Modeling super-spreading events for SARS

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Everlasting Father, everlasting Son, immortal Holy Ghost

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ABSTRACT

One of the intriguing characteristics of the 2003 severe acute respiratory syndrome (SARS) epidemics was the occurrence of super spreading events (SSEs). Super-spreading events for a specific infectious disease occur when infected individuals infect more than the average number of secondary cases. The understanding of these SSEs is critical to understanding the spread of SARS. In this thesis, we present a modification of the basic SIR (Susceptible - Infected - Removed) disease model, an SIPR (Susceptible - Regular Infected - Super-spreader - Removed) model, which captures the effect of the SSEs.

Chapter 1

Introduction

The Severe Acute Respiratory Syndrome (SARS) was the first epidemic of the 21st century. It emerged in China late 2002 and quickly spread to 32 countries causing more than 774 deaths and 8098 infections worldwide [14]. SARS is an example of the devastating epidemics of infectious diseases which have wiped out a significant percentage of the human population throughout history. The primary goal of this thesis is to formulate a mathematical model that captures the role of super-spreading events in the spread of the 2002-2003 SARS epidemic.

The first chapter is devoted to giving background and vital information about SARS. Our main goal here is to understand the basic epidemiology of this disease and the role of mathematical modeling in modeling the spread of the SARS epidemic. A review of two basic population models, the exponential and logistic growth model respectively, is given in Chapter 2. The next generation method, a method used for calculating an important parameter in the study of epidemics (the basic reproduction number) is presented in Chapter 3. An overview of the SIR (Susceptible - Infected - Removed) and SI_1I_2R (Susceptible - Infected Class 1 - Infected Class 2 - Removed) models, standard models in the study of infectious diseases, are presented in Chapter 4. Finally, a compartment SIPR (Susceptible - Regular Infected - Super-spreader - Removed) model is presented in Chapter 5. This model captures super-spreading events as a main feature that is believed to have been responsible for the progression of the SARS epidemic.

We start by looking at an overview of the SARS epidemic as it applies to this thesis.

1.1 What is SARS?

Severe Acute Respiratory Syndrome (SARS) is a highly contagious respiratory disease which is caused by the SARS Coronavirus. It is a serious form of pneumonia, resulting in acute respiratory distress and sometimes death.

The SARS epidemic originated in China, in late 2002. Although the Chinese government tried to control the the outbreak of the SARS epidemic without the awareness of the World Health Organization (WHO), it continued to spread. Failure of the Chinese government to seek international aid to fight the spread of SARS contributed to the epidemic spreading to most parts of the country. A Chinese doctor reported the SARS epidemic crisis to the WHO in early April of 2003, which then resulted in a system being set up to improve reporting and control in the SARS crisis [14]. The SARS outbreak is believed to have occurred between November 2002 and June 2003 between November 2002 and July 2003 [2].

1.1.1 Spread to other countries

An American businessman traveling in southern China in the fall of 2002 was the first known foreigner to contract the disease. He did not show symptoms or become ill until after he had flown from Guangzhou, China, to Hanoi, Vietnam. It is not known how many people the businessman might have infected during his travel from China to Vietnam [16]. In an age of international travel, global business, and tourism, there is no longer such a thing as a purely localized contagious disease. Diseases originating in the most remote inhabited regions can be spread globally in a matter of hours. The first line of defense is accurate and timely information. While the unfortunate American businessman was the carrier who took SARS beyond China's borders, the "head in the sand" obstructionist attitude of Beijing officials was the real culprit [16].

From Table 1.1, we see that the SARS epidemic claimed over 700 lives and infected over 8000 people worldwide between November 2002 and July 2003 [2]. There were 7780 SARS cases in the continent of Asia where the first outbreak was reported of which 729 of them died bringing the fatality rate in Asia to 9.4%. Other notable continents where the SARS epidemic was reported include Europe and Africa.

Table 1.1: Probable cases of SARS by continent, November 2002 to July 31, 2003 [2]

Continent	Cases	Deaths	Death cases not related to SARS	Fatality(%)
Europe	492	45	0	9.1
Asia	7780	729	60	9.4
Africa	1	1	0	100
Total	8273	775	60	9.6

1.1.2 SARS symptoms and signs

People affected by SARS develop a fever greater than $100.4°F$ ($38.0°C$), followed by respiratory symptoms such as cough, shortness of breath or difficulty breathing. In some cases, the symptoms become increasingly severe and patients may require oxygen support and mechanical help to breath. Symptoms found in more than half of the first 138 patients included (in the order of how they commonly appeared): fever, chills and shaking, muscle aches, cough, and headache. Less common symptoms include (also in order): dizziness, productive cough (sputum), sore throat, runny nose, nausea and vomiting, and diarrhea [2].

In most cases, symptoms appear within 2 to 3 days of infection [14]. The most prominent symptoms of SARS are high fever and coughing or shortness of breath. According to the World Health Organization (WHO), the vast majority of those infected have an incubation period less than ten days [14]. There may be many factors related to the person's immune system or factors in the environment that affect the symptoms and severity of SARS [14].

1.1.3 Transmission

SARS is caused by a previously unknown type of coronavirus, the same type that cause common cold. SARS is spread by droplet contact. When someone with SARS coughs or sneezes, infected droplets are

spread into the air. Like other coronaviruses, the SARS virus may live on hands, tissues, and other surfaces for up to six hours in these droplets and up to three hours after droplets have dried. After studying the virus, SARS was given a basic reproduction number (R_0) of three by Lipstich, a relatively low number [20]. This value is a measure of the potential of a disease to spread to susceptible populations when control measures are not taken. We explain the details of R_0 in Chapter 3.

SARS can only travel a few meters, which limits its transmissibility [4]. In order to become infected, a person usually must have either close contact with an infected person (such as in a household), intense exposure (such as in a small area like an airplane or taxi) or have been in a high risk area (such as a health care setting).

1.2 The role of mathematical modeling in the spread of the SARS epidemic

Mathematical models have become important tools in analyzing the spread and control of infectious diseases. The model formulation process clarifies assumptions, variables, and parameters; moreover, models provide conceptual results such as the basic reproduction number discussed in Chapter 3. Mathematical models and computer simulations are useful experimental tools for building and testing theories, assessing quantitative conjectures, answering specific questions, determining sensitivity to changes in parameter values, and estimating key parameters from data [9].

Our study will make use of mathematical models in epidemiology (discussed in detail in Chapter 4) which involve the use of ordinary differential equations. The models describe population behavior in continuous time, t. Ordinary differential equations describe many physical situations. Their prominence in applied mathematics is due to the fact that most of the scientific laws are more readily expressed in terms of rates of change. The SIPR model we develop eventually is a modification of the SIR model discussed in Section 4.1.

We conclude this section by giving a brief survey of SARS models developed after the 2002-2003 SARS epidemic:

- Lipsitch developed a model for the spread of Severe Acute Respiratory Syndrome (SARS) and used the model to make predictions on the impact of public health efforts to reduce disease transmis-

sion [5]. Such efforts included quarantine of exposed individuals to separate them (perhaps by confinement to their homes) from the susceptible population, and isolation of those who had SARS in strictly supervised hospital areas with no contacts other than by healthcare personnel. The Lipsitch model is an extension of the SEIR model, which is an extension of the SIR model. Besides the populations considered by SIR, the SEIR Model (Susceptible-Exposeds-Infecteds-Removeds) has an intermediate Exposed (E) population of individuals who have the disease but are not yet infectious. The Lipsitch model modifies SEIR to allow for quarantine, isolation, and death [11].

- Riley, developed a stochastic metapopulation model with hospitalized and presymptom stages to study SARS in Hong Kong. The focus of the model was to estimate the basic reproduction number, R_0, discussed in Chapter 3, in the absence of super-spreading events, control measures and nosocomial transmission. Riley concluded that the number of transmissions fell during the course of the outbreak as result of control measures and reduced contact; movement restrictions can be effective; and hospital transmission is significant [17].

- Wang developed a simplified deterministic compartment model to study the outbreak of SARS in Beijing. Their focus was parameter estimation and assessment of control measures. They concluded that applying control measures early is important, in order to avoid endemic persistence [19].

- Gumel, developed a deterministic model with quarantine, isolation to study the SARS outbreak in Toronto. Their focus was to assess the efficiency of control measures. They concluded that a perfect isolation policy alone is sufficient to control SARS, with or without quarantine; and that resources should be devoted disproportionately to isolation programs [7].

1.3 Super-spreading events in infectious diseases

Super-spreading events for a specific infectious disease occur when infected individuals infect more than the average number of secondary cases [10]. Super-spreading events pose a serious threat to public health and their influence on the course of diseases must be studied in order effectively control the spread of a disease characterized by SSEs. The 2002-2003 outbreak of severe acute respiratory syndrome (SARS)

brought the notion of super-spreading events to the forefront of epidemiological modeling simply because of the high numbers of secondary cases they caused.

In the following discussion we highlight two models that were developed to model super-spreading events for the SARS epidemic.

- Masuda, et al, developed a contact network model to study the outbreak of SARS. Their focus was to model super-spreading events, spatial effects, and social networks. They concluded that social network structure impacts spread; highly connected SSEs are crucial [13].
- Meyers, et al, also developed a network model specifically to study the outbreak of SARS in Vancouver. Their focus was to understand heterogeneity in SARS transmission (super-spreading events, geographic variation in outbreak occurrences). They concluded that network structure, and the location of index cases within a network, can influence size of outbreaks and chances of an epidemic occurring [15].

1.4 Aim and Objectives

The principal aim of this thesis is to construct the appropriate mathematical model in the form of a system of ordinary differential equations that captures the effect of super-spreading events for SARS. We then analyze the stability of the model. The main objectives of this thesis are:

- To develop a model for Severe Acute Respiratory Syndrome (SARS) that captures the effect the super-spreading events (SSEs)
- To analyze the stability of the SARS model which includes finding equilibria, showing that a unique global solution of the model exists. We also show that solutions for the constituent ODEs of the SIPR model stay positive for all time, $t \geq 0$.
- To present sample graphs to illustrate the behavior of solutions in continuous time of the SARS outbreak.
- To describe some benefits and limitations of the model.

Chapter 2

Basic population models

In this chapter we present a detailed explanation of two basic theoretical population models, the exponential growth model and the logistic growth model. Each subsection in this chapter includes an explanation of the model, the assumptions associated with the model, its analytical solution, an illustration of the behavior of the model and finally a discussion of its merits and shortcomings.

2.1 The exponential growth model

The exponential growth model, also called the Malthusian model, describes exponential growth (including exponential decay) based on a constant rate of population growth or decay. The model is named after the Reverend Thomas Malthus, who authored *An Essay on the Principle of Population* [12], one of the earliest and most influential books on population. We discuss the formulation of this model, its analytical solution, equilibrium solution, and finally its merits and limitations in the following subsections.

2.1.1 Model formulation

In many natural phenomena, quantities grow or decrease at a rate that is proportional to their size. Human population growth is no exception to this phenomena. Precisely, if $N = N(t)$ denotes the human population size in a particular location at time t, then it seems reasonable to expect that the population growth rate, $\frac{dN}{dt}$, is directly proportional to the population size N, that is, $\frac{dN}{dt} \propto N$. This implies that $\frac{dN}{dt} = rN$, where $r = b - d$ the difference between the constant birth rate b and the constant death rate d. The constant r is called the instantaneous

rate of increase if $b > d$ [6]. The value of r determines whether a population increases exponentially ($r > 0$) as shown in Figure 2.1, remains constant in size ($r = 0$) as shown in Figure 2.3 or declines to extinction ($r < 0$) as shown in Figure 2.2. The complete exponential growth model is given by the following equation:

$$\frac{dN}{dt} = rN \tag{2.1}$$

subject to the initial condition condition

$$N(0) = N_0 \tag{2.2}$$

where $N(0) = N_0$ is the initial population size.

