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Quasi-stationarity of stochastic models for the spread of infectious diseases

by

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Dedication

I would like to dedicate this piece of work to my family especially my parents for according me the opportunity to be educated and for the love and encouragement I received during my primary, secondary and tertiary education.

I am also dedicating this thesis to my twin brother Pierre Francis Mendy, to my beloved wife Awa Gomez and lovely daughters Frances Ann-Marie Mendy and Maria Sangnatu Mendy. Finally, I would like to dedicate this thesis to Mr Jawo and the family. I have become an integral part of the family and have benefited a lot in terms of moral, material, social and spiritual support. May God bless them and reward them immensely for their kindness.

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Abstract

Many mathematical models for the spread of infectious diseases predict that, eventually, the disease will die out of the population. However, the expected time to extinction can be long. When this is the case, interest focuses upon the long-term behaviour of the disease process prior to extinction, which is described by the quasi-stationary distribution.

Mathematically, if the infection process is modelled as a Markov process, then the quasi-stationary distribution is given by the left eigenvector of the reduced transition rate matrix, and can thus be evaluated numerically using computer packages such as Matlab. However, the transition rate matrix may be very large, or indeed infinite. Thus simple approximating methods can be of great value, and often yield qualitative insight into the structure of the quasi-stationary distribution. The most widely used method is to approximate the infection process by a Gaussian diffusion process, which leads to a normally distributed approximation for the quasi-stationary distribution. This approximation works well when time to fade-out is very long, but less well when time to fade-out is expected to be short or moderately long (Nåsell(1996)). Another method used to approximate the infection process is the moment closure method.

In this thesis, we analyse the basic SIS (Susceptible-Infected-Susceptible) model, in which individuals who have been infected recover to the susceptible state without acquiring any immunity to future infection. We work out the quasi-stationary distribution given by the left eigenvector corresponding to the eigenvalue with the maximal real part of the reduced transition rate matrix and approximate the quasi-stationary distribution by a Gaussian diffusion process and compare the two results. Cumulant equations are then derived and moment closure method based on distributional assumption is applied on them. The performance of these distributions

(Normal, Log-normal, Binomial, Poisson and Beta-binomial) are compared against each other and the true quasi-stationary distribution (left eigenvector) using the total variation distance. We then analyse a two group SIS model without demography in which within-group and between-group transmission parameters are the same for both groups. We approximate the quasi-stationary distribution using diffusion approximation and the result is compared with the true quasi-stationary distribution. Cumulant equations are derived and moment closure applied on them to derive an approximation of the quasi-stationary distribution.

The basic SIS model is then extended to incorporate demographic process of immigration and death. This is a two dimensional process with infinite state space so it is not possible to work out the left leading eigenvector. Thus diffusion approximation and moment closure method applied on cumulant equations are used to derive approximations for the quasi-stationary distribution. To validate these results, we carry out a simulation of the disease process and compare this with our approximations results. Nåsell(2005) carried out a detailed analysis of the the SIR (Susceptible-Infected-Removed) model with demography. We compare our results with the results of Nåsell(2005). It is shown that the SIR and SIS models have the same mean susceptible population in equilibrium, but the SIS model has a higher infection prevalence. The variance for the number of susceptible individuals at quasi-stationarity for the SIR model is greater than that of the SIS model but the SIS model has a larger variance than the SIR model for the number of infected individuals.

A two-group SIS model incorporating demographic process of immigration and death is then analysed. The result of the diffusion approximation is rather messy and not illuminating so we use numerical values to evaluate the result. We run a numerical simulation of the stochastic model and comparison with the result we obtained from the diffusion approximation shows that the diffusion approximation provides a good approximation of the quasi-stationary distribution for the parameter values studied.

Finally, we analyse the SIRS (Susceptible-Infected-Removed-Susceptible) in which there is temporary immunity. Thus we focus particularly upon the effect of waning of immunity. Here we analyse the SIRS model with and without demography.

Like with the SIS model with demography, we derive approximations for the quasi-stationary distribution using diffusion approximation and moment closure method applied on cumulant equations and the results are compared with simulation result. It is shown that when the loss of immunity rate $\nu = 0$ then we get an SIR model and when $\nu \to \infty$ we get the SIS model. Thus, the introduction of loss of immunity allows the disease to settle to an endemic equilibrium, but the number of infected individuals in endemic equilibrium is less than in the SIS model. It is also shown that any decrease in average immune period, for fixed $R_0 > 1$, corresponds to an increase in expected time to extinction of infection from the population.

Contents

Chapter 1

Introduction

It is well known that a person suffering from an infectious disease poses a threat to others. Susceptible individuals who come in contact with or in some cases are in the vicinity of an infectious individual may involuntarily contract the disease. The study of epidemic diseases has received a great deal of attention from mathematicians and population biologists. Different types of models have been proposed and discussed. This thesis explores the two standard modelling procedures: deterministic and stochastic. The deterministic model considers a structured mathematical framework, where the actual number of new cases in a short interval of time is taken to be proportional to the number of both susceptibles and infectives. The stochastic model on the other hand considers conditional realisation, where it is assumed that the probability of one new case in a short interval of time is proportional to both susceptibles and infectives, as well as the length of the time interval. Although both definitions sound similar, there is a subtle difference: the deterministic model considers a set mathematical structure, while the stochastic model works on the conditional probability structure. Deterministic models may be analysed with either difference or differential equations. Difference equations describe the transitions between compartments using discrete time steps and by expressing the number of cases at a given time $t+1$ in terms of that at preceding time t. Differential equations, on the other hand, describe the change in each compartment during a small time interval, δt, say, where the time is continuous. In this thesis we will analyse deterministic models using differential equations. Deterministic models are very popular in epidemic theory because of their tractability. The stochastic approach, however, when it can be performed is more realistic, powerful and flexible. For Anderson and

Britton (2000), the main advantage of the deterministic models lies in their simpler (but not necessarily simple!) analysis. For them, for a stochastic epidemic model to be mathematically manageable it has to be quite simple and thus not entirely realistic. Deterministic models, on the other hand, can be more complex yet still possible to analyse, at least when numerical solutions are adequate. Anderson and Britton (2000) gave some good reasons (which are presented below) why the stochastic models are to be preferred when their analysis is possible. First, the most natural way to describe the spread of a disease is stochastic; one defines the probability of disease transmission between two individuals, rather than stating certainly whether or not transmission will occur. Deterministic models usually describe the spread under the assumption of mass action, relying on the law of large numbers. Secondly, there are phenomena which are genuinely stochastic and do not satisfy a law of large numbers. For example, in a large community, many models will lead either to a minor outbreak infecting only a few individuals, or else to a major outbreak infecting a more or less deterministic proportion of the community. Calculation of the probability of the two events is only possible in a stochastic setting. The third advantage concerns estimation. Knowledge about uncertainty in estimates requires a stochastic model, and an estimate is not much use without some knowledge of uncertainty. Therefore stochastic models are to be preferred when their analysis is possible; otherwise deterministic models should be used. There is no conflict between the two. Both types of models play an important role in better understanding the mechanism of disease spread.

As stated above stochastic models are not easy to analyse. Usually the transition probabilities exhibits non-linear dependence on population size or number of infectives which makes the resultant stochastic process analytically intractable (Krishnarajah et al. (2004)). So techniques of approximation are needed to capture the underlying behaviour of the stochastic process. We can approximate the behaviour of the stochastic process, when the population size is large, by an essentially deterministic motion, with a random diffusion of smaller order superimposed upon it (Barbour (1975)). Here we look at the behaviour of the process near the equilibrium point of the deterministic equations. The deterministic trajectory starting from near an equilibrium point of the deterministic equations reduces to the same point for all time, and the stochastic fluctuation around it is approximated by the

Ornstein-Uhlenbeck process (see section 1.2). If the deterministic equilibrium is unstable, the original infection process can be expected to eventually diffuse away from it, and then to possibly follow some deterministic trajectory, with smaller order diffusion around it before entering another special phase (Barbour (1975)). On the other hand, if the deterministic equilibrium is stable, the original process will also enjoy a stable equilibrium behaviour similar to that of the approximating Ornstein-Uhlenbeck process. It is, however, possible that there exists one or more absorbing states which the process must eventually reach, in which case the apparent equilibrium is a quasi-equilibrium.

Here we analyse the SIS model with and without demography, two-group SIS model with and without demography and the SIRS model with and without demography. The letters S, I and R refer to susceptible, infective and recovered individuals respectively. S, I and R are random variables with discrete state space in the stochastic models and continuous variables in the corresponding deterministic models. The state variables are generally functions of time, although the main focus of this research is the quasi-stationary behaviour. The SIS model is a model for an infection without immunity, where recovery is possible and where recovered individuals are immediately susceptible. The SIRS model deals with a situation where the immunity is temporary. The number of susceptible, infected and recovered (and immune) individuals will be denoted by S, I and R respectively, where $R = 0$ in the SIS model. All infected hosts are assumed to be infective. The treatment of the stochastic version of each of the models is preceded by the formulation and analysis of the corresponding deterministic model.

The immigration rate will be put equal to μN and the death rate per individual μ, where N is the expected population size when infection is absent. We assume here that there are no disease related deaths. All models are based on homogeneous mixing. We also assume a constant contact rate β. The infection rate at time t will in each of the models be expressed as $\beta si/N$, where s and i are the values taken by the state variables S and I respectively at time t. N is the population size for epidemic models without demography whilst it is equal to the steady-state expected population size if no infection is present in the population for epidemic models with demography. The recovery rate will be expressed as γi. The latent

period (the period between the time of exposure to the disease and the time when infectiousness begins) is zero. So the average period of infectivity for models without demography is $1/\gamma$. The removal rate from the infective class by both recovery and death is $\gamma + \mu$, so the death-adjusted average period of infectivity is $1/(\gamma + \mu)$.

The basic reproduction number R_0 may be defined as the number of new infected individuals that a solitary infected individual is able to produce in a wholly susceptible population. This parameter is useful because it helps determine whether or not an infectious disease will spread through the population. The basic reproduction number is affected by several factors including: duration of infectivity of the infectives, how infectious the organism is and the number of susceptible hosts in the population. In other words, the expression for R_0 usually consist of a term for the rate of transmission divided by the expression for the rate of recovery and death.

One way of understanding the dynamics of the model is through the derivation of differential equations for the cumulants (the mean, variance etc.) of the distribution of the states of the process. The difficulty in applying this approach, however, is that nonlinearities in the equations governing the behaviour of the system lead to coupling between the equations for cumulants of different orders (Lloyd (2004)). For, instance, the equation for the first-order cumulants may involve second-order cumulants and those of second-order cumulants may involve third-order cumulants and so on. However, an approximation, moment closure approximation, which can truncate this set of equations can be used. The simplest moment closure method assumes that the distribution of states follows some given distribution and then uses the relationship between the moments of that distribution to truncate the set of cumulant equations (Nåsell (2003), Lloyd (2004)). For example Nåsell (2003) assumes that the distribution is normal and so the third-order and higher order cumulants vanish and closure of the set of cumulant equations is achieved by setting the third and higher order cumulants to zero. Here we shall use this moment closure method for the SIS model without demography and an extension of it used by Nåsell (2005) for multi-dimensional processes.

Another way of understanding the dynamics of the epidemic is the use of diffusion approximation. We say that a particle is diffusing about a space $\mathbb{R}^n$ whenever it experiences erratic and disordered motion through the space (Grimmett and Stirza-

ker (1982)). For example, radioactive particles diffusing through the atmosphere or a rumour diffusing through the population. Here we use the Ornstein-Uhlenbeck diffusion process to approximate the quasi-stationary distribution.

The performance of these approximations can be compared against each other and against the results obtained from numerical simulations of the stochastic model.

In this project we will start by give a brief discussion of the quasi-stationary distribution and the Ornstein-Uhlenbeck process. A literature review is given in chapter 2. In chapter 3, 4, 5, 6 and 7 we define and analyse in turn the SIS model without demography, the two-group SIS model without demography, the SIS model with demography, the two-group SIS model with demography and the SIRS model with and without demography. For each of the models in turn, we first analyse the deterministic version of the model. We then consider the stochastic model conditioned on non-extinction of infection. We use Ornstein-Uhlenbeck diffusion approximation to approximate the fluctuations about the deterministic endemic equilibrium to approximate the quasi-stationary distribution. An alternative approximation is then derived for all models except for the two-group SIS model with demography using cumulant differential equations and moment closure. Finally, we present numerical simulation results to validate our approximations. All numerical work was carried out using Matlab 7 on a desktop PC. In the final chapter, we give concluding remarks.

1.1 Quasi-stationary distribution

One of the main targets of this project is the quasi-stationary distribution. As stated earlier stochastic processes are widely used to model real-world phenomena. Some of these processes terminate due to the presence of an absorbing state. However, the behaviour of these processes prior to absorption can be of great interest. Certain processes, especially those for which the time to absorption is large, display some form of equilibrium on the non-absorbing states (Schrijner (1995)). 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 occurred (Nåsell (1996)). This distribution is referred to as the quasi-stationary distribution or limiting conditional distribution. The limiting conditional distribution can be described

by means of the limit, as time tends to infinity, of the conditional distribution of a Markov process, given that absorption has not yet occurred. This distribution is important for all the models we treat in this project as an approximation of the distribution of state prior to extinction. It is a useful approximation of the state of the process when it has been going on for a long time without extinction. It is a counterpart to the endemic infection level in the deterministic model (Nåsell (2005)). The goal of the analysis is to derive information about the quasi-stationary distribution of each of the models analysed.

