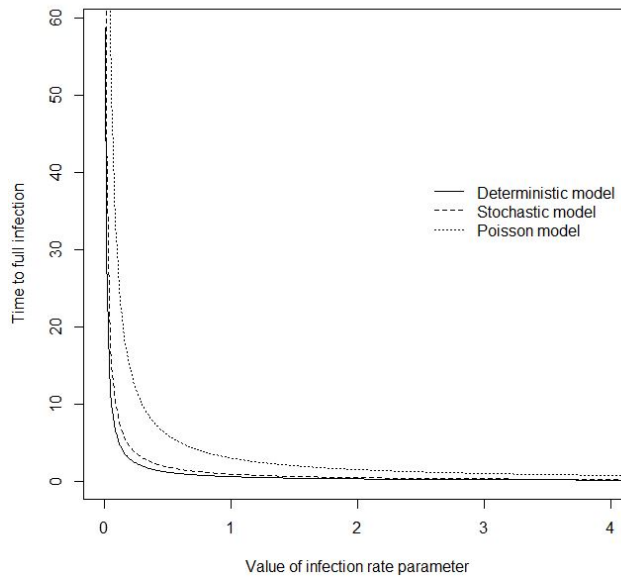


Figure 6.2: Times to full infection plotted against the value of infection rate parameter  $\lambda$  for  $I = 1$  and  $N = 3$ .

By using a similar method as the one used in this section, the density for the total of any number of transition times can be found, however this would be very labour intensive, so a slightly different way of approaching the model in equation (6.1) is required. This will be done by using the Laplace transform, suggested by Daley and Gani (1999, p59) and Bailey (1957, p39) and produced in more detail in the following subsection.

## 6.5 Deriving Kolmogorov equations for the epidemic

Writing equation (6.1) in terms of  $X(t)$  gives

$$\begin{aligned} Pr(X(t+h) = i-1 | X(t) = i) &= \lambda i(N+I-i)h + o(h) \\ Pr(X(t+h) = i | X(t) = i) &= 1 - \lambda i(N+I-i)h + o(h) \end{aligned}$$

with an absorbing state at  $X(t) = 0$ , because in the simple epidemic once all susceptibles are infected, the epidemic is over.

Denoting  $p_i(t) = Pr(X(t) = i | X(0) = N)$ , consider all possible transitions for state  $i$ , where  $0 < i < N$  over a small time period  $h$ . To be in state  $i$  at time  $t+h$  the system could be in state  $i+1$  at time  $t$ , and transition down in the short time period  $h$ , which happens with probability  $\lambda(i+1)(N+I-i-1)h + o(h)$ . Alternatively, the system could be in state  $i$  at time  $t$ , and remain in that state through time period  $h$ , which happens with probability  $1 - \lambda i(N+I-i)h + o(h)$ . For small enough  $h$ , and since the number of susceptibles can only remain the same or decrease, these are the only two transitions that can occur. This leads to the equation

$$\begin{aligned} p_i(t+h) &= p_{i+1}(t) [\lambda(i+1)(N+I-i-1)h + o(h)] \\ &\quad + p_i(t) [1 - \lambda i(N+I-i)h + o(h)]. \end{aligned}$$

Rearranging and dividing through by  $h$  gives

$$\frac{p_i(t+h) - p_i(t)}{h} = \lambda(i+1)(N+I-i-1)p_{i+1}(t) - \lambda i(N+I-i)p_i(t) + \frac{o(h)}{h}$$

and in the limit as  $h \rightarrow 0$ ,

$$\frac{dp_i(t)}{dt} = \lambda(i+1)(N+I-i-1)p_{i+1}(t) - \lambda i(N+I-i)p_i(t) \quad (6.3)$$

for  $i = 1, \dots, N-1$ .

Upon closer inspection, equation (6.3) also holds for the case  $i = 0$ . Since  $i = 0$ , the negative term in equation (6.3) disappears, leaving

$$\frac{dp_0(t)}{dt} = \lambda(N+I-1)p_1(t). \quad (6.4)$$

Finally, by defining  $p_{N+1}(t) = 0$  for all  $t$  so that it is impossible to have more than  $N$  susceptibles infected over the course of the epidemic, equation (6.3) also holds for the case  $i = N$ , giving

$$\frac{dp_N(t)}{dt} = -\lambda N I p_N(t). \quad (6.5)$$

Therefore by defining  $p_{N+1}(t) = 0$  for all  $t$ , equation (6.3) holds for  $i = 0, \dots, N$ . In the general case, these kind of equations relating the time differential of the state probabilities to the transition rates and the probabilities themselves are called the forward Kolmogorov equations. Equations (6.3), (6.4) and (6.5) are an example of the forward Kolmogorov equations for the simple epidemic.

Direct solving of these equations is difficult, however Bailey (1957, p39) outlines how the use of the Laplace transform can be used to simplify the solution, which is given in more detail below.

## 6.6 The Laplace transform

The Laplace transform is an integral transform that can be used to obtain solutions to some equations in a simpler way than direct computation, explained further by Braun (1983, p223).

The Laplacian operator  $\mathcal{L}$  acting on the probability  $p_i(t)$ , which is continuous between 0 and 1, gives the Laplace transform  $\mathcal{L}[p_i(t)] = \hat{p}_i(\theta)$  which is defined to be

$$\mathcal{L}[p_i(t)] = \hat{p}_i(\theta) = \int_0^{\infty} e^{-\theta t} p_i(t) dt \quad (6.6)$$

with  $0 \leq i \leq N$  and  $\text{Re}(\theta) > 0$ ; further details about Laplace transforms are included in Rainville (1963) and Davies (1978).

Equations (6.3), (6.4) and (6.5) can be transformed into the  $\theta$  domain by equation (6.6), then solved and converted back into the  $t$  domain by inverting the Laplace transform. To conclude this subsection, two important transforms and one important transform property will be proved which will be required later.



### 6.6.1 Properties of the Laplace transform

For constant  $a$ , if  $p(t) = e^{at}$ , then

$$\begin{aligned}\hat{p}(\theta) &= \int_0^{\infty} e^{at} e^{-\theta t} dt \\ &= \left[ -\frac{1}{\theta - a} e^{-(\theta - a)t} \right]_0^{\infty} \\ &= \frac{1}{\theta - a}.\end{aligned}\tag{6.7}$$

If  $p(t) = te^{at}$ , then

$$\hat{p}(\theta) = \int_0^{\infty} te^{-(\theta - a)t} dt.$$

Integrating by parts gives

$$\begin{aligned}\hat{p}(\theta) &= \left[ \frac{-t}{\theta - a} e^{-(\theta - a)t} \right]_0^{\infty} + \int_0^{\infty} \frac{1}{\theta - a} e^{-(\theta - a)t} dt \\ &= \left[ -\frac{1}{(\theta - a)^2} e^{-(\theta - a)t} \right]_0^{\infty} \\ &= \frac{1}{(\theta - a)^2}.\end{aligned}\tag{6.8}$$

Finally, the Laplace transform has the linearity property. For functions  $f_1(t)$ ,  $f_2(t)$  and constants  $a$  and  $b$ ,

$$\begin{aligned}\mathcal{L}[af_1(t) + bf_2(t)] &= \int_0^{\infty} (af_1(t) + bf_2(t)) e^{-\theta t} dt \\ &= a \int_0^{\infty} f_1(t) e^{-\theta t} dt + b \int_0^{\infty} f_2(t) e^{-\theta t} dt \\ &= a\hat{f}_1(t) + b\hat{f}_2(t).\end{aligned}\tag{6.9}$$

### 6.6.2 Applying the Laplace transform to the model

Applying the Laplace transform to equation (6.4) gives

$$\int_0^{\infty} e^{-\theta t} \frac{dp_0(t)}{dt} dt = \int_0^{\infty} \lambda(N + I - 1) p_1(t) dt.$$

Integrating by parts gives

$$\left[ -p_0(t) e^{-\theta t} \right]_0^{\infty} + \theta \int_0^{\infty} p_0(t) e^{-\theta t} dt = \lambda(N + I - 1) \hat{p}_1(t)\tag{6.10}$$

and because the system starts with  $N$  susceptibles,  $p_N(0) = 1$ , this means  $p_0(0) = 0$  which causes the square bracket term to be zero at  $t = 0$ . The exponential to a negative power causes the square bracket term to be zero as  $t \rightarrow \infty$ . Equation (6.10) then becomes

$$\theta \hat{p}_0(t) = \lambda(N + I - 1) \hat{p}_1(\theta).$$

Hence

$$\hat{p}_0(t) = \frac{\lambda(N + I - 1)}{\theta} \hat{p}_1(\theta).$$

Applying the same method to equations (6.5) and (6.3) gives the results

$$\hat{p}_N(t) = \frac{1}{\theta + \lambda NI}$$

and

$$\hat{p}_i(t) = \frac{\lambda(i + 1)(N + I - i - 1)}{\theta + \lambda i(N + I - i)} \hat{p}_{i+1}(\theta)$$

for  $1 \leq i \leq N - 1$ .

This set of equations can be solved recursively from  $\hat{p}_N(\theta)$  to give

$$\hat{p}_i(\theta) = \prod_{j=i}^{N-1} \frac{\lambda(j + 1)(N + I - j - 1)}{\theta + \lambda j(N + I - j)} \cdot \frac{1}{\theta + \lambda NI} \quad (6.11)$$

for  $0 \leq i \leq N - 1$ . This is the corrected form of the incorrect formula given in Daley and Gani (1999, p60). This method can be used for any number of susceptibles and infectives. However inverting each Laplace transform for a large population will again be labour intensive.

### 6.6.3 Applying the Laplace transform to an example

Consider again the example with  $N = 3$ ,  $I = 1$  and  $\lambda = 0.5$ . Using equation (6.11), the Laplace transforms of the probabilities are

$$\begin{aligned} \hat{p}_3(\theta) &= \frac{1}{\theta + 1.5} \\ \hat{p}_2(\theta) &= \frac{1.5}{(\theta + 1.5)(\theta + 2)} \\ \hat{p}_1(\theta) &= \frac{3}{(\theta + 1.5)^2(\theta + 2)} \\ \hat{p}_0(\theta) &= \frac{4.5}{\theta(\theta + 1.5)^2(\theta + 2)}. \end{aligned}$$

These transforms can now be inverted using partial fractions and the three facts proved in Section 6.6.1 to give

$$p_3(t) = e^{-1.5t} \quad (6.12)$$

$$p_2(t) = 3(e^{-1.5t} - e^{-2t}) \quad (6.13)$$

$$p_1(t) = 12e^{-2t} - 12e^{-1.5t} + 6te^{-1.5t} \quad (6.14)$$

$$p_0(t) = 1 - 9e^{-2t} + 8e^{-1.5t} - 6te^{-1.5t} \quad (6.15)$$

for all  $t \geq 0$ . The method is shown below for the case of  $p_1(t)$ , and the working for the other three probabilities follows the same approach.

Firstly, using partial fractions

$$\hat{p}_1(\theta) = \frac{3}{(\theta + 1.5)^2(\theta + 2)} = \frac{A}{\theta + 2} + \frac{B}{\theta + 1.5} + \frac{C}{(\theta + 1.5)^2},$$

where  $A, B$  and  $C$  are constants to be determined. Multiplying through by  $(\theta + 1.5)^2(\theta + 2)$  leads to

$$3 = A(\theta + 1.5)^2 + B(\theta + 2)(\theta + 1.5) + C(\theta + 2).$$

Now, substituting  $\theta = -1.5$  gives  $C = 6$ ,  $\theta = -2$  gives  $A = 12$  and  $\theta = -1$  gives  $B = -12$ . Hence

$$\hat{p}_1(\theta) = \frac{3}{(\theta + 1.5)^2(\theta + 2)} = \frac{12}{\theta + 2} - \frac{12}{\theta + 1.5} + \frac{6}{(\theta + 1.5)^2}.$$

Finally, using equations (6.7), (6.8) and (6.9) to invert the Laplace transforms gives

$$p_1(t) = 12e^{-2t} - 12e^{-1.5t} + 6te^{-1.5t}$$

as required.

The four probabilities in equations (6.12) to (6.15) are plotted against time  $t$  in Figure 6.3.

By looking at equations (6.12) to (6.15) and as illustrated by Figure 6.3, as  $t \rightarrow \infty$ ,  $p_0(t) \rightarrow 1$  whilst the other three probabilities tend to zero. This means that for large  $t$ , the probability that there are no susceptible members left tends to unity. This reinforces the result that in the simple epidemic, all susceptible members become infected.