Equation 2.1 is a simple model of population growth. The simplicity of this model is due to the fact that r, the instantaneous rate of increase, is constant as a result of constant birth and death rates, b and d, respectively. Further simplification of the model is brought by the closure (immigration and emigration not taken into consideration) of the population.

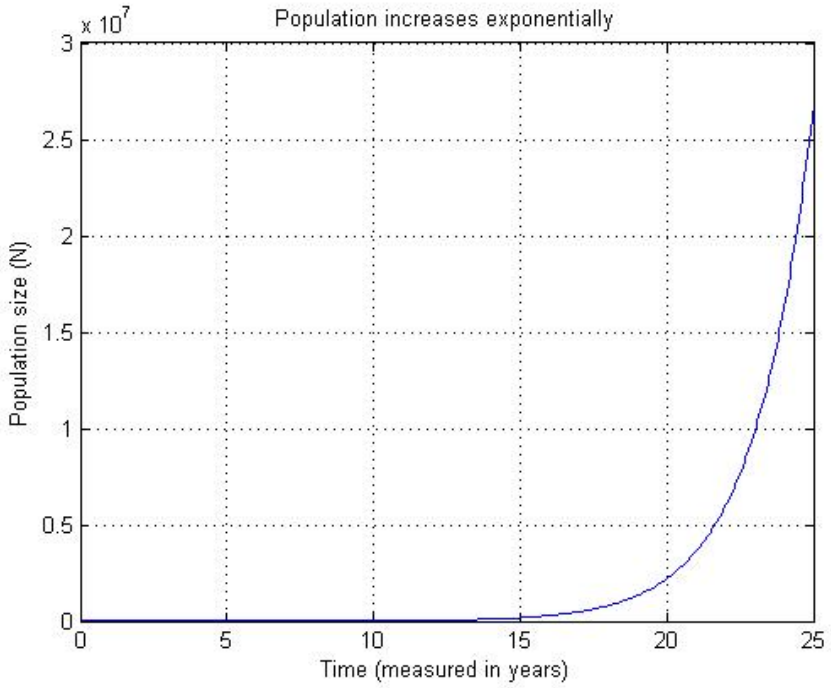
2.1.2 Analytical and equilibrium solutions of the exponential model

We proceed to find the exact solution of the first order linear ordinary differential equation, model 2.1 so to express the population size N as a function of time, t. To accomplish the latter, we use the method of separation of variables:

$$\begin{aligned} \frac{dN}{dt} &= rN \\ \frac{dN}{N} &= rdt \\ \ln(N) &= rt + c_1 \\ N(t) &= \exp(rt + c_1) \\ &= c_2 \exp(rt) \end{aligned} \tag{2.3}$$

To obtain the actual value of the constant c_2 we apply the initial condition 2.2 in equation 2.3 such that $N(0) = N_0$ which implies that $N(0) = c_2 \exp(r(0)) = c_2 \exp(0)$ so that $c_2 = N_0$. Hence the analytical

Figure 2.1: Population grows exponentially, using $r = 0.5$ and $N = 100$



solution of exponential growth model is given by:

$$N(t) = N_0 \exp(rt) \tag{2.4}$$

The equilibrium solution, $N = 0$, of this model is obtained by setting $\frac{dN}{dt} = 0$ in Equation 2.1 and solving for N when $r \neq 0$. For a population experiencing exponential growth/decay, the equilibrium solution means that in the long run population size will decrease to zero.

2.1.3 Merits and limitations of the exponential model

The exponential model has the following benefits:

- Exponential growth (or decay) forms the cornerstone of population biology [6] in the sense that even though no population can increase forever without a limit as shown in Figure 2.1, all populations have the potential for exponential increase. This potential for exponential increase in population size is one of the key factors that can be used to distinguish living from non-living

Figure 2.2: Population declines to extinction, using $r = -0.5$ and $N = 100$

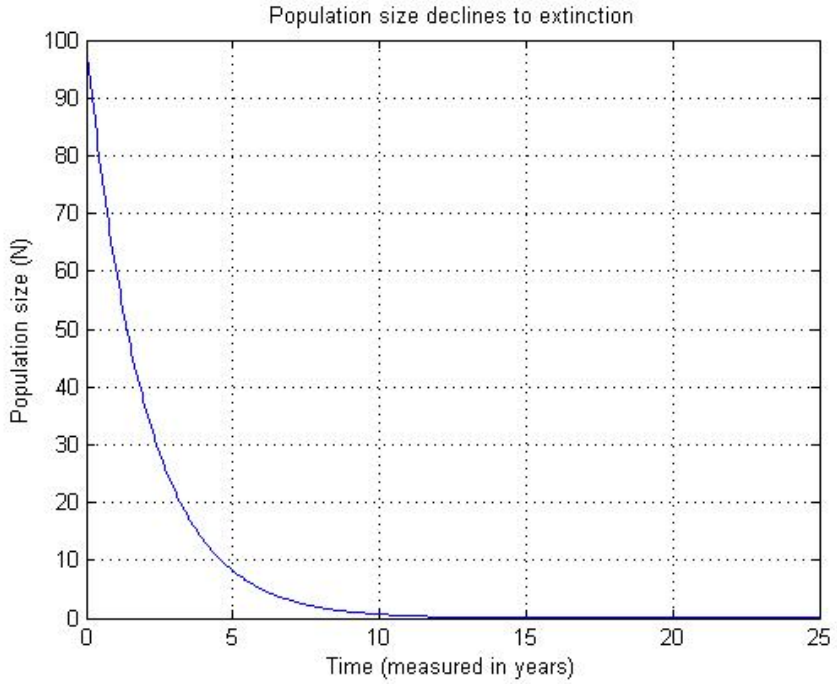
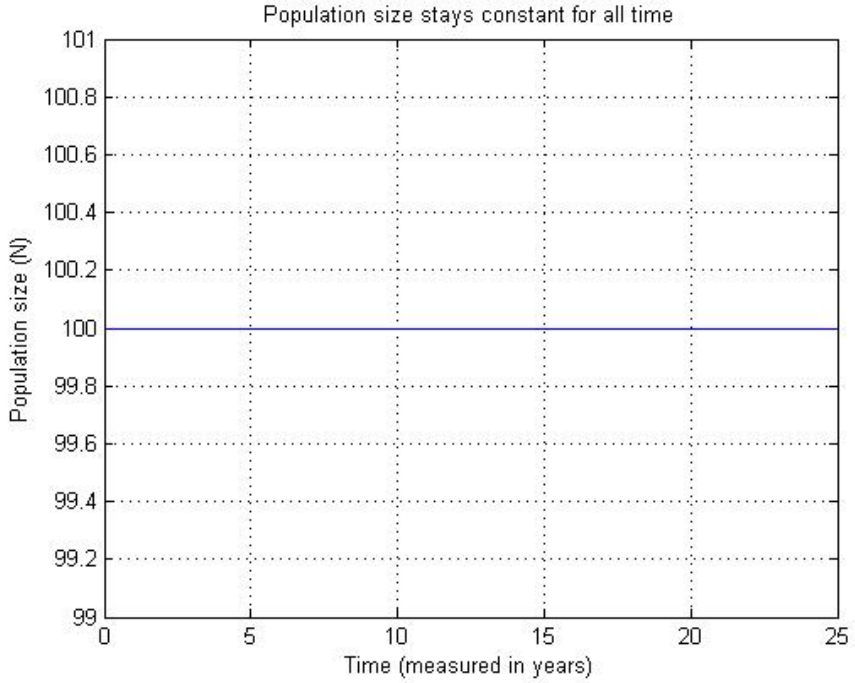


Figure 2.3: Population size stays constant for all time, using $r = 0$ and $N = 100$



organisms [6]. Exponential growth is observed in small populations with seemingly unlimited resources. Exponential decay is observed in large populations with limited resources.

- For $r \neq 0$, the exponential population model predicts either population growth without bound or inevitable extinction as shown in Figures 2.1 and 2.2. The difference is based on whether the growth rate r is positive or negative.
- The model is very simple with only one parameter, the intrinsic growth/decay rate, r.

The exponential model suffers from the following limitations:

- In reality, no population grows/decays indefinitely; i.e. from a biological point of view the missing feature of the exponential model is the idea of carrying capacity. The carrying capacity is the maximum size of the population that can be supported by the environment in terms of resources like availability of food. As the population increases in size the environment's ability to support the population decreases. As the population increases per capita food availability decreases, waste products may accumulate and birth rates tend to decline while death rates tend to increase. It seems reasonable to consider a mathematical model which explicitly incorporates the idea of carrying capacity.
- In the exponential model, we think of the population being closed i.e. we ignore immigration and emigration.
- Finally, the intrinsic growth/decay rate is constant. In reality the intrinsic growth/decay rate is more likely to be time dependent i.e. it changes over time.

2.2 The logistic growth model

In the following discussion, we discuss in detail the logistic growth model developed by a Belgian mathematician Pierre Verhulst (1838), who suggested that the rate of population increase may be limited by several factors such as availability of food, outbreak of diseases, etc. This model addresses the unbounded population growth behavior observed in the exponential model discussed in Section 2.1. We find its analytical solution, its equilibrium solution, and finally we discuss its merits and limitations.

2.2.1 Model formulation

The logistic model is a modification of the exponential population model discussed in Section 2.1. As with the exponential population model, the logistic model includes a rate r. The constant r is called the instantaneous rate of increase/decrease [6]. The value of r determines whether a population grows logistically ($N < K$ and $r > 0$) as shown in Figure 2.4, remains constant in size ($r = 0$) or declines to carrying capacity ($N > K$ and $r < 0$) as shown in Figure 2.5 where K is the carrying capacity of the environment, a constant.

A second parameter, K, represents the carrying capacity of the system being studied. Carrying capacity is the population level at which the birth and death rates of a species precisely match, resulting in a stable population over time. In simple terms, for any particular species in a given environment, the carrying capacity is the maximum sustainable population. That is, the largest population the environment can support for extended periods of time.

When the population size is small relative to the carrying capacity, logistic growth is exponential with growth rate close to the rate r. As the population approaches the carrying capacity, the logistic growth rate approaches zero. Likewise, when the population size is large relative to the carrying capacity, the population size decreases exponentially and approaches the carrying capacity. The logistic growth/decay rate at any time depends on the population at that time, the carrying capacity, and the rate r.

Letting $N = N(t)$ represent the population size at any time period t, the logistic model is:

$$\frac{dN}{dt} = r\left(1 - \frac{N}{K}\right)N \tag{2.5}$$

subject to the initial condition

$$N(0) = N_0,$$

where $N(0) = N_0$ is the initial population size.

Equation 2.5 above is a separable ordinary differential equation which can be solved analytically using the method of separation of variables.