The quasi-stationary distribution for a continuous time Markov chain $\{X(t) : t \geq 0\}$ with finite state space was first discussed by Darroch and Seneta (1967), under the assumption that the state space C may be partitioned as $C = D \cup \{0\}$ where 0 is the unique absorbing state while the transient states D form a single communicating class. Two years earlier, Darroch and Seneta (1965) solved the problem of the existence of the quasi-stationary distribution for a discrete time Markov chain with finite state space. They proved that there always exists precisely one quasi-stationary distribution. That is, there exists a unique distribution π_x defined on D such that if π_x is taken as the initial distribution of the process then $P(X(t) = x|X(t) \in D) = \pi_x$ for all $t \geq 0$, all $x \in D$. Furthermore, the quasi-stationary distribution π_x is also the unique limiting conditional distribution. That is, for any initial distribution of the process on D we have $\lim_{t\to\infty} P(X(t) = x|X(t) \in D) = \pi_x$ for all $x \in D$.

Consider a Markov process $\{X(t) : t \geq 0\}$ on the finite state space $C = \{0, 1, \ldots, N\}$, where 0 is an absorbing state while $D = \{1, 2, \ldots, N\}$ is a communicating class of transient states. We define the transition probabilities $p_{i,j}(t) = \Pr(X(t+s) = j|X(s) = i)$, where $\sum_{j=0}^{N} p_{i,j}(t) = 1$ for $i = 0, 1, \ldots, N, \quad t \geq 0$. The state probabilities $p_j(t) = \Pr(X(t) = j)$ are determined by the transition probabilities and the distribution of $X(s)$, $s < t$, through

$$p_j(t + \delta t) = \sum_{i=0}^{N} p_i(t) p_{i,j}(\delta t). \tag{1.1}$$

Subtracting $p_j(t)$ from both sides of equation (1.1) and taking limits as $\delta t \to \infty$ we have

$$\lim_{\delta t \to 0} \frac{p_j(t + \delta t) - p_j(t)}{\delta t} = \lim_{\delta t \to 0} \sum_{i \neq j} \frac{p_i(t) p_{i,j}(\delta t)}{\delta t} + \frac{p_j(t)(p_{j,j}(\delta t) - 1)}{\delta t}$$

Using Lemma 5.4.1 of Ross (1996) which can be stated as

1. $\lim_{\delta t \to 0} \frac{1-p_{i,i}}{\delta t} = \lambda_i$,

2. $\lim_{\delta t \to 0} \frac{p_{i,j}}{\delta t} = \lambda_{i,j}, \quad i \neq j$,

we have

$$\dot{p}_j(t) = \sum_{i \neq j} \lambda_{i,j} p_i(t) - \lambda_j p_j(t) \tag{1.2}$$

where $\lambda_{i,j}$ are the infinitesimal transition rates of the continuous-time Markov process $\{X(t)\}$, $\lambda_j = \sum_{i \neq j} \lambda_{i,j}$, and we use a dot to represent differentiation with respect to time. Putting $j = 0$ in equation (1.2) yields

$$\dot{p}_0(t) = \sum_{i \neq 0} \lambda_{i,0} p_i(t). \tag{1.3}$$

Now a sequence $\{q_j\}_{j=1}^N$ is a quasi-stationary distribution if $q_j \geq 0$ for all j, $\sum_{j=1}^N q_j = 1$, and

$$q_j = p_j(t)/(1 - p_0(t)) \qquad j = 1, 2, 3, \ldots, N; \quad t \geq 0, \tag{1.4}$$

where $p_j(t)$ are the state probabilities of the process with initial distribution $\Pr(X(0) = j) = q_j$, $j = 1, 2, \ldots, N$ and $\Pr(X(0) = 0) = 0$. 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 j at time t , given that absorption has not taken place by that time, is independent of time t for all j (Darroch and Seneta (1967)).

The sequence $\{q_j\}$ constitutes a quasi-stationary distribution if and only if $\{q_j\}$ solves the system

$$\sum_{i \neq j,\, i \geq 1} \lambda_{i,j} q_i - \lambda_j q_j = -\sum_{i \geq 1} \lambda_{i,0} q_i q_j \qquad j = 1, 2, \ldots, N, \tag{1.5}$$

and satisfies $q_j \geq 0$ and $\sum_{j=1}^N q_j = 1$. To prove this, we follow van Doorn (1991). First, let $\{q_j\}$ be a quasi-stationary distribution. Thus $q_j \geq 0$ and $\sum_{j=1}^N q_j = 1$. The process with initial distribution $\{q_j\}$ has state probabilities (from (1.4))

$$p_j(t) = q_j(1 - p_0(t)) \qquad j = 1, 2, \ldots, N. \tag{1.6}$$

Differentiating equation (1.6) we have

$$\dot{p}_j(t) = -q_j \dot{p}_0(t). \tag{1.7}$$

Substituting equation (1.3) into equation (1.7) we have

$$\dot{p}_j(t) = -q_j \sum_{i \neq 0} \lambda_{i,0} p_i(t). \tag{1.8}$$

Substituting equation (1.8) into equation (1.2) we have

$$\sum_{i \neq j} \lambda_{i,j} p_i(t) - \lambda_j p_j(t) = -q_j \sum_{i \neq 0} \lambda_{i,0} p_i(t).$$

Now substituting for $p_i(t), p_j(t)$ from equation (1.6), dividing through by $(1-p_0(t))$, and noting that $\lambda_{0,j} = 0$ for all j, yields equation (1.5).

Conversely, suppose that $\{q_j\}$ is a probability distribution on $\{1, 2, \ldots, N\}$ satisfying equation (1.5). Define $m_0(t)$ such that $m_0(0) = 0$ and $\dot{m}_0(t) = (1 - m_0(t)) \sum_{i \neq 0} q_i \lambda_{i,0}$, and define $m_j(t) = q_j(1 - m_0(t))$ for $j = 1, 2, \ldots, N$. Differentiating $m_j(t)$ with respect to time,

$$\dot{m}_j(t) = -q_j \dot{m}_0(t) = -q_j(1 - m_0(t)) \sum_{i \neq 0} q_i \lambda_{i,0} = (1 - m_0(t)) \left(- \sum_{i \neq 0} \lambda_{i,0} q_i q_j \right).$$

Since $\{q_j\}$ is assumed to satisfy (1.5), this becomes

$$\dot{m}_j(t) = (1 - m_0(t)) \left(\sum_{i \neq j,\, i \geq 1} \lambda_{i,j} q_i - \lambda_j q_j \right) = \sum_{i \neq j,\, i \geq 1} \lambda_{i,j} m_i(t) - \lambda_j m_j(t).$$

That is, for $j = 1, 2, \ldots, N$, the functions $m_j(t)$ satisfy equation (1.2). Similarly, we can show that (1.3) is satisfied. Since $\sum_{j=1}^{N} m_j(t) = (1 - m_0(t)) \sum_{j=1}^{N} q_j = 1 - m_0(t)$, then the functions $m_j(t), j = 0, 1, \ldots, N$, satisfy equations (1.2) and (1.3) together with $\sum_{j=0}^{N} m_j(t) = 1$, and so must be the state probabilities of the process $X(t)$ with initial distribution $\Pr(X(0) = j) = m_j(0) = q_j$ for $j = 1, 2, \ldots, N$ and $\Pr(X(0) = 0) = m_0(0) = 0$. Since (1.4) is satisfied by $\{m_j(t)\}$, then $\{q_j\}$ must be a quasi-stationary distribution.

Denoting by Λ_D the transition rate matrix restricted to the transient states equation (1.5), for the finite-state process, can be written

$$\mathbf{q}\Lambda_D = -\mu \mathbf{q}$$

where $\mathbf{q} = (q_1, q_2, \ldots, q_N)$ and $\mu = \sum_{i \in D} q_i \lambda_{i,0}$. Darroch and Seneta (1967) showed that the quasi-stationary distribution equals the left eigenvector of Λ_D corresponding to the eigenvalue with the maximal real part.

For processes on an infinite state space, in general there is no guarantee of existence of a unique quasi-stationary distribution or limiting conditional distribution. In the case of birth-death processes it is known that the quasi-stationary distribution need not be unique, but that provided the initial distribution of the process has finite support then the limiting conditional distribution corresponds to one particular member of the set of quasi-stationary distributions (van Doorn (1991)). For more general infinite state space processes, every limiting conditional distribution is a quasi-stationary distribution, but little else is known. See Pakes (1995) for a review of known results. We shall proceed by simulating our processes of interest over a sufficiently long time that convergence towards some limiting conditional distribution appears to have occurred, and considering approximation methods under the assumption that a unique limiting conditional distribution exists. From now on we shall use the term quasi-stationary distribution rather than limiting conditional distribution.

1.2 The Ornstein Uhlenbeck Process

As stated in section 1.1, the main goal of this analysis is to derive information about the quasi-stationary distribution of each of the models analysed. The pursuit of this goal, however, leads to mathematical problems where exact solutions cannot be found. There are no analytic solutions to the forward Kolmogorov equations derived for each model, so approximations are used. One of the approximations we will use to approximate the quasi-stationary distribution is the diffusion approximation (Ornstein Uhlenbeck). The material on the Ornstein Uhlenbeck process is taken from Tuckwell (1995).

The Ornstein Uhlenbeck process was introduced by Uhlenbeck and Ornstein 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. They used the following stochastic differential equation for the

velocity $v(t)$ of a particle at time t.

$$\frac{dv}{dt} + kv = w(t)$$

where k is constant and w is a white noise. In addition to its initial use in studies of Brownian motion, the Ornstein Uhlenbeck process has found application in diverse areas such as astrophysics, stochastic models for neuronal activity, birth and death theory, population biology etc.

The Ornstein Uhlenbeck process can be defined as a time - homogenous diffusion process with

1. first infinitesimal moment proportional to the value of the process, so

$$\alpha(x,t) = -ax \tag{1.9}$$

where a is a positive constant. The drift is therefore directed towards the origin. A constant drift sometimes occurs naturally in addition to the drift proportional to x and this does not affect the overall qualitative properties of the process so the general form of the first infinitesimal moment is

$$\alpha(x,t) = -ax + b$$

where b is a constant which can be any real number.

2. a constant second infinitesimal moment, so

$$\beta(x,t) = \sigma^2 \tag{1.10}$$

where σ is a non-negative real constant.

The Ornstein Uhlenbeck process unrestricted on $(-\infty, \infty)$ has a non-degenerate stationary distribution. Another important feature of the Ornstein Uhlenbeck process is that any finite point is eventually reached with probability one in a finite time, regardless of the values of the parameters a, b and σ. The process makes excursions away from the equilibrium, but the farther away from equilibrium the stronger is the drift towards equilibrium.

If the initial value of an Ornstein Uhlenbeck process is x then at time t, the random variable $X(t)$ i.e, the value of an Ornstein Uhlenbeck process at time t, is a

Gaussian random variable with mean

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

and variance

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

Hence, on using the standard formula for a normal density, we have

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

where $p(y,t|x)$ is the probability density function of the random variable $X(t)$ given that the initial value $X(0)$ is x.

1.2.1 Limiting behaviour at $t = \infty$ (stationary distribution)

As stated earlier 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 the variance of $X(t)$ take the following values as $t \to \infty$ regardless of the initial value $X(0)$:

$$E[X(t)] \to 0;$$

$$\text{Var}[X(t)] \to \frac{\sigma^2}{2a}.$$

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

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

Since the Ornstein Uhlenbeck process is a Gaussian process, and since the quasi-stationary distribution of the processes we are studying 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 each of the models studied.

The other reason for using the Ornstein Uhlenbeck Process is because it has a drift that is directed towards the origin (in our case the endemic deterministic

equilibrium). The theory for diffusion approximation (Etheir and Kurtz, (1986)) 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 deterministic equilibrium is stable, we expect the Ornstein Uhlenbeck process to drift towards it. The Ornstein Uhlenbeck process satisfies

$$dX_t = -\theta(X_t - \mu)dt + \sigma dW_t \tag{1.11}$$

where θ is the speed of the drift back to the mean μ, X_t denotes the Ornstein Uhlenbeck process $X(t)$ and W_t is a Wiener process.

Chapter 2

Literature Review

2.1 Brief history

Material on the brief history is based on Bailey (1975).

The study of epidemiology began well before the 19th century. However, genuine progress was only achieved in the 19th century. Hamer (1906) considered that the course of an epidemic must depend inter alia on the number of susceptibles and the contact-rate between susceptibles and infectious individuals (Bailey 1975). These are basic to all subsequent deterministic theories, and indeed appear in probability versions as well. Ross (1911 and later) worked with a more structured mathematical model taking into account a whole set of basic parameters describing various aspects of the transmission of malaria. Although Ross employed the idea of chance or probability in formulating his basic equations, they were actually still deterministic in character. That is, the future state of the epidemic can be determined when the initial numbers of susceptibles and infectious individuals, together with the attack, recovery, birth and death rates are given. This was the first time a well-organised mathematical theory was used as a research tool in epidemiology.

Kermack and McKendrick (1927 to 1939) carried out more elaborate mathematical studies of the same general types of models. They introduced a greater degree of generality, including variable rates of infection, recovery etc. Their most outstanding result was the celebrated Threshold Theorem. This theorem states that the introduction of infectious cases into a community of susceptibles would not give rise to an epidemic outbreak if the density of susceptibles was below a certain critical value. If, on the hand, the critical value was exceeded, then there would be

an epidemic. Soper (1929) carried out further deterministic work specifically with measles.

