UNIVERSITY OF
LIVERPOOL

Department of Mathematical Sciences

Thesis submitted in accordance with the requirements of
the University of Liverpool for PhD in Mathematical Sciences

Entitled:

Analysis of heterogeneity in the early and late stages of disease spread for a multi-group SIS model

by

Christopher Pearce

Supervised by

Dr D. Clancy

Analysis of heterogeneity in the early and late stages of disease spread for a multi-group SIS model

Thesis submitted in accordance with the requirements of
the University of Liverpool for the degree of Doctor in Philosophy
by
Christopher Pearce

September 2011

Abstract

Chapter 1 gives a brief introduction to modelling epidemics in both a deterministic and stochastic framework. Chapter 2 gives a brief introduction to the single-group Susceptible-Infected-Susceptible (SIS) model and we mention and establish all the necessary background theory we apply to the model with the aim of extending these theories and techniques to our own multi-group SIS model in order to obtain results concerning the short and long-term behaviour of the epidemic.

In Chapter 3 we define a k-group SIS model which will allow us to examine the effects of heterogeneity in three different categories - the infectivity of infectious individuals, their mixing behaviour and an individual's susceptibility to the disease. In doing this, we describe the dynamics of the model including how to represent it in a deterministic framework, the quasi-stationary distribution and the time to extinction. We apply a branching process approximation to the model, viable for the early stages of a disease, using well established theory.

In Chapter 4 we look specifically at the early stages of the epidemic based on the branching process approximation and produce numerical results on how the probability of disease emergence behaves as the basic reproduction number R_0 increases. We contrast 2-group heterogeneous models against a homogeneous model, for epidemics assuming either an exponential or constant infectious period. We then analyse these results with an iterative and inductive proof showing that the emergence probability for a heterogeneous model will always be less than that for a homogeneous model, not just in the limit but at all stages of iterative convergence. Next we provide a proof which shows that for the non-separable general model this ordering exists for any given infectious period. We then go on to look at comparing two heterogeneous models to one another under various sets of parameters and use majorization theory as a tool for doing so. We use orderings referred to as ordinary majorization, **p**-majorization and **pq**-majorization to show that there is an inferred ordering of emergence probabilities when comparing multi-group heterogeneous models to one another.

In Chapter 5 we study the long-term behaviour of the stochastic multi-group SIS model. We begin by formulating conditions for the general model under which

feasible equilibria exist and conditions where either the disease-free or endemic equilibria are stable. For a 2-group version, we calculate numerically the deterministic equilibrium values, stochastic means and quasi-stationary distributions for a range of R_0 values. We use an Ornstein-Uhlenbeck process to approximate the quasi-stationary distribution and assess the accuracy of the approximation. We then calculate the expected time to extinction and use a coefficient of variation approximation as a proxy for this and discuss the suitability of such an approximation to the exact results. These analyses are all carried out for models which exhibit heterogeneity in infectivity, mixing or susceptibility.

Contents

List of Figures

Acknowledgements

My sincere thanks and gratitude goes to my multi-talented supervisor Dr. Damian Clancy, without whose guidance and support this project would not have been possible. My thanks also go to my parents, Harvey and Julie Pearce, for believing in me and to my partner Thomasin Smith for continually keeping me on the right path whenever I wandered astray. I am also greatly appreciative for my scholarship provided by the EPSRC and to the University of Liverpool.

Chapter 1

Introduction

The outbreak and spread of disease has been questioned and studied for several centuries and infectious disease is still the leading cause of human mortality worldwide. The ability to make predictions about diseases enables scientists to evaluate vaccination or isolation plans that may have significant effect on the mortality rate of a particular epidemic. The modelling of infectious diseases is a tool which has been widely used to study the mechanisms by which diseases spread, to predict the future course of an outbreak and to evaluate the strategies to control an epidemic (Daley & Gani [33]).

Two types of models used are deterministic and stochastic models. When dealing with large populations, deterministic models are typically used. In these models, transition rates from one class to another are mathematically expressed as time-derivatives, hence the model is formulated using differential equations. While building such models, it must be assumed that a population size within a compartment is differentiable with respect to time and that the epidemic process is deterministic. In other words, the changes in population of a compartment can be calculated using only the history of the process. The deterministic model considers a structured mathematical framework, where for instance the actual number of new cases in a short time interval may be taken to be proportional to the number of both susceptibles and infectives. A stochastic model is a tool for estimating probability distributions of potential outcomes by allowing for random variation in one or more inputs over time. Stochastic models depend on the chance variations in risk of exposure, disease and other dynamics. They are used when these fluctuations are important, as in small populations. A stochastic model considers conditional realisation, where for instance it may be assumed that the probability of one new case in a short time interval is proportional to numbers of both susceptibles and infectives, as well as the length of the time interval. The difference between the two approaches is that the deterministic model considers a set mathematical structure whereas the stochastic model works on the conditional probability structure.

For this thesis we analyse a stochastic model referred to as the Susceptible-Infected-Susceptible (SIS) model, which in real-world application, has been used as a model for sexually transmitted diseases and macroparasites. The SIS model can easily be derived from the more widely used Susceptible-Infected-Removed (SIR) model by simply considering that the individuals recover with no immunity to the disease, that is, individuals are immediately susceptible once they have recovered. For a stochastic model to be mathematically manageable it has to be quite simple, and thus perhaps not entirely realistic. The beauty of the SIS model however, is that it allows us to examine long-term behaviour of a disease once an epidemic is established due to an unchanging population size, where theoretically the disease may persist for a very long time indeed. This in itself is not an easy task and the simplifying assumptions of the model make it more mathematically tractable. That said, the assumption that the total population size remains constant is argued as reasonable if the disease spreads quickly through the population, or when modelling the disease over many years if natural births are approximately balanced by the natural deaths (see eg. Anderson & May [7], Bailey [14], Hethcote [50]). Many studies of epidemic models focus on the final sizes of the epidemic (see eg. Artalejo et al. [11], Daley [32]) which are often considered as products of marginals. However these can be not entirely intuitive. There is indeed a significant challenge for meeting with applied insights from epidemic modelling.

Stochastic models, even the simpler ones, are not easy to analyse. Usually the transition probabilities exhibit non-linear dependence on population size or number of infectives which makes the resultant stochastic process analytically intractable (Krishnarajah et al [65]). Therefore techniques of approximation are needed to capture the underlying behaviour of the stochastic process. We can in fact approximate the behaviour of the stochastic process, when the population size is large, by an essentially deterministic motion which will be discussed in much more detail shortly. The stochastic approach, however, when it can be performed is more realistic, powerful and flexible.

Chapter 2

Literature review and model formulation

2.1 History

The mathematical study of diseases is at most three centuries old. To give a full account of the history of the subject would require a book in itself. The interested reader may refer to Burnet & White [26] for a natural history of diseases, Bailey [14], Anderson & Britton [4] and Anderson & May [7] for an outline of the development of mathematical theories for the spread of epidemics.

The first stochastic model was proposed by McKendrick in 1926 [77] which was a stochastic continuous-time version of the deterministic model of Kermack & McKendrick (1927) [62], but perhaps the most used was the chain binomial model of Reed & Frost in 1928. Abbey [1] later gave a detailed account of it (see also Wilson & Burke [103]). It wasn't until 1949 when Bartlett [20] formulated the model for the general stochastic epidemic by analogy with the Kermack-McKendrick deterministic model that stochastic models proliferated. The first pioneering monograph was written by Bailey in 1957 [13]. Anderson & May's book [7] received most attention, modelling the spread of disease for several different situations with many practical applications. More recently, Daley & Gani [33] focused on stochastic modelling and statistical inference for epidemics. Most stochastic models have relied on discrete or continuous time Markov Chain structure. Reviews of the literature of epidemic models (see eg. Dietz & Schenzle [39], Hethcote [52]) indicate that their number has grown rapidly in the past half century.

Several models have been proposed for the quantitative analysis of an epidemic. The most classical among them are the Susceptible-Infected (SI), Susceptible-Infected-Susceptible (SIS) and Susceptible-Infected-Removed (SIR) models. All of them model the outbreak and spread of contagious diseases under different assumptions (eg. according to whether an infected individual remains forever infected, re-

covers and becomes re-susceptible or is removed due to death/immunity/quarantine). The textbooks and monographs [2],[3],[15],[33],[37] give recent accounts of the main results in this area, with many examples.

The spread of infectious disease is a random process; when the number of individuals is very large, it is customary to represent the infectious process deterministically as Anderson & May [7] mostly do. For study of the spread of an epidemic in a large population, investigators use primarily deterministic models. Recent studies deal with refinements of the SI (Susceptible-Infected), SIS (Susceptible-Infected-Susceptible) and SIR (Susceptible-Infected-Removed) models using ordinary and partial differential equations, eg. see [97],[101]. However, deterministic models are unsuitable for small populations, while even in larger populations, the mean number of infectives in a stochastic model may not always be approximated satisfactorily by the equivalent deterministic model. On the other hand, stochastic methods complement the deterministic approach and are particularly useful for the study of epidemics in small populations. However, the dynamics of the underlying processes yield intractible models, even in the simplest cases of the SIS and SIR models. For this reason interest to this day is still focused on various aspects of the fundamental Markovian models and some variants eg. see [3],[18],[30],[69],[98],[105].

We focus on stochastic epidemic models making practical use of several probabilistic techniques. This way, the spread of disease is described by defining the probability of disease transmission between two individuals rather than stating certainly whether or not transmission will occur thus not necessitating a need to rely on the law of large numbers, as deterministic models do. This will be done without focusing on any specific disease, but instead analyzing rather simple generic models.

There is a main feature that makes the modelling of infectious disease different from other types of disease. Strong dependencies are naturally present: whether or not an individual becomes infected depends on the states of other individuals in its vicinity. This complicates the stochastic analysis. For non-transmittable disease, this is usually not the case and such diseases are usually modelled using survival analysis (a thorough treatment is given in Anderson and May [7]).

2.2 The SIS model

The SIS model was first discussed by Weiss & Dishon [102] and has since been used by authors in a variety of contexts, see Nåsell [84] and references therein. We consider a closed population of individuals, each of whom is classified as either susceptible or infectious. When an infectious individual makes contact with a susceptible individual, the susceptible becomes immediately infectious for a period of time and can infect other susceptibles during that period. After this period, an infectious individual then returns to a susceptible state and can again be infected. The abbreviation for this construct, and referred to henceforth, is the SIS-model (Susceptible-Infected-Susceptible). Historically, most analyses of SIS processes have been based on various versions of the forward Kolmogorov differential equations. We regard the epochs where individuals change their classification as randomly determined points in continuous-time. For mathematical convenience but with sufficient simplistic realism, we assume the processes involved are Markovian. When simulating this model, we assume there is no interference to the disease, eg. vaccination/confinement, in the interests of keeping the model simplified. If we were to consider such effects, we would have to account for additional groups of individuals in our system thus adding complexity and making explicit algebraic expressions much more difficult to find, if at all they exist. We also assume a homogeneously mixing group of N individuals and suppose the epidemic starts at time $t = 0$ with $I(0)$ infectives and $S(0)$ susceptibles. Further assumptions made at this stage for our model are that individuals are born susceptible, no individual has automatic immunity to the disease. At the start of the model, $I(0) \neq 0$. There are no births/deaths, ie. N is constant and the number of infectives increases/decreases by one at a time. One particular reason of interest for analysing the SIS model is that it can be used to model long-term endemic behaviour due to the fact that individuals become re-susceptible as opposed to SIR (Susceptible-Infected-Removed) models, for example, where recovered individuals are removed from the population. Therefore including immunity, for example, in a finite population model with no births results in a linear death process and so analysis of long-term behaviour would cease to be possible.

The model is an example of a discrete state space, continuous-time Markov process (eg. see Karlin & Taylor [59], [60] or Ross [93]). The SIS model describes an infection spreading in a closed population of N individuals, where individuals recover but do not develop immunity, being immediately susceptible to re-infection. So the population under consideration is divided into disjoint classes which change with time t. We have

$$S(t) + I(t) = N \qquad t \in [0, \infty)$$

where $S(t)$ is the number of susceptible individuals at time t, $I(t)$ is the number of infectives at time t, N is the fixed population size. The variables I, S take

discrete values, $I, S \in \{0, 1, 2, \ldots, N\}$. Since $S(t) + I(t) = N \quad \forall t$ it is sufficient to concentrate on $I(t)$. The process $\{I(t) : t \geq 0\}$ is a finite-state space univariate continuous-time Markov chain with state space $C = \{0, 1, \ldots, N\}$. During a sufficiently small time interval $[t, t + \delta t]$ there are two possibilities for a transition, and denoting $p_{i,j}(s,t) = P\{I(t) = j \mid I(s) = i\}$ for $i, j \in C, 0 \leq s \leq t$, we have, for $i \in C$,

$$\begin{array}{lll} p_{i,i+1}(t, t+\delta t) = & (\frac{\beta}{N}(N-i)i)\delta t + o(\delta t) & \text{infection} \\ p_{i,i-1}(t, t+\delta t) = & \gamma i \delta t + o(\delta t), & \text{recovery} \end{array}$$

all other transitions having probability $o(\delta t)$, where β, γ are the infection and recovery parameters respectively. The time between each transition is memoryless, meaning the future event only depends on the current event and is independent of all other events.

All states except the origin are transient and the stationary distribution is degenerate with probability 1 at the origin. The infection rate at time t is expressed as $\frac{\beta si}{N}$ where s, i are values taken by the state variables, S, I at time t. The recovery rate is γi. As disease transmission is instantaneous, ie. there is no latent period, the average period of infectivity is $1/\gamma$. The time between each successive transmission is exponentially distributed with parameter $\lambda = \frac{\beta}{N}(N - I)I + \gamma I$ which is the sum of the transition rates, and called the 'jump rate'. The exponential distribution has mean $\frac{1}{\lambda}$ so the mean for this system is $[\frac{\beta}{N}(N - I)I + \gamma I]^{-1}$. All parameters are assumed to be strictly positive.

We define R_0, a function of the model, as the 'average number of new infected individuals that a single infected individual produces in a population of susceptible individuals during the early stages of an epidemic' (Diekmann et al [36]). R_0 determines whether or not an outbreak is likely to happen. It is referred to as the **basic reproduction number** and given by $R_0 = \frac{\beta}{\gamma}$. The threshold limit theorem states that if and only if $R_0 > 1$ can a major outbreak occur in a large population. If $R_0 \leq 1$, the disease will not spread and will eventually die out. Since $R_0 = \beta/\gamma$, increases in the rate of infection tend to increase R_0 and increases in the rate of recovery tends to reduce the spread of the disease in the population. This is intuitive.

The state space C can be decomposed as $C = \{0\} \cup D$ where 0 is an absorbing state and D comprises the transient states. Absorption at 0 is certain within a finite time. Let $p_i(t) = P(I(t) = i), i \in \{0, 1, \ldots, N\}$ denote the state probabilities. These depend on the initial distribution $\{p_i(0)\}$. The intensity matrix Q is of tridiagonal type with entries

$$\begin{array}{lll} q_{i,i-1} = & \gamma i & i = 1, 2, \ldots, N, \\ q_{i,i+1} = & \frac{\beta}{N} i(N-i) & i = 0, 1, \ldots, N-1, \\ q_{i,i} = & -(\gamma i + \frac{\beta}{N} i(N-i)) & i = 0, 1, \ldots, N, \\ q_{i,j} = & 0 & \text{for } i, j = 0, 1, \ldots, N \text{ and } j \neq \{i-1, i, i+1\}. \end{array}$$

For a general Markov process, with discrete state space and transition rate matrix Q, the Kolmogorov Forward Equations are expressed as

$$\frac{d\mathbf{p}}{dt} = \mathbf{p}Q$$

where $\mathbf{p}(t)$ denotes the vector of state probabilities. For the SIS model, the Forward Kolmogorov Equations for the state probabilities can be written as

$$\frac{dp_i}{dt} = \frac{\beta}{N}(i-1)(N-i+1)p_{i-1}(t) + \gamma(i+1)p_{i+1}(t) - \left[\frac{\beta}{N}i(N-i) + \gamma i\right]p_i(t) \quad (2.1)$$

where $p_{-1}(t) = p_{N+1}(t) = 0$ for all t. Two different behaviours are possible at any given time. Either the process is extinct after having reached the absorbing state at the origin, or the process remains in the transient states. In the latter case the distribution of the process is found by conditioning on absorption not having taken place, which shall be discussed later. In the remainder of this chapter, we describe some well-known theory for the basic SIS model, before moving on in the next chapter to the multigroup SIS model which is the main focus of this thesis.

2.3 Deterministic representation of the SIS model and stability

A deterministic process is one whose outcome can be predicted exactly from knowledge of initial conditions. Unlike the stochastic process, the deterministic is not random and its outcome can be predicted from $\frac{dx}{dt}$ and any initial conditions we set. The deterministic approximation can be useful to give qualitative information about the process. As N increases the stochastic system would resemble the deterministic more closely. It is worth mentioning that a deterministic model is not useful in the early and late stages of an epidemic process, since in the early stages, I is small, and in the latter stages I is small again. In terms of modelling duration of the outbreak, the deterministic model is arguably not useful at all. What it is useful for is approximations when the disease process has 'taken off' and is in or around some sort of endemic equilibrium, which could in theory persist for an extremely long time.

We introduce scaling $x(t) = \frac{I(t)}{N}$ and $y(t) = \frac{S(t)}{N}$ to denote the fractions of the population which are infective and susceptible. N is considered sufficiently large so that the size of each class can be considered a continuous variable. The differential equations for the deterministic version of the epidemic are

$$\frac{dx}{dt} = \beta xy - \gamma x, \quad \frac{dy}{dt} = -\beta xy + \gamma x.$$

So we have a 2 dimensional, non-linear, differential equation system. The constant population size is built into the system since adding these two equations gives

$$\frac{d(x+y)}{dt} = \frac{dx}{dt} + \frac{dy}{dt} = 0,$$

so $\frac{dx}{dt}$ along with the fact that $y = 1 - x$ gives a complete description of the model,

$$\frac{dx}{dt} = \beta(1-x)x - \gamma x. \tag{2.2}$$

Let x^* be the equilibrium point. If x^* is stable then after any 'disturbance' ϵ near it, the system will return to equilibrium. Therefore, if x^* is stable $\frac{dx}{dt}\,|_{x^*-\epsilon} > 0$ since if we move along the horizontal line slightly to the left we will be attracted back towards the equilibriuim point. The reasoning is the same for $x^* + \epsilon$, hence $\frac{dx}{dt}\,|_{x^*+\epsilon} < 0$. $\frac{\partial}{\partial x}$ corresponds to changes in x and for a stable equilibrium

$$\frac{\partial}{\partial x}\left(\frac{dx}{dt}\right)_{|_{x^*}} < 0$$

is true if we move along the horizontal line from left to right, $\frac{dx}{dt}$ goes from positive to negative. A similar argument holds for proving an equilibrium is unstable.

When system (2.2) is in equilibrium,

$$x(\beta - \beta x - \gamma) = 0 \quad \text{which gives} \quad x = 0 \text{ or } x = x^* = 1 - \frac{\gamma}{\beta}.$$

To determine the stability conditions for $x = 0$,

$$\frac{\partial}{\partial x}\left(\frac{dx}{dt}\right)_{|_{x=0}} = \beta - \gamma,$$

so $x = 0$ is stable if $\gamma > \beta$, unstable if $\beta > \gamma$. So the disease-free equilibrium is only stable if $R_0 < 1$. If $\beta < \gamma$, ie. $R_0 < 1$, then $x(t)$ is strictly decreasing and therefore must approach an equilibrium since the process is bounded at zero. Since the only non-negative equilibrium of the process is zero, this is the point of equilibrium.

For $x = x^* = 1 - \frac{\gamma}{\beta} = 1 - \frac{1}{R_0}$,

$$\frac{\partial}{\partial x}\left(\frac{dx}{dt}\right) = \beta(1-2x) - \gamma \Rightarrow \frac{\partial}{\partial x}\left(\frac{dx}{dt}\right)_{x=1-\frac{\gamma}{\beta}} = \beta\left(1 - 2\left(1 - \frac{\gamma}{\beta}\right)\right) - \gamma = \gamma - \beta.$$

Thus x^* is stable if $\beta > \gamma$, ie. $R_0 > 1$.

2.4 The quasi-stationary distribution

A question which has received a lot of attention in the literature is the behaviour of an endemic disease after a long time, see e.g. Nåsell [86] and the references therein ([5],[48],[88]). Diseases that are able to persist in a population for a long time

without the need of introducing new infectious individuals from an external population are called endemic, see e.g. pg. 73 in [5]. Certain processes, especially those for which the time to absorption is large, display some form of equilibrium on the non-absorbing states (Schrijner [95]). The distribution of the state of the process during this long waiting time is close to the distribution of some random variable under the condition that extinction has not occured (Nåsell [84]). In the case where the disease becomes endemic, the stochastic system will stay in what seems like an equilibrium for a very long period of time before I reaches 0, so in the long-term the disease becomes extinct. This equilibrium that the system seems to be in is the **quasi-stationary distribution** (or limiting conditional distribution). So the quasi-equilibrium resembles an equilibrium although it is not a true equilibrium (the true equilibrium being extinction). The importance of the quasi-stationary distributions of Markov chains in the study of biological problems has been shown in a series of papers, see eg. [87], [100]. Since eventual absorption at the origin is certain, the stationary distribution is degenerate with probability 1 at the origin. Our interest is therefore the quasi-stationary distribution, which describes the long-term behaviour of the process prior to eventual extinction. More precisely, the process has a unique limiting conditional distribution $\mathbf{q} = (q_1, q_2, \ldots, q_n)$ such that

$$q_i = lim_{t\to\infty} P(I(t) = i \mid I(t) > 0)$$

whatever the distribution of the initial state $I(0)$ (Darroch & Senata, [34]). This distribution is also quasi-stationary in that if $P(I(0) = i) = q_i$ then $P(I(t) = i \mid I(t) > 0) = q_i \quad \forall t > 0$. That is: if you start the process off according to distribution $\mathbf{q}$, then at any later time the state of the process is still distributed according to $\mathbf{q}$. It is the unique solution of the equations

$$\frac{\beta}{N}(i-1)(N-i+1)q_{i-1} + \gamma(i+1)q_{i+1} - \left(\frac{\beta}{N}i(N-i) + \gamma i\right) q_i = -\gamma q_1 q_i$$

for $i = 1, 2, \ldots, N$, where $q_0 = q_{N+1} = 0$.

The quasi-stationary distribution of the SIS model was analysed by Nåsell [85], [87]. This distribution is important for the SIS model as an approximation of the distribution of state prior to extinction and is a counterpart to the endemic infection level in the deterministic model (Nåsell, [88]). Nåsell showed that the quasi-stationary distribution $\mathbf{q}$ has forms depending on the value $R_0 = \beta/\lambda$ and its relationship to the total population size N. He identified three parameter regions that determine the form of the quasi-stationary distribution. When $R_0 < 1$, the distribution is approximately geometric and when $R_0 > 1$, it is approximately Normal. However, there exists a transition region when R_0 is near 1, where the form of the distribution is more complex. By rescaling $R_0 = 1 + \frac{\rho}{\sqrt{N}}$ to make R_0 a function of N in such a way that for fixed ρ, R_0 approaches 1 as $N \to \infty$, he defined this region by requiring ρ to be fixed as $N \to \infty$. The time to disease extinction is also determined by these 3 regions. Extinction of the infection is

predicted to occur for all initial values of the proportion of infected individuals whenever $R_0 \leq 1$, its threshold value. If $R_0 > 1$ then the deterministic model predicts that an endemic infection will occur whenever the initial proportion of infected individuals is positive.

To actually find the quasi-stationary distribution for the SIS model, argue as follows: The Kolmogorov Forward Equations (2.1) are

$$\begin{aligned} p_i(t+\delta t) = \; & p_{i-1}(t)\left(\tfrac{\beta}{N}(N-(i-1))(i-1)\delta t\right) \\ & +p_{i+1}(t)(\gamma(i+1)\delta t) + p_i(t)\left(1-\tfrac{\beta}{N}(N-i)i\delta t - \gamma i\delta t\right) + o(\delta t) \end{aligned}$$

$$\begin{aligned} \Rightarrow \quad \tfrac{p_i(t+\delta t)-p_i(t)}{\delta t} = \; & p_{i-1}(t)\left(\tfrac{\beta}{N}(N-(i-1))(i-1)\right) \\ & +p_{i+1}(t)(\gamma(i+1)) - p_i(t)\left(\tfrac{\beta}{N}(N-i)i+\gamma i\right) + o(1) \end{aligned}$$

$$\begin{aligned} \Rightarrow \quad \tfrac{dp_i(t)}{dt} = \; & p_{i-1}(t)\left(\tfrac{\beta}{N}(N-(i-1))(i-1)\right) \\ & +p_{i+1}(t)(\gamma(i+1)) - p_i(t)\left(\tfrac{\beta}{N}(N-i)i+\gamma i\right) \end{aligned}$$

for $i = 0, 1, \ldots, N$, with $p_{-1}(t) = p_{N+1}(t) = 0$ for all t, so that the equations make sense for every i value.

As previously stated, the SIS process ultimately ends in state zero. That is, the stationary distribution assigns probability 1 to state $I = 0$. The infection eventually goes extinct. States $D = \{1, 2, \ldots, N\}$ are an irreducible class. As we're interested in the behaviour of the process in the long-term, conditional upon non-extinction we appeal to the conditional Kolmogorov equations, studying $\{I(t)\}$ conditioned on non-extinction. The state probabilities at time t conditional on non-extinction are given by

$$q_i(t) = P(I(t) = i \mid I(t) \neq 0) = \frac{p_i(t)}{1 - p_0(t)} \tag{2.3}$$

where $i = 1, 2, \ldots, N$ and $\mathbf{q}(t) = (q_1(t), q_2(t), \ldots, q_N(t))$, with $q_i(t) = 0$ if $i \notin [1, N]$. That is, a quasi-stationary distribution is an initial distribution on $\{1, 2, \ldots, N\}$ such that the conditional probability of the process being in state i at time t, given that absorption has not taken place by that time, is independent of time t for all i (Darroch & Seneta [34]).Using the quotient rule and Forward Kolmogorov equations (2.1) we find equations in terms of q_{i-1}, q_i, q_{i+1} and q_1.

$$\frac{dq_i}{dt} = \frac{(1-p_0(t))\left(\frac{dp_i(t)}{dt}\right) - (p_i(t))\frac{d}{dt}(1-p_0(t))}{(1-p_0(t))^2} = \frac{(1-p_0(t))\left(\frac{dp_i(t)}{dt}\right) + (p_i(t))\frac{d}{dt}(p_0(t))}{(1-p_0(t))^2}$$

$$= \frac{(1-p_0(t))(\frac{\beta}{N}(i-1)(N-i+1)p_{i-1}(t) + \gamma(i+1)p_{i+1}(t) - (\frac{\beta}{N}i(N-i)+\gamma i)p_i(t)}{(1-p_0(t))^2}$$

$$+\left(\frac{p_i(t)}{1-p_0(t)}\right)\left(\frac{\frac{\beta}{N}(-1)(N+1)p_{-1}(t)+\gamma(1)p_1(t)-(\frac{\beta}{N}0(N-0)+\gamma 0)p_0(t)}{1-p_0(t)}\right)$$

$$=\frac{\frac{\beta}{N}(i-1)(N-i+1)p_{i-1}(t)+\gamma(i+1)p_{i+1}(t)-(\frac{\beta}{N}i(N-i)+\gamma i)p_i(t)}{(1-p_0(t))}$$

$$+\left(\frac{p_i(t)}{1-p_0(t)}\right)\left(\frac{\gamma p_1(t)}{1-p_0(t)}\right)$$

The Forward Kolmogorov equations can now be used to derive differential equations for the conditional state probabilities $q_i(t)$.

$$\frac{dq_i}{dt}=\frac{\beta}{N}(i-1)(N-i+1)q_{i-1}(t)+\gamma(i+1)q_{i+1}(t)-\left(\frac{\beta}{N}i(N-i)+\gamma i\right)q_i(t)+q_i(t)\gamma q_1(t) \tag{2.4}$$

for $i=1,2,\ldots,N$ where $q_0(t)=q_{N+1}(t)=0$. Note that setting the time derivatives in (2.4) to zero yields the quasi-stationary probabilities of the SIS system.

Denoting by Q^C the intensity matrix Q with the first row and column deleted, the above equations can be written as

$$\frac{d\mathbf{q}}{dt}=\mathbf{q}Q^C+\gamma q_1\mathbf{q}.$$

In quasi-equilibrium, $\frac{dq_i}{dt}=0$ gives

$$\frac{\beta}{N}(i-1)(N-i+1)q_{i-1}+\gamma(i+1)q_{i+1}-\left(\frac{\beta}{N}i(N-i)+\gamma i\right)q_i=-\gamma q_1 q_i.$$

That is,

$$\mathbf{q}Q^C=-\gamma q_1\mathbf{q}. \tag{2.5}$$

There exists for the SIS model a unique quasi-stationary distribution $\mathbf{q}$ with $\mathbf{q}Q^C=-\gamma q_1\mathbf{q}$. This equation is the same as the forward conditional equation but expressed in matrix notation, where Q^C is a truncated $N\times N$ matrix, and $q_i=lim_{t\to\infty}q_i(t)$ is the stationary solution to this system of equations. However, explicit solutions are not possible so approximations are sought. It is known (see [85]) that the quasi-stationary distribution $\mathbf{q}$ is given by the left leading eigenvector of the $N\times N$ matrix Q^C. In other words, $\mathbf{q}$ is a left eigenvector of the matrix Q^C corresponding to the eigenvalue of maximal real part, $-\gamma q_1$. The limiting conditional behaviour is given by $lim_{t\to\infty}P(I(t)=i\mid I(t)\neq 0)=q_i$.

Kryscio & Lefèvre [66] and Nåsell [84], [86] used two birth and death processes to approximate the SIS model. The two approximations lack absorbing states and have non-degenerate stationary distributions that Nåsell called $p^{(1)}$ and $p^{(0)}$. The state space of each of these two approximations differs from the state space of the SIS model by not including the state 0. The approximation $p^{(1)}$ can be interpreted

as the SIS model with one permanently infected individual. In this approximation every recovery rate γi is replace by $\gamma(i-1)$ while all the infection rates remain unchanged. The second approximation, $p^{(0)}$, is interpreted as the SIS model with the origin removed. In this approximation the recovery rate from state 1. $\gamma 1 = \gamma$, is replace by 0, while all other transition rates remain unchanged. Nåsell's results from the approximations confirmed those of Kryscio & Lefèvre [66] that the quasi-stationary distribution is well approximated by distribution $p^{(0)}$ for $R_0 > 1$ and $p^{(1)}$ when $R_0 < 1$. Nåsell also derived approximations for the expected time to extinction from the quasi-stationary distribution.

2.5 Ornstein-Uhlenbeck approximation

Deriving information about the quasi-stationary distribution can be problematic where exact solutions cannot be found. There are no analytic solutions to the Forward Kolmogorov equations and so approximations can be useful. One such is the diffusion approximation known as the **Ornstein-Uhlenbeck** approximation (Tuckwell, [99]), which was initially introduced in 1930 as a mathematical model for the velocity of a Brownian motion particle. The assumption is that the velocity of the particle, rather than its position, undergoes a random walk. The following stochastic differential equation was given for the velocity $v(t)$ of a particle at time t.

$$\frac{dV}{dt} + av = \sigma w(t)$$

where a is constant and w is a white noise. The Ornstein-Uhlenbeck process is a time-homogeneous diffusion process.

If the initial value of an Ornstein-Uhlenbeck process is x then at time t, the random variable $X(t)$ (the value of the Ornstein-Uhlenbeck process at time t) is a Gaussian random variable with mean

$$\mathbb{E}[X(t) \mid X(0) = x] = xe^{-at}$$

and variance

$$Var[X(t) \mid X(0) = x] = \frac{\sigma^2}{2a}\left(1 - e^{-2at}\right).$$

Using the standard formula for a normal density, we have

$$p(y, t \mid x) = \left(\frac{a}{\pi\sigma^2\left(1 - e^{-2at}\right)}\right)^{1/2} \times exp\left(\frac{-[y - xe^{-at}]^2}{\frac{\sigma^2}{a}\left(1 - e^{-2at}\right)}\right),$$

where $p(y, t \mid x)$ is the probability density function of the random variable $X(t)$ given that the initial value $X(0)$ is x. The Ornstein-Uhlenbeck process on $(-\infty, \infty)$ has a stationary density for all parameter values. This time-independent density

can be found by noting that the mean and variance of $X(t)$ take the following values as $t \to \infty$ regardless of the initial value $X(0)$:

$$\mathbb{E}[X(t)] \to 0 \qquad Var[X(t)] \to \frac{\sigma^2}{2a}$$

The stationary density is that of a Gaussian random variable with these values for its mean and variance and is thus

$$P^*(y) = \frac{1}{\sqrt{\frac{\pi\sigma^2}{a}}} exp\left[\frac{-y^2}{\sigma^2/a}\right].$$

An Ornstein-Uhlenbeck process is stationary, Gaussian, Markovian and continuous in probability. Since the Ornstein-Uhlenbeck process is a Gaussian process, and since the quasi-stationary distribution of the SIS model can be approximated by a Normal distribution when $R_0 > 1$ and the population size is large, we shall use the stationary distribution of the Ornstein-Uhlenbeck process to approximate the quasi-stationary distribution of the SIS model.

The theory for diffusion approximation (Ethier & Kurtz, [42]) suggests that, in the endemic case, the deviation from equilibrium converges weakly as $N \to \infty$ to an Ornstein-Uhlenbeck process where the system fluctuates about the equilibrium but is always drawn back to it. So if the endemic equilibrium is stable, we expect the Ornstein-Uhlenbeck process to drift towards it. So the Ornstein-Uhlenbeck process is a diffusion process representing the random movement about the deterministic equilibrium.

A stochastic process is stationary if the random variables $(X(t_1), \ldots, X(t_n))$ and $(X(t_1 + s), \ldots, X(t_n + s))$ have identical joint distributions. The Gaussian distribution is continuous and has probability density function, in one dimension $f(x) = \frac{1}{\sqrt{2\pi}\sigma} e^{-\frac{(x-\mu)^2}{2\sigma^2}}$. For a process to be Gaussian, the samples generated in the simulation must follow a multivariate Normal distribution which has density

$$f(x_1, x_2, \ldots, x_n) = \frac{1}{\sqrt{|\sum|}(2\pi)^{n/2}} e^{-\frac{1}{2}(\mathbf{X}-\mu)^T \sum^{-1}(\mathbf{X}-\mu)}$$

where μ is the vector of the means and $\sum$ the covariance matrix. In a Markovian process the future only depends on the current event, it is independent of all past events and the time between each transition is memoryless.

A stochastic process is continuous in probability if $\forall u \in \mathbb{R}^+$ and $\epsilon > 0$ the following holds:

$$P(|\ X_v - X_u\ | \geq \epsilon) \to 0 \text{ as } v \to u$$

More precisely, assuming N is large, an approximating diffusion process is looked for using the result used in Chapter 5 of Anderson and Britton [4]. The approximation theory is a form of Central Limit Theorem. This means we can approximate the epidemic process when there are many infective individuals, thus excluding the initial and final phases of the epidemic.

We focus on $R_0 > 1$. Since the process has a finite state space and all states j with $j \geq 1$ communicate, the process will become absorbed into the disease-free state 0 in finite time. Prior to absorption we expect to observe small fluctuations around the endemic level. The deterministic model has a unique stable equilibrium at $x^* = 1 - \frac{1}{R_0}$ if $R_0 > 1$. It follows that if the stochastic process $I(t)$ starts close to the endemic equilibrium Nx^* it will tend to stay close to Nx^* for a considerable time subject to small random fluctuations. In order to study these fluctuations of the process I, we define $\sqrt{N}$-scaled process

$$\bar{I}(t) = \sqrt{N}\left(\frac{I(t)}{N} - x^*\right) \quad t \geq 0.$$

This process $\bar{I}(t)$ can be approximated by the Ornstein-Uhlenbeck process (Ethier & Kurtz [42]).

More precisely, if $x(t)$ denotes the trajectory of the deterministic process, and $I(0) = [Nx(0)]$, the integer part of $Nx(0)$, then for any $T > 0$ we have $lim_{N\to\infty} sup_{0\leq t\leq T} \mid \frac{I(t)}{N} - x(t) \mid = 0$ and the process $\sqrt{N}\left(\frac{I(t)}{N} - x(t)\right)$ converges weakly in the space of all sample paths on any finite time interval $[0, T]$ to a diffusion process (Ethier & Kurtz [42]). In the case $x(0) = x^*$ then $x(t) = x^*$ for all t and the relevant diffusion is an Ornstein-Uhlenbeck process.

We have

$$\frac{\mathbb{E}[\Delta I]}{\Delta t} = \frac{\beta}{N} I(N - I) + \gamma I(-1) = \frac{\beta}{N} I(N - I) - \gamma I \tag{2.6}$$

where ΔI is the change in the number of infectives. The Ornstein-Uhlenbeck variance, Σ, can be determined by solving for Σ:

$$\frac{d\Sigma}{dt} = B\Sigma + \Sigma B^T + G, \tag{2.7}$$

see e.g. [57], pg. 357. Here B and G are the local drift and local variance of our centred process. The local drift is the Jacobian of the first order infinitesimal moment of $\bar{I}(t)$ and the local variance is the infinitesimal covariance matrix of $\bar{I}(t)$. For the SIS model, we approximate using I for Nx and use the fact that $\frac{dx}{dt}$ corresponds to $\frac{1}{N}\frac{\mathbb{E}[\Delta I]}{\Delta t}$ to obtain $\frac{dx}{dt} = \beta x(1 - x) - \gamma x$, the deterministic representation of the stochastic system. We take the partial derivative with respect to x and substitute the equilibrium value $x^* = 1 - \frac{\gamma}{\beta}$, which is a solution of $\frac{dx}{dt} = 0$, for

x to obtain B.

$$B = \frac{\partial}{\partial x}\left(\frac{dx}{dt}\right)_{|_{x^*=1-\frac{\gamma}{\beta}}} = \gamma - \beta.$$

We obtain the local variance, G, by noting that

$$\frac{\mathbb{E}[(\Delta I)]^2}{\Delta t} = \frac{\beta}{N} I(N-I)(+1)^2 + \gamma I(-1)^2 = \frac{\beta}{N} I(N-I) + \gamma I$$

and substituting the deterministic equilibrium value Nx^* for I to obtain:

$$G = \beta x(1-x) + \gamma x = \beta\left(1-\frac{\gamma}{\beta}\right)\frac{\gamma}{\beta} + \gamma\left(1-\frac{\gamma}{\beta}\right) = 2\gamma\left(1-\frac{\gamma}{\beta}\right)$$

$$\Rightarrow \frac{d\Sigma}{dt} = (\gamma-\beta)\Sigma + \Sigma(\gamma-\beta) + 2\gamma\left(1-\frac{\gamma}{\beta}\right).$$

We equate this to zero, as we are looking for the equilibrium value of Σ, and not how it converges with time to yield

$$2\Sigma(\gamma-\beta) = -2\gamma\left(1-\frac{\gamma}{\beta}\right) \Rightarrow \Sigma = \frac{\gamma}{\beta} = \frac{1}{R_0}.$$

Therefore the equilibrium distribution of the Ornstein-Uhlenbeck process is Normal with mean 0, variance $\frac{1}{R_0}$. So the quasi-stationary distribution of $I(t)$ can be approximated by a Normal distribution with mean Nx^*, variance $\frac{N}{R_0}$ (result first obtained by Kryscio & Lefèvre [66]). This can be compared with the quasi-stationary distribution obtained using the truncated transition matrix Q^C and equation (2.5).

2.6 A branching process approximation and extinction probability

Branching processes are appropriate for describing the early stages of disease outbreak, when susceptible individuals are not limited and stochastic effects are most important (Ball, [17], Metz, [78]). This is precisely the time during which extinctions may occur. Discrete time branching process models have been used to estimate R_0 from epidemic data (Becker, [23], Farrington et al. [43]) Multi-type branching processes have also been used to predict the outcome of vaccination strategies in populations with different levels of mixing (Ball & Becker, [21]). Lloyd-Smith et al. [71] used single-type branching processes to study the influence of heterogeneity on the emergence of non-evolving pathogens.

We now develop a branching process approximation to the SIS model applicable to the initial stage of the epidemic process. For details on why a branching

process approximation is applicable to the SIS model see Neal, [89]. We approximate the spread of infection by means of a homogeneous Galton-Watson branching process (see Harris [49]), defined as follows.

Suppose an individual produces a random number ξ of offspring with probability distribution

$$P\{\xi = k\} = p_k \qquad k = 0, 1, 2, \ldots \tag{2.8}$$

where $p_k \geq 0$ and $\Sigma_{k=0}^{\infty} p_k = 1$. We assume the offspring act independently of each other and have progeny in accordance with the probability distribution (2.8). Let $Z_0, Z_1, Z_2, \ldots$ denote successive states in our process where Z_n =number of objects in the n'th generation of a population. We shall always assume $Z_0 = 1$. p_k is the probability that an object existing in the n'th generation has k offspring in the $(n+1)$'th generation. We assume p_k does not depend on the generation number n. The process $\{Z_n : n = 0, 1, 2, \ldots\}$ is a Markov Chain called a **Galton-Watson process** (see Harris [49]).

In the n'th generation the Z_n individuals independently give rise to numbers of offspring $\xi_1^{(n)}, \xi_2^{(n)}, \ldots, \xi_{Z_n}^{(n)}$ and hence the cumulative number produced for the $(n+1)$'th generation is

$$Z_{n+1} = \xi_1^{(n)} + \xi_2^{(n)} + \cdots + \xi_{Z_n}^{(n)}.$$

The conditional distribution of Z_{n+1}, given $Z_n = k$ is appropriate to the assumption that different objects reproduce independently, that is Z_{n+1} is distributed as the sum of k independent random variables, each distributed like Z_1. Thus we have defined the transition probabilities of our Markov process: $P_{ij} = P(Z_{n+1} = j | Z_n = i) \quad i, j, n = 0, 1, 2, \ldots$. Having defined the process, we want to know its properties: the probability distribution and moments of Z_n, the probability that the random sequence $Z_0, Z_1, Z_2, \ldots$ eventually goes to zero and the behaviour of the sequence in case it does not go to zero.

Consider the non-negative integer-valued random variable ξ whose population distribution is given by (2.8). The probability generating function $\phi(s)$ associated with this random variable is defined by

$$\phi(s) = \mathbb{E}\left[s^{\xi}\right] = \sum_{k=0}^{\infty} p_k s^k \qquad 0 \leq s \leq 1. \tag{2.9}$$

If $Z_n = \xi_1^{(n)} + \xi_2^{(n)} + \cdots + \xi_{Z_{n-1}}^{(n)}$ is itself random, then the probability generating function of Z_n is given by

$$\mathbb{E}[s^{Z_n}] = \phi_{Z_n}(s) = \phi_{Z_{n-1}}(\phi(s)).$$

For ease of notation we can write $\phi_{Z_n}(s) = \phi_n(s), \phi_{Z_{n-1}}(s) = \phi_{n-1}(s)$ and thus $\phi_n(s) = \phi_{n-1}(\phi(s))$. This is the branching process recursion formula. This is an

expression for the probability generating function of the population size at generation n although there is no guarantee it is possible to write down or manipulate it easily for large n. For example, if $Y \sim Pois(\lambda)$, then $\phi(s) = e^{\lambda(s-1)}$ and by generation $n = 3$ we have $\phi_3(s) = e^{\lambda(e^{\lambda(e^{\lambda(s-1)}-1)}-1)}$. From the point of view of probability theory, it enables us to calculate the moments of Z_n and to obtain various asymptotic laws of behaviour for Z_n when n is large. Thus knowing the generating function is equivalent, in some sense, to knowing the distribution.

Extinction occurs when the population size becomes zero. In Markov Chain terminology, 0 is an absorbing state and we can calculate the extinction probability by invoking a first step analysis. Let

$$q_n = P\{Z_n = 0\}$$

be the probability of extinction by generation n. If a single parent $Z_0 = 1$ gives rise to $\xi_1^{(0)} = k$ offspring, in turn, each of these offspring will generate a population of its own descendants. If the original population is due to die out in n generations then each of these k lines of descent must die out in $n-1$ generations.

The k subpopulations generated by the distinct offspring of the original parent are independent and have the same properties as the original population. The probability that any particular one of them dies out in $n-1$ generations is q_{n-1} by definition and the probability that all k subpopulations die out in $n-1$ generations is $(q_{n-1})^k$ by independence. Upon weighting this factor by the probability of k offspring and summing according to the law of total probability, we obtain

$$q_n = \sum_{k=0}^{\infty} p_k (q_{n-1})^k \qquad n = 1, 2, \ldots \tag{2.10}$$

with $q_0 = 0$, and $q_1 = p_0$, the probability that the original parent had no offspring.

Recalling that $\phi(s) = \mathbb{E}[s^{\xi}] = \Sigma_k s^k p_k$, then the recursion (2.10) becomes

$$q_n = \sum_{k=0}^{\infty} p_k (q_{n-1})^k = \phi(q_{n-1}).$$

That is, knowing the generating function $\phi(s)$, we may successively compute the generation n extinction probabilities q_n beginning with $q_0 = 0, q_1 = \phi(q_0), q_2 = \phi(q_1)$ and so on. The extinction probability converges upwards to the smallest root of the equation $q = \phi(q)$. If q_∞ denotes the smallest solution of $q = \phi(q)$ then q_∞ gives the probability the population eventually becomes extinct at some indefinite, but finite, time. The alternative is that the population grows infinitely large occuring with probability $1 - q_\infty$.

In general, the key is whether $\phi(s)$ crosses the 45^o line $\phi(s) = s$ for $s < 1$ and this can be determined from the slope $\phi'(1) = \frac{d\phi(s)}{ds} \mid_{s=1}$ of the generating function at $s = 1$. If $\phi'(1) \leq 1$ then no crossing takes place and $q_\infty = 1$. If $\phi'(1) > 1$ then

the equation $q = \phi(q)$ has a solution that is less than 1 and extinction is not a certain event. Note that $R_0 = \mathbb{E}[\xi] = \phi'(1)$, so that if $R_0 \leq 1$, extinction is certain; if $R_0 > 1$ then the process may never go extinct.

In the branching process, an individual gives birth to n offspring. In the epidemic, the parent is equivalent to an infected individual. Rather than 'giving birth' to n new individuals, the infected individual 'makes contact' with n other individuals, therefore infecting them, thus describing the disease spread. Each newly infected individual then makes contact with k other individuals, constituting the next generation in a branching process. This process is used as the approximation and continues up until a point where an infected individual makes contact with an individual that has already been infected. In this case, a 'contact' has already been made with this individual during the history of the process. As this individual is not susceptible, it and its descendants in the branching process are ignored in the epidemic process. This individual is referred to as a **ghost**, following Mollison [81].

During its infective period, each infective makes 'contacts' at the points of a Poisson process of rate β. Each contact is with an individual chosen uniformly at random from the N available (allowing self-contacts). If the individual contacted is susceptible, it becomes infected otherwise the contact has no effect. This means the total rate of infectious contacts is $I_t \times \beta \times (S_t/N)$. So each infective 'gives birth' to new infectives at constant rate β, but sometimes fails due to trying to infect a previously-infected individual. In the early stages of an outbreak, provided N is large, then whenever an infective tries to infect another individual the chances are it will succeed, because there's a very large population N, of which only a few individuals have yet been infected.

Now think about a trace of infection introduced into a large susceptible population; that is keep I_0 fixed, and allow $N \to \infty$. Consider any fixed (finite) time interval $[0, T]$. During $[0, T]$, only a finite number of attempted 'contact' events will occur. Hence in the limit as $N \to \infty$, the probability that any attempted contact is with an already infected individual converges to zero. In fact, given any finite interval $[0, T]$, a sequence of epidemic processes with $N = 1, 2, 3, \ldots$ can be constructed in such a way that for N sufficiently large, all attempted 'contacts' during the interval $[0, T]$ are successful (see Ball [17], Metz [78]). That is, for $N \geq N_T$, some N_T, the process $\{I_t : 0 \leq t \leq T\}$ is identical to a linear birth-death process. Studying the early stages of an epidemic is thus reduced to studying the early stages of a linear birth-death process, which is much simpler. The numbers of individuals in successive generations of this birth-death process are described by a Galton-Watson branching process.

Applying this theory to the SIS model: an individual, with infectious period I, 'makes contacts' at rate β, as a Poisson process. Given I, then $(\xi \mid I) \sim Pois(\beta I)$.

We must consider all contacts, including those with ghosts so,

$$p_k = \mathbb{E}\left[\frac{e^{-\beta I}(\beta I)^k}{k!}\right] = \frac{\beta^k}{k!}\mathbb{E}[I^k e^{-\beta I}].$$

So to find p_k, we need to know $\mathbb{E}[I^k e^{-\beta I}]$. We have $\phi(s) = \mathbb{E}[s^\xi] = \mathbb{E}[\mathbb{E}[s^\xi \mid I]]$, where

$$\mathbb{E}[s^\xi \mid I] = \sum_{k=0}^{\infty} s^k \frac{e^{-\beta I}(\beta I)^k}{k!} = e^{-\beta I}\sum_{k=0}^{\infty}\frac{(\beta s I)^k}{k!} = e^{-\beta I}e^{\beta s I} = e^{\beta I(s-1)},$$

so $\phi(s) = \mathbb{E}[e^{\beta I(s-1)}]$. We suppose $I \sim Exp(\gamma)$. Then

$$\mathbb{E}[e^{\beta I(s-1)}] = \int_0^\infty e^{\beta(s-1)t}\gamma e^{-\gamma t}dt = \gamma\int_0^\infty e^{(\beta(s-1)t-\gamma)t}dt = \gamma\left[\frac{e^{(\beta(s-1)-\gamma)t}}{\beta(s-1)-\gamma}\right]_0^\infty$$

$$\Rightarrow \phi(s) = \frac{\gamma}{\gamma - \beta(s-1)}$$

provided $s < 1 + \frac{\gamma}{\beta}$. The extinction probability is given by $q = \phi(q)$, so $q = \frac{\gamma}{\gamma-\beta(q-1)}$,

$$\Rightarrow \gamma q - \beta q(q-1) = \gamma \quad \Rightarrow -\beta q^2 + (\beta+\gamma)q - \gamma = 0.$$

This implies $(q-1)(-\beta q + \gamma) = 0$. So $q = 1$ or $q = \gamma/\beta$. That is,

$$q = min\left\{1, \frac{\gamma}{\beta}\right\} = min\left\{1, \frac{1}{R_0}\right\}.$$

If the Galton-Watson process goes extinct in a finite number of generations, then the approximation is good over the whole course of the epidemic, which dies out quickly. If the Galton-Watson process survives indefinitely, then a large epidemic outbreak occurs, and after the early stages the Galton-Watson process ceases to be a good approximation.

Chapter 3

Heterogeneous population models

3.1 Literature review

The classical simple epidemic models (Diekmann & Heesterbeek [37], Arino et al. [9], Ma & Earn [74]) assume homogeneous mixing of members of the population being studied, and this is certainly unrealistically simple. Frequently, there are what are termed 'super-spreaders', who make many contacts and are instrumental in spreading disease. In general, some members of a population make more contacts than others hence a need to account for heterogeneity.

The study of heterogeneity in epidemic modelling is vast. Of course, the need for heterogeneity in contact mentioned above is just one type of heterogeneity. One of the main issues is that heterogenity itself can be dependent upon a myriad factors. Furthermore, deciding on how you want to parameterize heterogeneity will lead to the question of which epidemic model in particular you should use. For example, choosing to model heterogeneity in the susceptibilities of individuals to a directly transmitted disease in a population that develops immunity may lead to the choice of a SIR (Susceptible-Infected-Removed) model. If you then wanted to incorporate a latent period into the model and accommodate for that source of heterogeneity, we might then require a SEIR (Susceptible-Exposed-Infected-Removed) model. There is by no means a unifying template to model factors that may affect disease dynamics. Another issue is choosing the actual disease, or type of disease, to model. Real-world diseases have different sets of heterogeneous factors, be it environmental, age-dependant, seasonal or contact to name but a few. One final issue is at what stage in a diseases 'lifetime' you want to examine the effects of heterogeneity. Whether it be prior to break out, or long-term persistence, the model choice and underlying assumptions will be affected.

The long-term dynamics of an epidemic are simple: either the disease dies out

or a stable (quasi-) equilibrium is reached in which case the disease is endemic. As discussed in chapter 2, a threshold condition determines which of these two fixed points is stable. If $R_0 > 1$, then the system settles down in the endemic state. In this case, the equilibrium may be approached via oscillations. Bartlett [20] argued such oscillations are sustained if a stochastic formulation is used, as the random effects prevent the system from settling into the stable endemic equilibrium. Dietz [38] and London & Yorke [72] produced work showing that in the deterministic framework, oscillations can be sustained if the contact rate is allowed to vary seasonally.