2.2.2 Analytical and equilibrium solutions for the logistic model

We proceed to find the exact solution of the first order non-linear ordinary differential equation 2.5 expressing the population size N as a function of time, t. To accomplish the latter, we use the method of separation of variables and the concept of partial fractions:

$$\begin{aligned}
\frac{1}{N}\frac{dN}{dt} &= r\left(1-\frac{N}{K}\right) \\
\frac{1}{N}\frac{dN}{\left(1-\frac{N}{K}\right)} &= rdt \\
\int\left(\frac{1}{N}+\frac{\frac{1}{K}}{1-\frac{N}{K}}\right)dN &= \int rdt \\
\ln\left(\frac{N}{1-\frac{N}{K}}\right) &= rt+C_1 \\
N &= \frac{C\exp(rt)}{1+\frac{C}{K}\exp(rt)}
\end{aligned}$$

Next we solve for the constant C by applying the initial condition in Equation 2.2:

$$N(0)=N_0 = \frac{C}{1+\frac{C}{K}}$$

which implies that

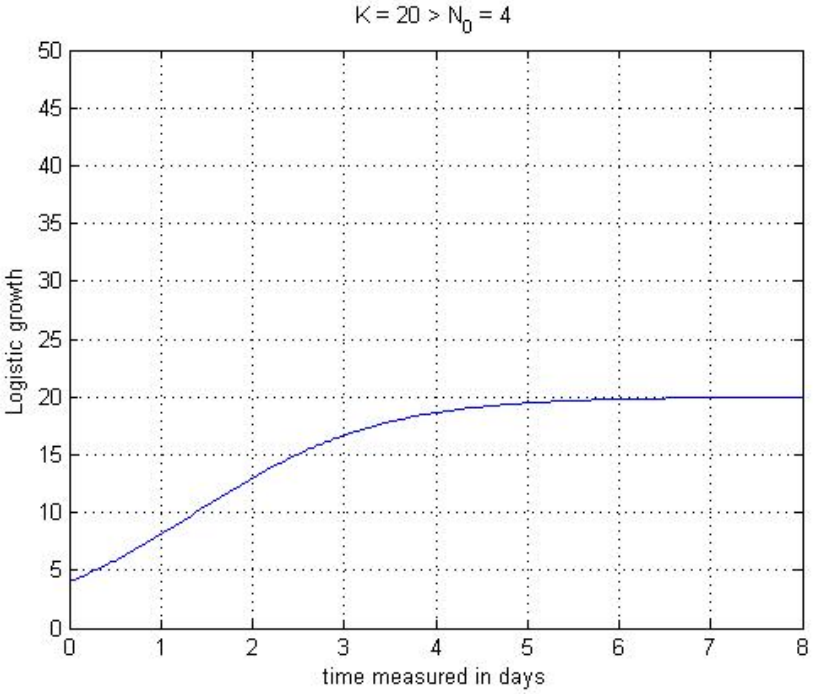
$$C = \frac{KN_0}{K-N_0}\,.$$

Hence the exact solution of the logistic model is given by:

$$N(t)=\frac{KN_0\exp(rt)}{K+N_0(\exp(rt)-1)} \tag{2.6}$$

The equilibrium solutions $N=0$ and $N=K$, of this model are obtained by setting $\dfrac{dN}{dt}=0$ in Equation 2.5 and solving for N when $r\neq 0$. These solutions play a crucial role in predicting the population growth behavior in continuous time.

Figure 2.4: Population increases and approaches the carrying capacity asymptotically, using $N_0 = 4$ and $K = 20$



2.2.3 Merits and limitations of the logistic model

The logistic model has the following benefits:

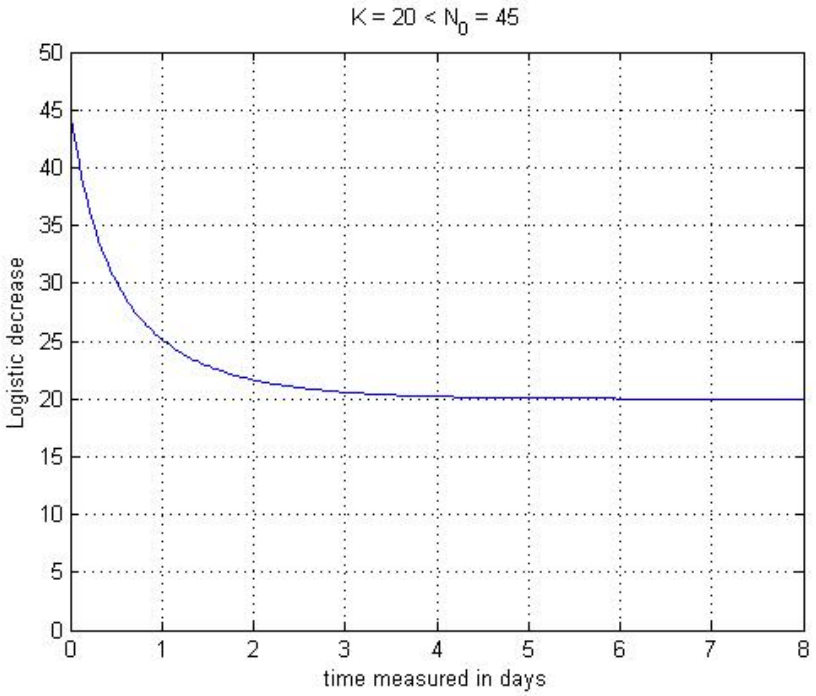
- Unlike the exponential model, the logistic model takes into consideration the limited resources of the environment. This is done by introducing the carrying capacity K in the exponential model discussed in Section 2.1. Birth/death rates depend on population size.

- The general form of the logistic model prevents unbounded growth since the per capita growth rate drops to zero when $N = K$. Thus, the population asymptotically approaches K instead of growing indefinitely as shown in Figure 2.4. If $N > K$ the population decreases and approaches the carrying capacity asymptotically as shown in Figure 2.5.

- The logistic model is suitable for both population growth and decay in environments with limited resources.

- The logistic model is simple with two parameters, K, the carrying capacity, and r the intrinsic growth/deacy rate.

Figure 2.5: Population decreases and approaches the carrying capacity asymptotically, using $N_0 = 45$ and $K = 20$



The logistic model suffers from the following limitations:

- We observe that the logistic model still exhibits similar problems as those of the exponential model. Precisely, the logistic model is also autonomous. Also, in reality environmental conditions influence the carrying capacity. As a consequence it can be time-varying, i.e. $K = K(t) > 0$, which is not so in the basic logistic model discussed in this section.
- Like the exponential model, we think of the population being closed; i.e. we ignore immigration and emigration.
- Finally, the intrinsic growth/decay rate is constant. In reality the intrinsic growth/decay rate is more likely to be time dependent, i.e. it changes overtime.

Chapter 3

The basic reproduction number, R_0

An important parameter when modeling diseases is the basic reproductive number, denoted as R_0. It is defined as the "average number of secondary infections caused by a single infectious individual during their entire infectious lifetime" in a fully susceptible population [18]. It's a measure of how quickly a disease spreads in its initial phase and can predict whether a disease will become endemic (prevalent) or will die out [18].

The basic reproductive number is an important threshold parameter because it tells us wether a population is at risk from a given disease or not [9]. When $R_0 > 1$, the occurrence of the disease will increase and when $R_0 < 1$ the disease spreads slower than people recover. When $R_0 = 1$, the disease occurrence will be constant. R_0 is affected by the infection and recovery rates. For example, the basic reproduction number for a measles epidemic in Niamey, Niger was found to be between 12 and 18 [3]. Table 3.1 shows reproduction numbers for well known diseases.

3.1 The Next Generation Method

The next generation method is a general method of deriving R_0 in situations in which the population is divided into discrete, disjoint compartments discussed extensively in Chapter 4 [18].

In the next generation method, R_0 is defined as the largest eigenvalue of the next generation matrix. The formulation of this matrix involves determining two classes, infected and non-infected, from the model.

Table 3.1: The value of R_0 for some well-known diseases [9]

Disease	R_0
AIDS	2 to 5
Smallpox	3 to 5
Measles	16 to 18
Malaria	> 100

Assume that there are p compartments of which q are infected. We define the vector $\overline{x} = x_i, i = 1, 2, ..., p$, where x_i denotes the number of individuals in the ith compartment. Let $F_i(\overline{x})$ be the rate of appearance of new infections in compartment i and let $V_i(\overline{x}) = V_i^-(\overline{x}) - V_i^+(\overline{x})$, where $V_i^+(\overline{x})$ is the rate of transfer of individuals into compartment i by all other means and $V_i^-(\overline{x})$ is the rate of transfer of individuals out of the ith compartment. The difference $F_i(\overline{x}) - V_i(\overline{x})$, gives the rate of change of x_i. F_i only includes infections that are newly arising, but does not include terms which describe the transfer of infectious individuals from one infected compartment to another.

The next generation matrix FV^{-1} is formed from partial derivatives of F_i and V_i. V^{-1} is the inverse of matrix V. We have $F = \left[\frac{\partial F_i(x_0)}{\partial x_j}\right]$ and $V = \left[\frac{\partial V_i(x_0)}{\partial x_j}\right]$ where $i, j = 1, 2, ..., q$ and where x_0 is the disease free equilibrium (when everyone remains susceptible which is to say that there are no infections at all). The entries of FV^{-1} give the rate at which infected individuals in x_j produce new infections in x_i, times the average length of time an individual spends in a single visit to compartment j. R_0 is given by the largest eigenvalue of the matrix FV^{-1} [18] [3].

Chapter 4

Compartmental models in epidemiology

In order to model the progress of an epidemic in a large population comprising of many different individuals with different characteristics, such a population diversity must be reduced to a few key characteristics which are relevant to the infection under consideration [1]. For example, for most common childhood diseases that confer long-lasting immunity it makes sense to divide the population into those who are susceptible to the disease, those who are infected and those who have recovered and are immune. These subdivisions of the population are called compartments.

A compartmental model is one for which the individuals in a population are classified into compartments depending on their status with regard to the infection under study. A person cannot be in more than one compartment at any given time during the course of the disease. However, a person can move from one compartment to another. The compartments are usually classified by a string of letters that provides information about the model structure. We consider two such compartment models in this chapter namely the SIR and SI_1I_2R compartment models.

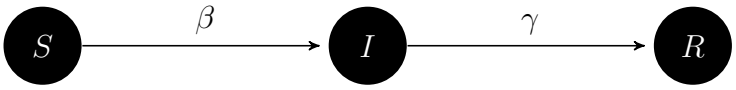
4.1 The standard SIR epidemic model

The SIR model is a classical model used to study diseases including SARS [14]. In an SIR model, the population is divided into three compartments namely:

- Susceptible individuals, $S(t)$

- Infected individuals, $I(t)$
- Removed individuals, $R(t)$

Schematically, we can think of the model as:



where β is the transmission rate and γ is the recovery rate. We describe the variables S, I, and R in detail as follows:

- $S = S(t)$, denotes the number of susceptible individuals at any given time, t. Susceptible people are those who are not infected but they can contract the disease if they they come in contact with infected people. Under normal circumstances, we would expect the number of susceptible people to decrease in continuous time during a disease outbreak.
- $I = I(t)$, denotes the number of infected individuals who also have the potential to infect others at any time, t. At the initial stages of the outbreak, we would expect the number of infected people to increase (if R_0 discussed in Chapter 3 is greater than one). This is because many people would be susceptible and probably less informed about the disease in the early stages of the outbreak. I will also decrease as S gets small.
- $R = R(t)$, denotes the number of individuals leaving the infected class I who become permanently immune (typically because of immunological response, but "immunity" may also include permanent quarantine or even death [10].

The only way an individual leaves the susceptible group is by becoming infected. The only way a person leaves the infected group is by being moved to a quarantine camp, isolation (home) or death. If a person recovers from the disease, he does not become susceptible again but rather remains in the removed compartment forever.

4.1.1 SIR model assumptions

The following assumptions are made for the SIR model:

- The population size N, is large enough and fixed. It is also closed i.e. there is neither emigration nor immigration taking place.
- The population consists of susceptible, infected, and removed individuals at all times with population size, N, defined by $N = N(t) = S(t) + I(t) + R(t)$.
- We assume that the population is subject to homogeneous mixing, which is to say the individuals (susceptible and infected) of the population under study make contacts at random.
- Contacts between either two susceptible people or two infected people are considered as 'waste' since they do not result in a new infection (even though not all contacts between S and I result in a new infection) and hence do not contribute toward the spread of the disease.
- A susceptible joins the infected compartment if he acquires an infection by being in contact with an infected person. In the SIR model, the latter statement is represented by the term, SI.
- Infected people are produced by the infection of susceptible people, S, by infected people, I, with constant transmission rate β.
- An infected person joins the removed compartment through isolation, quarantine or death at a constant rate proportional to the size of the infected population I.
- Infected people who recover on any given day leave the infected compartment with constant recovery rate γ and join the removed compartment. For example, if the average duration of the infection period is three days, then on average, one third of the currently infected population recovers each day, i.e. $\gamma = \frac{1}{3}$.
- β and γ are average rates for the population.
- We do not take birth and death rates into consideration.