Furthermore, for small  $t$ , the probability density of  $p_3(t)$  is the largest, implying that at this time it is most likely that there has been no new infections. Following this, both  $p_2(t)$  and  $p_1(t)$  have very short periods when they take the largest value respectively, meaning that one and two new infections are most likely at these times respectively. The fact that  $p_2(t)$  spends the least time being most likely is because when there are two susceptibles remaining, there

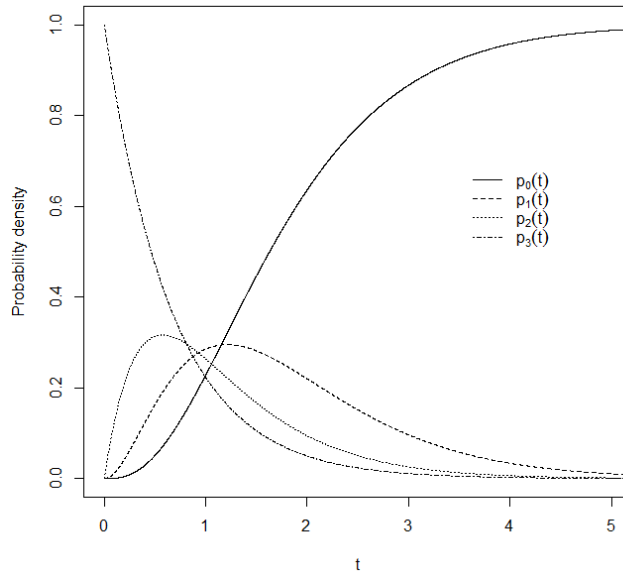


Figure 6.3: Probabilities  $p_0(t)$ ,  $p_1(t)$ ,  $p_2(t)$ ,  $p_3(t)$  plotted against  $t$ , with  $N = 3$ ,  $I = 1$  and  $\lambda = 0.5$ .

are two infectives, so contact between infectives and susceptibles is most likely to occur. This is similar to the deterministic case derived in equation (3.8), which shows the infection rate is quickest when the number of infectives is half of the total population. Finally, once  $p_0(t)$  becomes largest it will remain so, as once full infection is most likely, passing time will only make it more likely.

## 6.7 Probability generating functions

An alternative method to solving the differential equations using the Laplace transform, and one that returns an important final result, is to consider the probability generating function of the probabilities given by equation (6.3).

### 6.7.1 Properties of probability generation functions

The probability generating function  $G(z, t)$  of a Markov chain  $X(t)$  with  $N + 1$  possible states is defined by Iosifescu (1980, p34) to be

$$\begin{aligned} G(z, t) &= E(z^{X(t)}) = \sum_{i=0}^N Pr(X(t) = i | X(0) = N) z^i \\ &= \sum_{i=0}^N p_i(t) z^i \end{aligned}$$

where the series is absolutely convergent for  $|z| \leq 1$ . Furthermore, for  $1 \leq r \leq N$ , the probability generating function has the important property that

$$\lim_{z \rightarrow 1^-} \frac{\partial^r G(z, t)}{\partial z^r} = E(X(X-1)\dots(X-r+1)).$$

This is because, assuming the order of the sum and differentiation can be changed,

$$\begin{aligned} \lim_{z \rightarrow 1^-} \frac{\partial^r G(z, t)}{\partial z^r} &= \lim_{z \rightarrow 1^-} \frac{\partial^r}{\partial z^r} \sum_{i=0}^N p_i(t) z^i \\ &= \lim_{z \rightarrow 1^-} \sum_{i=0}^N p_i(t) \frac{d^r z^i}{dz^r} \\ &= \lim_{z \rightarrow 1^-} \sum_{i=0}^N p_i(t) i(i-1)\dots(i-r+1) z^{i-r} \\ &= \sum_{i=0}^N p_i(t) i(i-1)\dots(i-r+1) \\ &= E(X(t)(X(t)-1)\dots(X(t)-r+1)). \end{aligned}$$

Note also that

$$\frac{\partial G(z, t)}{\partial t} = \sum_{i=0}^N \frac{dp_i(t)}{dt} z^i, \quad (6.16)$$

$$\frac{\partial G(z, t)}{\partial z} = \sum_{i=1}^N i p_i(t) z^{i-1} = \sum_{i=0}^N i p_i(t) z^{i-1} \quad (6.17)$$

and

$$\frac{\partial^2 G(z, t)}{\partial z^2} = \sum_{i=2}^N i(i-1) p_i(t) z^{i-2} = \sum_{i=0}^N i(i-1) p_i(t) z^{i-2}. \quad (6.18)$$

## 6.7.2 Application to the state probabilities

Substituting equation (6.3) in for  $\frac{dp_i(t)}{dt}$  in equation (6.16) gives

$$\begin{aligned} \frac{\partial G(z, t)}{\partial t} &= \sum_{i=0}^N \frac{dp_i(t)}{dt} z^i \\ &= \sum_{i=0}^N \lambda z^i [-i(N+I)p_i(t) + i^2 p_i(t) + (i+1)(N+I)p_{i+1}(t) - (i+1)^2 p_{i+1}(t)] \\ &= \sum_{i=0}^N \lambda z^i [-i(N+I)p_i(t) + i^2 p_i(t)] + \sum_{i=0}^{N-1} \lambda z^i [(i+1)(N+I)p_{i+1}(t) - (i+1)^2 p_{i+1}(t)] \end{aligned}$$

as recalling that  $p_{N+1}(t) = 0$  means the second sum is zero when  $i = N$ . Writing  $j = i$  in the first sum, and  $j = i + 1$  in the second sum leads to

$$\frac{\partial G(z, t)}{\partial t} = \sum_{j=0}^N \lambda z^j [-j(N+I)p_j(t) + j^2 p_j(t)] + \sum_{j=1}^N \lambda z^{j-1} [j(N+I)p_j(t) - j^2 p_j(t)].$$

By writing  $j^2 = j(j-1) + j$  and because the second sum would be zero when  $j = 0$ , the  $j = 0$  term can be included in the sum, giving

$$\begin{aligned} \frac{\partial G(z, t)}{\partial t} &= \sum_{j=0}^N \lambda z^j [-j(N+I)p_j(t) + j(j-1)p_j(t) + jp_j(t)] \\ &\quad + \sum_{j=0}^N \lambda z^{j-1} [j(N+I)p_j(t) - j(j-1)p_j(t) - jp_j(t)] \\ &= \sum_{j=0}^N \lambda z^j [-j(N+I-1)p_j(t) + j(j-1)p_j(t)] + \lambda z^{j-1} [j(N+I-1)p_j(t) - j(j-1)p_j(t)]. \end{aligned}$$

Taking a single factor of  $z$  into the brackets in the first sum gives

$$\begin{aligned} \frac{\partial G(z, t)}{\partial t} &= \sum_{j=0}^N \lambda z^{j-1} [-zj(N+I-1)p_j(t) + zj(j-1)p_j(t) + j(N+I-1)p_j(t) - j(j-1)p_j(t)] \\ &= \sum_{j=0}^N \lambda z^{j-1} [(z-1)j(j-1)p_j(t)] - z^{j-1} [(z-1)j(N+I-1)p_j(t)] \\ &= \lambda z(z-1) \sum_{j=0}^N z^{j-2} j(j-1)p_j(t) - \lambda(z-1) \sum_{j=0}^N z^{j-1} j(N+I-1)p_j(t) \end{aligned}$$

and by recalling equations (6.17) and (6.18) this is

$$\frac{\partial G(z, t)}{\partial t} = \lambda z(z-1) \frac{\partial^2 G(z, t)}{\partial z^2} - \lambda(z-1) \frac{\partial G(z, t)}{\partial z}.$$

Now, from the previous subsection it is known that  $\lim_{z \rightarrow 1^-} \frac{\partial G(z, t)}{\partial z} = E[X(t)]$  and  $\lim_{z \rightarrow 1^-} \frac{\partial^2 G(z, t)}{\partial z^2} = E[X(t)(X(t)-1)]$ . To obtain an expectation term on the left hand side, the whole equation must be differentiated by  $z$  once more to give

$$\frac{\partial}{\partial z} \left( \frac{\partial G(z, t)}{\partial t} \right) = \frac{\partial^3 G(z, t)}{\partial z^3} \lambda z(z-1) + \frac{\partial^2 G(z, t)}{\partial z^2} \lambda(2z-1) - \frac{\partial G(z, t)}{\partial z} \lambda(N+I-1)$$

and assuming the order of differentiation can be changed, taking the limit  $z \rightarrow 1^-$  gives

$$\begin{aligned} \frac{dE[X(t)]}{dt} &= \lambda E[X(t)(X(t)-1)] - \lambda(N+I-1)E[X(t)] \\ &= \lambda E[X(t)^2] - \lambda E[X(t)]^2 + \lambda E[X(t)]^2 - \lambda E[X(t)] - (N+I-1)\lambda E[X(t)] \\ &= \lambda Var[X(t)] - \lambda E[X(t)](N+I-E[X(t)]). \end{aligned} \quad (6.19)$$

This is analogous to the simple deterministic epidemic curve for population size  $n$  and  $x(t)$  susceptibles at time  $t$  given by equation (3.2) to be

$$\frac{dx}{dt} = -\beta x(t)(n-x(t))$$

with the addition of the variance caused by the randomness in the stochastic model. Here  $X(0) = x(0)$  and  $N+I = n$ . Therefore when the variance of  $X(t)$  is small relative to  $E[X(t)](N+I-E[X(t)])$  the deterministic and stochastic epidemic curves are well matched for the same parameter values. This can be deduced because if  $Var(X(t)) \rightarrow 0$ , then  $E[X(t)] \rightarrow x(t)$ , causing the stochastic epidemic to tend to the deterministic case.

To investigate further, the variance of  $X(t)$  multiplied by  $\lambda$  can be written as

$$\begin{aligned} \lambda Var[X(t)] &= \lambda E[X(t)^2] - \lambda E[X(t)]^2 \\ &= \lambda \sum_{i=0}^N p_i(t) i^2 - \lambda \left( \sum_{i=0}^N p_i(t) i \right)^2, \end{aligned}$$

whilst

$$-\lambda E[X(t)](N+I-E[X(t)]) = -\lambda(N+I) \sum_{i=0}^N p_i(t) i + \lambda \left( \sum_{i=0}^N p_i(t) i \right)^2.$$

Therefore equation (6.19) becomes

$$\frac{dE[X(t)]}{dt} = \lambda \sum_{i=0}^N p_i(t) i^2 - \lambda \sum_{i=0}^N p_i(t) i(N + I). \quad (6.20)$$

Here the first summation in equation (6.20) is the contribution of the  $\lambda Var[X(t)]$  term from equation (6.19) and the second term is the contribution of  $-\lambda E[X(t)](N + I - E[X(t)])$  from equation (6.19).

Now, since  $i < N + I$  for all  $i$ ,  $\sum_{i=0}^N p_i(t) i(N + I)$  is always greater than  $\sum_{i=0}^N p_i(t) i^2$ . Furthermore, when the population  $N + I$  is large,

$$\lambda \sum_{i=0}^N p_i(t) i^2 \ll \lambda \sum_{i=0}^N p_i(t) i(N + I)$$

so that the variance of  $X(t)$  is small compared to the  $E[X(t)](N + I - E[X(t)])$  term. Hence for large populations, the stochastic and deterministic models are well matched. However, for short term epidemics there is no such guarantee as the randomness of the stochastic model will have more of an effect.

## 6.8 Numerical solution

To illustrate how this epidemic behaves, realisations of equations (6.1) can be simulated numerically by recalling that susceptibles transitioning to infective can be modelled by a Poisson process with rate  $\lambda X(t)(N + I - X(t))$ . This is done with the R code below

```
#setting up the constants
N=3; lambda=0.5; tt=0
#initial value
x=N
#initialising counters
tevent=numeric(0)
while(x>0){
pxy=lambda*x*(N-x+1)
u=rexp(1,pxy)
tt=tt+u
x=x-1
tevent=c(tevent,tt)
}

#plotting the evolution
plot(0,0,type="n",xlim=c(0,tt),ylim=c(0,4),
```



```

xlab="Time t",ylab="Number of susceptibles")
#set n as the length of tevent and initialising the susceptibles to N
n=length(tevent)
xx=N
#drawing the first horizontal line
lines(c(0,tevent[1]),c(xx,xx),lty=1)
for(i in 1:n){
#drawing vertical lines
lines(c(tevent[i],tevent[i]),c(xx,xx-1),lty=3); xx=xx-1
if(i!=n){
#drawing horizontal lines providing i is not equal to n
lines(c(tevent[i],tevent[i+1]),c(xx,xx),lty=1)
}
}

#setting up 1000 repeats of the system to estimate the mean and end time
tend=numeric(1000)
xend=numeric(1000)

for(isim in 1:1000){
x=N; tt=0
while((x>0)){
pxy=lambda*x*(N-x+1)
u=rexp(1,pxy)
tt=tt+u
x=x-1
}
#store the end time in tend and the final number of susceptibles in xend
tend[isim]=tt
xend[isim]=x
}
max(xend)
[1] 0
min(xend)
[1] 0
max(tend)
[1] 9.956497
min(tend)
[1] 0.1413819
mean(tend)
[1] 1.827053

```

This produces the plot in Figure 6.4 of the simple stochastic epidemic in the case  $N = 3$ ,  $I = 1$  and  $\lambda = 0.5$ .

The fact that the maximum and minimum value of `xend` is 0 once more confirms that, as shown for the simple deterministic epidemic, all susceptibles are infected during the course of

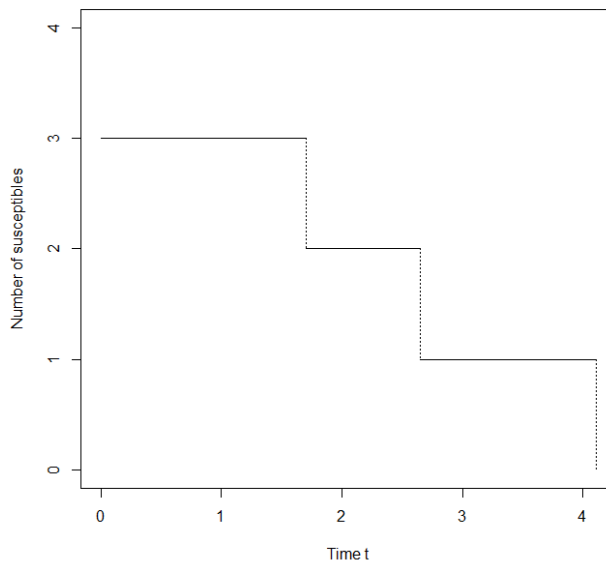


Figure 6.4: One realisation of the simple stochastic epidemic over time with  $\lambda = 0.5$ ,  $N = 3$  and  $I = 1$ .

the epidemic. Furthermore, the mean of the 1000 simulated end times of the epidemic, 1.83, is the same to two decimal places as the end time predicted in Figure 6.4, and close to the deterministic prediction of 1.52.

