Modelling Repeated Epidemics with General Infection Kernels.

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Abstract

This thesis is on mathematical modelling in epidemiology, exploring the generic characteristics of diseases in two different population structures.

Integral equations are used, to model the epidemics in each generation (of the epidemic). Difference equations are then used to model the change in the populations between epidemics. Initially, single dimension populations are modelled, where the entire population is considered to be one class. Then the population is split into two classes and a similar analysis is performed, with critical differences noted between the two structures. An analytical approach is taken, with numerical examples.

The work in this thesis is not specific to one disease, the main focus is to develop a stepped process between generations of the epidemic and analyse the behaviour.

Acknowledgements

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Chapter 1 Introduction.

Since 1760, when Daniel Bernoulli developed a mathematical model of the impact of vaccination against smallpox[1], there has been an increasing demand for models of various infections. Mathematical models help us achieve a better understanding of the dynamics of infections, which may then allow us to efficiently implement control techniques.

Infections are continually changing, whether it is change due to drug resistance or just mutation within the infectious agent. Our population dynamics are also changing, which has a large effect on the transmission and probability of infection – and so the mathematical models must also change.

This thesis will look at a simple model for an infection, with six generic examples given throughout the analysis. An integral equation technique is used to model the epidemic and then a discrete mapping system is used to model the dynamics of the population between successive epidemics. We first need to describe the assumptions and terminology used when modelling a disease.

1.1 The Model

Consider a population that can be split into three classes (in relation to an epidemic): those who are susceptible to the infection, the infectious people, and those who are removed from the epidemic (through immunity or

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[1] Dietz & Heesterbeek (2002)

death), i.e. no one member of the population may be infected twice. In the following analysis, we assume that the total population is constant.

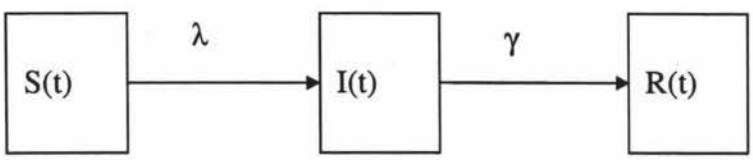

Figure 1.1 SIR Model – the population is divided into three compartments in relation to the infection: susceptibles (*S*), infectives (*I*)and removed (*R*).

The simplest model is depicted in Figure 1.1. The three compartments can represent population density or population size – as the total population size is assumed to be constant it makes no difference. Susceptibles becomes infected at a rate λ resulting from contact with infectives. Contact here is very loosely defined, as the amount of contact needed to become infected will be depend on the infection being modelled. Infectives then become part of the removed compartment at a constant rate γ. As the population size is constant, we know that the change in the population will be zero, .i.e.

$$\frac{dS}{dt}+\frac{dI}{dt}+\frac{dR}{dt}=0 \tag{1.1}$$

The differential equations to describe this model are:

$$\begin{aligned}\frac{dS}{dt}&=-\beta\chi\frac{SI}{N}\\ \frac{dI}{dt}&=\beta\chi\frac{SI}{N}-\gamma I\\ \frac{dR}{dt}&=\gamma I\end{aligned} \tag{1.2}$$

Where χ is the rate at which susceptibles contact other members of the population and β is the probability of a susceptible being infected given contact with an infected member of the population. We have assumed that the population size is constant, that is: $S(t)+I(t)+R(t)=N$, so it is easy to see that one of the above equations is redundant.

The rate λ is the force of the infection, that is, the rate that susceptibles become infected[2]. We have

$$\lambda = \beta\chi\frac{I}{N} \tag{1.3}$$

We can solve equations (1.2) to find a relation between the susceptibles and the infectives in the population[3].

A differential equations approach has been used for numerous mathematical models, and there is a large amount of information available for the analysis of such systems. However, with constant contact parameters, the time spent in each compartment is exponentially distributed among the members of the population – this does not fit actual results. So we turn to a slightly different way of constructing a model with the use of integral equations.

Using integral equations to model an infection is more intuitive than a differential equations approach, and will match the actual data more closely. However, the down side is, there is not a lot of information

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[2] Anderson & May (1991)

[3] See Roberts & Heesterbeek (2000).

published relating to the analysis of such systems. This thesis is based on the integral equation approach that will now be defined[4].

1.2 Probability of Infection

The probability of a susceptible being infected depends on their contact with an infective and the probability of infection given this contact, which depends on the time since the infective was itself infected. If we let $p(\tau)$ be the probability of contact and infection, and $\chi(\tau)$ be the contact rate with an infective, where τ is the time since the infective was initially infected, we let

$$A(\tau) = p(\tau)\chi(\tau) \tag{1.4}$$

So the function $A(\tau)$ represents the probability of contact and infection with an infective at infection time τ (the time since infection took place).