4.1.2 The governing equations

We formulate a system of three ordinary differential equations which best describe the SIR model:

$$\begin{aligned} \frac{dS}{dt} &= -\beta SI \\ \frac{dI}{dt} &= \beta SI - \gamma I \\ \frac{dR}{dt} &= \gamma I \end{aligned} \tag{4.1}$$

β denotes the transmission rate, between susceptible people and infected people, which is expected to result in a new infection; and γ is the recovery rate.

Adding the above three equations we have that

$$S'(t) + I'(t) + R'(t) = 0. \tag{4.2}$$

This, after integration, gives

$$S(t) + I(t) + R(t) = N \quad \forall t \geq 0, \tag{4.3}$$

where N, the integration constant, defines our fixed population size assumed earlier in Section 4.1.1.

4.1.3 Initial conditions

At time $t = t_0$, (i.e. at the outbreak of the epidemic) we have a relatively small group of infected individuals, $I = I_0 > 0$, in the infected group of the population. They are allowed to move and interact freely with the individuals in the susceptible group as a result of the population being subjected to homogenous mixing. Also, at time $t = t_0$, there are no individuals in the removed group (i.e. $R(t_0) = 0$) and everybody is susceptible excluding the the small group of infected people, I_0. We therefore formulate initial conditions for the SIR model as follows:

$$\begin{aligned} S(t_0) &= N - I_0 = S_0 \\ I(t_0) &= I_0 \\ R(t_0) &= 0, \end{aligned}$$

where $S_0 > 0$ and $I_0 > 0$. When S_0 and I_0 are added, N is obtained. Therefore our complete SIR model is

$$\begin{aligned} \frac{dS}{dt} &= -\beta SI \\ \frac{dI}{dt} &= \beta SI - \gamma I \\ \frac{dR}{dt} &= \gamma I \end{aligned} \tag{4.4}$$

subject to the following initial conditions

$S(t_0) = S_0,\ I(t_0) = I_0$, and $R(t_0) = 0$.

4.1.4 The SIR model analysis

In the following subsections, we not only show that a global solution to the SIR model exist but also that it is unique. We further show that the number of people in each compartment is nonnegative and it stays finite for all time $t > 0$. We also present solution graphs, calculate the basic reproduction number, R_0, using the next generation method discussed in Section 3.1 and further analyze the equilibrium points of the model. Finally we highlight some of the benefits and limitations of the SIR model.

Existence and uniqueness of a global solution

The system of equations given in Section 4.1.2, which best describes the SIR model, can be written in the form:

$y' = f(t, y),\ y(t_0) = y_0$ where $y = \begin{bmatrix} S(t) \\ I(t) \\ R(t) \end{bmatrix}$. The function $f(t, y)$ is continuous everywhere on $\mathbb{R}^3$ and its partial derivatives are continuous. The function $f(t, y)$ is bounded (since all solutions are bounded). Hence Peano's existence theorem in conjunction with Theorem 8.1 (on page 441) in Philip Hartman's book [8] guarantees the existence of a unique global solution for the SIR model.

Positivity and boundedness of solutions

The SIR model in Section 4.1 describes a human population, and, therefore, it is very important to prove that all quantities (susceptible, infected and removed) will be positive for all time, $t > 0$. In other

words, we want to prove that all solutions of system (given by Equation 4.4 with nonnegative initial data) will remain positive for all times $t > 0$.

Theorem 4.1.1. *Let the initial data be* $S(0) = S_0 > 0$, $I(0) = I_0 > 0$ *and* $R(0) = 0$. *Then the components of the solution* $S(t)$, $I(t)$ *and* $R(t)$ *of Equation 4.4 are positive for all time,* $t > 0$.

Proof. In this proof we try to show that if we start with nonnegative initial conditions (as indicated by our initial conditions given in Section 4.1.3) of the SIR model given by equation 4.4, we also end up with nonnegative solutions.

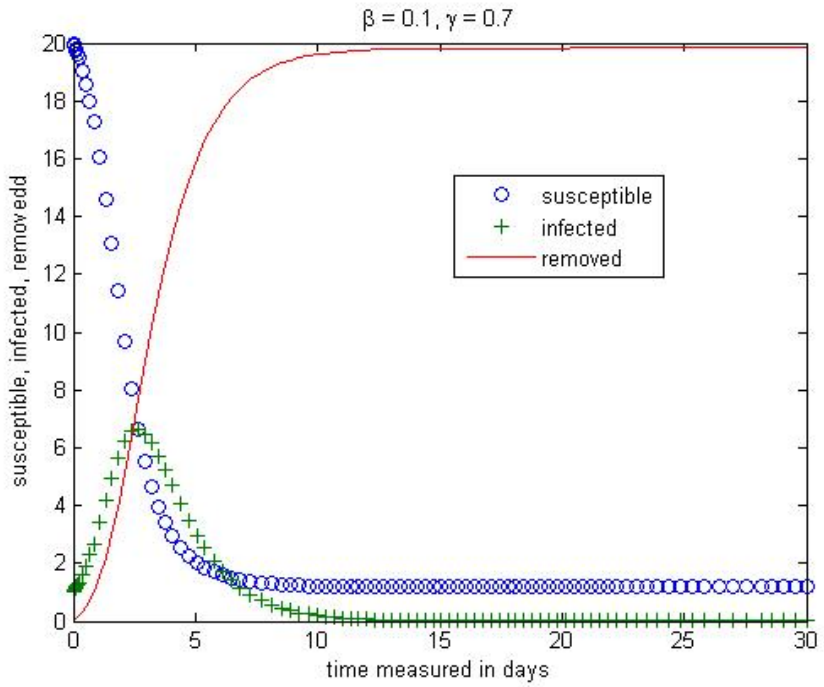
To see this, we assume that $S(t) = 0$ for some time $t > t_0$, $I(t) \geq 0$, $R(t) \geq 0$ and show that $\frac{dS}{dt} \geq 0$. Clearly in view of the SIR model given by Equation 4.4, $\frac{dS}{dt} = -\beta SI = 0$ when $S(t) = 0$ which shows that the component of the solution $S(t)$ will be nonnegative for all time $t > 0$.

To show that the component of the solution $I(t)$ will be nonnegative for all time, $t > 0$ we assume that $I(t) = 0$ for some time $t > t_0$, $S(t) \geq 0$, $R(t) \geq 0$ and show that $\frac{dI}{dt} \geq 0$. Looking at the system of equations in the SIR model given by Equation 4.4, $\frac{dI}{dt} = \beta SI - \gamma I = 0$ when $I(t) = 0$ which shows that the component of the solution $I(t)$ will be nonnegative for all time $t > 0$.

Finally, to show that the component of the solution $R(t)$ stays positive for all time we assume that $R(t) = 0$ for some time $t > t_0$, $S(t) \geq 0$, $I(t) \geq 0$ and show that $\frac{dR}{dt} \geq 0$. Looking at the SIR model given by Equation 4.4, $\frac{dR}{dt} = \gamma I \geq 0$ when $I(t) \geq 0$ since the constant recovery rate γ is positive which shows that the solution $R(t)$ will be nonnegative for all time $t > 0$ which completes the proof. □

The boundedness of the components of the solution $S(t)$, $I(t)$ and $R(t)$ follows from the fact that $N = S(t)+I(t)+R(t)$ and that $S(t), I(t)$ and $R(t) \geq 0$ for all time $t > 0$. Therefore we have that each component of the solution is at most equal to N. That is $S(t)$, $I(t)$, $R(t) \leq N \; \forall t \geq 0$. It was shown in Section 4.1.3 that each component of the solution is nonnegative at the outbreak of the disease ($t = 0$). This shows that

Figure 4.1: SIR solutions behavior in continuous time of disease outbreak, using $\beta = 0.1$ and $\gamma = 0.7$



each component of the solution $S(t)$, $I(t)$ and $R(t)$ is bounded between zero and the total population size, N.

Equilibrium solutions and their stability analysis

In this section we analyze the SIR model shown in Equation 4.4 by finding its equilibria. Steady states (equilibrium solutions) of the system in 4.4 satisfy the following system of equations:

$$\begin{aligned} -\beta SI &= 0 \\ \beta SI - \gamma I &= 0 \\ \gamma I &= 0 \end{aligned} \tag{4.5}$$

It is easy to check that 4.4 has the disease free equilibrium $E = (N, 0, 0)$ and , $Q = (S^*, 0, R^*)$ for any S^* (based on initial condition) and $R^* = N - S^*$. We can see from Figure 4.1 that when the transmission rate is small, not every body gets sick. However, if the transmission rate is high, almost everybody gets sick in the population as it can seen from Figures 4.2 and 4.3.

Figure 4.2: SIR solutions behavior in continuous time of disease outbreak, using $\beta = 0.4$ and $\gamma = 0.4$

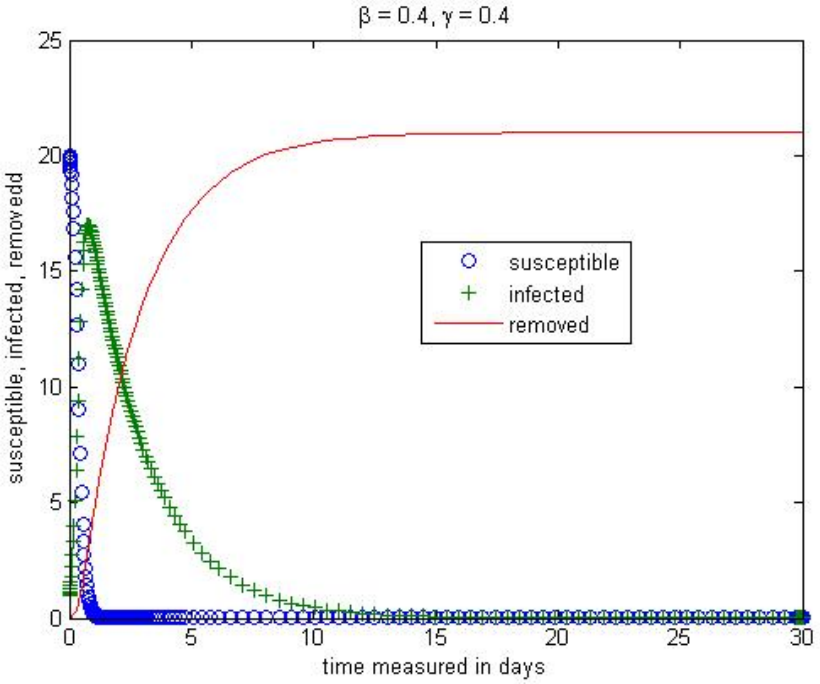
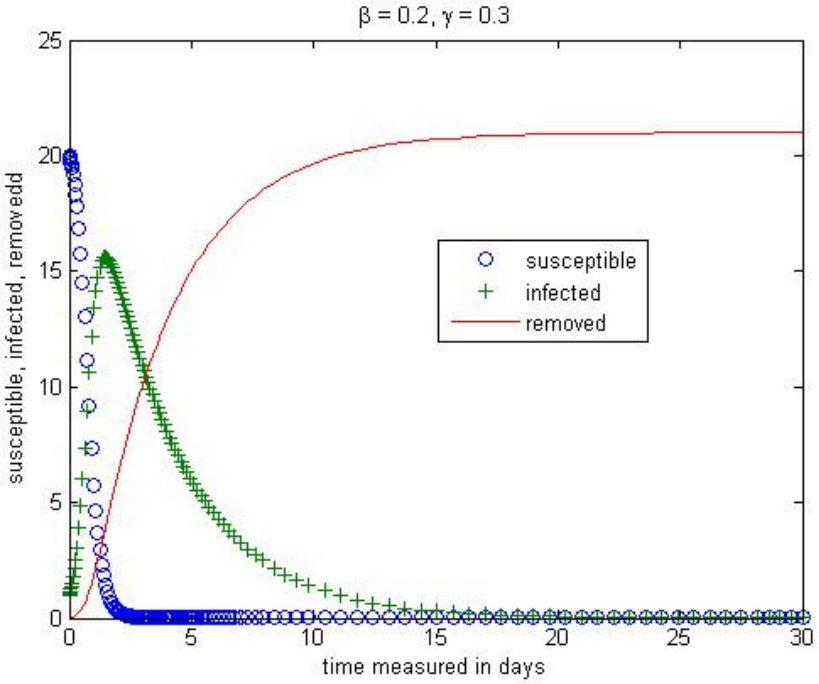


Figure 4.3: SIR solutions behavior in continuous time of disease outbreak, using $\beta = 0.2$ and $\gamma = 0.3$



R_0 for SIR using The Next Generation method

The SIR model has only one class of the infected population, I. We describe the rate of change of the infected population, I, by the following equation:

$$\frac{dI}{dt} = \beta SI - \gamma I \tag{4.6}$$

New infections are produced by the infection of susceptible people, S, by infected people, I, with transmission rate, β. We further assume that infected people recover from the infection with rate γ. For the SIR model shown in Equation 4.6 above, we find that

$F = (\beta S)$ and $V = (\gamma)$, where F and V were defined in Section 3.1, and where there is only one infected compartment.