McKendrick (1926) was the first to published a genuinely stochastic treatment of an epidemic process. Whereas in deterministic models one takes the actual number of new cases in a short interval of time to be proportional to the numbers of both susceptibles and infectious cases as well as to the length of the interval, McKendrick assumed that the probability of one case in a short interval was proportional to the same quantity. This model entails an individual being himself infectious from the instant he receives infection until the moment he or she dies, recovers, or is isolated. Since McKendrick's publication a lot of stochastic treatments of the epidemic process have been carried out (for further information see Bailey (1975)).

2.2 Simple epidemic model

Here we consider the simplest type of epidemic model in which infection spreads by contact between the members of a community, but in which there is no removal from circulation by death, recovery or isolation (Bailey 1975). This is the basic SI (susceptible $\rightarrow$ infective) model. In this model, all susceptibles will eventually become infected.

2.2.1 Deterministic model

The assumption here is homogenously mixing group of individuals of total size $n+1$. Suppose the epidemic starts at time $t = 0$ with one infected individual who is infectious and n susceptible individuals. We let s and i be the number of susceptibles and infectives, respectively, at time t, so that $s + i = n + 1$. We assume here that the rate of occurrence of infection is proportional to both the number of infectives and the number of susceptibles. So the number of new infectives in the time-interval δt can be written as $\beta si\delta t$ where β is the infection rate (or contact rate). So the process is described by the differential equation

$$\begin{aligned} \frac{di}{dt} &= \beta si \\ &= \beta i(n - i + 1). \end{aligned} \tag{2.1}$$

At equilibrium $i = 0$ or $i^* = n + 1$, i.e, no infectives or everybody becomes infected. This confirms our initial assertion that eventually everyone will be infected. We can solve equation (2.1) with the initial condition $i(0) = 1$. This gives

$$i(t) = \frac{n+1}{1 + ne^{-\beta(n+1)t}}.$$

This equation is called the logistic law of growth. As $t \to \infty$, $e^{-\beta(n+1)t} \to 0$ and therefore $i(t) \to n + 1 = i^*$.

2.2.2 Stochastic model

Whether or not an infective actually communicates his disease to susceptibles in his vicinity is plainly a matter of chance. The magnitude of this chance may depend on the virulence of the organisms, the extent at which they are discharged, the degree of the susceptibles' proximity to the infectives and so on. All this can be subsumed under a single concept called adequate contact (Bailey (1975)). So the spread of an infectious disease is a random process. For example, in a small group of individuals, a few of whom have a cold, some will catch the infection others will not. The simple stochastic epidemic was first mentioned by Bartlett (1949). This is the probability version of the deterministic model discussed in the previous section. As before, the assumption is a homogeneously mixing group of $n + 1$ individuals, one of whom is infective and n susceptibles. This time, however, the number of infectives and susceptibles at time t are random variables $I(t)$ and $S(t)$, respectively, where $S(t) + I(t) = n + 1$. So the epidemic is completely described by the process $\{I(t); \quad t \geq 0\}$. The epidemic is modelled by a continuous time Markov Chain. See Taylor and Karlin (1998) (chapter 3, page 95) for a definition of Markov Chain.

Modelling individual infection

The consideration here is that infection takes place at random, and the assumption is that only one infection can happen at a time. The time between events is some random variable which will be modelled. Considering a time interval of length δt, namely $(t, t + \delta t)$ say, the chance of a contact between any two individuals is $\beta\delta t + o(\delta t)$. The assumption here is that β is the contact rate. It follows then that the probability of an infection occurring in δt is $\beta SI\delta t + o(\delta t)$ (i.e. the chance of

one new case in a very short interval of time is jointly proportional to the length of the interval, the number of susceptibles and the number of infectives plus something small relative to that length). Therefore the probability of no infection is $1-\beta SI\delta t+ o(\delta t)$ (the sign of the term $o(\delta t)$ is irrelevant since it is very small). So the probability of i infectives at time $t+\delta t$ can be expressed as

$$p_i(t+\delta t) = \beta(i-1)(n-i+2)\delta t p_{i-1}(t) + (1-\beta i(n-i+1))\delta t p_i(t).$$

The above transition probabilities give a continuous-time Markov jump process where the number of infectives follows a pure birth process and the time between jumps is given by an exponential distribution with mean $\frac{1}{\beta SI}$.

2.3 General epidemic model

We now consider the general epidemic model of Kermack and Mckendrick (1927) also known as the SIR model. Let $S(t)$, $I(t)$ and $R(t)$ respectively denote the number of susceptibles, infectives and removed (recovered and immune) individuals. The main characteristics of this epidemic process are roughly as follows. A closed population is subdivided into susceptibles, infectives and removed individuals. So $S(t)+I(t)+R(t)=N$ for all t. So the model we study here is a bivariate Markov chain $\{S(t), I(t),\ t \geq 0\}$. Each infective is infectious during a random period of time that is exponentially distributed with intensity γ. While infected, it behaves independently of the others and is able to contact susceptibles, who will then become infected at a rate $\frac{\beta}{N}SI$. After that period, the individual recovers and become immune or dies and plays no further role in the propagation of the disease (Mollison (1995)).

2.3.1 Deterministic model

We introduce the scaling $s=\frac{S}{N}$ and $i=\frac{I}{N}$. The deterministic version of the model is defined by the following set of differential equations

$$\frac{ds}{dt} = -\beta si, \tag{2.2}$$

$$\frac{di}{dt} = \beta si - \gamma i, \tag{2.3}$$

$$\frac{dr}{dt} = \gamma i. \tag{2.4}$$

The term βsi is the crucial non-linear term, indicating that infections occur at high rate when there are many susceptibles and infectives.

At the start of the epidemic, when $t = 0$, let (s, i, r) take values $(s_0, i_0, 0)$. The question now is, 'when will there be an epidemic?' For there to be an epidemic, we expect $\left[\frac{di}{dt}\right]_{t=0} > 0$. So from equation (2.3)

$$\begin{aligned} \frac{di}{dt} &= \beta si - \gamma i \\ &= \beta i\left(s - \frac{\gamma}{\beta}\right). \end{aligned} \tag{2.5}$$

Therefore if $s_0 > \frac{\gamma}{\beta}$ then $\left[\frac{di}{dt}\right]_{t=0} > 0$. So initially the number of infected individuals will increase and there will be an epidemic. However, if $s_0 < \frac{\gamma}{\beta}$ then $\left[\frac{di}{dt}\right]_{t=0} < 0$ and no epidemic can occur because the number of infectives decreases with time. So there must be sufficient susceptibles for an epidemic to be possible. Therefore $\rho = \frac{\gamma}{\beta}$ gives a threshold density of susceptibles.

As stated earlier , the above equation cannot be solved easily because of the non-linearity (βsi). Now we consider the approximate solution to the system of equation obtained by Kermack and McKendrick (1927).

We eliminate i from the first and third equations (2.2 and 2.4) by division

$$\begin{aligned} \frac{ds}{dr} &= -\frac{\beta s}{\gamma} \\ &= -\frac{s}{\rho}, \\ s &= s_0 e^{-r/\rho}. \end{aligned}$$

Since $s + i + r = 1$, we can write equation (2.4) as

$$\begin{aligned} \frac{dr}{dt} &= \gamma(1 - s - r), \\ \frac{dr}{dt} &= \gamma\left(1 - s_0 e^{-r/\rho} - r\right). \end{aligned} \tag{2.6}$$

Explicit solution to equation (2.6) giving r as a function of t does not appear possible so we consider approximation by first expanding the exponential factor as far as the term in r^2.

$$\frac{dr}{dt} = \gamma\left(1 - s_0\left(1 - \frac{r}{\rho} + \frac{1}{2}\frac{r^2}{\rho^2}\right) - r\right). \tag{2.7}$$

Solving equation (2.7) gives

$$r = \frac{\rho^2}{s_0}\left(\left(\frac{s_0}{\rho} - 1\right) + \alpha \tanh\left[\frac{1}{2}\alpha\gamma t - \tanh^{-1}\left(\left(\frac{s_0}{\rho} - 1\right)/\alpha\right)\right]\right). \tag{2.8}$$

The epidemic curve, which gives the rate at which new infectives accrue, is therefore

$$\frac{dr}{dt} = \frac{\gamma\alpha^2\rho^2}{2s_0}\cosh^{-2}\left(\frac{1}{2}\alpha\gamma t - \tanh^{-1}\left(\left(\frac{s_0}{\rho} - 1\right)/\alpha\right)\right), \tag{2.9}$$

where

$$\alpha = \left(\frac{2s_0(1-s_0)}{\rho^2} + \left(\frac{s_0}{\rho} - 1\right)^2\right)^{\frac{1}{2}}.$$

This is in general a symmetrical bell-shaped curve (Bailey (1975)). This illustrates the common observation that in many actual epidemics the number of new cases reported each day climbs to a peak value and then dies away again.

We find the total size of the epidemic i.e. the total number of removal after the elapse of a very long period of time by letting $t \to \infty$ in (2.8). Since $\tanh(t) \to 1$ as $t \to \infty$,

$$r(\infty) = \frac{\rho^2}{s_0}\left(\frac{s_0}{\rho} - 1 + \alpha\right).$$

Assuming that there are a few initial infectives, then the first term in α is approximately zero. So the second term is dominant. Therefore

$$r(\infty) = 2\rho\left(1 - \frac{\rho}{s_0}\right).$$

This result can also be achieved by putting $dr/dt = 0$ and $s_0 = 1$ in (2.7). Kermack and McKendrick first got the above result and rewrote it again as follows:

$$s_0 = \rho + \nu,$$

where ν is the (scaled) number of susceptibles by which we are initially above threshold. So

$$\begin{aligned} r(\infty) &= 2\rho\left(\frac{\rho + \nu - \rho}{\rho + \nu}\right) \\ &= 2\nu\left(1 - \frac{\nu}{\rho} + \cdots\right). \end{aligned}$$

To the first order $r = 2\nu$. It follows then that $s_\infty = \rho - \nu$, i.e. the initial (scaled) number of susceptibles s_0, reduces finally to a value as far below the threshold, ρ, as it was originally above.

2.3.2 Stochastic model

Now we consider the stochastic version of the general epidemic. The stochastic version of the model was proposed by McKendrick (1926), but did not receive much attention. It was not until the late 1940's when Bartlett (1949) studied the stochastic version of the model (Kermack-Mckendrick model) that stochastic continuous-time epidemic models began to be analysed extensively.

Here there are two types of transition - infection and removal. As before, we write the chance of one new infection in time δt as $\frac{\beta}{N} SI\delta t$. When this transition occurs, S decreases by one unit and I increases by one unit. The chance of one removal in δt can be taken as $\gamma I \delta t$, where γ is the removal-rate. I decreases by one unit after the transition but S remains unchanged.

Let there be n susceptibles and a infectives at time $t = 0$. We denote $p_{s,i}(t)$ the probability that at time t there are s susceptibles and i infectives. The forward Kolmogorov equation is

$$\frac{dp_{s,i}}{dt} = \frac{\beta}{N}(s+1)(i-1)p_{s+1,i-1}(t) + \gamma(i+1)p_{s,i+1}(t) - \left(\frac{\beta}{N}si + \gamma i\right) p_{s,i}(t)$$

where $0 \leq i + s \leq n + a$, $0 \leq s \leq n$ and $0 \leq i \leq n + a$.

Gani(1965) and Siskind (1965) solve this problem using probability-generating function and Laplace transform. The probability-generating function they used is given by

$$p(z, w, t) = \sum_{s=0}^{N} \sum_{i=0}^{N-s} z^s w^i p_{s,i}(t). \tag{2.10}$$

It can be shown that equation (2.10) satisfies the partial differential equation

$$\frac{\partial p}{\partial t} = (w^2 - zw)\frac{\partial^2 p}{\partial z \partial w} + \rho(1-w)\frac{\partial p}{\partial w}. \tag{2.11}$$

See Bailey (1975) for further investigation on this topic.

2.4 SIR epidemic model with demography

Andersson and Britton (2000) and Nåsell (1996, 2002 and 2005) analysed the SIR model with demography. Individuals are born into the population at a constant rate

μN and each of them has an exponentially distributed lifetime with intensity μ, i.e. the average lifetime is given by $1/\mu$. Therefore the population size will fluctuate around the quantity N. Nåsell (2002) allows for disease related deaths. Andersson and Britton (2000) and Nåsell (1999 and 2005) assumed no disease related deaths. We will follow this approach. The choice of size-independent birth rates is to avoid population extinction or explosion.

As in the previous section, a given infective stays infectious for a time period that is exponentially distributed with intensity γ. During that time he or she contacts a given individual at rate β/N. If the contacted individual is susceptible, he or she immediately becomes infectious and proceeds to infect other individuals. All random variables and Poisson processes involved are assumed to be mutually independent.

As before, we use $S(t)$ and $I(t)$ to denote the number of susceptibles and infectives respectively at time t. Therefore $(S, I) = \{(S(t), I(t)); \quad t \geq 0\}$ is a bivariate continuous time Markov process with the following transition rates:

$$\begin{aligned}
(s,i) &\rightarrow (s+1,i) = \mu N, \\
(s,i) &\rightarrow (s-1,i+1) = \frac{\beta}{N} si, \\
(s,i) &\rightarrow (s-1,i) = \mu s, \\
(s,i) &\rightarrow (s,i-1) = (\mu+\gamma) i.
\end{aligned}$$

All states $(s, 0)$ communicate with each other, but not with any state (s, i) with $i \geq 1$. The states $(s, 0)$ form an absorbing set and the states (s, i), $i \geq 1$, are transient. The Kolmogorov forward equation for the model is

$$\begin{aligned}
\frac{dp_{s,i}}{dt} &= \mu N p_{s-1,i}(t) + \frac{\beta}{N}(s+1)(i-1)p_{s+1,i-1}(t) + \mu(s+1)p_{s+1,i}(t) + \mu(i+1)p_{s,i+1}(t) \\
&\quad +\gamma(i+1)p_{s,i+1}(t) - \left(\mu N + \frac{\beta}{N} si + \mu s + \mu i + \gamma i\right) p_{s,i}(t), \qquad (2.12)
\end{aligned}$$

where $s = 0, 1, 2, \ldots$ and $i = 0, 1, 2, \ldots$.