Throughout the following work, six different functions $A(\tau)$ will be used to illustrate the model, where $\tau \geq 0$.

1.2.1 Distribution 1

$$A(\tau) = \begin{cases} 0, & \tau < T_1 \\ a, & T_1 \leq \tau \leq T_2 \\ 0 & \tau > T_2 \end{cases}$$

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[4]Please refer to Diekmann & Heesterbeek (2000) for further elaboration on the integral equation approach.

When τ is less than some specified time T_1 or greater than a second specified time T_2 there is no chance of a susceptible being infected when contacting an infective. When τ lies between the two specified times, there is a constant probability of infection when a susceptible comes in contact with an infective. The period between time zero and T_1 can be seen as a latency period in the infection.

1.2.2 Distribution 2

$$A(\tau)=\begin{cases} a, & 0\le\tau\le T_1 \\ 0, & \tau>T_1 \end{cases}$$

This is similar to distribution one, but now there is a constant probability of contact and infection with an infective from time zero to time T_1. At any other time there is no chance of infection.

1.2.3 Distribution 3

$$A(\tau)=ae^{-c\tau},\ \tau\ge 0$$

Where a and c are positive constants. For this distribution, the probability of contact and infection decreases in a negative exponential in the time since infection. Note that this is the same as for the differential equations model, as a member of the population will spend an exponential amount of time within a compartment.

1.2.4 Distribution 4

$$A(\tau)=a\tau e^{-c\tau},\ \tau\ge 0$$

Again, a and c are positive constants. Here, the probability of contact and infection has a similar shape to the gamma distribution (see Figure 1.2 for further clarification).

1.2.5 Distribution 5

$$A(\tau) = ae^{-c(\tau - T_1)^2}, \ \tau \geq 0$$

As expected, a, c and T_1 are positive constants. The probability of contact and infection takes the shape of a shifted normal distribution curve, but we further truncate this, as we are dealing only on a positive time scale.

1.2.6 Distribution 6

$$A(\tau) = \begin{cases} \dfrac{a}{T_2 - T_1}(\tau - T_1), & T_1 \leq \tau \leq T_2 \\ a, & T_2 < \tau < T_3 \\ \dfrac{-a}{T_4 - T_3}(\tau - T_4), & T_3 \leq \tau \leq T_4 \\ 0, & \textit{otherwise} \end{cases}$$

The probability of contact and infection takes the form of a trapezium. From $\tau = 0$ to T_1 there is a latency period, and the from T_1 to T_2 the probability of contact and infection increases linearly, to reach its maximum at T_2. This maximum lasts until T_3 when it starts to decrease linearly to zero at T_4. This is one of the most flexible distributions and was recently used by Roberts[5] to model SARS.

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[5] Refer Roberts (in prep.)

Example plots are given below to further elaborate on the above explanations.

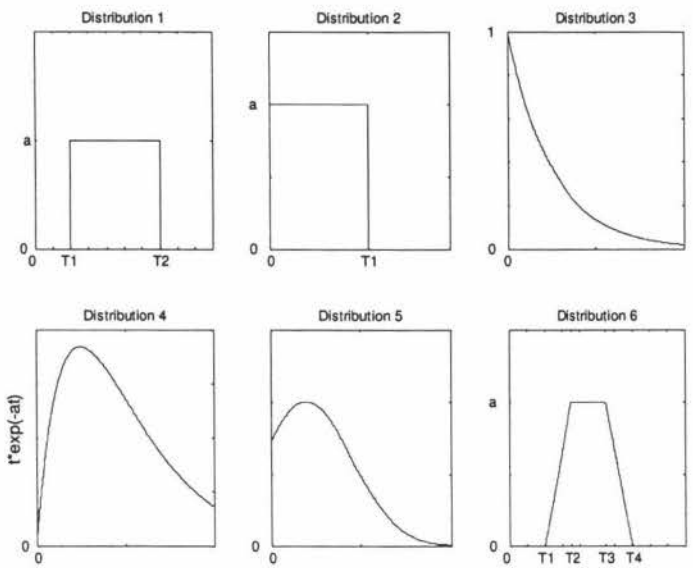

Figure 1.2 Contact Rate/Probability Distributions, time on the x axis

1.3 The Basic Reproduction Ratio

To see if an infection will persist within a population, we consider the basic reproduction ratio, represented by R_0, of the epidemic. We define the basic reproduction ratio as follows:

> The basic reproduction ratio is the number of secondary cases that arise from a primary case in a susceptible population (Diekmann & Heesterbeek 2000).