Since the determinant of V is not equal to 0, we can determine the inverse of V, V^{-1}:

$V^{-1} = \left(\frac{1}{\gamma}\right)$,
$FV^{-1} = \left(\frac{\beta S}{\gamma}\right)$, and
$\det(FV^{-1} - \lambda I_0) = \det\left(\frac{\beta S}{\gamma} - \lambda\right) = \frac{\beta S}{\gamma} - \lambda.$

Setting $\det(FV^{-1} - \lambda I_0)$ equal to 0, and solving for λ we obtain one eigenvalue:

$\lambda = \left(\frac{\beta S}{\gamma}\right)$. Since λ is the only eigenvalue obtained, it is the largest eigenvalue of FV^{-1}. We conclude by the next generation method described in Section 3.1 that $\lambda = \left(\frac{\beta S}{\gamma}\right)$ is the basic reproduction number of the SIR model where $S = S_0 = N - I_0$, the population size. That is $R_0 = \frac{\beta S}{\gamma}$.

4.1.5 Benefits and limitations of the SIR model

The SIR model is a good, simple, model for many infectious diseases including measles, SARS, foot and mouth, influenza, H_1N_1, mumps and rubella [2]. The SIR model is dynamic in the following way:

- The population size, N, is fixed making the model relatively simple to use. A model with fixed population size is good for modeling short-term outbreaks.

- The SIR model is dynamic in the sense that a majority of the whole population start susceptible at the outbreak of a disease, some or all them may acquire the infection (move into the infectious compartment) and finally die or recover (move into the removed compartment). Thus each member of the population typically progresses from susceptible to infectious and finally to the removed compartment.

The SIR model suffers from the following limitations:

- We assume that the transmission and recovery rates (β and γ) are fixed. However, in the practical sense these rates are more likely to vary with time. For example, if there is an outbreak of smallpox in a particular community there would be more transmission of the disease among students at school than there probably would when school is not in session.

- Many diseases, such as measles or chickenpox, are primarily disease of children. By further subdividing the population into differing age-classes researchers have been able to capture age-structured transmission in more detail [9].

- For childhood infections, such as those diseases stated above, there is greater mixing (the contact rate is larger) during school terms. Such seasonal dependence leads to regular epidemics or more complex dynamics, as the disease oscillates between the high-contact and low-contact solutions [9].

- For some diseases, other organisms are involved in the transmission, e.g. the mosquito is essential for transmission of malaria, and, together, rats and fleas are responsible for the majority of bubonic plague cases [9]. For such diseases we need to couple an SIR model for humans with an SIR model for the other organisms.

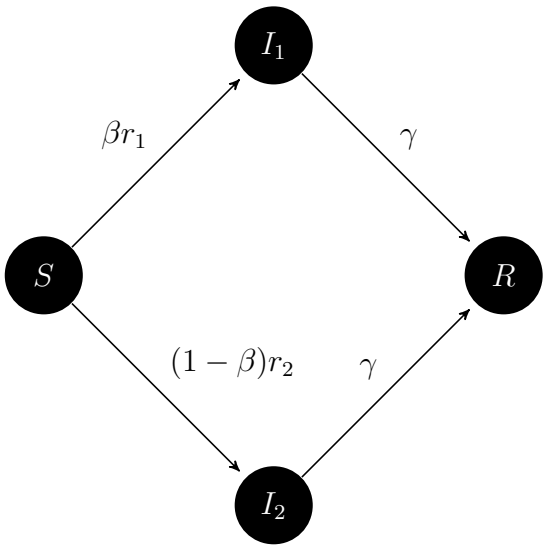
- Finally, we ignore immigration and emigration which has a great influence in the outbreak of an epidemic, as was the case in the outbreak of the 2002 - 2003 SARS epidemic and the recent H_1N_1 flu.

4.2 The SI_1I_2R model

The SI_1I_2R model was developed by John T. Kemper [10]. This model incorporates the existence of super-spreaders for a disease without immunity. In the SI_1I_2R model, the population is divided into four compartments namely:

- Susceptible individuals, $S(t)$
- First class of infected individuals, $I_1(t)$
- Second class of infected individuals, $I_2(t)$
- Removed (immune) individuals, $R(t)$

Schematically, we can think of the model as:



where β in this model is a fraction of all infections who result in an I_1 infective and $1-\beta$ is a fraction of all infections who result in an I_2 infective. The constants r_1 and r_2 are two different transmission rates and γ is the recovery rate. We explain the variables S, I_1, I_2 and R in the discussion that follows:

- $S = S(t)$, denotes the number of susceptible people at any given time, t. Susceptible people are those who are not infected but they can contract the disease if they they come in contact with infected people (people from class I_1 or I_2).

- $I = I_1(t)$ and $I_2(t)$, denotes two classes of infected people differing only in their transmission rates, r_1 and r_2 respectively [10]. Higher (than normal) transmission rates indicate the presence of super-spreading events in the SI_1I_2R model.
- $R = R(t)$, this is a class of people leaving the infected classes (I_1 and I_2) become permanently immune (typically because of immunological response, but "immunity" may also include permanent quarantine or even death) [10].

The only way an individual leaves the susceptible group is by becoming infected and hence either join I_1 class or I_2 class. The only way a person leaves the infected groups is through permanent immunity which also includes permanent quarantine or even death.

4.2.1 The SI_1I_2R model assumptions

The following assumptions were made for the SI_1I_2R model:

- The population size N, is large enough and fixed. It is also closed i.e. there is neither emigration nor immigration taking place.
- There are two classes of infected people, I_1 and I_2, differing only in their transmission rates, r_1 and r_2 respectively.
- We assume that the population is subject to homogeneous mixing which is to say the individuals (susceptible and infected) of the population under scrutiny make contacts at random.
- The population consists of susceptible, infected, and recovered people at all times with population size, N, defined $N = N(t) = S(t) + I_1(t) + I_2(t) + R(t)$.
- Contacts between either two susceptible people or two infected people are considered as 'waste' since they do not result in a new infection and hence do not contribute to the spread of the disease.
- A susceptible joins the infected compartment if he acquires an infection through being in contact with an infected person from class I_1 or class I_2.
- Also, an infected person joins the removed compartment through permanent immunity defined in Section 4.2 [10].
- A fraction, β, of all infections result in an I_1 infective, all others being I_2 infectives [10].

- Infection terminates in permanent immunity (or some other kind of removal) [10].
- γ is the removal rate from I_1 and I_2 [10].
- We do not take birth and death rates into consideration.

4.2.2 The governing equations

Based on the previous description of Section 4.2.1, the SI_1I_2R model was formulated by the following system of equations:

$$\begin{aligned} \frac{dS}{dt} &= -(r_1I_1 + r_2I_2)S \\ \frac{dI_1}{dt} &= \beta(r_1I_1 + r_2I_2)S - \gamma I_1 \\ \frac{dI_2}{dt} &= (1-\beta)(r_1I_1 + r_2I_2)S - \gamma I_2 \\ \frac{dR}{dt} &= \gamma(I_1 + I_2) \end{aligned} \tag{4.7}$$

with initial conditions $S(0) = S_0 > 0,\ I_1(0) \geq 0, I_2(0) \geq 0,$ $I_1(0)+I_2(0) = N-S_0$, and $R(0) = 0$, where $\beta \in (0,1)$, and $\gamma,\ r_1$, and r_2 are positive [10].

The constant β is the fraction of all infections who result in an I_1 infective, all others being I_2 infectives [10]. There are two classes of infected people, I_1 and I_2, differing only in their transmission rates, r_1 and r_2 respectively. γ is the removal rate from I_1 and I_2 to R [10].

4.2.3 SI_1I_2R model analysis

In the following subsections, we not only show that a global solution of the SI_1I_2R model exist but also that it is unique. We further show that the number of people in each compartment is nonnegative and it stays finite for all time $t > 0$. We then compute and analyze the equilibrium solutions for the SI_1I_2R model. We also present solution graphs and calculate the basic reproduction number, R_0 for the SI_1I_2R model using the next generation method discussed in Section 3.1. Finally we highlight some of the benefits and limitations of the SI_1I_2R model.

Existence and uniqueness of a global solution

The system of equations given in Section 4.2.2 which best describe the SI_1I_2R model can be written in the form:

$y' = f(t,y),\ \ y(t_0) = y_0$ where $y = \begin{bmatrix} S(t) \\ I_1(t) \\ I_2(t) \\ R(t) \end{bmatrix}$. The function $f(t,y)$ is continuous everywhere on $\mathbb{R}^4$. The function $f(t,y)$ is continuous everywhere on $\mathbb{R}^4$ and its partial derivatives are continuous. The function $f(t,y)$ is bounded (since all solutions are bounded). Hence Peano's existence theorem in conjunction with Theorem 8.1 (on page 441) in Philip Hartman's book [8] guarantees the existence of a unique global solution for the SI_1I_2R model.

Positivity and boundedness of solutions

The SI_1I_2R model discussed in Section 4.2 describes a human population, and, therefore, it is very important to prove that all quantities (susceptible, regularly infected, super-spreading events, and removed) will be positive for all time. In other words, we want to prove that all components of the solution of system 4.2 with nonnegative initial data will remain positive for all times $t > 0$.

Theorem 4.2.1. *Let the initial data be $S(0) = S_0 > 0$, $I_1(0) \geq 0$, $I_2 \geq 0$ and $R(0) = 0$. Then the components of the solution $S(t)$, $I_1(t)$, $I_2(t)$, and $R(t)$ of system 4.2.2 are positive for all time, $t > 0$.*

Proof. In this proof we show that if we start with nonnegative initial conditions of the SI_1I_2R model, given by the equations in Section 4.2.2, we also end up with nonnegative solutions.

To see this, we assume that $S(t) = 0$ for some time $t > t_0$, $I_1(t) \geq 0,\ I_2(t) \geq 0, R(t) \geq 0$ and show that $\dfrac{dS}{dt} \geq 0$. Clearly in view of the system in Section 4.2.2, $\dfrac{dS}{dt} = 0$ when $S(t) = 0$ which shows that the component of the solution $S(t)$ will be nonnegative for all time $t > 0$.

To prove that the component of the solution $I_1(t)$ will be nonnegative for all time $t > 0$, we assume that $I_1(t) = 0$ for some time $t > t_0$, $S(t) \geq 0, I_2(t) \geq 0, R(t) \geq 0$ and show that $\dfrac{dI_1}{dt} \geq 0$. Looking at the SI_1I_2R system of equations discussed in Section 4.2.2, $\dfrac{dI_1}{dt} = \beta r_2 I_2 S \geq 0$ when $I_1(t) = 0$ which shows that the solution $I_1(t)$ will be nonnegative for

all time $t > 0$.