2.4.1 Deterministic model

We now define the scaled process $1/N(S(t), I(t)) = (s(t), i(t))$. The deterministic model of the scaled process is given by

$$\frac{ds}{dt} = \mu(1-s) - \beta si, \tag{2.13}$$

$$\frac{di}{dt} = \beta si - (\mu+\gamma)i. \tag{2.14}$$

Here the basic reproduction number is given by $R_0 = \beta/(\gamma+\mu)$, since the true infectious period is exponentially distributed with intensity $\gamma+\mu$, taking into account the possibility of death before recovery. Also let $\alpha = (\gamma+\mu)/\mu$ be the ratio of average lifetime to the average duration of infection.

Equations (2.13) and (2.14) have two stationary points, namely $(1, 0)$ which is the disease free state and

$$(s^*, i^*) = \left(\frac{1}{R_0}, \frac{R_0 - 1}{\alpha R_0}\right),$$

which is the endemic level. It can be shown that the first stationary point is stable if $R_0 < 1$ and unstable if $R_0 > 1$ while the second one is stable if $R_0 > 1$. The second stationary point is unfeasible if $R_0 < 1$. So if $R_0 < 1$ the infection is predicted to die out fairly quickly. On the other hand, if $R_0 > 1$ then the infection will rise towards the endemic level.

2.4.2 Diffusion approximation

We now proceed by studying the scaled and centred process $(S(t) - Ns^*, I(t) - Ni^*)/\sqrt{N}$. The theory for diffusion approximation (Etheir and Kurtz, (1986)) suggests that this process may be approximated by a two-dimensional Ornstein-Uhlenbeck process, $(\tilde{S}(t), \tilde{I}(t))$, which is the limiting process as the population size, N, tends to infinity. Since the limiting process is of Ornstein-Uhlenbeck type, it has a bivariate Gaussian stationary distribution with mean (0, 0) and covariance matrix $\mathbf{\Sigma}$ where $\mathbf{\Sigma}$ solves the matrix equation

$$\mathbf{J}(s^*, i^*)\mathbf{\Sigma} + \mathbf{\Sigma}\mathbf{J}(s^*, i^*)^T + \mathbf{G}(s^*, i^*) = 0 \tag{2.15}$$

(Gardiner (1985)). Here $\mathbf{J}(s, i)$ and $\mathbf{G}(s, i)$ are the local drift and covariance matrices of $(\tilde{S}(t), \tilde{I}(t))$. The local drift matrix is the Jacobian matrix of the first order

infinitesimal moments of the scaled process and the local covariance matrix is the infinitesimal covariance matrix of the scaled process. We are interested in the behaviour of the epidemic process close to the endemic level and therefore we approximate $\mathbf{J}(s,i)$ and $\mathbf{G}(s,i)$ at the endemic level, which become $\mathbf{J}(s^*,i^*)$ and $\mathbf{G}(s^*,i^*)$. The local drift matrix $\mathbf{J}(s^*,i^*)$ (which corresponds to θ in equation (1.11)) and the local covariance matrix $\mathbf{G}(s^*,i^*)$ (which corresponds to σ in the same equation) of the limiting process, $(\tilde{S}(t),\tilde{I}(t))$, are

$$\mathbf{J}(s^*,i^*) = \begin{pmatrix} -\beta i^* - \mu & -\beta s^* \\ \beta i^* & \beta s^* - (\gamma+\mu) \end{pmatrix} = \mu \begin{pmatrix} -R_0 & -\alpha \\ R_0 - 1 & 0 \end{pmatrix}$$

and

$$\mathbf{G}(s^*,i^*) = \begin{pmatrix} \beta s^* i^* + \mu(1+s^*) & -\beta s^* i^* \\ -\beta s^* i^* & \beta s^* i^* + (\gamma+\mu) i^* \end{pmatrix} = \frac{\mu}{R_0} \begin{pmatrix} 2R_0 & -(R_0-1) \\ -(R_0-1) & 2(R_0-1) \end{pmatrix}$$

respectively. The stationary distribution of the process $(\tilde{S}(t),\tilde{I}(t))$ can be used to provide an approximation of the quasi-stationary distribution of the process (S,I). That is, the quasi-stationary distribution of (S,I) can be approximated by a bivariate normal distribution with mean $N(s^*,i^*)$ and covariance matrix $N\boldsymbol{\Sigma}$. Solving equation (2.15) we derive the explicit expression for the covariance matrix for the stationary solution, $\boldsymbol{\Sigma}$.

$$\boldsymbol{\Sigma} = \frac{1}{R_0^2} \begin{pmatrix} \alpha + R_0 & -R_0 \\ -R_0 & R_0 - 1 + R_0^2/\alpha \end{pmatrix}.$$

For the approximation to be valid, we require that the step size $1/N$ of the scaled process is sufficiently small for it to be approximated by a process with continuous sample paths; that the equilibrium point (s^*,i^*) is stable, so that the process will tend to spend a long time in the vicinity of (s^*,i^*) and that i^* is sufficiently large that the Ornstein-Uhlenbeck process is unlikely to reach the boundary $I=0$ (Clancy (2005)). Therefore, we expect the approximation to be good if the infection process is above threshold, that is $R_0 > 1$ and N is sufficiently large.

Nåsell (2005) also used cumulant equations to approximate the quasi-stationary distribution. He derived the cumulant equations and used moment closure methods to solve them. For details see Nåsell (2005). However, the derivation of cumulant equations will be discussed in detail in later chapters.

2.5 SIS model

The susceptible-infected-susceptible (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 define $S(t)$ and $I(t)$ as the number of susceptible individuals and the number of infected individuals at time t respectively. The susceptible class consists of those individuals who can incur the disease and the infective class consists of those who are infected and are transmitting the disease to others. Since $S(t) + I(t) = N$ for all t, it is sufficient to concentrate on $I(t)$. $\{I(t) : t > 0\}$ is a finite-state space univariate continuous-time Markov chain with state space $C = \{0, 1, 2, \ldots N\}$ and transition rates

$$\begin{aligned}
\Pr\left(I(t+\delta t) = i+1 \mid I(t) = i\right) &= (\beta/N)i(N-i)\delta t + o(\delta t) \text{ for } i = 1, 2, \ldots, N-1, \\
\Pr\left(I(t+\delta t) = i-1 \mid I(t) = i\right) &= \gamma i \delta t + o(\delta t) \text{ for } i = 1, 2, \ldots, N,
\end{aligned}$$

for some $\beta, \gamma > 0$, all other transitions having probability $o(\delta t)$.

The origin is an absorbing state in this model, and eventual absorption at the origin is certain. All states except the origin are transient, and the stationary distribution is degenerate with probability one at the origin.

As stated earlier, we assume a constant contact rate β. The infection rate at time t will be expressed as $\beta si/N$, where s and i are the values taken by the state variables S and I respectively at time t. The recovery rate will be expressed as γi. The latent period (the period between the time of exposure to the disease and the time when infectiousness begins) is zero. So the average period of infectivity is $1/\gamma$.

The SIS model was first discussed by Weiss and Dishon (1971)and has since been used by other authors in a variety of contexts – see Nåsell (1996) and references therein. Since this model has a degenerate stationary distribution with probability one at the origin, our interest therefore focuses upon 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

$$q_i = \lim_{t\to\infty} \Pr\left(I(t) = i \mid I(t) > 0\right),$$

whatever the distribution of the initial state $I(0)$ (Darroch and Seneta (1967)). This distribution is also quasi-stationary in that if $\Pr(I(0) = i) = q_i$, then $\Pr(I(t) = i | I(t) > 0) = q_i$ for all $t > 0$, and, it is the unique solution of the equations

$$\begin{aligned}&(\beta/N)(i-1)(N-i+1)q_{i-1} + \gamma(i+1)q_{i+1} - ((\beta/N)i(N-i) + \gamma i)\, q_i \\ &= -\gamma q_1 q_i \end{aligned} \tag{2.16}$$

for $i = 1, 2, \ldots, N$, where we adopt the convention that $q_0 = q_{N+1} = 0$. Note that (2.16) is a special case of equation (1.5).

The SIS model without demography was analysed in detail by Nåsell (1996, 1999). He showed that the quasi-stationary distribution q has forms depending on the value of $R_0 = \beta/\gamma$ and its relationship to the total population size, N. He identified three different parameter regions that determine the form of the quasi-stationary distribution. When R_0 is distinctly below 1, the quasi-stationary distribution is approximated by a geometric distribution and when R_0 is distinctly above 1, it is approximated by a Normal distribution. However, there exists a transition region when R_0 is near 1, where the form of the distribution is more complex. He found it by rescaling $R_0 = 1 + \rho/\sqrt{N}$ to make R_0 a function of N in such a way that for fixed ρ, R_0 approaches 1 as N approaches infinity. He defined this region by requiring ρ to be fixed as $N \to \infty$.

Kryscio and Lefèvre (1989) and later Nåsell (1996, 1999) 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 (1996, 1999) 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 first approximation, $p^{(1)}$, can be interpreted as the SIS model with one permanently infected individual. In this approximation, every recovery rate γi is replaced by $(i-1)\gamma$ 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 replaced by 0, while all other transition rates remain unchanged. Nåsell's results from the approximations confirmed those of Kryscio and Lefèvre (1989) that the quasi-stationary distribution q is well approximated by the distribution $p^{(0)}$ for R_0 distinctly larger than 1 and by the distribution $p^{(1)}$ when R_0 is distinctly smaller than 1. He showed that in the transition region,

the quasi-stationary distribution q makes a transition from close to $p^{(1)}$ to close to $p^{(0)}$ as R_0 grows past value 1. Nåsell (1996, 1999) also derived approximations for the expected time to extinction from the quasi-stationary distribution for the three parameter regions of R_0. Andersson and Djehiche (1998) also investigated the time to extinction. They derived the asymptotic distribution for the extinction time as the population grows to infinity, under different initial conditions and for different values of the infection rate.

Ovaskainen (2001) approximated the quasi-stationary distribution in two different limits. In the first case the number of individuals N is fixed, but the basic reproduction ratio $R_0 \to \infty$ (with relative error of the approximations of the order $O(1/R_0)$). In the second case, the basic reproduction ratio $R_0 > 1$ is fixed but the number of individuals $N \to \infty$ (with relative error of the approximations of the order $O(1/N)$).

Detailed analysis of the SIS model without and with demography is given in chapter 3 and chapter 5 respectively.

For models incorporating demographic processes, we allow for recruitment of new susceptibles to the population at constant rate μN. This is often referred to in the literature as 'birth', but since a birth rate might be expected to depend upon current population size we use the term 'immigration'. Other recruitment rates considered by previous authors include (a) birth of susceptibles at rate proportional to current population size (Hethcote (1994)); (b) birth of susceptibles at rate proportional to number of susceptibles present (Clancy, O'Neill and Pollett (2001)); (c) logistic birth rate (Krishnarajah et al. (2007)). However, birth rates (a) and (b) lead to exponential growth or decay of the total population size, while (c) results in a somewhat more complicated model. We choose constant immigration to give a relatively simple model with stable total population size.

Chapter 3

SIS model without demography

In section 2.5 we briefly defined the SIS (susceptible-infected-susceptible) model so we will now analyse it in detail. In some of the sections (3.1 - 3.6) we present known results which we will develop further in later chapters for more complicated models. Section 3.7 presents results slightly different from those previously obtained by Nåsell (2003). The results in section 3.8 and 3.9 are entirely new.

Nåsell (2003) studied the quasi-stationary distribution of the stochastic logistic model in the parameter region where its body is approximately Normal. He used moment closure methods to approximate the quasi-stationary distribution by the Normal, Binomial, Poisson and the Log-normal distributions. Krishnarajah et al. (2004) also used moment closure methods to approximate the stochastic epidemic. They, like Nåsell, used a moment closure approximation based on distributional assumptions. However, they used raw moments instead of central moments or cumulants. They used the Beta-binomial and Log-normal approximations to model the distribution of states of the process at fixed time t. In addition, they developed a closure approximation based on a mixture distribution in order to capture the behaviour of the stochastic SIS model around the threshold between persistence and extinction. This mixture approximation comprises a probability distribution (Log-normal or Beta-binomial) designed to capture the probabilities of the system conditioned on non-extinction and a probability mass at 0 which represents the probability of extinction.

In this chapter we will investigate the closed SIS epidemic model using a diffusion approximation similar to the one used by Clancy and French (2001). We also derive cumulant equations and use moment closure methods based on distributional

assumptions – specifically, we assume a normal, poisson, log-normal, binomial or beta-binomial distribution. Some of our approximating distributions are those of Nåsell (2003), others are new. We then work out the total variation distance of each of the approximating distributions from the exact quasi-stationary distribution. For comparison, we also compute the total variation distance away from the true quasi-stationary distribution of the asymptotic approximations of Nåsell (1996, 1999).