In addition, Figure 6.5 shows four realisations of the infective deterministic curve, as found in Section 3.3, and the stochastic infective curve for  $N = 95$  initial susceptibles,  $I = 5$  initial infectives, and an infection rate parameter of 0.01. This shows that for larger population sizes, the two models are fairly well matched.

Figure 6.6 shows four realisations of the deterministic and stochastic models with again  $\lambda = \beta = 0.01$ , but now there is only a fifth of the population, so  $I = 1$ ,  $N = 19$ . Note that because there is no randomness in the deterministic model, the deterministic curve is uniquely determined by the initial parameters, meaning the deterministic curve for each of the four plots is identical.

Comparing Figures 6.5 and 6.6 seems to suggest that the deterministic and stochastic models agree relatively more strongly for larger population sizes, and that the probabilistic element of the stochastic model matters more in a smaller population. This is as expected from the result derived in Section 6.7.2

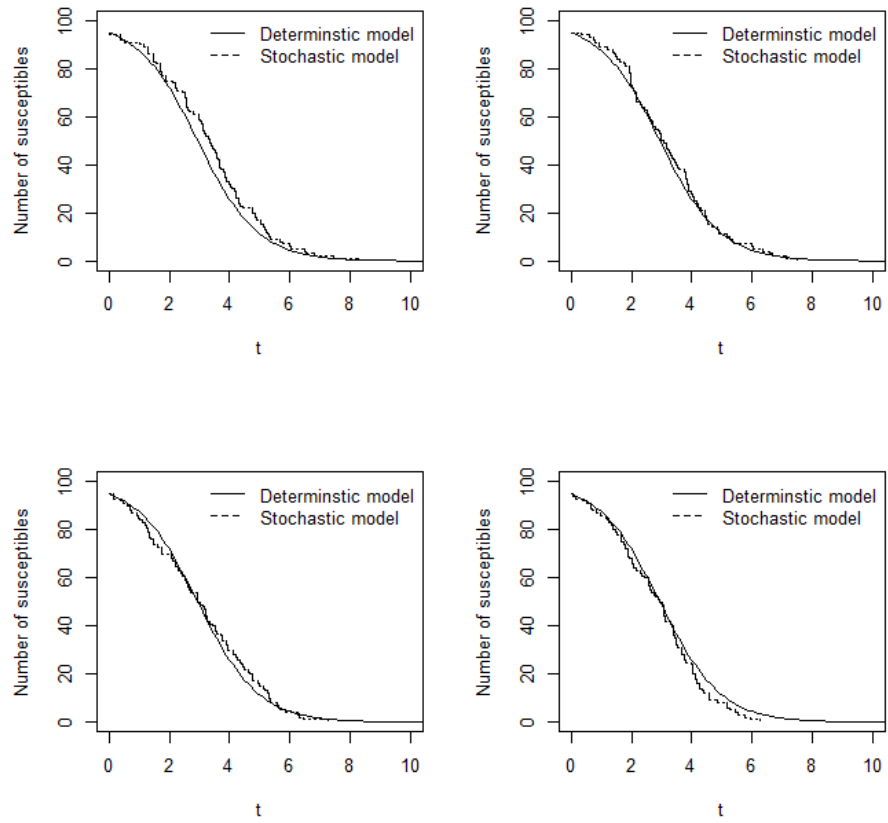


Figure 6.5: Deterministic and stochastic models for the number of infectives with  $N = 95$ ,  $I = 5$  and  $\lambda = \beta = 0.01$ .

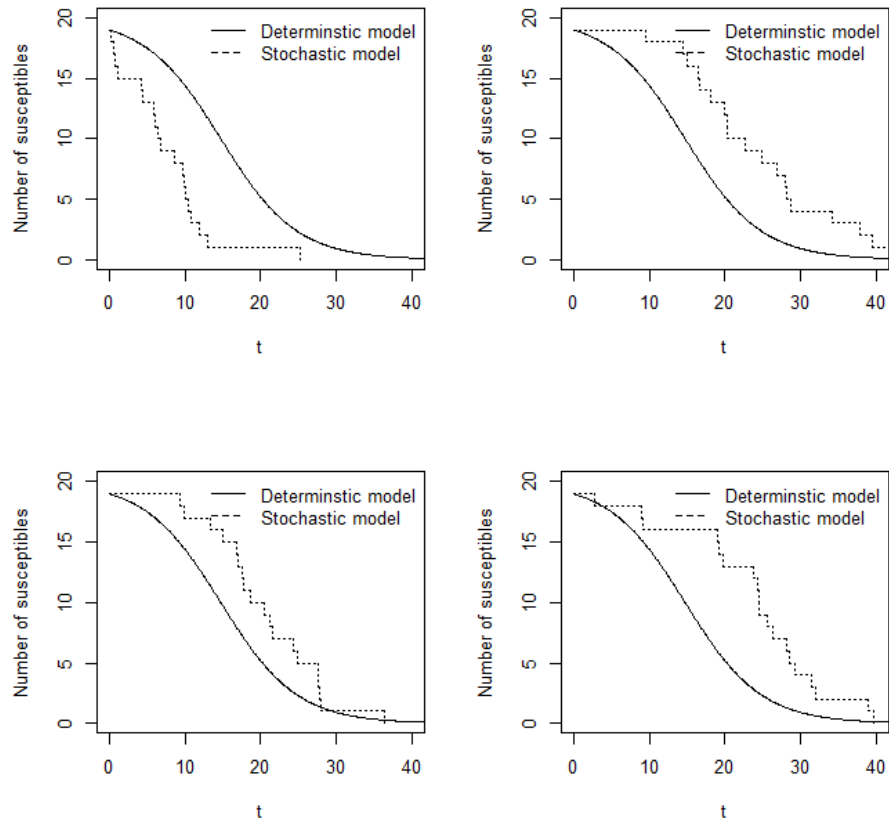


Figure 6.6: Deterministic and stochastic models for the number of infectives with  $N = 19$ ,  $I = 1$  and  $\lambda = \beta = 0.01$ .

# Chapter 7

## The General Stochastic Epidemic

### 7.1 Modelling the general epidemic stochastically

The general stochastic epidemic is the natural extension of the simple case considered in Chapter 6 obtained by including a class of removals  $Z$ , where  $Z(t)$  denotes the number of removals at time  $t$ . Analogously to Chapter 4, the rate at which each population member can enter the removal class from the class of infectives is modelled by a Poisson process with rate  $\gamma$ , but once in the removal class a member cannot leave. Homogeneous mixing of all population members is also again assumed.

The population is once more assumed to be closed, and since there cannot be any removals before the epidemic has begun it must be the case that  $Z(0) = 0$ . This means for an epidemic with  $N$  initial susceptibles and  $I$  initial infectives,

$$X(t) + Y(t) + Z(t) = N + I$$

for all  $t$ .

Due to this closed population constraint the state of the infectives and susceptibles uniquely determines the system, as then  $Z(t) = N + I - X(t) - Y(t)$ . Therefore the bivariate Markov process  $\mathbf{U}(t)$  defined in Section 6.1 is enough to describe the behaviour of the general epidemic system.

By considering a small time period  $h$ , the transition probabilities can be written as

$$Pr(\mathbf{U}(t+h) = (i-1, j+1) | \mathbf{U}(t) = (i, j)) = \lambda ijh + o(h)$$

$$Pr(\mathbf{U}(t+h) = (i, j-1) | \mathbf{U}(t) = (i, j)) = \gamma jh + o(h)$$

$$Pr(\mathbf{U}(t+h) = (i, j) | \mathbf{U}(t) = (i, j)) = 1 - \lambda ijh - \gamma jh + o(h)$$

where  $\lambda$  is the stochastic pairwise infection rate parameter and  $0 \leq i + j \leq N + I$ ,  $0 \leq i \leq N$  and  $0 \leq j \leq N + I$ .

## 7.2 Investigating the general stochastic epidemic

Following the method of Daley and Gani (1999, p66), by writing

$$p_{ij}(t) = Pr(\mathbf{U}(t) = (i, j) | \mathbf{U}(0) = (N, I))$$

the forward Kolmogorov equations can be derived in a similar way to Section 6.5. Considering all possible transitions to be in state  $(i, j)$  after a short time period  $h$ , for  $0 \leq i + j \leq N + I$ ,  $0 \leq i \leq N - 1$  and  $1 \leq j \leq N + I - 1$ , then

$$p_{ij}(t + h) = p_{i+1, j-1}(t)\lambda(i+1)(j-1)h + p_{i, j+1}(t)\gamma(j+1)h + p_{ij}(t)(1 - \lambda ijh - \gamma jh) + o(h).$$

After rearrangement and taking the limit  $h \rightarrow 0$ , this becomes

$$\frac{dp_{ij}(t)}{dt} = \lambda(i+1)(j-1)p_{i+1, j-1}(t) + \gamma(j+1)p_{i, j+1}(t) - j(i\lambda + \gamma)p_{ij}(t) \quad (7.1)$$

with  $p_{NI}(0) = 1$ . Defining  $p_{ij}(t) = 0$  for all  $t$  whenever  $i > N$ ,  $j < 0$  or  $j > N + I$  causes equation (7.1) to also hold when  $i = N$ ,  $j = 0$  and  $j = N + I$ .

Also note that, by recalling the general deterministic epidemic, it may not be the case that all susceptibles become infected. Since there is an extra class of removals all states may not be visited by this system, unlike the case of the simple stochastic epidemic.

The method of Laplace transforms from the previous chapter could be employed to find a general recursive solution. However, because the system being considered is now a bivariate Markov chain, it becomes extremely complicated for any population size of interest. Alternatively a less laborious, however still complex method to solve this system is proposed by Gani (1967) which involves the use of Laplace transforms, bivariate probability generating functions and matrix manipulation. In this report these equations will be simulated numerically in Section 7.4. Before this, the link between the general deterministic and stochastic models, analogous to the previous chapter, will be derived.

## 7.3 Probability generating functions

To find the corresponding link between the general stochastic and deterministic epidemics, an extension of the results proved in Section 6.7.1 is required.

### 7.3.1 Bivariate probability generating functions

Two random variables  $X(t)$  and  $Y(t)$ , taking states indexed by  $i$  and  $j$  respectively, constrained by  $0 \leq i + j \leq N + I$ ,  $0 \leq i \leq N$  and  $0 \leq j \leq N + I$ , have a bivariate probability generating

function  $G(z, w; t)$  defined as

$$G(z, w; t) = E(z^{X(t)}w^{Y(t)}) = \sum_{i=0}^N \sum_{j=0}^{N+I-i} p_{ij}(t)z^i w^j.$$

Investigating this probability generating function leads to a similar set of results proved in Section 6.7.1.

Firstly, under partial differentiation with respect to  $z$ ,

$$\frac{\partial G(z, w; t)}{\partial z} = \sum_{i=0}^N \sum_{j=0}^{N+I-i} p_{ij}(t)iz^{i-1}w^j.$$

Now in the double limit  $z \rightarrow 1^-$ ,  $w \rightarrow 1^-$  this becomes

$$\lim_{z \rightarrow 1^-} \lim_{w \rightarrow 1^-} \frac{\partial G(z, w; t)}{\partial z} = \sum_{i=0}^N \sum_{j=0}^{N+I-i} p_{ij}(t)i$$

which is the expectation of  $X(t)$ , hence

$$\lim_{z \rightarrow 1^-} \lim_{w \rightarrow 1^-} \frac{\partial G(z, w; t)}{\partial z} = E[X(t)]. \quad (7.2)$$

Partial differentiation with respect to  $w$  using the exact same method leads to the same result for  $Y(t)$ ,

$$\lim_{z \rightarrow 1^-} \lim_{w \rightarrow 1^-} \frac{\partial G(z, w; t)}{\partial w} = E[Y(t)]. \quad (7.3)$$

Additionally, differentiating with respect to both  $w$  and  $z$  and taking limits leads to,

$$\begin{aligned} \lim_{z \rightarrow 1^-} \lim_{w \rightarrow 1^-} \frac{\partial^2 G(z, w; t)}{\partial z \partial w} &= \lim_{z \rightarrow 1^-} \lim_{w \rightarrow 1^-} \sum_{i=0}^N \sum_{j=0}^{N+I-i} p_{ij}(t)ijz^{i-1}w^{j-1} \\ &= \sum_{i=0}^N \sum_{j=0}^{N+I-i} p_{ij}(t)ij \\ &= E[X(t)Y(t)]. \end{aligned} \quad (7.4)$$

### 7.3.2 Application to the general epidemic

These results can now be applied to the general epidemic Kolmogorov equation given by equation (7.1). Here

$$\begin{aligned}
\frac{\partial G(z, w; t)}{\partial t} &= \sum_{i=0}^N \sum_{j=0}^{N+I-i} \frac{dp_{ij}(t)}{dt} z^i w^j \\
&= \sum_{i=0}^N \sum_{j=0}^{N+I-i} z^i w^j \lambda(i+1)(j-1)p_{i+1, j-1}(t) + \sum_{i=0}^N \sum_{j=0}^{N+I-i} z^i w^j \gamma(j+1)p_{i, j+1}(t) \\
&\quad - \sum_{i=0}^N \sum_{j=0}^{N+I-i} z^i w^j j(i\lambda + \gamma)p_{ij}(t).
\end{aligned}$$

Defining  $k = i + 1$ ,  $l = j - 1$  in the first sum,  $k = i$ ,  $l = j + 1$  in the second sum, and  $k = i$ ,  $l = j$  in the third sum gives

$$\begin{aligned}
\frac{\partial G(z, w; t)}{\partial t} &= \sum_{k=1}^{N+1} \sum_{l=-1}^{N+I-(k-1)-1} z^{k-1} w^{l+1} \lambda k l p_{kl}(t) + \sum_{k=0}^N \sum_{l=1}^{N+I-k+1} z^k w^{l-1} \gamma l p_{kl}(t) \\
&\quad - \sum_{k=0}^N \sum_{l=0}^{N+I-i} z^k w^l l(k\lambda + \gamma) p_{kl}(t). \tag{7.5}
\end{aligned}$$

Now a closer inspection of each of the three double sums is required.