Various kinds of heterogeneities have been proposed and their effects on particular models studied. Age structure has been widely studied (Anderson & May [6], Schenzle [94]). This is intended to reflect situations where individuals of a particular age may be in contact with each other more frequently than those of differing age, during particular time periods. One of the most obvious examples is when children spend the duration of a working week in school together, which would cause an increase in the probability of disease transmission between individuals within these age classes. This setup can account for heterogeneity in mixing preferences and hence contact. Age structured models can reproduce the observed disease incidences fairly well and also lead to more realistic estimates of an average age individuals acquire infection (see Schenzle [94]).

It has been suggested that spatial heterogeneity may address many of the deficiencies of epidemic models. Spatial heterogeneity can be represented using a subpopulation framework, where the total population is divided into n subpopulations and we allow infective individuals in one population to infect susceptible individuals in another. The equilibrium behaviour of such models has been studied widely (Hethcote [51], Hethcote & Van Ark [53], Lajmanovich & Yorke [68], Nold [90]), particularly with regard to the effects of spatial heterogeneity on the design of immunization programs (Anderson & May [6]). Simulation studies have been presented (Murray & Cliff [83]), and it has been shown that spatial heterogeneity can reduce the occurrence of successful infections in epidemic models (Grenfell et al. [47]). Some attention has been directed towards understanding the dynamics of spatial models (Schwartz [96]). If spatial effects are important for the persistence of the disease it is crucial to examine the differences between each subpopulation of the types of models in question.

Some have added an immigration term to spatial SIR models, where infective individuals enter the system at a constant rate (Engbert & Drepper [41], Olsen et al. [91]). This clearly allows persistence of the disease because if it dies out in one region then the arrival of an infective from elsewhere can trigger another epidemic. Indeed, the arrival of new infectives has been demonstrated as being important in the outbreak of measles in particular. A constant immigration term has a mildly

stabilizing effect on the dynamics, and tends to increase the minimum number of infective individuals in the models (Bolker & Grenfell [25]).

How endemic disease persistence depends on the degree of spatial heterogeneity is not intuitively straightforward although useful insights have been gained within the context of diseases with strong oscillatory dynamics such as HIV, measles and influenza [8],[25],[43],[45]. More efforts are needed to obtain a better understanding of how spatial heterogeneity affects persistence across a variety of population-dynamical systems.

Lloyd-Smith et al. [71] analyzed the influence of individual variation in infectiousness on disease emergence. For directly transmitted infections, however, the number of others infected during the infectious period of a single infective arises from a complex mixture of host, pathogen and environmental factors. Consequently, the degree of infectiousness can be modelled as distributed continuously in any population (Diekmann & Heesterbeek [37], Koopman [64]). This differs to the conventional approach of adding heterogeneity to epidemic models, in which populations are divided into homogeneous subgroups (Anderson & May [7], Diekmann [37]). Research on continuous individual variation in infectiousness for directly transmitted infections has been largely restricted to within-household transmission (Bailey [14], Becker [22]), or to variation in infectious period (Keeling [61], Lloyd [70]) or social network (Meyers [79]).

Recently there has been a move to complicated network models for simulating epidemics (Andersson & Britton [3], Bansal et al. [19], Ferguson et al. [44], Gani et al. [45], Longini et al. [73]). These assume knowledge of the mixing patterns of groups of members of the population and make predictions based on simulations of a stochastic model. While network models can give very detailed predictions, they have disadvantages. For a complex network model, simulations take long enough to make it difficult to examine a significant range of parameter values, and it is difficult to estimate the sensitivity with respect to parameters of the model. If for example, the purpose is to compare various strategies in the event of an outbreak of a new strain of disease, this is a serious drawback, and simple compartmental models may actually be more useful predictors.

So model choice for heterogeneity is fraught with peril. The analysis of any temporal disease data in practice is invariably complicated by lack of complete data. Often the infection process is unobserved, so that data will at best consist of times at which infectious individuals are detected, usually via observable syptoms. When using stochastic models to describe an epidemic, this can lead to intractible expressions for all but the most trivial of models. One way to overcome this is to adopt simplifying assumptions although it may be fair to doubt the conclusions rendered from such assumptions.

It is not just the patterns of mixing between hosts, affected by spatial heterogeneity, that are important to epidemic modelling but also the transmission characteristics of the infectious disease. Transmission is a key process in the spread of disease. In most models, transmission is assumed to occur via so called **density-dependent** transmission: if the number of susceptible individuals is represented as S, and that of infected individuals as I, the number of new infected individuals per unit area, per unit of time is βSI, where β represents a transition rate, or infection 'pressure'. This model assumes that infected and susceptible individuals mix completely with each other and move randomly within an area of fixed size.

3.2 The transmission term

In 1995, De Jong et al. [35] published a paper that has been widely interpreted as claiming βSI did not represent this so-called 'true mass action', and was rather a model of 'pseudo mass action'. It was claimed transmission following 'true mass action' should be represented by $(\beta SI)/P$ where P is the total population size, which may vary in time. Since then, models have appeared that use either form of transmission and terminology has become confused.

De Jong et al. pointed out that βSI only represents 'true mass action' if S and I represent densities of individuals (numbers per unit area). In this situation, the number of random encounters between a susceptible and infective per unit time will be proportional to the density of infected individuals I. However, if S and I represent actual numbers, and if the total densities remain constant as numbers of both classes of individual change, the total number of encounters a randomly moving susceptible has with other individuals will not change. The probability that the susceptible becomes infected will depend on the proportion I/P of those encounters that are with infected individuals. Thus the transmission rate in this situation will be $(\beta SI)/P$.

If S and I represent densities rather than numbers βSI does represent 'true mass action'. However $(\beta SI)/P$ might still give a better representation of the rate of infection transmission. For a directly transmitted infection, the rate at which new infections occur in a population is the product of three things - the contact rate, proportion of those contacts that occur with susceptibles and proportion of such contacts that result in infection. The assumption underlying 'true mass action' is that the contact rate is directly proportional to density. Assuming that susceptible and infected hosts are randomly mixed, this would lead to transmission following $(\beta SI)/P$: on average, each susceptible S would make the same number of contacts regardless of host density, and a proportion I/P of these would be with infectives. This mode of transmission became known in modern literature as **frequency-dependent** transmission.

It is clear the transmission rate in this case depends on P, which reflects the fact that, whereas for constant density and increasing population size the number of individuals encountered per individual does not change, the probability of encountering any particular individual decreases. This transmission term can be derived using a direct argument in terms of numbers: as a fraction I/P of all encounters is with infectious individuals and there is a constant number of effective encounters per unit time per susceptible β, the total number of infections per unit of time for S susceptible individuals is $(\beta SI)/P$.

3.3 Stochastic multi-group SIS model

We now extend much of the theory for the one-dimensional SIS model to a k-dimensional SIS model. We now have a scenario whereby there are multiple distinct populations which not only have interactions occuring within-group but can interact with the other groups as well. The model we consider is a k-group (Multi-type) SIS model where each group consists of a fixed population of individuals, each with a particular number of infectives to begin with. Let there be k populations, which we shall refer to as groups $1, \ldots, k$, where N_1 individuals exist in group 1 of whom m_1 are initially infectives and N_2 individuals exist in group 2 of whom m_2 are initially infectives and so on. The combined total population $N = N_1 + \cdots + N_k$. The infectious periods of different infectives are independent and identically distributed according to a random variable I (the same for each group). We define infection rate as $\frac{\beta}{N}\lambda_s \pi_{sr} \mu_r$, in accordance with Becker and Marschner [24], Yates et al. [106] where β represents an overall force of infection, λ_s is the infectivity of any individual in group s, μ_r is the susceptibility of any individual in group r and π_{sr} is a mixing parameter represented by the matrix $\pi_{sr} = \begin{bmatrix} \pi_{11} & \cdots & \pi_{1k} \\ \vdots & \ddots & \vdots \\ \pi_{k1} & \cdots & \pi_{kk} \end{bmatrix}$.

During its infective period, an individual from group s makes contact with each individual from group r at a rate $\frac{\beta}{N}\lambda_s \pi_{sr} \mu_r$ where $N = N_1 + \cdots + N_k$. If the contacted individual is susceptible then it becomes infected and is immediately able to infect others. After the infectious period, the individual recovers and becomes susceptible to re-infection. This can be represented by the infection rate matrix

$$B_{sr} = \beta \begin{bmatrix} \lambda_1 \pi_{11} \mu_1 & \cdots & \lambda_1 \pi_{1k} \mu_k \\ \vdots & \vdots & \vdots \\ \lambda_k \pi_{k1} \mu_1 & \cdots & \lambda_k \pi_{kk} \mu_k \end{bmatrix}$$

where each entry in the matrix denotes the infection rate acting upon a group r susceptible from a group s infective.

If infection periods are exponentially distributed, $I \sim exp(\gamma)$, then this is a k-dimensional Markovian model. The Markov chain $(I_1(t), I_2(t), \ldots, I_k(t))$ describing the number of infected individuals at time t, takes values in the state space $S = \{0, 1, \ldots, N_1\} \times \{0, 1, \ldots, N_2\} \times \cdots \times \{0, 1, \ldots, N_k\}$. There are two types of transition - infection and removal. The transition rates are denoted by

$$(I_1, \ldots, I_k) \to (I_1, \ldots, I_r + 1, \ldots, I_k) \quad \text{with rate} \quad \frac{\beta}{N} \sum_{s=1}^{k} \lambda_s \pi_{sr} \mu_r I_s (N_r - I_r)$$

$$(I_1, \ldots, I_k) \to (I_1, \ldots, I_r - 1, \ldots, I_k) \quad \text{with rate} \quad \gamma I_r$$

corresponding to an infection in group r and a recovery in group r respectively where $r = 1, \ldots, k$. We also impose that $\sum_{r=1}^{k} \pi_{sr} = 1$ for each s and $\sum_r \lambda_r f_r = \sum_s \mu_s f_s = 1$ (in accordance with Becker & Marschner [24]) where we denote f_r as the relative frequency of group r ($f_r = N_r/(N_1 + \cdots + N_k)$) and so $\sum_r f_r = 1$ automatically. This simply imposes restrictions on the arbitrariness in the choice of scale of the λ's and μ's conveniently. Deterministic differential equations can be derived from the transition rates of this stochastic model by including $f_1 = N_1/N, f_2 = N_2/N$ as will be seen in section 3.6.

Let us denote $\mathbf{i} = (i_1, i_2, \ldots, i_k)$ and denote by $\mathbf{e}_j$ the vector with 1 in the j'th position and 0 elsewhere, so that $\mathbf{i} - \mathbf{e}_j = (i_1, i_2, \ldots, i_j - 1, \ldots, i_k)$ and $\mathbf{i} + \mathbf{e}_j = (i_1, i_2, \ldots, i_j + 1, \ldots, i_k)$. The Kolmogorov Forward equations for the state probabilities $p_{\mathbf{i}}(t)$ can be used to derive the differential equations for the conditional state probabilities $q_{\mathbf{i}}(t)$:

$$\begin{aligned}\frac{dp_{\mathbf{i}}}{dt} = \beta \sum_{r=1}^{k} \sum_{s \neq r} \lambda_s \pi_{sr} \mu_r i_s (N_r - i_r + 1) p_{(\mathbf{i}-\mathbf{e}_r)}(t) + \sum_{r=1}^{k} \gamma (i_r + 1) p_{(\mathbf{i}+\mathbf{e}_r)}(t) \\ + \beta \sum_{r=1}^{k} \lambda_r \pi_{rr} \mu_r (i_r - 1)(N_r - i_r + 1) p_{(\mathbf{i}-\mathbf{e}_r)}(t) \\ - p_{\mathbf{i}}(t) \left(\beta \sum_{r=1}^{k} \sum_{s=1}^{k} \lambda_s \pi_{sr} \mu_r i_s (N_r - i_r) + \sum_{r=1}^{k} \gamma i_r \right)\end{aligned}$$

for $\mathbf{i} \in S$ with boundary conditions $p_{\mathbf{i}}(t) = 0$ for $\mathbf{i} \notin S$ and $\sum p_{\mathbf{i}} = 1$.

Quasi-stationarity is defined by conditioning on non-extinction. The state probabilities conditioned on not being absorbed are denoted $q_{\mathbf{i}}(t)$. They can be determined from the unconditional probabilities $p_{\mathbf{i}}(t)$ via the relation

$$q_{\mathbf{i}}(t) = P((I_1(t), \ldots, I_k(t)) = (I_1, \ldots, I_k) \mid (I_1(t), \ldots, I_k(t) \neq (0, \ldots, 0)) = \frac{p_{\mathbf{i}}(t)}{1 - p_{\mathbf{0}}(t)}. \tag{3.1}$$

The state probabilities conditioned on not being absorbed can be calculated from the unconditioned probabilities $p_{\mathbf{i}}(t)$ via the relation (3.1). Differentiating (3.1) and using the equation $\dot{p}_{\mathbf{0}}(t) = \gamma \sum_{r=1}^{k} p_{\mathbf{e}_r}(t)$ which is obtained by setting $\mathbf{i} = \mathbf{0}$ in the Kolmogorov forward equations for the state probabilities $p_{\mathbf{i}}(t)$ gives

$$\dot{q}_{\mathbf{i}}(t) = \frac{\dot{p}_{\mathbf{i}}(t)}{1 - p_{\mathbf{0}}(t)} + \gamma \left(\sum_{r=1}^{k} q_{\mathbf{e}_r}(t) \right) \frac{p_{\mathbf{i}}(t)}{1 - p_{\mathbf{0}}(t)}. \tag{3.2}$$

$$= \frac{(\sum_{r=1}^{k} \sum_{s \neq r} \lambda_s \pi_{sr} \mu_r i_s + \sum_{r=1}^{k} \lambda_r \pi_{rr} \mu_r (i_r - 1)) \beta (N_r - i_r + 1) p_{(\mathbf{i}-\mathbf{e}_r)}(t) + \sum_{r=1}^{k} \gamma (i_r + 1) p_{(\mathbf{i}+\mathbf{e}_r)}(t)}{1 - p_{\mathbf{0}}(t)}$$

$$- \frac{(\beta \sum_{r=1}^{k} \sum_{s=1}^{k} \lambda_s \pi_{sr} \mu_r i_s (N_r - i_r) + \sum_{r=1}^{k} \gamma i_r) p_{\mathbf{i}}(t)}{(1 - p_{\mathbf{0}}(t))} + \left(\frac{p_i(t)}{1 - p_{\mathbf{0}}(t)} \right) \left(\frac{\sum_{r=1}^{k} \gamma p_{\mathbf{e}_r}(t)}{1 - p_{\mathbf{0}}(t)} \right)$$

Therefore

$$\frac{dq_i}{dt} = \left(\sum_{r=1}^{k} \sum_{s \neq r} \lambda_s \pi_{sr} \mu_r i_s + \sum_{r=1}^{k} \lambda_r \pi_{rr} \mu_r (i_r - 1) \right) \beta (N_r - i_r + 1) q_{(\mathbf{i}-\mathbf{e}_r)}(t) + \sum_{r=1}^{k} \gamma (i_r + 1) q_{(\mathbf{i}+\mathbf{e}_r)}(t)$$

$$- \left(\beta \sum_{r=1}^{k} \sum_{s=1}^{k} \lambda_s \pi_{sr} \mu_r i_s (N_r - i_r) + \sum_{r=1}^{k} \gamma i_r \right) q_{\mathbf{i}}(t) + q_{\mathbf{i}}(t) \gamma \sum_{r=1}^{k} q_{\mathbf{e}_r}(t).$$

Setting $\frac{d\mathbf{q}}{dt} = 0$ and rearranging we can write the above as

$$\mathbf{q} Q^C = -\gamma \mathbf{q}(t) \sum_{r=1}^{k} q_{\mathbf{e}_r}(t) \tag{3.3}$$

where Q^C is the truncated matrix as in equation (2.5) and the quasi-stationary distribution is found as the left leading eigenvector of the matrix on the left hand side of equation (3.3).

3.4 Time to extinction

The time to disease extinction, τ, is a random variable whose distribution is dependent on the distribution of the initial state. If the process has continued for a long period of time and is not extinct, then the quasi-stationary distribution is used as an approximation of the distribution of states (Nåsell, [85]). We can determine the distribution of time to extinction, τ of a k-group model from the probability $p_{\mathbf{0}}(t)$, where $\mathbf{0}$ is a k-length zero vector, since the event $\{\tau \leq t\}$ is equal to the event $\{I_1(t) = I_2(t) = \cdots = I_k(t) = 0\}$. Therefore $P(\tau \leq t) = P((I_1(t), I_2(t), \ldots, I_k(t)) = (0, 0, \ldots, 0)) = p_{\mathbf{0}}(t)$. Assuming the initial distribution equals the quasi-stationary distribution, ie. $p_{\mathbf{i}}(0) = q_{\mathbf{i}}$ for $\mathbf{i} \in S, \mathbf{i} \neq \mathbf{0}$ and $p_{\mathbf{0}}(0) = 0$, we can determine the distribution of the time to extinction as

follows.

Using equation (3.2) and setting $\frac{dq_{\mathbf{i}}}{dt} = 0$ we have

$$\dot{p}_{\mathbf{i}}(t) = -\gamma \left(\sum_{r=1}^{k} q_{\mathbf{e}_r} \right) p_{\mathbf{i}}(t) \qquad \mathbf{i} \in S, \mathbf{i} \neq 0.$$

With an initial condition of $p_{\mathbf{i}}(0) = q_{\mathbf{i}}$, we can solve this differential equation to give

$$p_{\mathbf{i}}(t) = q_{\mathbf{i}} exp \left(-\gamma \left(\sum_{r=1}^{k} q_{\mathbf{e}_r} \right) t \right) \qquad \mathbf{i} \in S, \mathbf{i} \neq 0.$$

We can now solve $\dot{p}_{\mathbf{0}}(t) = \gamma(\sum_{r=1}^{k} p_{\mathbf{e}_r}(t))$, since $p_{\mathbf{e}_r}(t) = q_{\mathbf{e}_r} exp(-\gamma(\sum_{r=1}^{k} q_{\mathbf{e}_r})t)$, so we have that

$$\dot{p}_{\mathbf{0}}(t) = \left(\gamma \left(\sum_{r=1}^{k} q_{\mathbf{e}_r} \right) \right) exp \left(-\gamma \left(\sum_{r=1}^{k} q_{\mathbf{e}_r} \right) t \right).$$

Using initial value $p_{\mathbf{0}}(0) = 0$ implies

$$p_{\mathbf{0}} = 1 - exp \left(-\gamma \left(\sum_{r=1}^{k} q_{\mathbf{e}_r} \right) t \right).$$

This tells us that the time to extinction from the point when the system is in quasi-stationarity, τ_Q, has an exponential distribution with mean $\frac{1}{\gamma(\sum_{r=1}^{k} q_{\mathbf{e}_r})}$.

For a single group model, the quasi-stationary distribution would be a single vector $(q_1, \ldots, q_k)$ and so τ_Q would be exponentially distributed with mean $\frac{1}{\gamma q_1}$.

There is no time-dependence in the above equations; that is, in quasi-stationarity, the hazard rate for extinction remains constant. So the quasi-stationary probabilities $q_{\mathbf{e}_r}$ determine the mean time to extinction (from quasi-stationarity). If $\sum_{r=1}^{k} q_{\mathbf{e}_r}$ is big, the process will go extinct quickly. Consequently, if $\sum_{r=1}^{k} q_{\mathbf{e}_r}$ is big, then the quasi-stationary distribution isn't of much interest in practice; the process is likely to go extinct before it ever settles to quasi-stationarity. If $\sum_{r=1}^{k} q_{\mathbf{e}_r}$ is of moderate size, the process will settle to quasi-equilibrium in the medium term, then go extinct according to an exponential distribution of mean above. If $\sum_{r=1}^{k} q_{\mathbf{e}_r}$ is small, the process will settle to quasi-equilibrium in the long-term, and although extinction is sure to happen eventually, it may not occur for a very long time indeed.

3.5 Multi-type branching process and extinction

Many of the branching process approximation results of chapter 2 can be extended to the situation where we consider more than one population. Let T be the set of all k-dimensional vectors whose components are non-negative integers. A **Multitype branching process** is a temporally homogeneous vector-valued Markov process $\mathbf{Z}_0, \mathbf{Z}_1, \mathbf{Z}_2 \ldots$ whose states are vectors in T (see eg. [56], [80]). We assume $\mathbf{Z}_0$ is nonrandom. Write Z_n^i = the number of objects of type i in the n'th generation. If $\mathbf{Z}_0 = \mathbf{e}_i = (0, \ldots, 0, 1, 0, \ldots, 0)$ where the 1 occurs at the i'th component then the law for this process is as follows; the generating function of $\mathbf{Z}_1$ is

$$\phi^i(s_1, \ldots, s_k) = \sum_{r_1, \ldots, r_k = 0}^{\infty} p^i(r_1, \ldots, r_k) s_1^{r_1} \ldots s_k^{r_k} \quad | s_1 |, \ldots, | s_k | \leq 1 \qquad (3.4)$$

where $p^i(r_1, \ldots, r_k)$ is the probability an infective from group i makes r_1 contacts of type 1,..., r_k contacts of type k.

In general, if $\mathbf{Z}_n = (r_1, \ldots, r_k) \in T$, then $\mathbf{Z}_{n+1}$ is the sum of $r_1 + \cdots + r_k$ independent random vectors, r_1 having generating function ϕ^1, r_2 having generating function ϕ^2, ..., r_k having generating function ϕ^k. The generating function of $\mathbf{Z}_n$ has components denoted by $\phi_n^i(s_1, \ldots, s_k) = \phi_n^i(\mathbf{s}), n = 0, 1, \ldots, i = 1, \ldots, k$. Then ϕ_1^i is the function ϕ^i of (3.4).

The generating functions are functional iterates, defined by the relations

$$\begin{cases} \phi_{n+1}^i(\mathbf{s}) & = \phi^i[\phi_n^1(\mathbf{s}), \ldots, \phi_n^k(\mathbf{s})], \\ \phi_0^i(\mathbf{s}) & = s_i. \end{cases}$$

The progeny matrix, or **next-generation mean matrix**, is the matrix of expected number of progeny of all types of parent objects. In terms of our application this translates as the mean number of contacts.

$$M = \begin{bmatrix} m_{11} & \ldots & m_{1k} \\ m_{21} & \ldots & m_{2k} \\ \vdots & & \vdots \\ m_{k1} & \ldots & m_{kk} \end{bmatrix}, \quad \text{with} \quad M_{ij} = \mathbb{E}[Z_1^j \mid Z_0 = \mathbf{e}_i] = \frac{\partial \phi^i(1, \ldots, 1)}{\partial s_j}.$$

So $\mathbb{E}[\mathbf{Z}_{n+1} \mid \mathbf{Z}_n] = \mathbf{Z}_n \mathbf{M}$ or generally $\mathbb{E}[\mathbf{Z}_{n+N} \mid \mathbf{Z}_N] = \mathbf{Z}_N \mathbf{M}^n$.

More specifically, each entry of the mean offspring matrix is interpreted as the mean number of secondary infectious type j individuals that a single infectious type i individual infects in an otherwise disease-free population during its infectious period. Processes with several types are more complex than single branching processes because besides the branching pattern they contain another Markovian structure of movement between different states, the types. One extreme, pure branching is obtained if $r = 1$, the other extreme, a Markov Chain with r states and no branching if $\phi^i(\mathbf{s}) = \Sigma_{j=1}^k p_{ij} s_j \quad 1 \leq i \leq r$ for some numbers p_{ij}. Thus issues like classes of states and periodicity reappear here. It is common to avoid these difficulties by

assuming the process **positively regular**, which is what we shall do in terms of our application : A multitype branching process is positively regular if there is an $n \in N$ such that all entries in M^n are strictly positive. All states, except zero in a positively regular branching process are transient, ie. the probability of returning to the same state is less than 1; $P(\mathbf{Z}_n = \mathbf{z}$ for some n=1,2,... $\mid \mathbf{Z}_0 = \mathbf{z}) < 1$.

The maximal eigenvalue of M plays a similar role to the mean of the offspring distribution for regular branching processes in determining whether extinction occurs. For general multi-type epidemic models R_0 is defined as the largest eigenvalue of the mean offspring matrix, see e.g. Pg 51-61 in [37]. Let q^i = extinction probability if initially there is 1 object of type i, $i = 1, \ldots, k$.

$$q^i = P(\mathbf{Z}_n = 0 \text{ for some } n \mid \mathbf{Z}_0 = \mathbf{e}_i) \quad \mathbf{q} = (q^1, q^2, \ldots, q^k)$$

Then

$$\begin{cases} R_0 \leq 1 & \Rightarrow \quad \mathbf{q} = \mathbf{1}, \\ R_0 > 1 & \Rightarrow \quad 0 \leq \mathbf{q} < 1, \end{cases}$$
$$\text{and } \mathbf{q} = \phi(\mathbf{q}). \tag{3.5}$$

If $\mathbf{x}$ is any vector in the unit cube other than $\mathbf{1}$, then $lim_{n\to\infty}\phi_n(\mathbf{x}) = \mathbf{q}$ [63]. This ensures we can obtain a solution using successive approximations, using *any* initial vector in the unit cube other than $\mathbf{1}$. This implies that the only solutions of (3.5) in the unit cube are $\mathbf{q}$ and $\mathbf{1}$.

An individual in group i 'makes contacts' to group j at rate $\beta_{ij} = \frac{\beta}{N}\lambda_i\pi_{ij}\mu_j$ as a Poisson process. Given that the individual has infectious period I, then $(G_{ij} \mid I) \sim Pois(\frac{\beta}{N}\lambda_i\pi_{ij}\mu_j f_j I)$ where G_{ij} is the number of group j contacts emanating from a group i individual, λ_i is the group i infectivity, μ_j is the group j susceptibility, π_{ij} the mixing preference and f_j is a relative frequency of group j. So group i infects group j at rate $(\frac{\lambda_i\pi_{ij}\mu_j}{N})I_iS_j$ where we have assumed for our branching process approximation that $S_j = N_j$. Using a branching process approximation for our SIS infection model, we can write the next generation mean matrix as

$$M_{ij} = \beta\mathbb{E}[I]\begin{bmatrix} \lambda_1\pi_{11}\mu_1 f_1 & \ldots & \lambda_1\pi_{1k}\mu_k f_k \\ \vdots & \ddots & \vdots \\ \lambda_k\pi_{k1}\mu_1 f_1 & \ldots & \lambda_k\pi_{kk}\mu_k f_k \end{bmatrix}$$

where $f_j = N_j/N$ represents the relative frequency of group j, namely the proportion of individuals in group j against the overall population of all groups. If we now examine the branching process approximation where $\pi_{sr} = \frac{1}{k}$, the next-generation offspring mean matrix M is given by

$$M = \frac{\beta}{k\gamma}\lambda\mu^T diag(\mathbf{f})$$

Finding eigenvalues of this matrix,

$$M\boldsymbol{\lambda} = \frac{\beta}{k\gamma}\boldsymbol{\lambda}\boldsymbol{\mu}^T diag(\mathbf{f})\boldsymbol{\lambda} = \frac{\beta}{k\gamma}\boldsymbol{\lambda}(\boldsymbol{\mu}^T diag(\mathbf{f})\boldsymbol{\lambda})$$

where $\boldsymbol{\mu}^T diag(\mathbf{f})\boldsymbol{\lambda}$ is scalar. So $\boldsymbol{\lambda}$ is an eigenvector with eigenvalue $\frac{\beta}{k\gamma}(\boldsymbol{\mu}^T diag(\mathbf{f})\boldsymbol{\lambda})$. If we construct an orthogonal basis $\{\boldsymbol{\lambda}, \mathbf{w}_2, \ldots, \mathbf{w}_k\}$ of $\mathbb{R}^k$, then for each $i = 2, \ldots, k$

$$\mathbf{w}_i^T M = \frac{\beta}{k\gamma}\mathbf{w}_i^T\boldsymbol{\lambda}\boldsymbol{\mu}^T diag(\mathbf{f}) = \mathbf{0}$$

due to $\mathbf{w}_i^T\boldsymbol{\lambda} = 0$. Therefore, the matrix M has $(k-1)$ eigenvectors each with eigenvalue 0. With R_0 being the maximum eigenvalue, it is clear that

$$R_0 = \frac{\beta}{k\gamma}(\boldsymbol{\mu}^T diag(\mathbf{f})\boldsymbol{\lambda}) = \frac{\beta}{k\gamma}(\lambda_1\mu_1 f_1 + \cdots + \lambda_k\mu_k f_k).$$

For a 2-group process, we have $\phi_1(\mathbf{s}) = \mathbb{E}[s_1^{G_{11}}s_2^{G_{12}}]$ and $\phi_2(\mathbf{s}) = \mathbb{E}[s_1^{G_{21}}s_2^{G_{22}}]$. Note that

$$\mathbb{E}[s_1^{G_{11}}s_2^{G_{12}} \mid I] = \mathbb{E}[s_1^{G_{11}} \mid I]\mathbb{E}[s_2^{G_{12}} \mid I]$$

by independence of G_{11} and G_{12} conditional upon I. So, as before

$$\mathbb{E}[s_1^{G_{11}} \mid I] = e^{\beta_{11}I(s_1-1)}.$$

In a similar fashion $\mathbb{E}[s_2^{G_{12}} \mid I] = e^{\beta_{12}I(s_2-1)}$ since here we are looking at infection crossing from group 1 to group 2 as opposed to just infections occuring within group 1. Hence

$$\phi_1(\mathbf{s}) = \mathbb{E}[s_1^{G_{11}}s_2^{G_{12}} \mid I] = e^{\beta_{11}I(s_1-1)}.e^{\beta_{12}I(s_2-1)} = e^{-I(\beta_{11}(1-s_1)+\beta_{12}(1-s_2))}$$

Similarly, $\phi_2(\mathbf{s}) = \mathbb{E}[e^{-I(\beta_{21}(1-s_1)+\beta_{22}(1-s_2))}]$. If we assume each group has the same infectious period given by the exponential distribution $I \sim exp(\gamma)$ it follows that

$$\phi_1(\mathbf{s}) = \mathbb{E}\left[e^{-I(\beta_{11}(1-s_1)+\beta_{12}(1-s_2))}\right] = \frac{\gamma}{\gamma+\beta_{11}(1-s_1)+\beta_{12}(1-s_2)}.$$

Further details on exponential generating functions in epidemics can be seen in [16]. In terms of our vector equation for the extinction probability $\mathbf{q} = \phi(\mathbf{q})$ we have

$$q_1 = \frac{\gamma}{\gamma+\beta_{11}(1-q_1)+\beta_{12}(1-q_2)} \quad \text{and} \quad q_2 = \frac{\gamma}{\gamma+\beta_{21}(1-q_1)+\beta_{22}(1-q_2)}.$$

This yields

$$[\gamma + \beta_{11}(1-q_1) + \beta_{12}(1-q_2)]q_1 = \gamma \Rightarrow -\beta_{11}q_1^2 - \beta_{12}q_1q_2 + (\gamma + \beta_{11} + \beta_{12})q_1 = \gamma$$

and similarly for the second equation, giving rise to two 2-d quadratics:

$$\begin{cases} -\beta_{11}q_1^2 - \beta_{12}q_1q_2 + (\gamma + \beta_{11} + \beta_{12})q_1 - \gamma &= 0, \\ -\beta_{22}q_2^2 - \beta_{21}q_1q_2 + (\gamma + \beta_{21} + \beta_{22})q_2 - \gamma &= 0. \end{cases}$$

These equations can be solved for various forms of λ, μ for q_1, q_2 using Maple. Solving for these extinction probabilities will be necessary in calculating the emergence probability as will be seen in the following chapter.

We could simplify the model significantly by assuming a symmetry exists, ie. the within-group infection rates are equal to one another as are cross-group infection rates thus the infection rate matrix would be given by

$$\beta_{ij} = \begin{bmatrix} \beta & \lambda \\ \lambda & \beta \end{bmatrix}$$

If this were the case our extinction probability calculations would simplify further. In terms of our vector equation for the extinction probability $\mathbf{q} = \phi(\mathbf{q})$ we have

$$q_1 = \frac{\gamma}{\gamma + (\beta + \lambda) - \beta q_1 - \lambda q_2} \quad \text{and} \quad q_2 = \frac{\gamma}{\gamma + (\beta + \lambda) - \lambda q_1 - \beta q_2}$$

By symmetry, $q_1 = q_2$, so

$$q = \frac{\gamma}{\gamma + (\beta + \lambda) - (\beta + \lambda)q} \quad \Rightarrow \quad (q-1)(-(\beta + \lambda)q + \gamma) = 0.$$

So $q = 1$ or $q = \frac{\gamma}{\beta + \lambda}$ which means $q = \min\{1, \frac{\gamma}{\beta+\lambda}\} = \min\{1, \frac{1}{R_0}\}$. If R_0 were for example fixed, then the extinction probability for both the 1-group SIS model and this 2-group symmetric SIS model would be the same.

If we were to instead assume a constant infectious period I for this symmetric model as opposed to an exponential, there is no need to integrate the function over time and so $\mathbb{E}[s_1^{G_{21}} s_2^{G_{22}} \mid I] = e^{I(\lambda(s_1-1)+\beta(s_2-1))}$. So using $\mathbf{q} = \phi(\mathbf{q})$ and maintaining the assumption of symmetry ($q_1 = q_2$) we have

$$\begin{aligned} q &= e^{I(\beta(q-1)+\lambda(q-1))} \\ &= e^{R_0(q-1)} \end{aligned}$$

Note that $R_0 = \frac{\gamma}{\beta+\lambda}$ is still given by the eigenvalue of maximum real part, as before.

Of course, in the more general setting where this symmetry isn't assumed, for a constant infectious period I, the extinction probabilities would be given by the solution to the simultaneous equations

$$\begin{cases} q_1 = e^{I(\beta_{11}(q_1-1)+\beta_{12}(q_2-1))}, \\ q_2 = e^{I(\beta_{21}(q_1-1)+\beta_{22}(q_2-1))}. \end{cases}$$

3.6 Deterministic representation

The system of differential equations which describe the deterministic version of the general k-group SIS model defined in section 3.2 is

$$\frac{dI_r}{dt} = \frac{\beta}{N}\mu_r \left(\sum_{s=1}^{k} \lambda_s \pi_{sr} (N_r - I_r) I_s \right) - \gamma I_r \qquad r = 1, \ldots, k. \tag{3.6}$$

In this setup, I_r represents the actual number of infectives in group r, $r = 1, \ldots, k$. N_r are the total number of individuals in group r and $N = N_1 + \cdots + N_k$ is total population size. If we are to view this model in terms of densities, we set $x_r = I_r/N_r$ where x_r represents the proportion of infectives in group r. As $N \to \infty$, the process describing the density of infectives in each population $\left\{ \left(\frac{I_1}{N_1}, \ldots, \frac{I_k}{N_k} \right) ; t \geq 0 \right\}$ can be approximated by the deterministic model described by the following differential equations

$$\frac{dx_r}{dt} = \beta \mu_r (1 - x_r) \sum_{s=1}^{k} \lambda_s \pi_{sr} f_s x_s - \gamma x_r \tag{3.7}$$

for $r = 1, 2, \ldots, k$ where f_s represents the relative frequency of group s. In Chapter 5 we will investigate feasibility and stability of equilibria of this system, as well as using this representation to look at the effect varying individual parameters has on the system.

Chapter 4

Probability of emergence

4.1 Introduction

The emergence of a disease combines two elements: the introduction of the pathogen in a certain population and its subsequent spread within it. Mathematical models have been used to show that, given an introduction, an epidemic spreads more rapidly if there are heterogeneities in contact between individuals than in a homogeneous population with the same mean contact rate (Hethcote & Van Ark [53], May & Anderson [6]). Heterogeneities in epidemiological parameters can affect the probability that a pathogen can establish itself in a new population. Generally, for a given R_0, increasing heterogeneity leads to a decrease in the probability of emergence (Galvani & May [46], Lloyd-Smith et al. [71], Xiao et al. [104]). The intuitive reason for this effect is an increase in extinctions of the pathogen owing to stochastic effects in the early stages of the epidemic.

To model heterogeneity, we assume that the probability of infection occuring in a given encounter is proportional to the infectivity of the infected individual and susceptibility of the recipient. This assumption is known as proportionate mixing (Hethcote & Van Ark [53]). Host types may also mix with different preferences for one another, and so the number of potentially infective encounters between two types is determined by the frequency of each in the population and the mixing preference of the infectious and susceptible individuals.

From section 3.5, the next generation mean matrix of the multitype branching process approximation to our infection model has elements

$$M_{ij} = \beta \mathbb{E}[I] \lambda_i \pi_{ij} \mu_j f_j \quad \text{for } 1 \leq i, j \leq k$$

where λ_i represents the infectivity of an individual in group i, μ_j the susceptibility of an individual in group j, π_{ij} is a mixing parameter, f_j is the relative frequency of group j and β is a force of infection and I the infectious period (see model definition, chapter 3.3). For mathematical convenience we set the constraints

$\sum_{j=1}^{k} \pi_{ij} = 1$ for $i = 1, 2, \ldots, k$. As there is an arbitrariness in the choices of scale of the infectivity and susceptibility parameters λ_i and μ_i we resolve this by imposing the restrictions

$$\sum_{i=1}^{k} \mu_i f_i = 1 \quad , \quad \sum_{i=1}^{k} \lambda_i f_i = 1$$

(in accordance with Becker & Marschner [24]) where f_i denotes a relative frequency, ie. $S_j(t)/N$, the number of susceptibles of type j remaining at time t within the population. Because we are dealing with a large population we can approximate $S_j(t)/N$ by $S_j(0)/N = f_j$ during the early stage of an epidemic. This ensures in his case that when N is large, the f_j's sum to 1. These restrictions are important for the purposes of this thesis as they will also be imposed upon the stochastic model we analyze in the next chapter. In addition to these constraints, for the purposes of the models studied from now on we scale time so that $\mathbb{E}[I] = 1$. This allows us to change the rates of infection in each model by the same factor without altering the model dynamics.

There is some degeneracy in this parameterization, but it allows us to discuss how the conceptually distinct factors interact to determine the probability of emergence. We do not assume any correlation between λ, μ and π. Typically, this correlation is implicit in deterministic models in which the rate of new infections is represented by a term of the form βSI, where β is a single parameter expressing a combination of transmissability and susceptibility and I, S are the numbers of infectives and susceptibles respectively.

Conditional upon the infectious period, the number of secondary cases in type j individuals originating from one infected type i is a Poisson distributed random variable. This can be expressed with the probability generating function $\phi_i(\mathbf{s})$, which specifies the distribution of secondary cases generated by a case of type i in each of the k-host types. Specifically, $\phi_i(\mathbf{0})$ is the extinction probability after one generation, given a starting condition of one infected host of type i.

We have already established (section 3.5) using standard multi-type branching process theory (Harris, [49]), from the assumption of Poisson-distributed secondary cases between hosts of each type, that when a constant infectious period is assumed,

$$\phi_i(\mathbf{s}) = e^{\sum_j \beta_{ij}(s_j - 1)}$$

that the extinction probability after m generations starting with one infected host of type i is $\phi_i^{(m)}(\mathbf{0})$, the i'th component of the m'th iterate of the probability generating function. The ultimate extinction probability, q_i, the limit of $\phi_i^{(m)}(\mathbf{0})$ as $m \to \infty$, is the solution to

$$\phi_i(\mathbf{q}) = q_i \quad \text{for } i = 1, 2, \ldots, k.$$

Following Yates et al. [106] we then calculate the probability of emergence in the population as

$$P(Em) = 1 - P(Extinction) = 1 - \sum_i f_i \mu_i q_i, \tag{4.1}$$

where f_i is the relative frequency of group i and μ_i is the susceptibility of an individual in group i. This formula means that emergence probability is the probability of extinction, given the infected individual is in group i, multiplied by the probability that it is in group i, which is a quantity given by a combination of susceptibility and relative numbers. We can compare $P(Em)$ in a heterogeneous population with the reference case of $P(Em)$ in a homogeneous population with the same value for R_0. In this framework, disease spread can be described with a single-component probability generating function $\hat{\phi}(s) = \mathbb{E}[e^{R_0(s-1)I}]$ and $P(Em) = 1 - q$ where q is the solution to $q = \hat{\phi}(q)$.

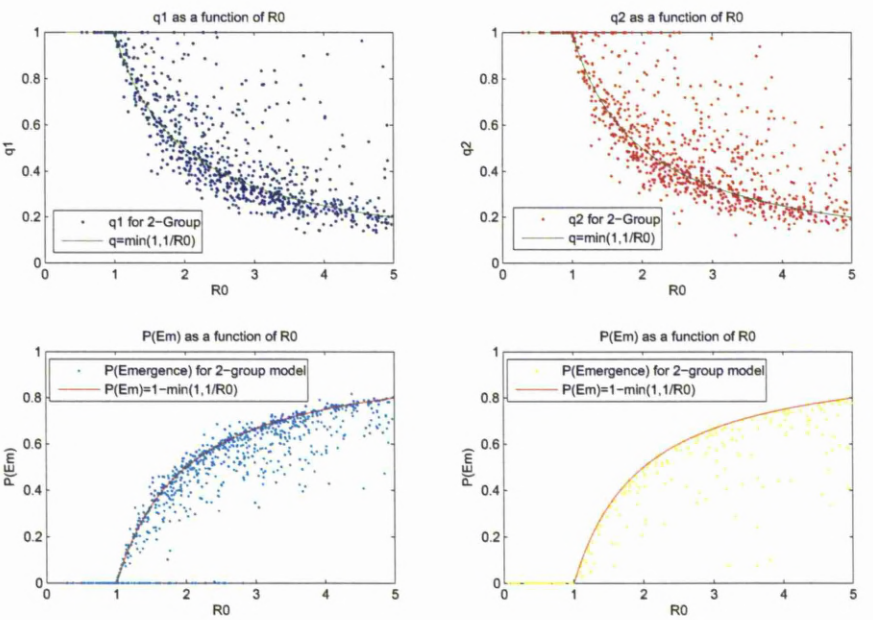

Figure 4.1: Extinction and Emergence probabilities for 2-group models with different starting conditions. Fixed parameters $f_1 = f_2 = 1/2$.

The motivation for this is made clear by the four subplots of Figure (4.1). Xiao et al. [104] start their model with one initial infective in a particular group. The top

two subplots of Figure (4.1) show that for a separable model where $\pi_{ij} = \frac{1}{k} \quad \forall i, j$, when picking λ_i, μ_j arbitrarily at random, with no constraints, leads to having extinction probabilities both above and below the homogeneous curve. The top left hand plot shows extinction probabilities given we start our 2-group model with one infective in group 1, the top right plot similarly for one infective starting in group 2. The bottom left hand plot shows emergence probabilities where λ_i, μ_j are again picked at random and we assign the probability f_j to an individual infective starting in group j. Here we can see under this setup, which is similar to Xiao et al. [104], that the emergence probability can lie both above and below the homogenous curve. However, the bottom right subplot takes the approach of Yates et al. [106], which is what we're interested in. They assign the group the infected individual starts in randomly according to $\mu_i f_i$. Here we see this results in an ordering on emergence probability, even when λ_i, μ_j are still chosen at random and it is this ordering which is of interest.

We begin by looking at a 2-group model as per Yates et al. [106]. We produce numerical results and examine the effects of various heterogeneities under an exponential infectious period and contrast these results with those of Yates et al. [106], who looked at a constant infectious period. Throughout these results our interest is in comparing the heterogeneous model to the reference case of a homogeneous model, in terms of their corresponding emergence probabilities.

Next we produce some analytical results for comparing a homogeneous model with the 2-group heterogeneous model where $\pi_{ij} = \frac{1}{k}$ for all i, j, so that $M_{ij} = \frac{\beta}{k}\lambda_i \mu_j f_j$. This formulation for the model is often referred to as a 'separable model'. We calculate the probability of emergence iteratively for both models and analyse both numerically and algebraically the differences in this probability. We offer a proof which shows that the emergence probability will always be lower for a heterogeneous model than for a homogeneous model not only in the limit but will show this ordering has an n-generational effect. What this proof yields is explicit algebraic expressions for the emergence probability at any stage of iterative convergence. Furthermore, the numerical results will indicate exactly how large this difference is and the magnitude of effect that different types of heterogeneity have. We then adapt a proof by Becker & Marschner [24] which shows something similar to this and extend this result to the general case for a non-separable model.

We set up the following notation in using our branching process approximation. For the homogeneous model let m_n be the probability that, starting from one infective individual at generation 0, the infection persists to generation n. We then define the probability of emergence to be

$$P(Em) = \lim_{n \to \infty} m_n.$$

For the heterogeneous model, let t_n be the probability that infection persists to

generation n, given that generation 0 consists of a single infective individual whose group is assigned at random with probability $\frac{\mu_i f_i}{\sum_j \mu_j f_j} = \mu_i f_i$ of being in group i. Note that $m_n = 1 - \hat{\phi}^n(0)$ and t_n is something similar, $t_n = 1 - \sum_{i=1}^{k} f_i \mu_i \phi_i^{(n)}(\mathbf{0})$.

Finally we examine various forms of majorization which allow us to compare two heterogeneous models to each other, for various forms of heterogeneity, and discuss how certain types of majorization allow us to make inferences on the orderings of emergence probabilities for heterogeneous models. Numerical and analytical results follow.

4.2 Preliminary numerical results

Using the same parameter values as used in Yates et al. [106], we are able to compare the effect of heterogeneity in infectivity, susceptibility and in mixing on the probability of emergence for the 2-group model for varying R_0. One set of results is consequential of assuming a constant infectious period, as Yates et al. [106] did. By contrast we generate results for the same parameter values but assuming an exponential infectious period, and compare. It is important to note that for these results the parameter values were chosen specifically in order to compare with Yates et al. [106]. So the elements of the infection rate matrix β_{ij} are prescribed and fixed. For the purposes of this 2-group model we set $\pi_{11} = \pi_{22} = \pi$ so π_{ij} reduces to a single parameter matrix $\begin{bmatrix} \pi & 1-\pi \\ 1-\pi & \pi \end{bmatrix}$. We define **assortative** mixing to be when $\pi > 0.5$. This represents the fact that each individual in a group is more likely to make contact with an individual from the same group as opposed to one from the other group. This is equivalent to saying an individual 'prefers' within-group contact. Similarly, we define **dissortative** mixing to be when $\pi < 0.5$. This represents the fact that each individual in a group is more likely to make contact with an individual from the other group as opposed to one from its own group. This is equivalent to saying an individual 'prefers' cross-group contact. When $\pi = 1 - \pi = 0.5$, this signifies that contact is just as likely to occur within-group as it is cross-group - that is, a homogeneously mixing scenario.

In all figures we have a population split such that 10% of the total population exist within group 1 and 90% exist within group 2. In every case, the plots generated for q_1, q_2 and $P(Em)$ are all compared to the homogeneous case. One reason for parameter choices is to investigate the effect of so-called '*superspreaders*'. By having a low frequency of highly infectious individuals in group one interacting with a high frequency of relatively low infectious individuals in group two we can model the degree by which this affects emergence probabilities. The MATLAB code (for details on software see [92]) used to generate the following numerical results can be seen in Appendix A.

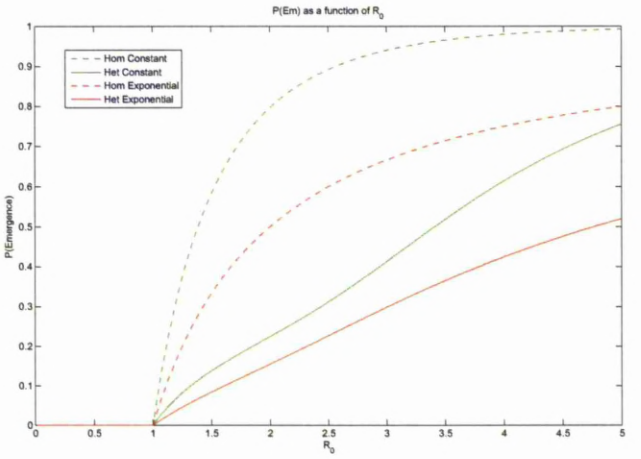

Figure 4.2: Emergence probability for homogeneous and heterogeneous 2-group models where heterogeneity exists in infectivity for both constant and exponential infectious periods. Parameters: $\lambda_1 = 200/29, \lambda_2 = 10/29, \mu_1 = \mu_2 = 1, f_1 = 1/10, f_2 = 9/10, \pi = 1/2$.

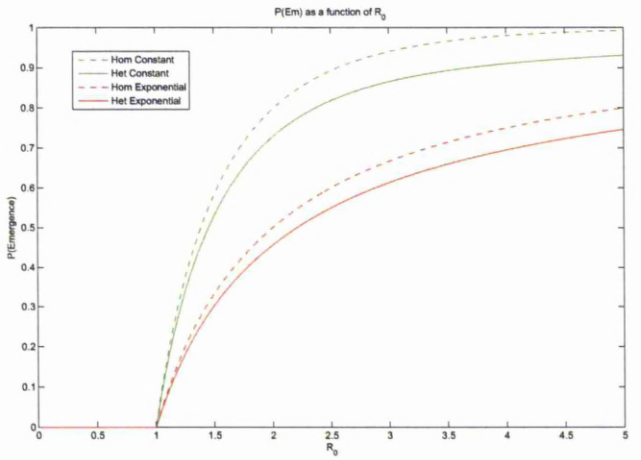

Figure 4.3: Emergence probability for homogeneous and heterogeneous 2-group models where heterogeneity exists in mixing (assortative) for both constant and exponential infectious periods. Parameters: $\lambda_1 = \lambda_2 = 1, \mu_1 = \mu_2 = 1, f_1 = 1/10, f_2 = 9/10, \pi = 0.95$.

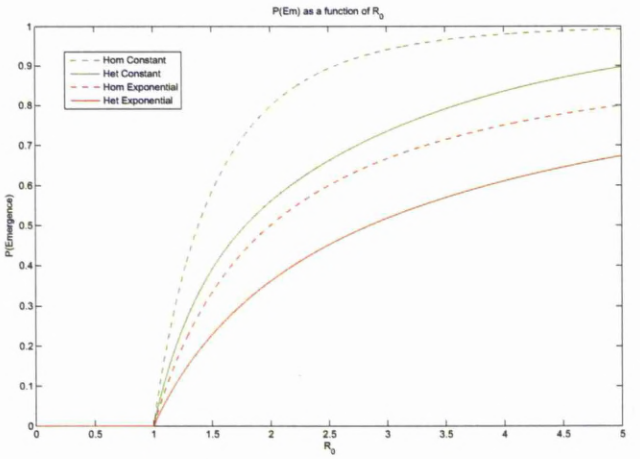

Figure 4.4: Emergence probability for homogeneous and heterogeneous 2-group models where heterogeneity exists in mixing (dissortative) for both constant and exponential infectious periods. Parameters: $\lambda_1 = \lambda_2 = 1, \mu_1 = \mu_2 = 1, f_1 = 1/10, f_2 = 9/10, \pi = 0.05$.

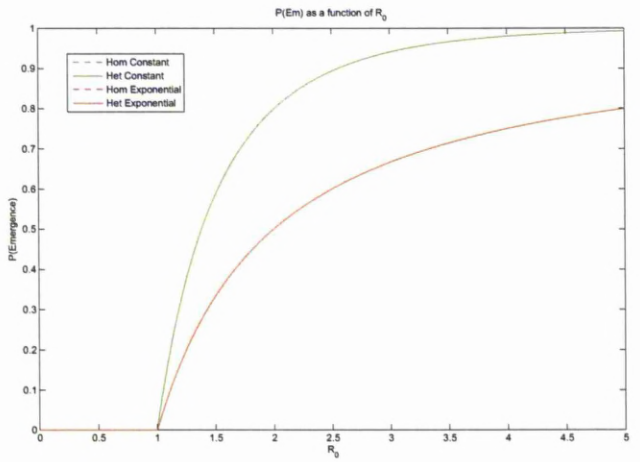

Figure 4.5: Emergence probability for homogeneous and heterogeneous 2-group models where heterogeneity exists in susceptibility for both constant and exponential infectious periods. Parameters: $\lambda_1 = \lambda_2 = 1, \mu_1 = 1000/109, \mu_2 = 10/109, f_1 = 1/10, f_2 = 9/10, \pi = 1/2$.