To prove that the component of the solution $I_2(t)$ will be nonnegative for all time $t > 0$, we assume $I_2(t) = 0$ for some time $t > t_0$, $S(t) \geq 0, I_1(t) \geq 0,\ R(t) \geq 0$ and show that $\frac{dI_2}{dt} \geq 0$. Looking at the SI_1I_2R system of equations discussed in Section 4.2.2, $\frac{dI_2}{dt} = (1-\beta)r_1I_1S \geq 0$ when $I_2(t) = 0$ which shows that the solution $I_2(t)$ will be nonnegative for all time $t > 0$.

Finally, to prove that the component of the solution $R(t)$ will be nonnegative for all time $t > 0$, we assume that $R(t) = 0$ for some time $t > t_0$, $S(t) \geq 0,\ I_1(t) \geq 0,\ I_2 \geq 0$ and show that $\frac{dR}{dt} \geq 0$. Looking at the SI_1I_2R system of equations discussed in Section 4.2.2, $\frac{dR}{dt} = \gamma(I_1 + I_2) \geq 0$ when $R(t) = 0$ which shows that the solution $R(t)$ will be nonnegative for all time $t > 0$ which completes the proof. □

The boundedness of the components of the solution $S(t),\ I_1(t),\ I_2(t)$ and $R(t)$ follows from the fact that $N = S(t) + I_1(t) + I_2(t) + R(t)$ and that $S(t),\ I_1(t),\ I_2(t),\ R(t) \geq 0$ for all time $t > 0$. Therefore we have that each component of the solution is at most equal to N. That is $S(t),\ I_1(t),\ I_2(t),\ R(t) \leq N$. It was shown in Section 4.2.1 that each component of the solution is nonnegative at the outbreak of the disease ($t = t_0$). This shows that each of the components of the solution $S(t),\ I_1(t),\ I_2(t)$ and $R(t)$ is bounded between zero and the total population size, N.

Equilibrium solutions and their stability analysis

In this Section we analyze the SIPR model shown in Equation 4.7 by finding the equilibria. Steady states (equilibrium solutions) of Equation 4.7 satisfy the following system of equations:

$$\begin{aligned} -(r_1I_1 + r_2I_2)S &= 0 \\ \beta(r_1I_1 + r_2I_2)S - \gamma I_1 &= 0 \\ (1-\beta)(r_1I_1 + r_2I_2)S - \gamma I_2 &= 0 \\ \gamma I_1 + \gamma I_2 &= 0 \end{aligned} \tag{4.8}$$

It is easy to check that Equation 4.8 above has the disease free equilibrium $E = (N, 0, 0, 0)$ and $Q = (S^*, 0, 0, R^*)$ for any S^* (based on the initial condition) and $R^* = N - S^*$. We can see from Figure 4.4

Figure 4.4: SI_1I_2R solutions behavior in continuous time for a generic epidemic disease outbreak, using $\beta = 0.2,\ r_1 = 0.1,\ r_2 = 0.3$ and $\gamma = 0.3$

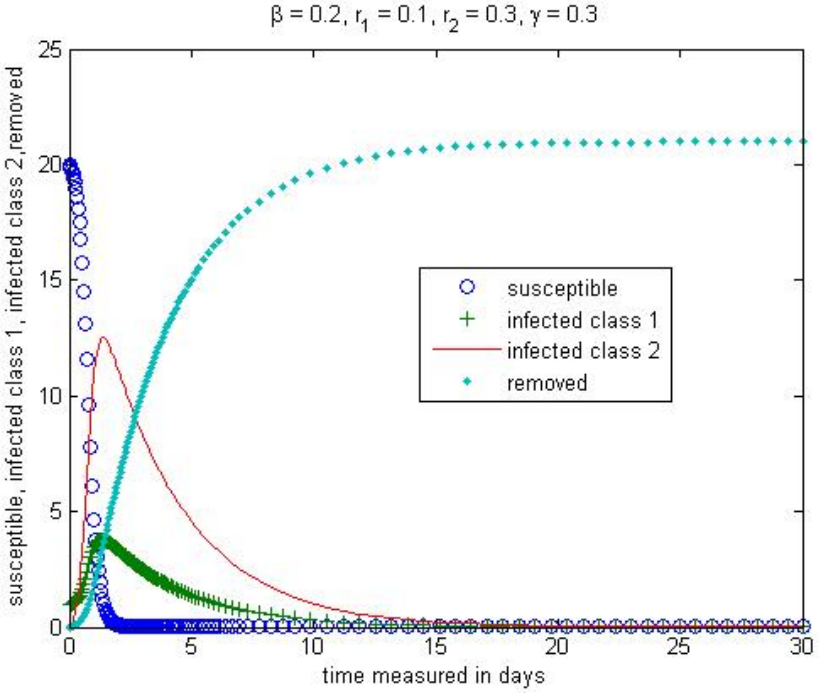
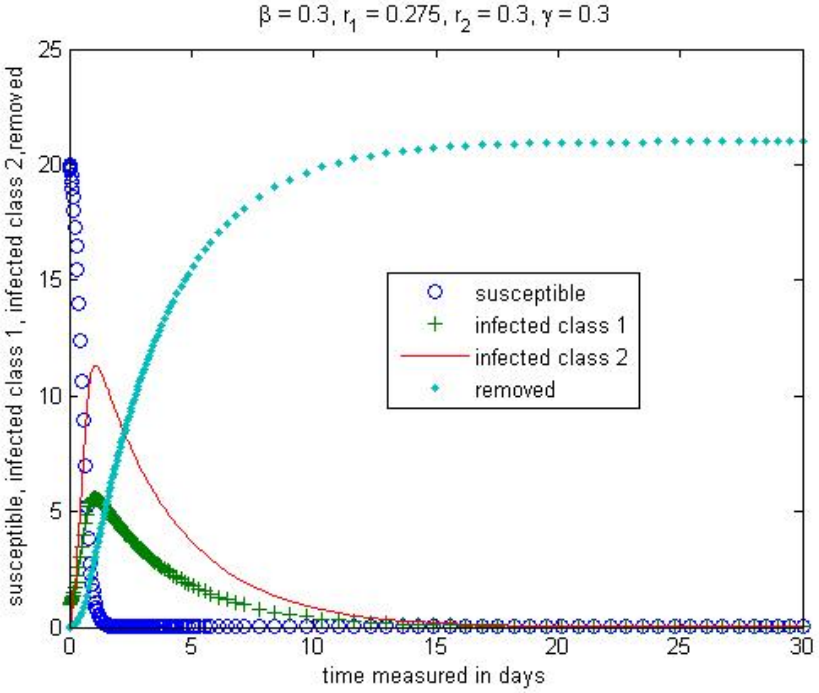


Figure 4.5: SI_1I_2R solutions behavior in continuous time for a generic epidemic disease outbreak, using $\beta = 0.3,\ r_1 = 0.275,\ r_2 = 0.3$ and $\gamma = 0.3$



that when the transmission rates are small, not everybody gets sick. However, if the transmission rate is high, almost everybody gets sick in the population as it can seen from Figure 4.5.

R_0 for SI_1I_2R using The Next Generation method

We describe the rate of change of the first class of infected people, I_1, and the second class of infected people, I_2, by the following equations:

$$\begin{aligned} \frac{dI_1}{dt} &= \beta(r_1 I_1 + r_2 I_2)S - \gamma I_1 \\ \frac{dI_2}{dt} &= (1-\beta)(r_1 I_1 + r_2 I_2)S - \gamma I_2 \end{aligned} \tag{4.9}$$

New cases are produced by the infection of susceptible people, S, by an infected person who is either from the first class of infected individuals or the second class of individuals with contact rates βr_1 and $(1-\beta)r_2$ respectively. We further assume that people from both infected classes (I_1 or I_2) recover from the infection with with the same rate γ. For the SI_1I_2R model shown in Equation 4.9 above, we find that

$$F = \begin{pmatrix} \beta r_1 S & \beta r_2 S \\ (1-\beta)r_1 S & (1-\beta)r_2 S \end{pmatrix} \quad \text{and} \quad V = \begin{pmatrix} \gamma & 0 \\ 0 & \gamma \end{pmatrix}$$

Since the determinant of V is not equal to 0, we can determine V^{-1}:

$$V^{-1} = \begin{pmatrix} \frac{1}{\gamma} & 0 \\ 0 & \frac{1}{\gamma} \end{pmatrix},$$

$$FV^{-1} = \begin{pmatrix} \frac{\beta r_1 S}{\gamma} & \frac{\beta r_2 S}{\gamma} \\ \frac{(1-\beta)r_1 S}{\gamma} & \frac{(1-\beta)r_2 S}{\gamma} \end{pmatrix}, \text{ and}$$

$$\det(FV^{-1} - \lambda I_2) = \det \begin{pmatrix} \frac{\beta r_1 S}{\gamma} & \frac{\beta r_2 S}{\gamma} \\ \frac{(1-\beta)r_1 S}{\gamma} & \frac{(1-\beta)r_2 S}{\gamma} \end{pmatrix}.$$

Setting $\det(FV^{-1} - \lambda I_2)$ equal to 0, and solving for λ we obtain two eigenvalues:

$\lambda_1 = 0$ and $\lambda_2 = \frac{(1-\beta)r_2 S}{\gamma} + \frac{\beta r_1 S}{\gamma}$ where $S = S(0) = S_0$. Clearly λ_2 is the largest eigenvalue of FV^{-1} and so we conclude, by the next

generation method described in Section 3.1, that λ_2 is the basic reproduction number of the SI_1I_2R model. We note that $R_0 = \lambda_2 = \frac{(1-\beta)r_2S}{\gamma} + \frac{\beta r_1 S}{\gamma}$ is composed of the $\frac{r_i s}{\gamma}$multiplied by their respective probabilities β, $(1-\beta)$ and then added together.

Benefits and limitations of the SI_1I_2R model

Like the SIR model, the SI_1I_2R is a good, simple, model for many infectious diseases including SARS, measles, foot and mouth, influenza, H_1N_1, mumps and rubella [10]. The SI_1I_2R model is dynamic in the following ways:

- As implied by the variable function of t, the SI_1I_2R model is dynamic in that the numbers in each compartment may fluctuate over time.
- When an epidemic occurs, the number of susceptible individuals fall rapidly as more of them get infected and thus enter the infectious compartments (I_1 and I_2) and eventually the removed compartment R.
- The SI_1I_2R is also dynamic in the sense that a much higher proportion of individuals are susceptible at the outbreak of an epidemic. They may acquire the infection (move into I_1 or I_2) and finally die, go to a quarantine camp, or recover (move into the removed compartment R). Thus each member of the population typically progresses from susceptible to infectious (I_1 or I_2) and finally to the removed compartment, R.
- The SI_1I_2R model has two compartments of infectious people (I_1 and I_2) to facilitate a better understanding of the spread of any epidemic disease.

Despite all the the benefits of the the SI_1I_2R, it still suffers from the following limitations.

- We ignore immigration and emigration; which sometimes has a great influence in the outbreak of an epidemic, as was the case in the outbreak of the 2009 H_1N_1 flu.
- The SI_1I_2R model is an autonomous system. In mathematics, a system of autonomous differential equations is a system of ordinary differential equations which does not depend on the independent variable.