In the first term on the right hand side of equation (7.5), the lower limit of both sums,  $k = 1$  and  $l = -1$  can be set to start from 0, since when  $k = 0$  the  $k$  term in the sum will be zero and when  $l = -1$ , by definition  $p_{k, -1}(t) = 0$ . Looking at the  $k = N + 1$  case, by definition  $p_{N+1, j}(t) = 0$  therefore the sum over  $k$  need only go up to  $N$ , and  $l = N + I - (k - 1) - 1$  simplifies to  $l = N + I - k$ . Therefore

$$\sum_{k=1}^{N+1} \sum_{l=-1}^{N+I-(k-1)-1} z^{k-1} w^{l+1} \lambda k l p_{kl}(t) = \sum_{k=0}^N \sum_{l=0}^{N+I-k} z^{k-1} w^{l+1} \lambda k l p_{kl}(t). \tag{7.6}$$

In the second term, the sum over  $k$  is in the required form, and the  $l$  term in the summation means the sum over  $l$  can be started from zero as opposed to  $l = 1$ , as it just adds a zero into the sum. Also by definition  $k + l \leq N + I$ , but in the case  $l = N + I - k + 1$ , the value of  $k + l = k + N + I - k + 1 = N + I + 1$ , so the probability of this event will be zero by definition, therefore this sum over  $l$  can be limited by  $N + I - k$  instead. Hence

$$\sum_{k=0}^N \sum_{l=1}^{N+I-k+1} z^k w^{l-1} \gamma l p_{kl}(t) = \sum_{k=0}^N \sum_{l=0}^{N+I-k} z^k w^{l-1} \gamma l p_{kl}(t) \tag{7.7}$$



The third term is already of the required form so does not need to be analysed further. Substituting the results from equations (7.6) and (7.7) back into equation (7.5) gives

$$\begin{aligned} \frac{\partial G(z, w; t)}{\partial t} &= \sum_{k=0}^N \sum_{l=0}^{N+I-k} z^{k-1} w^{l+1} \lambda k l p_{kl}(t) + \sum_{k=0}^N \sum_{l=0}^{N+I-k} z^k w^{l-1} \gamma l p_{kl}(t) \\ &\quad - \sum_{k=0}^N \sum_{l=0}^{N+I-i} z^k w^l l (k\lambda + \gamma) p_{kl}(t). \end{aligned}$$

Writing this all as one sum, and taking out relevant factors of  $z$  and  $w$  leads to

$$\begin{aligned} \frac{\partial G(z, w; t)}{\partial t} &= \sum_{k=0}^N \sum_{l=0}^{N+I-i} \left\{ \lambda w^2 (z^{k-1} w^{l-1} k l p_{kl}(t)) + \gamma (z^k w^{l-1} l p_{kl}(t)) \right. \\ &\quad \left. - \lambda w z (z^{k-1} w^{l-1} k l p_{kl}(t)) - \gamma w (z^k w^{l-1} l p_{kl}(t)) \right\}. \end{aligned} \quad (7.8)$$

Using the results from Section 7.3.1 gives

$$\frac{\partial G(z, w; t)}{\partial t} = \lambda w^2 \frac{\partial^2 G(z, w; t)}{\partial z \partial w} - \lambda w z \frac{\partial^2 G(z, w; t)}{\partial z \partial w} + \gamma \frac{\partial G(z, w; t)}{\partial w} - \gamma w \frac{\partial G(z, w; t)}{\partial w}. \quad (7.9)$$

As in Section 6.7.1, differentiating both sides of the equation with respect to  $z$  or  $w$  and taking the limit as they both  $\rightarrow 1^-$  will give the time differential of the respective expectation on the right hand side. This is shown for the more complex case of  $E[Y(t)]$ , with the result provided for  $E[X(t)]$ .

Partially differentiating both sides of equation (7.9) with respect to  $w$  gives

$$\begin{aligned} \frac{\partial^2 G(z, w; t)}{\partial w \partial t} &= \frac{\partial^3 G(z, w; t)}{\partial w^2 \partial z} [\lambda w^2 - \lambda w z] + \frac{\partial^2 G(z, w; t)}{\partial w \partial z} [2\lambda w - \lambda z] \\ &\quad + \frac{\partial^2 G(z, w; t)}{\partial w^2} [\gamma - \gamma w] + \frac{\partial G(z, w; t)}{\partial w} [-\gamma]. \end{aligned}$$

Then, assuming the order of differentiation on the right hand side can be changed, taking the limits  $z, w \rightarrow 1^-$  and using equations (7.3) and (7.4) gives

$$\begin{aligned} \frac{dE[Y(t)]}{dt} &= \lambda E[X(t)Y(t)] - \gamma E[Y(t)] \\ &= \lambda E[X(t)]E[Y(t)] - \gamma E[Y(t)] + \lambda \text{cov}[X(t), Y(t)]. \end{aligned} \quad (7.10)$$

This second equality in equation (7.10) is found by noting that the covariance between two random variables  $X(t)$  and  $Y(t)$  satisfies

$$\text{cov}[X(t), Y(t)] = E[X(t)Y(t)] - E[X(t)]E[Y(t)].$$

By the same method, the time differential of the expectation of  $X$  is

$$\begin{aligned}\frac{dE[X(t)]}{dt} &= -\lambda E[(t)Y(t)] \\ &= -\lambda E[X(t)]E[Y(t)] - \lambda cov[X(t), Y(t)].\end{aligned}\tag{7.11}$$

For  $\lambda = \beta$ , since  $E[X(t)] \approx x(t)$  and  $E[Y(t)] \approx y(t)$  if the covariance term is small compared to the other terms then equations (7.11) and (7.10) are well approximated by the general deterministic epidemic equations. These general deterministic equations are given by equations (4.1) and (4.2) to be

$$\begin{aligned}\frac{dy}{dt} &= \beta xy - \gamma y \\ \frac{dx}{dt} &= -\beta xy.\end{aligned}$$

Hence it is clear that the deterministic and stochastic models are closely related. Once the general stochastic epidemic can be plotted, as done in Section 7.4, the similarities between the two will be further commented upon.

## 7.4 Numerical solution

The general stochastic epidemic can be further investigated by numerically solving equations (7.10) and (7.11). This is done by using a generalisation of the code given in Section 6.8 to accommodate the fact the Markov process is now a function of two variables rather than one.

The code simulates to the time to the next transition of any kind by summing the probabilities of the two different transitions. This can be done as when in state  $(i, j)$ , infections and removals occur from independent Poisson processes, so the probability of an infection or a removal is the sum of the probabilities of the two events occurring. The code then determines which of the two transitions have occurred at this time using the probability of each event, storing an infection as  $k = 1$  in the vector `kevent` and a removal as  $k = 2$  in the same vector.

The R code below does this whilst simulating the Markov process numerically, also plotting the general deterministic numerical solution used in Section 4.4.5 with the same parameter values for comparison. Finally, a simulation of 1000 Markov processes with the same parameters is performed to identify a mean end time, stored in object `tend` and mean number of susceptibles that do not ever become infected, stored in object `xend`. The R code below does this, and produces the plot in Figure 7.1.

```
###stochastic###
N=95; I=5; nn=N; lambda=0.01; gamma=0.01; tt=0 #setting up constants
```

```

y=I; x=nn; z=0 #setting up initial population split
tevent=numeric(0) #will store the transition times
kevent=numeric(0) #will store the type of transition
while((y>0)){
#Finding the time to the next event
pxy=lambda*x*y; pyz=gamma*y; ptot=pxy+pyz
u=rexp(1,ptot)
#finding if a transition occurs, which one
tt=tt+u
k=sample(c(1,2),1,prob=c(pxy,pyz))
#dealing with x equal and not equal to 0 separately
if(x!=0){
if(k == 1){x=x-1;y=y+1}
if(k == 2){y=y-1;z=z+1}}
if(x==0){
if(k == 2){y=y-1;z=z+1}}
tevent=c(tevent,tt) #storing transition time
kevent=c(kevent,k)} #storing transition type

#plotting
plot(0,0,type="n",xlim=c(0,40),ylim=c(0,100),xlab="Time t",ylab="Number")
legend(12,90,c("Number of susceptibles","Number of infectives"),lty=c(1,2),bty="n")
n=length(tevent)
#setting up initials
xx=nn; yy=I
lines(c(0,tevent[1]),c(xx,xx),lty=1)
lines(c(0,tevent[1]),c(yy,yy),lty=2) #setting up the starting point
#iterating drawing lines for each transition
for (i in 1:n){
if(kevent[i] == 1){
lines(c(tevent[i],tevent[i]),c(xx,xx-1),lty=3); xx=xx-1
lines(c(tevent[i],tevent[i]),c(yy,yy+1),lty=3); yy=yy+1}
if(kevent[i] == 2){
lines(c(tevent[i],tevent[i]),c(yy,yy-1),lty=3); yy=yy-1}
#drawing the horizontal lines
if(i!=n){
lines(c(tevent[i],tevent[i+1]),c(xx,xx),lty=1)
lines(c(tevent[i],tevent[i+1]),c(yy,yy),lty=2)}}}

###1000 sims###
tend=numeric(1000) #will store all end times
xend=numeric(1000) #will store all final number susceptibles
for(isim in 1:1000){
y=I; x=nn; z=0; tt=0
while((y>0)){
#Finding the time to the next event
pxy=lambda*x*y; pyz=gamma*y; ptot=pxy+pyz
u=rexp(1,ptot)

```

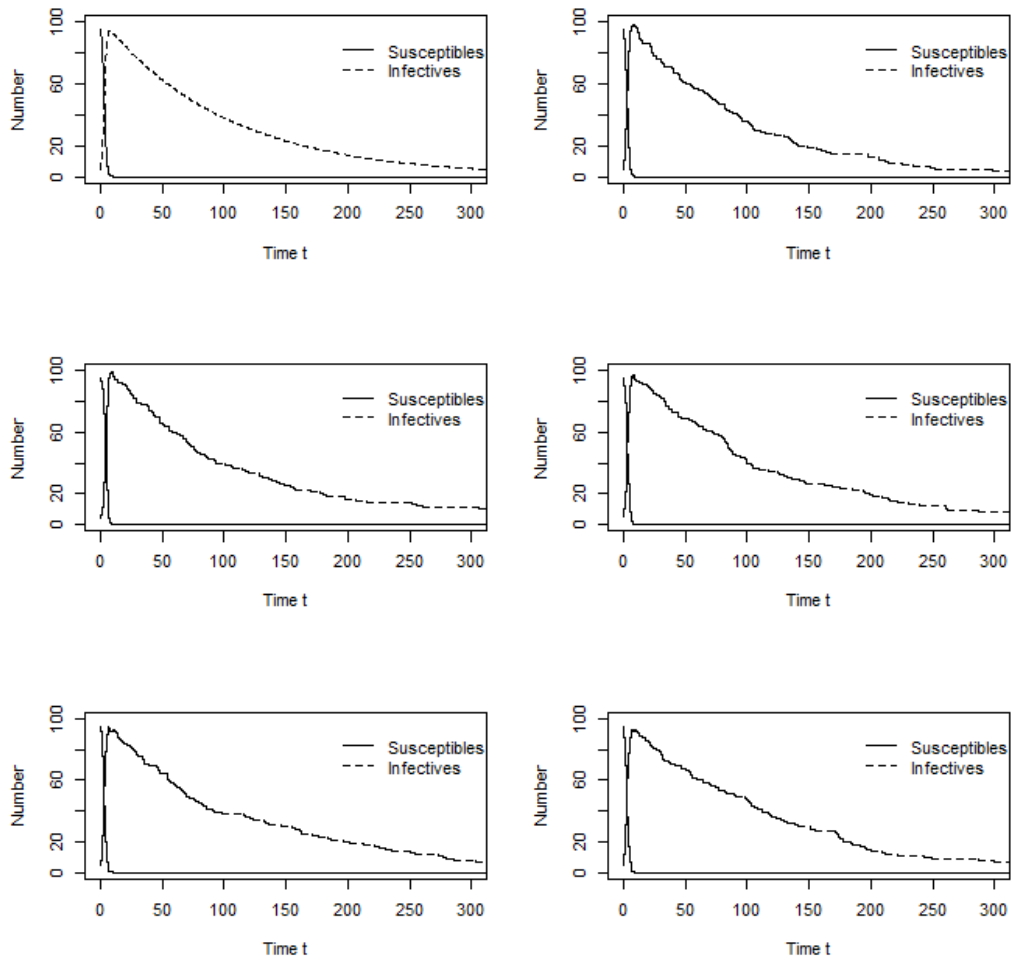


Figure 7.1: The deterministic (top left plot) and five stochastic realisations of the general stochastic epidemic with parameters  $N = 95$ ,  $I = 5$ ,  $\lambda = \beta = 0.01$  and  $\gamma = 0.01$ .

```

#finding if a transition occurs, which one
tt=tt+u
k=sample(c(1,2),1,prob=c(pxy,pyz))
if(x!=0){
if(k == 1){x=x-1;y=y+1}
if(k == 2){y=y-1;z=z+1}}
if(x==0){
if(k == 2){y=y-1;z=z+1}}
tend[isim]=tt
xend[isim]=x}

```

For these parameter values, R returns the results

```
mean(tend)
4199.36
mean(xend)
0.
```

This implies that all susceptibles become infected in this case, and due to the fact the removal rate is so small, the epidemic takes a long time, 4199.36 here, for all infective members to become removed.