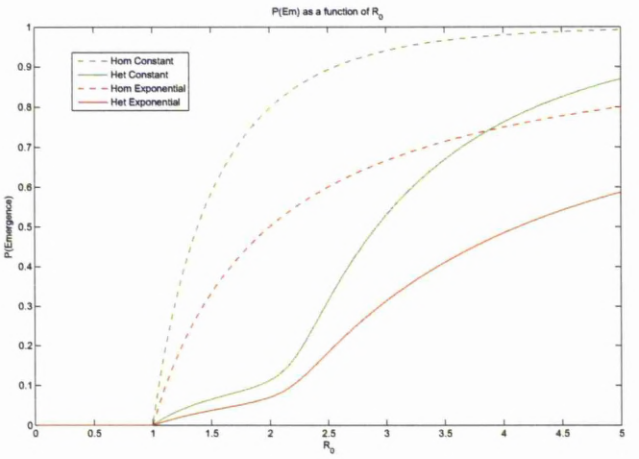

Figure 4.6: Emergence probability for homogeneous and heterogeneous 2-group models where heterogeneity exists in infectivity with assortative mixing for both constant and exponential infectious periods. Parameters: $\lambda_1 = 200/29, \lambda_2 = 10/29, \mu_1 = \mu_2 = 1, f_1 = 1/10, f_2 = 9/10, \pi = 0.95$.

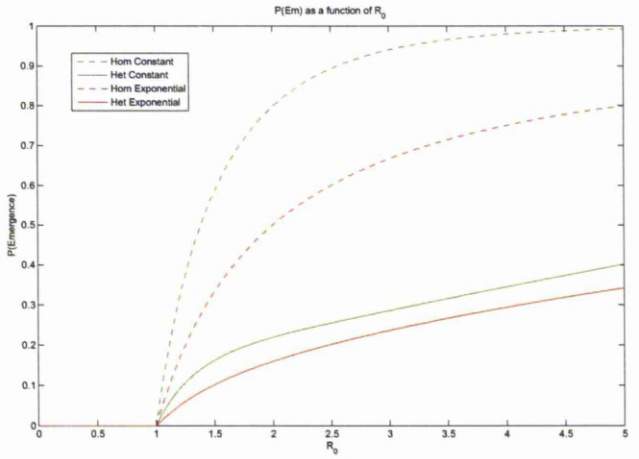

Figure 4.7: Emergence probability for homogeneous and heterogeneous 2-group models where heterogeneity exists in infectivity with dissortative mixing for both constant and exponential infectious periods. Parameters: $\lambda_1 = 200/29, \lambda_2 = 10/29, \mu_1 = \mu_2 = 1, f_1 = 1/10, f_2 = 9/10, \pi = 0.05$.

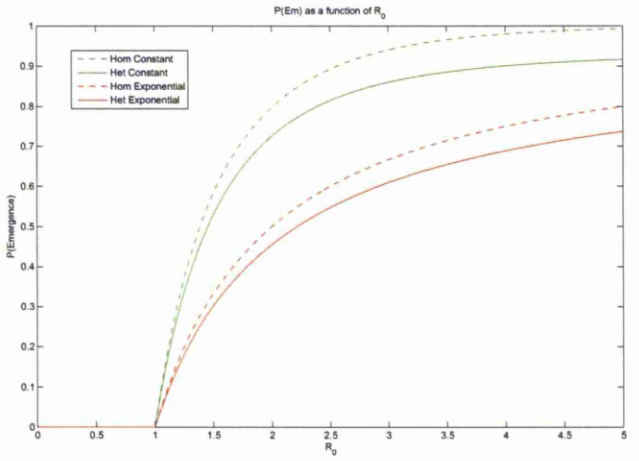

Figure 4.8: Emergence probability for homogeneous and heterogeneous 2-group models where heterogeneity exists in susceptibility with assortative mixing for both constant and exponential infectious periods. Parameters: $\lambda_1 = \lambda_2 = 1, \mu_1 = 1000/109, \mu_2 = 10/109, f_1 = 1/10, f_2 = 9/10, \pi = 0.95$.

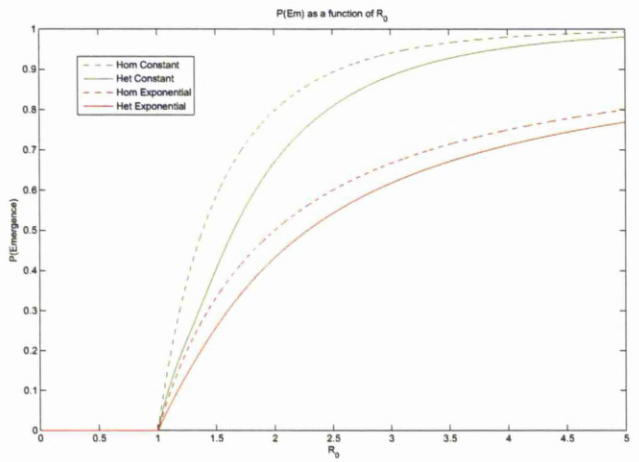

Figure 4.9: Emergence probability for homogeneous and heterogeneous 2-group models where heterogeneity exists in susceptibility with dissortative mixing for both constant and exponential infectious periods. Parameters: $\lambda_1 = \lambda_2 = 1, \mu_1 = 1000/109, \mu_2 = 10/109, f_1 = 1/10, f_2 = 9/10, \pi = 0.05$.

Figures (4.2)-(4.9) correspond to the graphs of Figure 2 of Yates et al. [106]. The difference with our results is that we have included emergence probabilities for both a constant and exponential infectious period assumption for all sets of parameter values. The first four figures of results we produce each show the effect of one type of heterogeneity, and each shows both constant and exponential cases. In Figure (4.2) we examine the effect of heterogeneity in infectivity. In this case, π is set to 0.5 to ensure that mixing has no effect, ie. there is no contact preference - group 1 individuals are just as likely to make contact with group 2 individuals as they are with themselves and vice versa. We set $\lambda_1 = 200/29$, $\lambda_2 = 10/29$, meaning that group 1 individuals are 20 times more infectious than group 2 individuals. As mentioned in Chapter 3, this small proportion of highly infectious individuals within the whole population are referred to as 'super spreaders'. Figure (4.3) shows the effect of assortative mixing. We set $\pi = 0.95 \Rightarrow 1 - \pi = 0.05$. This means that group 1 individuals are 95% likely to make contacts with other group 1 individuals and only 5% likely to make contacts with group 2 individuals and vice versa. The infectivity and susceptibility are equal between both groups. Figure (4.4) shows the effect of dissortative mixing. Here $\pi = 0.05$ so contact within-group is 5% likely and contact preference for the opposite group is 95% likely. Again, force of infectivity and susceptibility between groups is equal. Figure (4.5) shows the effect of heterogeneity in susceptibility. There is no contact preference and infectivity is equal between groups.

The remaining four figures show the effect of two types of heterogeneity simultaneously. Figure (4.6) shows heterogeneity in two parameters, infectivity with assortative mixing. Figure (4.7) shows heterogeneity in infectivity with dissortative mixing. Figure (4.8) shows heterogeneity in susceptibility with assortative mixing and figure (4.9) shows heterogeneity in susceptibility with dissortative mixng.

The probability of emergence is less for every value of R_0, in every instance, when an exponential infectious period is assumed as opposed to a constant infectious period in comparing corresponding homogeneous and heterogeneous models. It is also clear that the probability of emergence remains higher across the R_0 range for the homogeneous model than for the heterogeneous, irrespective of infectious period assumption and type of heterogeneity imposed. This is also true in the cases where multiple heterogeneities are imposed.

There are several observations to be made concerning these results. Firstly, Figure (4.5) shows that the emergence probability for the homogeneous model is identical to that of the heterogeneous model with the same R_0 value when considering heterogeneity in susceptibility only. This is true when both a constant and exponential infectious period is assumed. We will present an algebraic argument in section 4.3.3 showing this to be the case for k-groups under the constant infectious period assumption.

Another point of interest is that the type of mixing preference of otherwise identical individuals influences disease emergence. From Figures (4.3) and (4.4) we can see that both assortative and dissortative mixing lower the emergence probability compared to that of the homogeneous model and that strong dissortative mixing yields a lower emergence probability than the same model with strong assortative mixing. This observation is in line with one made by Marschner [75], who discussed that increasing the assortative mixing component of simpler models tends to allow an epidemic to grow more easily. Furthermore, the addition of multiple forms of heterogeneity result in complex outcomes. The results suggest that heterogeneity does not increase the probability of emergence and in every case but one, decreases it. This is consistent with results of Lloyd-Smith et al. [71] who considered the case of heterogeneity in infectivity alone. What is clear is that the influence of heterogeneity on disease emergence depends on the type of heterogeneity. For example, variation in susceptibility does not affect emergence whereas variation in infectivity reduces its likelihood. Multiple forms of heterogeneity yield more complex results, for example, whilst variation in susceptibility alone gives the same effect as a homogeneous population with the same R_0, when combined with heterogeneity in mixing, it reduces the risk of emergence compared to the homogeneous case.

So these graphs show that with only the exception of varying susceptibility alone, variation in infectiousness, susceptibility to infection and mixing preference makes the extinction of chains of disease transmission more likely, ie. epidemics are less likely to occur in epidemiologically diverse populations than in homogeneous ones (with the same R_0).

Another feature to note is that the probability of emergence is always lower when an exponential infectious period is assumed when compared to a model with constant infectious period of the same parameter values. This was proved for the case of a homogeneously mixing population by Daley [32]. The effect of the constant or exponential assumption is often greater than the effect of the type of heterogeneity.

Daley [32] states that it is feasible to have $\mathbb{E}[I_1] = \mathbb{E}[I_2]$ but $P^{I_1}(Em) = 0 < P^{I_2}(Em)$, because the critical threshold level above which major outbreaks occur depends not on the mean infectious period but rather on the mean number of contacts during such a period. This however is not possible with a Poisson process of contacts where $R_0 = \mathbb{E}[\text{Number of contacts}] = \mathbb{E}[\beta I] = \beta\mathbb{E}[I]$. Here, $R_0 \leq 1$ if $\mathbb{E}[I] \leq \frac{1}{\beta}$ thus $P^I(Em) = 0$ if $\mathbb{E}[I] \leq \frac{1}{\beta}$ where $P^I(Em)$ is determined by the mean infectious period otherwise if $R_0 > 1$, the value of $P^I(Em)$ is determined by $\mathbb{E}[e^{-\beta I}]$. In a general sense, as the variability of the infectious period increases for a given mean infectious period, so both the mean size of the epidemic and

probability of emergence decrease.

Figure (4.10) plots the extinction probabilities and emergence probabilities for a 3-group separable model where the values of λ and μ are chosen randomly from an exponential distribution with mean 3, and so the elements of the infection rate matrix are random. This random selection of parameters is iterated 1000 times and so we see a range of possible values for extinction probabilities of all three groups and emergence probabilities under these parameters. What is of interest is that the extinction probabilities (with initial infective in a specified group), although seemingly clustered around the homogeneous curve, lie above and below the curve for any R_0, entirely dependent upon chosen parameter values. However, the emergence probability (with the initial infective assigned to group i with probability $\mu_i f_i$) lies consistently below the homogeneous line for all R_0 and all parameter values.

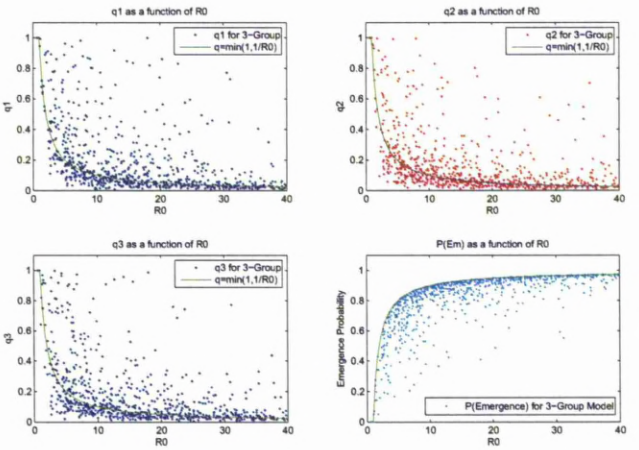

Figure 4.10: Extinction probabilities q_1, q_2, q_3 and P(Emergence) as a function of R_0. The solid green line represents the homogeneous model in each case. Fixed parameters $f_1 = f_2 = f_3 = 1/3$.

Furthermore we produce emergence probabilities for a more general, non-separable model (Figure (4.11)) where β_{ij} is no longer a product of separate parameters but is simply a number chosen at random. In this case, it is impossible to tell which characteristics contributed to the infection rate and by how much. What is interesting to note about this setup is that the emergence probabilities are still all bounded from above by the homogeneous curve. Here the emergence probability is calculated by $P_{Het}(Em) = 1 - q^{\mathbf{V}}$ where $\mathbf{V}$ is the normalised eigenvector of the next-generation mean matrix M corresponding to eigenvalue R_0.

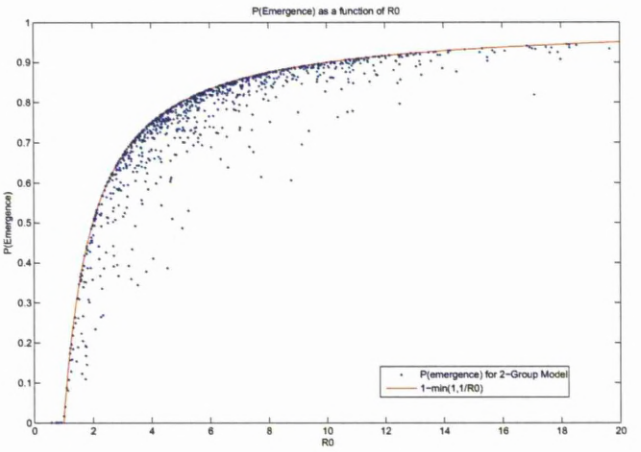

Figure 4.11: P(Emergence) as a function of R_0 for a non-separable infection model. Fixed parameters $f_1 = f_2 = 1/2$.

This is a point of interest. Here this eigenvector acts as a probability distribution of an infective starting in group i so we start the process off according to this dominant eigenvector. This is not biologically speaking a sensible way to start such a process but this vector does have a biological interpretation. We see that the process ends up after a long time in the same position as it was when it began. In other words, if we start the process at the 'ultimate state' then this is where the process ends at after a long time. This is enforced by Corollary 4.2.7, pg. 95 in [56] which states that for a supercritical positively regular process $\mathbf{Z}_n$,

$$\lim_{n\to\infty} \frac{\mathbf{Z}_n}{|\,\mathbf{Z}_n\,|} = \mathbf{V}$$

where $\mathbf{V}$ is a normalised eigenvector and $|\,.\,|$ denotes the sum of absolute values of elements. The notion that there is no change over time of this probability distribution at least makes mathematical sense. The MATLAB code used to generate the results of Figures (4.10) and (4.11) is viewable in appendices B and C.

4.3 Analytical results

For the purposes of these analytical proofs we define $M_{ij} = \beta \mathbb{E}[I]\lambda_i \pi_{ij} \mu_j f_j$ and set $\pi_{ij} = \frac{1}{k}$ so we can now view the model as being separable. If $f_j = \frac{1}{k}$ then, as already established [23], R_0 is defined as the maximal eigenvalue of our next generation mean matrix

$$M = \beta \mathbb{E}[I] \begin{bmatrix} \lambda_1\mu_1 & \dots & \lambda_1\mu_k \\ \lambda_2\mu_1 & \dots & \lambda_2\mu_k \\ \vdots & \dots & \vdots \\ \lambda_k\mu_1 & \dots & \lambda_k\mu_k \end{bmatrix} /k^2,$$

If we now take $\mathbb{E}[I] = 1$ we have that $M = \beta \frac{\lambda \mu^T}{k^2}$, so $\boldsymbol{\lambda}$ is an eigenvector of M with

$$M\boldsymbol{\lambda} = \left(\frac{\beta \boldsymbol{\lambda} \mu^T}{k^2}\right) \boldsymbol{\lambda} = \boldsymbol{\lambda} \left(\frac{\beta \mu^T \boldsymbol{\lambda}}{k^2}\right) = R_0 \boldsymbol{\lambda} \quad \text{where} \quad R_0 = \frac{\beta \mu^T \boldsymbol{\lambda}}{k^2}.$$

This shows that $\frac{\beta \mu^T \boldsymbol{\lambda}}{k^2}$ is an eigenvalue of M. In order to show that this is also the largest eigenvalue, see Galvani & May [46].

We examine a 2-group model under this parameterization, but we will allow for $f_1 \neq f_2$. For the homogeneous case, assuming an exponential infectious period with mean 1, the probability generating function is given by

$$\hat{\phi}(s) = \frac{1}{1 + R_0(1-s)} = \frac{1}{1 + \frac{\beta}{2}(\lambda_1\mu_1 f_1 + \lambda_2\mu_2 f_2)(1-s)}.$$

Thus $\hat{\phi}(0) = \frac{1}{1+R_0}$ which implies $m_1 = 1 - \frac{1}{1+R_0}$.

We now iterate the generating function a number of times in order to examine $\lim_{n\to\infty} \hat{\phi}^n(0)$. A procedure in MATLAB is created where for starting point $s = 0$, we iterate this generating function a specified number of times and examine how convergence occurs through iteration in order to gain insight into the probability of emergence. In other words we look at how $P(Em) = \lim_{n\to\infty}[1 - \hat{\phi}^n(0)]$ converges.

We set the number of iterations $n = 5$. Take starting points $s = 0$ and set arbitrarily $R_0 = 5$, for our homogeneous model. For the 2-group heterogeneous case, there are now two generating functions involved as opposed to one. We have

$$\phi_1(\mathbf{s}) = \frac{1}{1 + \frac{\beta}{2}(\lambda_1\mu_1 f_1(1-s_1) + \lambda_1\mu_2 f_2(1-s_2))}, \quad \phi_2(\mathbf{s}) = \frac{1}{1 + \frac{\beta}{2}(\lambda_2\mu_1 f_1(1-s_1) + \lambda_2\mu_2 f_2(1-s_2))}.$$

Taking $\mathbf{s} = \mathbf{0}$ then

$$t_1 = 1 - \mu_1 f_1 \left(\frac{1}{1 + \frac{\beta}{2}(\lambda_1\mu_1 f_1 + \lambda_1\mu_2 f_2)}\right) - \mu_2 f_2 \left(\frac{1}{1 + \frac{\beta}{2}(\lambda_2\mu_1 f_1 + \lambda_2\mu_2 f_2)}\right).$$

We iterate these generating functions each a number of times and examine $\phi_1^n(\mathbf{0})$, $\phi_2^n(\mathbf{0})$ and $t_n = 1 - \mu_1 f_1 \phi_1^n(\mathbf{0}) - \mu_2 f_2 \phi_2^n(\mathbf{0})$. We set the parameters for the heterogeneous model to match the R_0 value of the homogeneous model studied by setting $n = 5, \lambda_1 = 3, \lambda_2 = 1, \mu_1 = 1, \mu_2 = 2, R_0 = 5$. The table below shows the results for $\phi_1^n(s), \phi_2^n(s)$ and emergence probabilities m_n and t_n for both the heterogeneous and homogeneous models.

n	1	2	3	4	5
$\phi_1^n(\mathbf{0})$	0.0925	0.1202	0.1267	0.1282	0.1286
$\phi_2^n(\mathbf{0})$	0.2342	0.2908	0.3032	0.3061	0.3068
t_n	0.8130	0.7661	0.7556	0.7532	0.7526
m_n	0.8333	0.8065	0.8013	0.8002	0.8001

It is first of all clear to see that $m_n = 1 - \hat{\phi}^n(0)$ converges as n increases, to $P_{Hom}(Em)$. In fact $\lim_{n\to\infty} \hat{\phi}^n(s)$ is the same for all $s \in [0, 1)$. This is in keeping with the theory below where we can use equation (3.3) to calculate the extinction probability q and then use the fact that the emergence probability is $1 - q$.

$$q = \hat{\phi}(q) = \frac{1}{1 + R_0(1-q)} \quad \Rightarrow \quad q[1+R_0(1-q)] = 1 \quad \Rightarrow \quad -R_0q^2+(1+R_0)q-1 = 0$$

$$\Rightarrow (q-1)(-R_0q+1) = 0 \quad \Rightarrow \quad q = \frac{1}{R_0} = \frac{1}{5} = 0.2 \quad \Rightarrow \quad P(Em) = 1 - q = 0.8.$$

It is also clear to see that, $\phi_1^n(\mathbf{0})$ and $\phi_2^n(\mathbf{0})$ converge as n increases which implies $t_n = 1 - \mu_1 f_1 \phi_1^n(\mathbf{s}) - \mu_2 f_2 \phi_2^n(\mathbf{s})$ converges as n increases.

The below table shows results for $R_0 = 38$. Although this is arguably an unrealistic R_0 value, the data supports the following inference clearly. Again, by selecting $\lambda_1 = 6, \lambda_2 = 2, \mu_1 = 3, \mu_2 = 10$ for our heterogeneous model we can ensure $R_0 = 38$ matches the homogeneous model and tabulate m_n, t_n in order to show that increasing R_0 causes both to be larger, no matter the initial value of s, $(0 \leq \mathbf{s} < 1)$.

n	1	2	3	4	5
t_n	0.9711	0.9667	0.9676	0.9676	0.9676
m_n	0.9744	0.9737	0.9737	0.9737	0.9737

Increasing λ_i, μ_j, ie. R_0 causes $\hat{\phi}(s)$ to be smaller and so $\lim_{n\to\infty} \hat{\phi}^n(s)$ converges to a smaller value. Numerical results obtained (but not included) indicate that convergence occurs to the same value as above, no matter what value s takes $(0 \leq s < 1)$. In turn

$$\text{As } \lambda_i, \mu_j \to \infty, [\lim_{n\to\infty} \hat{\phi}^n(0)] \to 0 \quad \Rightarrow \quad [\lim_{n\to\infty} (1 - \hat{\phi}^n(s))] \to 1$$

So as we increase R_0, the probability of emergence tends to 1. Similarly to the homogeneous case, numerical results have been obtained (but not included) for the heterogeneous case to show that convergence to the same value occurs $\forall \quad 0 \leq s < 1$.

As in the homogeneous case, observe that for the heterogeneous case, as $R_0 \to \infty$, $\lim_{n\to\infty} t_n \to 1$.

Examining the above data, we can compare m_n with t_n for each n. One can see that t_n is smaller than m_n so that, in the limit, the probability of emergence for the heterogeneous case is always smaller than the probability of emergence for the homogeneous case. What follows is an algebraic proof showing that this is indeed the case, no matter what values λ_i, μ_j and so ultimately R_0 take. In addition, we will see that this result holds independently of group frequencies f_i.

4.3.1 Iterative proof for 2-group heterogeneous model with exponential infectious period

For the homogeneous case, define $s_0 = 0$ and

$$s_{n+1} = \hat{\phi}(s_n) = \frac{1}{1 + R_0(1 - s_n)} = \frac{1}{1 + \frac{\beta}{2}(\lambda_1\mu_1 f_1 + \lambda_2\mu_2 f_2)(1 - s_n)} \quad \text{for } n=1,2,\ldots, \tag{4.2}$$

$$m_n = 1 - s_n \quad \text{for } n=1,2,\ldots,$$

Then $s_n \to q$, the extinction probability and $m_n \to P_{Hom}(Em)$ as $n \to \infty$.

For the heterogeneous case, take $\mathbf{s}^0 = (0, 0)$ and define

$$\mathbf{s}^{n+1} = \phi(\mathbf{s}^n) \quad \text{for } n=1,2,\ldots,$$

that is,

$$s_1^{n+1} = \phi_1(\mathbf{s}^n), \qquad s_2^{n+1} = \phi_2(\mathbf{s}^n),$$

and define

$$t_n = 1 - \mu_1 f_1 s_1^n - \mu_2 f_2 s_2^n.$$

Then $\mathbf{s}^n \to \mathbf{q}$ and $t_n \to P_{Het}(Em)$ as $n \to \infty$.

The tabulated results (and Figures (4.1)-(4.8)) showed that, in the limit, $P_{Hom}(Em) \geq P_{Het}(Em)$. This is equivalent to saying that, in the limit, $t_n \leq m_n$ or $1 - t_n \geq 1 - m_n$. If we can show that $t_n \leq m_n$ for each n, then we can infer that in the limit the probability of emergence for the heterogeneous case is always less than or equal to the probability of emergence for the homogeneous case, no matter the

strength of infectivity and susceptibility of the population or relative frequency of each group.

To begin, take $s_0 = 0$ so $s_1 = \frac{1}{1+R_0}$ which implies $m_1 = 1 - \frac{1}{1+R_0}$. So for the homogeneous case:

$$m_1 = 1 - \frac{1}{1 + \frac{\beta}{2}(\lambda_1\mu_1 f_1 + \lambda_2\mu_2 f_2)}.$$

Similarly, for the heterogeneous case, take $s_1^0 = s_2^0 = 0$ and so $t_0 = 1$, and then

$$s_1^1 = \frac{1}{1 + \frac{\beta}{2}(\lambda_1\mu_1 f_1 + \lambda_1\mu_2 f_2 - \lambda_1\mu_1 f_1(s_1^0) - \lambda_1\mu_2 f_2(s_2^0))} = \frac{1}{1 + \frac{\beta}{2}(\lambda_1\mu_1 f_1 + \lambda_1\mu_2 f_2)},$$

$$s_2^1 = \frac{1}{1 + \frac{\beta}{2}(\lambda_2\mu_1 f_1 + \lambda_2\mu_2 f_2 - \lambda_2\mu_1 f_1(s_1^0) - \lambda_2\mu_2 f_2(s_2^0))} = \frac{1}{1 + \frac{\beta}{2}(\lambda_2\mu_1 f_1 + \lambda_2\mu_2 f_2)},$$

so

$$t_1 = 1 - \mu_1 f_1(s_1^1) - \mu_2 f_2(s_2^1)$$

$$t_1 = 1 - \mu_1 f_1\left(\frac{1}{1 + \frac{\beta}{2}(\lambda_1\mu_1 f_1 + \lambda_1\mu_2 f_2)}\right) - \mu_2 f_2\left(\frac{1}{1 + \frac{\beta}{2}(\lambda_2\mu_1 f_1 + \lambda_2\mu_2 f_2)}\right).$$

We are to show that $t_1 \leq m_1$, or equivalently, $1 - t_1 \geq 1 - m_1$. We have

$$1 - t_1 = \mu_1 f_1\left(\frac{1}{1 + \frac{\beta}{2}(\lambda_1\mu_1 f_1 + \lambda_1\mu_2 f_2)}\right) + \mu_2 f_2\left(\frac{1}{1 + \frac{\beta}{2}(\lambda_2\mu_1 f_1 + \lambda_2\mu_2 f_2)}\right). \tag{4.3}$$

Examining equation (4.3), we can simplify. We take the RHS, put over a common denominator and collect terms in the numerator:

$$1 - t_1 = \frac{\mu_1 f_1(1 + \frac{\beta}{2}(\lambda_2\mu_1 f_1 + \lambda_2\mu_2 f_2)) + \mu_2 f_2(1 + \frac{\beta}{2}(\lambda_1\mu_1 f_1 + \lambda_1\mu_2 f_2))}{(1 + \frac{\beta}{2}(\lambda_1\mu_1 f_1 + \lambda_1\mu_2 f_2))(1 + \frac{\beta}{2}(\lambda_2\mu_1 f_1 + \lambda_2\mu_2 f_2))},$$

which implies

$$t_1 = 1 - \frac{(1 + \frac{\beta}{2}(\lambda_1\mu_2 f_2 + \lambda_2\mu_1 f_1))}{(1 + \frac{\beta}{2}(\lambda_1\mu_1 f_1 + \lambda_1\mu_2 f_2))(1 + \frac{\beta}{2}(\lambda_2\mu_1 f_1 + \lambda_2\mu_2 f_2))}. \tag{4.4}$$

So we now compare (4.4) with m_1; wanting to show $t_1 \leq m_1$, that is,

$$1 - \frac{(1 + \frac{\beta}{2}(\lambda_1\mu_2 f_2 + \lambda_2\mu_1 f_1))}{(1 + \frac{\beta}{2}(\lambda_1\mu_1 f_1 + \lambda_1\mu_2 f_2))(1 + \frac{\beta}{2}(\lambda_2\mu_1 f_1 + \lambda_2\mu_2 f_2))} \leq 1 - \frac{1}{1 + \frac{\beta}{2}(\lambda_1\mu_1 f_1 + \lambda_2\mu_2 f_2)}.$$

This is equivalent to

$$\frac{1}{1 + \frac{\beta}{2}(\lambda_1\mu_1 f_1 + \lambda_2\mu_2 f_2)} \leq \frac{(1 + \frac{\beta}{2}(\lambda_1\mu_2 f_2 + \lambda_2\mu_1 f_1))}{(1 + \frac{\beta}{2}(\lambda_1\mu_1 f_1 + \lambda_1\mu_2 f_2))(1 + \frac{\beta}{2}(\lambda_2\mu_1 f_1 + \lambda_2\mu_2 f_2))}$$

$$\iff \lambda_1\lambda_2(\mu_1^2 f_1^2+2\mu_1\mu_2 f_1 f_2+\mu_2^2 f_2^2) \leq \lambda_1^2\mu_1\mu_2 f_1 f_2+\lambda_1\lambda_2\mu_1^2 f_1^2+\lambda_1\lambda_2\mu_2^2 f_2^2+\lambda_2^2\mu_1\mu_2 f_1 f_2$$

$$\iff 2\lambda_1\lambda_2\mu_1\mu_2 f_1 f_2 \leq \mu_1\mu_2 f_1 f_2(\lambda_1^2+\lambda_2^2)$$

Note at this stage that if $\mu_1 = 0$ or $\mu_2 = 0$ then this inequality holds. If not, then this reduces to

$$2\lambda_1\lambda_2 \leq \lambda_1^2+\lambda_2^2,$$

but now

$$(\lambda_1^2+\lambda_2^2) - 2\lambda_1\lambda_2 = (\lambda_1-\lambda_2)^2 \geq 0.$$

Since any real value squared is non-negative, we have shown that $t_1 \leq m_1$. We now extend this argument from m_1 and t_1 to m_{n+1} and t_{n+1}.

We defined for the homogeneous case,

$$s_{n+1} = \hat{\phi}(s_n) = \frac{1}{1+R_0(1-s_n)}$$

$$= \frac{1}{1+\frac{\beta}{2}(\lambda_1\mu_1 f_1+\lambda_2\mu_2 f_2)(1-s_n)} \quad \text{for } n=0,1,\ldots$$

We defined

$$m_n = 1 - s_n \quad \text{for } n=0,1,\ldots$$

so that, from (4.2),

$$m_{n+1} = 1 - \frac{1}{1+m_n R_0}. \tag{4.5}$$

For the heterogeneous case,

$$t_n = 1 - \mu_1 f_1 s_1^n - \mu_2 f_2 s_2^n$$

$$= 1 - \mu_1 f_1 \left(\frac{1}{1+\frac{\beta}{2}(\lambda_1\mu_1 f_1(1-s^{n-1})+\lambda_1\mu_2 f_2(1-s_2^{n-1}))}\right) - \mu_2 f_2 \left(\frac{1}{1+\frac{\beta}{2}(\lambda_2\mu_1 f_1(1-s_1^{n-1})+\lambda_2\mu_2 f_2(1-s_2^{n-1}))}\right)$$

Following rearrangement,

$$t_{n+1} = 1 - \frac{(1+\frac{\beta}{2}(\lambda_1\mu_2 f_2+\lambda_2\mu_1 f_1)t_n)}{(1+\frac{\beta\lambda_1}{2}(\mu_1 f_1+\mu_2 f_2)t_n)(1+\frac{\beta\lambda_2}{2}(\mu_1 f_1+\mu_2 f_2)t_n)}, \tag{4.6}$$

where $0 \leq t_n \leq 1$. Now $t_{n+1} \leq m_{n+1}$ if and only if

$$\frac{1}{1+m_n R_0} \leq \frac{(1+\frac{\beta}{2}(\lambda_1\mu_2 f_2+\lambda_2\mu_1 f_1)t_n)}{(1+\frac{\beta\lambda_1}{2}(\mu_1 f_1+\mu_2 f_2)t_n)(1+\frac{\beta\lambda_2}{2}(\mu_1 f_1+\mu_2 f_2)t_n)}$$

$$\iff 1+\frac{\beta}{2}(\lambda_1(\mu_1 f_1+\mu_2 f_2)t_n+\lambda_2(\mu_1 f_1+\mu_2 f_2)t_n)+\frac{\beta^2\lambda_1\lambda_2}{4}(\mu_1 f_1+\mu_2 f_2)^2 t_n^2 \quad \leq$$

$$1+\frac{\beta}{2}((\lambda_1\mu_1 f_1+\lambda_2\mu_2 f_2)m_n+(\lambda_1\mu_2 f_2+\lambda_2\mu_1 f_1)t_n)+\frac{\beta^2}{4}(\lambda_1\mu_2 f_2+\lambda_2\mu_1 f_1)(\lambda_1\mu_1 f_1+\lambda_2\mu_2 f_2)m_n t_n$$

if and only if

$$\frac{\beta t_n}{2}(\lambda_1\mu_1 f_1+\lambda_2\mu_2 f_2)+\frac{\beta^2 t_n^2\lambda_1\lambda_2}{4}(\mu_1 f_1+\mu_2 f_2)^2 \quad \leq$$

$$\frac{\beta m_n}{2}(\lambda_1\mu_1 f_1+\lambda_2\mu_2 f_2)+\frac{\beta^2 m_n t_n}{4}(\lambda_1\mu_1 f_1+\lambda_2\mu_2 f_2)(\lambda_1\mu_2 f_2+\lambda_2\mu_1 f_1)$$

Inductively, we know $t_n \leq m_n$ so $\frac{\beta t_n}{2}(\lambda_1\mu_1 f_1+\lambda_2\mu_2 f_2) \leq \frac{\beta m_n}{2}(\lambda_1\mu_1 f_1+\lambda_2\mu_2 f_2)$, so it is sufficient to show that

$$\frac{\beta^2 t_n^2\lambda_1\lambda_2}{4}(\mu_1 f_1+\mu_2 f_2)^2 \leq \frac{\beta^2 m_n t_n}{4}(\lambda_1\mu_1 f_1+\lambda_2\mu_2 f_2)(\lambda_1\mu_2 f_2+\lambda_2\mu_1 f_1)$$

$$\iff t_n\lambda_1\lambda_2(\mu_1^2 f_1^2+2\mu_1\mu_2 f_1 f_2+\mu_2^2 f_2^2) \leq m_n(\lambda_1^2\mu_1\mu_2 f_1 f_2+\lambda_1\lambda_2\mu_1^2 f_1^2+\lambda_1\lambda_2\mu_2^2 f_2^2+\lambda_2^2\mu_1\mu_2 f_1 f_2)$$

Again, since $t_n \leq m_n$ it is sufficient to show $\lambda_1\lambda_2(\mu_1 f_1+\mu_2 f_2)^2 \leq (\lambda_1\mu_1 f_1+\lambda_2\mu_2 f_2)(\lambda_1\mu_2 f_2+\lambda_2\mu_1 f_1)$. This can be done by exactly the same method as used when looking at t_1 and m_1. Thus we have proved that $t_n \leq m_n$ for $n = 0, 1, 2, \ldots$. Thus the probability of emergence, in the limit, for a 2-group model with exponential infectious period, is always smaller in the heterogeneous case than the homogeneous case, no matter the values of (λ_i, μ_j), the relative group frequencies and hence R_0.

4.3.2 Iterative proof for 2-group heterogeneous model with constant infectious period

As before, for the homogeneous case we take $s_0 = 0$, but now we define

$$s_{n+1} = \hat{\phi}(s_n) = e^{R_0(s_n-1)} = e^{\beta(\lambda_1\mu_1 f_1+\lambda_2\mu_2 f_2)(s_n-1)/2} \qquad \text{for } n = 1, 2, \ldots$$

In the same fashion as the exponential case we have that $m_n = 1 - s_n$ for $n = 0, 1, \ldots$ and that $s_n \to q$ and $m_n \to P_{Hom}(Em)$ as $n \to \infty$. The same proceedings as before apply to the heterogeneous case, namely that $\mathbf{s}^0 = (0, 0)$ and $\mathbf{s}^{n+1} = \phi(\mathbf{s}_n)$ for $n = 1, 2, \ldots$with $t_n = 1 - \mu_1 f_1 s_1^n - \mu_2 f_2 s_2^n$, then $\mathbf{s}^n \to \mathbf{q}$ and $t_n \to P_{Het}(Em)$ as $n \to \infty$.

To begin, $s_0 = 0$ therefore $s_1 = e^{R_0(0-1)} = e^{-R_0} \Rightarrow m_1 = 1 - e^{-R_0}$. For the heterogeneous model,

$$\phi_1(\mathbf{s}) = e^{\frac{\beta}{2}(\lambda_1\mu_1 f_1(s_1-1)+\lambda_1\mu_2 f_2(s_2-1))}, \quad \phi_2(\mathbf{s}) = e^{\frac{\beta}{2}(\lambda_2\mu_1 f_1(s_1-1)+\lambda_2\mu_2 f_2(s_2-1))},$$

so that

$$\begin{aligned} s_1^1 = e^{\frac{\beta}{2}(\lambda_1\mu_1 f_1(s_1^0-1)+\lambda_1\mu_2 f_2(s_2^0-1))} &= e^{-\frac{\beta}{2}(\lambda_1\mu_1 f_1+\lambda_1\mu_2 f_2)}, \\ s_2^1 = e^{\frac{\beta}{2}(\lambda_2\mu_1 f_1(s_1^0-1)+\lambda_2\mu_2 f_2(s_2^0-1))} &= e^{-\frac{\beta}{2}(\lambda_2\mu_1 f_1+\lambda_2\mu_2 f_2)}, \end{aligned}$$

and so

$$t_1 = 1 - \mu_1 f_1 e^{-\frac{\beta}{2}(\lambda_1\mu_1 f_1+\lambda_1\mu_2 f_2)} - \mu_2 f_2 e^{-\frac{\beta}{2}(\lambda_2\mu_1 f_1+\lambda_2\mu_2 f_2)}.$$

We now show $t_1 \leq m_1$, ie.

$$\begin{aligned} e^{-\beta(\lambda_1\mu_1 f_1+\lambda_2\mu_2 f_2)/2} &\leq \mu_1 f_1 e^{-\frac{\beta}{2}(\lambda_1\mu_1 f_1+\lambda_1\mu_2 f_2)} + \mu_2 f_2 e^{-\frac{\beta}{2}(\lambda_2\mu_1 f_1+\lambda_2\mu_2 f_2)} \\ \iff e^{-\beta(\lambda_1\mu_1 f_1+\lambda_2\mu_2 f_2)/2} &\leq \mu_1 f_1 e^{-\frac{\beta}{2}(\lambda_1\mu_1 f_1+\lambda_1\mu_2 f_2)} + \mu_2 f_2 e^{-\frac{\beta}{2}(\lambda_2\mu_1 f_1+\lambda_2\mu_2 f_2)}. \end{aligned}$$

This above inequality says that the left hand side is less than, or equal to, some weighted average on the right hand side. In fact, this inequality follows because e^{-x} is a convex function and

$$\lambda_1\mu_1 f_1 + \lambda_2\mu_2 f_2 = \mu_1 f_1(\lambda_1\mu_1 f_1 + \lambda_1\mu_2 f_2) + \mu_2 f_2(\lambda_2\mu_1 f_1 + \lambda_2\mu_2 f_2). \tag{4.7}$$

We have shown thus far that $t_1 \leq m_1$, for all values of λ, μ and f when we assume a constant infectious period. Now we extend the case, as before, to m_{n+1} and t_{n+1}. We have, in general,

$$\begin{aligned} m_{n+1} &= 1 - e^{-m_n R_0}, \\ t_{n+1} &= 1 - \mu_1 f_1(e^{\frac{\beta}{2}(\lambda_1\mu_1 f_1(s_1^n-1)+\lambda_1\mu_2 f_2(s_2^n-1))}) - \mu_2 f_2(e^{\frac{\beta}{2}(\lambda_2\mu_1 f_1(s_1^n-1)+\lambda_2\mu_2 f_2(s_2^n-1))}). \end{aligned}$$

Using the fact that $t_n = 1 - \mu_1 f_1 s_1^n - \mu_2 f_2 s_2^n$ we can assert that

$$t_{n+1} = 1 - \mu_1 f_1 e^{-\frac{\beta}{2}(\lambda_1 t_n(\mu_1 f_1+\mu_2 f_2))} - \mu_2 f_2 e^{-\frac{\beta}{2}(\lambda_2 t_n(\mu_1 f_1+\mu_2 f_2))}.$$

We now show that $t_{n+1} \leq m_{n+1}$. We require

$$\begin{aligned} 1-\mu_1 f_1 e^{-\frac{\beta}{2}(\lambda_1 t_n(\mu_1 f_1+\mu_2 f_2))} - \mu_2 f_2 e^{-\frac{\beta}{2}(\lambda_2 t_n(\mu_1 f_1+\mu_2 f_2))} &\leq 1-e^{-\beta m_n(\lambda_1\mu_1 f_1+\lambda_2\mu_2 f_2)/2} \\ \iff e^{-\beta m_n(\lambda_1\mu_1 f_1+\lambda_2\mu_2 f_2)/2} &\leq \mu_1 f_1 e^{-\frac{\beta}{2}(\lambda_1 t_n(\mu_1 f_1+\mu_2 f_2))} + \mu_2 f_2 e^{-\frac{\beta}{2}(\lambda_2 t_n(\mu_1 f_1+\mu_2 f_2))}. \end{aligned}$$

We know inductively that $t_n \leq m_n$. Thus the result follows from convexity of e^{-x} and (4.7).

4.3.3 The effects of varying λ_i, μ_j for k-group heterogeneous model with constant infectious period

We have as the generating function for a k-group model

$$\phi_i(\mathbf{s}) = e^{\beta\lambda_i/k \sum_{j=1}^{k} \mu_j f_j (s_j - 1)} \quad \text{for} \quad i = 1, \ldots, k$$

Following the previous section it is easy to see that

$$1 - m_1 \equiv e^{-\frac{\beta}{k} \sum_{i=1}^{k} \lambda_i \mu_i f_i} = e^{-\beta(\lambda^T \mu F)/k}$$

$$1 - t_1 \equiv \mu_1 f_1 e^{-\frac{\beta\lambda_1}{k} \sum_{j=1}^{k} \mu_j f_j} + \cdots + \mu_k e^{-\frac{\beta\lambda_k}{k} \sum_{j=1}^{k} \mu_j f_j}$$

We are trying to show that $P_{Het}(Em) \leq P_{Hom}(Em)$. Following the same reasoning as previously, first show that $s_1 \leq 1 - t_1$, ie.

$$e^{-\beta(\lambda^T \mu F)/k} \quad \leq \quad \mu_1 f_1 e^{-\frac{\beta\lambda_1}{k} \sum_{j=1}^{k} \mu_j f_j} + \cdots + \mu_k f_k e^{-\frac{\beta\lambda_k}{k} \sum_{j=1}^{k} \mu_j f_j}$$

That is,

$$e^{-\beta(\lambda^T \mu F)/k} \quad \leq \quad \sum_{i=1}^{k} \left(\mu_i f_i e^{-\beta\lambda_i/k} \right) \tag{4.8}$$

Now suppose we set $\boldsymbol{\lambda} = \mathbf{1}$ and allow μ to vary in (4.8) then we have

$$e^{-\frac{\beta}{k} \sum_{j=1}^{k} \mu_j f_j} \quad = \quad \sum_{i=1}^{k} \left(\mu_i f_i e^{-\frac{\beta}{k} \sum_{j=1}^{k} \mu_j f_j} \right)$$

The inequality becomes an equality and so $m_1 = t_1$. To extend this to m_n and t_n is simply a matter of comparing $exp\left(-\frac{\beta m_n}{k}(\lambda^T \mu F)\right)$ and $\sum \mu_i f_i exp\left(-\frac{\beta \lambda_i t_n}{k}\right)$. When $\boldsymbol{\lambda} = \mathbf{1}$ this becomes a matter of comparing $exp\left(-\frac{\beta m_n}{k}\right)$ and $exp\left(-\frac{\beta t_n}{k}\right)$. Since the inductive step in this case is $m_n = t_n$ we see that this is also an equality. So keeping infectivity uniform, and varying susceptibility means that $P_{Het}(Em) = P_{Hom}(Em)$ for any values of μ_j, for a k-group scenario, with constant infectious period. For an exponential assumption this follows from the fact that $\phi_i(\mathbf{s}) = \frac{1}{1 + \frac{\beta}{k}(\sum_j \lambda_i \mu_j f_j)(1 - s_j)}$ and the fact that $\phi_i(\mathbf{q}) = q_i$, since $\phi_i(\mathbf{s})$ doesn't depend on i in the case of heterogeneous susceptibility alone.

If on the other hand we set $\mu_i f_i = \frac{1}{k}$ for all i in (4.8), and allow $\boldsymbol{\lambda}$ to vary then we require

$$e^{-\frac{\beta}{k} \sum_{i=1}^{k} \lambda_i} \quad \leq \quad \frac{1}{k} \sum_{i=1}^{k} e^{-\beta\lambda_i/k}$$

At this stage, we establish some necessary definitions before proceeding with the remainder of our analysis. We define **majorization** as a partial ordering over vectors of real numbers from pg. 7 of [76], as

Definition 1 *Given $\boldsymbol{x}, \boldsymbol{y} \in \mathbb{R}^k$, we say $\boldsymbol{x}$ majorizes $\boldsymbol{y}$, written $\boldsymbol{x} \succ \boldsymbol{y}$, if*

$$\sum_{i=1}^{k} x_i^{\downarrow} = \sum_{i=1}^{k} y_i^{\downarrow} \quad \textit{and} \quad \sum_{i=1}^{n} x_i^{\downarrow} \leq \sum_{i=1}^{n} y_i^{\downarrow} \quad \textit{for all} \quad n \in \{1, \ldots, k-1\}$$

where $x_i^{\downarrow}, y_i^{\downarrow}$ are the elements of $\mathbf{x}, \mathbf{y}$ respectively sorted in decreasing order.

This definition is of central importance as it will be used when comparing two heterogeneous models in section 4.4. Furthermore we use the following definition from pg. 54 of [76]:

Definition 2 *A real-valued function ϕ defined on a set $A \subset \mathbb{R}^k$ is said to be Schur-convex on A if*

$$\boldsymbol{x} \prec \boldsymbol{y} \textit{ on } A \quad \Rightarrow \quad \phi(x) \leq \phi(y).$$

Finally, the proposition on pg. 64 of [76] states
Proposition: If $I \subset R$ is an interval and $g : I \to R$ is convex, then

$$\phi(\mathbf{x}) = \sum_{i=1}^{k} g(x_i)$$

is Schur-convex on I^k. Consequently, $\mathbf{x} \prec \mathbf{y}$ on I^k implies $\phi(\mathbf{x}) \leq \phi(\mathbf{y})$.

Now in the case $\mu_i f_i = \frac{1}{k}$ for all i, we have

$$\begin{aligned} 1 - m_1 &= e^{-\frac{\beta}{k^2} \sum_{i=1}^{k} \lambda_i}, \\ 1 - t_1 &= \tfrac{1}{k} \textstyle\sum_i e^{-\beta \lambda_i / k}. \end{aligned}$$

Take $g(x_i) = e^{-x_i}, \mathbf{x} = \frac{1}{k}\boldsymbol{\lambda}$ and $\mathbf{y} = \frac{\beta}{k^2}\left(\sum_{i=1}^{k} \lambda_i\right)\mathbf{1}$. Then $\mathbf{x} \succ \mathbf{y}$, and so

$$\begin{aligned} \textstyle\sum_{i=1}^{k} g(x_i) &\geq \textstyle\sum_{i=1}^{k} g(y_i) \\ \textstyle\sum_{i=1}^{k} e^{-\beta\lambda_i/k} &\geq \textstyle\sum_{i=1}^{k} e^{-\sum_{j=1}^{k} \beta\lambda_j/k^2} = k e^{-\sum_{j=1}^{k} \beta\lambda_j/k^2} \\ \Rightarrow \quad \tfrac{1}{k} \textstyle\sum_{i=1}^{k} e^{-\beta\lambda_i/k} &\geq e^{-\sum_{j=1}^{k} \beta\lambda_j/k^2} \\ \Rightarrow \quad 1 - t_1 &\geq 1 - m_1 \\ \Rightarrow \quad t_1 &\leq m_1 \end{aligned}$$

To show that $t_n \leq m_n$ for all n we observe that (4.8) becomes

$$exp\left(-\frac{\beta m_n}{k^2}\sum_{i=1}^{k}\lambda_i\right) \quad \leq \quad \sum_{i=1}^{k}\frac{1}{k}exp\left(-\frac{\beta\lambda_i}{k}t_n\right)$$

The same argument as above shows that

$$exp\left(-\frac{\beta t_n}{k^2}\sum_{i=1}^{k}\lambda_i\right) \quad \leq \quad \frac{1}{k}\sum_{i=1}^{k}exp\left(-\frac{\beta\lambda_i}{k}t_n\right)$$

and then since inductively we know $t_n \leq m_n$ then

$$exp\left(-\frac{\beta m_n}{k^2}\sum_{i=1}^{k}\lambda_i\right) \quad \leq \quad exp\left(-\frac{\beta t_n}{k^2}\sum_{i=1}^{k}\lambda_i\right)$$

and the required inequality follows. With equal group sizes $f_1 = \cdots = f_k = \frac{1}{k}$, then what we have in fact shown is that if susceptibility is uniform and equal amongst groups, and we vary the degree of infectivity only, then the probability of emergence for a heterogeneously mixing case is always less than or equal to the probability of emergence for a homogeneously mixing case for a model with any number of groups.

To summarise, heterogeneity in infectivity decreases the probability of emergence when susceptibility is uniform between groups and group sizes are equal. Heterogeneity in susceptibility yields the same probability of emergence as a homogenous model when infectivity is kept uniform between groups. This holds for any number of groups, irrespective of group size, when a constant infectious period is assumed.

4.3.4 Proof for k-group non-separable model

4.3.4.1 Comparing a heterogeneous model with a homogeneous model using a homogeneous process construction

We now construct processes by assigning to each individual its own offspring distribution. Firstly, we construct a homogeneous branching process. Whenever a new individual is born, it has offspring distribution $\sim G$. Set

$$G = \begin{cases} G_1 & \text{with probability } \mu_1 f_1, \\ \vdots & \\ G_k & \text{with probability } \mu_k f_k, \end{cases}$$

where G_k is the number of points in a Poisson process of rate λ_k in time period I. That is to say that an infected individual has a probability $\mu_i f_i$ of making G_i

contacts during its infectious period, meaning that it infects G_i other individuals since if a contact is made with an already infected individual, the branching process approximation ceases to become viable.

The probability generating function of the offspring distribution is

$$\begin{aligned}\phi(s) = \mathbb{E}\left[s^G\right] &= \mu_1 f_1 \mathbb{E}\left[s^{G_1}\right] + \cdots + \mu_k f_k \mathbb{E}\left[s^{G_k}\right] \\ &= \sum_{i=1}^{k} \mu_i f_i \phi_i(s)\end{aligned}$$

So comparing the heterogeneous model with the homogeneous model is equivalent to comparing two different homogeneous models with each other. Therefore it suffices to check that $\hat{\phi}(s) \leq \phi(s)$ for all $s \in [0,1)$. Equivalently, we can in a similar fashion to Marschner define a function for the heterogeneous model ϕ by

$$\phi(s) = \mathbb{E}\left[\sum_{i=1}^{k} \mu_i f_i e^{\frac{\beta}{k}\lambda_i I(s-1)}\right].$$

4.3.4.2 General Proof

To show that the probability of emergence is always less for a heterogeneous model than a homogeneous model, for k groups we can adapt an argument from Becker & Marschner [24]. Marschner defines R_0 in the same sense as in this chapter, as the maximum eigenvalue of the infectivity matrix. In the separable case (but not otherwise) this is the sum of the diagonal entries of the infectivity matrix

$$R_0 = \sum_{i=1}^{k} \beta_{ii}.$$

Marschner defines q_i as the unconditional probability that an epidemic started by a single infective is a minor epidemic, given the initial infective is of type i. He defines the unconditional probability that an epidemic started by a single infective is a minor epidemic as

$$q = 1 - P(Em) = \sum_{i=1}^{k} p_i q_i = \sum_{i=1}^{k} \mu_i f_i q_i$$

where p_i denotes the probability that the single infective starts in group i.

We denote by I the duration of the infectious period for a particular infective of type i, and G_{ij} the number of individuals of type j infected by this infective.