3.1 Model formulation

In this model there are two possible events (see Table 3.1), i.e. infection of a susceptible individual and recovery of an infected individual. Three parameters are used, namely the population size N, the contact rate β, and the recovery rate γ. All these parameters are assumed to be strictly positive. The basic reproduction number (the average number of new infected individuals that a solitary infected individual produces in a population of susceptible individuals) is $R_0 = \beta/\gamma$. The state space C can also be defined as $C = \{0\} \cup D$, where 0 is the absorbing state and D comprises the transient states. Absorption at 0 is certain within a finite time.

Let $p_i(t) = Pr(I(t) = i)$, $i \in \{0, 1, 2, \ldots N\}$, denote the state probabilities. These depend on the initial distribution $\{p_i(0)\}$. The intensity matrix A (matrix

Table 3.1: The transition rates for the model are given as:

Event	State Transition	Transiton Rate
Infection of a susceptible	$i \to i+1$	$\beta(i/N)(N-i)$
Recovery of an infective	$i \to i-1$	γi

which consists of the transition rates $a_{i,j}$ from state i to state j for $i \neq j$ and where $a_{i,i} = -a_i$ with $a_i = \sum_{i \neq j}^{N} a_{i,j}$) is of tri-diagonal type, with entries

$$a_{j,i-1} = \gamma i, \qquad i = 1, 2, \ldots N,$$

$$a_{i,i+1} = \beta \frac{i}{N}(N-i), \qquad i = 0, 1, 2, \ldots N-1,$$

$$a_{i,i} = -(\gamma i + \beta \frac{i}{N}(N-i)), \qquad i = 0, 1, 2, \ldots N,$$

$$a_{i,j} = 0 \quad \text{for} \quad i,j = 0,1,2,\ldots N \quad \text{and} \quad j \notin \{i-1, i, i+1\}.$$

The Kolmogorov forward equations for the state probabilities can be written as,

$$\frac{dp_i}{dt} = \beta\frac{i-1}{N}(N-i+1)p_{i-1}(t) + \gamma(i+1)p_{i+1}(t) - \left(\beta\frac{i}{N}(N-i) + \gamma i\right)p_i(t), \quad (3.1)$$

for $i = 0, 1, 2, \ldots, N$ and where $p_{-1}(t) = p_{N+1}(t) = 0$. In matrix notation,

$$\frac{dp}{dt} = pA.$$

As stated earlier, this process has a degenerate stationary distribution that puts probability one at the origin. Therefore 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. This will be analysed later in section (3.4).

3.2 Deterministic model

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

$$\frac{di}{dt} = \beta si - \gamma i, \quad (3.2)$$

$$\frac{ds}{dt} = -\beta si + \gamma i. \quad (3.3)$$

The constant population size is built into the system (3.2) and (3.3), since adding the equations gives:

$$\frac{d(s+i)}{dt} = \frac{ds}{dt} + \frac{di}{dt} = 0.$$

So the first equation (3.2) along with the fact that $s = 1 - i$ give a complete description of the model,

$$\frac{di}{dt} = \beta(1-i)i - \gamma i. \quad (3.4)$$

The basic reproduction number R_0 is

$$R_0 = \frac{\beta}{\gamma}. \tag{3.5}$$

Therefore, increases in the rate of transmission tend to increase R_0, and increase in the rate of recovery tends to reduce the spread of the disease in the population.

3.3 Equilibrium

At equilibrium equation (3.4) becomes

$$0 = \beta i(1-i) - \gamma i.$$

So, either

$$i = 0 \quad \text{or} \quad i = i^* = \left(1 - \frac{\gamma}{\beta}\right) = \left(1 - \frac{1}{R_0}\right).$$

The first critical point corresponds to the absorbing state of the stochastic system, which is the disease-free equilibrium, and the second one corresponds to the endemic equilibrium. The associated value of the proportion of susceptibles at the endemic equilibrium is $\frac{1}{R_0}$.

Here i^* is only feasible if $\frac{1}{R_0} < 1$, that is $R_0 > 1$. When $i = 0$ then the disease has died out and there is no more process to investigate. So we are interested in the process when $i \neq 0$. We investigate the value of i as $t \to \infty$ for $R_0 > 1$ and this is referred to as the endemic level.

3.3.1 Stability of equilibrium

The equilibrium states can be characterised as being stable or unstable. To investigate their stability properties we differentiate the function $f(i)$, the right hand side of (3.4), about each equilibrium value. If $\frac{df}{di} > 0$, then the equilibrium solution is unstable. However, if $\frac{df}{di} < 0$, then the equilibrium is stable. So

$$\frac{df}{di} = \beta - 2\beta i - \gamma.$$

At $i = 0$,

$$\frac{df}{di} = \beta - \gamma.$$

Thus $\frac{df}{di}$ is only less than 0 when γ is greater that β, indicating stability if $R_0 < 1$.

At $i = i^* = \left(1 - \frac{1}{R_0}\right)$,

$$\frac{df}{dt} = -\beta + \gamma.$$

Thus i^* is stable if $R_0 > 1$. That is, the endemic equilibrium is stable if it is feasible. However, if $R_0 \leq 1$ then the process 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 0, then it approaches 0.

3.4 Conditioning on non-extinction

Now we study the process $\{I(t)\}$ conditioned on non-extinction. This conditional distribution converges to a stationary conditional distribution called the quasi-stationary distribution. The quasi-stationary distribution mean can be approximated by the deterministic equilibrium. The state probabilities at time t conditioned on non-extinction are given by

$$\begin{aligned} q_i(t) &= P(I(t) = i | I(t) \neq 0) \\ &= \frac{p_i(t)}{1 - p_0(t)}, \end{aligned} \tag{3.6}$$

where $i = 1, 2, \ldots, N$ and $q(t)^T = (q_1(t), q_2(t), \ldots, q_N(t))$. So $q_i(t) = 0$ if $i \notin [1, N]$. Differentiating equation (3.6) and using the equation $\dot{p}_0(t) = \gamma p_1(t)$ (which is obtained by putting $i = 0$ in equation (3.1) and where the dot represents differentiation with respect to time) we have

$$\frac{dq_i}{dt} = \frac{\dot{p}_i(t)}{1 - p_0(t)} + \gamma q_1(t) \frac{p_i(t)}{1 - p_0(t)}. \tag{3.7}$$

The Kolmogorov forward equations (3.1) for the state probabilities $p_i(t)$ can now be used to derive differential equations for the conditional state probabilities $q_i(t)$,

$$\begin{aligned} \frac{dq_i}{dt} &= \beta \frac{i-1}{N}(N - i + 1)q_{i-1}(t) + \gamma(i+1)q_{i+1}(t) \\ &\quad - \left(\beta \frac{i}{N}(N - i) + \gamma i\right) q_i(t) + \gamma q_1 q_i(t), \end{aligned} \tag{3.8}$$

for $i = 1, 2, \ldots N$, where $q_0(t) = q_{N+1}(t) = 0$. Note that setting the time derivatives in equations (3.8) to zero yields equations (2.16).

Denoting by A_Q the intensity matrix A with the first column and row deleted, the above equations can be written as

$$\frac{dq}{dt} = qA_Q + \gamma q_1 q. \tag{3.9}$$

The quasi-stationary distribution $q_i = \lim_{t\to\infty} q_i(t)$ ($q^T = (q_1, q_2, \ldots, q_N)$) is the stationary solution of this system of equations. That is,

$$qA_Q = -\gamma q_1 q. \tag{3.10}$$

This shows that the quasi-stationary distribution q is the left eigenvector of the $N \times N$ matrix A_Q corresponding to the eigenvalue $-\gamma q_1$. This was solved using Matlab for parameter value $N = 200$, $\beta = 0.9$ and $\gamma = 0.4$. It can be seen in Figure 3.1 that the quasi-stationary distribution is approximately normal, for these parameter values.

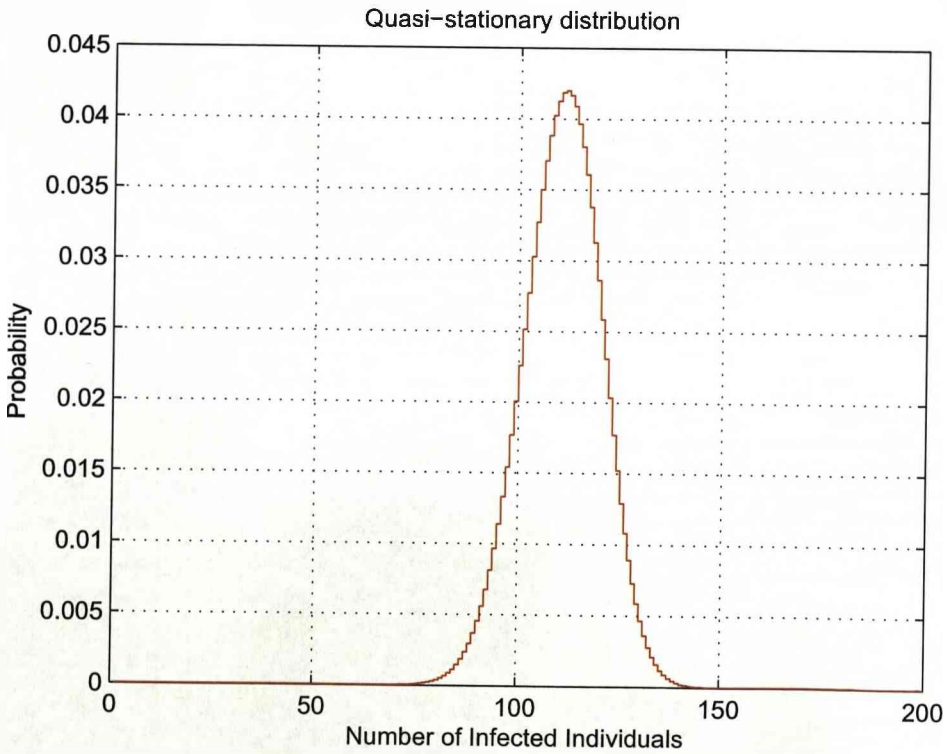

Figure 3.1: The quasi-stationary distribution of the number of infectives. The parameter values are $N = 200$, $\beta = 0.9$ and $\gamma = 0.4$ (so $R_0 = 2.25$)

3.5 Diffusion approximation

In order to study the behaviour of the disease process prior to extinction, it is assumed that the number N in the population is large and an approximating diffusion process is looked for using the result used in chapter 5 of Anderson and Britton (2000). The approximation theory is a form of central limit theorem. This means that we can only hope to approximate the epidemic process when there are many infective individuals, thus excluding the initial and final phases of the epidemic (Anderson and Britton, (2000)). In section 3.3, it was seen that the deterministic model has a unique stable equilibrium at $i^* = 1 - \frac{1}{R_0}$ if $R_0 > 1$. It follows then that if the stochastic process $I(t)$ is started close to the endemic level (Ni^*) it will tend to stay close to Ni^* for a considerable time subject to small random fluctuations. In order to study these fluctuations of the process I, we define the $\sqrt{N}$-scaled centred process

$$\overline{I}(t) = \sqrt{N}\left(\frac{I(t)}{N} - i^*\right), \qquad t \geq 0.$$

Here the focus is on the case where $R_0 > 1$. 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. This process $\overline{I}(t)$, for N large, can be approximated by a diffusion process called an Ornstein-Uhlenbeck process (Ethier and Kurtz, (1986)).

More precisely, if $i(t)$ denotes the trajectory of the deterministic process, and $I(0) = Ni(0)$, then for any $T > 0$ we have $\lim_{N\to\infty} \sup_{0\leq t\leq T} \left|\frac{I(t)}{N} - i(t)\right| = 0$ and the process $\sqrt{N}\left(\frac{I(t)}{N} - i(t)\right)$ converges weakly in the space of all sample paths on any finite time interval $[0, T]$ to a diffusion process (Ethier and Kurtz, (1986)). (See also Mandelbaum and Pats (1994).) In the case $i(0) = i^*$ then $i(t) = i^*$ for all t and the relevant diffusion is an Ornstein-Uhlenbeck process.

The Ornstein-Uhlenbeck process has a local drift constant

$$\begin{aligned} A(i^*) = \frac{\partial}{\partial i}\left(\frac{di}{dt}\right) &= \beta - \gamma - 2\beta i^* \\ &= \beta - \gamma - 2\beta\left(1 - \frac{\gamma}{\beta}\right) \\ &= -(\beta - \gamma), \end{aligned}$$

and its local variance around i^* is, from Table 3.1,

$$\begin{aligned} G(i^*) &= \beta i^*(1-i^*) + \gamma i^* \\ &= \beta\left(1-\frac{\gamma}{\beta}\right)\left(1-\left(1-\frac{\gamma}{\beta}\right)\right) + \gamma\left(1-\frac{\gamma}{\beta}\right) \\ &= \gamma\left(1-\frac{\gamma}{\beta}\right) + \gamma\left(1-\frac{\gamma}{\beta}\right) \\ &= 2\gamma\left(1-\frac{\gamma}{\beta}\right). \end{aligned}$$

The state of this Ornstein-Uhlenbeck process at time t is distributed according to a normal distribution with mean 0 and variance $\Sigma(t)$ satisfying

$$\frac{d\Sigma}{dt} = 2A(i^*)\Sigma + G(i^*)$$

(Gardiner (1985)).