The simple epidemic is classed as finished once all susceptibles are infected, however in the general case infective members can also become removed. Susceptibles stop becoming infected relatively early on in Figure 7.1, but if a government wanted to know how long they would need to provide support, supplies and help for, defining the end of an epidemic as when no infective members remain is probably a more realistic definition. Therefore the end of a general epidemic is defined as when there are no infectives remaining, this is the time given by the `tend` object in the R code above.

Furthermore, looking at the infective curves in Figure 7.1, after some initial variation including the exact locations of the peaks of the stochastic and deterministic curves, the stochastic and deterministic curves are well matched, especially asymptotically. Towards the end of this epidemic, the number of susceptibles is zero with no chance of changing, hence it is reasonable to assume that the covariance between  $X(t)$  and  $Y(t)$  is negligible, or even zero. At this point, the decay of the number of current infectives behaves like a death process discussed in Section 5.3.1. When this is the case, as mentioned earlier, the stochastic and deterministic models given by equations (7.10) and (7.11), and equations (4.1) and (4.2) respectively are well matched. This seems to be illustrated by the plots in Figure 7.1. However, earlier in the epidemic, when the number of susceptibles is changing,  $X(t)$  and  $Y(t)$  certainly are correlated. A decrease in susceptibles will certainly cause an immediate increase in infectives and therefore a correlation between the number of susceptibles and infectives would be expected.

Realisations of an epidemic with different parameter values, when all susceptibles do not become infected, is shown in Figure 7.2. These are the same parameter values used for the plot in Figure 4.10 of  $N = 9$ ,  $I = 1$ ,  $\lambda = \beta = 0.05$  and  $\gamma = 0.7$ . In this case, comparing with the deterministic case in Figure 4.10, the randomness seems to have much more of an effect on the outcome of the epidemic. The high removal rate, coupled with the fact there is only one infective means that for three of the plots, the infective member of the population is removed before they can infect any susceptibles. In the top left plot however the infective manages to infect a susceptible member resulting in more infections taking place and the epidemic evolving rather than just dying out straight away like in the other three plots. This seems to agree with the result derived in Section 6.7.2, that for larger populations, the stochastic and deterministic

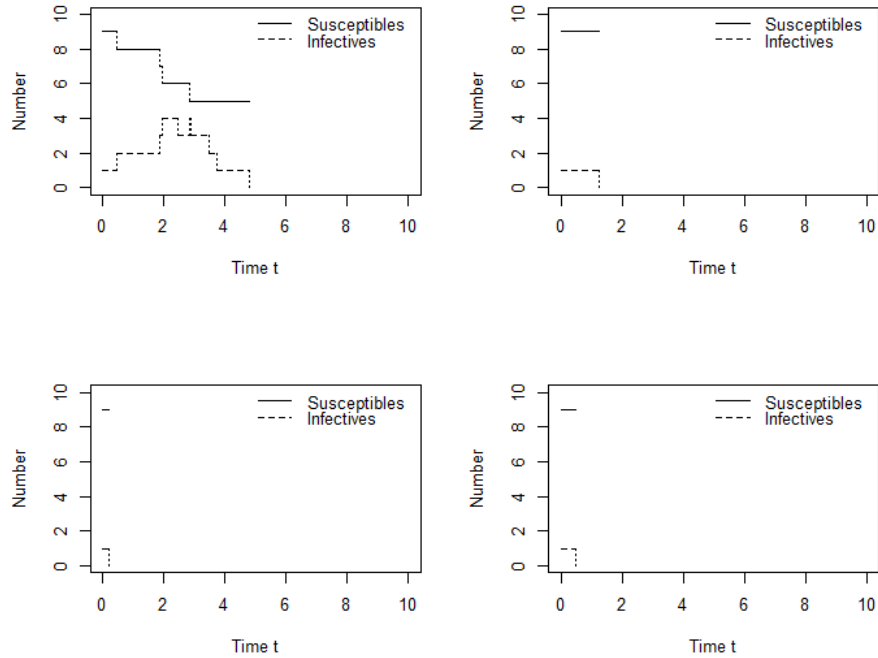


Figure 7.2: Four realisations of the general deterministic and stochastic model for  $N = 9$ ,  $I = 1$ ,  $\lambda = \beta = 0.05$  and  $\gamma = 0.7$ .

models are well matched; although the random nature of the stochastic model can make them differ in smaller populations.

In addition to the plots in Figure 7.2, the 1000 simulations of the epidemic where  $N = 9$ ,  $I = 1$ ,  $\lambda = 0.05$  and  $\gamma = 0.7$  were used to investigate the duration  $T$  of the epidemic, and the number of susceptibles remaining once the epidemic is over. The R commands

```
tupper=ceiling(max(tend))
hist(tend,freq=FALSE,breaks=c(0:tupper),xlab="Duration T",
ylab="Proportion",main="",ylim=c(0,0.6))
hist(xend,freq=FALSE,breaks=-0.5+c(0:(nn+1)),xlab="X(t)",
ylab="Proportion",main="",ylim=c(0,0.6),xlim=c(0,10))
```

were used to plot the histograms in Figure 7.3. Figure 7.3 (left) suggests that the duration of the epidemic is generally very short. This agrees with the plots in Figure 7.2 which sees three out of the four realisations end almost immediately with no secondary infections. The fact there are usually no secondary infections is consistent with Figure 7.3 (right) which implies the most likely outcome of the epidemic is that all nine susceptibles remain uninfected at the end, which happens roughly 60% of the time. The randomness of the model is highlighted by the fact that, whilst the most likely duration times are close to 0, times of up to 10 are observed. Similarly, the most likely number of susceptibles remaining at the end of the epidemic is 9,

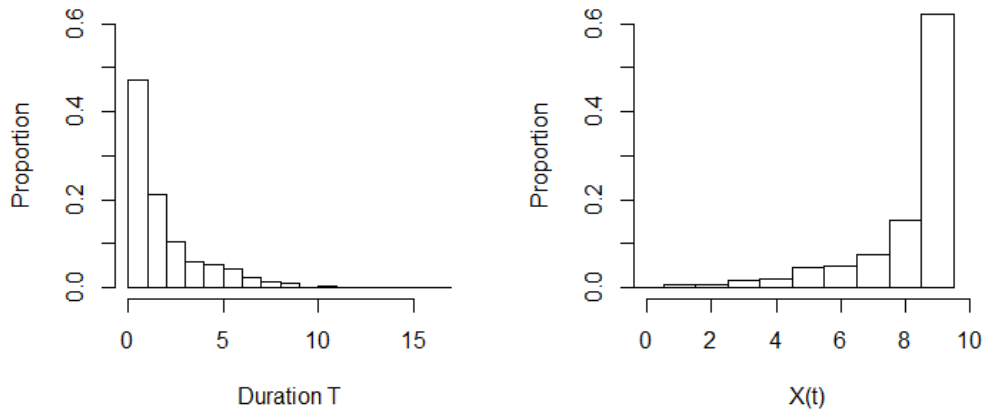


Figure 7.3: Histograms showing the proportion of end times (left) and remaining number of susceptibles (right) at the end of an epidemic with  $N = 9$ ,  $I = 1$ ,  $\lambda = 0.05$  and  $\gamma = 0.7$ .

but all situations between 1 and 9 susceptibles remaining are realised at some point during the 1000 simulations.

Whether or not the whole population of susceptibles will eventually become infected is dependent on the number of infectives, susceptibles and the parameters  $\gamma$  and  $\lambda$ , as well as the randomness of the model. If  $\gamma j > \lambda i j$  it is more likely that an infective will be removed than a susceptible be infected in state  $(i, j)$ .

In this example where the epidemic starts with one infective, initially there is a greater chance that the infective will be removed than infect another member, as  $\gamma = 0.7 > 0.45 = \lambda i$ . In the deterministic model this would be the condition for no epidemic to take place, however because of the randomness in the stochastic model, there is a chance that the single infective could infect a susceptible, causing  $\gamma$  to increase to  $2\gamma$  and making another infection more likely that it was before. This behaviour can be seen in the top left plot of Figure 7.2 where the epidemic fails to die out before any infections have taken place, in contrast to the other three plots.

# Chapter 8

## Epidemic Modelling In Reality

Now that models of disease spread have been introduced and investigated, they will be applied to some real world situations to see how well they can express what actually happens in reality.

As mentioned in Chapter 2, it is not clear how to estimate the parameters of the model from real world data. Dietz (1993) and Heffernan *et al.* (2005) discuss various involved methods of estimation, but in this report some overly simplistic assumptions will be made when estimating parameters, and hence some accuracy may be lost from the original data.

### 8.1 Measles

This section focuses on a Welsh measles outbreak, centred on the Swansea area, occurring between November 2012 and July 2013. The data used comes from the Public Health Wales (2015) website and gives the number of new cases for each month in the outbreak period. Also included in the data set is the number of under immunised and un-immunised children in the Swansea area on 1<sup>st</sup> November 2012, the time of the start of the outbreak.

As measles predominantly affects children, this number of under and un-immunised children is taken to be the total number of susceptibles in the population. The data is collected across the three large health boards close to the Swansea area, Abertawe Bro Morgannwg UHB, Hywel Dda HB and Powys Teaching HB. These are shown in Figure 8.1 taken from the NHS Wales website (2015). The total number of susceptibles at the beginning of the outbreak across these three health boards is 28870. In the first reported week of the outbreak, there are 34 reported cases of measles. This is taken to be the initial number of infectives used in the model.

Farrington *et al.* (2003, p126) discuss the measles infection process in detail. The average infectious period for measles is roughly one week, and when setting up the model it will be assumed that each member has an infectious period of one week. Measles also has a latent





Figure 8.1: Wales broken down into health board regions; taken from the NHS wales website (2015)

period between a population member becoming infected and infectious of around two weeks. However when a child displays the symptoms of measles, they are infective, so the latent period will be ignored here to simplify the model. Furthermore, once the body has produced the specific white blood cells needed to fight measles, these cells provide immunity from further cases, so once infective members are no longer infected, they become removed and immune from the disease.

### 8.1.1 The general deterministic model

Now, recalling the base reproduction number  $r_0$  from Chapter 2, it is stated in Section 2.4 that for an initial infective making  $\beta x_0$  transmissions of the disease in  $t$  time units, the base reproduction number can be written as

$$r_0 = \beta x_0 t.$$

Since  $y_0 = 34 \ll 28870 = x_0$  we can take the initial infective assumption needed when calculating  $r_0$  as approximately valid for this population and assume that the time when there was one infective was close to this time, in effect taking this to be the start of the epidemic.

Taking the time unit to be weeks, considering one week means  $t = 1$ . For measles in the UK, Gay (2004) suggests  $14 \leq r_0 \leq 18$ , so taking the middle of this region it is assumed here that  $r_0 = 16$ . Note that this value for  $r_0$  is also in the range suggested by Fine (1993) given in Chapter 2. For further reading, Mossong and Muller (2000) discuss methods of parameter estimation of  $r_0$  in their paper. Now, using  $r_0 = 16$ , the estimate for  $\beta$  is

$$\beta = \frac{r_0}{x_0 t} = \frac{16}{28870} = 0.000554.$$

to three significant figures. Furthermore,  $\gamma$  is the removal rate per infective member per unit time. Denoting  $A$  as the number of removals from  $B$  infectives over time period  $T$ ,  $\gamma$  can be estimated by

$$\gamma = \frac{A}{BT}.$$

By taking  $T$  as the average infectious period of measles which is roughly one and a half weeks, it would be expected that over this period, all  $B$  infectives present at the start of the period would become removed. This leads to the conclusion that

$$\gamma = \frac{1}{1.5} = \frac{2}{3}.$$

Now these parameters can be used to model the measles outbreak as a general deterministic epidemic, as in Chapter 4. Figure 8.2 shows the numerically simulated number of infectives

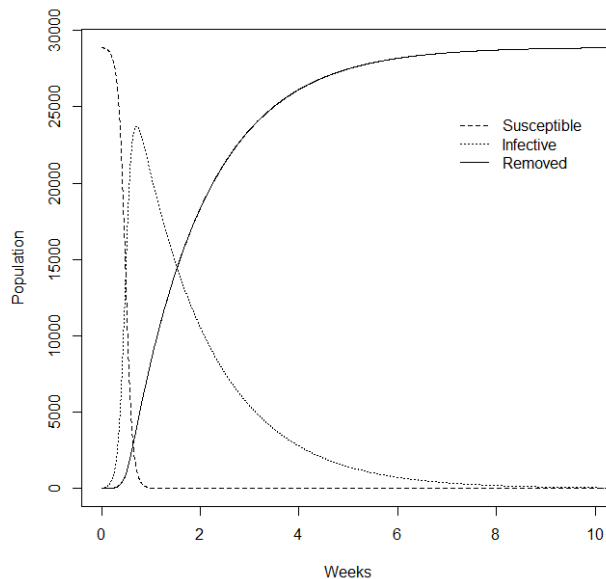


Figure 8.2: Modelling measles with the general deterministic epidemic with  $x_0 = 28870$ ,  $y_0 = 34$ ,  $\beta = 0.000554$  and  $\gamma = 0.667$ .

plotted against time, modelled by the general deterministic epidemic using the R code from Section 4.4.5.