We assume that given I, the $G_{i1}, \ldots, G_{ik}$ are independent Poisson variables with means $\lambda_i \mu_1 f_1 I, \ldots, \lambda_i \mu_k f_k I$, respectively for k groups and that the duration I has the same distribution for all types. So we have that G_1 which is the number of offspring from a G_1 individual is equivalent to $G_{11} + \cdots + G_{1k}$ which is the number of types of G_1 individuals. Then the extinction probabilities satisfy

$$q_i = \phi_i(\mathbf{q}) = \mathbb{E}\left[e^{\frac{\beta}{k}\lambda_i I \sum_{j=1}^{k} \mu_j f_j (q_j - 1)}\right]. \tag{4.9}$$

provided I is random. If I is constant then $q_i = e^{-\beta \lambda_i I \sum_{j=1}^{k} \mu_j f_j (q_j - 1)/k}$. Following Athreya and Ney [12], pg. 168 we can argue that

$$\begin{aligned} q &= \mathbb{E}\left[\sum_{i=1}^{k} \mu_i f_i e^{\frac{\beta}{k}\lambda_i I \sum_{j=1}^{k} \mu_j f_j (q_j - 1)}\right] \\ &= \mathbb{E}\left[\sum_{i=1}^{k} \mu_i f_i e^{\frac{\beta}{k}\lambda_i I (q - 1)}\right]. \end{aligned}$$

It is important at this stage to highlight the difference between how Marschner constructs his homogeneous model and how we do so. Marschner defines single parameters μ and λ to be the average of the susceptibilities and infectivities (which he allows to vary over time) respectively. He then inserts these parameters into his homogeneous model with an interest in the effect on R_0. This is equivalent to setting $\mu_i = \lambda_i = 1 \quad \forall i \Rightarrow R_0 = \beta \sum_{i=1}^{k} f_i = \beta$ and so his homogeneous model is given by $\phi_0(s) = \mathbb{E}\left[e^{\beta I (s-1)}\right]$. We, on the other hand, don't set such a constraint. In our case we start with a heterogeneous model, calculate R_0, then calculate a homogeneous model with the same R_0 and infectious period. We deliberately fix R_0 so that it is the same for both models, ie. $R_0 = \beta \sum_{i=1}^{k} \lambda_i \mu_i f_i$. This homogeneous model is given by

$$\hat{\phi}(s) = \mathbb{E}[e^{R_0(s-1)}] = \mathbb{E}\left[e^{\frac{\beta}{k}\sum_{i=1}^{k} \lambda_i \mu_i f_i (s-1)}\right].$$

In the same fashion, we compare the smaller roots of the equations $s = \phi(s)$ and $s = \hat{\phi}(s)$. Jensen's inequality (see [76], pg. 454) states that, for a general convex function, $g\left(\frac{\sum a_i x_i}{\sum a_i}\right) \leq \frac{\sum a_i g(x_i)}{\sum a_i}$, where a_i represents positive weights and the x_i are numbers in the domain of a real convex function g. By taking $a_i = \mu_i f_i$ and $x_i = \lambda_i$ we get

$$\begin{aligned} g\left(\frac{\sum \mu_i f_i \lambda_i}{\sum \mu_i f_i}\right) &\leq \frac{\sum \mu_i f_i g(\lambda_i)}{\sum \mu_i f_i} \\ \Rightarrow \quad g\left(\sum \mu_i f_i \lambda_i\right) &\leq \sum \mu_i f_i g(\lambda_i) \\ \Rightarrow \quad \exp\{\tfrac{\beta}{k} I (s-1) \textstyle\sum \lambda_i \mu_i f_i\} &\leq \sum \mu_i f_i \exp\{\tfrac{\beta}{k} I \lambda_i (s-1)\} \\ \Rightarrow \quad \mathbb{E}\left[\exp\{\tfrac{\beta}{k} I (s-1) \textstyle\sum \lambda_i \mu_i f_i\right] &\leq \mathbb{E}\left[\sum \mu_i f_i \exp\{\tfrac{\beta}{k} I \lambda_i (s-1)\}\right] \\ \Rightarrow \quad \hat{\phi}(s) &\leq \phi(s) \qquad \text{for } 0 \leq s \leq 1. \end{aligned}$$

In terms of Marschner's comparison, at this stage he uses the result to conclude that the smaller root of the heterogeneous model will be greater than that of his homogeneous model under certain constraints, hence the probability of a minor outbreak is greater for a heterogeneous community. That is, P(Emergence) is less for a heterogeneous community than for a homogeneous community.

In terms of our comparison, we can conclude that P(Emergence) is always less for a heterogeneous community than for a homogeneous community with the same R_0 value.

Using a similar argument we can reach the same conclusion for a non-separable model. Following Marschner, assuming a general infectious period, we have

$$q_i = \mathbb{E}\left[exp\left\{\sum_{j=1}^{k}\beta_{ij}(q_j-1)I\right\}\right]$$

where q_i is the extinction probability, $\beta_{ij} = \beta\lambda_i\pi_{ij}\mu_j f_j$ and I is the infectious period. We also have that

$$P(Emergence) = 1 - \sum_{j=1}^{k} q_j p_j \quad \text{where} \quad \sum_{j=1}^{k} p_j = 1.$$

This is true provided p_j is the probability that the initial infective is in group j. Suppose now we take $\mathbf{p}$ to be an eigenvector of B with eigenvalue R_0. So

$$\begin{aligned} q \;\; &= 1 - P(Emergence) \;\; = \textstyle\sum_{i=1}^{k} p_i q_i \\ q \;\; &= \textstyle\sum_{i=1}^{k} p_i \mathbb{E}\left[exp\{I\sum_{j=1}^{k}\beta_{ij}(q_j-1)\}\right]. \end{aligned} \tag{4.10}$$

We saw previously at this stage, Marschner finds a function $\phi(s)$ such that $\phi(q) = q$ for the separable model and compares with $\phi_0(s) = exp\{R_0(s-1)\}$. The homogeneous model has $\phi_0(q_0) = q_0$ and he shows that $\phi(s) \geq \phi_0(s)$ for all s and from this it follows that $q \geq q_0$. For our more general model, there is no such function $\phi(s)$, but we do have relationship (4.10), and want to show $q \geq q_0$.

Let us write $\Psi(\theta) = \mathbb{E}\left[e^{-\theta I}\right]$. Then Ψ is convex. Given one initial infective, in group i with probability p_i, then the overall extinction probability is given by

$$q = \sum_{i=1}^{k} p_i q_i = \sum_{i=1}^{k} p_i \Psi\left(\sum_{j=1}^{k}\beta_{ij}(1-q_j)\right).$$

Using Jensen's formula which states $g\left(\sum_{i=1}^{k} p_i x_i\right) \leq \sum_{i=1}^{k} p_i g(x_i)$ for convex g by

taking $g(x) = \Psi(x)$ and $x_i = I\sum_{j=1}^{k}\beta_{ij}(1-q_j)$, then

$$\begin{aligned} q = \sum_{i=1}^{k} p_i g(x_i) \geq & \; g\left(\sum_{i=1}^{k} p_i x_i\right) \\ = & \; \Psi\left(\sum_{i=1}^{k} p_i \sum_{j=1}^{k}\beta_{ij}(1-q_j)\right) \\ = & \; \Psi\left(\sum_{i=1}^{k}\sum_{j=1}^{k} p_i\beta_{ij}(1-q_j)\right). \end{aligned}$$

Let us take $(p_1, \ldots, p_k)$ to be an eigenvector of $\{\beta_{ij}\}$, with

$$\sum_{i=1}^{k} p_i\beta_{ij} = R_0 p_j.$$

Therefore $\mathbf{p}$ is an eigenvector corresponding to some eigenvalue of the infection rate matrix. For primitive and irreducible matrices, this has to be the dominant eigenvalue (ie. R_0) in order to have a strictly positive eigenvector, which is why we can take our eigenvector to be a probability vector. This eigenvector in fact corresponds to a state probability vector for which the process settles down to. We now have

$$\begin{aligned} q \; & \geq \Psi\left(\sum_{j=1}^{k} R_0 p_j(1-q_j)\right) \\ & = \Psi\left(R_0\left(\sum_{j=1}^{k} p_j\right) - R_0\left(\sum_{j=1}^{k} p_j q_j\right)\right) \end{aligned}$$

Recall that $\sum_{j=1}^{k} p_j = 1$ and that $q = \sum_{j=1}^{k} p_j q_j$ so that

$$q \geq \Psi\left(R_0\left(1 - \sum_{j=1}^{k} p_j q_j\right)\right) = \Psi\left(R_0(1-q)\right),$$

and for the corresponding homogeneous model, the extinction probability satisfies

$$q_0 = \Psi(R_0(1-q_0)).$$

In order to argue that this shows $q \geq q_0$ note that $f(s) = \Psi(R_0(1-s))$ is an increasing function that crosses the 45^o line at points q_0 and at 1 with it lying above this line between 0 and q_0, and below it between q_0 and 1. It is this part of the function curve we are interested in and so the solution lies between q_0 and 1. If we have that q is greater than or equal to this function, then it follows that $q \geq q_0$.

What we have argued here is that the emergence probability for a k-group non-separable heterogeneous model will always be less than or equal to the emergence probability of a corresponding non-separable homogeneous model with the same R_0 value, where the initial infective starts in group i with probabilities given by the eigenvector p_i, corresponding to eigenvalue R_0, for any infectious period.

4.4 Comparing two heterogeneous populations

4.4.1 Majorization and p-majorization results

We showed in section 4.3.4.2 that comparing a homogeneous process to a heterogeneous one was equivalent to showing that

$$\mathbb{E}\left[\exp\{\frac{\beta}{k}I\sum_{i=1}^{k}\lambda_i\mu_i f_i(s-1)\}\right] \quad \leq \quad \mathbb{E}\left[\sum_{i=1}^{k}\mu_i f_i e^{\frac{\beta}{k}I\lambda_i(s-1)}\right].$$

By taking $\phi(x) = e^{\frac{\beta I}{k}(s-1)x}$, $x_i = \lambda_i, a_i = \mu_i f_i$ noting that $\sum_{i=1}^{k}\mu_i f_i = 1$ and applying Jensen's inequality we obtain the result of section 4.3.4.2 in the separable case. We have also shown earlier that heterogeneity in susceptibility alone has no effect on emergence probability.

Our interest is now in comparing two heterogeneous models to each other and using majorization as a tool to show that orderings in emergence probabilities exist under certain circumstances.

In section 4.3.3, we used majorization to show that if $\mu_i f_i = \frac{1}{k}$ for all i then the probability of emergence for the heterogeneous model (with heterogeneity in $\boldsymbol{\lambda}$ only) is less than or equal to the probability of emergence for the homogeneous model. The proof depended upon the observation that for any $\boldsymbol{\lambda}$ we have $\frac{1}{k}\left(\sum_{i=1}^{k}\lambda_i\right)\mathbf{1} \prec \boldsymbol{\lambda}$.

Consider now two heterogeneous populations, each with $\mu_i f_i = \frac{1}{k}$ for all i, but with different infectivity vectors $\boldsymbol{\lambda}$ and $\boldsymbol{\delta}$. Define generating functions

$$\phi^{(\lambda)}(s) = \mathbb{E}\left[\frac{1}{k}\sum_{i=1}^{k}e^{\frac{\beta}{k}\lambda_i I(s-1)}\right],$$

$$\phi^{(\delta)}(s) = \mathbb{E}\left[\frac{1}{k}\sum_{i=1}^{k}e^{\frac{\beta}{k}\delta_i I(s-1)}\right].$$

Arguing as in section 4.3.3, the extinction probabilities for the two populations, given an initial infective in group i with probability $\mu_i f_i = \frac{1}{k}$, satisfy

$$q^{(\lambda)} = \phi^{(\lambda)}\left(q^{(\lambda)}\right) \quad \text{and} \quad q^{(\delta)} = \phi^{(\delta)}\left(q^{(\delta)}\right).$$

Suppose that $\boldsymbol{\lambda} \prec \boldsymbol{\delta}$. The function $\Psi(\theta) = \mathbb{E}\left[e^{-\theta I}\right]$ is convex, and

$$\phi^{(\lambda)}(s) = \frac{\beta}{k}\sum_{i=1}^{k}\Psi\left(\frac{\beta}{k}\lambda_i(1-s)\right).$$

Now $\boldsymbol{\lambda} \prec \boldsymbol{\delta}$ implies $\frac{\beta}{k}(1-s)\boldsymbol{\lambda} \prec \frac{\beta}{k}(1-s)\boldsymbol{\delta}$, so by the Proposition of section 4.3.3 we have

$$\phi^{(\boldsymbol{\lambda})}(s) \quad \leq \quad \phi^{(\boldsymbol{\delta})}(s) \quad \text{for} \quad 0 \leq s \leq 1.$$

Consequently, we have

$$q^{(\boldsymbol{\lambda})} = \phi^{(\boldsymbol{\lambda})}\left(q^{(\boldsymbol{\lambda})}\right) \quad \leq \quad \phi^{(\boldsymbol{\delta})}\left(q^{(\boldsymbol{\lambda})}\right).$$

Arguing as in section 4.3.4.2, the inequality $q^{(\boldsymbol{\lambda})} \leq \phi^{(\boldsymbol{\delta})}\left(q^{(\boldsymbol{\lambda})}\right)$ implies that $q^{(\boldsymbol{\lambda})}$ is less than or equal to the fixed point of the function $\phi^{(\boldsymbol{\delta})}$. That is,

$$q^{(\boldsymbol{\lambda})} \quad \leq \quad q^{(\boldsymbol{\delta})}.$$

Since the emergence probability is $1-q$, we have now shown that

$$\boldsymbol{\lambda} \prec \boldsymbol{\delta} \quad \Rightarrow \quad P_{\boldsymbol{\lambda}}(Em) \quad \geq \quad P_{\boldsymbol{\delta}}(Em).$$

That is, if heterogeneity is only in infectivity, then the 'less heterogeneous' population has the greater emergence probability.

Note that if groups are equally sized ($f_i = \frac{1}{k}$ for all i) then the constraint $\sum_{i=1}^{k} \lambda_i f_i = 1$ together with the condition $\boldsymbol{\lambda} \prec \boldsymbol{\delta}$ imply automatically that $\sum_{i=1}^{k} \delta_i f_i = 1$. If the groups are not of equal size, then the constraints $\sum_{i=1}^{k} \lambda_i f_i = \sum_{i=1}^{k} \delta_i f_i = 1$ must be checked separately.

Figures (4.12) and (4.13) show numerical results for the probability of emergence in comparing heterogeneous 2-group models to each other under various conditions. Firstly, we look at a 2-group model where a constant infectious period is assumed and group sizes are equal. We fix the susceptibility of each group to be equal but vary the infectivities, so that we have a 2-group model with heterogeneity in infectivity alone. We then compare this to other 2-group models with the same properties *except* the infectivity vector differs from that of the first in accordance with majorization constraints.

It is clear from the definition of majorization that $(1,1) \prec (1.2, 0.8) \prec \cdots \prec (1.8, 0.2)$. From Figures (4.12) and (4.13) we see that the most 'spread out' infectivity vector yields the lowest probability of emergence. In other words, the higher the degree of heterogeneity in infectivity, when susceptibility is homogeneous, the lower the emergence probability. This observation holds, as shown by Figures (4.12) and (4.13) when either a constant or exponential infectious period is assumed.

Consider now heterogeneity in both infectivity and susceptibility. We can write the generating functions of two heterogeneous models as

$$\phi^{(\boldsymbol{\lambda},\boldsymbol{\mu},\mathbf{f})}(s) = \sum_{i=1}^{k} \mu_i f_i \Psi\left(\frac{\beta}{k}\lambda_i(s-1)\right) \quad \text{and} \quad \phi^{(\boldsymbol{\delta},\boldsymbol{\psi},\boldsymbol{\rho})}(s) = \sum_{i=1}^{k} \psi_i \rho_i \Psi\left(\frac{\beta}{k}\delta_i(s-1)\right)$$

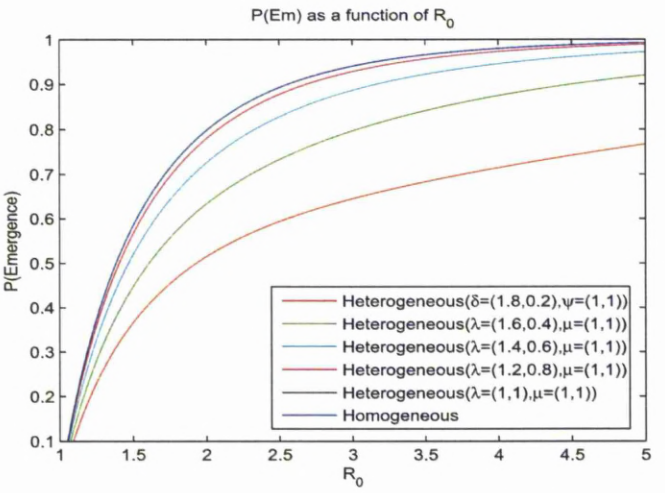

Figure 4.12: P(Emergence) for models with heterogeneity in infectivity, assuming constant infectious period. Group sizes are equal. Parameters: $\mu = (1, 1), \mathbf{f} = \rho = (0.5, 0.5), \delta = (1.8, 0.2), \lambda = (1.6, 0.4), (1.4, 0.6), (1.2, 0.8), (1, 1)$.

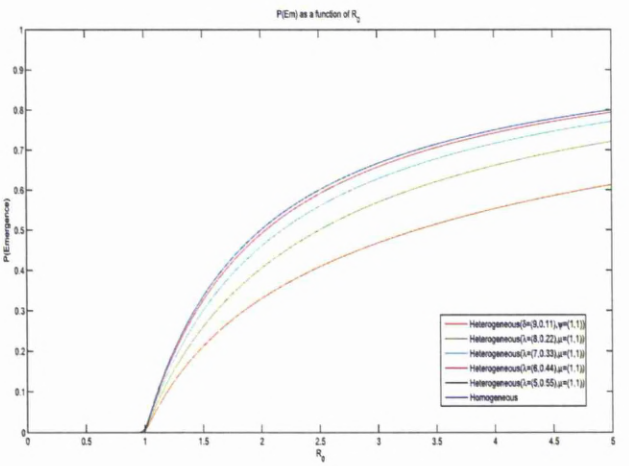

Figure 4.13: P(Emergence) for models with heterogeneity in infectivity, assuming exponential infectious period. Group sizes are equal. Parameters: $\mu = (1, 1), \mathbf{f} = \rho = (0.5, 0.5), \delta = (1.8, 0.2), \lambda = (1.6, 0.4), (1.4, 0.6), (1.2, 0.8), (1, 1)$.

where δ_i denotes the infectivity of a group i individual, ψ_i the susceptibility of a group i individual and ρ_i the relative frequency of group i, all these parameters being in our second heterogeneous model.

Recall we impose constraints $\sum_{i=1}^{k} \mu_i f_i = \sum_{i=1}^{k} \psi_i \rho_i = 1$. If we set $c_i = \mu_i f_i$ and $d_i = \psi_i \rho_i$ then our interest is in comparing

$$\sum_{i=1}^{k} c_i \Psi(K\lambda_i) \quad \text{with} \quad \sum_{i=1}^{k} d_i \Psi(K\delta_i)$$

where $K = \frac{\beta}{k}(s-1)$ subject to the conditions that $\sum c_i = \sum d_i = 1$, $\sum \lambda_i f_i = \sum \delta_i \rho_i = 1$ and $\sum c_i \lambda_i = \sum d_i \delta_i$. This latter condition ensures that the R_0 values for each model are the same.

Recall from definition 1 in section 4.3.3 that majorization is a partial ordering over vectors of real numbers. We now define **p-majorization.**

For any permutation π, write $x \in D^\pi$ to mean $x_{\pi_1} \geq \cdots \geq x_{\pi_n}$. When π is the identity permutation, $D^\pi = D$ where $D = \{(x_1, \ldots, x_n) : x_1 \geq \cdots \geq x_n\}$. We appeal to definition A.2 in [76], pg. 418 which states that for **any real numbers** $p_1, \ldots, p_n$, $\mathbf{x}$ is said to be **p-majorized by** $\mathbf{y}$ on D^π, written $\mathbf{x} \prec_{\mathbf{p}} \mathbf{y}$ on D^π, if

$$\sum_{1}^{k} p_{\pi_i} x_{\pi_i} \leq \sum_{1}^{k} p_{\pi_i} y_{\pi_i} \quad k = 1, \ldots, n-1,$$

$$\sum_{1}^{n} p_{\pi_i} x_{\pi_i} = \sum_{1}^{n} p_{\pi_i} y_{\pi_i}.$$

Further, Propositions A.3 and A.3.a on pg. 419 of [76] state that if $p_1, \ldots, p_n > 0$ then $\mathbf{x} \prec_{\mathbf{p}} \mathbf{y}$ on D^π for any permutation π if and only if

$$\sum_{1}^{n} p_i \phi(x_i) \quad \leq \quad \sum_{1}^{n} p_i \phi(y_i)$$

for all continuous convex functions $\phi : \mathbb{R} \to \mathbb{R}$, and Proposition A.1.a on pg. 418 of [76] states that this is equivalent to the existence of an $n \times n$ matrix $A = \{a_{ij}\}$ with the properties

$$\begin{array}{ll} (i) & a_{ij} \geq 0 \text{ for all } i, j \\ (ii) & \mathbf{e}A = \mathbf{e} \text{ where } \mathbf{e} = (1, \ldots, 1) \\ (iii) & A\mathbf{p}' = \mathbf{p}' \end{array}$$

such that $\mathbf{x} = \mathbf{y}A$.

In our case, p_i corresponds to $c_i = d_i$, $\mathbf{x} = \boldsymbol{\lambda}, \mathbf{y} = \boldsymbol{\delta}$. This allows us to fix the susceptibility vectors for both heterogeneous models so that they are equal to each other and then vary the infectivity vectors and see how this affects the probability of emergence. The definitions above show that $\mathbf{x}$ being **p**-majorized by $\mathbf{y}$ is equivalent to finding a matrix A with $\mathbf{x} = \mathbf{y}A$ such that constraints $(i) - (iii)$ hold. Constraints $(i) - (iii)$ require us to be able to solve a system of equations for a feasible A matrix such that its entries are greater than or equal to zero, the columns sum to 1 and $Ac' = c'$ can be solved such that we can satisfy $\boldsymbol{\lambda} = \boldsymbol{\delta}A$.

For our k-group epidemic model, these conditions can be written as

$$\sum_{j=1}^{k} a_{ij}\mu_j f_j = \mu_i f_i \quad \text{and} \quad \sum_{j=1}^{k} a_{ji}\delta_j = \lambda_i \qquad \text{for } i = 1, 2, \ldots, k.$$

With $\phi(x) = \Psi\left(\frac{\beta}{k}(s-1)x\right)$ then

$$\phi^{(\boldsymbol{\lambda},\boldsymbol{\mu},\mathbf{f})}(s) = \sum_{i=1}^{k} \mu_i f_i \Psi(\lambda_i)$$

so that $\boldsymbol{\lambda} \prec_{\mathbf{c}} \boldsymbol{\delta}$ implies $\phi^{(\boldsymbol{\lambda},\boldsymbol{\mu},\mathbf{f})}(s) \leq \phi^{(\boldsymbol{\delta},\boldsymbol{\mu},\mathbf{f})}(s)$ for $0 \leq s \leq 1$. Arguing as before it then follows that $P_{\boldsymbol{\lambda},\boldsymbol{\mu},\mathbf{f}}(Em) \geq P_{\boldsymbol{\delta},\boldsymbol{\mu},\mathbf{f}}(Em)$.

Examining two-group models, $k = 2$, with $\pi_{ij} = f_i = \frac{1}{2}$ for all i, j we have constraints $\mu_1 + \mu_2 = 2, \lambda_1 + \lambda_2 = 2$ and

$$\begin{aligned} R_0 &= \tfrac{\beta}{4}(\mu_1\lambda_1 + \mu_2\lambda_2) &&= \tfrac{\beta}{4}(\mu_1\lambda_1 + (2-\mu_1)(2-\lambda_1)) \\ &&&= \tfrac{\beta}{4}(4 + 2\mu_1\lambda_1 - 2\mu_1 - 2\lambda_1) \\ &&&= \beta + \tfrac{\beta}{2}(\mu_1\lambda_1 - \mu_1 - \lambda_1) \end{aligned}$$

We fix $\boldsymbol{\mu}$, vary $\boldsymbol{\lambda}$ and examine the effect on R_0 with the interest of comparing $(\boldsymbol{\mu}, \boldsymbol{\lambda})$ with $(\boldsymbol{\mu}, \boldsymbol{\delta})$.

$$\begin{aligned} R_0^{\boldsymbol{\lambda}} - R_0^{\boldsymbol{\delta}} &= \tfrac{\beta}{2}((\mu_1\lambda_1 - \mu_1 - \lambda_1) - (\mu_1\delta_1 - \mu_1 - \delta_1)) \\ &= \tfrac{\beta}{2}(\mu_1(\lambda_1 - \delta_1) - (\lambda_1 - \delta_1)) \\ &= \tfrac{\beta}{2}(\mu_1 - 1)(\lambda_1 - \delta_1) \end{aligned}$$

For the case $\mu_1 = 1$, we note that this has been dealt with previously by ordinary majorization. For the case $\mu_1 \neq 1$, the constraint $R_0^{\boldsymbol{\lambda}} = R_0^{\boldsymbol{\delta}}$ implies $\boldsymbol{\lambda} = \boldsymbol{\delta}$ and so there is no point trying to use **p**-majorization, because the only way to get $R_0^{\boldsymbol{\lambda}} = R_0^{\boldsymbol{\delta}}$ is to take $\boldsymbol{\lambda} = \boldsymbol{\delta}$, so the comparison becomes trivial.

For $k = 2$, with $\pi_{ij} = \frac{1}{2}$ for all i, j we have constraints $\mu_1 f_1 + \mu_2 f_2 = \lambda_1 f_1 + \lambda_2 f_2 = 1$ and $f_1 + f_2 = 1$. That is,

$$\begin{cases} \mu_1 f_1 + \mu_2(1 - f_1) = 1 \\ \lambda_1 f_1 + \lambda_2(1 - f_1) = 1 \end{cases} \Rightarrow \quad \mu_2 = \tfrac{1}{1-f_1}(1 - \mu_1 f_1)$$

$$\begin{aligned}
R_0 &= \tfrac{\beta}{2}(\mu_1\lambda_1 f_1 + \mu_2\lambda_2 f_2) \\
&= \tfrac{\beta}{2}(\mu_1\lambda_1 f_1 + \mu_2(1-\lambda_1 f_1)) \\
&= \tfrac{\beta}{2}(\mu_1\lambda_1 f_1 + \tfrac{1}{1-f_1}(1-\mu_1 f_1)(1-\lambda_1 f_1)) \\
&= \tfrac{\beta}{2}\left(\tfrac{1}{1-f_1}\right)(\mu_1\lambda_1 f_1(1-f_1) + (1-\mu_1 f_1)(1-\lambda_1 f_1)) \\
&= \tfrac{\beta}{2}\left(\tfrac{1}{1-f_1}\right)(\mu_1\lambda_1 f_1(1-f_1) + 1 - \mu_1 f_1 - \lambda_1 f_1 + \mu_1\lambda_1 f_1^2) \\
&= \tfrac{\beta}{2}\left(\tfrac{1}{1-f_1}\right)(\mu_1\lambda_1 f_1 + 1 - (\mu_1+\lambda_1) f_1) \\
&= \tfrac{\beta}{2}\left(\tfrac{f_1}{1-f_1}\right)(\tfrac{1}{f_1} + \mu_1\lambda_1 - \mu_1 - \lambda_1)
\end{aligned}$$

If we keep $\mathbf{f}$ and μ fixed, but vary $\boldsymbol{\lambda}$

$$\begin{aligned}
R_0^{(\lambda)} - R_0^{(\delta)} &= \tfrac{\beta}{2}\left(\tfrac{1}{1-f_1}\right)((\mu_1\lambda_1 - \mu_1 - \lambda_1) - (\mu_1\delta_1 - \mu_1 - \delta_1)) \\
&= \tfrac{\beta}{2}\left(\tfrac{f_1}{1-f_1}\right)(\mu_1 - 1)(\lambda_1 - \delta_1)
\end{aligned}$$

Again, constraint $R_0^{(\lambda} = R_0^{(\delta)}$ implies $\boldsymbol{\lambda} = \boldsymbol{\delta}$, for $\mu_1 \neq 1$.

The observation of interest is that in comparing heterogeneous models with $k = 2$ groups the only way to allow for heterogeneity in infectivity between the models is by having homogeneous susceptibility in each model.

For $k = 3$ where $\pi_{ij} = f_i = \frac{1}{3}$ for all i, j we have for general μ

$$\begin{cases}
\lambda_1 & \leq & \delta_1 \\
\mu_1\lambda_1 + \mu_2\lambda_2 & \leq & \mu_1\delta_1 + \mu_2\delta_2 \\
\mu_1\lambda_1 + \mu_2\lambda_2 + \mu_3\lambda_3 & = & \mu_1\delta_1 + \mu_2\delta_2 + \mu_3\delta_3
\end{cases}$$

where the third constraint, using the fact that $\lambda_3 = 3 - \lambda_1 - \lambda_2$, implies that

$$(\mu_1 - \mu_3)\lambda_1 + (\mu_2 - \mu_3)\lambda_2 = (\mu_1 - \mu_3)\delta_1 + (\mu_2 - \mu_3)\delta_2$$

$$\Rightarrow \quad \lambda_2 = \delta_2 + \left(\frac{\mu_1 - \mu_3}{\mu_2 - \mu_3}\right)(\delta_1 - \lambda_1)$$

and the second constraint becomes

$$\mu_1\lambda_1 + \mu_2\left(\delta_2 + \left(\frac{\mu_1 - \mu_3}{\mu_2 - \mu_3}\right)(\delta_1 - \lambda_1)\right) \quad \leq \quad \mu_1\delta_1 + \mu_2\delta_2$$

$$\lambda_1\left(\mu_1 - \mu_2\left(\frac{\mu_1 - \mu_3}{\mu_2 - \mu_3}\right)\right) \quad \leq \quad \delta_1\left(\mu_1 - \mu_2\left(\frac{\mu_1 - \mu_3}{\mu_2 - \mu_3}\right)\right)$$

so $\mu_2 - \mu_3 \geq 0$ and

$$\begin{aligned}
\lambda_1(\mu_1(\mu_2 - \mu_3) - \mu_2(\mu_1 - \mu_3)) &\leq \delta_1(\mu_1(\mu_2 - \mu_3) - \mu_2(\mu_1 - \mu_3)) \\
\lambda_1(-\mu_1\mu_3 + \mu_2\mu_3) &\leq \delta_1(-\mu_1\mu_3 + \mu_2\mu_3) \\
\lambda_1(\mu_2 - \mu_1) &\leq \delta_1(\mu_2 - \mu_1)
\end{aligned}$$

so $\mu_2 \geq \mu_3$. To avoid $\boldsymbol{\lambda} = \boldsymbol{\mu}$, we require $\mu_2 \geq \mu_1$ if $\mu_2 \geq \mu_3$. Note $\lambda_1 \geq \lambda_2 \geq \lambda_3$ and $\delta_1 \geq \delta_2 \geq \delta_3$. Either $\mu_2 \geq \mu_3$ and $\mu_2 \geq \mu_1$ or $\mu_2 \leq \mu_3$ and $\mu_2 \leq \mu_1$.

Figure (4.14) plots the emergence probabilities for two heterogeneous 3-group models for both an exponential and constant infectious period. The solid lines represent emergence probabilities for a constant infectious period and we see that the model with the most 'spread out' infectivity vector yields consistently the smallest emergence probability between the two across the R_0 range. The dotted lines represent emergence probabilities assuming an exponential infectious period and again we see the same ordering. We use parameter values $\mu = (0.5, 1.5, 1), \boldsymbol{\lambda} = (1.6, 1.1, 0.3), \delta = (1.5, 1, 0.5)$. A feasible matrix for these parameters under **p**-majorization conditions is $A = \begin{bmatrix} 12/13 & 1/39 & 0 \\ 0 & 5/6 & 1/4 \\ 1/13 & 11/78 & 3/4 \end{bmatrix}$, and $\delta \prec_\mu \boldsymbol{\lambda}$. This numerical example highlights the fact that for $k \geq 3$, we don't require uniform susceptibilities in order to find non-uniform infectivity vectors which satisfy **p**-majorization conditions, unlike the 2-group case.

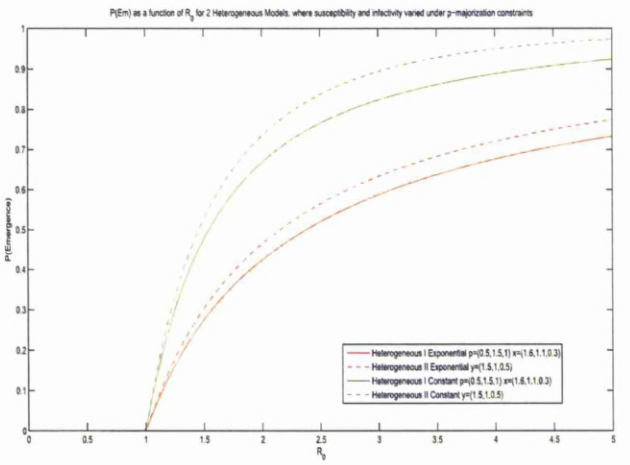

Figure 4.14: P(Emergence) for 3-group models where $\delta \prec_\mu \boldsymbol{\lambda}$ for different parameter values assuming constant and exponential infectious periods. Group sizes are equal. Parameters: $\boldsymbol{\mu} = (0.5, 1.5, 1), \boldsymbol{\lambda} = (1.6, 1.1, 0.3), \delta = (1.5, 1, 0.5)$.

We can also show that under **p**-majorization constraints, the emergence probability for a homogeneous model always bounds from above that of any heterogeneous model. Let us start with comparing two heterogeneous 2-group models and suppose the ordering is such that $\lambda_1 \geq \lambda_2$ and $\delta_1 \geq \delta_2$. The **p**-majorization definition then stipulates that $c_1\lambda_1 \leq c_1\delta_1$ and $c_1\lambda_1 + c_2\lambda_2 = c_1\delta_1 + c_2\delta_2$ in order

for $\boldsymbol{\lambda} \prec_{\mathbf{p}} \boldsymbol{\delta}$. Let us fix $\mathbf{c}$, so that the susceptibility vectors for each heterogeneous group are the same, and fix $\boldsymbol{\lambda}$ so we can vary the infectivities of the second heterogeneous group and examine its effect. We have that $\lambda_1 \leq \delta_1$ and

$$\delta_2 = \frac{c_1(\lambda_1 - \delta_1) + c_2\lambda_2}{c_2} = \frac{c_1}{c_2}(\lambda_1 - \delta_1) + \lambda_2$$

Suppose $\delta_1 = \delta_2$ and $\boldsymbol{\lambda} \prec_{\mathbf{p}} \boldsymbol{\delta}$, with $\lambda_1 \geq \lambda_2$. Then $c_1\lambda_1 + c_2\lambda_2 = (c_1 + c_2)\delta_1$. Rearranging

$$\delta_1 = \frac{c_1}{c_1 + c_2}\lambda_1 + \frac{c_2}{c_1 + c_2}\lambda_2$$

with the ordering condition that $\lambda_1 \leq \delta_1$. This implies that $\lambda_2 \geq \delta_1$. But then we have that $\lambda_2 \geq \delta_1 \geq \lambda_1$. But it is already a condition that $\lambda_1 \geq \lambda_2$ for p-majorization to hold so $\lambda_1 = \lambda_2$. From this it is clear that

$$\boldsymbol{\lambda} \prec_{\mathbf{p}} \delta\mathbf{1}$$

is only possible if $\boldsymbol{\lambda} = \delta\mathbf{1}$. A natural question to ask here is whether it is true that $\delta\mathbf{1} \prec_{\mathbf{p}} \boldsymbol{\lambda}$ for every $\boldsymbol{\lambda}$ with $\lambda_1 \geq \lambda_2$ and $c_1\lambda_1 + c_2\lambda_2 = (c_1 + c_2)\delta$?

In this case

$$\delta = \frac{c_1}{c_1 + c_2}\lambda_1 + \frac{c_2}{c_1 + c_2}\lambda_2$$

so $\lambda_1 \geq \delta_2$ and $\lambda_1 \geq \delta_1$. So $\delta\mathbf{1} \prec_{\mathbf{p}} \boldsymbol{\lambda}$ for all $\boldsymbol{\lambda}$ with $c_1\lambda_1 + c_2\lambda_2 = c_1\delta_1 + c_2\delta_2$. In other words, for 2-dimensional vectors, $\delta\mathbf{1}$ is the $\prec_{\mathbf{p}}$-minimal element. In other words, for any $\mathbf{p}$, the uniform distribution is $\prec_{\mathbf{p}}$-minimal, in the sense that for any $\boldsymbol{\delta}$ we have $\epsilon\mathbf{1} \prec_{\mathbf{p}} \boldsymbol{\delta}$ for some ϵ.

We can generalize this argument to a k-group situation. Under p-majorization conditions, a k-group population will be subject to k constraints, those being;

$$\begin{array}{lrcl}
(1) & \sum_{i=1}^{k} c_i\lambda_i & = & \sum_{i=1}^{k} c_i\delta_i \\
(2) & \sum_{i=1}^{1} c_i\lambda_i & \leq & \sum_{i=1}^{1} c_i\delta_i \\
(3) & \sum_{i=1}^{2} c_i\lambda_i & \leq & \sum_{i=1}^{2} c_i\delta_i \\
\vdots & & & \\
(k) & \sum_{i=1}^{k-1} c_i\lambda_i & \leq & \sum_{i=1}^{k-1} c_i\delta_i
\end{array}$$

We fix $\mathbf{c}$ and given any $\boldsymbol{\delta}$, with $\delta_1 \geq \delta_2 \geq \cdots \geq \delta_k$, set

$$\lambda_1 = \cdots = \lambda_k = \frac{c_1}{\sum_{i=1}^{k} c_i}\delta_1 + \frac{c_2}{\sum_{i=1}^{k} c_i}\delta_2 + \cdots + \frac{c_k}{\sum_{i=1}^{k} c_i}\delta_k = \sum_{i=1}^{k}\left(\frac{c_i}{\sum_{i=1}^{k} c_i}\delta_i\right) \tag{4.11}$$

Then $\boldsymbol{\lambda}$ satisfies $\lambda_1 \geq \lambda_2 \geq \cdots \geq \lambda_k$ and constraint (1) is satisfied. λ_1 is a weighted average of $(\delta_1, \delta_2, \ldots, \delta_k)$ so λ_1 lies in between the two extreme values $\delta_1 \geq \lambda_1 \geq \delta_k$ since λ_1 is a convex combination of $(\delta_1, \ldots, \delta_k)$ and hence constraint (2) is satisfied.

We argue as follows for the remainder of the constraints; Suppose $\sum_{i=1}^{j} c_i\lambda_i = \lambda_1 \sum_{i=1}^{j} c_i$. If $j = k-1$ then this equals

$$\begin{aligned} &\frac{c_1\sum_{i=1}^{k-1} c_i}{\sum_{i=1}^{k} c_i}\delta_1 + \frac{c_2\sum_{i=1}^{k-1} c_i}{\sum_{i=1}^{k} c_i}\delta_2 + \cdots + \frac{c_k\sum_{i=1}^{k-1} c_i}{\sum_{i=1}^{k} c_i}\delta_k \qquad (4.12)\\ &= \frac{\sum_{i=1}^{k-1} c_i}{\sum_{i=1}^{k} c_i}\sum_{i=1}^{k-1} c_i\delta_i + \frac{c_k}{\sum_{i=1}^{k} c_i}\sum_{i=1}^{k-1} c_i\delta_k \\ \leq\ &\frac{\sum_{i=1}^{k-1} c_i}{\sum_{i=1}^{k} c_i}\sum_{i=1}^{k-1} c_i\delta_i + \frac{c_k}{\sum_{i=1}^{k} c_i}\sum_{i=1}^{k-1} c_i\delta_i = \sum_{i=1}^{k-1} c_i\delta_i \end{aligned}$$

If $j = k-2$ then equation (4.12) becomes

$$\begin{aligned} &\frac{\sum_{i=1}^{k-2} c_i}{\sum_{i=1}^{k} c_i}\sum_{i=1}^{k-2} c_i\delta_i + \frac{c_{k-1}}{\sum_{i=1}^{k} c_i}\sum_{i=1}^{k-2} c_i\delta_{k-1} + \frac{c_k}{\sum_{i=1}^{k} c_i}\sum_{i=1}^{k-2} c_i\delta_k \\ \leq\ &\frac{\sum_{i=1}^{k-2} c_i}{\sum_{i=1}^{k} c_i}\sum_{i=1}^{k-2} c_i\delta_i + \frac{c_{k-1}}{\sum_{i=1}^{k} c_i}\sum_{i=1}^{k-2} c_i\delta_i + \frac{c_k}{\sum_{i=1}^{k} c_i}\sum_{i=1}^{k-2} c_i\delta_i \end{aligned}$$

So writing this in terms of any number of j constraints $1 \leq j \leq k-1$ for a k-group population, the j'th constraint can be written

$$\begin{aligned} &\frac{\sum_{i=1}^{j} c_i}{\sum_{i=1}^{k} c_i}\sum_{i=1}^{j} c_i\delta_i + \sum_{n=j+1}^{k}\left(\frac{c_n}{\sum_{i=1}^{k} c_i}\sum_{i=1}^{j} c_i\delta_n\right) \\ \leq\ &\frac{\sum_{i=1}^{j} c_i}{\sum_{i=1}^{k} c_i}\sum_{i=1}^{j} c_i\delta_i + \sum_{n=j+1}^{k}\left(\frac{c_n}{\sum_{i=1}^{k} c_i}\sum_{i=1}^{j} c_i\delta_i\right) \end{aligned}$$

So for a k-group population the remaining j constraints are satisfied hence, just as was the case for the 2-group, for a k-group population, for any δ, $\epsilon\mathbf{1} \prec_{\mathbf{p}} \delta$ where ϵ is given by equation (4.11).

A natural question to ask at this stage is what happens if $c_i \neq d_i$? Can an ordering on emergence probabilities still be found? In Figure (4.15) we fix our infectivity vector $\lambda = \delta$ to be $(1.6, 0.4)$ for a 2-group model so heterogeneity exists in infectivity, and we then compare this model against other models having different susceptibilities. We see that $P_{Het}(Em) \neq P_{Hom}(Em)$ and that we do have an ordering, but one which is different from previously. As shown in Figure (4.15), the more 'spread out' the susceptibility vector is, the higher the probability of emergence.

This suggests that if the infectivity vector is fixed but non-uniform and susceptibility vectors satisfy $(\mu_1, \mu_2) \prec (\psi_1, \psi_2)$ then $P_{(\mu_1,\mu_2)}(Em) \leq P_{(\psi_1,\psi_2)}(Em)$. This example would not satisfy p-majorization conditions of course but there is yet another type of majorization which could be used.

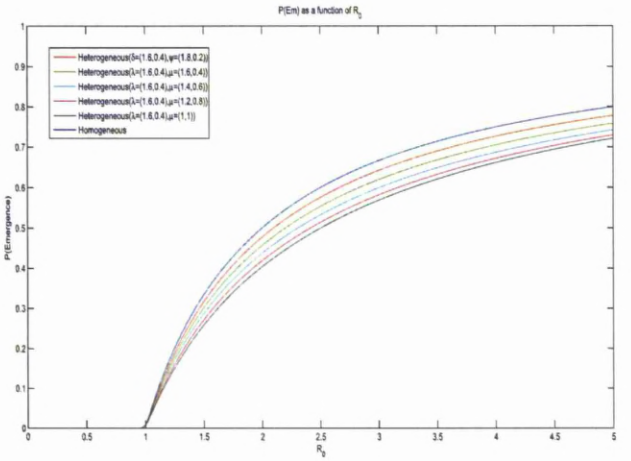

Figure 4.15: P(Emergence) for models where infectivity vector fixed, $(\lambda_1, \lambda_2) = (1.6, 0.4)$ and susceptibility vector (μ_1, μ_2) varies assuming exponential infectious period. Parameters: $\psi = (1.8, 0.2), \mu = (1.6, 0.4), (1.4, 0.6), (1.2, 0.8), (1, 1), \delta = \lambda = (1.6, 0.4), \mathbf{f} = \rho = (0.5, 0.5)$.

4.4.2 Probability of emergence and *pq*-majorization

A natural extension to these arguments is to consider comparing models of different susceptibility and infectivity vectors. There is a more general extension to the **p**-majorization conditions which again can be used to make inferences of the orderings of emergence probabilities. Blackwell's (1951) proposition, cited as Proposition A.1 on pg. 417 of [76], states

Let $c = (c_1, \ldots, c_n)$ and $d = (d_1, \ldots, d_m)$ be fixed vectors with nonnegative components such that $\sum_1^n c_i = \sum_1^m d_j = 1$. For $\boldsymbol{\lambda} \in \mathbb{R}^n, \boldsymbol{\delta} \in \mathbb{R}^m$,

$$\sum_1^n c_i \phi(\lambda_i) \quad \leq \quad \sum_1^m d_i \phi(\delta_i)$$

for all continuous convex functions $\phi : \mathbb{R} \to \mathbb{R}$ iff there exists an $m \times n$ matrix $A = \{a_{ij}\}$ with the properties

$$\begin{array}{ll} (i) & a_{ij} \geq 0 \text{ for all } i, j \\ (ii) & \mathbf{e}A = \mathbf{e} \text{ where } \mathbf{e} = (1, \ldots, 1) \\ (iii) & A\mathbf{c}' = \mathbf{d}' \end{array}$$

such that $\boldsymbol{\lambda} = \boldsymbol{\delta} A$.

In terms of our application, we now have a situation where one heterogeneous system doesn't have to contain the same number of groups as another, and that the susceptibility vectors of these systems do not have to be equal to one another.

For simplicity, we consider two groups ($k = 2$) with $f_1 = f_2 = \frac{1}{2}$. For our numerical results, we choose a non-uniform $\mu = (1.5, 0.5)$, and various non-uniform infectivity vectors δ. We then choose various matrices A satisfying conditions (i) and (ii). Finally, we can compute the corresponding ψ and λ using $\psi' = A\mu'$ and $\lambda = \delta A$. To ensure that the constraints $\sum \psi f_i = \sum \lambda_i f_i = 1$ we choose matrices A whose rows (as well as columns) sum to 1. We use the following four A matrices:

$$A_1 = \begin{bmatrix} 2/3 & 1/3 \\ 1/3 & 2/3 \end{bmatrix}, A_2 = \begin{bmatrix} 3/4 & 1/4 \\ 1/4 & 3/4 \end{bmatrix}, A_3 = \begin{bmatrix} 4/5 & 1/5 \\ 1/5 & 4/5 \end{bmatrix}, A_4 = \begin{bmatrix} 5/6 & 1/6 \\ 1/6 & 5/6 \end{bmatrix}.$$

It is important to mention that when $\mu = (1.5, 0.5)$ then under $A_1, \psi = (1.16, 0.833)$, under $A_2, \psi = (1.25, 0.75)$, under $A_3, \psi = (1.3, 0.7)$ and under $A_4, \psi = (1.33, 0.66)$.

(δ_1, δ_2)	(λ_1, λ_2) A_1	(λ_1, λ_2) A_2	(λ_1, λ_2) A_3	(λ_1, λ_2) A_4
(1.1, 0.9)	(1.03, 0.97)	(1.05, 0.95)	(1.06, 0.94)	(1.07, 0.93)
(1.2, 0.8)	(1.07, 0.93)	(1.1, 0.9)	(1.12, 0.88)	(1.13, 0.87)
(1.3, 0.7)	(1.1, 0.9)	(1.15,0.85)	(1.18, 0.82)	(1.2, 0.8)
(1.4, 0.6)	(1.13, 0.87)	(1.2, 0.8)	(1.24, 0.76)	(1.27, 0.73)
(1.5, 0.5)	(1.17, 0.83)	(1.25, 0.75)	(1.3, 0.7)	(1.33, 0.67)
(1.6, 0.4)	(1.2, 0.8)	(1.3, 0.7)	(1.36, 0.64)	(1.4, 0.6)
(1.7, 0.3)	(1.23, 0.77)	(1.35, 0.65)	(1.42, 0.58)	(1.47, 0.53)
(1.8, 0.2)	(1.27, 0.73)	(1.4, 0.6)	(1.48, 0.52)	(1.53, 0.47)
(1.9, 0.1)	(1.3, 0.7)	(1.45, 0.55)	(1.54, 0.46)	(1.6, 0.4)
(2, 0)	(1.33, 0.67)	(1.5, 0.5)	(1.6, 0.4)	(1.67, 0.33)

For all cases, the probability of emergence of heterogeneous model (λ, μ) is always higher than that of the heterogeneous model (δ, ψ) for all R_0, ie. $P_{\mathrm{d},\delta}(Em) < P_{\mathrm{c},\lambda}(Em)$. What we notice is that as $A \to \begin{bmatrix} 1 & 0 \\ 0 & 1 \end{bmatrix}$ the difference bewteen the emergence probability of the two models decreases, but provided $A \neq \begin{bmatrix} 1 & 0 \\ 0 & 1 \end{bmatrix}$ these probabilities will always be ordered. Figure (4.16) shows a comparison of two scenarios in the tabulated results. First we take one heterogeneous model to have parameters $\delta = (1.9, 0.1), \psi = (1.166, 0.833)$ and compare it to a model having parameters $\lambda = (1.3, 0.7), \mu = (1.5, 0.5)$ where $A = A_1$. It is clear the model with the most 'spread out' infectivity vector has the lowest emergence probability. We then compare two models where δ and μ are the same but because we now take $A = A_2$ this implies $\lambda = (1.45, 0.55), \psi = (1.25, 0.75)$. Again, we see the same ordering but the difference between the emergence probabilities is smaller than when we compared under condition $A = A_1$. This trend continues to remain true

for $A = A_3$ and $A = A_4$.

What we also see evidence of is that provided $\boldsymbol{\lambda} \prec_{\mu\psi} \boldsymbol{\delta}$ then $P_{\psi,\delta}(Em) < P_{\mu,\lambda}(Em)$ as was similar for **p-majorization.**

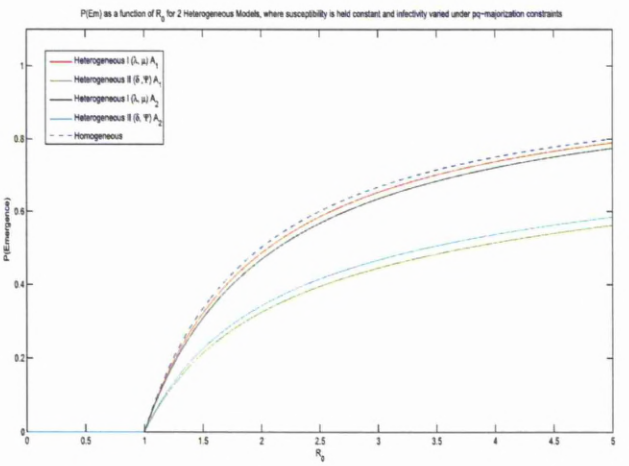

Figure 4.16: Comparison of P(Emergence) for two heterogeneous models assuming exponential infectious period under different A matrices: $\boldsymbol{\lambda} = (1.3, 0.7), \boldsymbol{\mu} = (1.5, 0.5)$ vs $\boldsymbol{\delta} = (1.9, 0.1), \boldsymbol{\psi} = (1.166, 0.833)$ under A_1 and $\boldsymbol{\lambda} = (1.45, 0.55), \boldsymbol{\mu} = (1.5, 0.5)$ vs $\boldsymbol{\delta} = (1.9, 0.1), \boldsymbol{\psi} = (1.25, 0.75)$ under A_2.