To find the variance of the Ornstein-Uhlenbeck process in equilibrium, the equation above is equated to zero.

$$\begin{aligned} 2A(i^*)\Sigma &= -G(i^*), \\ 2\Sigma(\beta-\gamma) &= 2\gamma\left(1-\frac{\gamma}{\beta}\right), \\ \Sigma(\beta-\gamma) &= \frac{\gamma}{\beta}(\beta-\gamma), \\ \Sigma &= \frac{\gamma}{\beta}. \end{aligned}$$

Therefore the equilibrium distribution of the Ornstein-Uhlenbeck process is normal with mean 0 and variance $\frac{1}{R_0}$. So the quasi-stationary distribution of the disease process $I(t)$ can be approximated by a normal distribution with mean Ni^* and variance $\frac{N}{R_0}$. This can be compared with the quasi-stationary distribution obtained using the truncated transition matrix A_Q. Figure 3.2 shows a comparison of the Ornstein-Uhlenbeck approximation of the quasi-stationary distribution and the quasi-stationary distribution given by the left leading eigenvector of the truncated transition matrix. It shows that with parameter values $N = 200$, $\beta = 0.9$ and $\gamma = 0.4$ the Ornstein-Uhlenbeck approximation gives a very good approximation of the quasi-stationary distribution.

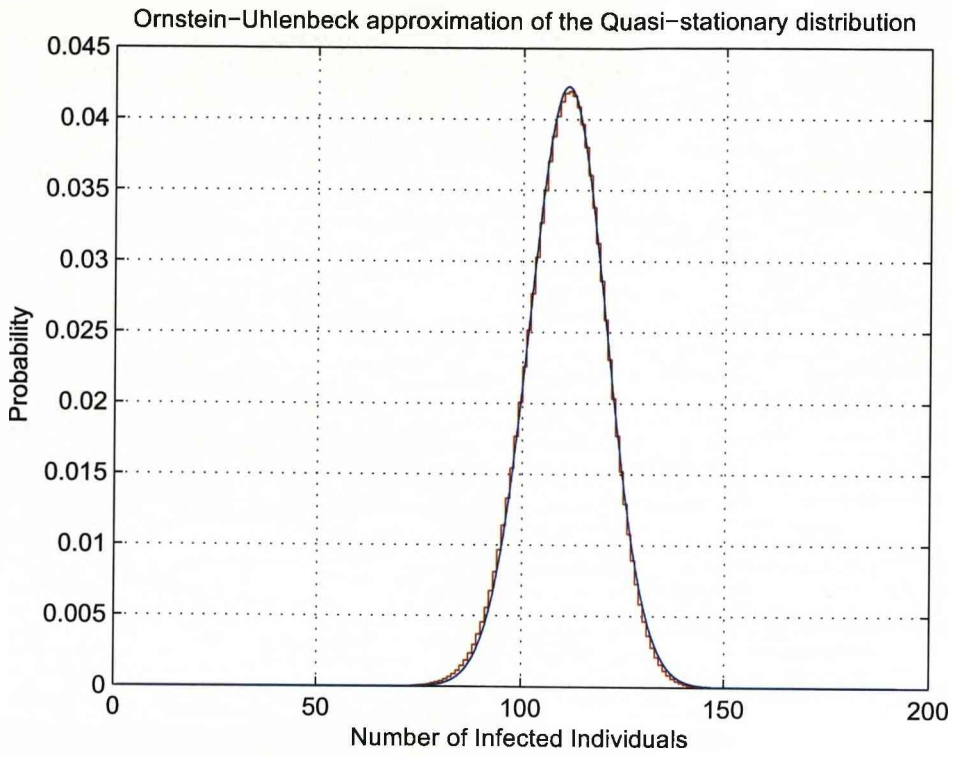

Figure 3.2: The Ornstein-Uhlenbeck approximation of the number of infectives at quasi-stationarity. The red solid line represents the quasi-stationary distribution for the number of infectives calculated from the truncated transition matrix A_Q. The blue line represents the Ornstein-Uhlenbeck approximation of the number of infectives at quasi-stationarity. The parameter values are $N = 200$, $\beta = 0.9$ and $\gamma = 0.4$ (so $R_0 = 2.25$)

3.6 Cumulant equations

Moment closure approximations are used to provide analytic approximations to non-linear stochastic population models (Krishnarajah et al. (2004)). They provide insights into the model behaviour and help validate simulation results. We will use methods from Bailey (1964) and Matis and Kiffe (1996) to derive the cumulant equations for our process similar to the ones given by Nåsell (2003). Equation (3.8) can be used to derive equations for the rate of change of the expected number of infectives $E[I]$ and higher cumulants such as the variance and skewness. Let $M(\theta, t)$ and $K(\theta, t)$ denote the moment and cumulant generating function of $I(t)$ conditioned on non-extinction; that is, for $t \geq 0$,

$$M(\theta, t) = E[e^{I(t)\theta} | I(t) > 0] = \sum_{i=1}^{N} q_i e^{i\theta} \qquad \theta \in \mathbb{R} \tag{3.11}$$

and $K(\theta, t) = \log M(\theta, t)$.

Multiplying equation (3.8) by $e^{i\theta}$ and summing over all values of i and simplifying (see Appendix A) gives

$$\begin{aligned} \sum_{i=1}^{N} \frac{dq_i}{dt} e^{i\theta} &= \sum_{i=2}^{N} \beta \frac{(i-1)}{N} (N-i+1) q_{i-1} e^{i\theta} - \sum_{i=1}^{N-1} \beta \frac{i}{N} (N-i) q_i e^{i\theta} \\ &\quad + \sum_{i=1}^{N-1} \gamma (i+1) q_{i+1} e^{i\theta} - \sum_{i=1}^{N} \gamma i q_i e^{i\theta} + \sum_{i=1}^{N} \gamma q_1 q_i e^{i\theta}. \end{aligned}$$

Simplifying,

$$\begin{aligned} \sum_{i=1}^{N} \frac{dq_i}{dt} e^{i\theta} &= \left(\beta(e^{\theta} - 1)\right) \sum_{i=1}^{N-1} i q_i e^{i\theta} - \frac{\beta}{N} (e^{\theta} - 1) \sum_{i=1}^{N-1} i^2 q_i e^{i\theta} \\ &\quad + \left(\gamma(e^{-\theta} - 1)\right) \sum_{i=2}^{N} i q_i e^{i\theta} - \gamma q_1 e^{\theta} + \sum_{i=1}^{N} \gamma q_1 q_i e^{i\theta}. \end{aligned} \tag{3.12}$$

From equation (3.11) we have

$$\frac{\partial M(\theta, t)}{\partial \theta} = \sum_{i=1}^{N} i q_i e^{i\theta}$$

and

$$\frac{\partial^2 M(\theta, t)}{\partial \theta^2} = \sum_{i=1}^{N} i^2 q_i e^{i\theta} = \sum_{i=1}^{N-1} i^2 q_i e^{i\theta} + N^2 q_N e^{N\theta}.$$

Therefore equation (3.12) becomes

$$\frac{\partial M}{\partial t} = \left[\beta(e^{\theta}-1)+\gamma(e^{-\theta}-1)\right]\frac{\partial M}{\partial \theta} - \frac{\beta}{N}\left(e^{\theta}-1\right)\frac{\partial^2 M}{\partial \theta^2} + \gamma q_1(M(\theta,t)-1).$$

Using the transformation $K(\theta,t) = \log M(\theta,t)$ gives

$$\frac{\partial K}{\partial t} = \left[\beta(e^{\theta}-1)+\gamma(e^{-\theta}-1)\right]\frac{\partial K}{\partial \theta} - \frac{\beta}{N}\left(e^{\theta}-1\right)\left[\frac{\partial^2 K}{\partial \theta^2} + \left(\frac{\partial K}{\partial \theta}\right)^2\right] + \gamma q_1(1-e^{-K}).$$

Using the definition $K(\theta,t) = \sum_{m=1}^{\infty} k_m(t)\frac{\theta^m}{m!}$, where $k_m(t)$ denotes the mth cumulant, and expanding in powers of θ, gives the following differential equations for the first three cumulants (see Appendix A for derivation).

$$\dot{k}_1(t) = \frac{\gamma R_0}{N}\left[\left(N\left(1-\frac{1}{R_0}\right)-k_1(t)\right)k_1(t) - k_2(t)\right] + \gamma q_1 k_1(t), \quad (3.13)$$

$$\begin{aligned}\dot{k}_2(t) = \frac{\gamma R_0}{N}\Bigg[&\left(N\left(1+\frac{1}{R_0}\right)-k_1(t)\right)k_1(t) + \left(2N\left(1-\frac{1}{R_0}\right)-1\right)k_2(t) \\ &-4k_1(t)k_2(t) - 2k_3(t)\Bigg] + \gamma q_1(k_2(t)-(k_1(t))^2),\end{aligned} \quad (3.14)$$

$$\begin{aligned}\dot{k}_3(t) = \frac{\gamma R_0}{N}\Bigg[&\left(N\left(1-\frac{1}{R_0}\right)-k_1(t)\right)k_1(t) - 6k_1(t)k_2(t) - 6k_1(t)k_3(t) - 6(k_2(t))^2 \\ &-\left(3N\left(1+\frac{1}{R_0}\right)-1\right)k_2(t) + 3\left(N\left(1-\frac{1}{R_0}\right)-1\right)k_3(t) - 3k_4(t)\Bigg] \\ &+\gamma q_1(k_1(t) - 3k_1(t)k_2(t) + k_3(t)),\end{aligned} \quad (3.15)$$

These equations can be used to approximate the quasi-stationary distribution. The cumulants of a distribution are closely related to moments; in particular, the first cumulant k_1 is equal to the mean while the second cumulant k_2 is the variance. Here we are interested in the first two cumulants so we find them by setting $\dot{k}_1 = \dot{k}_2 = 0$ and solve equations (3.13, 3.14) for k_1, k_2. However, the equation describing the rate of change of the jth cumulant depends on the $(j+1)$th cumulant. So the above equations (3.13)-(3.15) are not closed because the equation for k_2 contains the unknown k_3, and the equation for k_3 contains the unknown k_4. One way of closing the system of equations is to approximate the cumulant functions of order j with cumulants of higher order set to zero, a technique known as the cumulant truncation procedure (Matis and Kiffe (1996)). However, we will employ an alternative approach used by Nåsell (2003) whereby we assume a particular distribution. This assumption

imposes a functional relationship between the $(j+1)$th cumulant and lower order cumulants. So from the assumptions we will be able to close the equations (3.13, 3.14) by expressing k_3 in terms of k_1 and k_2. Therefore the two equations (3.13, 3.14) now contain three unknowns: k_1, k_2 and q_1. Having assumed a distributional form for $\mathbf{q}$ we can express q_1 in terms of the cumulants of the distribution; however, initially we shall follow the simpler route of Nåsell(2003) in assuming that $q_1 = 0$, which is equivalent to the condition that R_0 be distinctly above 1. For Nåsell these assumptions lead to a variable number of spurious solutions for the critical points of the moment closure equations. The only point that is accepted as stable is the point whose k_1-coordinate (where k_1 is the first cumulant) is asymptotically equal to the deterministic model prediction of the endemic level. From Nåsell (2003) it can be shown that our stochastic model has a quasi-stationary distribution which with $R_0 > 1$ approaches a Normal distribution in its body as $N \to \infty$, with mean $N\frac{(R_0-1)}{R_0}$ and variance $\frac{N}{R_0}$.

From previous studies of the stochastic logistic model, it is seen that in the region where $R_0 > 1$ the quasi-stationary distribution is approximately Normal. Here we will consider approximating the quasi-stationary distribution by the Normal, Poisson, Log-normal, Binomial and Beta-binomial distributions.

Thus the problem of approximating the quasi-stationary distribution $\mathbf{q}$ for R_0 distinctly above 1 amounts to solving for k_1, k_2 the equations

$$\left(N\left(1-\frac{1}{R_0}\right)-k_1\right)k_1 - k_2 = 0, \qquad (3.16)$$

$$\left(N\left(1+\frac{1}{R_0}\right)-k_1\right)k_1 + \left(2N\left(1-\frac{1}{R_0}\right)-1\right)k_2 - 4k_1k_2 - 2k_3 = 0, \qquad (3.17)$$

with k_3 given by an expression in terms of k_1, k_2 determined by our choice of approximating distribution.

3.7 Distributional approximations for $R_0 > 1$

Nåsell (2003) derived approximations for the quasi-stationary distribution using the Normal, Poisson, Log-normal and Binomial distributions. We shall follow a similar approach for Normal, Log-normal and Binomial but a slightly different approach for the Poisson. The Beta-binomial approximation is entirely new.