This model suggests that, under the standard assumption of homogeneous mixing, roughly no susceptibles remain after one week, with no infective members left after around eight weeks.

The conclusion that every child not fully vaccinated in the Swansea area will become infected with measles during the epidemic seems quite extreme. The fact the model displays this is a consequence of the very high value of  $r_0$  and the homogeneous mixing assumption. It does not take into account once a child is infected with measles they will most likely be isolated in hospital or stay in bed at home, and hence would struggle to infect other susceptibles, meaning homogeneous mixing between all population members is probably not a valid assumption. In addition, the health boards affected by the outbreak implemented a variety of preventative measures.

Different methods of preventative measures including vaccination, updating public awareness and population screening and are discussed in depth by Carneiro and Howard (2011, p137) and Beaglehole *et al.* (1993, p83). The methods used in this instance were highlighted in the Public Health Wales post epidemic report. They included additional immunisation of susceptible members leading to an extra 30000 vaccinations across vulnerable areas, and a specialist measles control call centre for quicker diagnosis and to provide advice to keep infectious members from passing the disease on.

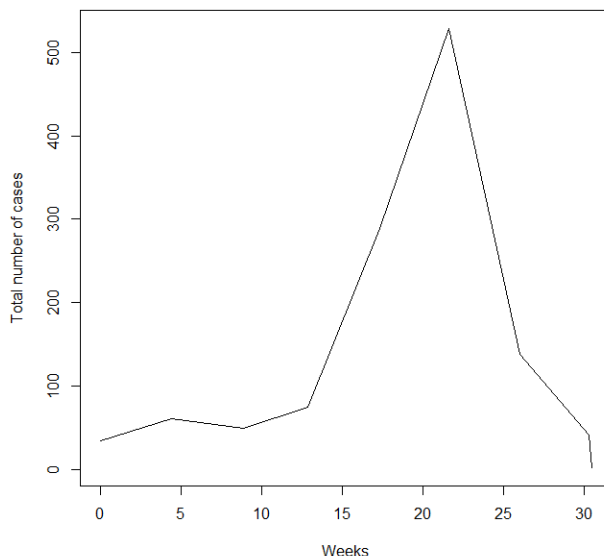


Figure 8.3: The monthly number of reported cases through the evolution of the epidemic, data taken from Public Health Wales.

Again, using the data from the Public Health Wales website, the number of new cases reported each month is plotted in Figure 8.3. The cumulative number of people infected throughout the course of the epidemic was 1219. The total number of reported cases given by Public Health Wales is shown in Figure 8.4.

The difference between the deterministic model and the real data is large. In the model all 28870 susceptibles become infected within one week, whereas in reality only 1219 people became infected in 30 weeks. This could be down to a variety of factors. Certainly the homogeneous mixing assumption may not be correct in this case as explained above. Also, the assumptions made to estimate  $\beta$  and  $\gamma$  for this model may interfere with the data. However, the preventative measures put in place by the health boards trying to control the outbreak may also play a big part. If nearly 30000 susceptible members were homogeneously mixing with a disease as highly contagious as measles, it is easy to imagine that all members may become infected. In practice, homogeneous mixing between around 30000 children is not a wholly realistic assumption to make. In this instance the health boards managed to drastically slow the spread of the disease, strongly limiting the number of infections to roughly 5% of the under or un-vaccinated child population.

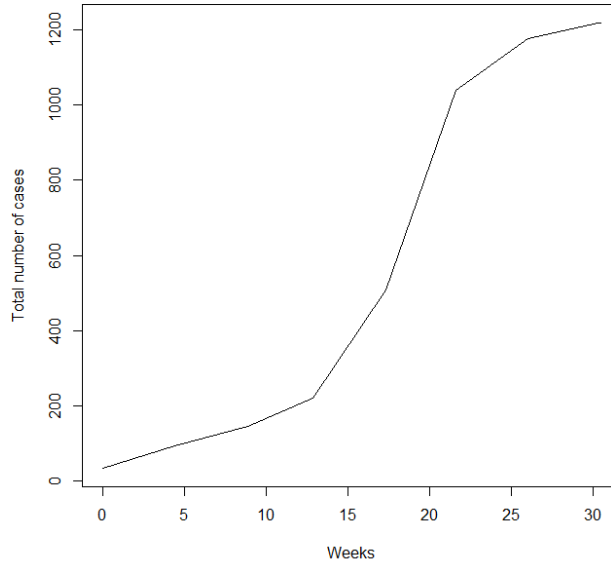


Figure 8.4: The total number of reported cases through the evolution of the epidemic, data taken from Public Health Wales.

### 8.1.2 Vaccinating in the general deterministic model

The preventative measure of vaccination can be imitated by adding a vaccination rate  $v$  to the general deterministic differential equations given by Equations (4.1), (4.2) and (4.3) in a similar fashion to Keeling *et al.* (2013). This vaccination rate would aim to keep vaccinating a constant rate  $v$  of current susceptibles, taking them straight to the removal class. This leads to the modified set of differential equations

$$\begin{aligned} \frac{dx}{dt} &= -\beta xy - vx \\ \frac{dy}{dt} &= \beta xy - \gamma y \\ \frac{dz}{dt} &= \gamma y + vx. \end{aligned}$$

Assuming that the aim was to keep constant a rate of vaccination of 10% of the susceptible population, numerically solving these equations in the case  $v = 0.1$  with  $\beta = 0.000554$  and  $\gamma = 0.667$  gives the plot shown in Figure 8.5.

Here the time until no susceptibles remain is slightly longer, and with the vaccination policy removing a proportion of susceptibles, they will not all pass through the infected state. This is highlighted by the slightly lower peak of the curve illustrating the number of infectives.

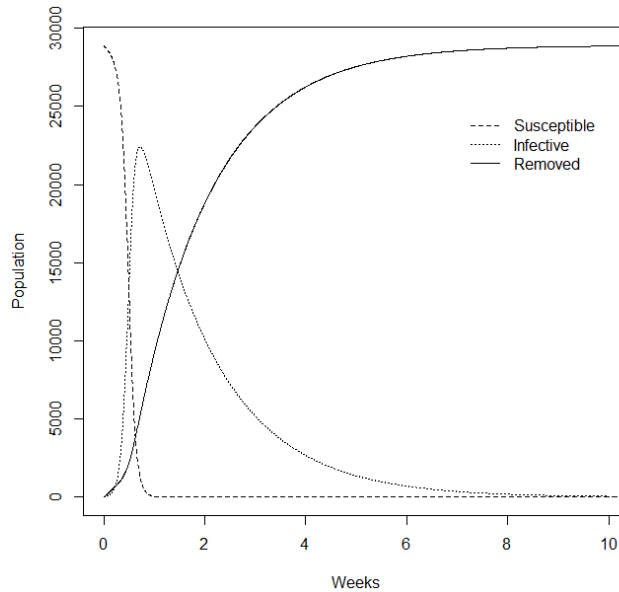


Figure 8.5: Modelling measles with the general deterministic epidemic with  $x_0 = 28870$ ,  $y_0 = 34$ ,  $\beta = 0.000554$ ,  $\gamma = 0.667$  and  $v = 0.1$ .

### 8.1.3 Increasing the removal rate parameter

Furthermore, the measles control call centre would lead to quicker diagnosis and hence removal from the infective class, and the increased public awareness of the outbreak through news and word of mouth may lead to an increased removal rate from the infective class. Assuming this action could double the removal rate of infective members, equivalent to taking  $\gamma = \frac{4}{3} = 1.33$ , with all other parameters unchanged, gives the plot in Figure 8.6.

Again this reduces the size of the infective curve, giving a shorter time until no infectives remain of around four weeks. This is to be expected, as increasing only the rate at which infectives are removed should reduce the size and length of the epidemic. Comparing the infective evolution in Figure 8.6 to the actual evolution in Figure 8.4 suggests that the model is still some way off reality, overestimating the number of infectives and under estimating the time taken for these infections to occur.

### 8.1.4 Adapting the model to include inhomogeneous mixing

As mentioned earlier, homogeneous mixing between the whole population is likely to be unrealistic. Adapting the interacting groups model explained for the simple deterministic epidemic in Section 3.6 could help gain an understanding into the dynamics of having more than one group. In this instance, it is assumed that each individual health board area is a single

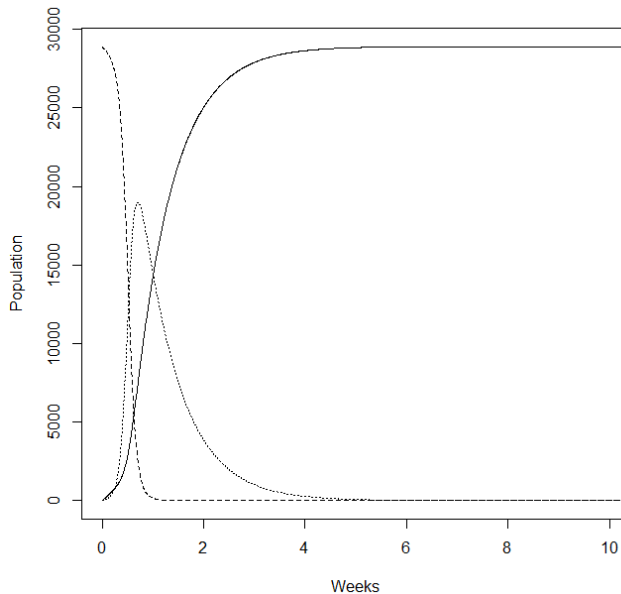


Figure 8.6: Modelling measles with the general deterministic epidemic with  $x_0 = 28870$ ,  $y_0 = 34$ ,  $\beta = 0.000554$ ,  $\gamma = 1.33$  and  $v = 0.1$

group, giving  $m = 3$  groups. For simplicity it is also assumed that the internal infection rates  $\beta_1 = \beta_2 = \beta_3 = \beta$  are the same and the external infection rates  $\beta_{ij} = 0.01\beta$  for  $i \in \{1, 2, 3\}$ ,  $j \in \{1, 2, 3\}$  and  $i \neq j$ . Finally assuming the initial number of susceptibles and infectives are the same in each group, means there will be three groups evolving identically. This can be incorporated into the general deterministic differential equations. Further building on the model including vaccination discussed up to Section 8.1.3, each group will evolve according to the equations

$$\begin{aligned} \frac{dx}{dt} &= -\beta xy - 0.01\beta(m-1)xy - vx \\ \frac{dy}{dt} &= \beta xy + 0.01\beta(m-1)xy - \gamma y \\ \frac{dz}{dt} &= \gamma y + vx. \end{aligned}$$

As each group is identical and the model is deterministic, the solution for the population as a whole is the solution for one group multiplied by  $m = 3$ . Numerically simulating these equations for the current number of infectives gives the plot in Figure 8.7.

Here the actual number of infectives predicted by the model is substantially reduced by the interacting group model between the three health boards. However, this model still overestimates the number of infectives and fails to encapsulate the lag before the large increase

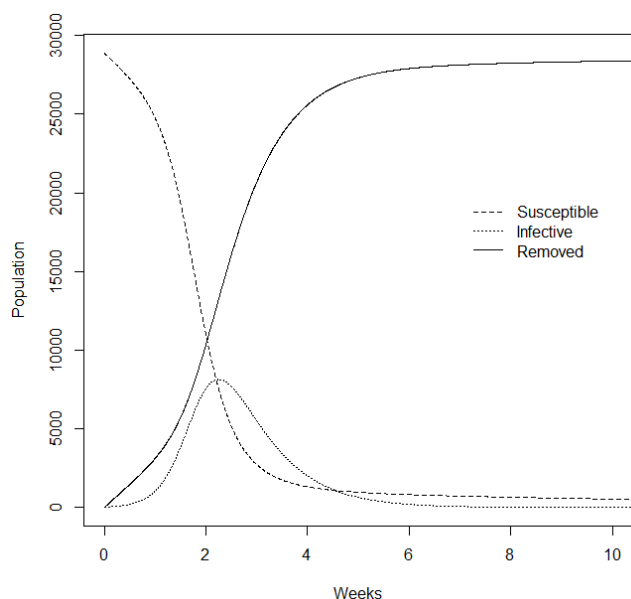


Figure 8.7: Modelling measles with the general deterministic epidemic with  $m = 3$  groups,  $x_0 = 28870$ ,  $y_0 = 34$ ,  $\beta = 0.000554$ ,  $\gamma = 1.33$  and  $v = 0.1$

in the number of infectives in the real world data. This lag in the real world data that is not present in the model could be caused by the model failing to express the latent period of measles where members are infected but not infectious to other susceptibles.