Let us now consider comparing models of different group sizes. **If we were to compare 2-group and 3-group heterogeneous models where the frequencies of each group were equal in each model, we would now be required to solve**

$$A\mathbf{c}' = \mathbf{d}' \Rightarrow \quad \frac{1}{2}\begin{bmatrix} a_{11} & a_{12} \\ a_{21} & a_{22} \\ 1-(a_{11}+a_{21}) & 1-(a_{12}+a_{22}) \end{bmatrix}\begin{bmatrix} \mu_1 \\ \mu_2 \end{bmatrix} = \frac{1}{3}\begin{bmatrix} \psi_1 \\ \psi_2 \\ \psi_3 \end{bmatrix}.$$

Using the fact that $\mu_2 = 2 - \mu_1$ we can write

$$A\mathbf{p}' = \mathbf{q}' = \frac{1}{2}\begin{bmatrix} a_{11}+a_{12}(2-\mu_1) \\ a_{21}+a_{22}(2-\mu_1) \\ 2-(a_{11}+a_{21})\mu_1-(a_{12}+a_{22})(2-\mu_1) \end{bmatrix} = \frac{1}{3}\begin{bmatrix} \psi_1 \\ \psi_2 \\ \psi_3 \end{bmatrix}$$

$$= \frac{1}{2}\begin{bmatrix} 2a_{12}+\mu_1(a_{11}-a_{12}) \\ 2a_{22}+\mu_1(a_{21}-a_{22}) \\ 2-2(a_{12}+a_{22})+\mu_1(a_{12}+a_{22}-a_{11}-a_{21}) \end{bmatrix} = \frac{1}{3}\begin{bmatrix} \psi_1 \\ \psi_2 \\ 3-\psi_1-\psi_2 \end{bmatrix}$$

where the third equation becomes redundant. These equations must be solved subject to the conditions

$$\begin{bmatrix} \lambda_1 \\ \lambda_2 \end{bmatrix} = \begin{bmatrix} a_{11}\delta_1 + a_{21}\delta_2 + (1 - (a_{11} + a_{21}))\delta_3 \\ a_{12}\delta_1 + a_{22}\delta_2 + (1 - (a_{12} + a_{22}))\delta_3 \end{bmatrix}.$$

Using $\lambda_2 = 2 - \lambda_1$ this leads to

$$\begin{bmatrix} \lambda_1 \\ 2 - \lambda_1 \end{bmatrix} = \begin{bmatrix} \delta_1(2a_{11} + a_{21} - 1) + \delta_2(2a_{21} + a_{11} - 1) + 3(1 - (a_{11} + a_{21})) \\ \delta_1(2a_{12} + a_{22} - 1) + \delta_2(2a_{22} + a_{12} - 1) + 3(1 - (a_{12} + a_{22})) \end{bmatrix}.$$

So **pq**-majorization for a 2vs3-group model becomes a problem of solving

$$\begin{cases} a_{12} + \frac{1}{2}\mu_1(a_{11} - a_{12}) &= \frac{1}{3}\psi_1 \\ a_{22} + \frac{1}{2}\mu_1(a_{21} - a_{22}) &= \frac{1}{3}\psi_2 \end{cases} \quad \text{subject to}$$

$$\begin{aligned} \lambda_1 = &\ a_{11}(2\delta_1 + \delta_2 - 3) + a_{21}(\delta_1 + 2\delta_2 - 3) + (3 - \delta_1 - \delta_2) \\ 2 - \lambda_1 = &\ a_{12}(2\delta_1 + \delta_2 - 3) + a_{22}(\delta_1 + 2\delta_2 - 3) + (3 - \delta_1 - \delta_2) \end{aligned}$$

with constraints $0 \leq \lambda_1, \mu_1 \leq 2, \psi_1 + \psi_2 \leq 3, \delta_1 + \delta_2 \leq 3, a_{11} + a_{21} \leq 1, a_{12} + a_{22} \leq 1$ and all parameters must be greater than or equal to zero. Obviously, the more groups there are in the models we are comparing, the more complicated a system of equations we have to solve. Figure (4.17) shows a comparison of 2, 3 and 4-group heterogeneous models where each model has uniform susceptibility and the infectivities of each model are feasible solutions to **pq**-majorization. The figure shows that under these circumstances, as we increase group size, the probability of emergence decreases for the heterogeneous models.

4.5 An alternative heterogeneous population model

In [75] Marschner defines a different heterogeneous model, represented by the infection rate matrix

$$M_{ij} = \begin{cases} af_j & \text{if } i = j, \\ bf_j & \text{if } i \neq j, \end{cases}$$

where a and b represent relative magnitudes of a mixing parameter, a symbolizing within-group mixing and b cross-group mixing. The homogeneous model has $a = b$ and is a standard Galton-Watson branching process. What he then does is compare a homogeneous and heterogeneous process by restricting a and b such that the average offspring mean of the heterogeneous process is the same as the offspring mean of the homogeneous process. That is, individuals differ in infectivity but the average level of infectiousness stays constant. He takes this average in 2 ways:

$$R_0^{(1)} = \sum_{i=1}^{k} f_i \sum_{j=1}^{k} \beta_{ij} = \sum_{i=1}^{k} f_i(\beta_{ii} + \sum_{j \neq i} \beta_{ij})$$

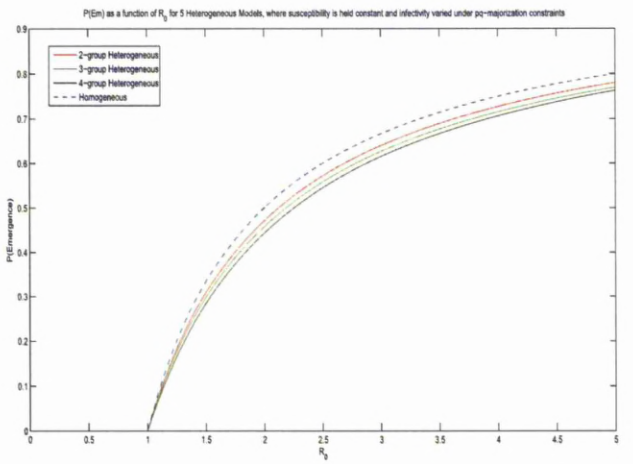

Figure 4.17: P(Emergence) for 2, 3 and 4-group heterogeneous models under pq-majorization constraints assuming an exponential infectious period. $\lambda = (1.33, 0.66), \mu = (1, 1)$ vs $\delta = (1.0222, 0.6222, 0.3556), \psi = (1, 1, 1)$ vs $\delta = (0.9333, 0.4333, 0.3667, 0.2667), \psi = (1, 1, 1, 1)$. For each k-group model, $f_i = 1/k$.

$$= \sum_{i=1}^{k} f_i(af_i + \sum_{j \neq i} bf_j) = a\sum_{i=1}^{k} f_i^2 + b\sum_{i=1}^{k}\sum_{j \neq i} f_i f_j$$

$$= a\sum_{i=1}^{k} f_i^2 + b\sum_{i=1}^{k} f_i(1 - f_i) = a\sum_{i=1}^{k} f_i^2 + b(1 - \sum_{i=1}^{k} f_i^2)$$

$$= (a - b)\sum_{i=1}^{k} f_i^2 + b,$$

$$R_0^{(2)} = \frac{1}{k}\sum_{i=1}^{k}\sum_{j=1}^{k} \beta_{ij} = \frac{1}{k}(a\sum_{i=1}^{k} f_i + \sum_{i=1}^{k}\sum_{j \neq i}^{k} \beta_{ij})$$

$$= \frac{1}{k}(a + \sum_{i=1}^{k}\sum_{j \neq i}^{k} bf_j) = \frac{1}{k}(a + \sum_{j=1}^{k} bf_j(\sum_{i \neq j} 1))$$

$$= \frac{1}{k}(a + b\sum_{j=1}^{k} f_j(k-1)) = \frac{1}{k}(a + b(k-1)\sum_{j=1}^{k} f_j)$$

$$= \frac{1}{k}(a + b(k-1)).$$

Thus he compares a heterogeneous process with two homogeneous processes each having offspring mean $R_0^{(1)}$ and $R_0^{(2)}$ respectively.

The extinction probability in this scenario is defined $q = \sum_{i=1}^{k} f_i q_i$ and the homogeneous extinction probabilities are labelled $q^{(1)}$ and $q^{(2)}$ corresponding to $R_0^{(1)}, R_0^{(2)}$ respectively. Following [12] in this case leads to

$$q_i = exp[af_i(q_i - 1) + b \sum_{j=1, j\neq i}^{k} f_j(q_j - 1)] \quad i = 1, \ldots, k.$$

Since $\sum_{j\neq i} f_j q_j = q - q_i f_i$ we have that

$$q_i = exp[af_i(q_i - 1) + b(q - q_i f_i - \sum_{j\neq i} f_j)] = exp[af_i(q_i - 1) + b(q - q_i f_i - (1 - f_i)]$$

$$= exp[af_i(q_i - 1) + b((q - 1) - f_i(q_i - 1))] = exp[f_i(a - b)(q_i - 1) + b(q - 1)]$$

for $i = 1, \ldots, k$. Marschner then asserts the following theorem:

Theorem Under the assumption $a \leq b$, $q^{(1)} \geq q^{(2)}$.

This is stating that the probability for a minor outbreak is greater for a heterogeneous population than that of a homogeneous population where the offspring mean is given by $R_0^{(2)}$. For details see [75].

In Figures (4.18) and (4.19) we compare the probability of emergence for a heterogeneous model with that of the homogeneous model with corresponding R_0 as previously, but also with two other types of homogeneous models where R_0 in these cases is not calculated as the maximal eigenvalue of the next generation mean matrix but by $R_0^{(1)}$ and $R_0^{(2)}$. Note that $R_0 = R_0^{(1)} = R_0^{(2)}$ when groups are equally proportioned. We compare all three models to the heterogeneous one where a, b are chosen such that the average offspring mean of the heterogeneous process is the same as that of the homogeneous process where $R_0 = \rho$. We compare R_0 with its homogeneous counterparts by rescaling a, b such that the homogeneous threshold level stays constant. That is, a proportionate change in $R_0^{(i)}$ implies a proportionate change in a, b which from the form of the mean matrix, implies a proportionate change in R_0. In the first plot we have that $a < b$ and it is clear that $P_{R_0^{(2)}}(Em)$ is consistently less than $P_{R_0}^{Het}(Em)$ and that $P_{R_0^{(1)}}(Em)$ is consistently larger than $P_{R_0}^{Het}(Em)$. In the second plot $a > b$ and we can here see that $P_{R_0^{(2)}}(Em)$ is consistently larger than $P_{R_0}^{Het}(Em)$ as is $P_{R_0^{(1)}}(Em)$. In both cases an exponential infectious period is assumed. It is obvious that the emergence probability is extremely sensitive to how we define R_0. For this model,

treating the homogeneous case as having offspring mean $R_0^{(1)}$ or $R_0^{(2)}$ will affect whether the emergence probability is higher or lower than that of a corresponding heterogeneous model.

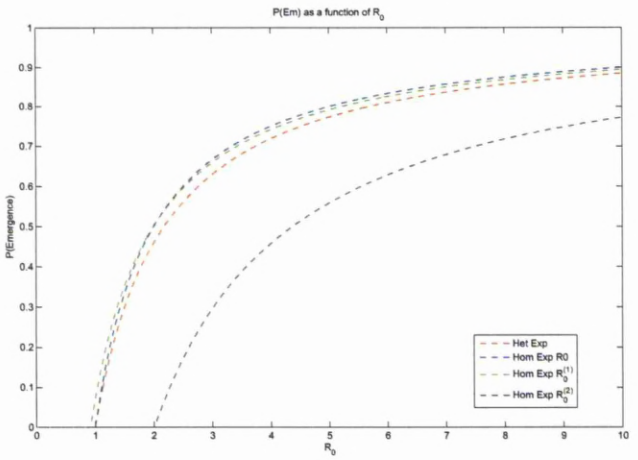

Figure 4.18: P(Emergence) for models under different definitions of R_0. Model parameters; $a = 1, b = 3$. Frequency split 10% group 1 90% group 2.

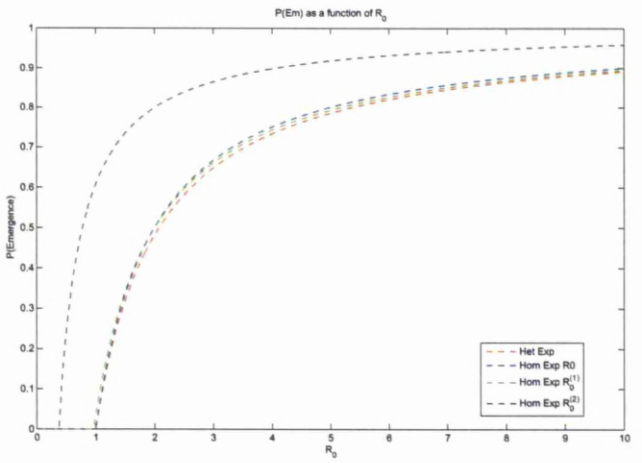

Figure 4.19: P(Emergence) for models under different definitions of R_0. **Model parameters; $a = 3, b = 1$. Frequency split 10% group 1 90% group 2.**

Chapter 5

Long-term behaviour

5.1 k-group stochastic model and deterministic representation

Let there be k populations, which we shall refer to as groups 1 to k, where N_1 individuals exist in group 1 of whom m_1 are initially infectives, N_2 individuals exist in group 2 of whom m_2 are initially infectives and so on. We assume that $N_1 + N_2 + \cdots + N_k = N$ and define $f_s = N_s/N$ assuming without loss of generality that $f_s > 0$ for $s = 1, 2, \ldots, k$. Throughout this chapter we also assume an exponential infectious period for all models considered. We define the infection rate from group s to group r as $\frac{1}{N}\beta_{sr} = \frac{\beta}{N}\lambda_s\pi_{sr}\mu_r$, in accordance with Becker and Marschner [24], Yates et. al [106] where β represents an overall force of infection, λ_s is the infectivity of any individual in group s, μ_r is the susceptibility of any individual in group r and π_{sr} is a mixing parameter.

This setup for our stochastic model was previously fully described in section 3.3. We have a k-dimensional Markov Chain $(I_1(t), I_2(t), \ldots, I_k(t))$ describing the number of infected individuals at time t with transition rates

$$(I_1, \ldots, I_k) \to (I_1, \ldots, I_r + 1, \ldots, I_k) \quad \text{with rate} \quad \tfrac{\beta}{N}\textstyle\sum_{s=1}^{k} \lambda_s\pi_{sr}\mu_r I_s(N_r - I_r),$$

$$(I_1, \ldots, I_k) \to (I_1, \ldots, I_r - 1, \ldots, I_k) \quad \text{with rate} \quad \gamma I_r,$$

corresponding to an infection in group r and a recovery in group r respectively where $r = 1, \ldots, k$ and I_k represents the actual number of infectives in group k. The next generation mean matrix is given by

$$M = \frac{\beta}{\gamma}\begin{bmatrix} \lambda_1\pi_{11}\mu_1 f_1 & \cdots & \lambda_1\pi_{1k}\mu_k f_k \\ \vdots & \ddots & \vdots \\ \lambda_k\pi_{k1}\mu_1 f_1 & \cdots & \lambda_k\pi_{kk}\mu_k f_k \end{bmatrix}.$$

As in section 3.6 the system of differential equations describing the deterministic

version of this general k-group SIS model is

$$\frac{dI_r}{dt} = \frac{\beta}{N}\mu_r \left(\sum_{s=1}^{k} \lambda_s \pi_{sr} (N_r - I_r) I_s \right) - \gamma I_r \qquad r = 1, \ldots, k. \tag{5.1}$$

By setting $x_r = I_r/N_r$ to represent the proportion of infectives in group r, we can rewrite this system as (see section 3.5)

$$\frac{dx_r}{dt} = \beta\mu_r(1 - x_r) \sum_{s=1}^{k} \lambda_s \pi_{sr} f_s x_s - \gamma x_r \tag{5.2}$$

for $r = 1, 2, \ldots, k$ where f_s represents the relative frequency of group s.

5.2 Feasibility of equilibria for k-group model

To find equilibria, we set the derivatives in (5.2) to zero, and so the system becomes

$$\beta\mu_r(1 - x_r) \sum_{s=1}^{k} \lambda_s \pi_{sr} f_s x_s = \gamma x_r \qquad \text{for } r = 1, 2, \ldots, k. \tag{5.3}$$

It is clear that there is always a solution $\mathbf{x} = \mathbf{0}$. In other words the disease-free equilibrium is always a feasible equilibrium point for the k-group model.

There will be a non-zero symmetrical solution $\mathbf{x} = x\mathbf{1}$ if there exists $x \neq 0$ satisfying

$$\beta x(1 - x)\mu_r \sum_{s=1}^{k} \lambda_s f_s \pi_{sr} = \gamma x \qquad \text{for all r .}$$

That is,

$$(1 - x)\beta\mu_r \sum_{s=1}^{k} \lambda_s f_s \pi_{sr} = \gamma,$$

$$1 - x = \frac{\gamma}{\beta\mu_r \sum_{s=1}^{k} \lambda_s f_s \pi_{sr}}. \tag{5.4}$$

This solution is valid provided the value of $\mu_r \sum_{s=1}^{k} \lambda_s f_s \pi_{sr}$ is the same for all r. In particular, if there is equal mixing amongst all groups (ie. each individual in any group is equally likely to make contact with any individual in any other group) $\pi_{sr} = \frac{1}{k}$ for all s, r and all individuals are equally susceptible, $\mu_r = \mu$ for all r then

$$x = 1 - \frac{\gamma}{\beta\mu \left(\sum_{s=1}^{k} \lambda_s f_s \right) / k}.$$

This solution is feasible provided $0 \leq x \leq 1$; that is,

$$\frac{\beta\mu}{k}\sum_{s=1}^{k}\lambda_s f_s \quad > \quad \gamma$$

$$\iff \quad \frac{\beta\mu}{k\gamma}\boldsymbol{\lambda}^T\mathbf{f} \quad > \quad 1.$$

From section 3.5 we have $R_0 = \frac{\beta\mu}{k\gamma}\boldsymbol{\lambda}^T\mathbf{f}$, so that in the case $\pi_{sr} = \frac{1}{k}$ for all r, s and $\mu_r = \mu$ for all r, the endemic equilibrium simplifies to

$$x_r^* = 1 - \frac{1}{R_0} \quad \text{for} \quad r = 1, 2, \ldots, k. \tag{5.5}$$

which is feasible for $R_0 > 1$. In general, (5.4) implies that if a symmetrical solution $\mathbf{x} = x\mathbf{1}$ exists then $x = 1 - \frac{\gamma}{\beta\mu_r \sum_s \lambda_s f_s \pi_{sr}}$ for all r.

Denote by B the matrix with entries β_{sr}, and write $F = diag(f_1, f_2, \ldots, f_k)$. We have $x = 1 - \frac{\gamma}{\sum_s f_s \beta_{sr}}$ for all r, so that a symmetrical solution exists provided the value of $\sum_s f_s\beta_{sr}$ does not depend upon r. That is, we require that the column sums of the matrix FB are all equal, and then $x = 1 - \frac{\gamma}{c}$ where $c = \sum_s f_s\beta_{sr}$.

Now the next-generation mean matrix is $M = \frac{1}{\gamma}BF = \frac{1}{\gamma}F^{-1}(FB)F$, so that M and $\frac{1}{\gamma}FB$ are similar matrices, and have the same eigenvalues as each other. Also, $\frac{1}{c}(FB)^T$ is a stochastic matrix, with dominant eigenvalue 1, so that $\frac{1}{\gamma}FB$ has dominant eigenvalue $\frac{c}{\gamma}$. It follows that $\frac{c}{\gamma} = R_0$. We have now shown that provided $\sum_s f_s\beta_{sr}$ does not depend upon r then (5.3) has the symmetrical endemic equilibrium solution $x_r^* = 1 - \frac{1}{R_0}$ for $r = 1, 2, \ldots, k$.

Let us suppose now that $\pi_{sr} = \frac{1}{k}$ for all r, s but that $\mu, \boldsymbol{\lambda}, \mathbf{f}$ are kept general. The equilibrium equations (5.3) become

$$\beta\mu_r(1 - x_r)\frac{1}{k}\sum_{s=1}^{k}\lambda_s f_s x_s = \gamma x_r.$$

Let $A = \frac{\beta}{k\gamma}\sum_{s=1}^{k}\lambda_s f_s x_s$ and note that A does not depend on r. Then

$$A\mu_r(1 - x_r) = x_r \quad \Rightarrow \quad A\mu_r = (1 + A\mu_r)x_r \quad \Rightarrow \quad x_r = \frac{A\mu_r}{1 + A\mu_r}.$$

Note for $A > 0$ we have $0 < x_r < 1$. But then

$$A = \frac{\beta}{k\gamma}\sum_{s=1}^{k}\lambda_s f_s x_s = \frac{\beta}{k\gamma}\sum_{s=1}^{k}\frac{\lambda_s f_s A\mu_s}{1 + A\mu_s}$$

Either $A = 0$ or $1 = \frac{\beta}{k\gamma}\sum_{s=1}^{k}\frac{\lambda_s f_s \mu_s}{1+A\mu_s}$. We require $A > 0$ with

$$\sum_{s=1}^{k}\left(\frac{\frac{\beta}{k\gamma}\lambda_s f_s \mu_s}{1+A\mu_s}\right) = 1.$$

That is,

$$\frac{\beta}{k\gamma}\boldsymbol{\lambda}^T diag(\mathbf{f})(I + Adiag(\boldsymbol{\mu}))^{-1}\boldsymbol{\mu} = 1.$$

Note that $R_0 = \frac{\beta}{k\gamma}\boldsymbol{\lambda}^T diag(\mathbf{f})\boldsymbol{\mu}$. For $R_0 > 1$ we must solve $\sum_{s=1}^{k}\left(\frac{\frac{\beta}{k\gamma}\lambda_s f_s \mu_s}{1+A\mu_s}\right) = 1$ to find A, and then set $x_r = \frac{A\mu_r}{1+A\mu_r}$ for $r = 1, 2, \ldots, k$. Note that the function

$$h(A) = \sum_{s=1}^{k}\left(\frac{\frac{\beta}{k\gamma}\lambda_s f_s \mu_s}{1+A\mu_s}\right)$$

is continuous, with $h(0) = R_0$ and $h(A) \to 0$ as $A \to \infty$. Also $h(A)$ is a decreasing function of $A \geq 0$. This ensures uniqueness of the solution to $h(A) = 1$. So a solution exists if and only if $R_0 \geq 1$. In other words, if $\pi_{rs} = \frac{1}{k}$ for all r, s then there is a unique feasible endemic equilibrium point provided $R_0 > 1$.

The endemic equilibrium point may be written $x_r = 1 - \frac{1}{1+A\mu_r}$ for $r = 1, \ldots, k$ where $h(A) = 1$. Now

$$\begin{aligned} h(A) = \sum_{s=1}^{k}\left(\frac{\frac{\beta}{k\gamma}\lambda_s f_s \mu_s}{1+A\mu_s}\right) &= \sum_{s=1}^{k}\frac{\beta}{k\gamma}\lambda_s f_s \mu_s (1 - x_s) \\ &= R_0 - \sum_{s=1}^{k}\frac{\beta}{k\gamma}\lambda_s f_s \mu_s x_s. \end{aligned}$$

The equation $h(A) = 1$ thus becomes

$$\sum_{s=1}^{k}\frac{\beta}{k\gamma}\lambda_s f_s \mu_s x_s = R_0 - 1 \tag{5.6}$$

Setting $a_s = \frac{\beta}{k\gamma}\lambda_s f_s \mu_s / R_0$ then we have $a_1 + a_2 + \cdots + a_k = 1, a_s \geq 0$, and (5.6) becomes

$$\sum_{s=1}^{k} a_s x_s = 1 - \frac{1}{R_0},$$

extending equation (5.5) to the non-symmetric case, provided $\pi_{sr} = \frac{1}{k}$ for all s, r.

5.3 Stability of disease-free equilibrium

Differentiating (5.2) with respect to x_r we have that

$$\frac{\partial}{\partial x_r}\left(\frac{dx_r}{dt}\right) = \beta\mu_r(1-2x_r)\lambda_r\pi_{rr}f_r - \beta\mu_r\sum_{s\neq r}\lambda_s\pi_{sr}f_s x_s - \gamma,$$

and for $p \neq r$,

$$\frac{\partial}{\partial x_p}\left(\frac{dx_r}{dt}\right) = \beta\mu_r(1-x_r)\lambda_p\pi_{pr}f_p.$$

The Jacobian has elements $J_{rp} = \frac{\partial}{\partial x_p}\left(\frac{dx_r}{dt}\right)$. Note that

$$\frac{\partial}{\partial x_r}\left(\frac{dx_r}{dt}\right) = \beta\mu_r(1-x_r)\lambda_r\pi_{rr}f_r - \beta\mu_r\sum_{s=1}^{k}\lambda_s\pi_{sr}f_s x_s - \gamma,$$

so for all r, p we have

$$J_{rp} = \beta\mu_r(1-x_r)\lambda_p\pi_{pr}f_p - \delta_{rp}\left(\beta\mu_r\sum_{s=1}^{k}\lambda_s\pi_{sr}f_s x_s + \gamma\right). \tag{5.7}$$

It is (5.7) we must analyse in order to deduce stability properties. At disease-free equilibrium, then

$$J_{rp}(\mathbf{0}) = \beta\mu_r\lambda_p\pi_{pr}f_p - \gamma\delta_{rp}.$$

That is,

$$J(\mathbf{0}) = \gamma(FM^TF^{-1} - I)$$

where M is the next generation mean matrix and $F = diag(f_1, f_2, \ldots, f_k)$. Now if $\mathbf{w}$ is any eigenvector of M^T with eigenvalue ρ, then

$$\begin{aligned} J(\mathbf{0})(F\mathbf{w}) &= \gamma(FM^TF^{-1}F\mathbf{w} - F\mathbf{w}) = \gamma F(\rho\mathbf{w} - \mathbf{w}) \\ &= \gamma(\rho-1)F\mathbf{w}, \end{aligned}$$

so that $F\mathbf{w}$ is an eigenvector of $J(\mathbf{0})$ with eigenvalue $\gamma(\rho-1)$. The condition for stability of the disease-free equilibrium is that all eigenvalues of $J(\mathbf{0})$ have negative real part. We have now shown that this is equivalent to all eigenvalues of M having real part less than 1. That is, the disease-free equilibrium is stable if and only if $R_0 < 1$. To put it another way, the deterministic model has the same threshold condition as the branching process model.

5.4 Stability of endemic equilibrium

Denoting by $\mathbf{x}^*$ the endemic equilibrium point, then from (5.7),

$$J_{rp}(\mathbf{x}^*) = \beta\mu_r(1-x_r^*)\lambda_p\pi_{pr}f_p - \delta_{rp}\left(\beta\mu_r\sum_{s=1}^{k}\lambda_s\pi_{sr}f_s x_s + \gamma\right)$$

and substituting from (5.3) this simplifies to

$$\begin{aligned} J_{rp}(\mathbf{x}^*) &= \beta\mu_r(1-x_r^*)\lambda_p\pi_{pr}f_p - \delta_{rp}\left(\tfrac{\gamma x_r^*}{1-x_r^*} + \gamma\right) \\ &= \beta\mu_r(1-x_r^*)\lambda_p\pi_{pr}f_p - \delta_{rp}\left(\tfrac{\gamma}{1-x_r^*}\right). \end{aligned}$$

In the symmetrical case when $x_r^* = x^* = 1 - \frac{1}{R_0}$ for all r, then

$$J_{rp}(\mathbf{x}^*) = \beta(1-x^*)\mu_r\lambda_p\pi_{pr}f_p - \delta_{rp}\left(\frac{\gamma}{1-x^*}\right).$$

That is,

$$J(\mathbf{x}^*) = \frac{\gamma F M^T F^{-1}}{R_0} - \gamma R_0 I.$$

If $\mathbf{w}$ is any eigenvector of M^T, with eigenvalue ρ, then

$$\begin{aligned} J(\mathbf{x}^*)(F\mathbf{w}) &= \tfrac{\gamma F M^T F^{-1} F\mathbf{w}}{R_0} - \gamma R_0 F\mathbf{w} \\ &= \tfrac{\gamma F\rho\mathbf{w}}{R_0} - \gamma R_0 F\mathbf{w} \\ &= \tfrac{\gamma}{R_0}\left(\rho - R_0^2\right) F\mathbf{w}. \end{aligned}$$

That is, $F\mathbf{w}$ is an eigenvector of $J(\mathbf{x}^*)$ with eigenvalue $\gamma(\rho - R_0^2)/R_0$. For stability, we require $Re(\rho) < R_0^2$ for all eigenvalues ρ of M. Now since all eigenvalues of M satisfy $Re(\rho) < R_0$, we require $R_0 < R_0^2$, or equivalently, $R_0 > 1$. We have now shown that a symmetric endemic equilibrium point is stable if and only if $R_0 > 1$.

Writing the equilibrium equations (5.3) in a more general form, we have that, at equilibrium

$$(1-x_r^*)\sum_{s=1}^{k} x_s f_s \beta_{sr} = \gamma x_r^* \qquad \text{for} \quad r = 1, \ldots, k.$$

The Jacobian can therefore be written as having elements

$$\begin{aligned} J_{rp}(\mathbf{x}^*) &= (1-x_r^*)f_p\beta_{pr} - \delta_{rp}\left(\textstyle\sum_{s=1}^{k} x_s f_s \beta_{sr} + \gamma\right) \\ &= (1-x_r^*)f_p\beta_{pr} - \left(\tfrac{\gamma}{1-x_r^*}\right)\delta_{rp}. \end{aligned}$$

If we write $X = diag(\mathbf{1} - \mathbf{x}^*)$, then

$$J(\mathbf{x}^*) = XFB^T - \gamma X^{-1}.$$

The equilibrium equations can be written as

$$(1 - x_r^*)((\mathbf{x}^*)^T FB)_r = \gamma x_r^*$$

$$\Rightarrow \quad (\mathbf{x}^*)^T FBX = \gamma (\mathbf{x}^*)^T.$$

Unfortunately, in the asymmetric case it is not immediately obvious how to identify eigenvalues of the Jacobian $J(\mathbf{x}^*)$.

5.5 The effect of heterogeneity: numerical results for 2-group deterministic and stochastic systems

For the following numerical results we shall assume equal group sizes and will examine heterogeneity in infectivity only, mixing only and susceptibility only as separate cases. In this section we define the deterministic differential system which approximates the full stochastic model for each case. The deterministic equilibrium values and stochastic means for the heterogeneous model are then plotted alongside those of the homogeneous model for a range of R_0 values. For the stochastic mean, we calculate the joint quasi-stationary distribution $P(I_1 = x_1, I_2 = x_2)$ at successive R_0 values, and then the distribution of total infected $P(I_1 + I_2 = x), 0 \leq x \leq 2N$ at that particular R_0. It is this total distribution from which the mean is calculated and this procedure is then iteratively repeated for increasing values of R_0. We calculate this stochastic mean for both the homogeneous and heterogeneous 2-group models.

Figure 5.1 is an example of such a joint quasi-stationary distribution with heterogeneity in infectivity. In section 5.6 we prove algebraically the results for deterministic equilibrium values in this section for each case, but extend to a k-group scenario. The models we look at in this section constitute special cases from the general theory already discussed. Due to this, in section 5.7, the stability conditions for the disease-free and endemic equilibrium points will be calculated. For the case of heterogeneity in susceptibility, this is complicated. In section 5.8, the variance matrix for each of these 2-group models will be approximated using an Ornstein-Uhlenbeck approximation and this will be used as an approximation to the quasi-stationary distribution and its accuracy assessed.

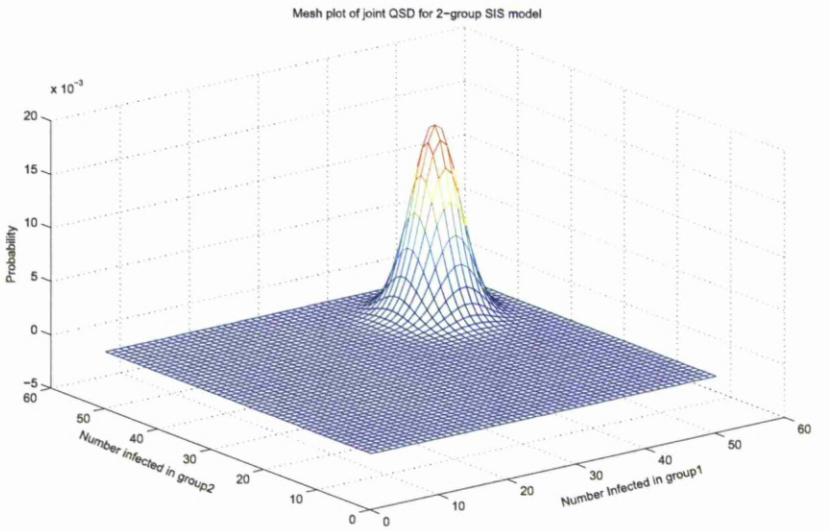

Figure 5.1: Mesh plot of joint quasi-stationary distribution of a 2-group SIS model with heterogeneity in infectivity. Parameter values $N = 100, \lambda_1 = 40/21, \lambda_2 = 2/21, \mu_1 = \mu_2 = 1, f_1 = f_2 = 1/2, \pi = 1 - \pi = 1/2$.

5.5.1 Heterogeneity in infectivity

We begin by examining the effect of varying infectivity only. In this scenario, susceptibility of the 2 groups is equal ($\mu_1 = \mu_2 = 1$), the number of individuals in each group is the same ($f_1 = f_2 = 1/2$) and all individuals are as likely to mix with their own group as with the other ($\pi = 1 - \pi = 1/2$). So our deterministic system of differential equations becomes

$$\begin{cases} \frac{dx_1}{dt} = & \frac{\beta}{4}[\lambda_1 x_1(1-x_1) + \lambda_2 x_2(1-x_1)] - \gamma x_1, \\ \frac{dx_2}{dt} = & \frac{\beta}{4}[\lambda_1 x_1(1-x_2) + \lambda_2 x_2(1-x_2)] - \gamma x_2. \end{cases}$$

The next generation mean matrix now becomes simply

$$M = \frac{\beta}{4\gamma}\begin{bmatrix} \lambda_1 & \lambda_1 \\ \lambda_2 & \lambda_2 \end{bmatrix}$$

with $R_0 = \frac{\beta(\lambda_1+\lambda_2)}{4\gamma}$. The deterministic endemic equilibrium value for the homogeneous case is given by $N(1 - \frac{1}{R_0})$ and for the heterogeneous case is given by $N(x_1^* + x_2^*)/2$ where (x_1^*, x_2^*) is the equilibrium point of the system of differential equations above.

Figures (5.2) and (5.3) show the endemic equilibrium values and stochastic means for both the homogeneous and heterogeneous cases. The MATLAB code used to carry out these calculations can be seen in appendix D (for deterministic equilibrium values) and appendix E (for stochastic means). Figure (5.2) shows that the deterministic equilibrium values for the homogeneous and heterogeneous models remain equal to each other for all values of R_0. What follows in section 5.6.1 is an algebraic argument showing these two quantities are equal for k-groups.

Figure (5.3) shows that the stochastic means for the homogeneous and heterogeneous models, when varying infectivity only, differ only slightly across the range of R_0 values. For $0.5 \leq R_0 \leq 1.25$ the stochastic mean for the heterogeneous model exceeds that of the homogeneous. Around $1.3 \leq R_0 \leq 3$ this mean then becomes less than the homogeneous. The bottom panel of Figure (5.3) shows more clearly this crossover. It is also clear from Figures (5.2) and (5.3) that the deterministic endemic equilibrium values for both the homogeneous and heterogeneous cases is larger than the corresponding stochastic mean, for $R_0 \geq 1$. Looking at Figure (5.4) showing the mean number of infected individuals across the plotted R_0 range we can see that it appears the deterministic approximations and stochastic means for both heterogeneous and homogeneous models are tending towards the same value as R_0 increases and that there is an ordering between these plotted values.

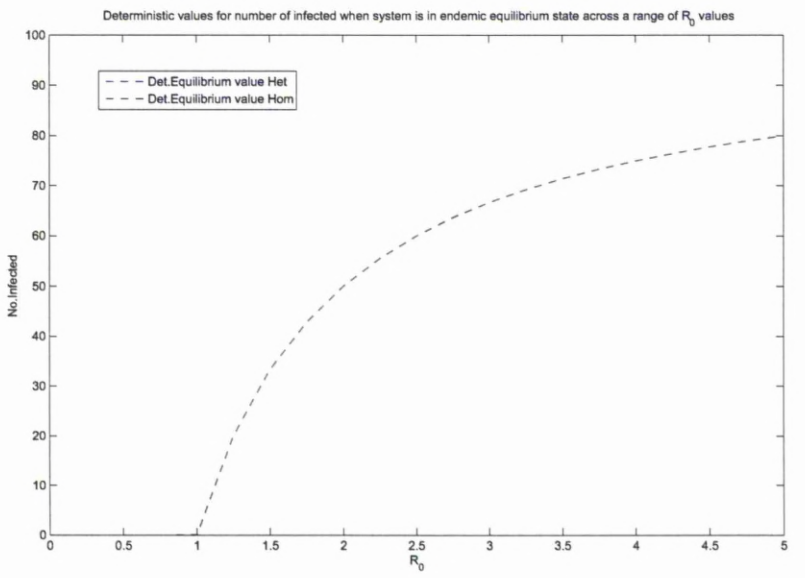

Figure 5.2: Deterministic equilibrium values of numbers infected for the homogeneous and heterogeneous 2-group model with heterogeneity in infectivity. Parameter values $N = 100, \lambda_1 = 40/21, \lambda_2 = 2/21, \mu_1 = \mu_2 = 1, f_1 = f_2 = 1/2, \pi = 1 - \pi = 1/2$.

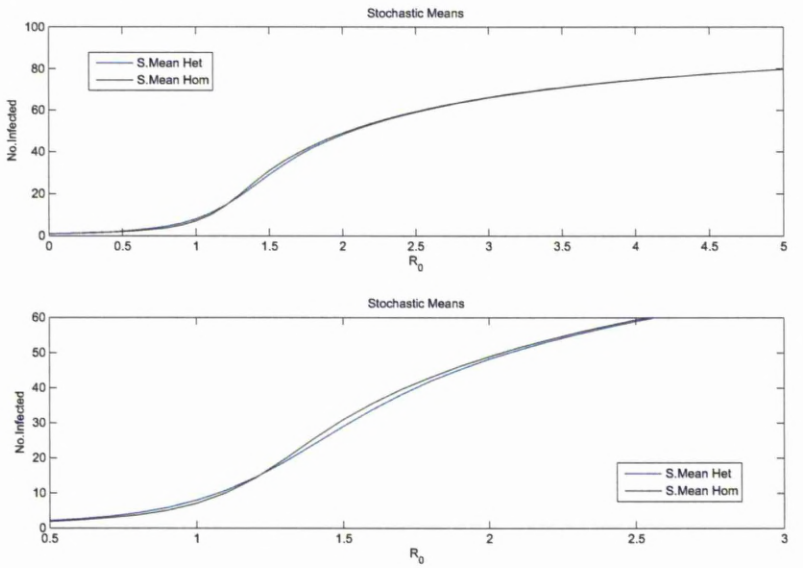

Figure 5.3: Stochastic means of the homogeneous and heterogeneous quasi-stationary distribution of total number infected for a 2-group model with heterogeneity in infectivity. Parameter values $N = 100, \lambda_1 = 40/21, \lambda_2 = 2/21, \mu_1 = \mu_2 = 1, f_1 = f_2 = 1/2, \pi = 1 - \pi = 1/2$.

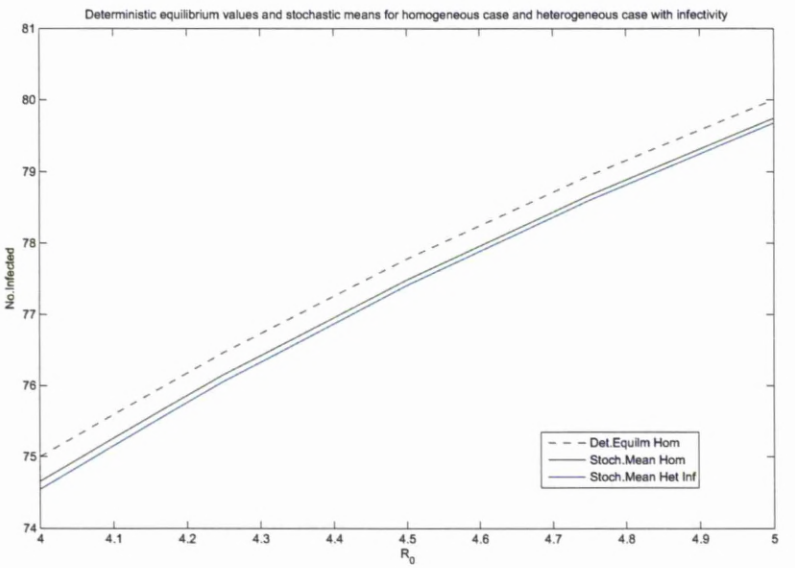

Figure 5.4: Deterministic endemic equilibrium values and stochastic means of the quasi-stationary distribution for both homogeneous and heterogeneous cases where heterogeneity is in infectivity. Parameter values $N = 100, \lambda_1 = 40/21, \lambda_2 = 2/21, \mu_1 = \mu_2 = 1, f_1 = f_2 = 1/2, \pi = 1 - \pi = 1/2$

5.5.2 Heterogeneity in Mixing

In this scenario, susceptibility of the 2 groups is equal as is the infectivity ($\mu_1 = \mu_2 = 1, \lambda_1 = \lambda_2 = 1$), the number of individuals in each group is the same ($f_1 = f_2 = 1/2$) but individuals have mixing preferences. For assortative mixing we assume within-group mixing is strongly preferential to cross-group mixing and set $\pi = 0.95$. For dissortative mixing we assume cross-group mixing is strongly preferential to within-group mixing and $\pi = 0.05$. This is in accordance with parameter values chosen by Yates et al. [106]. So our deterministic system of differential equations becomes

$$\begin{cases} \frac{dx_1}{dt} = \frac{\beta}{2}[\pi x_1(1-x_1) + (1-\pi)x_2(1-x_1)] - \gamma x_1, \\ \frac{dx_2}{dt} = \frac{\beta}{2}[(1-\pi)x_1(1-x_2) + \pi x_2(1-x_2)] - \gamma x_2. \end{cases}$$

The next generation mean matrix now becomes

$$M = \frac{\beta}{2\gamma}\begin{bmatrix} \pi & 1-\pi \\ 1-\pi & \pi \end{bmatrix}.$$

The eigenvalues are $\frac{\beta}{2\gamma}$ and $\frac{\beta\pi}{\gamma} - \frac{\beta}{2\gamma}$ where $0 \leq \pi \leq 1$. If $\pi = 1$, then these two eigenvalues are equal. If $\pi < 1$ then $\frac{\beta}{2\gamma}$ is the larger eigenvalue so $R_0 = \frac{\beta}{2\gamma}$.

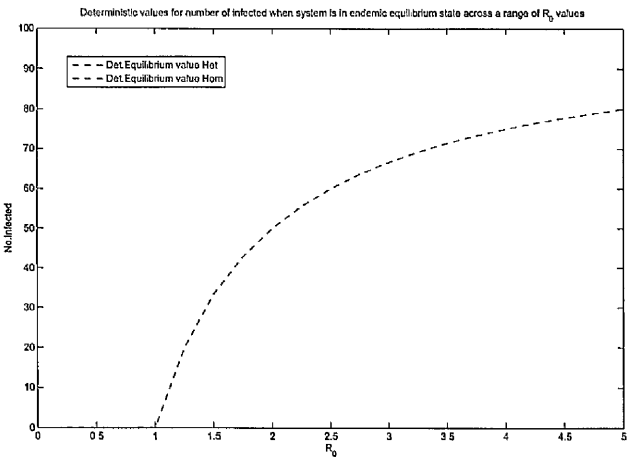

Figure 5.5: Deterministic equilibrium values of number infected for the homogeneous and heterogeneous 2-group model where assortative mixing is assumed. Parameter values $N = 100, \lambda_1 = \lambda_2 = 1, \mu_1 = \mu_2 = 1, f_1 = f_2 = 1/2, \pi = 0.95$.

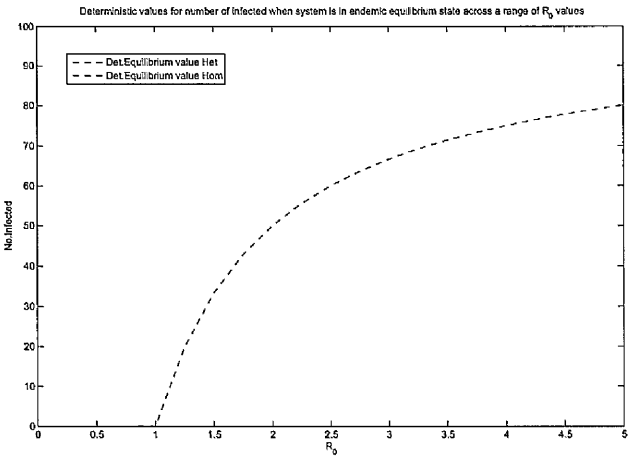

Figure 5.6: Deterministic equilibrium values of number infected for the homogeneous and heterogeneous 2-group model where dissortative mixing is assumed. Parameter values $N = 100, \lambda_1 = \lambda_2 = 1, \mu_1 = \mu_2 = 1, f_1 = f_2 = 1/2, \pi = 0.05$.

Figure (5.5) shows the deterministic equilibrium values for both the homogeneous and heterogeneous case where the only source of heterogeneity is in the mixing parameter and assortative mixing is assumed. Figure (5.6) shows the deterministic equilibrium values for both the homogeneous and heterogeneous case of a 2-group model where this time the mixing parameter reflects dissortative mixing.

As was the case for heterogeneity in infectivity we can see from Figures (5.5) and (5.6) that despite the type of heterogeneity in mixing between the 2 groups, the deterministic equilibrium values for both the homogeneous and heterogeneous models remain equal to each other for all values of R_0. This will be proven similarly as for infectivity for k-groups in section 5.6.2.

Figure (5.7) shows that the stochastic mean for the homogeneous model is consistently larger than the stochastic mean for the heterogeneous model for the range of R_0 values when assortative mixing is assumed. For $R_0 > 3$ the difference between the two becomes very small, but certainly for $1 \leq R_0 \leq 2$ there is significant difference. In Figure (5.8) however, the stochastic mean for the homogeneous model is consistently less than the stochastic mean for the heterogeneous model for the range of R_0 values when dissortative mixing is assumed. This difference is very small, as shown by the bottom panel of Figure (5.8), across the range.

We therefore cannot conclude that the stochastic heterogeneous mean is bounded by the stochastic homogeneous mean in the case of heterogeneous mixing. In fact, the type of mixing assumed dictates whether the stochastic heterogeneous

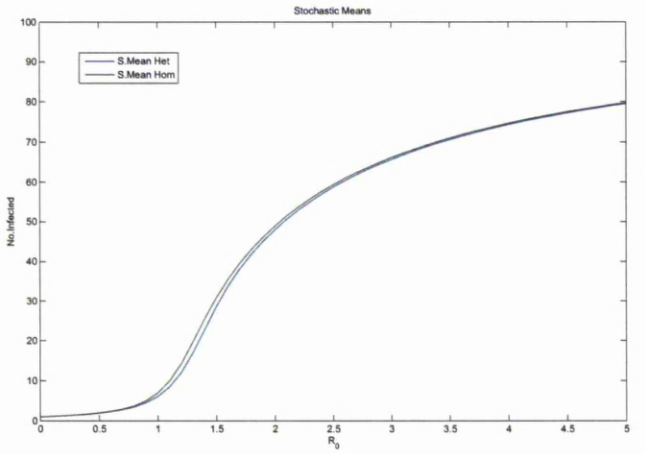

Figure 5.7: Stochastic means of the homogeneous and heterogeneous quasi-stationary distribution of total number infected for a 2-group model where assortative mixing is assumed. Parameter values $N = 100, \lambda_1 = \lambda_2 = 1, \mu_1 = \mu_2 = 1, f_1 = f_2 = 1/2, \pi = 0.95$.

mean lies above or below the stochastic homogeneous mean. What we can state is that the stochastic mean when dissortative mixing is assumed bounds from above the stochastic mean when assortative mixing is assumed. When mixing is equal across the 2 groups, ie. $\pi = 1 - \pi = 0.5$, infectives are just as likely to make contact with individuals from their own group as with individuals from the other, these two values are equal.

As was the observation when infectivity was the only source of heterogeneity, the deterministic endemic equilibrium value for both homogeneous and heterogeneous cases and stochastic mean of the quasi-stationary distribution for the homogeneous and heterogeneous models appear to converge to the same value as R_0 increases, and a consistent ordering holds, evidenced by Figure (5.9).

5.5.3 Heterogeneity in Susceptibility

In this scenario, infectivity of the 2 groups is equal ($\lambda_1 = \lambda_2 = 1$), the number of individuals in each group is the same ($f_1 = f_2 = 1/2$) and all individuals are equally likely to mix with their own group as with the other ($\pi = 1 - \pi = 1/2$).

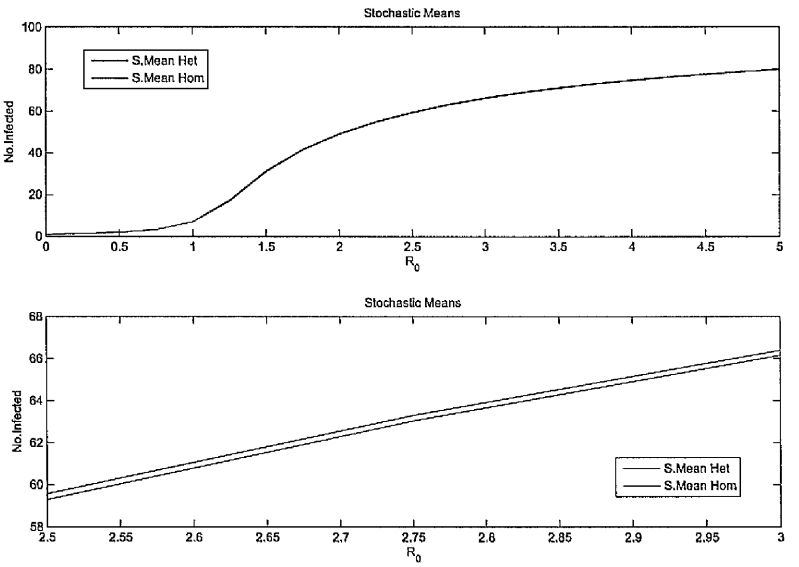

Figure 5.8: Stochastic means of the homogeneous and heterogeneous quasi-stationary distribution of total number infected for a 2-group model where dissortative mixing is assumed. Parameter values $N = 100, \lambda_1 = \lambda_2 = 1, \mu_1 = \mu_2 = 1, f_1 = f_2 = 1/2, \pi = 0.05$.

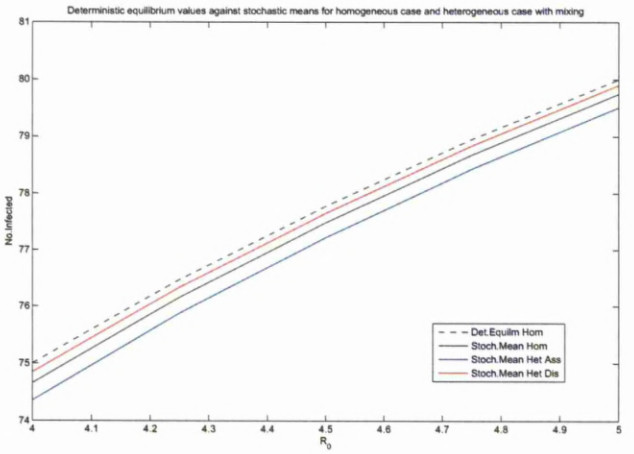

Figure 5.9: Deterministic endemic equilibrium values and stochastic means of the quasi-stationary distribution for both homogeneous and heterogeneous cases where heterogeneity is in mixing.

So our deterministic system of differential equations becomes

$$\begin{cases} \frac{dx_1}{dt} = \frac{\beta}{4}[\mu_1 x_1(1-x_1) + \mu_1 x_2(1-x_1)] - \gamma x_1, \\ \frac{dx_2}{dt} = \frac{\beta}{4}[\mu_2 x_1(1-x_2) + \mu_2 x_2(1-x_2)] - \gamma x_2. \end{cases}$$

The next generation mean matrix now becomes

$$M = \frac{\beta}{4\gamma}\begin{bmatrix} \mu_1 & \mu_2 \\ \mu_1 & \mu_2 \end{bmatrix}$$

with $R_0 = \frac{\beta(\mu_1+\mu_2)}{4\gamma}$. The deterministic endemic equilibrium value for the homogeneous case is given by $N(1-\frac{1}{R_0})$ and for the heterogeneous case is given by $N_1 x_1^* + N_2 x_2^*$ and (x_1^*, x_2^*) is the equilibrium point of the system of differential equations above.

Figure (5.10) shows that the deterministic equilibrium value across the range of R_0 for the heterogeneous model is consistently less than or equal to the deterministic equilibrium value for the homogeneous model. Previously, when examining heterogeneity in infectivity and mixing these two quantities were equal but for heterogeneity in susceptibility we have a different result. In section 5.6.3 we will provide an algebraic argument showing this to be the case for a k-group model.