So the critical value of R_0 is one. If $R_0 < 1$ then the epidemic will not persist in the population, and the number of infectives will decrease. If $R_0 > 1$ then the epidemic will continue through the population, and the number of

infectives will increase while the number of susceptibles will decrease. We can see that R_0 will depend on the population size, the contact rates and the probability of infection, hence:

$$R_0 = S(0)\int_0^{\infty} A(\tau)\mathrm{d}\tau \tag{1.5}$$

1.4 The Incidence of Infection.

The incidence of infection $i(t)$ is the number of new cases per unit time. So we see that it will be equal to the change in the susceptible population (as we have ignored changes in the susceptible population due to other causes).

At time t, the number of new cases of the infection depends on the contacts between susceptibles and infectives – those who were infected themselves before time t. So we have:

$$i(t) = i_0\delta(t) + S(t)\int_0^t A(\tau)i(t-\tau)\mathrm{d}\tau \tag{1.6}$$

where the $i_0\delta(t)$ accounts for the initial introduction of the infection into the population[6].

We may also rewrite this in terms of the change in the susceptible population:

$$-\frac{\mathrm{d}S(t)}{\mathrm{d}t} = i_0\delta(t) - S(t)\int_0^t A(\tau)\frac{\mathrm{d}S(t-\tau)}{\mathrm{d}t}\mathrm{d}\tau \tag{1.7}$$

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[6] $\delta(t)$ is the Dirac's delta function

1.5 The Initial Growth Rate

The number of infectives can be modelled by an exponential during the initial phases of infection. So we let

$$i(t) \approx ke^{rt} \tag{1.8}$$

for some positive constant r, which we call the initial growth rate of the infection. As we said above, the change in infectives is proportional to the incidence of infection. We can then state:

$$ke^{rt} = i_0\delta(t) + S(t)k\int_0^\infty A(\tau)e^{r(t-\tau)}\mathrm{d}\tau \tag{1.9}$$

As we are examining the initial growth of the infection, we do not need to include the initial introduction of the infection into our population; hence we can omit the $i_0\delta(t)$ term. We also set the size of the susceptible population equal to its initial value[7], $S(t) \equiv S(0)$. So we solve:

$$1 = S(0)\int_0^\infty A(\tau)e^{-r\tau}\mathrm{d}\tau \tag{1.10}$$

It is shown in Diekmann and Heesterbeek (2000), that there is a unique real r that solves equation (1.10). Note that equation (1.10) is similar to our equation for the basic reproduction ratio (equation (1.5)) The correlation between the two lead to two important facts: $r > 0$ if and only if the basic reproduction ratio is greater than one, and $r < 0$ if and only if the basic

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[7] Note: $S(t) \gg i_0$, and so we let $S(0^+) = S(0^-)$. i_0 will usually be assumed to be equal to one, i.e. there will be one initial case to introduce the infection into the susceptible population.

reproduction ratio is less than one. That is, we only have initial growth of the infection if we have an epidemic.

1.6 Overview

The purpose of the following exercises is to determine R_0 (the basic reproduction ratio), r (the initial growth rate) and the final size equation of an epidemic, given a function $A(\tau)$ that characterises the epidemic. The susceptible population will first be viewed as one class, and will then be split into two classes with intra-class mixing introduced. All the calculations will be based on the following relation for the incidence of the epidemic

$$i(t)=i_0\delta(t)+S(t)\int_0^t A(\tau)i(t-\tau)\mathrm{d}\tau \qquad (1.11)$$

for our six functions $A(\tau)$ and for constant and non-constant $S(t)$.

Two methods will be used to calculate the final size of the infection. For a small epidemic, $R_0<1$, we assume that $S(t)$ is constant and equal to the initial susceptible population (as there will be no major epidemic, so the change in the population due to the infection is slower that any other change in the population). For a larger epidemic, $R_0>1$, we can not assume that the susceptible population is constant, so we use a direct method applied to equation (1.7) to calculate the final size of the epidemic.

Using the methods outlines above, we then construct a repeated epidemic process, where we consider epidemics on a discrete generation basis. Initially we assume that the entire population is susceptible, and we let an epidemic occur. We then calculate the final number of susceptibles and let

a portion of them continue on to the next epidemic generation. New susceptibles are introduced into the population to maintain a constant population. We then let another epidemic occur, calculate the final number of susceptibles from this second generation and let a proportion continue and introduce new members into the population. This is repeated, with either an epidemic occurring each generation or the infection not persisting within the population. Numerical calculations are given for this, and then a full analytic proof into the nature of the solution is given.

We then repeat out analysis of the six functions $A(\tau)$ when the population is split into two subclasses. The basic reproduction ratio will be calculated for four different mixing schemes between classes. The same methods can be used as for the one dimensional case, with slight alterations to the equations. The final size equations are calculated, and a brief introduction into applying a repeated epidemic process is given.

MATLAB has been used to generate the numerical examples with this thesis, and Maple was used for some of the analytical work.