### 8.1.5 Adapting the model to include a latent period

To model the exposed period between the periods in which a member is susceptible and infective, an extension of the susceptible - infective - removal model is required. Different extensions of this model are discussed by Brauer *et al.* (2008). In this case, introducing an exposed class  $W$  between the susceptible and infective class is required, with  $w$  representing the number of population members waiting to become infected in the exposed class. Now, instead of going straight from susceptible to infective, each infected member becomes exposed for some period of time, before leaving this exposed class with some rate  $\mu$  per unit time. This leads to the system of equations



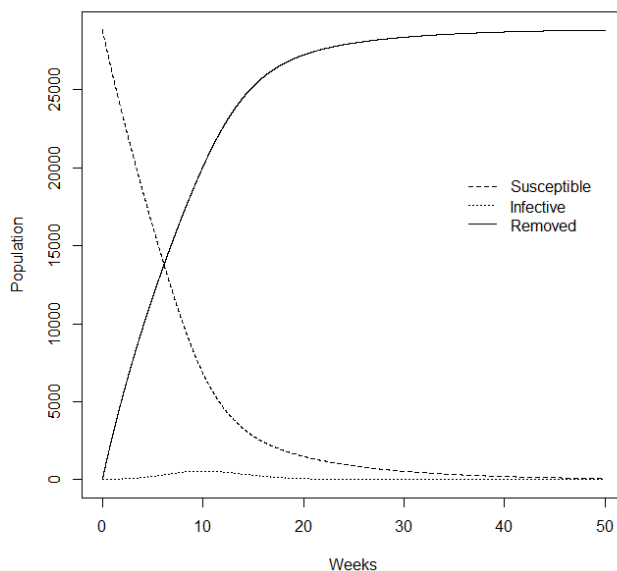


Figure 8.8: Modelling measles with the general deterministic epidemic, modified to include an exposed class, with  $m = 3$  groups,  $x_0 = 28870$ ,  $y_0 = 34$ ,  $\beta = 0.000554$ ,  $\gamma = 1.33$  and  $v = 0.1$

$$\begin{aligned}\frac{dx}{dt} &= -\beta xy - 0.01\beta(m-1)xy - vx \\ \frac{dw}{dt} &= \beta xy + 0.01\beta(m-1)xy - \mu w \\ \frac{dy}{dt} &= \mu w - \gamma y \\ \frac{dz}{dt} &= \gamma y + vx.\end{aligned}$$

In the Public Health Wales post epidemic report the incubation, or exposed, period of the outbreak was given to be between 6 and 21 days. For simplicity here it is taken to be 2 weeks, so by the same reasoning used earlier to estimate  $\gamma$ ,  $\mu = \frac{1}{2}$ , as roughly half the exposed members present at the start of one week will have left the exposed class at the end of one week. Adapting the R code used in Section 4.4.5 to include this new latent class and to simulate this numerically gives the plot in Figure 8.8.

This significantly reduces the height of the infective curve, and extends the time taken for the small amount of infectives present to reduce to zero to over ten weeks. Figure 8.9 shows just the infective curve for this model, plotted with the real data.

Modifying the model to include an exposed period seems to have a large effect on reducing the height of the infective curve, bringing the model with these parameters close to the actual

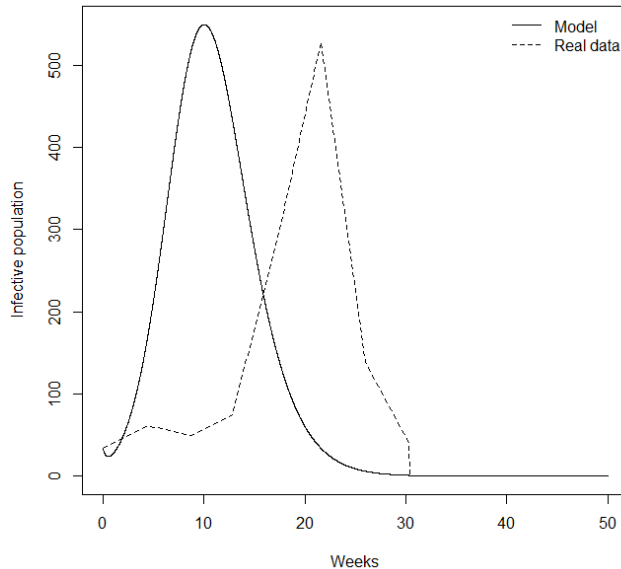


Figure 8.9: Infectives in the general deterministic epidemic, modified to include an exposed class, with  $m = 3$  groups,  $x_0 = 28870$ ,  $y_0 = 34$ ,  $\beta = 0.000554$ ,  $\gamma = 1.33$  and  $v = 0.1$  plotted alongside the real data.

data for the measles outbreak. This modification still fails to fully explain the lag before the large peak in the real world data, this could be down to the randomness that cannot be expressed by the deterministic model. As there are only a small number of infectives initially, removals may occur before infections start to have a large influence on the data, and this randomness cannot be expressed by the deterministic model. The lag could also be due to the validity of the model failing at these early times before epidemic has really taken hold in the population.

Overall the large number of assumptions made in this section suggest these parameter values used may not be wholly accurate and believable. In spite of this, whilst not mirroring the reality of the measles outbreak exactly, these plots show that preventative measures such as vaccination, actions that can increase the rate of removals from the infective state, looking closer at the homogeneous mixing assumption and including a latent period in the model can all have large effects on reducing the predicted size of an epidemic.

An in depth look at developing at introducing an exposed class is discussed by Goufo *et al.* (2014). This lead to a whole family of compartmental models which have been adapted with the aim of modeling many different disease states and types of epidemics, see Brauer *et al.* (2008) and Brauer and Castillo-Chavez (2013).

## 8.2 Disease spread in care homes

Another situation in which the rapid spread of disease could be devastating is in confined populations with weak immune systems. Hospitals, nurseries and schools could all possibly fall into this category, however this section will consider the spread of respiratory tract infections (RTIs) in care homes for the elderly. Loeb *et al.* (2000) monitored 16 care homes in Toronto over 3 years finding that 24% of respiratory tract infections in this period occurred due to outbreaks in the homes, and that the overall case fatality rate from RTIs was 8%. If the outbreaks of RTIs could be limited, staff efforts and money spent on caring for infected patients could be redistributed, and lives of patients could even be saved.

In this instance, RTIs are classed as any infection of the sinuses, throat, airways or lungs that can be passed between care home residents such as influenza and pneumonia. These kind of infectious diseases are comparatively common and more deadly in the elder populations than in the population as a whole.

### 8.2.1 Modelling an outbreak stochastically

As most care homes only usually house up to around 100 patients, the small population means a stochastic epidemic model may be appropriate to investigate this kind of situation.

Loeb *et al.* (2000) reported that the infection rate for one member was 0.42 per 1000 resident days. Therefore for a care home with 100 members starting with one infective, there would be 0.42 infections in 10 days, and so the infection rate can be approximated by  $\lambda = 0.042$  per day. Furthermore, the recovery time between different RTIs varies, as does the infectious period. Here the average recovery time is taken to be 2 weeks, or 14 days, and it is assumed that an infective member is infectious during this period. This means the removal rate can be estimated by  $\gamma = \frac{1}{14} = 0.0714$  to three significant figures. As in the previous section, these are strong simplification assumptions made to gain a set of usable parameters and hence should be treated with caution. Even if the parameters are not wholly accurate, they will provide a good insight into how altering these parameters can change the outcome of an epidemic.

Inputting  $I = 1$ ,  $N = 99$ ,  $\lambda = 0.042$  and  $\gamma = 0.0714$  into the numerical model of the general stochastic epidemic from Section 7.4 gives the plots in Figure 8.10. This seems to suggest that under the homogeneous mixing assumption used in this model, that all susceptibles will become infected within the space of a few days, and that it takes a long time for infectives to recover afterwards. The homogeneous mixing assumption seems more valid here than in measles example considered in Section 8.1 as the population size is much smaller, and the whole population is confined to one care home.

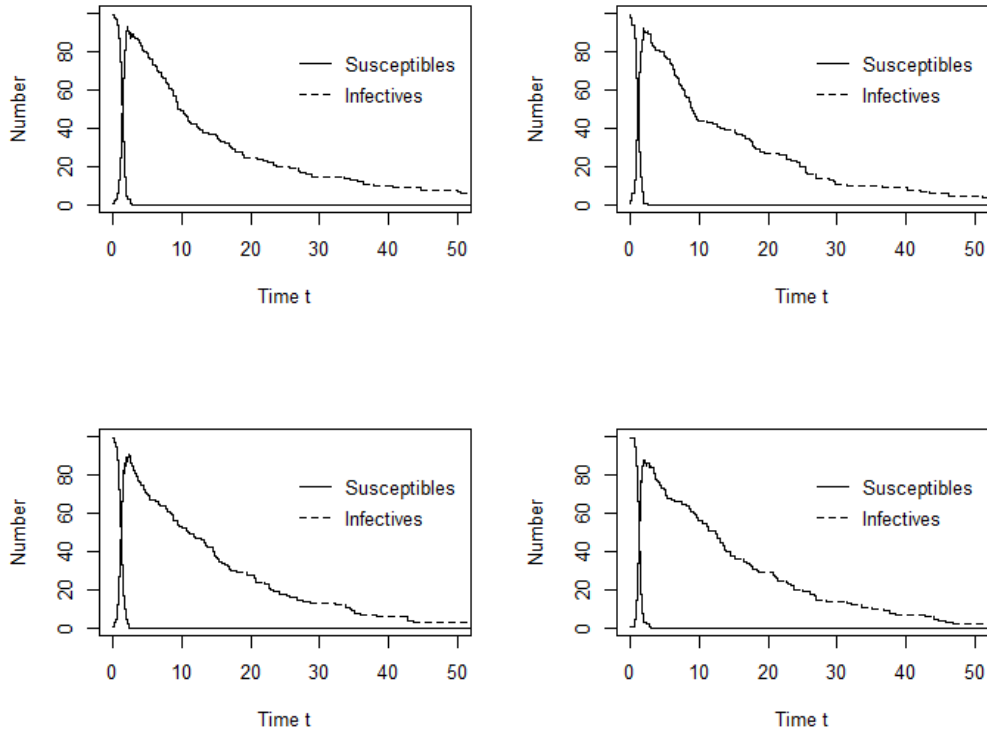


Figure 8.10: Four realisations of the general stochastic epidemic in a care home with  $I = 1$ ,  $N = 99$ ,  $\lambda = 0.042$  and  $\gamma = 0.0714$ .

Figure 8.11 shows the proportions of end times and remaining susceptibles once the epidemic is over averaged over 1000 simulations. The vast majority of simulations end with all susceptibles becoming infected and removed, however a very small proportion of the epidemics end very quickly, illustrated by the small proportion around 0 in Figure 8.11 (left) and 99 in Figure 8.11 (right).

A situation such as this, where a large number of residents become infected and possibly die, would obviously be disastrous for a care home. Using the historical care home RTI mortality data from the investigation conducted by Loeb *et al.* (2000), 8 patients could be expected to die as a result of this outbreak. A variety of preventative measures discussed in the previous section could be implemented by the care home to counter an outbreak like this. The next section will focus on the importance of early identification and isolation of infected members, recommended by the Department of Health as a key measure in the prevention of care home outbreaks.

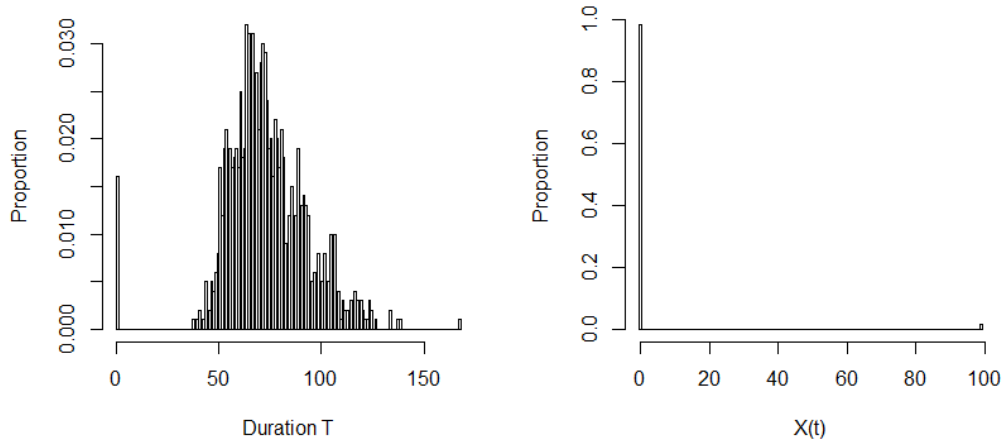


Figure 8.11: Proportions of durations (left) and remaining susceptibles (right) from the general stochastic epidemic in a care home with  $I = 1$ ,  $N = 99$ ,  $\lambda = 0.042$  and  $\gamma = 0.0714$ .