Figure (5.11) shows that the stochastic heterogeneous mean is significantly lower than the stochastic homogeneous mean and lies consistently below it for all

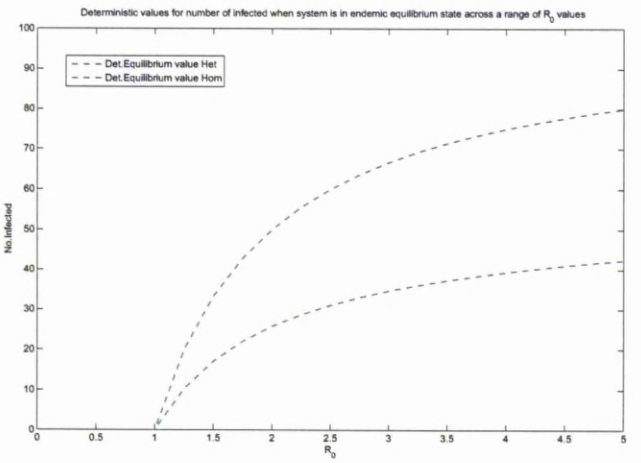

Figure 5.10: Deterministic equilibrium value of number infected for the homogeneous and heterogeneous 2-group model with heterogeneity in susceptibility. Parameter values $N = 100, \lambda_1 = \lambda_2 = 1, \mu_1 = 200/101, \mu_2 = 2/101, f_1 = f_2 = 1/2, \pi = 1 - \pi = 1/2$.

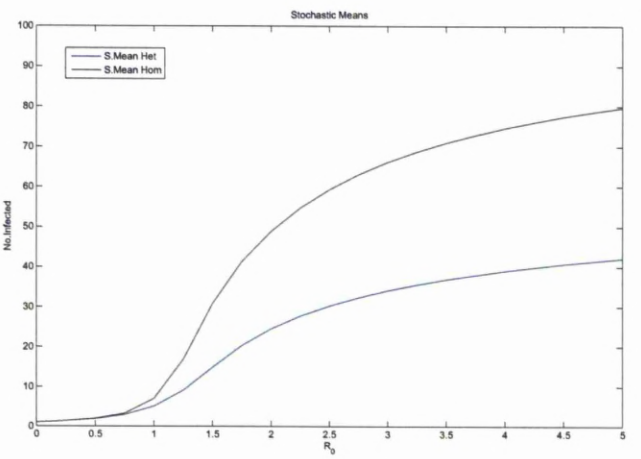

Figure 5.11: Stochastic means of the homogeneous and heterogeneous quasi-stationary distribution of a 2-group model with heterogeneity in susceptibility. Parameter values $N = 100, \lambda_1 = \lambda_2 = 1, \mu_1 = 200/101, \mu_2 = 2/101, f_1 = f_2 = 1/2, \pi = 1 - \pi = 1/2$.

R_0 values. In this instance, convergence doesn't appear to occur towards the same value. However, the stochastic mean and deterministic equilibrium value for the heterogeneous model converge towards the same value as R_0 increases.

5.6 Analytical results

In section 5.5 we observed that the deterministic equilibrium values for both the homogeneous and heterogeneous models were the same across the R_0 range when heterogeneity existed in infectivity, and in mixing. We will prove this to be the case for k-groups. We also had the result that the determinstic equilibrium value for the heterogeneous model was consistently less than or equal to that of the homogeneous model when heterogeneity existed in susceptibility. We will also prove this to be the case for a k-group model, where group sizes are equal.

5.6.1 Heterogeneity in infectivity

We have that if for k-groups $\pi_{sr} = 1/k$, $\mu_r = 1$, for all r, s,

$$\frac{dx_r}{dt} = \frac{\beta}{k}(1 - x_r)\sum_{s=1}^{k} \lambda_s f_s x_s - \gamma x_r.$$

Now $\sum_s f_s \beta_{sr} = \sum_s \beta f_s \lambda_s \pi_{sr} \mu_r = \frac{\beta}{k}\sum_s f_s \lambda_s = \frac{\beta}{k}$ which is independent of r, so from section 5.2 we know that the endemic equilibrium point is given by $x_r^* = 1 - \frac{1}{R_0}$ for $r = 1, 2, \ldots, k$, where $R_0 = \frac{\beta}{k\gamma}$.

So for the heterogeneous model, the total number infected in endemic equilibrium is

$$N_1\left(1 - \frac{1}{R_0}\right) + N_2\left(1 - \frac{1}{R_0}\right) + \cdots + N_k\left(1 - \frac{1}{R_0}\right)$$

whereas the corresponding quantity for the homogeneous model is $N\left(1 - \frac{1}{R_0}\right)$. Clearly these two quantities are in fact equal. Note that in our numerical results we had equal group sizes but we have now shown however that this relationship holds for any frequencies.

5.6.2 Heterogeneity in mixing

We have that if for k-groups $\lambda_s = \mu_r = 1$ and $f_s = 1/k$ for all r, s, taking $\pi_{rr} = \pi$ and $\pi_{sr} = \frac{1-\pi}{k-1}$ for all $s \neq r$, then

$$\frac{dx_r}{dt} = \frac{\beta}{k}(1 - x_r)\left[\pi x_r + \sum_{s=1}^{k-1} \frac{(1-\pi)}{k-1} x_s\right] - \gamma x_r.$$

In this case $\sum_s f_s\beta_{sr} = \sum_s \beta f_s\lambda_s\pi_{sr}\mu_r = \frac{\beta}{k}\sum_r \pi_{sr} = \frac{\beta}{k}$, which again is independent of r, so that the endemic equilibrium point is

$$x_r^* = 1 - \frac{1}{R_0} \quad \text{for} \quad r = 1, 2, \ldots, k$$

Exactly as in the case of heterogeneity in infectivity, it follows that the total number infected in endemic equilibrium is the same for the heterogeneous model and the corresponding homogeneous model. Note here that we do need to assume $f_s = \frac{1}{k}$.

It is important to also note that this is the case due to the symmetry we impose in our mixing parameter causing the differential equations to become equal under this constraint. If, for example, the mixing parameter had been defined by $\pi_{sr} = \begin{bmatrix} \pi_{11} & \pi_{12} \\ \pi_{21} & \pi_{22} \end{bmatrix}$ and neither row had to sum to 1, then we wouldn't have this symmetry and so the endemic equilibrium would be of a more complex form.

5.6.3 Heterogeneity in susceptibility

For k groups with $\lambda_s = 1$ and $\pi_{sr} = f_s = \frac{1}{k}$ for all r, s then $\sum_s f_s\beta_{sr} = \beta\sum_s \lambda_s f_s\pi_{sr}\mu_r = \frac{\beta}{k}\mu_r$. In this case, the sum is not independent of r, so that the endemic equilibrium point is not of symmetric form. Our system of differential equations is

$$\frac{dx_r}{dt} = \frac{\beta}{k^2}\left[\mu_r(1 - x_r)\left(\sum_{s=1}^{k} x_s\right)\right] - \gamma x_r.$$

Adding these equations gives, in equilibrium,

$$\sum_{s=1}^{k} x_s\left(\frac{\beta\mu_1(1 - x_1)}{k^2} + \cdots + \frac{\beta\mu_k(1 - x_k)}{k^2} - \gamma\right) = 0.$$

Solving this leads to $\mathbf{x} = \mathbf{0}$ or $\frac{\beta(\mu_1 x_1 + \cdots + \mu_k x_k)}{k^2} = \frac{\beta}{k^2}(\mu_1 + \cdots + \mu_k) - \gamma$

$$\Rightarrow \quad \left(\frac{\mu_1}{\mu_1 + \cdots + \mu_k}\right)x_1 + \left(\frac{\mu_2}{\mu_1 + \cdots + \mu_k}\right)x_2 + \cdots + \left(\frac{\mu_k}{\mu_1 + \cdots + \mu_k}\right)x_k = 1 - \frac{k^2\gamma}{\beta(\mu_1 + \cdots + \mu_k)}.$$

Note that the condition $\sum_{s=1}^{k} \mu_s f_s = 1 \Rightarrow \sum_{s=1}^{k} \mu_s = k$ in this case, that $x_r^* = \frac{A\mu_r}{1 + A\mu_r}$ from section 5.2 and that $R_0 = \frac{\beta}{\gamma k}$. The total infected for the heterogeneous case is

$$N\sum_{s=1}^{k} \frac{1}{k}x_s^*$$

From section 5.2 we have in this case that

$$h(A) = \sum_{s=1}^{k} \left(\frac{\frac{\beta}{k^2\gamma}\mu_s}{1 + A\mu_s} \right) = \sum_{s=1}^{k} \frac{\beta}{k^2\gamma}\mu_s(1 - x_s) = R_0 - \sum_{s=1}^{k} \frac{\beta}{k^2\gamma}\mu_s x_s = 1.$$

Thus $h(A) = 1$ becomes

$$\sum_{s=1}^{k} \frac{\beta}{k^2\gamma}\mu_s x_s = R_0 - 1.$$

If we then divide through by R_0 we have that

$$\sum_{s=1}^{k} \frac{1}{k}\mu_s x_s^* = 1 - \frac{1}{R_0}$$

That is,

$$\sum_{s=1}^{k} \frac{1}{k}\mu_s(1 - x_s) = \frac{1}{R_0}$$

That is,

$$\sum_{s=1}^{k} \frac{1}{k} \frac{\mu_s}{1 + A\mu_s} = \frac{1}{R_0}. \tag{5.8}$$

This algebra has shown that this quantity corresponds to the number of susceptibles in a homogeneous population, $\frac{1}{R_0}$. The total number of susceptibles in a heterogeneous population is given by

$$N \sum_s \frac{1}{k}(1 - x_s) = N \sum_s \frac{1}{k} \frac{1}{1 + A\mu_s}. \tag{5.9}$$

It is equations (5.8) and (5.9) we want to compare. We'd expect there to be fewer suceptible individuals in a homogeneous population than a heterogeneous. In other words we'd expect there to be more infected individuals in a homogeneous population than in a heterogeneous. This is equivalent to expecting the inequality

$$\sum_s \frac{\mu_s}{1 + A\mu_s} \quad \leq \quad \sum_s \frac{1}{1 + A\mu_s}$$

to hold. This is easy to see because $\{\mu_s\}$ and $\left\{\frac{1}{1+A\mu_s}\right\}$ are oppositely ordered. Let us set $a_r = \mu_r, b_r = \frac{1}{1+A\mu_r}$. If $a_1 > a_2 > \cdots > a_k$ then $b_1 < b_2 < \cdots < b_k$. The above inequality then follows directly from the fact that

$$\sum_{r=1}^{k} a_r b_r \quad < \quad \frac{1}{k} \left(\sum_{r=1}^{k} a_r \right) \left(\sum_{r=1}^{k} b_r \right).$$

Thus we have shown for k-groups that the deterministic equilibrium value for a heterogeneous model will always be less than that of a homogeneous model when group sizes and mixing are equal and heterogeneity exists in susceptibility alone.

5.7 Stability for special 2-group cases

At the beginning of this chapter we formulated some stability results for equilibria for a general k-group model, predominantly where the mixing parameter was equal for all groups. In this section we specialise to the 2-group numerical examples in section 5.5. In the cases of heterogeneity in infectivity and heterogeneity in mixing only this is in accordance with the general results stated earlier. For the case of heterogeneity in susceptibility, stability conditions are much more complex to find. We demonstrate why and find as simple a form as possible.

5.7.1 Heterogeneity in infectivity

From section 5.3 we know that the disease-free equilibrium is stable if and only if $R_0 < 1$. With heterogeneity in infectivity only, the endemic equilibrium is symmetric, $x_r^* = 1 - \frac{1}{R_0}$ for all r, and so from section 5.4 we have that the endemic equilibrium is stable if and only if $R_0 > 1$.

5.7.2 Heterogeneity in mixing

The Jacobian is

$$J(x_1, x_2) = \frac{\beta}{2} \begin{bmatrix} \pi - \pi x_1 - x_1 - \frac{2\gamma}{\beta} & 1 - x_1 - \pi + \pi x_1 \\ 1 - x_1 - \pi + \pi x_1 & \pi - \pi x_1 - x_1 - \frac{2\gamma}{\beta} \end{bmatrix}.$$

If we examine the trace and determinant of this matrix at both the disease-free and endemic equilibrium point, algebra leads us to some unusual conditions which make sense under particular assumptions. We expect the disease-free equilibrium to be stable if and only if $R_0 < 1$ and the endemic equilibrium point to be stable if and only if $R_0 > 1$. As the eigenvalues of the Jacobian are easy to find explicitly in this case it is much simpler to show that these are negative in order to find stability conditions.

At the disease-free equilibrium point $(0, 0)$,

$$J(0,0) = \frac{\beta}{2} \begin{bmatrix} \pi - \frac{2\gamma}{\beta} & 1 - \pi \\ 1 - \pi & \pi - \frac{2\gamma}{\beta} \end{bmatrix}.$$

The eigenvalues of the Jacobian are $\frac{\beta}{2} - \gamma$ and $\beta\pi - \gamma - \frac{\beta}{2}$. We have

$$\frac{\beta}{2} - \gamma < 0 \quad \Longleftrightarrow \quad 1 < \frac{2\gamma}{\beta} = \frac{1}{R_0} \quad \Longleftrightarrow \quad R_0 < 1$$

and

$$\beta\pi - \gamma - \frac{\beta}{2} < 0 \quad \Longleftrightarrow \quad 2\pi - 1 < \frac{2\gamma}{\beta} = \frac{1}{R_0} \quad \Longleftrightarrow \quad R_0 < \frac{1}{2\pi - 1}.$$

In order for us to reciprocate in this latter inequality we must assume both sides are positive, ie $2\pi - 1 > 0$ and therefore $\pi > 1/2$. Note that $0 \leq \pi \leq 1$ so when $\pi = 1$ this inequality equates to $R_0 < 1$. Thus both inequalities are satisfied and the disease-free point stable if $R_0 < 1$.

For endemic equilibrium,

$$J(x_1, x_2) = \frac{\beta}{2}\begin{bmatrix} \frac{2\gamma\pi}{\beta} - 1 & \frac{2\gamma}{\beta}(1-\pi) \\ \frac{2\gamma}{\beta}(1-\pi) & \frac{2\gamma\pi}{\beta} - 1 \end{bmatrix} = \begin{bmatrix} \frac{\beta}{2}\left(\frac{2\gamma\pi}{\beta} - 1\right) & \gamma(1-\pi) \\ \gamma(1-\pi) & \frac{\beta}{2}\left(\frac{2\gamma\pi}{\beta} - 1\right) \end{bmatrix}.$$

The eigenvalues are $\gamma - \frac{\beta}{2}$ and $\gamma(2\pi - 1) - \frac{\beta}{2}$. We have that

$$\gamma - \frac{\beta}{2} < 0 \quad \Longleftrightarrow \quad 1 < \frac{\beta}{2\gamma} \quad \Longleftrightarrow \quad R_0 > 1$$

and

$$\gamma(2\pi - 1) - \frac{\beta}{2} < 0 \quad \Longleftrightarrow \quad 2\pi - 1 < \frac{\beta}{2\gamma} = R_0.$$

It is clear that the only way these two inequalities are satisfied is when $R_0 > 1$. Thus the results we expected are true in this case.

5.7.3 Heterogeneity in susceptibility

In this case, the endemic equilibrium is not symmetric. We still have that the disease-free equilibrium is stable if and only if $R_0 < 1$, but the situation for the endemic equilibrium is now more complicated. The Jacobian is

$$J(x_1^*, x_2^*) = \frac{\beta}{4}\begin{bmatrix} \mu_1 - 3\mu_1 x_1^* - \frac{4\gamma}{\beta} & \mu_1(1 - x_1^*) \\ \mu_2(1 - x_1^*) & \mu_2 - 3\mu_2 x_1^* - \frac{4\gamma}{\beta} \end{bmatrix}.$$

At the disease-free equilibrium point $(0, 0)$

$$J(0,0) = \frac{\beta}{4}\begin{bmatrix} \mu_1 - \frac{4\gamma}{\beta} & \mu_1 \\ \mu_2 & \mu_2 - \frac{4\gamma}{\beta} \end{bmatrix}$$

$$tr(J(0,0)) = \frac{\beta}{4}\left[\mu_1 + \mu_2 - \frac{8\gamma}{\beta}\right] < 0 \text{ for stability}$$

$$\Rightarrow \frac{\beta}{4}(\mu_1 + \mu_2) < 2\gamma \quad \Rightarrow \quad \frac{\beta(\mu_1 + \mu_2)}{4\gamma} < 2 \quad \Rightarrow \quad R_0 < 2$$

$$det(J(0,0)) = \frac{\beta}{4}\left[(\mu_1 - \frac{4\gamma}{\beta})(\mu_2 - \frac{4\gamma}{\beta}) - \mu_1\mu_2\right] > 0 \text{ for stability}$$

$$\Rightarrow \frac{\beta}{4}\left[\frac{16\gamma^2}{\beta^2} - \frac{4\gamma}{\beta}(\mu_1+\mu_2)\right] > 0 \quad \Rightarrow \quad \frac{4\gamma^2}{\beta} > \gamma(\mu_1+\mu_2) \quad \Rightarrow \quad \frac{4\gamma}{\beta(\mu_1+\mu_2)} > 1$$

Which is equivalent to $R_0 < 1$. If the determinant condition is satisfied then the trace condition automatically follows if $R_0 < 1$. If $R_0 < 1$ then these criteria are satified and equilibrium point $(0,0)$ is stable. If $R_0 \geq 1$ then the trace condition doesn't hold and so $(0,0)$ becomes an unstable equilibrium point.

For the endemic equilibrium it is not sufficient in this scenario to assume $x_1^* = x_2^*$. Intuitively, if we have an overall infection pressure acting on 2 groups with different susceptibilities, one would expect, on average, more infections to occur in the group that is more susceptible to the infection and so this asymmetry makes sense. To find the endemic equilibrium we solve the system

$$\begin{cases} \frac{\beta}{4}\mu_1(1-x_1)(x_1+x_2) - \gamma x_1 &= 0, \\ \frac{\beta}{4}\mu_2(1-x_2)(x_1+x_2) - \gamma x_2 &= 0. \end{cases}$$

Solving this system using Maple yields the disease-free equilibrium and also the solution

$$x_1^* = \frac{-(\beta\mu_1 x_2^* + \beta\mu_2 x_2^* + 4\gamma - \beta\mu_1 - \beta\mu_2)}{\beta(\mu_2-\mu_1)(x_2^*-1)} = \frac{\beta(\mu_1+\mu_2)(1-x_2^*) - 4\gamma}{\beta(\mu_2-\mu_1)(x_2^*-1)}$$

where x_2^* is the solution to a quadratic given by

$$f(Z) = (-\beta\mu_1\mu_2 + \beta\mu_2^2)Z^2 + (-4\gamma\mu_1 + 4\gamma\mu_2 - 2\beta\mu_2^2)Z + \beta\mu_1\mu_2 - 4\gamma\mu_2 + \beta\mu_2^2$$

$$f(Z) = -\beta\mu_2(\mu_1-\mu_2)Z^2 - 2(2\gamma(\mu_1-\mu_2) + \beta\mu_2^2)Z + \mu_2(\beta(\mu_1+\mu_2) - 4\gamma). \quad (5.10)$$

In order to establish the feasibility of the roots of this quadratic, we check the sign of $f(Z)$ by evaluating at 0 and 1:

$$f(0) = \frac{\mu_2}{4\gamma}\left(\frac{\beta(\mu_1+\mu_2)}{4\gamma} - 1\right) = \frac{\mu_2}{4\gamma}(R_0 - 1),$$

$$f(1) = \beta\mu_2(\mu_1+\mu_2-2\mu_2-\mu_1+\mu_2) - 4\gamma(\mu_1-\mu_2) - 4\gamma\mu_2 = -4\gamma\mu_1 \quad < 0,$$

so for $R_0 > 1$,

$$\begin{aligned} f(0) &> 0, \\ f(1) &< 0, \end{aligned}$$

which means there is precisely one root in $(0,1)$. The roots of quadratic (5.10) (solved in Maple) are given by

$$x_2^* = \frac{-2\gamma\mu_1 + 2\gamma\mu_2 - \beta\mu_2^2 \pm \sqrt{4\mu_1^2\gamma^2 - 8\mu_1\mu_2\gamma^2 + 4\mu_2^2\gamma^2 + \beta^2\mu_1^2\mu_2^2}}{\beta\mu_2(\mu_1-\mu_2)}$$

$$= \frac{-2\gamma(\mu_1-\mu_2) - \beta\mu_2^2 \pm \sqrt{4\gamma^2(\mu_1-\mu_2)^2 + \beta^2\mu_1^2\mu_2^2}}{\beta\mu_2(\mu_1-\mu_2)}.$$

Both roots are always real but only one of these roots is feasible. Let us set $\mu_1 \geq \mu_2$ by labelling groups appropriately. If we take the root where the square root term is subtracted then we get $x_2^* < 0$ so the only possible feasible root is obtained by taking the square root term being added in the numerator. Taking this root as x_2^* and substituting back into x_1^*, using Maple after simplification we obtain an endemic equilibrium point of $(x_1^*, x_2^*) =$

$$\left(\frac{-2\gamma(\mu_2-\mu_1) - \beta\mu_1^2(\sqrt{4\gamma^2(\mu_2-\mu_1)^2 + \beta^2\mu_1^2\mu_2^2})}{\beta\mu_1(\mu_2-\mu_1))}, \frac{-2\gamma(\mu_1-\mu_2) - \beta\mu_2^2 + \sqrt{4\gamma^2(\mu_1-\mu_2)^2 + \beta^2\mu_1^2\mu_2^2}}{\beta\mu_2(\mu_1-\mu_2)}\right).$$

Evaluating the trace and determinant of the Jacobian at this endemic equilibrium we have

$$tr(J(x_1^*, x_2^*)) = \frac{\beta}{4}\left[\mu_1 + \mu_2 - 2\mu_1 x_1^* - 2\mu_2 x_2^* - \mu_1 x_2^* - \mu_2 x_1^* - \frac{8\gamma}{\beta}\right]$$

$$= \frac{\beta}{4}\left(\mu_1 + \mu_2 - x_1^*(2\mu_1+\mu_2) - x_2^*(2\mu_2+\mu_1) - \frac{8\gamma}{\beta}\right),$$

so $tr < 0$ if and only if

$$\frac{\beta}{4}\left[x_1^*(2\mu_1+\mu_2) + x_2^*(2\mu_2+\mu_1)\right] \quad > \quad \frac{\beta}{4}(\mu_1+\mu_2) - 2\gamma.$$

Next,

$$det(J(\mathbf{x}^*)) = \frac{\beta^2}{16}\left[\left(\mu_1 - 2\mu_1 x_1^* - \mu_1 x_2^* - \frac{4\gamma}{\beta}\right)\left(\mu_2 - 2\mu_2 x_2^* - \mu_2 x_1^* - \frac{4\gamma}{\beta}\right) - (\mu_1(1-x_1^*))(\mu_2(1-x_1^*)\right]$$

$$= \frac{\beta^2}{16}\left[\frac{16\gamma^2}{\beta^2} - \frac{4\gamma}{\beta}(\mu_1+\mu_2) + 2\mu_1\mu_2(x_1^{*2}+x_2^{*2}) - 2\mu_1\mu_2(x_1^*+x_2^*) + 4\mu_1\mu_2 x_1^* x_2^*\right.$$

$$\left. + \frac{4\gamma\mu_1}{\beta}(2x_1^*+x_2^*) + \frac{4\gamma\mu_2}{\beta}(2x_2^*+x_1^*)\right]$$

so $det > 0$ if and only if

$$\frac{4\gamma^2}{\beta} - \gamma(\mu_1+\mu_2) + \frac{\beta\mu_1\mu_2}{2}(x_1^{*2}+x_2^{*2}) - \frac{\beta\mu_1\mu_2}{2}(x_1^*+x_2^*) + \beta\mu_1\mu_2 x_1^* x_2^* + \gamma\mu_1(2x_1^*+x_2^*) + \gamma\mu_2(2x_2^*+x_1^*) > 0$$

This is as simplified an expression as manageable. We'd expect this inequaility to hold only for $R_0 > 1$. This is easy to check numerically at least.

5.8 Quasi-stationarity and the Ornstein-Uhlenbeck approximation

5.8.1 Heterogeneity in infectivity

We now use Ornstein-Uhlenbeck theory to calculate the approximate variance matrix Σ of the 2-group heterogeneous model of section 5.5.1. This will allow us to calculate the variance within groups 1 and 2 and the covariance between the groups. Recall that the quasi-stationary distribution is given by the left leading eigenvector of the matrix of the system (see section 3.3, equation (3.3)). Over the time interval $[t, t+\delta t]$ we have the transition rates

$$\begin{aligned}
(I_1, I_2) &\to (I_1+1, I_2) \text{ with rate } \frac{\beta}{4}\lambda_1 I_1(1-I_1) + \frac{\beta}{4}\lambda_2 I_2(1-I_1),\\
(I_1, I_2) &\to (I_1, I_2+1) \text{ with rate } \frac{\beta}{4}\lambda_1 I_1(1-I_2) + \frac{\beta}{4}\lambda_2 I_2(1-I_2),\\
(I_1, I_2) &\to (I_1-1, I_2) \text{ with rate } \gamma I_1,\\
(I_1, I_2) &\to (I_1, I_2-1) \text{ with rate } \gamma I_2.
\end{aligned}$$

So close to endemic equilibrium, since $x_1^* = x_2^*$,

$$E[(\partial x_1)^2] = \frac{\beta}{4}[\lambda_1 x_1^*(1-x_1^*) + \lambda_2 x_1^*(1-x_1^*)] + \gamma x_1^* = \frac{\beta}{4}[(\lambda_1+\lambda_2)x_1^*(1-x_1^*)] + \gamma x_1^*.$$

Similarly

$$E[(\partial x_2)^2] = \frac{\beta}{4}[(\lambda_1+\lambda_2)x_1^*(1-x_1^*)] + \gamma x_1^*.$$

Finally, since we are dealing in one step-transitions where only an infection or recovery can occur in one group per time interval, $E[(\partial x_1 \partial x_2)] = 0$. Therefore the approximating Ornstein-Uhlenbeck process around (x_1^*, x_2^*) has local covariance matrix

$$G = \begin{bmatrix} \frac{\beta}{4}[(\lambda_1+\lambda_2)x_1^*(1-x_1^*)] + \gamma x_1^* & 0 \\ 0 & \frac{\beta}{4}[(\lambda_1+\lambda_2)x_1^*(1-x_1^*)] + \gamma x_1^* \end{bmatrix}.$$

Substituting $x_1^* = 1 - \frac{1}{R_0} = 1 - \frac{4\gamma}{\beta(\lambda_1+\lambda_2)}$ gives

$$\begin{aligned}
G_{11} &= \tfrac{\beta}{4}\left[(\lambda_1+\lambda_2)\left(1-\tfrac{4\gamma}{\beta(\lambda_1+\lambda_2)}\right)\left(\tfrac{4\gamma}{\beta(\lambda_1+\lambda_2)}\right)\right] + \gamma\left(1-\tfrac{4\gamma}{\beta(\lambda_1+\lambda_2)}\right)\\
&= \tfrac{\beta}{4}\left[(\lambda_1+\lambda_2)\left(\tfrac{4\gamma}{\beta(\lambda_1+\lambda_2)} - \tfrac{16\gamma^2}{\beta^2(\lambda_1+\lambda_2)^2}\right)\right] + \gamma - \tfrac{4\gamma^2}{\beta(\lambda_1+\lambda_2)}\\
&= \tfrac{\gamma\lambda_1}{\lambda_1+\lambda_2} + \tfrac{\gamma\lambda_2}{\lambda_1+\lambda_2} - \tfrac{4\gamma^2\lambda_1}{\beta(\lambda_1+\lambda_2)^2} - \tfrac{4\gamma^2\lambda_2}{\beta(\lambda_1+\lambda_2)^2} - \tfrac{4\gamma^2}{\beta(\lambda_1+\lambda_2)} + \gamma\\
&= 2\gamma - \tfrac{4\gamma^2}{\beta(\lambda_1+\lambda_2)} - \tfrac{4\gamma^2}{\beta(\lambda_1+\lambda_2)}\left(\tfrac{\lambda_1}{\lambda_1+\lambda_2} + \tfrac{\lambda_2}{\lambda_1+\lambda_2}\right)\\
&= 2\gamma\left(1-\tfrac{4\gamma}{\beta(\lambda_1+\lambda_2)}\right).
\end{aligned}$$

We have $J(x_1^*, x_2^*)\Sigma + \Sigma J^T(x_1^*, x_2^*) = -G(x_1^*, x_2^*)$ which can be written

$$\begin{pmatrix} J_{11} & J_{12} \\ J_{21} & J_{22} \end{pmatrix}\begin{pmatrix} \Sigma_{11} & \Sigma_{12} \\ \Sigma_{21} & \Sigma_{22} \end{pmatrix} + \begin{pmatrix} \Sigma_{11} & \Sigma_{12} \\ \Sigma_{21} & \Sigma_{22} \end{pmatrix}\begin{pmatrix} J_{11} & J_{21} \\ J_{12} & J_{22} \end{pmatrix} = -\begin{pmatrix} G_{11} & G_{12} \\ G_{21} & G_{22} \end{pmatrix}$$

$$\Rightarrow \begin{pmatrix} J_{11}\Sigma_{11} + J_{12}\Sigma_{21} & J_{11}\Sigma_{12} + J_{12}\Sigma_{22} \\ J_{21}\Sigma_{11} + J_{22}\Sigma_{21} & J_{21}\Sigma_{12} + J_{22}\Sigma_{22} \end{pmatrix} + \begin{pmatrix} J_{11}\Sigma_{11} + J_{12}\Sigma_{12} & J_{21}\Sigma_{11} + J_{22}\Sigma_{12} \\ J_{11}\Sigma_{21} + J_{12}\Sigma_{22} & J_{21}\Sigma_{21} + J_{22}\Sigma_{22} \end{pmatrix} = -G$$

$$\begin{pmatrix} 2J_{11}\Sigma_{11} + J_{12}\Sigma_{12} + J_{12}\Sigma_{21} & J_{11}\Sigma_{12} + J_{12}\Sigma_{22} + J_{21}\Sigma_{11} + J_{22}\Sigma_{12} \\ J_{11}\Sigma_{21} + J_{12}\Sigma_{22} + J_{21}\Sigma_{11} + J_{22}\Sigma_{21} & 2J_{22}\Sigma_{22} + J_{21}\Sigma_{12} + J_{21}\Sigma_{21} \end{pmatrix} = -\begin{pmatrix} G_{11} & G_{12} \\ G_{21} & G_{22} \end{pmatrix}.$$

where Σ_{11} represents the variance of the number of infected individuals within group 1, Σ_{22} the variance of the number of infected indivudals within group 2 and Σ_{12}, Σ_{21} the covariance between group 1 and group 2 when the system is in quasi-stationarity. To solve for the components of Σ, this can be written as

$$\begin{bmatrix} 2J_{11} & J_{12} & J_{12} & 0 \\ J_{21} & (J_{11}+J_{22}) & 0 & J_{12} \\ J_{21} & 0 & (J_{11}+J_{22}) & J_{12} \\ 0 & J_{21} & J_{21} & 2J_{22} \end{bmatrix}\begin{bmatrix} \Sigma_{11} \\ \Sigma_{12} \\ \Sigma_{21} \\ \Sigma_{22} \end{bmatrix} = -\begin{bmatrix} G_{11} \\ G_{12} \\ G_{21} \\ G_{22} \end{bmatrix},$$

so

$$\begin{bmatrix} \Sigma_{11} \\ \Sigma_{12} \\ \Sigma_{21} \\ \Sigma_{22} \end{bmatrix} = -\begin{bmatrix} 2J_{11} & J_{12} & J_{12} & 0 \\ J_{21} & (J_{11}+J_{22}) & 0 & J_{12} \\ J_{21} & 0 & (J_{11}+J_{22}) & J_{12} \\ 0 & J_{21} & J_{21} & 2J_{22} \end{bmatrix}^{-1}\begin{bmatrix} G_{11} \\ G_{12} \\ G_{21} \\ G_{22} \end{bmatrix}$$

$$\begin{bmatrix} \Sigma_{11} \\ \Sigma_{12} \\ \Sigma_{21} \\ \Sigma_{22} \end{bmatrix} =$$

$$-\frac{\beta}{4}\begin{bmatrix} 2(\lambda_1 - 2\lambda_1 x_1^* - \lambda_2 x_1^* - \frac{4\gamma}{\beta}) & \lambda_2(1-x_1^*) & \lambda_2(1-x_1^*) \\ \lambda_1(1-x_1^*) & \lambda_1+\lambda_2-3\lambda_1 x_1^* - 3\lambda_2 x_1^* - \frac{8\gamma}{\beta} & 0 \\ \lambda_1(1-x_1^*) & 0 & \lambda_1+\lambda_2-3\lambda_1 x_1^* - 3\lambda_2 x_1^* - \frac{8\gamma}{\beta} \\ 0 & \lambda_1(1-x_1^*) & \lambda_1(1-x_1^*) \end{bmatrix}$$

$$\begin{bmatrix} 0 \\ \lambda_2(1-x_1^*) \\ \lambda_2(1-x_1^*) \\ 2(\lambda_2 - 2\lambda_2 x_1^* - \lambda_1 x_1^* - \frac{4\gamma}{\beta}) \end{bmatrix}^{-1} \times \begin{bmatrix} G_{11} \\ G_{12} \\ G_{21} \\ G_{22} \end{bmatrix}.$$

After substituting $x_1^* = 1 - \frac{1}{R_0}$ and simplifying we get

$$\begin{bmatrix} \Sigma_{11} \\ \Sigma_{12} \\ \Sigma_{21} \\ \Sigma_{22} \end{bmatrix} = -\frac{\beta}{4} \begin{bmatrix} \frac{2(4\gamma\lambda_1-\beta(\lambda_1+\lambda_2)^2)}{\beta(\lambda_1+\lambda_2)} & \frac{4\gamma\lambda_2}{\beta(\lambda_1+\lambda_2)} & \frac{4\gamma\lambda_2}{\beta(\lambda_1+\lambda_2)} & 0 \\ \frac{4\gamma\lambda_1}{\beta(\lambda_1+\lambda_2)} & -2(\lambda_1+\lambda_2)+\frac{4\gamma}{\beta} & 0 & \frac{4\gamma\lambda_2}{\beta(\lambda_1+\lambda_2)} \\ \frac{4\gamma\lambda_1}{\beta(\lambda_1+\lambda_2)} & 0 & -2(\lambda_1+\lambda_2)+\frac{4\gamma}{\beta} & \frac{4\gamma\lambda_2}{\beta(\lambda_1+\lambda_2)} \\ 0 & \frac{4\gamma\lambda_1}{\beta(\lambda_1+\lambda_2)} & \frac{4\gamma\lambda_1}{\beta(\lambda_1+\lambda_2)} & \frac{2(4\gamma\lambda_2-\beta(\lambda_1+\lambda_2)^2)}{\beta(\lambda_1+\lambda_2)} \end{bmatrix}^{-1}$$

$$\times \begin{bmatrix} 2\gamma\left(1-\frac{4\gamma}{\beta(\lambda_1+\lambda_2)}\right) \\ 0 \\ 0 \\ 2\gamma\left(1-\frac{4\gamma}{\beta(\lambda_1+\lambda_2)}\right) \end{bmatrix}.$$

Using Maple we can calculate explicit algebraic solutions for the elements of the variance matrix, given below for $\Sigma_{11}, \Sigma_{12} = \Sigma_{21}$ and Σ_{22} respectively.

$$-\frac{4\gamma(\beta^2(\lambda_1^4+\lambda_2^4)+\beta^2(4\lambda_1^3\lambda_2+4\lambda_1\lambda_2^3+6\lambda_1^2\lambda_2^2)+16\lambda_2^2\gamma^2-2\beta\gamma(\lambda_1^3+5\lambda_1^2\lambda_2+7\lambda_1\lambda_2^2+3\lambda_2^3)}{\beta^2(2\gamma\lambda_1+2\gamma\lambda_2-\beta\lambda_1^2-\beta\lambda_2^2-2\beta\lambda_1\lambda_2)(\lambda_1+\lambda_2)^3}$$

$$\frac{8\gamma^2(8\lambda_1\lambda_2\gamma-\beta\lambda_1^3-\beta\lambda_2^3-3\beta\lambda_1^2\lambda_2-3\beta\lambda_1\lambda_2^2)}{\beta^2(2\gamma\lambda_1+2\gamma\lambda_2-\beta\lambda_1^2-\beta\lambda_2^2-2\beta\lambda_1\lambda_2)(\lambda_1+\lambda_2)^3}$$

$$-\frac{4\gamma(\beta^2(\lambda_1^4+\lambda_2^4)+\beta^2(4\lambda_1^3\lambda_2+4\lambda_1\lambda_2^3+6\lambda_1^2\lambda_2^2)+16\lambda_1^2\gamma^2-2\beta\gamma(\lambda_2^3+5\lambda_1\lambda_2^2+7\lambda_1^2\lambda_2+3\lambda_1^3)}{\beta^2(2\gamma\lambda_1+2\gamma\lambda_2-\beta\lambda_1^2-\beta\lambda_2^2-2\beta\lambda_1\lambda_2)(\lambda_1+\lambda_2)^3}$$

We can now plot the quasi-stationary distribution of total infected $I_1 + I_2$ in this scenario, against the Ornstein-Uhlenbeck approximation, a normal distribution having mean given by the deterministic equilibrium and variance $N\sqrt{\Sigma_{11}+\Sigma_{12}+\Sigma_{21}+\Sigma_{22}}$.

Figure (5.12) shows that the Ornstein-Uhlenbeck approximation gives a good approximation to the quasi-stationary distribution, with probabilities differing with that of the quasi-stationary distribution by no more than 0.0034 across the population range, for these parameter values. Appendix F shows the MATLAB code used to perform these operations including the algebraic variance output from Maple (for the case of heterogeneity in infectivity).

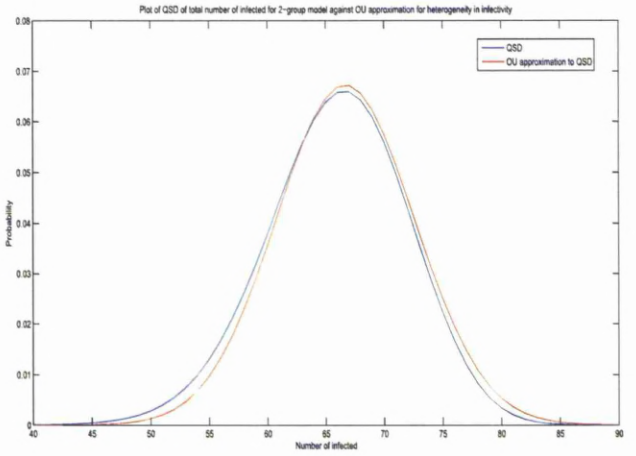

Figure 5.12: Quasi-stationary distribution of total number of infected for the 2-group case with heterogeneity in infectivity against Ornstein-Uhlenbeck approximation. Parameter values $N_1 = N_2 = 50, \lambda_1 = 40/21, \lambda_2 = 2/21, \mu_1 = \mu_2 = 1, f_1 = f_2 = 1/2, \pi = 1 - \pi = 1/2, R_0 = 3, \gamma = 1$.

5.8.2 Heterogeneity in mixing

For our Ornstein-Uhlenbeck approximation, we have that

$$J(x_1^*, x_2^*) = \frac{\beta}{2}\begin{bmatrix} \pi - 2\pi x_1^* - x_1^* + \pi x_1^* - \frac{2\gamma}{\beta} & 1 - x_1^* - \pi + \pi x_1^* \\ 1 - x_1^* - \pi + \pi x_1^* & \pi - 2\pi x_1^* - x_1^* + \pi x_1^* - \frac{2\gamma}{\beta} \end{bmatrix}.$$

From the transition rates, since $x_1^* = x_2^*$,

$$E[(\partial x_1)^2] = \frac{\beta}{2}[\pi x_1^*(1 - x_1^*) + (1 - \pi)x_1^*(1 - x_1^*)] + \gamma x_1^*,$$

$$E[(\partial x_2)^2] = \frac{\beta}{2}[\pi x_1^*(1 - x_1^*) + (1 - \pi)x_1^*(1 - x_1^*)] + \gamma x_1^*,$$

$$E[(\partial x_1 \partial x_2)] = 0,$$

so that

$$G = \begin{bmatrix} \frac{\beta}{2}[\pi x_1^*(1 - x_1^*) + (1 - \pi)x_1^*(1 - x_1^*)] + \gamma x_1^* & 0 \\ 0 & \frac{\beta}{2}[\pi x_1^*(1 - x_1^*) + (1 - \pi)x_1^*(1 - x_1^*)] + \gamma x_1^* \end{bmatrix}$$

$$G = \begin{bmatrix} \frac{\beta}{2}[x_1^*(1 - x_1^*)] & 0 \\ 0 & \frac{\beta}{2}[x_1^*(1 - x_1^*)] \end{bmatrix}.$$

Substituting $x_1^* = 1 - 1/R_0$ leads to diagonal elements

$$G_{11} = G_{22} = \frac{\beta}{2}\left[\left(1 - \frac{2\gamma}{\beta}\right)\left(\frac{2\gamma}{\beta}\right)\right] = \gamma - \frac{2\gamma^2}{\beta} = \gamma\left(1 - \frac{2\gamma}{\beta}\right).$$

Using the same approach as we did when examining heterogeneity in infectivity, we substitute algebraic expressions from the Jacobian into the equation $J\Sigma + \Sigma J^T + G = 0$, evaluate the elements of the J matrix at equilibrium point $1 - 1/R_0$ and use the elements calculated above for the G matrix. After algebra and simplification we acquire the relation

$$\begin{bmatrix} \Sigma_{11} \\ \Sigma_{12} \\ \Sigma_{21} \\ \Sigma_{22} \end{bmatrix} = -\frac{\beta}{2}\begin{bmatrix} \frac{4\gamma\pi}{\beta} - 2 & \frac{2\gamma}{\beta} - \frac{2\gamma\pi}{\beta} & \frac{2\gamma}{\beta} - \frac{2\gamma\pi}{\beta} & 0 \\ \frac{2\gamma}{\beta} - \frac{2\gamma\pi}{\beta} & \frac{4\gamma\pi}{\beta} - 2 & 0 & \frac{2\gamma}{\beta} - \frac{2\gamma\pi}{\beta} \\ \frac{2\gamma}{\beta} - \frac{2\gamma\pi}{\beta} & 0 & \frac{4\gamma\pi}{\beta} - 2 & \frac{2\gamma}{\beta} - \frac{2\gamma\pi}{\beta} \\ 0 & \frac{2\gamma}{\beta} - \frac{2\gamma\pi}{\beta} & \frac{2\gamma}{\beta} - \frac{2\gamma\pi}{\beta} & \frac{4\gamma\pi}{\beta} \end{bmatrix}^{-1}$$
$$\times \begin{bmatrix} \gamma\left(1 - \frac{2\gamma}{\beta}\right) \\ 0 \\ 0 \\ \gamma\left(1 - \frac{2\gamma}{\beta}\right) \end{bmatrix}$$

Solving this in Maple, leads to algebraic solutions for the variance matrix given by

$$\begin{bmatrix} \Sigma_{11} & \Sigma_{12} \\ \Sigma_{21} & \Sigma_{22} \end{bmatrix} = \begin{bmatrix} \frac{\gamma(2\gamma\pi-\beta)}{\beta(4\gamma\pi-2\gamma-\beta)} & \frac{2\gamma^2(\pi-1)}{\beta(4\gamma\pi-2\gamma-\beta)} \\ \frac{2\gamma^2(\pi-1)}{\beta(4\gamma\pi-2\gamma-\beta)} & \frac{\gamma(2\gamma\pi-\beta)}{\beta(4\gamma\pi-2\gamma-\beta)} \end{bmatrix}.$$

We can now plot the actual quasi-stationary distribution of total infected in this scenario, against the Ornstein-Uhlenbeck theory approximation, a normal distribution having mean equal to the deterministic equilibrium and variance $N\sqrt{\Sigma_{11} + \Sigma_{12} + \Sigma_{21} + \Sigma_{22}}$.

Figure (5.13) shows that the Ornstein-Uhlenbeck approximation, although not exactly equal to the quasi-stationary distribution, is a very close approximation with probabilities differing from that of the quasi-stationary distribution by no more than 0.0052 across the range of predicted numbers of infected individuals when assortative mixing is assumed for these parameter values. Figure (5.14) shows, again, the closeness of the Ornstein-Uhlenbeck approximation to the quasi-stationary distribution with probabilities differing from that of the quasi-stationary distribution by no more than 0.0016 when dissortative mixing is assumed. What is interesting to note is that the Ornstein-Uhlenbeck approximation is close to the quasi-stationary distribution when the two different types of heterogeneity in mixing are assumed, but the type of mixing assumed does impact the accuracy of the approximation. It is closer to the quasi-stationary distribution when dissortative mixing is assumed but nonetheless remains a good approximation for either mixing type.

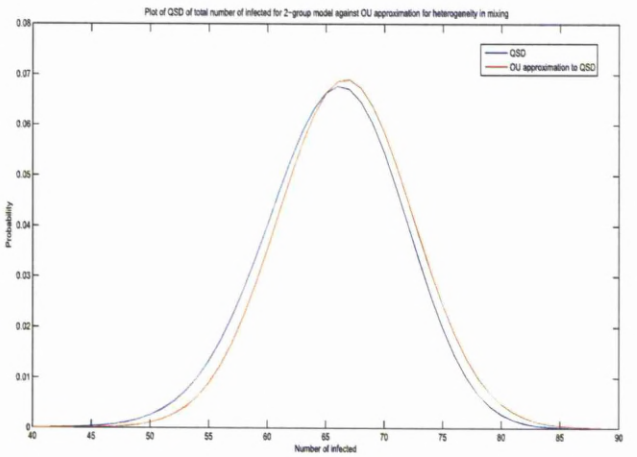

Figure 5.13: Quasi-stationary distribution for total number of infected for the 2-group case with heterogeneity in mixing against Ornstein-Uhlenbeck approximation. Parameter values $N_1 = N_2 = 50, \lambda_1 = \lambda_2 = 1, \mu_1 = \mu_2 = 1, f_1 = f_2 = 1/2, \pi = 0.95, R_0 = 3, \gamma = 1$.

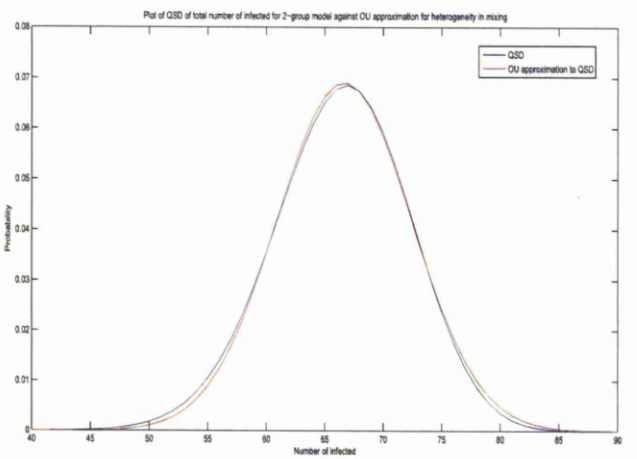

Figure 5.14: Quasi-stationary distribution for total number of infected for the 2-group case with heterogeneity in mixing against Ornstein-Uhlenbeck approximation. Parameter values $N_1 = N_2 = 50, \lambda_1 = \lambda_2 = 1, \mu_1 = \mu_2 = 1, f_1 = f_2 = 1/2, \pi = 0.05, R_0 = 3, \gamma = 1$.

5.8.3 Heterogeneity in susceptibility

For our Ornstein-Uhlenbeck approximation, we have that

$$J(x_1^*, x_2^*) = \frac{\beta}{4}\begin{bmatrix} \mu_1 - 2\mu_1 x_1^* - \mu_1 x_2^* - \frac{4\gamma}{\beta} & \mu_1(1-x_1^*) \\ \mu_2(1-x_2^*) & \mu_2 - 2\mu_2 x_2^* - \mu_2 x_1^* - \frac{4\gamma}{\beta} \end{bmatrix}.$$

From the transition rates

$$E[(\partial x_1)^2] = \frac{\beta}{4}[\mu_1(1-x_1^*)(x_1^*+x_2^*)] + \gamma x_1^*,$$

$$E[(\partial x_2)^2] = \frac{\beta}{4}[\mu_2(1-x_2^*)(x_1^*+x_2^*)] + \gamma x_2^*,$$

$$E[(\partial x_1 \partial x_2)] = 0,$$

$$\Rightarrow G = \begin{bmatrix} \frac{\beta}{4}[\mu_1(1-x_1^*)(x_1^*+x_2^*)] + \gamma x_1^* & 0 \\ 0 & \frac{\beta}{4}[\mu_2(1-x_2^*)(x_1^*+x_2^*)] + \gamma x_2^* \end{bmatrix}.$$

Substituting x_1^* and x_2^* into this matrix leads to

$$G_{11} = \frac{-2\gamma(2\gamma(\mu_1-\mu_2) - \beta\mu_1^2 + \sqrt{4\gamma^2(\mu_1-\mu_2)^2 + \beta^2\mu_1^2\mu_2^2}}{\beta\mu_1(\mu_1-\mu_2)}.$$

Similarly

$$G_{22} = \frac{-2\gamma(2\gamma(\mu_1-\mu_2) + \beta\mu_2^2 + \sqrt{4\gamma^2(\mu_1-\mu_2)^2 + \beta^2\mu_1^2\mu_2^2}}{\beta\mu_2(\mu_1-\mu_2)}.$$

Substituting algebraic expressions from the Jacobian into the equation $J\Sigma + \Sigma J^T + G = 0$, evaluating the elements of the J matrix at equilibrium point (x_1^*, x_2^*) and using the elements calculated above for the G matrix. After algebra and simplification we acquire the relation

$$\begin{bmatrix} \Sigma_{11} \\ \Sigma_{12} \\ \Sigma_{21} \\ \Sigma_{22} \end{bmatrix} = -\frac{\beta}{4}\begin{bmatrix} 2\mu_1 - 4\mu_1 x_1^* - 2\mu_1 x_2^* - \frac{8\gamma}{\beta} & \mu_1(1-x_1^*) \\ \mu_2(1-x_2^*) & \mu_1 + \mu_2 - x_1^*(2\mu_1+\mu_2) - x_2^*(2\mu_2+\mu_1) - \frac{8\gamma}{\beta} \\ \mu_2(1-x_2^*) & 0 \\ 0 & \mu_2(1-x_2^*) \end{bmatrix}$$

$$\begin{bmatrix} \mu_1(1-x_1^*) & 0 \\ 0 & \mu_1(1-x_1^*) \\ \mu_1 + \mu_2 - x_1^*(2\mu_1+\mu_2) - x_2^*(2\mu_2+\mu_1) - \frac{8\gamma}{\beta} & \mu_1(1-x_1^*) \\ \mu_2(1-x_2^*) & 2\mu_2 - 4\mu_2 x_2^* - 2\mu_2 x_1^* - \frac{8\gamma}{\beta} \end{bmatrix}^{-1} \times \begin{bmatrix} G_{11} \\ 0 \\ 0 \\ G_{22} \end{bmatrix}.$$

Using Maple this leads to explicit algebraic solutions for the variance matrix. Calculations and explicit solutions for $\Sigma_{11}, \Sigma_{12} = \Sigma_{21}$ and Σ_{22} are shown in appendix H under these conditions. Substitution of x_1^*, x_2^* for their corresponding roots is simple enough giving the variances and covariances explicitly in terms of γ, β and μ but such solutions are both lengthy and complicated.

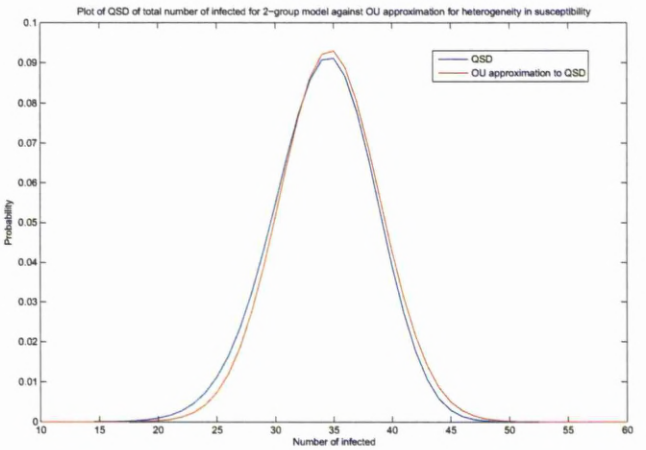

Figure 5.15: Quasi-stationary distribution for total number of infected for the 2-group case with heterogeneity in susceptibility against Ornstein-Uhlenbeck approximation. Parameter values $N_1 = N_2 = 50, \lambda_1 = \lambda_2 = 1, \mu_1 = 200/101, \mu_2 = 2/101, f_1 = f_2 = 1/2, \pi = 0.5, R_0 = 3, \gamma = 1$.