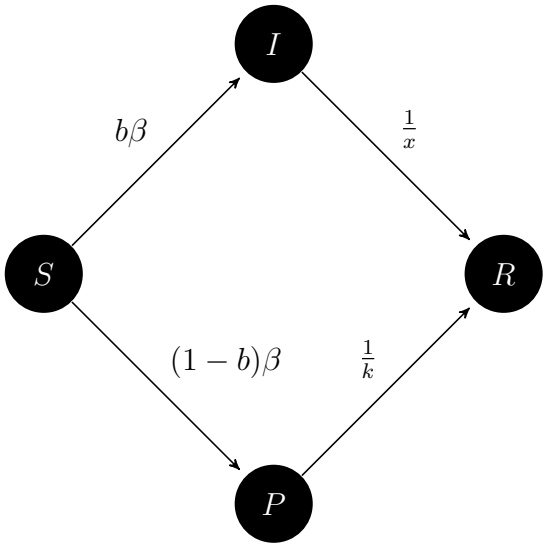
Chapter 5

The SIPR epidemic model

This chapter is devoted to the formulation and analysis of an SIPR model that captures one of the several main features which enhanced the progression and transmission of the SARS epidemic. In particular, this model captures super-spreading events, infected individuals who in turn had an extra ordinary number of secondary cases. In the SIPR model we divide the population size N, into four groups namely:

- Susceptible individuals, $S(t)$
- Regular infected individuals, $I(t)$
- Super-spreading events, $P(t)$
- Removed individuals, $R(t)$

Schematically, we can think of the model as:



where β is the transmission rate and b the probability that a new infection will be a regular infected person. On the other hand, $1 - b$ is the probability that a new infection will be a super-spreading event. The constant x denotes the average number of days spent by a regularly infected person outside isolation. The constant k denotes the average number of days spent by a super-spreading event outside isolation. We explain the variables S, I, P, and R in detail in the following piece of writing:

- $S = S(t)$, denotes the number of susceptible people at any given time, t. Susceptible people are those who are not infected but they can contract the disease if they they come in contact with infected people (from either I or P). Under normal circumstances, we would expect the number of susceptible people to decrease in continuous time during a disease outbreak.

- $I = I(t)$, denotes the number of regularly infected people (infected people who are not super-spreading events) who also have the potential to infect others at any time, t. At the initial stages of the outbreak, we would expect the number of infected people to increase (if R_0 discussed in Chapter 3 is greater than one). This is because many people would be susceptible and probably less informed about the disease in the early stages of the outbreak. As the people get informed and control measures are imposed such as isolation, quarantine, and medication is available, the number of infected people is expected to decrease. That is, if the latter control measures are effective enough.

- $P = P(t)$, denotes the number of super-spreading events at any given time, t. This is a group of infected people that would normally generate a larger number of secondary cases than a regularly infected person would. More super spreaders would mean that the disease would spread quickly. The class of super-spreading events forms a small proportion of the infected class.

- $R = R(t)$, denotes the number of people (regular infected and super-spreading events) who have been removed, recovered or died at any given time, t during a disease outbreak. Precisely, the removed people are those who are kept in isolation such as in quarantine camps, and maybe at home. Recovered people are those who receive treatment and hence become immune to the disease. They are then kept in isolation (asked to stay at home).

It is worth mentioning that the class, $I = I(t)$ now has a slightly different meaning than the one defined in Sections 4.1 and 4.1.1. This is because it no longer refers to the entire class of infected people but a specific class of infected people, called regularly infected people i.e. infected people who are not super-spreading events.

The only way an individual leaves the susceptible group is by becoming infected and hence moves either into the regularly infected compartment or the super-spreading event compartment. The only way a person leaves either the regularly infected class or super-spreading events compartment is by being moved to a quarantine camp, isolation (home) or death. If a person recovers from the disease, he does not become susceptible again but rather remains in the removed compartment forever.

5.1 The SIPR model assumptions

The following assumptions are made for the SIPR model:

- The population size N, is large enough and fixed. It is also closed, i.e. there is neither emigration nor immigration taking place.
- We assume that the population is subject to homogeneous mixing which is to say the individuals (susceptible, regularly infected, and the super-spreading events) of the population under scrutiny will assort and make contacts at random.
- The populations consists of susceptible, regular infected, super-spreaders, and recovered people at all times such that the population size $N = N(t) = S(t) + I(t) + P(t) + R(t)$. Also, a person cannot be in more than one compartment at the same time.
- Contacts between either two regular infected people, two super-spreading events or between a regular infected person and a super spreader are considered as 'waste' since they do not contribute towards the spread of the disease.
- We do not take birth and death rates into consideration in view of the short duration of the outbreak.
- Super-spreading events spend more time outside quarantine than regularly infected people.

- A susceptible person joins either the regularly infected compartment or the super-spreading event compartment if he acquires an infection through being in contact with a person who is in any of the infected compartments (regularly infected or super-spreading events).
- Also, an infected person (regular or super-spreader) joins the removed compartment through isolation, quarantine or death.
- Each time there is an interaction between the infected compartments (I or P) and the susceptible population S, there is a probability b that the new infection will be regularly infected (I) and a probability $(1-b)$ that the new infection will be a super spreading event (P).
- Infected people (regularly infected or super-spreading events) are produced by the infection of susceptible people, S, by either regularly infected people, I, or super-spreading events, P, with transmission rate β.
- Regularly infected people who recover on any given day leave the regularly infected compartment with recovery rate $\frac{1}{x}$ and join the removed compartment. The constant x denotes the average number of days spent by a regularly infected person outside isolation.
- Super-spreading events who recover on any given day leave the super-spreading events compartment with recovery rate $\frac{1}{k}$ and join the removed compartment. The constant k denotes the average number of days spent by a super-spreading event outside isolation.

5.2 Governing equations of the SIPR model

Based on the previous descriptions and assumptions we formulate a system of four ordinary differential equations which best describe the SIPR model:

$$\begin{aligned}
\frac{dS}{dt} &= -\beta(I+P)S \\
\frac{dI}{dt} &= b\beta(I+P)S - \frac{1}{x}I \\
\frac{dP}{dt} &= (1-b)\beta(I+P)S - \frac{1}{k}P \\
\frac{dR}{dt} &= \frac{1}{x}I + \frac{1}{k}P
\end{aligned} \tag{5.1}$$

where b is the probability of having contacts between super-spreading events and regular infected peoples at any given day, x is a constant with units of time in days which is a measure of the average number of days spent by a regularly infected person outside isolation, and k is a constant with units of time in days which is a measure of the average number of days spent by a person who is a super-spreading event outside isolation.

Adding these four equations we have that

$$S' + P' + I' + R' = 0 \tag{5.2}$$

This upon integration gives

$$S + P + I + R = N, \tag{5.3}$$

where N, the integration constant, is the fixed population size.

5.3 Initial conditions

Assuming that at time, $t = t_0$, of the outbreak of the SARS epidemic there were no super-spreading events, we formulate the initial condition $P(t_0) = 0$. Also, at the outbreak of the SARS epidemic there was a relatively small number of regularly infected people, $I = I_0 > 0$. They are allowed to move and interact freely with the individuals in the susceptible group as a result of the population being subjected to homogenous mixing.

At the outbreak of the SARS epidemic, there were no people in the removed compartment, i.e. $R(t_0) = 0$). Thus everybody is susceptible, excluding the the small group of regularly infected people, I_0. We

therefore formulate initial conditions for the SIPR model as follows:

$$\begin{aligned} S(t_0) &= N - I_0 = S_0 \\ I(t_0) &= I_0 \\ P(t_0) &= 0 \\ R(t_0) &= 0 \end{aligned}$$

where $S_0 > 0$ and $I_0 > 0$. When S_0 and I_0 are added, N is obtained. Therefore our complete SIPR model is

$$\begin{aligned} \frac{dS}{dt} &= -\beta SI - \beta PS \\ \frac{dI}{dt} &= b\beta SI + b\beta PS - \frac{1}{x}I \\ \frac{dP}{dt} &= (1-b)\beta PS + (1-b)\beta SI - \frac{1}{k}P \\ \frac{dR}{dt} &= \frac{1}{x}I + \frac{1}{k}P \end{aligned}$$

subject to the following initial conditions

$$S(t_0) = N - I_0 = S_0,\ I(t_0) = I_0,\ P(t_0) = 0,\ \text{ and }\ R(t_0) = 0$$

5.4 Relationships between the variables

- We assume that $I > P$ and $k > x \Rightarrow SI > SP$. This means that since we have more regularly infected people than super-spreading events at the outbreak of the disease, we expect in the long run to have more contacts between between the susceptible population and the regularly infected people than we would with the susceptible people with the super-spreading events [5].
- We also assume that $b > 0.5 \Rightarrow b > 1 - b$ which implies that $\beta SI > (1-b)\beta SI$. This means that each time there is an interaction between an infected person (either I or P) and a susceptible person, there is a high likelihood that the resulting infected will be join the regularly infected population. The "20/80" rule states that 20% of cases cause 80% of transmission.

5.5 SIPR model analysis

In the following subsections, we not only show that a global solution to the SIPR model exists but also that it is unique. We further show

that the number of people in each compartment is nonnegative and it stays finite for all time $t > 0$. We then compute and analyze the equilibrium solutions of the SIPR model. We also present solution graphs and calculate the basic reproduction number, R_0, using the next generation method discussed in Section 3.1. Finally we highlight some of the benefits and limitations of the SIPR model.

5.5.1 Existence and uniqueness of a global solution

The system of equations given in Section 5.1 which best describe the SIPR model can be written in the form:

$y' = f(t, y),\ \ y(t_0) = y_0\ \ \text{where}\ \ y = \begin{bmatrix} S(t) \\ I(t) \\ P(t) \\ R(t) \end{bmatrix}$. The function $f(t, y)$ is continuous everywhere on $\mathbb{R}^4$ and its partial derivatives are continuous. The function $f(t, y)$ is bounded (since all solutions are bounded). Hence Peano's existence theorem in conjunction with Theorem 8.1 (on page 441) in Philip Hartman's book [8] guarantees the existence of a unique global solution for the SIPR model.

5.5.2 Positivity and boundedness of solutions

The SIPR model discussed in Section 5.1 describes a human population, and, therefore, it is very important to prove that all quantities (susceptible, regularly infected, super-spreading events, and removed) will be positive for all time. In other words, we want to prove that all components of the solution of system 5.1 with nonnegative initial data will remain positive for all times $t > 0$.

Theorem 5.5.1. *Let the initial data be* $S(0) = S_0 > 0$, $I(0) = I_0 > 0,\ P(0) = P_0 = 0$ *and* $R(0) = 0$. *Then the components of the solution* $S(t)$, $I(t), P(t)$, *and* $R(t)$ *of the SIPR model are positive for all time,* $t > 0$.

Proof. In this proof we show that if we start with nonnegative initial conditions (given in Section 5.3) of the SIPR model given by Equation 5.1, we also end up with nonnegative solutions.

To see this, we assume that $S(t) = 0$ for some time $t > t_0$, $I(t) \geq 0,\ P(t) \geq 0,\ R(t) \geq 0$ and show that $\dfrac{dS}{dt} \geq 0$. Clearly in view

of the SIPR model, $\frac{dS}{dt} = 0$ when $S(t) = 0$ which shows that the solution $S(t)$ will be nonnegative for all time $t > 0$.

To prove that the component of the solution $I(t)$ will be positive for all time $t > 0$, we assume that $I(t) = 0$ for some time $t > t_0$, $S(t) \geq 0,\ P(t) \geq 0, R(t) \geq 0$ and show that $\frac{dI}{dt} \geq 0$. Looking at the SIPR system of equations, $\frac{dI}{dt} = b\beta PS \geq 0$ when $I(t) = 0$ which shows that the component of the solution $I(t)$ will be nonnegative for all time $t > 0$.

To prove that the component of the solution $P(t)$ will be positive for all time $t > 0$, we assume $P(t) = 0$ for some time $t > t_0$, $S(t) \geq 0,\ I(t) \geq 0,\ R(t) \geq 0$ and show that $\frac{dP}{dt} \geq 0$. Looking at the SIPR system of equations, $\frac{dP}{dt} = (1-b)\beta IS \geq 0$ when $P(t) = 0$ which shows that the component of the solution $P(t)$ will be nonnegative for all time $t > 0$.