3.7.1 Normal distribution

Here we assume that the quasi-stationary distribution is approximately Normal, so all cumulants of order higher than 2 are (approximately) zero. Putting $k_3 = 0$ in equations (3.16, 3.17) gives

$$k_1 = 0 \qquad \text{or} \qquad k_1 = \frac{3N\left(1-\frac{1}{R_0}\right)}{4} \pm \frac{1}{4}N\left(1-\frac{1}{R_0}\right)\sqrt{1-\frac{8\frac{N}{R_0}}{\left(N\left(1-\frac{1}{R_0}\right)\right)^2}}.$$

$N\left(1-\frac{1}{R_0}\right)$ and $\frac{N}{R_0}$ are $O(N)$. Therefore $\frac{N}{R_0}/\left(N\left(1-\frac{1}{R_0}\right)\right)^2$ is of order $1/N$. So as $N \to \infty$ the one term expansion of the square root is one. Therefore to first order in N, $k_1 = N\left(1-\frac{1}{R_0}\right)$ or $k_1 = N\left(1-\frac{1}{R_0}\right)/2$ or $k_1 = 0$. Two of these values of k_1 are spurious solutions and should be rejected. Taking the assumption of normality into consideration only $k_1 = N\left(1-\frac{1}{R_0}\right)$ is consistent with it. Taking $k_1 = N\left(1-\frac{1}{R_0}\right)/2$, for instance, the ratio of the mean to the standard deviation is equal to 1, which is not large. For the normal approximation to be valid, we require that the ratio of the mean to the standard deviation be greater than or equal to 3. This is because a normally distributed random variable takes values larger than 3 standard deviations below its mean with high probability, so that provided the ratio of mean to standard deviation is at least 3 then the normal approximation assigns high probability to values larger than zero. Note that the true quasi-stationary distribution $\mathbf{q}$ assigns zero probability to negative values. Any normal distribution with mean $k_1 = 0$ assigns probability 0.5 to negative values, so cannot provide an acceptable approximation. So $k_1 = 0$ is also rejected. Taking two terms in the approximation of the square root as $N \to \infty$ leads to

$$k_1 = N\left(1-\frac{1}{R_0}\right) - \frac{1}{R_0-1} + O\left(\frac{1}{N}\right), \qquad k_2 = \frac{N}{R_0} - \left(\frac{1}{R_0-1}\right)^2 + O\left(\frac{1}{N}\right).$$

From Figure 3.3 it can be seen that the Normal distribution is a very good approximation of the quasi-stationary distribution of our model, for $N = 200$ and $R_0 = 2.25$.

3.7.2 Poisson distribution

Here the assumption is that the quasi-stationary distribution is approximately Poisson. For the Poisson distribution the first two cumulants are equal so we can use

equation (3.16) alone. This gives

$$k_1 = 0 \qquad \text{or} \qquad k_1 = N\left(1 - \frac{1}{R_0}\right) - 1.$$

By the same argument as in the normal case above we have that $k_1 = 0$ is a spurious solution and so we have

$$k_1 \;=\; N\left(1 - \frac{1}{R_0}\right) - 1.$$

This differs slightly from the corresponding result of Nåsell(2003), where both of equations (3.16, 3.17) were used together with the relationship $k_3 = k_1$.

From Figure 3.3 it can be seen that the Poisson is not a good approximation of our model for these parameter values. Although it gives a very good approximation of the first cumulant, there is nothing to regulate the spread. Therefore it is not good to fit a Poisson distribution to our model. It is important to note similar results were obtained when Nåsell's approximation was fitted.

3.7.3 Log-normal distribution

With the assumption that the quasi-stationary distribution is approximately Log-normal, then the third cumulant k_3 can be expressed in terms of the first two,

$$k_3 = 3\frac{k_2^2}{k_1} + \frac{k_2^3}{k_1^3}. \qquad \text{(Nåsell (2003))}$$

Substituting this into equation (3.17), solving equations (3.16, 3.17) for k_1, k_2 and discarding the spurious solution at $k_1 = 0$ gives

$$k_1 \;=\; \frac{N^2\left(R_0 - 1\right)^3}{R_0\left(N\left(R_0 - 1\right)^2 + R_0\right)}$$

$$\text{and} \quad k_2 = \frac{\frac{N}{R_0}\left(N\left(1 - \frac{1}{R_0}\right)\right)^4}{\left(\frac{N}{R_0} + \left(N\left(1 - \frac{1}{R_0}\right)\right)^2\right)^2}.$$

This result can be further simplified in the form $k_1 = aN + b + O(1/N)$ and allowing $N \to \infty$. This yields

$$k_1 = N\left(1 - \frac{1}{R_0}\right) - \frac{1}{1 - R_0} + O\left(\frac{1}{N}\right)$$

and

$$k_2 = \frac{N}{R_0} - \frac{2}{(1-R_0)^2} + O\left(\frac{1}{N}\right)$$

Looking at Figure 3.3, it can be seen that the Log-normal distribution is a good approximation of the quasi-stationary distribution for these parameter values.

3.7.4 Binomial distribution

Here the assumption is that the quasi-stationary distribution is approximately Binomial (Bin(n,p)). Here we will allow n to vary. So we will approximate both n and p. The alternative is to set $n = N - 1$ and approximate the quasi-stationary distribution by Bin $(N-1, p) + 1$ with only p to be estimated. The advantage is that there is only one parameter to approximate and therefore less mathematical complication. However, this may affect the shape of the distribution since n and p determine where the peak of the distribution lies. Therefore n and p will be approximated. With the assumption of the binomial distribution the third cumulant k_3 can be expressed in terms of the first two,

$$k_3 = \frac{2k_2^2}{k_1} - k_2. \qquad \text{(Nåsell (2003))}$$

Substituting this into equation (3.17) and solving equations (3.16, 3.17) for k_1, k_2 and discarding the spurious solution $k_1 = 0$ gives

$$k_1 = N\left(1 - \frac{1}{R_0}\right) - \frac{N}{R_0\left(N\left(1 - \frac{1}{R_0}\right) - 1\right)}$$

and

$$k_2 = \frac{N^2(N(R_0-1)^2 - 2R0 + 1)}{R_0(NR_0 - N - 1)^2}.$$

These results can be further simplified to:

$$k_1 = N\left(1 - \frac{1}{R_0}\right) - \frac{1}{R_0 - 1} + O\left(\frac{1}{N}\right)$$

and

$$k_2 = \frac{N}{R_0} - \frac{1}{R_0(R_0-1)^2} + O\left(\frac{1}{N}\right).$$

From Figure 3.3 it can be seen that the Binomial is a very good approximation of the quasi-stationary distribution for these parameter values.

3.7.5 Beta-binomial distribution

Here the assumption is that the quasi-stationary distribution is approximately Beta-binomial. A variable with Beta-binomial distribution is distributed as a Binomial distribution with parameters N and p, where p is distributed with a Beta distribution with parameters a and b. The probability mass function for N trials is,

$$P(x) = \frac{B(x+a, N-x+b)\begin{pmatrix} N \\ x \end{pmatrix}}{B(a,b)}$$

where $B(a,b)$ is a beta function and $\begin{pmatrix} N \\ x \end{pmatrix}$ is a binomial coefficient. Here we will assume that N is constant and equal to the population size. The first three raw moments of the Beta-binomial in terms of its parameters (a and b) are

$$\mu_1' = E[x] = \frac{Na}{a+b},$$

$$\mu_2' = E[x^2] = \frac{Na(Na+N+b)}{(a+b)(a+b+1)},$$

$$\mu_3' = E[x^3] = \frac{Na[N^2(1+a)(2+a) + 3N(1+a)b + b(a+b)}{(a+b)(a+b+1)(2+a+b)}$$

(http://mathworld.wolfram.com/BetaBinomialDistribution.html).

The cumulants are:

$$k_1 = \mu_1',$$

$$k_2 = \frac{Nab(N+a+b)}{(a+b)^2(a+b+1)},$$

$$k_3 = \mu_3' - k_1^3 - 3k_1k_2. \tag{3.18}$$

We now need to express the third cumulant in terms of the first and second cumulant. So

$$\begin{aligned} \frac{k_2}{k_1^2} &= \frac{b(N+a+b)}{Na(a+b+1)} \\ &= \frac{\frac{b}{a+b}\left(\frac{N}{a+b}+1\right)}{N\frac{a}{a+b}(1+\frac{1}{a+b})} \\ &= \frac{\left(1-\frac{k_1}{N}\right)\left(\frac{k_1}{a}+1\right)}{k_1\left(1+\frac{k_1}{Na}\right)}. \end{aligned}$$

Therefore

$$a = \frac{(N-k_1)k_1^2 - k_1k_2}{N(k_2-k_1)+k_1^2}. \tag{3.19}$$

Substituting this into

$$k_1 = \frac{Na}{a+b}$$

and simplifying gives

$$b = \frac{((N-k_1)k_1 - k - 2)(N-k_1)}{N(k_2-k_1)+k_1^2}. \tag{3.20}$$

From (3.15)

$$k_3 = \frac{Na[N^2(1+a)(2+a) + 3N(1+a)b + b(a+b)}{(a+b)(a+b+1)(2+a+b)} - k_1^3 - 3k_1k_2. \tag{3.21}$$

Substituting equation (3.19) and equation (3.20) into equation (3.21) we have

$$k_3 = \frac{k_2(2k_1^3 - 3k_1^2N + k_1N^2 + 4k_1k_2N - 2k_1k_2 - 2N^2k_2 + Nk_2)}{k_1N - k_1N^2 - Nk_2 + 2k_1N - 2k_1^2}. \tag{3.22}$$

Substituting this into equation (3.17) and solving equations (3.16, 3.17) for k_1, k_2 and discarding the spurious solution $k_1 = 0$ gives

$$k_1 = \frac{N\left(N^2 - 3NR_0^2 - 2N^2R_0 + N^2R_0^2 + 2R_0^2 + 2NR_0\right)}{R_0\left(2R_0 - 3NR_0 + N^2R_0 - N^2\right)}.$$

As with the Log-normal and the binomial distribution, the second result can be expressed as $aN + b + O(1/N)$. So

$$k_1 = N\left(1 - \frac{1}{R_0}\right) - \frac{1}{R_0 - 1} + O\left(\frac{1}{N}\right)$$

and

$$k_2 = \frac{N}{R_0} + \frac{R_0^2 - 2}{R_0(R_0-1)^2} + O\left(\frac{1}{N}\right).$$

Taking the first two terms for each cumulant k_1, k_2 gives

$$a \simeq \frac{N(N(R_0-1)^2 - R_0)}{R_0(N-R_0)}, \qquad b \simeq \frac{N(N(R_0-1) - R_0)}{R_0(N-R_0)}.$$

From Figure 3.3 it can be seen that the Beta-binomial is a very good approximation of the quasi-stationary distribution of our model, for these parameter values.

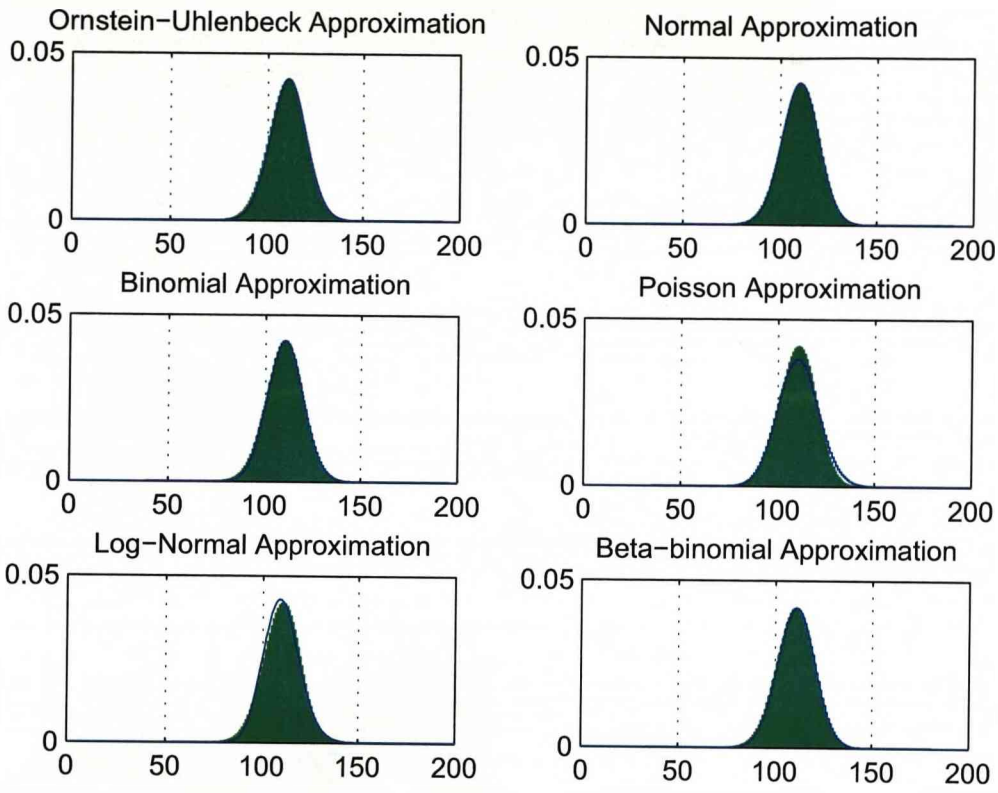

Figure 3.3: Different distributional approximations of the quasi-stationary distribution using moment closure. The green represents the quasi-stationary distribution and the blue solid line represents the fitted approximating distribution. The parameter values are $N = 200$, $\beta = 0.9$ and $\gamma = 0.4$ (so $R_0 = 2.25$).