Figure (5.15) shows that the Ornstein-Uhlenbeck approximation, although not exactly equal to the quasi-stationary distribution, is a very close approximation with probabilities differing from that of the quasi-stationary distribution by no more than 0.0049 across the range of predicted numbers of infected individuals for these parameter values. It is reasonable to conclude from each of the Ornstein-Uhlenbeck approximations we have analysed that the Ornstein-Uhlenbeck approximation is a good approximation to the quasi-stationary distribution irrespective of the type of heterogeneity imposed for the parameter values we have used. As was touched upon earlier however, the actual type of heterogeneity does affect the closeness of the approximation. From these results, the Ornstein-Uhlenbeck approximation is least accurate when heterogeneity in susceptibility exists, and is most accurate when dissortative mixing exists. Note that we only expect the Ornstein-Uhlenbeck approximation to be good for N_1, N_2 large and for $R_0 >> 1$.

5.9 Time to extinction

For all scenarios examined so far, where we have looked at differing parameters of heterogeneity we now calculate numerical results for the mean time to extinction from quasi-stationarity for each heterogeneous model and compare it to the corresponding mean time to extinction of a homogenoeus model.

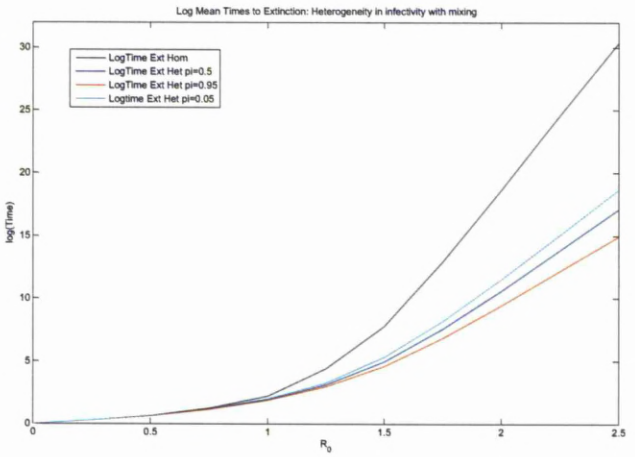

Figure 5.16: Log mean times to extinction for both a homogeneous 2-group model and heterogeneous 2-group model where heterogeneity is in infectivity, infectivity with assortative mixing and infectivity with dissortative mixing. Parameter values $N_1 = N_2 = 50, \lambda_1 = 40/21, \lambda_2 = 2/21, \mu_1 = \mu_2 = 1, \gamma = 1$ for all cases, $f_1 = f_2 = 1/2$ for all cases. We use mixing parameters $\pi = 0.5, 0.95, 0.05$.

Let us denote by τ_Q^{Hom} the mean time to extinction of a homogeneous 2-group process, and by τ_Q^{Het} the mean time to extinction of a heterogeneous 2-group process. In addition to this notation, let us further define τ_Q^x to be the mean time to extinction of a heterogeneous 2-group process where x describes a particular type, or types, of heterogeneity. The types x can take are $\{Inf, Ass, Dis, Sus\}$ or a combination, where $\{Inf\}$ refers to infectivity, $\{Ass\}$ assortative mixing, $\{Dis\}$ dissortative mixing and $\{Sus\}$ susceptibility.

From all results, a similarity to notice is that the mean time to extinction is strictly increasing in R_0 irrespective of the types of heterogeneity introduced. This is an intuitive notion, because as we increase the rate at which individuals become infected (R_0), we would expect more infections to occur and so the longer the process would take to die out due to a larger proportion of infected individuals in the whole population. The type of heterogeneity however does strongly influence the

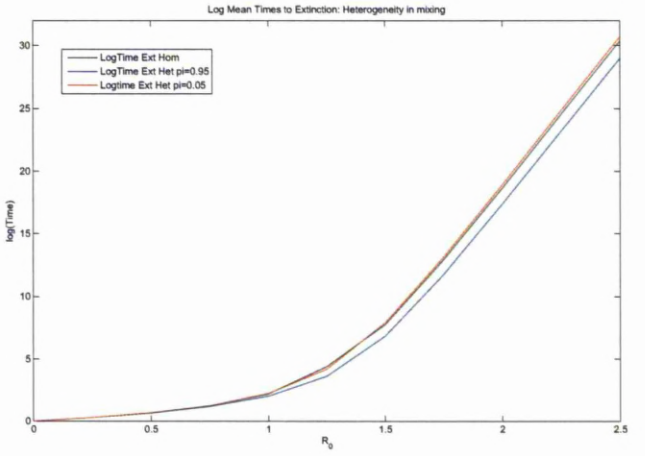

Figure 5.17: Log mean times to extinction for both a homogeneous 2-group model and heterogeneous 2-group model where heterogeneity is in mixing. Parameter values $N_1 = N_2 = 50, \lambda_1 = \lambda_2 = 1, \mu_1 = \mu_2 = 1, \gamma = 1$ for all cases, $f_1 = f_2 = 1/2$ for all cases. We use mixing parameters $\pi = 0.95, 0.05$.

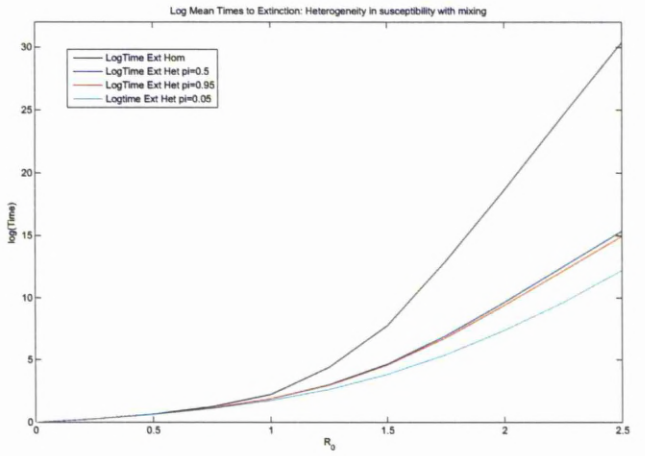

Figure 5.18: Log mean times to extinction for both a homogeneous 2-group model and heterogeneous 2-group model where heterogeneity is in susceptibility, susceptibility with assortative mixing and susceptibility with dissortative mixing. Parameter values $N_1 = N_2 = 50, \lambda_1 = \lambda_2 = 1, \mu_1 = 200/101, \mu_2 = 2/101, \gamma = 1$ for all cases, $f_1 = f_2 = 1/2$ for all cases. We use mixing parameters $\pi = 0.5, 0.95, 0.05$.

mean time to extinction and the range by which it differs from the homogeneous mean time to extinction.

From Figures (5.16) and (5.17) we can see that heterogeneity in infectivity decreases τ_Q^{Het} significantly more than heterogeneity in mixing. τ_Q^{Inf} is significantly lower for this 2-group heterogeneous model than τ_Q^{Hom}. In fact τ_Q^{Inf} is consistently bounded from above by τ_Q^{Hom} for all R_0 values. When we combine heterogeneity in infectivity with assortative mixing we find that this lowers τ_Q^{Het} further still and therefore the process is expected to die out more quickly. If however we combine with dissortative mixing, the results show that this process will take longer to die out than a process where heterogeneity in infectivity exists and there is no mixing preference. The homogeneous case bounds all three of these cases from above. In fact, we have the ordering

$$\tau_Q^{Hom} \geq \tau_Q^{Inf,Dis} \geq \tau_Q^{Inf} \geq \tau_Q^{Inf,Ass}.$$

It is clear to see that as $\pi \to 0.5$ from above $\tau_Q^{Inf,Ass} \to \tau_Q^{Inf}$ and that as $\pi \to 0.5$ from below $\tau_Q^{Inf,Dis} \to \tau_Q^{Inf}$. In other words, the stronger the preference for within-group mixing, when combined with heterogeneity in infectivity, the quicker the time to extinction and the stronger the preference for cross-group mixing when combined with heterogeneity in infectivity, the longer the time to extinction with the case of equal mixing preference taking some time in between. The degree of the impact each mixing-type has on τ_Q^{Het} appears to increase as R_0 increases.

Although heterogeneity in mixing impacts τ_Q^{Het}, its impact is not as strong as heterogeneity in other parameters as evidenced by Figure (5.17). What is interesting to note is that when we have assortative mixing, time to extinction is lower than that for a homogeneously mixing model and so the process is expected to die out more quickly. In fact τ_Q^{Hom} bounds from above τ_Q^{Ass} in this case for all R_0 values. However, when we impose dissortative mixing, this isn't the case. The plots show that $\tau_Q^{Hom} \geq \tau_Q^{Dis}$ up until an R_0 value of approximately 1.4, but then for R_0 values above this, a process with heterogeneity in dissortative mixing is expected to persist longer than a homogeneous process, although the difference in time is not large. The important result here is that we cannot conclude that τ_Q^{Hom} is always greater than τ_Q^{Het} irrespective of the type of heterogeneity.

From Figure (5.18) it is also clear to see that heterogeneity in susceptibility has a much larger impact on τ_Q^{Het} than heterogeneity in mixing only. $\tau_Q^{Hom} \geq \tau_Q^{Sus}$ for all R_0 values. Combining heterogeneity in susceptibility with assortative mixing decreases τ_Q^{Het} further and combining heterogeneity in susceptibility with dissortative mixing decreases τ_Q^{Het} further still. So we have the ordering

$$\tau_Q^{Hom} \geq \tau_Q^{Sus} \geq \tau_Q^{Sus,Ass} \geq \tau_Q^{Sus,Dis},$$

where the homogeneous process is expected to persist the longest. What is interesting to note here is the difference between this ordering and the previous two. When we examined heterogeneity in mixing only, we found that dissortative mixing raised τ_Q^{Het} and assortative lowered τ_Q^{Het}. When we examined heterogeneity in infectivity and combined it with dissortative mixing, again τ_Q^{Het} was raised above τ_Q^{Inf} with no mixing preference and assortative mixing lowered τ_Q^{Het} below τ_Q^{Inf} with no mixing preference. When looking at heterogeneity in susceptibility, both types of mixing decrease τ_Q^{Het} below τ_Q^{Sus} with no mixing preference. Another feature is that combining heterogeneity in susceptibility with assortative mixing has a lesser impact on τ_Q^{Inf} than combining heterogeneity in susceptibility with dissortative mixing. The degree of this impact appears to become more significant as R_0 increases.

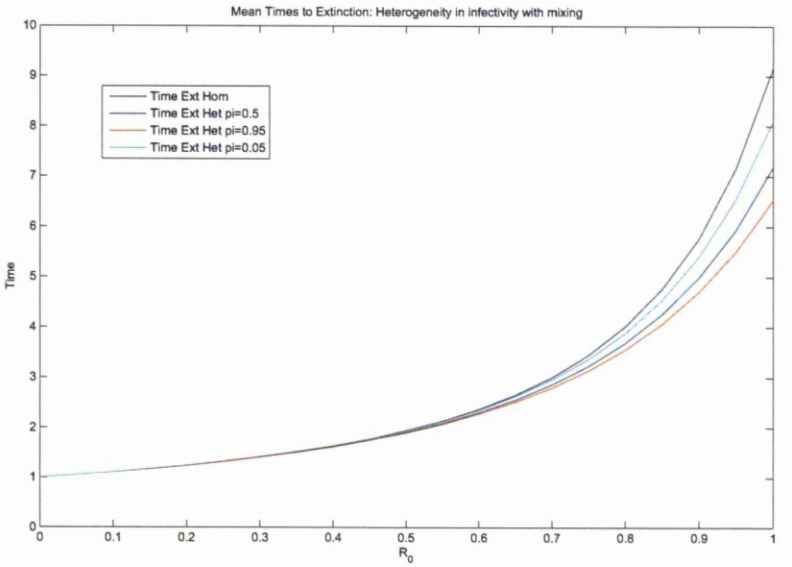

Figure 5.19: Mean times to extinction for $R_0 \leq 1$ for both a homogeneous 2-group model and heterogeneous 2-group model where heterogeneity is in infectivity, infectivity with assortative mixing and infectivity with dissortative mixing. Parameter values $N_1 = N_2 = 50, \lambda_1 = 40/21, \lambda_2 = 2/21, \mu_1 = \mu_2 = 1, \gamma = 1$ for all cases, $f_1 = f_2 = 1/2$ for all cases. We use mixing parameters $\pi = 0.5, 0.95, 0.05$.

Figures (5.19), (5.20) and (5.21) show the mean times to extinction for $R_0 < 1$ for heterogeneity in infectivity, mixing and susceptibility respectively. In the cases of infectivity and susceptibility we look at the effects of assortative and dissortative mixing in addition. Each of these plots show more closely the effects

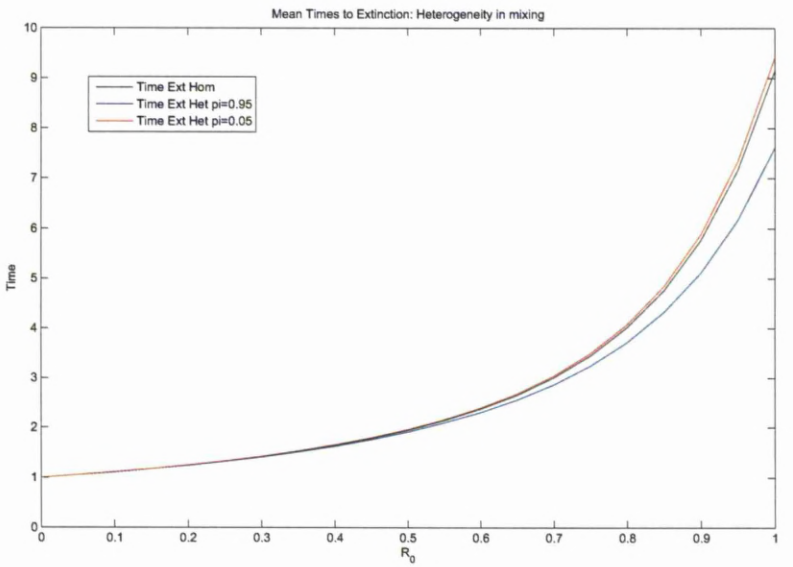

Figure 5.20: Mean times to extinction for $R_0 \leq 1$ for both a homogeneous 2-group model and heterogeneous 2-group model where heterogeneity is in mixing. Parameter values $N_1 = N_2 = 50, \lambda_1 = \lambda_2 = 1, \mu_1 = \mu_2 = 1, \gamma = 1$ for all cases, $f_1 = f_2 = 1/2$ for all cases. We use mixing parameters $\pi = 0.95, 0.05$.. We use mixing parameters $\pi = 0.5, 0.95, 0.05$.

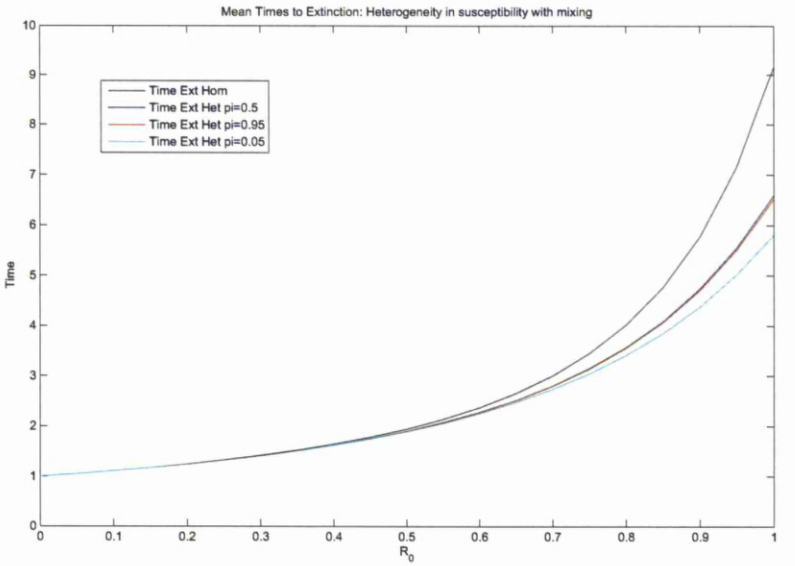

Figure 5.21: Mean times to extinction for $R_0 \leq 1$ for both a homogeneous 2-group model and heterogeneous 2-group model where heterogeneity is in susceptibility, susceptibility with assortative mixing and susceptibility with dissortative mixing. Parameter values $N_1 = N_2 = 50, \lambda_1 = \lambda_2 = 1, \mu_1 = 200/101, \mu_2 = 2/101, \gamma = 1$ for all cases, $f_1 = f_2 = 1/2$ for all cases. We use mixing parameters $\pi = 0.5, 0.95, 0.05$.

of heterogeneities for the below-threshold parameter region. Every observation discussed above remains true for these cases.

5.10 Coefficient of variation

A measure used to get an idea of how far the process is from extinction, is the coefficient of variation. Having obtained numerical results for time to extinction, it is useful to examine the coefficient of variation of the Ornstein-Uhlenbeck approximation, and deduce whether we can use this as a good approximation to the time to extinction of the stochastic model. The coefficient of variation is a normalized measure of dispersion of a probability distribution. It is defined as the ratio of the standard deviation σ to the mean μ:

$$CV = \frac{\sigma}{\mu}.$$

This is only defined for non-zero mean, and is most useful for variables that are always positive. We can analyse CV^2 as a function of either the infectivities or susceptibilities instead. Intuitively, as CV^2 increases, we are more likely to make larger fluctuations around the endemic level, and are hence more likely to hit the disease-free set of states. Thus increasing the variance ought to shorten the expected time to extinction and vice versa. The key idea behind this approximation is to relate the conditional process to the quasi-stationary process, for which the distribution of the time to extinction can be expressed in terms of quasi-stationary distributions. This technique was first introduced by Nåsell [86]. Having used Ornstein-Uhlenbeck theory we have explicit algebraic expressions for the mean and variance of the stationary distribution of the Ornstein-Uhlenbeck process, which we are in turn using as an approximation to the stochastic system, and so calculating this ratio is relatively straightforward. What we are then able to do is investigate the relationship between coefficients of variation for both the heterogeneous and homogeneous models, and indeed analyse how the coefficient of variation of the number of individuals depends on the type of heterogeneity between the two groups. What we find is that the analytical coefficient of variation approximations are not perfect, but can capture the qualitative behaviour of the epidemic in relevant regions of the parameter space. An increase of the difference in infectivity between the two groups ought to decrease the expected time to extinction, whereas it is a more complicated situation when the difference in susceptibility between the two groups is changed, and non-monotonic behaviour may occur.

5.10.1 Heterogeneity in infectivity

For the case of heterogeneity in infectivity, we can simplify the expressions for the variance matrix by using the fact that $\lambda_2 = 2 - \lambda_1$ from $\sum \lambda_i f_i = 1$. Substituting this into the variance results of section 5.8.1 and simplification yield

$$\Sigma_{11} = \frac{-2\gamma(\beta^2 + \gamma^2\lambda_1^2 - 4\gamma^2\lambda_1 - 3\gamma\beta + \gamma\beta\lambda_1 + 4\gamma^2)}{\beta^2(\gamma - \beta)},$$

$$\Sigma_{12} = \Sigma_{21} = \frac{-2\gamma^2(\beta - 2\gamma\lambda_1 + \gamma\lambda_1^2)}{\beta^2(\gamma - \beta)},$$

$$\Sigma_{22} = \frac{-2\gamma(\beta^2 + \gamma^2\lambda_1^2 - \gamma\beta + \gamma\beta\lambda_1)}{\beta^2(\gamma - \beta)},$$

so that

$$\Sigma_{11} + \Sigma_{12} + \Sigma_{21} + \Sigma_{22} = \frac{-4\gamma(\beta^2 - \gamma\beta - 4\gamma^2\lambda_1 + 2\gamma^2\lambda_1^2 + 2\gamma^2)}{\beta^2(\gamma - \beta)}.$$

We want to compare CV_{Het}^2 and CV_{Hom}^2, that is

$$\left(\frac{\sqrt{(\Sigma_{11} + \Sigma_{12} + \Sigma_{21} + \Sigma_{22})\frac{N}{2}}}{N(1 - \frac{1}{R_0})}\right)^2 \quad \text{and} \quad \left(\frac{\sqrt{N\left(\frac{1}{R_0}\right)}}{N(1 - \frac{1}{R_0})}\right)^2.$$

Because the denominator is equal in both cases, the problem becomes a comparison of the squares of the numerators only;

$$(\Sigma_{11} + \Sigma_{12} + \Sigma_{21} + \Sigma_{22})\frac{N}{2} \quad \text{and} \quad N\left(\frac{1}{R_0}\right).$$

We have $CV_{Het}^2 \geq CV_{Hom}^2$ if and only if

$$\frac{N}{2}\left(\frac{-4\gamma(\beta^2 - \gamma\beta - 4\gamma^2\lambda_1 + 2\gamma^2\lambda_1^2 + 2\gamma^2)}{\beta^2(\gamma - \beta)}\right) \geq N\left(\frac{4\gamma}{\beta(\lambda_1 + \lambda_2)}\right)$$

$$\iff \quad \frac{-2\gamma(\beta^2 - \gamma\beta - 4\gamma^2\lambda_1 + 2\gamma^2\lambda_1^2 + 2\gamma^2)}{\beta^2(\gamma - \beta)} \geq \frac{4\gamma}{\beta(\lambda_1 + \lambda_2)} = \frac{2\gamma}{\beta}.$$

Rearranging this expression leads to

$$-2\gamma\beta(\beta^2 - \gamma\beta - 4\gamma^2\lambda_1 + 2\gamma^2\lambda_1^2 + 2\gamma^2) \leq 2\gamma\beta^2(\gamma - \beta)$$

$$\iff \quad -(\beta^2 - \gamma\beta - 4\gamma^2\lambda_1 + 2\gamma^2\lambda_1^2 + 2\gamma^2) \leq \beta(\gamma - \beta)$$

$$\iff \quad 4\gamma^2\lambda_1 - 2\gamma^2\lambda_1^2 - 2\gamma^2 \leq 0$$

$$\iff \quad 2 \leq \frac{\lambda_1^2 + 1}{\lambda_1}.$$

$$\iff \lambda_1^2 - 2\lambda_1 + 1 \geq 0 \quad \Rightarrow \quad (\lambda_1 - 1)^2 \geq 0.$$

Note that if we set $\lambda_1 = 1$ (which in turn implies $\lambda_2 = 1$), then the assumed inequality is an equality. To have $\lambda_1 = \lambda_2 = 1$ would indeed be a homogeneous

model and so this equality is showing that under such parameter values the coefficient of variation for both the homogeneous and heterogeneous model would be the same. If we are to assume any degree of heterogeneity under model constraints (ie. $0 < \lambda_1 < 1, 1 < \lambda_1 \leq 2$), then for any value of λ_1 the fraction is larger than 2. Therefore any heterogeneous parameter value in the model will yield a coefficient of variation larger than that for a homogeneous model. Note that because this fraction is independent of β and γ, it holds for all R_0. This is consistent with numerical results (Figure (5.22)). The algebraic argument concludes that the coeffiecient of variation for the heterogeneous model with heterogeneity in infectivity will always be larger than the coefficient of variation for a homogeneous model. Furthermore, if $f(\lambda_1) = \frac{\lambda_1^2+1}{\lambda_1}$ then $\frac{d}{d\lambda_1} = 1 - \frac{1}{\lambda_1^2}$. Setting the derivative to zero and solving gives $\lambda_1 = 1$. $\frac{d^2}{d\lambda_1^2} = \frac{2}{\lambda_1^3} > 0$ and so it is clear that $\lambda_1 = 1$ is a minimum point therefore the homogeneous case gives us an absolute lower bound for coefficient of variation and increasing heterogeneity increases the coefficient of variation.

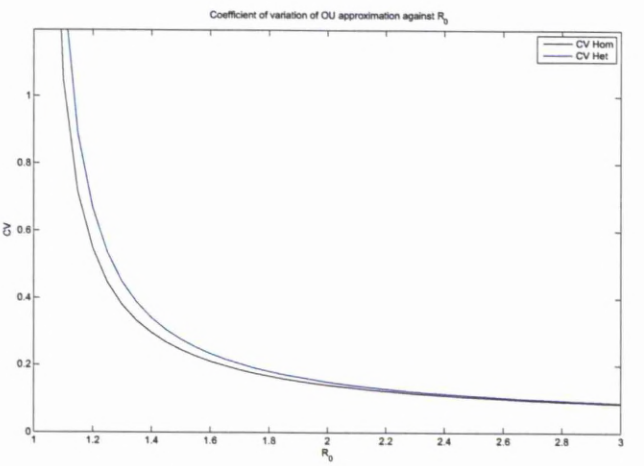

Figure 5.22: Coefficient of variation of Ornstein-Uhlenbeck approximation against R_0 for homogeneous and heterogeneous case with heterogeneity in infectivity. Parameter values $N_1 = N_2 = 50, \lambda_1 = 40/21, \lambda_2 = 2/21, \pi = 0.5, \mu_1 = \mu_2 = 1, f_1 = f_2 = 1/2, \gamma = 1$.

If we were to instead compare coefficients of variation for two models of differing degrees of heterogeneity in infectivity we would have a comparison of two

expressions given by

$$\left(\frac{\sqrt{(\Sigma_{11}+\Sigma_{12}+\Sigma_{21}+\Sigma_{22})\frac{N}{2}}}{N\left(1-\frac{1}{R_0}\right)} \right)^2.$$

Due to the denominators being the same and the numerators both being multiplied by the same constant this comparison would simplify down to simply comparing the sum of the variance matrices $\Sigma_{11}+\Sigma_{12}+\Sigma_{21}+\Sigma_{22}$ for each heterogeneous model. Writing this sum in terms of γ, β, λ_1, as before, the comparison now becomes

$$\frac{-4\gamma\left(\beta^2-\gamma\beta-4\gamma^2\lambda_1+2\gamma^2\lambda_1^2+2\gamma^2\right)}{\beta^2(\gamma-\beta)} \quad \text{with} \quad \frac{-4\gamma\left(\beta^2-\gamma\beta-4\gamma^2\tilde{\lambda_1}+2\gamma^2\tilde{\lambda_1}^2+2\gamma^2\right)}{\beta^2(\gamma-\beta)}$$

where λ_1 is the infectivity of model I and $\tilde{\lambda_1}$ is the infectivity of model II. Note here that

$$\frac{4\gamma(\beta(\beta-\gamma)-2\gamma^2\lambda_1(2-\lambda_1)+2\gamma^2)}{\beta^2(\beta-\gamma)} = \frac{4\gamma}{\beta}+\frac{8\gamma^3}{\beta^2(\beta-\gamma)}-\frac{8\gamma^3}{\beta^2(\beta-\gamma)}\lambda_1(2-\lambda_1)$$

where only the last term is negative, provided $\beta > \gamma$. Thus the larger λ_1, the smaller the coefficient of variation. This amounts to comparing

$$\lambda_1(2-\lambda_1) \quad \text{with} \quad \tilde{\lambda_1}(2-\tilde{\lambda_1}).$$

Clearly this quadratic has a maximum when $\lambda_1 = 1$, the homogeneous case, and is monotonically increasing towards this point. From this it is clear that $CV^2_{Het,\lambda_1} \geq CV^2_{Het,\tilde{\lambda_1}}$ provided $\lambda_1 \leq \tilde{\lambda_1} \leq 1$. In other words, the higher the degree of heterogeneity in infectivity, the larger the coefficient of variation. This conclusion for this approximation would in turn suggest that the higher the degree of heterogeneity in infectivity, the lower the time to extinction and so the process would die out more quickly.

Figure (5.23) shows the means, variances, standard deviations and coefficients of variation for both the stationary distribution calculated by Ornstein-Uhlenbeck theory and the quasi-stationary distribution of the actual stochastic systems when heterogeneity in infectivity is imposed. We can see that the mean and variance, thus the coefficient of variation for the Ornstein-Uhlenbeck approximation converges to that of the full stochastic system as $R_0 \to \infty$ with some discrepancy between $1 \leq R_0 \leq 2$. We shall discuss this discrepancy in section 5.10.2.

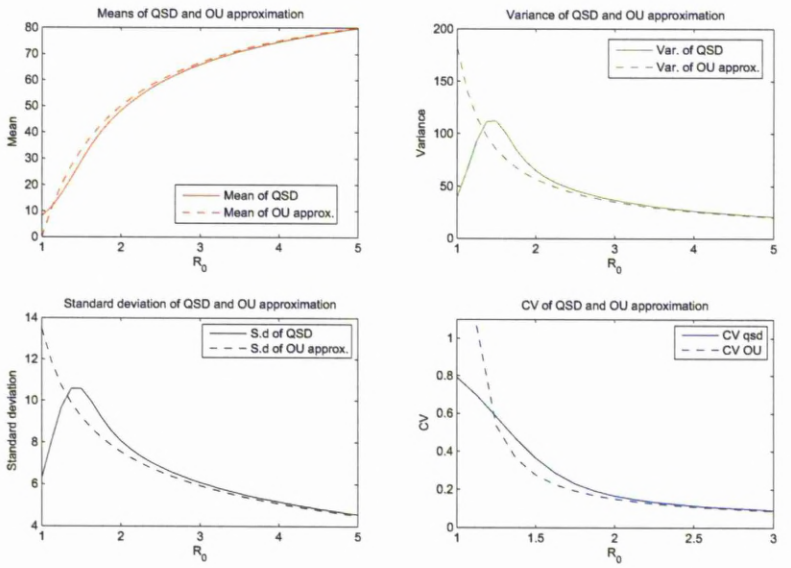

Figure 5.23: The mean, variance, standard deviation and coefficient of variation for the Ornstein-Uhlenbeck approximation and stochastic system for heterogeneity in infectivity. Parameter values $N_1 = N_2 = 50, \lambda_1 = 40/21, \lambda_2 = 2/21, \pi = 0.5, \mu_1 = \mu_2 = 1, f_1 = f_2 = 1/2, \gamma = 1$.

5.10.2 Heterogeneity in mixing

For the case of heterogeneity in mixing we have that

$$CV_{Hom} = \frac{\sqrt{N\left(\frac{1}{R_0}\right)}}{N\left(1-\frac{1}{R_0}\right)} = \frac{\sqrt{N\left(\frac{2\gamma}{\beta}\right)}}{N\left(1-\frac{2\gamma}{\beta}\right)} \quad \Rightarrow \quad CV^2_{Hom} = \frac{N\left(\frac{2\gamma}{\beta}\right)}{\left(N\left(1-\frac{2\gamma}{\beta}\right)\right)^2},$$

$$CV_{Het} = \frac{\sqrt{N_1(\Sigma_{11}+\Sigma_{12}+\Sigma_{21}+\Sigma_{22})}}{N\left(1-\frac{1}{R_0}\right)} = \frac{\sqrt{N_1(2\Sigma_{11}+2\Sigma_{12})}}{N\left(1-\frac{1}{R_0}\right)}$$

$$\Rightarrow \quad CV^2_{Het} = \frac{N_1\left(\frac{4\gamma(2\gamma\pi-\beta)}{\beta(4\gamma\pi-2\gamma-\beta)} + \frac{8\gamma^2(\pi-1)}{\beta(4\gamma\pi-2\gamma-\beta)}\right)}{\left(N\left(1-\frac{2\gamma}{\beta}\right)\right)^2} = \frac{\frac{N}{2}\left(\frac{16\gamma^2\pi-8\gamma^2-4\gamma\beta}{\beta(4\gamma\pi-2\gamma-\beta)}\right)}{\left(N\left(1-\frac{2\gamma}{\beta}\right)\right)^2}$$

$$= \frac{\frac{N}{2}\left(\frac{4\gamma(4\gamma\pi-2\gamma-\beta)}{\beta(4\gamma\pi-2\gamma-\beta)}\right)}{\left(N\left(1-\frac{2\gamma}{\beta}\right)\right)^2} = \frac{\frac{N}{2}\left(\frac{4\gamma}{\beta}\right)}{\left(N\left(1-\frac{2\gamma}{\beta}\right)\right)^2} = \frac{N\left(\frac{2\gamma}{\beta}\right)}{\left(N\left(1-\frac{2\gamma}{\beta}\right)\right)^2} = CV^2_{Hom}.$$

So we have shown algebraically that the coefficient of variation for the heterogeneous model is the same as that for the homogeneous model, irrespective of the type of mixing assumed. This is no surprise as we can reduce the formula for CV_{Het} down to one which does not rely on the mixing parameter π at all. This is consistent with the numerical results in Figure (5.25). What is interesting to see is that when calculating the actual mean times to extinction, they are indeed influenced by the type of mixing we assume, and dependent on the parameter, can actually dictate whether the process will die out quicker or slower than the corresponding homogeneous case (Figures (5.17) and (5.20)). In both the assortative and dissortative cases the mean time to extinction is very close to that of the homogeneous. This is in some way similar to the coefficient of variation approximation. The approximation dictates this 'closeness', but from it we cannot infer that a heterogeneous process will die out more quickly than a homogeneous. The time to extinction results reveal just that, for particular values of π. So although useful in some sense as an approximation, we cannot rely on the coefficient of variation approximation to give us a full indication of the behaviour of our stochastic heterogeneous model.

Another issue to address is the validity of the Ornstein-Uhlenbeck approach to the coefficient of variation as an approximation to the coefficient of variation of the actual stochastic system.

Figure (5.24) shows the means, variances, standard deviations and coefficients of variation for both the stationary distribution calculated by Ornstein Uhlenbeck

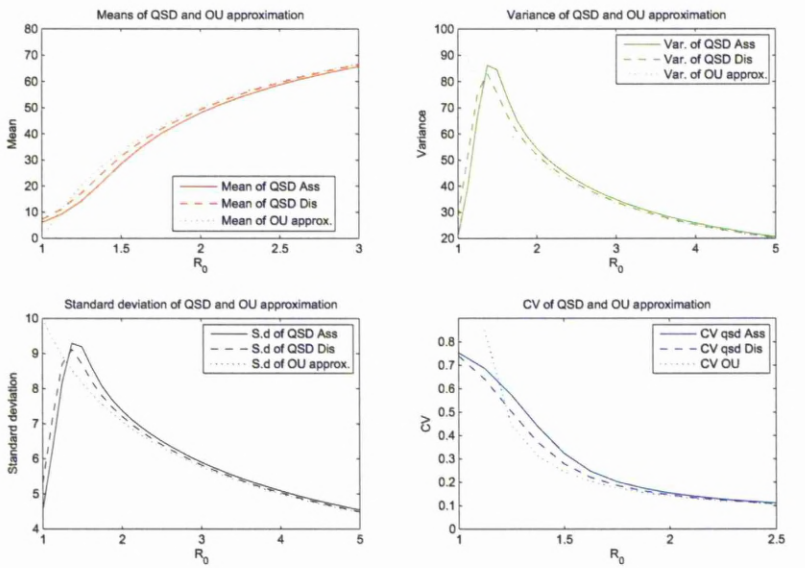

Figure 5.24: The mean, variance, standard deviation and coefficient of variation for the Ornstein-Uhlenbeck approximation and stochastic system for both assortative and dissortative mixing. Parameter values $N_1 = N_2 = 50, \lambda_1 = \lambda_2 = 1, \pi = 0.05, 0.95. \mu_1 = \mu_2 = 1, f_1 = f_2 = 1/2, \gamma = 1.$

theory and the quasi-stationary distribution of the actual stochastic systems with both assortative and dissortative mixing imposed. As previously mentioned, the Ornstein-Uhlenbeck approximation in this case is the same whatever the type of mixing, but not so for the stochastic system. It is clear to see that for R_0 close to 1 there is significant difference between the actual variance of the stochastic system and the Ornstein-Uhlenbeck approximated variance. Also, the Ornstein-Uhlenbeck approximation places a mean of zero at threshold ($R_0 = 1$) whereas the mean of the stochastic system at this point is non-zero. Consequently, at $R_0 = 1$, the Ornstein-Uhlenbeck approximation gives an infinite value for the coefficient of variation. For R_0 values slightly above 1 we see that the Ornstein-Uhlenbeck approximation is overestimating the variance and underestimating the mean. There then comes a point between $1 < R_0 \leq 2$ where the Ornstein-Uhlenbeck approximation underestimates the variance and overestimates the mean. As shown, this yields a coefficient of variation quite different to that of the full stochastic systems for R_0 between 1 and 2. We are however using the Ornstein-Uhlenbeck approximation as a limiting approximation and we can see that as R_0 exceeds 2, the Ornstein-Uhlenbeck approximation rapidly converges to the stochastic system and thus can be considered a reliable approximation for large R_0. This feature we have discussed is important as it allows us to verify exactly what was claimed before, that the coefficient of variation approximation can be considered as an estimate and therefore in use, should be looked at as a proxy to time to extinction results for the actual stochastic system. In particular, for R_0 values around threshold, it should not be considered a particularly good approximation in this case.

The difference in variances between the Ornstein-Uhlenbeck approximation and actual quasi-stationary distribution for R_0 around 1 is due to the difference in shape of the actual distributions themselves. At $R_0 = 1$, the Ornstein-Uhlenbeck approximation is a Normal curve which peaks at precisely the origin. As we are interested in positive values only, the entire probability distribution lies on the right hand side of the y-axis. The true quasi-stationary distribution at $R_0 = 1$ however is different. Rather than a Normal curve with peak at the origin it more resembles a skewed right tail of the Normal curve. As R_0 increases, the actual quasi-stationary distribution starts to look more like a complete Normal curve to the right of the origin, but this happens at a slower rate than that for the Ornstein-Uhlenbeck curve. Consequently, at R_0 values around 1, the quasi-stationary distribution has more probability closer to the origin, whereas for the Ornstein-Uhlenbeck curve, the probability is spread more 'Normally'. This in turn implies a higher variance for the Ornstein-Uhlenbeck which is what we see in this region of the plots.

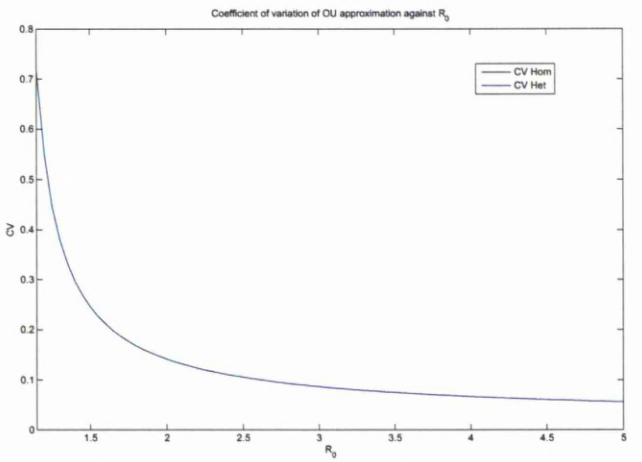

Figure 5.25: Coefficient of variation of Ornstein-Uhlenbeck approximation against R_0 for homogeneous and heterogeneous case with heterogeneity in mixing. Parameter values $N_1 = N_2 = 50, \lambda_1 = \lambda_2 = 1, \pi = 0.95, \mu_1 = \mu_2 = 1, f_1 = f_2 = 1/2, \gamma = 1$. This graph is identical whether assortative or dissortative mixing is assumed.

5.10.3 Heterogeneity in susceptibility

For the case of heterogeneity in susceptibility we have

$$CV_{Het} = \frac{\sqrt{(\Sigma_{11} + \Sigma_{12} + \Sigma_{21} + \Sigma_{22})N_1}}{N_1 x_1^* + N_2 x_2^*} \quad \Rightarrow \quad CV_{Het}^2 = \frac{N_1(\Sigma_{11} + 2\Sigma_{12} + \Sigma_{22})}{(N_1 x_1^* + N_2 x_2^*)^2},$$

$$CV_{Hom} = \frac{\sqrt{\frac{N}{R_0}}}{N\left(1 - \frac{1}{R_0}\right)} \quad \Rightarrow \quad CV_{Hom}^2 = \frac{N/\frac{\beta}{2\gamma}}{\left(N\left(1 - \frac{2\gamma}{\beta}\right)\right)^2}.$$

So we need to show that

$$\begin{aligned} & \frac{\frac{N}{2}(\Sigma_{11} + 2\Sigma_{12} + \Sigma_{22})}{(N_1 x_1^* + N_2 x_2^*)^2} \geq \frac{2\gamma\beta}{N(2\gamma - \beta)^2} \\ \iff & \tfrac{N^2}{2}(2\gamma - \beta)^2(\Sigma_{11} + 2\Sigma_{12} + \Sigma_{22}) \geq 2\gamma\beta(N_1 x_1^* + N_2 x_2^*)^2 \\ & = 2\gamma\beta\left(\tfrac{N^2}{4}(x_1^{*2} + x_2^{*2}) + \tfrac{N^2}{2}x_1^* x_2^*\right) \\ \iff & \frac{N^2(2\gamma - \beta)^2}{4\gamma\beta}(\Sigma_{11} + 2\Sigma_{12} + \Sigma_{22}) \geq \frac{N^2}{4}(x_1^{*2} + x_2^{*2}) + \frac{N^2}{2}x_1^* x_2^* \end{aligned}$$

$$\iff \Sigma_{11} + 2\Sigma_{12} + \Sigma_{22} \geq \frac{\gamma\beta(x_1^{*2} + x_2^{*2} + 2x_1^* x_2^*)}{(2\gamma - \beta)^2} = \frac{\gamma\beta(x_1^* + x_2^*)^2}{(2\gamma - \beta)^2}$$

$$\iff \frac{(2\gamma - \beta)^2}{\gamma\beta(x_1^* + x_2^*)^2}(\Sigma_{11} + 2\Sigma_{12} + \Sigma_{22}) \geq 1.$$

Due to the complicated nature of x_1^* and x_2^* and thus Σ_{rs} this is as neat a form algebraically as can be managed. It is easy to see that the left hand side of the inequality will be positive, but much more difficult to prove it is greater than unity.

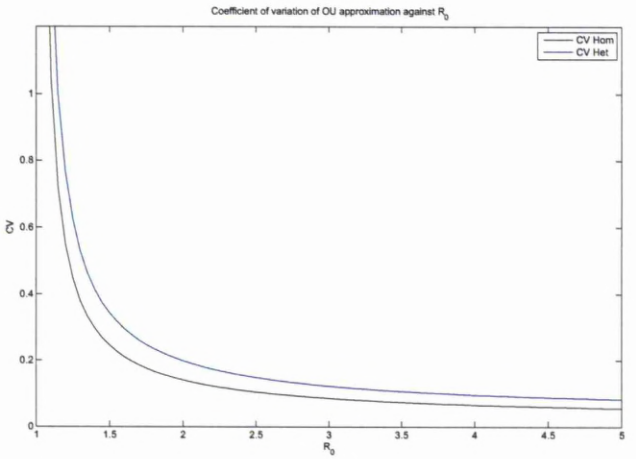

Figure 5.26: Coefficient of variation of Ornstein-Uhlenbeck approximation against R_0 for homogeneous and heterogeneous case with heterogeneity in susceptibility. Parameter values $N_1 = N_2 = 50, \lambda_1 = \lambda_2 = 1, \pi = 0.5, \mu_1 = 200/101, \mu_2 = 2/101, f_1 = f_2 = 1/2, \gamma = 1$.

Figure (5.26) shows the coefficient of variation for the heterogeneous model to be consistently higher than that of the homogeneous for all R_0 suggesting the heterogeneous model will die out more quickly than the homogeneous. This is consistent with the time to extinction numerical results in Figures (5.18) and (5.21). Figure (5.27) shows the means, variances, standard deviations and coefficients of variation for both the stationary distribution calculated by Ornstein Uhlenbeck theory and the quasi-stationary distribution of the actual stochastic systems with heterogeneity in susceptibility imposed. We see similarly to the other cases examined, a convergence as $R_0 \to \infty$ between the two processes with the previously discussed difference close to threshold.

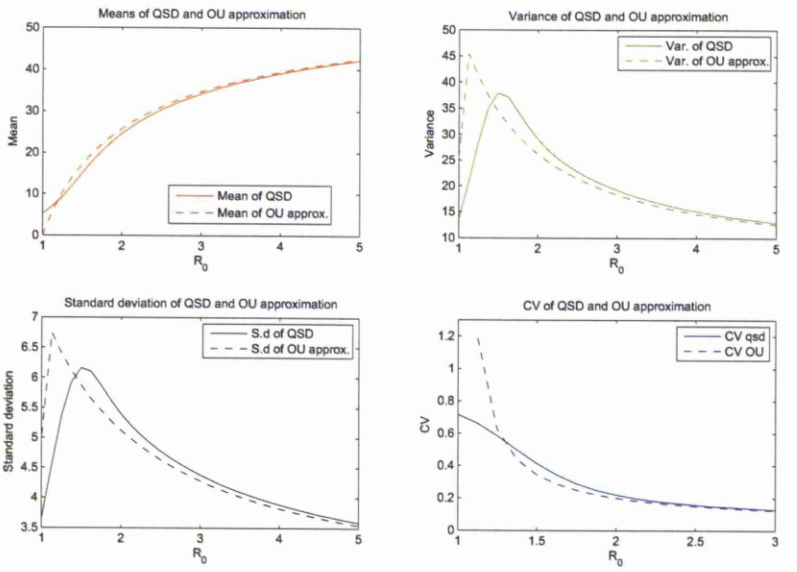

Figure 5.27: The mean, variance, standard deviation and coefficient of variation for the Ornstein-Uhlenbeck approximation and stochastic system for heterogeneity in susceptibility. Parameter values $N_1 = N_2 = 50, \lambda_1 = \lambda_2 = 1, \pi = 0.5, \mu_1 = 200/101, \mu_2 = 2/101, f_1 = f_2 = 1/2, \gamma = 1$.

Chapter 6

Conclusion

We examined the effects of three distinct types of heterogeneity for a multi-group SIS model in both the early stages of disease spread and long-term stage conditional on non-extinction using both a branching process model and deterministic model as approximations to the actual stochastic model respectively. Our interest was in comparing a heterogeneous model with a corresponding homogeneous model, for each type of heterogeneity at each of these stages in the disease evolution of the SIS model.

We demonstrated that a model with heterogeneity in infectivity had a lower emergence probability than a corresponding homogeneous model and provided a proof which showed this to be the case, not just in the limit, but at every generational iteration for all R_0, when both a constant and exponential infectious period are assumed. Furthermore, the higher the degree of heterogeneity in infectivity, the lower the emergence probability leading us to the result that if $\lambda \prec_\mu \delta$ then $P_{\mu,\delta}(Em) \leq P_{\mu,\lambda}(Em)$ and thus a means of ordering emergence probabilities of different heterogeneous models. Not only this, but a model with heterogeneity in infectivity has the same deterministic endemic equilibrium value as a corresponding homogeneous model for all R_0, which slightly overestimates the number infected in equilibrium compared to the homogeneous and heterogeneous stochastic models, particularly for R_0 values close to 1. Heterogeneity in infectivity also yields a lower time to extinction and we showed that the Ornstein-Uhlenbeck approximation was a close approximation to the quasi-stationary distribution for this type of heterogeneity, with its coefficient of variation providing a useful estimate of time to extinction.

We demonstrated numerically and proved that heterogeneity in susceptibility alone had no effect on emergence probability and the heterogeneous model yielded the same emergence probability as the corresponding homogeneous model. A deterministic model with heterogeneity in susceptibility had a lower endemic equilibrium value than a corresponding homogeneous model and the determinis-

tic heterogeneous model only slightly overestimated the number infected when in equilibrium compared to the stochastic heterogeneous model. Heterogeneity in susceptibility yielded a lower time to extinction and this was reflected by the coefficient of variation of the Ornstein-Uhlenbeck approximation. Again, the Ornstein-Uhlenbeck approximation remained close to the actual quasi-stationary distribution for this type of heterogeneity. Heterogeneity in susceptibility made it difficult to find stability conditions for a feasible endemic equilibrium due to us not being able to assume a symmetric solution, unlike the other cases.

For heterogeneity in mixing, we showed numerically that both assortative and dissortative mixing lowered the probability of emergence when compared with a homogeneous model but had less of an impact than the other types of heterogeneity. We also showed that a model with heterogeneity in mixing had the same deterministic endemic equilibrium value as a corresponding homogeneous model irrespective of mixing type, which again overestimated slightly the number infected in equilibrium compared to the stochastic models, which themselves were affected by the type of mixing. Numerical results showed heterogeneity in mixing marginally affected time to extinction and could produce both a higher and lower time to extinction depending on type and that although the coefficient of variation approximation was reasonable, it could not account for this effect of type. However, the Ornstein-Uhlenbeck approximation remained a close approximation to the quasi-stationary distribution for both types of mixing. The inclusion of this mixing parameter made finding explicit endemic equilibrium points difficult.

We also provided a proof for a general non-separable model showing emergence probability to be lower for a k-group heterogeneous model than that of a corresponding homogeneous model irrespective of group size or infectious period. We also proved that the deterministic model gave the same threshold condition as the branching process model.

What is interesting is the difference in effect each type of heterogeneity has on the model from the other. What is seemingly a simple parameterization leads to distinctly different sets of results when considering each parameter effect individually. For some of our algebraic results we had to assume equal group sizes to make the mathematics more tractable and it would be worth investigating some effects in more detail for varying group sizes and perhaps without an assumption of homogeneous mixing. However, there are computational difficulties in producing suitable ranges of results in MATLAB, especially when there are multiple forms of heterogeneity. It is important to note that although the model we analysed was complicated in its own right, it was in essence based on many simplified assumptions. We could allow for a more robust contact pattern to exist within the model, by incorporating demography for example, where we could allow for the immigration and death of susceptible and infected individuals. We could also examine,

either as an alternative or in addition, a model with a latent period (SEIS) or even one where we allowed the inclusion of age varying infectivity. The technicality of such models would be more complicated, but it would be interesting to see if these types of heterogeneity yielded different results under such constructions to that of this thesis and may certainly be an avenue for future work. However, as initially mentioned, even under this simpler model, the approximations yield results close to those of the actual model and have allowed us to make some useful theoretical inferences. It is reasonable to conclude that the results obtained give a good indication of the dynamics of the disease process for the parameters studied.