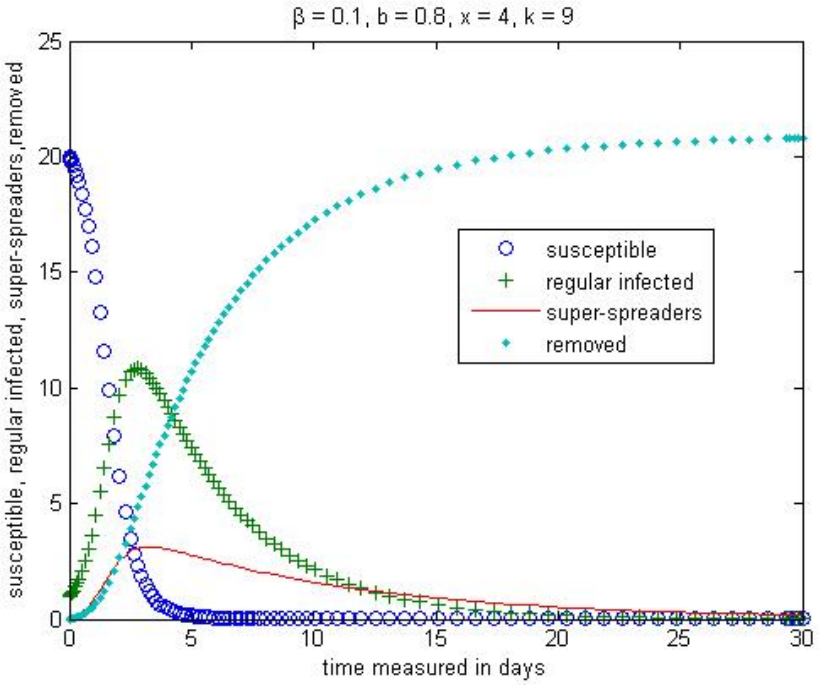
Finally, to prove that the component of the solution $R(t)$ will be positive for all time $t > 0$, we assume that $R(t) = 0$ for some time $t > t_0$, $S(t) \geq 0, I(t) \geq 0,\ P(t) \geq 0$ and show that $\frac{dR}{dt} \geq 0$. Looking at the SIPR system of equations, $\frac{dR}{dt} = \frac{1}{x}I + \frac{1}{k}P \geq 0$ which shows that the component of the solution $R(t)$ will be nonnegative for all time $t > 0$ which completes the proof. □

The boundedness of the components of the solution $S(t)$, I(t), P(t) and $R(t)$ follows from the fact that $N = S(t) + I(t) + P(t) + R(t)$ and that $S(t),\ I(t),\ P(t), R(t) \geq 0$ for all time $t > 0$. Therefore we have that each component of the solution is at most equal to N. That is $S(t),\ I(t),\ P(t),\ R(t) \leq N$. It was shown in Equation 5.1 that each component of the solution is nonnegative at the outbreak of the disease ($t = t_0$). This shows that each of the components of the solution $S(t)$, $I(t)$, $P(t)$ and $R(t)$ is bounded between zero and the total population size, N.

5.5.3 SIPR Equilibrium points and their stability analysis

In this section we analyze the SIPR model shown in Equation 5.1 by finding the equilibria. Steady states (equilibrium solutions) of Equa-

Figure 5.1: SIPR solutions behavior in continuous time of SARS outbreak, using $\beta = 0.1,\ b = 0.8,\ x = 4$ and $k = 9$



tion 5.1 satisfy the following system of equations:

$$\begin{aligned} -\beta SI - \beta PS &= 0 \\ b\beta SI + b\beta PS - \frac{1}{x}I &= 0 \\ (1-b)\beta PS + (1-b)\beta SI - \frac{1}{k}P &= 0 \\ \frac{1}{x}I + \frac{1}{k}P &= 0 \end{aligned} \tag{5.4}$$

It is easy to check that Equation 5.4 has the disease free equilibrium $E = (N, 0, 0, 0)$ and $Q = (S^*, 0, 0, R^*)$ for any S^* (based on the initial condition) and $R^* = N - S^*$. We can see from Figure 5.1 that when the transmission rate is small, not every body gets sick. However, if the transmission rate is high, almost everybody gets sick in the population as it can seen from Figures 5.2 and 5.3.

5.5.4 R_0 for SIPR using The Next Generation method

We describe the rate of change of the regularly infected individuals, I, and the super-spreading events, P, populations by the following

Figure 5.2: SIPR solutions behavior in continuous time of SARS outbreak, using $\beta = 0.1,\ b = 0.8,\ x = 2$ and $k = 3$

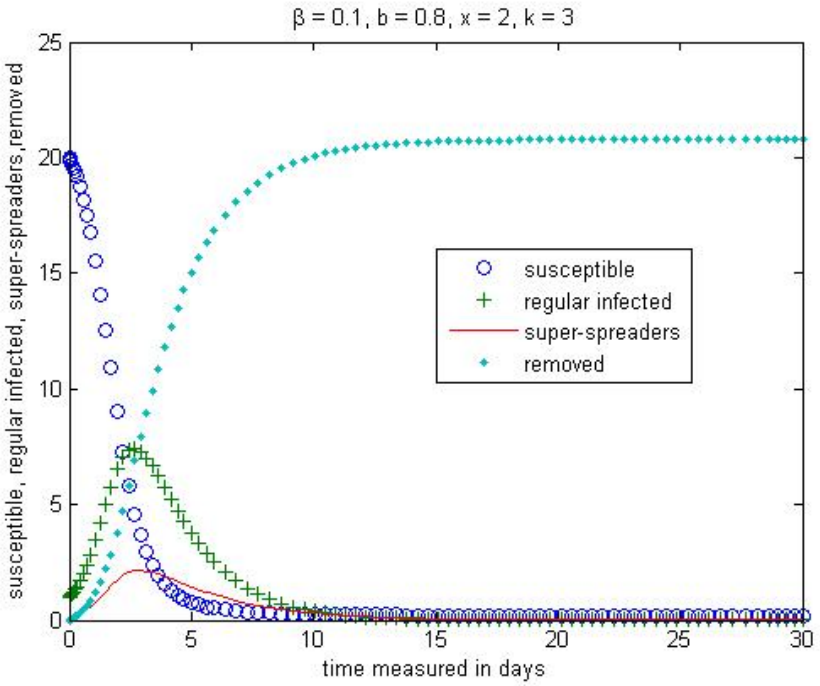
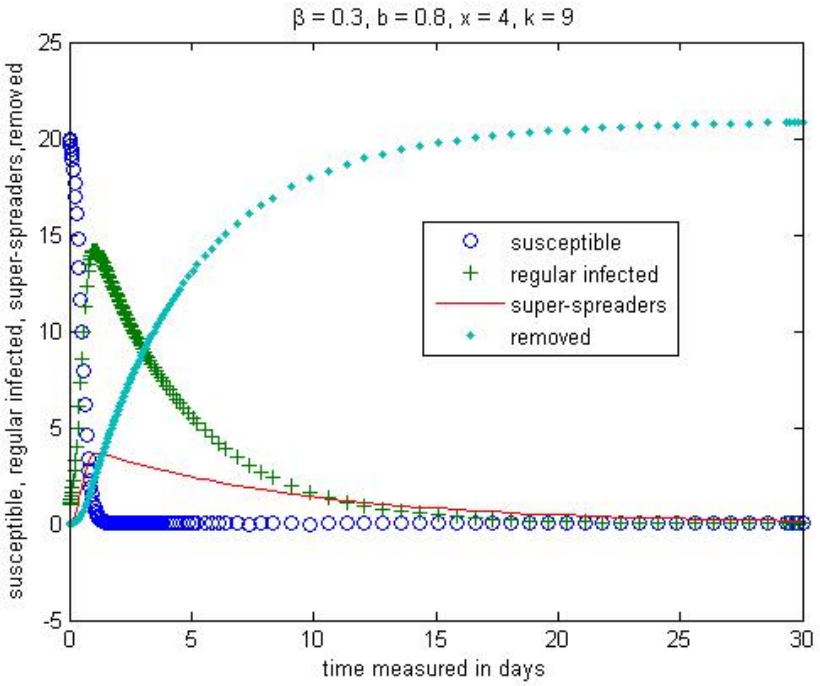


Figure 5.3: SIPR solutions behavior in continuous time of SARS outbreak, using $\beta = 0.3,\ b = 0.8,\ x = 4$ and $k = 9$



equations:

$$\begin{aligned} \frac{dI}{dt} &= b\beta SI + b\beta PS - \frac{1}{x}I \\ \frac{dP}{dt} &= (1-b)\beta PS + (1-b)\beta SI - \frac{1}{k}P \end{aligned} \tag{5.5}$$

New cases are produced by the infection of susceptible people, S, by an infected person who is either regularly infected or a super-spreading event with contact rates $b\beta$ and $(1-b)\beta$ respectively. We further assume that regularly infected people recover from the infection with rate $\frac{1}{x}$ and super-spreading events recover from the infection with rate $\frac{1}{k}$. For the SIPR model shown in Equation 5.5 above, we find that

$$F = \begin{pmatrix} b\beta S & b\beta S \\ (1-b)\beta S & (1-b)\beta S \end{pmatrix} \quad \text{and} \quad V = \begin{pmatrix} \frac{1}{x} & 0 \\ 0 & \frac{1}{k} \end{pmatrix}$$

Since determinant of V is not equal to 0 we can determine V^{-1}:

$V^{-1} = \begin{pmatrix} x & 0 \\ 0 & k \end{pmatrix}$,

$FV^{-1} = \begin{pmatrix} bx\beta S & bk\beta S \\ (1-b)x\beta S & (1-b)k\beta S \end{pmatrix}$, and

$$\det(FV^{-1} - \lambda I_2) = \det \begin{pmatrix} xb\beta S - \lambda & kb\beta S \\ x(1-b)\beta S & k(1-b)\beta S - \lambda \end{pmatrix}.$$

setting $\det(FV^{-1} - \lambda I_2)$ equal to 0, and solving for λ we obtain two eigenvalues:

$\lambda_1 = 0$ and $\lambda_2 = \frac{(1-b)\beta S}{\frac{1}{k}} + \frac{b\beta S}{\frac{1}{x}}$ where $S = S(0) = S_0$. We note that λ_2 is the largest eigenvalue of FV^{-1} and so we conclude by the next generation method described in Section 3.1 that λ_2 is the basic reproduction number of the SIPR model. We note that $R_0 = \lambda_2 = \frac{(1-b)\beta S}{\frac{1}{k}} + \frac{b\beta S}{\frac{1}{x}}$ is the R_0 for I and P (as SIR models), multiplied by their respective probabilities b, $(1-b)$ then added together.

5.6 Benefits and limitations of the SIPR model

The SIPR model has the following valuable benefits:

- Like the SIR model, the SIPR is a good, simple, model for many infectious diseases including SARS, measles, foot and mouth, influenza, H_1N_1, mumps and rubella. It is simple in the sense that it has few parameters and hence easy to study.
- It captures the aspect of SSE behavior (i.e. SSE stays longer out of quarantine).
- The system of equations in the SIPR model is autonomous which makes it easier to study the model mathematically.

Despite all the the benefits of the the SIPR, it still suffers from the following limitations.

- It does not capture all aspects of the disease. It assumes the same transmission rate for both infected compartments and only certain combinations of parameters truly show SSE.
- The generalization of the SIR (base) model, i.e. no birth/death rates, makes the model only reasonable for short term diseases. The rates are assumed to be constant (time independent), population averages, and permanent immunity is also assumed.
- We ignore immigration and emigration which had a great influence in the outbreak of the SARS epidemic. The 2002-2003 SARS was spread mainly through air travel.

5.7 Possible future directions of work for the SIPR model

One may wish improve the SIPR model by considering the following aspects:

- Test the SIPR model against real data and make necessary adjustments if need be. One possible source for the data could be the Center for Disease Control (CDC) in Georgia.
- Make changes to the model in order to extend the model to other diseases.
- Convert the model to non-autonomous system. This includes considering a time transmission and recovery rates that are are time dependent instead of the fixed ones used in our model.

- Do a detailed study of the SIPR steady state solutions (equilibrium solutions) therefore determining whether they are locally stable or not.
- Consider a population that is not closed, one which takes immigration as well as emigration into consideration in the modeling of the SARS epidemic.

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