### 8.2.2 The influence of the removal rate parameter

The aim of early identification and isolation is to increase the value of the removal rate  $\gamma$  so that removals happen regularly enough to counter the effect of increasing number of susceptibles becoming infective. Introducing a weekly screening of the care home residents and putting any found infective patients in isolation until they recover would mean that a member could be infective to the susceptible residents for at most one week. This would cause an approximate increase in  $\gamma$  from  $\frac{1}{14}$  to  $\frac{1}{7} = 0.143$  to three significant figures. Performing 1000 simulations with these parameters leads to the histograms in Figure 8.12.

Compared to Figure 8.11 there has been a slight increase in the proportion of simulations where nearly all of the susceptible members remain susceptible until the epidemic is over. This increase is only negligible though, and the proportion of cases where all susceptibles are infection is still much greater.

To get a better idea of how regularly health checks for symptoms of the care home residents would be needed to make a significant difference, Figure 8.13 shows the histogram of remaining susceptibles for the care home outbreak model with  $I = 1$ ,  $N = 99$ ,  $\lambda = 0.042$  and  $\gamma = \frac{1}{14}$  (top left),  $\gamma = \frac{1}{7}$  (top right),  $\gamma = \frac{1}{1} = 1$  (bottom left) and  $\gamma = \frac{1}{0.5} = 2$  (bottom right). These values for  $\gamma$  correspond to two weekly, weekly, daily and half daily regular checks and then isolation for infective members respectively.

With daily checks, illustrated in Figure 8.13 (bottom left), the chance of a serious epidemic expressed by the proportion bars on the left hand side of the plot is roughly equal to the proportion of outbreaks where there is no real spread, indicated by the bars on the right hand

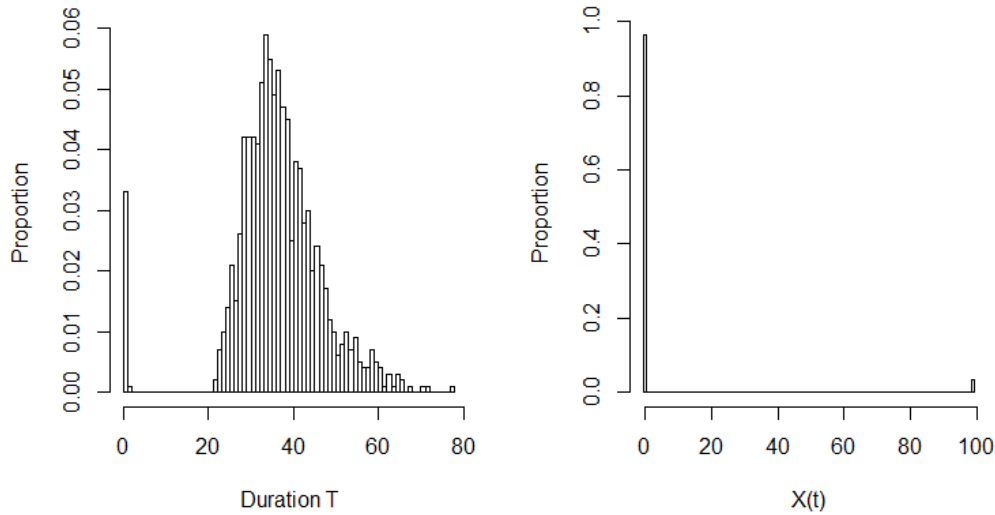


Figure 8.12: Proportions of durations (left) and remaining susceptibles (right) from the general stochastic epidemic in a care home with  $I = 1$ ,  $N = 99$ ,  $\lambda = 0.042$  and  $\gamma = 0.0714$ .

side of the plot. Furthermore the plot with half daily checks on the bottom right shows that the chance of avoiding an epidemic where the majority of patients become infected is more likely than not. Intuitively, as the removal rate  $\gamma \rightarrow \infty$ , the proportion of epidemics with a large number of infections should fall to 0, while the proportion of ‘epidemics’ finishing before any infections have been made should tend to 1. This is reinforced by the histogram in Figure 8.14 which shows the proportions of remaining susceptibles from 1000 simulations when hourly checks are made on the care home residents for symptoms of RTIs, and discovered infectives isolated immediately. Here because of the hourly check on patients, the removal rate is estimated as  $\gamma = \frac{1}{24} = 24$ .

In this case none of the simulations result in a large spread of disease, with 99 remaining susceptibles being the case with the highest proportion by far, and in all other simulated cases the vast majority of susceptibles pass through the process uninfected. In this instance, the lack of any proportions around 0 suggest there seems to be hardly any chance of a large number of care home residents becoming infected.

This indicates that the regular monitoring of care home residents for, not just RTIs, but all infectious diseases, and isolating any patient showing symptoms can vastly reduce the impact of an infectious disease on a closed population. It is therefore vital that staff are regularly observing and talking to residents to try to identify and eliminate possibly fatal disease spread between them.

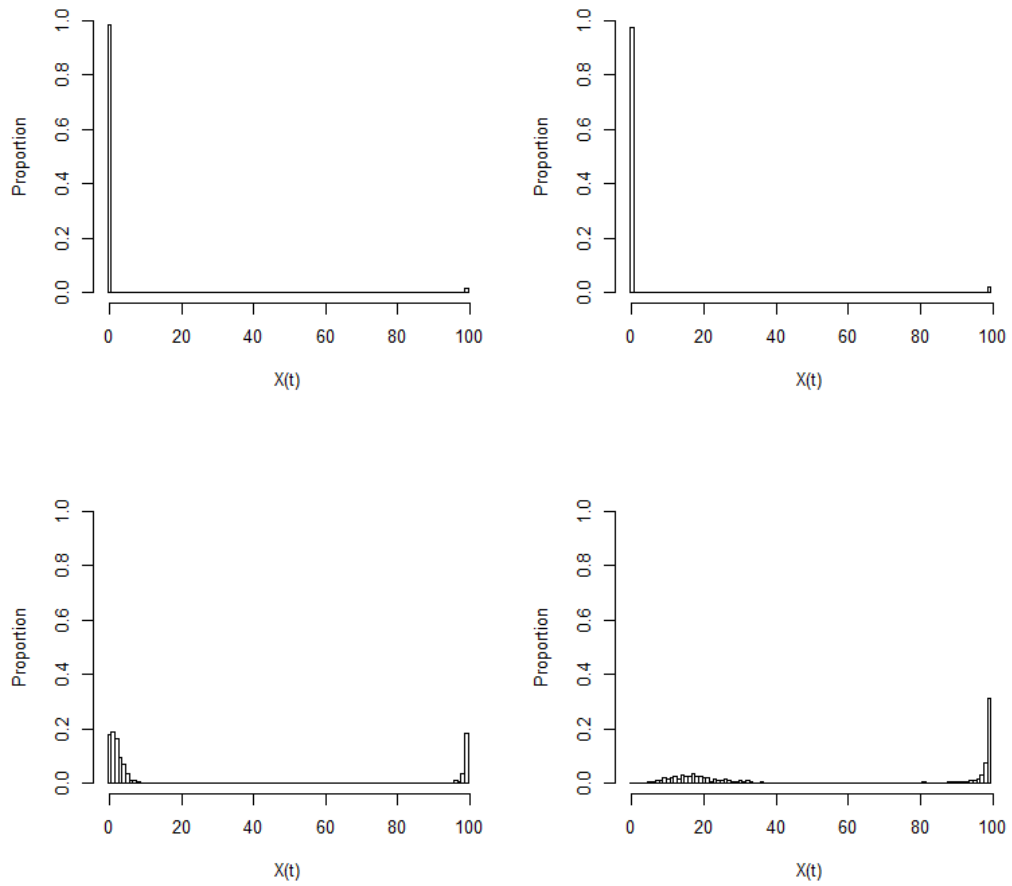


Figure 8.13: Proportions of remaining susceptibles from the general stochastic epidemic in a care home with  $I = 1$ ,  $N = 99$ ,  $\lambda = 0.042$  and  $\gamma = \frac{1}{14}$  (top left),  $\gamma = \frac{1}{7}$  (top right),  $\gamma = 1$  (bottom left) and  $\gamma = 2$  (bottom right).

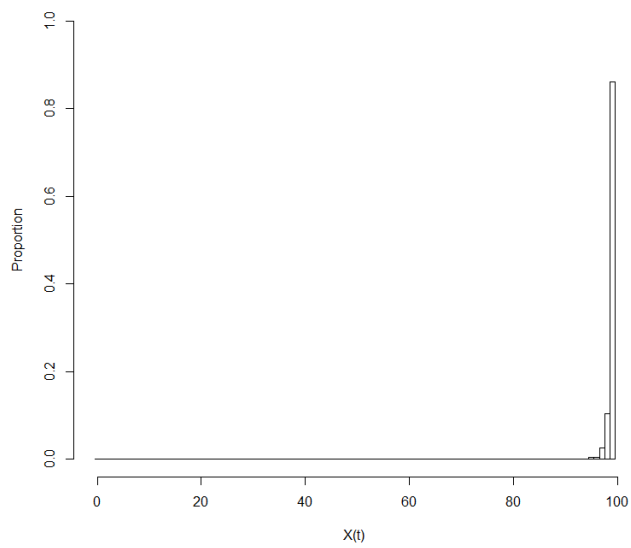


Figure 8.14: Proportions of remaining susceptibles from the general stochastic epidemic in a care home with  $I = 1$ ,  $N = 99$ ,  $\lambda = 0.042$  and  $\gamma = 24$ .



# Chapter 9

## Discussion

After developing the tools and investigating some of the interesting theoretical results that have arisen as a consequence of modelling an epidemic deterministically and stochastically as done up to Chapter 7, Chapter 8 demonstrates how these models can be applied to real world situations. The models discussed can be used to examine the sensitivity of an epidemic to the variation and introduction of new parameters and preventative measures.

The power to implement these modelling techniques whilst an epidemic is in process could be vital to decision makers and medical professionals dealing with an outbreak of an infectious disease. Being able to model the effect of introducing preventative measures such as mass vaccination or isolation into a population can be quantified by mathematics and should be able to provide additional, useful information when trying to control an epidemic outbreak.

With more time, the theory needed to extend and develop more involved versions of the models discussed in this report would be investigated. This could lead to developing more complex models such as the extended general stochastic models discussed by Gani (1967) and adapting and introducing different versions of the compartmental model discussed briefly at the end of Chapter 8 to better model reality, as done by Brauer and Castillo-Chavez (2013). In addition, the chain binomial model discussed by Becker (1981) provides an alternative way to view an epidemic, describing an epidemic as a sequence of binomial random variables. Daley and Gani (1999, p105) comment on how this class of model is useful when dealing with diseases with a short infective period in comparison to their latent period. Developing this chain binomial model could also lead to more accurate real world models of some situations.

Alongside this, more effective and realistic methods of model parameter estimation would be explored in a similar fashion to Dietz (1993), who provides different estimates for  $r_0$  depending on the parameters for the disease in consideration and the stage of the epidemic. Also Heffernan *et al.* (2005) describe how the base reproduction ratio can be defined, and estimated,

through the use of integrated hazard rates.

The combination of these two improvements to the models introduced in this report would lead to many more realistic, interesting and accurate applications to the real world spread of epidemics.

One of most serious examples of mathematical epidemic modelling influencing disease outbreak policy in recent years is the outbreak of foot and mouth disease in 2001. The mathematical models of how the disease was expected to evolve made up part of the information used by policy makers when deciding to cull all farms close to, or infected with, foot and mouth disease. This led to over 10 million sheep and cattle being killed, with the loss of livestock and tourism estimated to have cost the UK over £8 billion.

The models used during the foot and mouth epidemic are described by Talyor (2003) in a review of the use of models in forming disease policy for the Department for Environment and Rural Affairs. These models were developed quickly during the early stages of the outbreak and backed up the veterinary suggestions that culling all neighbouring farms, and farms within 3km of an infected premises, within 24 hours of diagnosis would reduce the length and severity of the epidemic.

In his review of the main models used, Keeling (2005) describes how disease spread is modelled on a local scale by using spatial clustering to express the closeness of farms. This was required because as farms are in fixed locations with animals usually staying resident on only one farm, homogeneous mixing between all farm animals in the country would not be a valid assumption to make. Keeling (2005) also describes how these huge models, which involved the diseased status of every farm in the country, were updated daily with the aim of giving policy makers an insight into how any course of preventative measures they may undertake would unfold in the future.

Despite all the epidemiological and modelling developments using these highly technical and complex models, there were still some points in reality which the model failed to express. The spatial clustering of farms only modelled the location of the farm houses. This was a problem as the boundary of a farm where animals could graze may lie far from the actual farm house, which is something that could not be described by the model. Additionally the changing of infectivity of the disease throughout the outbreak could not be modelled, meaning a constant infection rate for the different animals was used for all times throughout the modelling of the disease.

This example highlights how difficult modelling large scale epidemics in reality is, there is always multitude of factors that could have an effect on the outbreak. However, as shown in this report, epidemic models can be an important decision making tool, illustrating how introducing and changing different factors, parameters and preventative measures can effect

the outbreak as a whole.

It is important that care is taken when presenting the results found from a mathematical epidemic model to decision makers who may not necessarily have a strong mathematical grounding. But, when used as part of a well informed decision making process, and as modelling techniques, theory and research continue to improve, epidemic modelling of infectious diseases will continue to establish itself as a key resource in the handling of epidemiological crises in the future.

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