Appendix A

MATLAB code for probability of emergence

```
% Calculates the Probability of Emergence assuming both a constant and
% exponential infectious period and plots these probabilities against R0.

clear

N1=10;    % Group 1 Size
N2=90;    % Group 2 Size
N=N1+N2;    % Total Population Size
gamma=1;
lambda1=1;    % Infectivity for Group 1
lambda2=1;    % Infectivity for Group 2
mu1=1;    % Susceptibility for Group 1
mu2=1;    % Susceptibility for Group 2
pi=0.95;    % Mixing parameter pi=0.5 equal mixing of 2 types
% pi > 0.5 assortative mixing
% pi < 0.5 dissortative mixing
freq1=N1/N;    % Population split between two groups
freq2=N2/N;

int=0.125;
S=40;

beta=1;
betaall(i)=beta;
beta11=lambda1*mu1*beta*pi*freq1;
beta12=lambda1*mu2*beta*(1-pi)*freq2;
beta21=lambda2*mu1*beta*(1-pi)*freq1;
beta22=lambda2*mu2*beta*pi*freq2;
```

```
B=[beta11  beta12  ;  beta21  beta22];

R0=eigs(B,1,'LM');   % calculation of reproductive ratio

B-basic=B/R0;

for i=(1:S)

B=B-basic*(int*i);
beta11=B(1,1);
beta12=B(1,2);
beta21=B(2,1);
beta22=B(2,2);
beta11all(i)=beta11;
beta12all(i)=beta12;
beta21all(i)=beta21;
beta22all(i)=beta22;

R0=int*i;
R0all(i)=R0;   % retain all values of R0

%Calculating extinction probabilities for EXPONENTIAL infectious period

q(1)=0.5;
q(2)=0.5;
for loop-number=1:10000
PGF(1)=gamma./(gamma+(beta11+beta12)-beta11*q(1)-beta12*q(2));
PGF(2)=gamma./(gamma+(beta21+beta22)-beta22*q(2)-beta21*q(1));
q(1)=PGF(1);
q(2)=PGF(2);
end

q1all(i)=q(1);   % retain all iterates of extinction probs
q2all(i)=q(2);

%Calculating extinction probabilities for CONSTANT infectious period

q(3)=0.5;
q(4)=0.5;
for loop-number=1:10000
PGF(3)=exp((1/gamma)*(beta11*q(3)+beta12*q(4)-beta11-beta12));
PGF(4)=exp((1/gamma)*(beta21*q(3)+beta22*q(4)-beta21-beta22));
```

```
q(3)=PGF(3);
q(4)=PGF(4);
end

q3all(i)=q(3);    % retain all iterates of extinction probs
q4all(i)=q(4);

%Calculating P(Emergence)

Emexp = 1 - (freq1*q(1)+freq2*q(2));
Emconst = 1 - (freq1*q(3)+freq2*q(4));

end

Emexpall = 1 - (freq1*q1all+freq2*q2all);    %Retains all iterates of P(Emergence)
Emconstall = 1 - (freq1*q3all+freq2*q4all);

%Calculating Homogeneous Line for assumption of exponential infectious period

c=sort(R0all);
t1=[min(c):1:max(c)];
for i=(1:S)
a(i)=min(1,1/c(i));
b(i)=min(1,1-1/c(i));
end

%Calculating Homogeneous Line for assumption of constant infectious period

for i=(1:S)
q-homogeneous=0.5;
for loop-number=1:100
PGF-homogeneous=exp(c(i)*(q-homogeneous-1));
q-homogeneous=PGF-homogeneous;
end
y(i)=min(1,exp(c(i)*(q-homogeneous-1)));
z(i) = 1-q-homogeneous;
end

%Plotting Graphs

plot(c,z,'g-'),xlabel('R0'),ylabel('P(Emergence)'),title('P(Em) as a function of R0')
hold on
plot(R0all,Emconstall,'g-')
```

```
hold on
plot(c,b,'r--')
hold on
plot(R0all,Emexpall,'r-')
legend('Hom Constant','Het Constant','Hom Exponential','Het Exponential')
axis([0   R0   0   1])
```

Appendix B

MATLAB code for probability of emergence of a k-group model

```
% Calculates the Probability of Emergence assuming an exponential
% infectious period, extinction probabilities for each group and
% plots these probabilities against R0.

clear

n=3;    % Number of groups
gamma=1;
S=1000; for i=(1:S)
for group=1:n
lambda(group)=random('exp',3);    % infectivity of group individuals
lambda-all(i,group)=lambda(group);
mu(group)=random('exp',3);
mu-all(i,group)=mu(group);
end

for group-from=1:n
for group-to=1:n
beta(group-from,group-to)=lambda(group-from)*mu(group-to);
beta-all(i,group-from,group-to)=lambda(group-from)*mu(group-to);
end
end

B=beta;    % infection rate matrix in general form

R0=eigs(B,1,'LM');    % calculation of reproductive ratio
```

```
R0all(i)=R0;    % retain all values of R0
curve(i)=min(1,1/R0all(i));

for group=1:n    % calculating extinction probabilities
q(group)=0.5;
end

for loop-number=1:100
product=beta*q';
for group=1:n
betasum=sum(beta(group,:));
PGF(group)=gamma./(gamma+betasum-sum(product(group,:)));
end
q=PGF;
end

for group=1:n
q-all(i,group)=q(group);    % retain all iterates of extinction probs
end

Em=1-sum((mu(1,:).*q(1,:)))/(sum(mu));    % calculating P(emergence)
Em=1-(mu-all(i,1).*q-all(i,1)+mu-all(i,2).*q-all(i,2)+mu-all(i,3).*q-all(i,3))/(mu-all(i,1)
+mu-all(i,2)+mu-all(i,3));
Emall(i)=Em;

end

x=sort(R0all);
t=[min(x):1:max(x)];
for i=1:S
y(i)=min(1,1/x(i));
z(i)=min(1,1-1/x(i));
end

subplot(2,2,1)
plot(R0all,q-all(:,1),'b.'),xlabel('R0'),ylabel('q1'),title('q1 as a function of R0')
hold on
axis([0   40   0   1.1])
plot(x,y,'g-')
legend('q1 for 3-group','q=min(1,1/R0)')
hold on
subplot(2,2,2)
plot(R0all,q-all(:,2),'r.'),xlabel('R0'),ylabel('q2'),title('q2 as a function of R0')
```

```
axis([0   40   0   1.1])
hold on
plot(x,y,'g-')
legend('q2 for 3-group','q=min(1,1/R0)')
subplot(2,2,3)
plot(R0all,q-all(:,3),'b.'),xlabel('R0'),ylabel('q3'),title('q3 as a function of R0')
hold on
axis([0   40   0   1.1])
plot(x,y,'g-')
legend('q3 for 3-group','q=min(1,1/R0)')
subplot(2,2,4)
plot(R0all,Emall,'c.'),xlabel('R0'),ylabel('Emergence Probability'),title('P(Em) as
a function of R0')
hold on
axis([0   40   0   1.1])
plot(x,z,'g-')
legend('P(Emergence) for 3-Group Model')
```

Appendix C

MATLAB code for probability of emergence for model with general infection rates

```
% Calculates the Probability of Emergence assuming an exponential
% infectious period, where infection rates are non-separable
% using normalised eigenvectors corresponding to R0.

clear

gamma=1;

S=1000;
for i=(1:S)

B=random('exp',3,2,2);

[evect,R0]=eigs(B',1,'LM');    % calculation of reproductive ratio
evect=evect/sum(evect);   % calculation of the normalised eigenvector corresponding to R0

R0all(i)=R0;   % retain all values of R0

q=[0.5 0.5];   % calculating extinction probabilities
for loop-number=1:100
PGF(1)=gamma./(gamma+(B(1,1)+B(1,2))-B(1,1)*q(1)-B(1,2)*q(2));
PGF(2)=gamma./(gamma+(B(2,1)+B(2,2))-B(2,2)*q(2)-B(2,1)*q(1));
q=PGF;
end
```

```
Em-all(i)=1-q*evect;

end

x=sort(R0all);
t=[min(x):1:max(x)];
for i=1:S
y(i)=min(1,1-1/x(i));
end

plot(R0all,Em-all,'b.'),xlabel('R0'),ylabel('P(Emergence)'),title('P(Emergence) as
a function of R0')
hold on
axis([0   20   0   1.3])
plot(x,y,'r-')
legend('P(emergence) for 2-Group Model','1-1/R0')
```

Appendix D

MATLAB code for deterministic equilibrium values

```
% Calculates the deterministic equilibrium value for chosen parameters
% and plots the deterministic equilibrium value against R0 for the 2-group model
both
% for homogeneous and heterogeneous case.

clear

global Bdet beta gamma

N1=50;    % Group 1 Size
N2=50;    % Group 2 Size
N=N1+N2;    % Total Population Size
freq1=N1/N;    % Population split between two groups
freq2=N2/N;

beta=1;
gamma=1;
lambda1=1;    % Infectivity for Group 1
lambda2=(1-lambda1*freq1)/freq2;    % Infectivity for Group 2
mu1=0.0198;    % Susceptibility for Group 1
mu2=(1-mu1*freq1)/freq2;    % Susceptibility for Group 2
pi=0.5;    % Mixing parameter pi=0.5 equal mixing of 2 types

% pi > 0.5 assortative mixing
% pi < 0.5 dissortative mixing
```

```
if lambda2<0 | mu2<0
break
end

    B-branching=(beta/gamma)*[lambda1*mu1*pi*freq1    lambda1*mu2*(1-pi)*freq2
;  lambda2*mu1*(1-pi)*freq1    lambda2*mu2*pi*freq2];
R0-initial=eigs(B-branching,1,'LM');

Bdet=beta*[lambda1*mu1*pi*freq1    lambda2*mu1*(1-pi)*freq2    ;    lambda1*mu2*(1-
pi)*freq1    lambda2*mu2*pi*freq2];
Bdet-basic=Bdet/R0-initial;

R0set=[0.25:0.25:5];
S=length(R0set);

for i=(1:S)

Bdet = Bdet-basic*R0set(i);
R0det(i)=eigs(Bdet,1,'LM')/gamma;

%Calculating deterministic mean
detmeanvector=fsolve('twogroupv3',[1    1]);

detmean = N1*detmeanvector(1)+N2*detmeanvector(2);
detmeanall(i)=detmean;
detmeanhomog=max(0,N*(1-1/R0set(i)));
detmeanhomogall(i)=detmeanhomog;
end


    %Plotting Graphs

plot(R0set,detmeanall,'b-'),xlabel('R0'),ylabel('No.Infected'),title('Deterministic va-
lues for number of infected when system is in endemic equilibrium state across a
range of R0 values')
hold on
plot(R0set,detmeanhomogall,'k-')
legend('Det.Equilibrium value Het'    ,    'Det.Equilibrium value Hom')
axis([0    R0set(end)    0    N])
```

```
% Calculating deterministic equilibrium values for system (Separate code)

function twogroupv3 = twogroupv3(I)

global Bdet gamma

twogroupv3 = [ Bdet(1,1)*I(1)*(1-I(1))+Bdet(1,2)*I(2)*(1-I(1))-gamma*I(1)    Bdet(2,1)
*I(1)*(1-I(2))+Bdet(2,2)*I(2)*(1-I(2))-gamma*I(2) ];
```

Appendix E

MATLAB code for stochastic means and time to extinction

```
% Calculates the Quasi-stationary distribution for parameter values
% and plots the total stochastic mean against R0 for the 2-group model both
% for homogeneous and heterogeneous case. Also calculates mean times to
% extinction.

clear

N1=50;    % Group 1 Size
N2=50;    % Group 2 Size
N=N1+N2;    % Total Population Size

freq1=N1/N;    % Population split between two groups
freq2=N2/N;

beta=1;
gamma=1;
lambda1=1;    % Infectivity for Group 1
lambda2=1;    % Infectivity for Group 2
mu1=2*(100/101);    % Susceptibility for Group 1
mu2=2*(1/101);    % Susceptibility for Group 2
pi=0.5;    % Mixing parameter pi=0.5 equal mixing of 2 types
% pi > 0.5 assortative mixing
% pi < 0.5 dissortative mixing

Next-gen-mean-matrix=(beta/gamma)*[lambda1*mu1*pi*freq1    lambda1*mu2*(1-
pi)*freq2    ;    lambda2*mu1*(1-pi)*freq1    lambda2*mu2*pi*freq2];
R0-initial=eigs(Next-gen-mean-matrix,1,'LM');
```

```
Bstoc = (beta/gamma)*[lambda1*mu1*pi   lambda1*mu2*(1-pi)   ;   lambda2*mu1*(1-
pi)   lambda2*mu2*pi];

Bstoc-basic=Bstoc/R0-initial;
beta-basic=beta/R0-initial;
R0set=[0:0.1:5];
S=length(R0set);
for i=(1:S)

Bstoc = Bstoc-basic*R0set(i);

%Calculating QSD for heterogeneous case

k=0;
for I1=0:N1
for I2=0:N2
k=k+1;
number(I1+1,I2+1)=k;    %number all combinations of (I1,I2) to produce (N+1)x(N+1)
matrix
end
end
kmax=k;

Q=sparse(kmax,kmax);    %zero matrix

for I1=1:N1
for I2=0:N2
Q(number(I1+1,I2+1),number(I1-1+1,I2+1)) = gamma*I1;    %recovery in group
1
end
end

for I1=0:N1
for I2=1:N2
Q(number(I1+1,I2+1),number(I1+1,I2+1-1)) = gamma*I2;    %recovery in group
2
end
end

for I1=0:N1-1
for I2=0:N2
Q(number(I1+1,I2+1),number(I1+1+1,I2+1)) = ( Bstoc(1,1)/N)*I1*(N1-I1)+(Bstoc(2,1)/N)
*I2*(N1-I1);    %infection in group 1
```

```
end
end

for I1=0:N1
for I2=0:N2-1
Q(number(I1+1,I2+1),number(I1+1,I2+1+1)) = ((Bstoc(2,2))/N)*I2*(N2-I2)+((Bstoc(1,2))/N)
*I1*(N2-I2);    %infection in group 2
end
end

Q = Q - diag(sum(Q'));    %each row to equal zero
QT=Q(2:kmax,2:kmax);    %truncated matrix QT
[EGVT,lambdaT]=eigs(QT',1,'LR');    %eigens & eigenvs of QT - returns eigenv
of largest real part
q=EGVT;    %denote eigenv of truncated matrix by q
q=q/sum(q);    %divide each q by sum of q's
q=[0;q];    %add a zero to start of vector in order to have kmax elements ow we'd
have kmax-1

for I1=0:N1
for I2=0:N2
qdist(I1+1,I2+1) = q(number(I1+1,I2+1));    %converting k back to form (I1,I2)
⇒ kmax by kmax matrix with q in place of the corresponding k
end
end

qdist-I1 = sum(qdist');
qdist-I2 = sum(qdist);

dist-total=zeros(1,N1+N2);
for I1=0:N1
for I2=double((I1==0)):N2
dist-total(I1+I2)=dist-total(I1+I2)+qdist(I1+1,I2+1);
end
end

MeanTimeHetExt=1/(gamma.*(qdist(1+1,0+1)+qdist(0+1,1+1)));    %Calculates
mean time to extinction
LogMeanTimeHetExt=log(MeanTimeHetExt);
MeanTimeHetExtall(i)=MeanTimeHetExt;
LogMeanTimeHetExtall(i)=LogMeanTimeHetExt;

%Calculating QSD for Homogeneous case
```

```
QH=zeros(N+1,N+1);    %zero matrix

for ii=1:N
QH(ii+1,ii)=ii;    %recovery rate ie. I-1 (gamma set to 1)
end

for ii=0:N-1
QH(ii+1,ii+2)=(R0set(i)/N)*(N-ii)*ii;    %infection rate ie. I+1
end

QH = QH - diag(sum(QH'));    %each row to equal zero

QTH=QH(2:N+1,2:N+1);    %truncated matrix QTH
[EVC,lambdaC]=eigs(QTH',1,'LR');    %eigens & eigenvs of QTH - returns eigenv
of largest real part
qH=EVC;    % denote eigenv of truncated matrix by qH
qH=qH/sum(qH);

MeanTimeHomExt=1/(gamma*qH(1));    %Calculates mean time to extinction
LogMeanTimeHomExt=log(MeanTimeHomExt);
MeanTimeHomExtall(i)=MeanTimeHomExt;
LogMeanTimeHomExtall(i)=LogMeanTimeHomExt;

%Calculating Stochastic Means

W=(1:N1+N2)';
X=(0:N1)';
Y=(0:N2)';
G1=qdist-I1(:).*X;
G2=qdist-I2(:).*Y;
GH=qH(:).*W;
meanG1=sum(G1);
meanG1all(i)=meanG1;
meanG2=sum(G2);
meanG2all(i)=meanG2;
StochmeanHomog=sum(GH);
StochmeanHomogall(i)=StochmeanHomog;
Stochmeanhet=sum(meanG1)+sum(meanG2);
Stochmeanhetall(i)=Stochmeanhet;


   end
```

```
%Plotting Graphs

plot(R0set,Stochmeanhetall,'b-'),xlabel('R0'),ylabel('No.Infected'),title('Stochastic
Means')
hold on
plot(R0set,StochmeanHomogall,'k-')
legend('S.Mean Het','S.Mean Hom')
axis([0   5   0   N])
figure
subplot(2,1,1)
plot(R0set,MeanTimeHomExtall,'k-'),xlabel('R0'),ylabel('Time'),title('Mean Times
to Extinction')
hold on
plot(R0set,MeanTimeHetExtall,'b-')
legend('Time Ext Hom','Time Ext Het')
axis([0   1   0   10])
subplot(2,1,2)
plot(R0set,LogMeanTimeHomExtall,'k-'),xlabel('R0'),ylabel('log(Time)'),title('Log
Mean Times to Extinction')
hold on
plot(R0set,LogMeanTimeHetExtall,'b-')
legend('LogTime Ext Hom','LogTime Ext Het')
axis([1   2.5   0   40])
figure
mesh(qdist),xlabel('Number Infected in group1'),ylabel('Number infected in group2'),zlabel
('Probability'),title('Mesh plot of joint QSD for 2-group SIS model')
```

Appendix F

MATLAB code for Ornstein-Uhlenbeck approximation

```
% Calculates the quasi-stationary distribution for parameter values
% and plots the total stochastic mean against R0 for the 2-group model both
% for homogeneous and heterogeneous case. Calculates OU approximation.

clear

N1=50;    % Group 1 Size
N2=50;    % Group 2 Size
N=N1+N2;    % Total Population Size

freq1=N1/N;    % Population split between two groups
freq2=N2/N;

beta=6;
gamma=1;
lambda1=2*(20/21);    % Infectivity for Group 1
lambda2=2*(1/21);    % Infectivity for Group 2
mu1=1;    % Susceptibility for Group 1
mu2=1;    % Susceptibility for Group 2
pi=0.5;    % Mixing parameter pi=0.5 equal mixing of 2 types
% pi > 0.5 assortative mixing
% pi < 0.5 dissortative mixing

Next-gen-mean-matrix=(beta/gamma)*[lambda1*mu1*pi*freq1    lambda1*mu2*(1-
pi)*freq2    ;    lambda2*mu1*(1-pi)*freq1    lambda2*mu2*pi*freq2];
R0=eigs(Next-gen-mean-matrix,1,'LM')
```

```
Bstoc = (beta/gamma)*[lambda1*mu1*pi  lambda1*mu2*(1-pi)  ;  lambda2*mu1*(1-
pi)  lambda2*mu2*pi];

%Calculating QSD for heterogeneous case

k=0;
for I1=0:N1
for I2=0:N2
k=k+1;
number(I1+1,I2+1)=k; %number all combinations of (I1,I2) to produce (N+1)x(N+1)
matrix
end
end
kmax=k;

Q=sparse(kmax,kmax); %zero matrix

for I1=1:N1
for I2=0:N2
Q(number(I1+1,I2+1),number(I1-1+1,I2+1)) = I1; %recovery in group 1
end
end

for I1=0:N1
for I2=1:N2
Q(number(I1+1,I2+1),number(I1+1,I2+1-1)) = I2; %recovery in group 2
end
end

for I1=0:N1-1
for I2=0:N2
Q(number(I1+1,I2+1),number(I1+1+1,I2+1)) = ( Bstoc(1,1)/N)*I1*(N1-I1)+(Bstoc(2,1)/N)
*I2*(N1-I1); %infection in group 1
end
end

for I1=0:N1
for I2=0:N2-1
Q(number(I1+1,I2+1),number(I1+1,I2+1+1)) = ((Bstoc(2,2))/N)*I2*(N2-I2)+((Bstoc(1,2))/N)
*I1*(N2-I2); %infection in group 2
end
end
```

```
Q = Q - diag(sum(Q'));    %each row to equal zero
QT=Q(2:kmax,2:kmax);    %truncated matrix QT
[EGVT,lambdaT]=eigs(QT',1,'LR');    %eigens  eigenvs of QT - returns eigenv of
largest real part
q=EGVT;    %denote eigenv of truncated matrix by q
q=q/sum(q);    %divide each q by sum of q's
q=[0;q];    %add a zero to start of vector in order to have kmax elements ow we'd
have kmax-1

for I1=0:N1
for I2=0:N2
qdist(I1+1,I2+1) = q(number(I1+1,I2+1));    %converting k back to form (I1,I2)
⇒ kmax by kmax matrix with q in place of the corresponding k
end
end

qdist-I1 = sum(qdist');
qdist-I2 = sum(qdist);

dist-total=zeros(1,N1+N2);
for I1=0:N1
for I2=double((I1==0)):N2
dist-total(I1+I2)=dist-total(I1+I2)+qdist(I1+1,I2+1);
end
end

Det-equilm=N*(1-4*gamma/(beta*(lambda1+lambda2)));

%Calculating sigma-matrix (OU) for varying infectivity only
%These values are only applicable when we vary INFECTIVITY only

OUI11=-4*gamma*(beta^2*lambda2^4+16*gamma^2*lambda2^2+beta^2*lambda1^4-
10*gamma*beta*lambda1^2*lambda2-14*gamma*beta*lambda1*lambda2^2-2*gamma*beta
*lambda1^3+6*beta^2*lambda1^2*lambda2^2+4*beta^2*lambda1*lambda2^3-6*beta*gamma
*lambda2^3+4*beta^2*lambda1^3*lambda2)/(beta^2*(lambda1+lambda2)^3*(2*gamma
*lambda1+2*gamma*lambda2-beta*lambda2^2-beta*lambda1^2-2*beta*lambda1*lambda2));
OUI12=8*gamma^2*(-3*beta*lambda1^2*lambda2-3*beta*lambda1*lambda2^2-
beta
*lambda1^3-beta*lambda2^3+8*gamma*lambda1*lambda2)/(beta^2*(lambda1+lambda2)^3
*(2*gamma*lambda1+2*gamma*lambda2-beta*lambda2^2-beta*lambda1^2-2*beta*lambda1
*lambda2));
OUI21=OUI12;
```

```
OUI22=-4*gamma*(beta^2*lambda1^4+beta^2*lambda2^4+16*gamma^2*lambda1^2-
14*gamma*beta*lambda1^2*lambda2-10*gamma*beta*lambda1*lambda2^2-6*gamma*beta
*lambda1^3+6*beta^2*lambda1^2*lambda2^2+4*beta^2*lambda1*lambda2^3-2*gamma*beta
*lambda2^3+4*beta^2*lambda1^3*lambda2)/(beta^2*(lambda1+lambda2)^3*(2*gamma
*lambda1+2*gamma*lambda2-beta*lambda2^2-beta*lambda1^2-2*beta*lambda1*lambda2));
OU-VarianceI=(OUI11+OUI12+OUI21+OUI22)*N1;

figure
plot(dist-total,'.b'),xlabel('Number of infected'),ylabel('Probability'),title('Plot of
QSD of total number of infected for 2-group model against OU approximation for
heterogeneity in infectivity')
hold on
plot(1:N,normpdf(1:N,Det-equilm,sqrt(OU-VarianceI)),'r')
legend('QSD','OU approximation to QSD')
axis([40   90   0   0.08])
```

Appendix G

MATLAB code for coefficient of variation approximation

```
% Calculates the coefficient of variation of a heterogeneous
% model across a range of R0 values.

clear

N1=50;   % Group 1 Size
N2=50;   % Group 2 Size
N=N1+N2;   % Total Population Size

freq1=N1/N;   % Population split between two groups
freq2=N2/N;

gamma=1;
lambda1=2*(20/21);   % Infectivity for Group 1
lambda2=2*(1/21);   % Infectivity for Group 2
mu1=1;   % Susceptibility for Group 1
mu2=1;   % Susceptibility for Group 2
pi=0.5;   % Mixing parameter pi=0.5 equal mixing of 2 types
% pi > 0.5 assortative mixing
% pi < 0.5 dissortative mixing

beta=1.75;
int=0.25;
S=33;

for i=(1:S)
beta=beta+int;
betaall(i)=beta;
```

```
Next-gen-mean-matrix=(beta/gamma)*[lambda1*mu1*pi*freq1  lambda1*mu2*(1-
pi)*freq2  ;  lambda2*mu1*(1-pi)*freq1  lambda2*mu2*pi*freq2];
R0=eigs(Next-gen-mean-matrix,1,'LM')
R0all(i)=R0;

Bstoc = (beta/gamma)*[lambda1*mu1*pi  lambda1*mu2*(1-pi)  ;  lambda2*mu1*(1-
pi)  lambda2*mu2*pi];

Det-equilm=N*(1-4*gamma/(beta*(lambda1+lambda2)));
Det-equilmall(i)=Det-equilm;

%Calculating sigma-matrix (OU) for varying infectivity only
%These values are only applicable when we vary INFECTIVITY only

OUI11=-4*gamma*(beta^2*lambda2^4+16*gamma^2*lambda2^2+beta^2*lambda1^4-
10*gamma*beta*lambda1^2*lambda2-14*gamma*beta*lambda1*lambda2^2-2*gamma*beta
*lambda1^3+6*beta^2*lambda1^2*lambda2^2+4*beta^2*lambda1*lambda2^3-6*beta*gamma
*lambda2^3+4*beta^2*lambda1^3*lambda2)/(beta^2*(lambda1+lambda2)^3*(2*gamma
*lambda1+2*gamma*lambda2-beta*lambda2^2-beta*lambda1^2-2*beta*lambda1*lambda2));
OUI11all(i)=OUI11;
OUI12=8*gamma^2*(-3*beta*lambda1^2*lambda2-3*beta*lambda1*lambda2^2-
beta
*lambda1^3-beta*lambda2^3+8*gamma*lambda1*lambda2)/(beta^2*(lambda1+lambda2)^3
*(2*gamma*lambda1+2*gamma*lambda2-beta*lambda2^2-beta*lambda1^2-2*beta*lambda1
*lambda2));
OUI12all(i)=OUI12;
OUI21=OUI12;
OUI21all(i)=OUI21;
OUI22=-4*gamma*(beta^2*lambda1^4+beta^2*lambda2^4+16*gamma^2*lambda1^2-
14*gamma*beta*lambda1^2*lambda2-10*gamma*beta*lambda1*lambda2^2-6*gamma*beta
*lambda1^3+6*beta^2*lambda1^2*lambda2^2+4*beta^2*lambda1*lambda2^3-2*gamma*beta
*lambda2^3+4*beta^2*lambda1^3*lambda2)/(beta^2*(lambda1+lambda2)^3*(2*gamma
*lambda1+2*gamma*lambda2-beta*lambda2^2-beta*lambda1^2-2*beta*lambda1*lambda2));
OUI22all(i)=OUI22;
OU-VarianceI=(OUI11+OUI12+OUI21+OUI22)*N;
OU-VarianceIall(i)=OU-VarianceI;

%Calculates Coefficient of Variation
CVHom=sqrt(N/R0all(i))/(N*(1-(2*gamma)/beta));
CVHomall(i)=CVHom;
CVHet=sqrt(N*(OUI11+OUI12+OUI21+OUI22))/((N*(1-(2*gamma)/beta)));
CVHetall(i)=CVHet;
```

```
end

figure
plot(R0all,CVHomall,'k-'),xlabel('R0'),ylabel('CV'),title('Coefficient of variation
of OU approximation against R0')
hold on
plot(R0all,CVHetall,'b-')
legend('CV Hom', 'CV Het')
```

Appendix H

Maple Code for OU approximations with heterogeneity in suceptibility

```
> with(linalg):
> restart;
> A := (1/4)*beta*mu[1]*(1-i[1])*(i[1]+i[2])-gamma*i[1] = 0:
> B := (1/4)*beta*mu[2]*(1-i[2])*(i[1]+i[2])-gamma*i[2] = 0:
> solution := solve(A, B, [i[1], i[2]])
```

$$solution := [[i[1] = 0, i[2] = 0], [i[1] = -(beta * mu[2] * RootOf((-beta * mu[1] * mu[2] + mu[2]^2 * beta) * Z^2 + (-4 * mu[1] * gamma + 4 * gamma * mu[2] - 2 * mu[2]^2 * beta) * Z + beta * mu[1] * mu[2] - 4 * gamma * mu[2] + mu[2]^2 * beta) + beta * RootOf((-beta * mu[1] * mu[2] + mu[2]^2 * beta) * Z^2 + (-4 * mu[1] * gamma + 4 * gamma * mu[2] - 2 * mu[2]^2 * beta) * Z + beta * mu[1] * mu[2] - 4 * gamma * mu[2] + mu[2]^2 * beta) * mu[1] - beta * mu[1] + 4 * gamma - beta * mu[2])/((-mu[1] + mu[2]) * beta * (RootOf((-beta * mu[1] * mu[2] + mu[2]^2 * beta) * Z^2 + (-4 * mu[1] * gamma + 4 * gamma * mu[2] - 2 * mu[2]^2 * beta) * Z + beta * mu[1] * mu[2] - 4 * gamma * mu[2] + mu[2]^2 * beta) - 1)), i[2] = RootOf((-beta * mu[1] * mu[2] + mu[2]^2 * beta) * Z^2 + (-4 * mu[1] * gamma + 4 * gamma * mu[2] - 2 * mu[2]^2 * beta) * Z + beta * mu[1] * mu[2] - 4 * gamma * mu[2] + mu[2]^2 * beta)]]$$

```
> Quad := (-beta * mu[1] * mu[2] + mu[2]^2 * beta) * Z^2 + (-4 * mu[1] * gamma +
4 * gamma * mu[2] - 2 * mu[2]^2 * beta) * Z - 4 * gamma * mu[2] + beta * mu[1] *
mu[2] + mu[2]^2 * beta :
> i[2] := solve(Quad, Z)
```

i[2] := $Z = -($mu[2]^2*beta+2*mu[1]*gamma-2*gamma*mu[2]-sqrt(4*mu[1]^2*gamma^2-8*mu[1]*gamma^2*mu[2]+4*gamma^2*mu[2]^2+beta^2*mu[1]^2*mu[2]^2))/(beta*mu[2]*(mu[1]-mu[2])), $Z = -($mu[2]^2*beta+2*mu[1]*gamma-2*gamma*mu[2]+sqrt(4*mu[1]^2*gamma^2−

8*mu[1]*gamma^2*mu[2]+4*gamma^2*mu[2]^2+beta^2*mu[1]^2*mu[2]^2))/(beta*mu[2]*(mu[1]-mu[2]))

```
> G[11] := simplify((1/4)*beta*mu[1]*(1-i[1])*(i[1]+i[2])+gamma*i[1]):
> G[22] := simplify((1/4)*beta*mu[2]*(1-i[2])*(i[1]+i[2])+gamma*i[2]):

> M := -(1/4)*beta*Matrix([[2*mu[1]-4*mu[1]*i[1]-2*mu[1]*i[2]-8*gamma/beta,
mu[1]*(1-i[1]), mu[1]*(1-i[1]), 0], [mu[2]*(1-i[2]), mu[1]+mu[2]-i[1]*(2*mu[1]+mu[2])-
i[2]*(2*mu[2]+mu[1])-8*gamma/beta, 0, mu[1]*(1-i[1])], [mu[2]*(1-i[2]), 0, mu[1]+mu[2]-
i[1]*(2*mu[1]+mu[2])-i[2]*(2*mu[2]+mu[1])-8*gamma/beta, mu[1]*(1-i[1])], [0, mu[2]*(1-
i[2]), mu[2]*(1-i[2]), 2*mu[2]-4*mu[2]*i[2]-2*mu[2]*i[1]-8*gamma/beta]]):
> G := transpose(Matrix([[2*gamma*i[1], 0, 0, 2*gamma*i[2]]])):
> S := simplify(linsolve(M, G)):
```

$$S[1,1] = 2*gamma*(32*gamma^2*i[1]-12*i[1]*beta*mu[2]*gamma+24*gamma*i[1]*i[2]*beta*mu[2]+12*gamma*i[1]^2*beta*mu[2]+4*gamma*i[1]*i[2]*beta*mu[1]+8*gamma*i[1]^2*beta*mu[1]-4*i[1]*beta*mu[1]*gamma-2*beta^2*mu[2]*mu[1]*i[2]*i[1]+mu[1]^2*beta^2*i[2]-2*i[1]*beta^2*mu[1]^2*i[2]-2*i[1]^2*beta^2*mu[2]*mu[1]+i[1]^2*beta^2*mu[1]^2*i[2]+2*i[1]^3*beta^2*mu[2]*mu[1]+4*beta^2*mu[2]*mu[1]*i[2]*i[1]^2+2*i[2]^2*beta^2*mu[2]*mu[1]*i[1]+mu[2]^2*beta^2*i[1]-2*i[1]^2*beta^2*mu[2]^2-4*i[1]*beta^2*mu[2]^2*i[2]+4*i[1]^2*beta^2*mu[2]^2*i[2]+4*i[1]*beta^2*mu[2]^2*i[2]^2+i[1]^3*mu[2]^2*beta^2)/((8*gamma^2+2*i[1]*beta*mu[2]*gamma+4*i[2]*beta*mu[2]*gamma-2*mu[2]*beta*gamma+4*i[1]*beta*mu[1]*gamma-2*mu[1]*beta*gamma+2*i[2]*beta*mu[1]*gamma+2*beta^2*mu[2]*mu[1]*i[2]*i[1]-beta^2*mu[2]*mu[1]*i[1]-beta^2*mu[2]*mu[1]*i[2]+i[1]^2*beta^2*mu[2]*mu[1]+i[2]^2*beta^2*mu[2]*mu[1])*(-mu[1]*beta-mu[2]*beta+2*i[1]*beta*mu[1]+i[1]*beta*mu[2]+2*i[2]*beta*mu[2]+i[2]*beta*mu[1]+8*gamma))$$

$$S[2,1] = S[3,1] = -2*beta*(-4*mu[2]*gamma*i[1]-4*gamma*i[2]*mu[1]+4*mu[2]*gamma*i[1]*i[2]+4*gamma*i[2]*mu[1]*i[1]+mu[1]^2*beta*i[2]+mu[2]^2*beta*i[1]-i[1]^2*beta*mu[2]^2-i[2]^2*beta*mu[1]^2-3*mu[1]^2*beta*i[2]*i[1]-3*mu[2]^2*beta*i[2]*i[1]+2*i[1]^2*beta*mu[1]^2*i[2]+i[1]^2*beta*mu[2]^2*i[2]+2*i[2]^2*beta*mu[2]^2*i[1]+i[2]^2*beta*mu[1]^2*i[1])*gamma/((-mu[1]*beta-mu[2]*beta+2*i[1]*beta*mu[1]+i[1]*beta*mu[2]+2*i[2]*beta*mu[2]+i[2]*beta*mu[1]+8*gamma)*(8*gamma^2+2*i[1]*beta*mu[2]*gamma+4*i[2]*beta*mu[2]*gamma-2*mu[2]*beta*gamma+4*i[1]*beta*mu[1]*gamma-2*mu[1]*beta*gamma+2*i[2]*beta*mu[1]*gamma+2*beta^2*mu[2]*mu[1]*i[2]*i[1]-beta^2*mu[2]*mu[1]*i[1]-beta^2*mu[2]*mu[1]*i[2]+i[1]^2*beta^2*mu[2]*mu[1]+i[2]^2*beta^2*mu[2]*mu[1]))$$

$$S[4,1] = 2*gamma*(32*gamma^2*i[2]-4*i[2]*beta*mu[2]*gamma+12*i[2]^2*beta*mu[1]*gamma-12*i[2]*beta*mu[1]*gamma+24*gamma*i[1]*i[2]*beta*mu[1]+8*i[2]^2*beta*mu[2]*gamma+4*gamma*i[1]*i[2]*beta*mu[2]-2*beta^2*$$

$$mu[2]*mu[1]*i[2]*i[1]+mu[1]^2*beta^2*i[2]-2*i[2]^2*beta^2*mu[1]^2-4*i[1]*beta^2*mu[1]^2*i[2]-2*i[2]^2*beta^2*mu[2]*mu[1]+4*i[2]^2*beta^2*mu[1]^2*i[1]+4*i[1]^2*beta^2*mu[1]^2*i[2]+2*beta^2*mu[2]*mu[1]*i[2]*i[1]^2+4*i[2]^2*beta^2*mu[2]*mu[1]*i[1]+mu[2]^2*beta^2*i[1]+i[2]^3*beta^2*mu[1]^2-2*i[1]*beta^2*mu[2]^2*i[2]+2*i[2]^3*beta^2*mu[2]*mu[1]+i[1]*beta^2*mu[2]^2*i[2]^2)/((-mu[1]*beta-mu[2]*beta+2*i[1]*beta*mu[1]+i[1]*beta*mu[2]+2*i[2]*beta*mu[2]+i[2]*beta*mu[1]+8*gamma)*(8*gamma^2+2*i[1]*beta*mu[2]*gamma+4*i[2]*beta*mu[2]*gamma-2*mu[2]*beta*gamma+4*i[1]*beta*mu[1]*gamma-2*mu[1]*beta*gamma+2*i[2]*beta*mu[1]*gamma+2*beta^2*mu[2]*mu[1]*i[2]*i[1]-beta^2*mu[2]*mu[1]*i[1]-beta^2*mu[2]*mu[1]*i[2]+i[1]^2*beta^2*mu[2]*mu[1]+i[2]^2*beta^2*mu[2]*mu[1]))$$

Bibliography

[1] Abbey, H. "An examination of the Reed-Frost theory of epidemics" (1952) Human Biology, **24**, 201-233.

[2] Allen, L.J.S. "An Introduction to stochastic processes with application to biology" (2003) Prentice-Hall, New Jersey.

[3] Andersson, H., & Britton, T. "Heterogeneity in epidemic models and its effect on the spread of infection" (1998) J. Appl. Probab. **35**, 651-661.

[4] Andersson, H., & Britton, T. "Stochastic epidemic models and their statistical analysis" (2000) Lecture Notes in Statistics, vol. **151**. Springer-Verlag, New York.

[5] Andersson, H., & Britton, T. "Stochastic epidemics in dynamic populations : quasi-stationarity and extinction" (2000) J. Math. Biol. **41**, 559-580.

[6] Anderson, R.M., & May, R.M. "Spatial, temporal and genetic heterogeneity in host populations and the design of immunization programmes" (1984) J. Math. Appl. Med. Biol. **1**, 233-266.

[7] Anderson, R.M., & May, R.M. "Infectious diseases of humans : dynamics and controls" (1991) Oxford Univ. Press, Oxford. [xii,1,8,11,16-17,46,85,154,179-182].

[8] Anderson, R.M., & May, R.M. "The transmission dynamics of human immunodeficiency virus" (1988) Phil. Trans. R. Soc. Biol. **321** , 565-607.

[9] Arino, J., Brauer, F., Van den Driessche, P., Watmough, J., & Wu, J. "Simple models for containment of a pandemic" (2006) J. R. Soc. Interface, **3**, 453-457.

[10] Arnold, B.C. "Majorization and the Lorenz Order : A Brief Introduction" (1987) Springer-Verlag, 1-17, 91-93.

[11] Artalejo, J.R., Economou A., & Lopez-Herrero, M.J. "The maximum number of infected individuals in SIS epidemic models: computational techniques and quasi-stationary distributions" (2010) J. Computational & Appl. Math. **233**, 2563-2574.

[12] Athreya, K.B., & Ney, P.E. "Branching Processes" (1972) Springer-Verlag, Berlin.

[13] Bailey, N.T.J. "The mathematical theory of epidemics" (1957) Charles Griffin, London.

[14] Bailey, N.T.J. "The mathematical theory of infectious diseases and its applications" (1975) Charles Griffin, London. [xii,1,16,21,60,77,99,107,117-118,154-155,162,165,168,186].

[15] Bailey, N.T.J. "The elements of stochastic processes with application to natural sciences" (1990) John Wiley & Sons, New York.

[16] Ball, F. "The threshold behaviour of epidemic models" (1983) J. Appl. Probab. **20** , 227-241.

[17] Ball, F., & Becker, N.G. "Control of transmission with two types of infection" (2006) Math. Biosci. **200**, 170-187.

[18] Ball, F., & Neal, P. "Network epidemic models with two levels of mixing" (2008) Math. Biosci. **212**, 69-87.

[19] Bansal, S., Pourbohloul, B., & Meyers, L.A. "A comparative analysis of influenza vaccination programs" (2006) PLoS Med. **3**, 1816-1825.

[20] Bartlett, M.S. "Deterministic and stochastic models for recurrent epidemics" (1956) Proceedings of the Third Berkley Symposium on Mathematical statistics & Probability, **4**, 81-109. Berkley : University of California Press.

[21] Becker, N.G. "Estimation for discrete time branching processes with application to epidemics" (1977) Biometrics. **3**, 515-522.

[22] Becker, N.G. "Analysis of infectious disease data" (1989) 48-59, Chapman & Hall, London.

[23] Becker, N.G., & Hall, R. "Immunization levels for preventing epidemics in a community of households made up of individuals of various types" (1996) Math. Biosci. **132** , 205-216.

[24] Becker, N., & Marschner, I. "The effect of heterogeneity on the spread of disease" (1990) Stochastic processes in epidemic theory, **86**, 90-103.

[25] Bolker, B.M., & Grenfell, B.T. "Space, persistence, and dynamics of measles epidemics" (1995) Phil. Trans. R. Soc. Lond. **B348**, 309-320.

[26] Burnett, F.M., & White, D.O. "The natural history of infectious disease" (1972) Cambridge University Press, 4th Edition.

[27] Cheng, K.W. "Majorization : It's extensions and preservation theorems" (1977) Tech. Rep. No.121, Dept Statistics, Stanford University, California.

[28] Clancy, D. "Carrier-Borne epidemic models incorporating population mobility" (1995) Math. Biosci. **132**, 185-204.

[29] Clancy, D., O'Neill, P.D., & Pollett, P.K. "Approximations for the long-term behaviour of an open-population epidemic model" (2001) Methodology & Comp. in Appl. Probab. **3**, 75-95.

[30] Clancy, D. "A stochastic SIS infection model incorporating indirect transmission" (2005) J. Appl. Probab. **42**, 726-737.

[31] Coolen-Schrijner, P., & Van Doorn, E.A. "Quasi-stationary distributions for a class of discrete-time Markov chains" (2006) Methodology & Comp. in Appl. Probab. **8**, 449-465.

[32] Daley, D.J. "The size of epidemics with variable infectious periods" (unpublished) Statistics Research Section, School of Mathematical Sciences, Australian National University.

[33] Daley, D.J., & Gani, J. "Epidemic modelling: An Introduction" (1999) Cambridge Studies in Mathematical Biology, 15, Cambridge University Press, Cambridge.

[34] Darroch, J.N., & Senata, E. "On the quasi-stationary distribution in absorbing continuous-time finite Markov chains" (1967) J. Appl. Probab. **4**, 192-196.

[35] De Jong, M.C.M., Diekmann, O., & Heesterbeek, J.A.P. "How does transmission of infection depend on population size?" (1995) In Epidemic Models: Their structure and relation to data (Mollison, D.,ed.), pp. 84-94, Cambridge University Press.

[36] Diekmann, O., Heesterbeek, J.A.P & Metz, J.A.J. "On the definition and the computation of the basic reproduction number R_0 in models for infectious diseases in heterogeneous populations" (1990) J. Math. Biol. **28**, 365-382.

[37] Diekmann, O., & Heesterbeek, J.A.P. "Mathematical epidemiology of infectious diseases" (2000) Wiley Series in Mathematical and computational Biology, John Wiley & Sons, Chichester, Model builing, analysis & interpretation.

[38] Dietz, K. "The incidence of infectious diseases under the influence of seasonal fluctuations" (1976) Lecture Notes BioMath. **11**, 1-15.

[39] Dietz, K., & Schenzle, D. "Mathematical models for infectious disease statistics" (1985) In A Celebration of Statistics, A.C Atkinson & S.E Fienberg, Springer-Verlag, New York, 167-204 [13,165]

[40] Durrett, R. "Essentials of stochastic processes" (1999) Berlin, Germany, Springer.

[41] Engbert, R., & Drepper, F.R. "Chance and chaos in population biology - models for recurrent epidemics and food chain dynamics" (1994) Chaos Solitions and Fractals **4**, 1147-1169.

[42] Ethier, S.N., & Kurtz, T.G. "Markov Processes : Characterization and convergence" (1986) John Wiley & Son, New York.

[43] Farrington, C.P., Kanaan, M.N., & Gray, N.J. "Branching process models for surveillance of infectious diseases controlled by mass vaccination" (2003) Biostatistics. **4**, 279-295.

[44] Ferguson, N.M., Cummings, D.A.T., Cauchemez, S., Fraser, C., Riley, S., Meeyai, A., Iamsirithaworn, S., & Burke, D.S. "Strategies for containing an emerging influenza pandemic in Southeast Asia" (2005) Nature. **437**, 209-214.

[45] Gani, R., Hughes, H., Fleming, D., Griffin, T., Medlock, J., & Leach, S. "Potential impact of antiviral drug use during influenza pandemic" (2005) EID, **11.9**, 1355-1362.

[46] Galvani, A.P., & May, R.M. "Epidemiology: dimensions of superspreading" (2005) Nature. **438**, 293-305.

[47] Grenfell, B.T., Bolker, B.M. & Kleczkowski, A. "Seasonality and extinction in chaotic metapopulations" (1995) Proc. R. Soc. London. B**259**, 97-103.

[48] Hagenaars, T.J. "Spatial heterogeneity and the persistence of infectious diseases" (2004) J. Theor. Biol. **229**, 349.

[49] Harris, T.E. "The theory of branching processes" (1963) Berlin, Germany, Springer.

[50] Hethcote, H.W. "Qualitative analysis of communicable disease models" (1976) Math. Biosci. **28**, 335-356.

[51] Hethcote, H.W. "An immunization model for a heterogeneous population" (1978) Theor. Popul. Biol. **14**, 338-349.

[52] Hethcote, H.W. "A thousand and one epidemic models" (1994) Lecture Notes in Biomathematics **100**, 504-515.

[53] Hethcote, H.W., & Van Ark, W. "Epidemiological models for heterogeneous populations: proportionate mixing, parameter estimation and immunization programs" (1987) Math. Biosci. **33** , 85-118.

[54] Hyman, J.M. & Li, J. "An intuitive formulation for the reproductive number for the spread of diseases in heterogeneous populations" (2000) Math. Biosci. **167** , 65-86.

[55] Jacquez, J.A., & Simon, C.P. "The stochastic SI model with recruitment and deaths I; comparison with the SIS model" (1993) Math. Biosci. **117**, 77-125.

[56] Jagers, P. "Branching Processes with biological applications" (1975) John Wiley & Sons.

[57] Karatzas, I., & Shreve, S.E. "Brownian motion and stochastic calculus" (1991) 2nd Ed. Graduate Texts in Mathematics, Vol.**113**, Springer-Verlag, New York.

[58] Karlin, S., & Taylor, H.M. "A first course in stochastic processes" (1975) (2nd Edtn) Academic Press, New York.

[59] Karlin, S., & Taylor, H.M. "An introduction to stochastic models" (1984) Academic Press, New York.

[60] Karlin, S., & Taylor, H.M. "An introduction to stochastic modelling" (1998) Academic Press, 3rd Edition.

[61] Keeling, M.J., & Grenfell, B.T. "Disease extinction and community size : modelling the persistence of measles" (1997) Science. **275**, 65-67.

[62] Kermack, W.O., & McKendrick, A.G. "A contribution to the Mathematical Theory of epidemics" (1927) Proc. R. Soc. London. **A115**, 700-721.

[63] Kimmel, M., & Axelrod, D.E. "Branching Processes in biology" (2002) Springer-Verlag, New York.

[64] Koopman, J. "Modelling infection transmission" (2004) Annu. Rev. Public. Health. **25**, 303-326.

[65] Krishnarajah, I., Marion, G., & Gibson, G. "Novel closure approximations in stochastic epidemics" (2005) Bull. Math. Biol. **67**, 855-873.

[66] Kryscio, R.J., & Lefèvre, C. "On the extinction of the SIS stochastic logistic epidemic" (1989) J. Appl. Probab. **26**, 685-694.

[67] Kurtz, T.G. "Limit theorems for sequences of jump Markov processes approximating ordinary differential processes" (1971) J. Appl. Probab. **8**, 344-356.

[68] Lajmanovich, A., & Yorke, J.A. "A deterministic model for gonorrhea in a nonhomogeneous population" (1976) Math. Biosci. **28**, 221-236.

[69] Lindholm, M. "On the time to extinction for a two-type version of Bartlett's epidemic model" (2008) Math. Biosci. **212**, 99-108.

[70] Lloyd, A.L. "Destabilization of epidemic models with the inclusion of realistic distributions of infection periods" (2001) Proc. R. Soc. Lond. **B268**, 985-993.

[71] Lloyd-Smith, J.O., Schrieber S.J., Kopp P.E., & Getz W.M. "Superspreading and the effect of individual variation on disease emergence" (2005) Nature. **438** , 355-359.

[72] London, W.P., & Yorke, J.A. "Recurrent outbreaks of measles, chickenpox and mumps. I. Seasonal variation in contact rates" (1973) Am. J. Epidemic. **98**, 453-468.

[73] Longini, I.M., Nizam, A., Xu, S., Ungchusak, K., Hanshaoworakul, W., Cummings, D.A., & Halloran, M.E. "Containing pandemic influenza at the source" (2005) Science. **308**, 1083-1087.

[74] Ma, J., & Earn, D.J.D. "Generality of the final size formula for an epidemic of a newly invading infectious disease" (2006) Bulletin of Mathematical Biology, **68**, 679-702.

[75] Marschner, I. "The effect of preferential mixing on the growth of an epidemic" (1992) Math. Biosci. **109**, 39-67.

[76] Marshall, A.W., & Olkin, I. "Inequalities: theory of Majorization and its applications" (1979) Academic press, New York, Ch. 1 & 9.

[77] McKendrick, A.G. "Applications of mathematics to medical problems" (1926) Kapil Proceedings of the Edinburgh Mathematical Society, **44**, 1-34.

[78] Metz, J.A. "The epidemic in a closed population with all susceptibles equally vulnerable; some results for large susceptible populations and small initial infections" (1978) Acta. Biotheor. **27** , 75-123.

[79] Meyers, L.A., Pourbohloul, B., Newman, M.E.J., Skowronski, D.M., & Brunham, R.C. "Network theory and SARS : predicting outbreak diversity" (2005) J. Theor. Biol. **232**, 71-81.

[80] Mode, C.J. "Multitype branching processes: theory and applications" (1971) in Modern Analytic and Computational Methods in Science and Mathematics, R.Bellman, Ed., American Elsevier, New York.

[81] Mollison, D. "Spatial contact models for ecological and epidemic spread" (1977) J. R. Stat. Soc. **B39**, 283-326.

[82] Mollison, D. "Epidemic Models: Their structure and relation to data" (1995) Cambridge University Press : Cambridge [xii,16]

[83] Murray, G.D., & Cliff, A.D. "A stochastic model for measles epidemics in a multi-region setting" (1975) Trans. Inst. Brit. Geog. **2**, 158-174.

[84] Nåsell, I. "The quasi-stationary distribution of the closed endemic SIS model" (1996) Adv. Appl. Probab. **28**, 895-932.

[85] Nåsell, I. "On the quasi-stationary distribution of the stochastic logistic epidemic" (1999) Math. Biosci. **156**, 21-40.

[86] Nåsell, I. "On the time to extinction in recurrent epidemics" (1999) J. R. Stat. Soc. **B61**, (Part 2) 309.

[87] Nåsell, I. "Extinction and quasi-stationarity in the Verhulst logistic model" (2001) J. Theor. Biol. **211**, 11-27.

[88] Nåsell, I. "Stochastic models of some endemic infections" (2002) Math. Biosci. **179**, 1.

[89] Neal, P. "The SIS Great Circle Epidemic model" (2008) J. Appl. Probab. **45**, 513-530.

[90] Nold, A. "Heterogeneity in disease-transmission modelling" (1980) Math. Biosci. **52**, 227-240.

[91] Olsen, L.F., Truty, G.L., & Schaffer, W.M. "Oscillations and chaos in epidemics : a nonlinear dynamic study of six childhood diseases in Copenhagen, Denmark" (1988) Theor. Popul. Biol. **33**, 344-370.

[92] Patrap, R. "Getting started with MATLAB 7" (2006) OUP, USA.

[93] Ross, S.M. "Stochastic Processes 2nd Edition" (1996) John Wiley, New York.

[94] Schenzle, D. "An age-structured model of pre- and post-vaccination measles transmission" (1984) J. Math. Appl. Med. Biol. **1**, 169-191.

[95] Schrijner, P. "Quasi-stationarity of discrete-time Markov Chains" (1995) Thesis Universiteit Twente Enschede.

[96] Schwartz, I.B. "Small amplitude, long period outbreaks in seasonally driven epidemics" (1992) J. Math. Biol. **30**, 473-491.

[97] Song, M., Ma, W., & Takeuchi. Y. "Permanence of a delayed SIR epidemic model with density dependent birth and death rates" (2007) J. Computational & Appl. Math. **201**, 339-347.

[98] Stone, P., Wilkinson-Herbots, H., & Isham, V. "A stochastic model for head lice infections" (2008) J. Math. Biol. **56**, 743-763.

[99] Tuckwell, H.C. "Elementary applications of probability theory" (1995) Chapman & Hall, 2nd Edition.

[100] Van Doorn, E.A., & Pollett, P.K. "Survival in a quasi-death process" (2008) Linear Algebra & its applications **429**, 776-791.

[101] Wei, J., & Zhou, X. "Bifurcation analysis of a population model and the resulting SIS model with delay" (2006) J. Computational & Appl. Math. **197**, 169-187.

[102] Weiss, G.H., & Dishon, M. "On the asymptotic behaviour of the stochastic and deterministic models of an epidemic" (1971) Math. Biosci. **11**, 261-265.

[103] Wilson, E.B., & Burke, M.H. "The epidemic curve I and II" (1942,43) Proc. Nat. Acad. Sci. Washington. **29**,43-48 [11,19,33,154]

[104] Xiao Y., Clancy D., French N.P., & Bowers R.G. "A semi-stochastic model for salmonella infection in a multi-group herd" (2006) Math. Biosci. **200**, 214-233.

[105] Xu, Y., Allen, L.J.S., & Perelson, A.S. "Stochastic model of an influenza epidemic with drug resistance" (2007) J. Theor. Biol. **248**, 179-193.

[106] Yates A., Rustom A., & Roland, R.R. "How do pathogen evolution and host heterogeneity interact in disease emergence?" (2006) Proc. R. Soc. B. **273**, 3075-3083.