3.8 Total variation distance

In the previous section we compared the different approximations of the quasi-stationary distribution for one fixed set of parameter values. We are looking for the best approximation for the quasi-stationary distribution. We have already seen that although the means of all the approximating distributions give good approximations of the mean of the quasi-stationary distribution, not all distributions fit well. In this section, we will compare the approximating distributions over a range of parameter values using total variation distance. In classical analysis, the variation of a real-valued function f on the bounded interval $[a,b]$ is

$$\sup_p \sum |f(x_{i+1}) - f(x_i)|,$$

where the supremum runs over all partitions $p = \{x_1, \ldots, x_n\}$ of the interval $[a,b]$. In effect, the total variation is the vertical component of the arc length of the graph of f. The function f is said to be of bounded variation precisely if the total variation of f is finite. In probability theory, the total variation distance between two probability measures P and Q on the sigma-algebra F is

$$\delta(P,Q) = \sup\{|P(A) - Q(A)| : A \in F\}.$$

Informally, this is the largest possible difference between the probabilities (in our case the quasi-stationary distribution and each of the approximating distributions) that the two probability distributions can assign to the same event. For a finite space we can write

$$\delta(P,Q) = \frac{1}{2}\sum_x |P(x) - Q(x)|.$$

Working out the total variation distance for each of the approximating distributions using different parameter values, results are plotted in Figure 3.4. From Figure 3.4 it can be seen that the Beta-binomial distribution (green solid line), the normal distribution (the red broken line), the binomial distribution (blue asterisks), have the lowest total variation distance when $R_0 > 1$ followed by the Log-normal distribution (red solid line). The Poisson has the largest total variation distance. This confirms our earlier conclusion that the Beta-binomial, Normal, Binomial and the Log-normal distributions give better approximation to the quasi-stationary distribution than

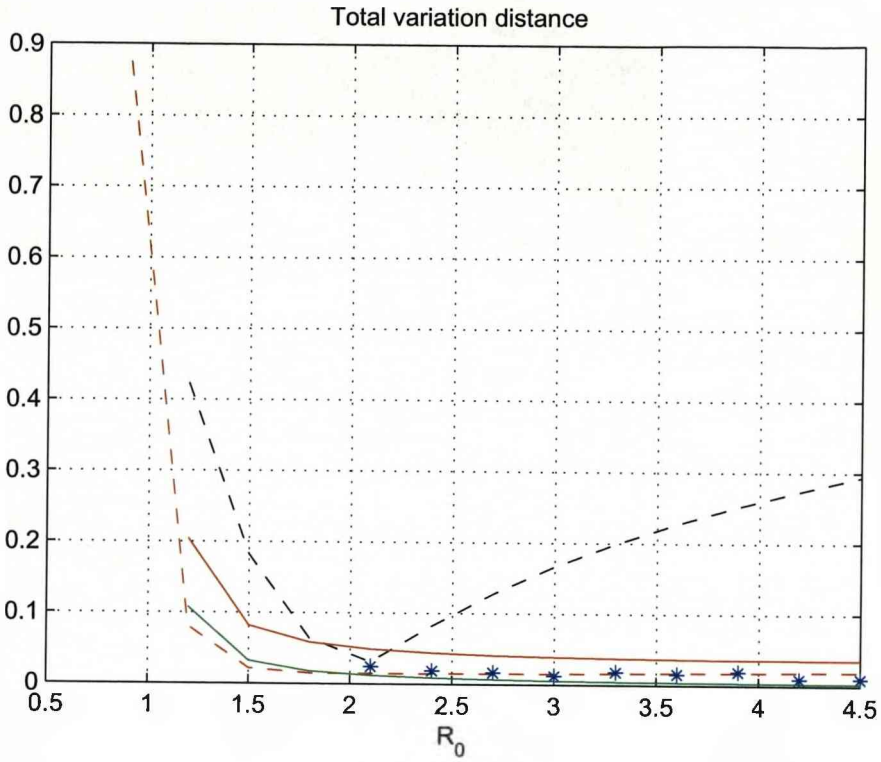

Figure 3.4: The total variation distance is calculated for $N = 200$ and different values of R_0 (R_0 from 0.9 to 4.5 in step size of 0.3). The green solid line represents the total variation distance of the Beta-binomial distribution from the quasi-stationary distribution. The red broken line represents the total variation distance of the normal distribution from the quasi-stationary distribution, the red solid line the the Log-normal distribution from the quasi-stationary distribution. The blue asterisks represent the total variation distance of the binomial distribution from the quasi-stationary distribution. The black broken line represents the total variation distance of the Poisson distribution from the quasi-stationary distribution. This graph shows the behaviour of each approximation as R_0 grows from 0.9 to 4.5. The results agree with the conclusions drawn earlier concerning goodness of each approximating distribution.

the Poisson distribution. The total variation distance for the Normal distribution shows that the Normal distribution is a bad approximation for the quasi-stationary distribution for $R_0 < 1$. Its total variation distance falls rapidly as R_0 approaches 1. However, as R_0 grows very large, the total variation distance grows slowly. This is due to the fact that the quasi-stationary distribution is skewed to the left (number of infected individuals is close to the boundary at N) as R_0 grows very large.

It can also be seen in Figure 3.4 that the total variation distance for the Poisson distribution is only low when R_0 is about 2. It is very high initially (when R_0 is less than 1) then drops as R_0 approaches 2. It then rises as R_0 moves further away from 2. This is due to the fact that at $R_0 = 2$, the mean of the quasi-stationary distribution is approximately equal to its variance, as we can see from the diffusion approximation formulae for the mean, $N\left(1 - \frac{1}{R_0}\right)$, and variance, $\frac{N}{R_0}$.

Looking back at the Ornstein-Uhlenbeck approximation it can be seen that the mean and variance of the number of susceptibles at quasi-stationarity are the same and equal to N/R_0. This is a property of the Poisson distribution. So we fit a Poisson distribution to the quasi-stationary distribution of the number of susceptibles rather than the number of infectives from the truncated transition matrix. It can been seen from Figure 3.5 that the Poisson distribution gives a very good fit. Therefore it will be better to use the Poisson distribution to approximate the quasi-stationary distribution for the number of susceptibles than to use it to approximate the quasi-stationary distribution for the number of infectives. Figure 3.6, which is the total variation distance between the fitted Poisson distribution and the quasi-stationary distribution for the number of susceptibles, shows that the Poisson distribution doesn't give a good approximation of the quasi-stationary distribution when R_0 is close to 1 but a very good approximation when R_0 grows larger than 1. Its total variation distance falls rapidly as R_0 moves towards 2. However, as R_0 grows very large, the total variation distance grows slowly. This is due to the fact that the quasi-stationary distribution for the number of susceptibles is skewed to the right (number of susceptible individuals is close to the boundary at 0) as R_0 grows very large.

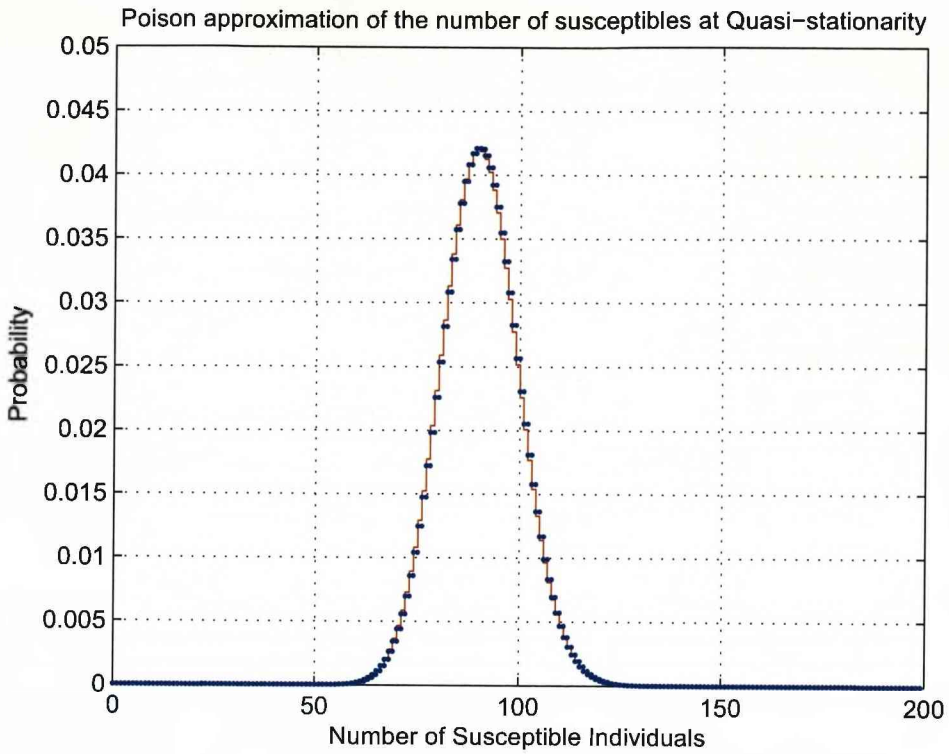

Figure 3.5: The Poisson distribution approximation of the quasi-stationary distribution for the number of susceptibles. The red solid line represents the quasi-stationary distribution for the number of susceptibles calculated from the truncated transition matrix. The blue dots represent the Poisson approximation of the number of susceptibles at quasi-stationarity. The parameter values are $N = 200$, $\beta = 0.9$ and $\gamma = 0.4$ (so $R_0 = 2.25$).

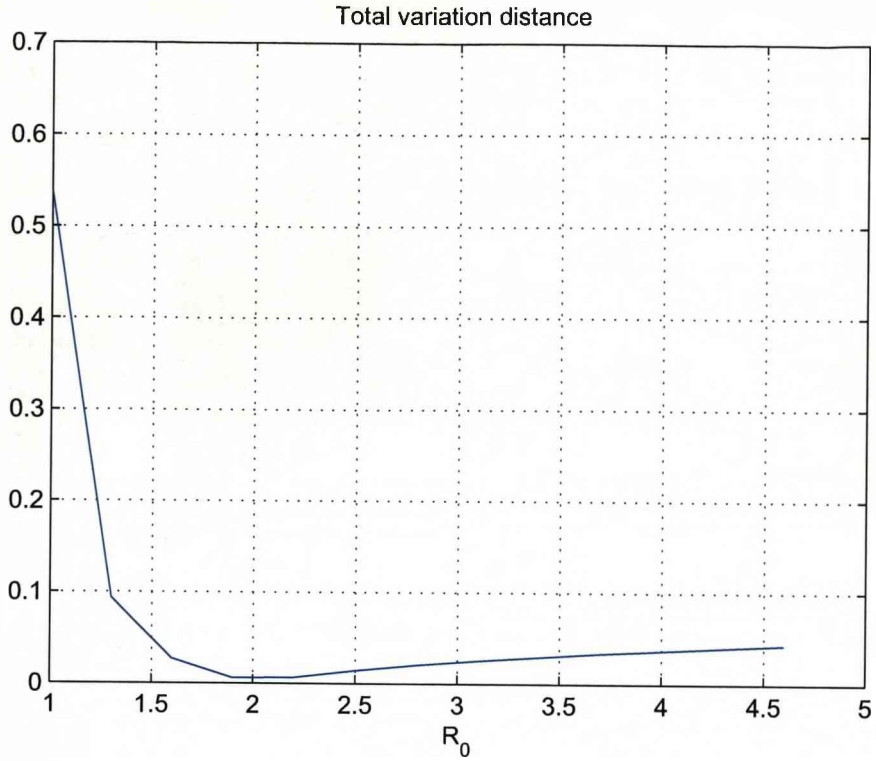

Figure 3.6: The total variation distance between the Poisson approximation of the quasi-stationary distribution for the number of susceptibles and the true quasi-stationary distribution for the number of susceptibles. The total variation distance is calculated for $N = 200$ and different values of R_0 (R_0 from 1 to 4.5 in step size of 0.3).

3.8.1 Nåsell's (1996 and 1999) approximations of the quasi-stationary distribution

Nåsell (1996) derived an approximation for the quasi-stationary distribution q. He gave the following approximation of the cumulative distribution function of the quasi-stationary distribution

$$F(K) = \frac{\phi(u_0(K)) - \phi(v_0(1))}{1 - \phi(v_0(1))},$$

where the functions u and v are defined by

$$\begin{aligned} u_0(j) &= y(j + H(z(j))) = \frac{j + H(z(j)) - \mu}{\sigma}, \\ v_0(j) &= y(j + H(z(j)) - 1 = y(j - H(-z(j))), \end{aligned}$$

where

$$y(j) = \frac{j-\mu}{\sigma}, \qquad z(j) = \frac{y(j)}{\sigma},$$

$$\mu = \frac{N(R_0-1)}{R_0} \qquad \text{and} \qquad \sigma = \sqrt{\frac{N}{R_0}} \qquad \text{for} \qquad R_0 > 1$$

and

$$\mu = N \log R_0 \qquad \text{and} \qquad \sigma = \sqrt{N} \qquad \text{for} \qquad R_0 < 1$$

and where the function H is defined by

$$H(z) = \begin{cases} \frac{1}{z}\log\frac{e^z-1}{z}, & \text{for} \quad z \neq 0, \\ \frac{1}{2} & \text{for} \quad z = 0. \end{cases}$$

Nåsell (1999) gives the following approximation for the quasi-stationary distribution q.

$$q_j = \begin{cases} \frac{1}{\sigma}\varphi(y(j)) & \text{for} \quad R_0 > 1, \\ (1-R_0)R_0^{j-1} & \text{for} \quad R_0 < 1, \end{cases}$$

where $\varphi(x) = exp(-x^2/2)/\sqrt{2\pi}$ denotes the normal density function. μ, σ and $y(j)$ are as defined above.

We will now analyse the total variation distance between these approximations of the quasi-stationary distribution and the quasi-stationary distribution calculated using the truncated transition matrix. From Figure 3.7 it can be seen that these approximations give very good approximations of the the quasi-stationary distribution and they get better as R_0 grows bigger. We now compare Nåsell's (1996 and 1999) approximations with the other approximations (Normal, Binomial, Log-normal and Beta-binomial) but this time we allow N to vary.

3.8.2 Comparison of all the above approximating distribution with varying N

Now we allow N to vary and fix R_0 ($R_0 = 3$) and work out the total variation distances. Figure 3.8 shows the total variation distance between each approximation and the true quasi-stationary distribution as N grows from 100 to 400 with step size of 20 and R_0 fixed at 3. It can be seen in Figure 3.8 that the Beta-binomial gives the best approximation of the quasi-stationary distribution q for these parameter values. This is followed by the Normal distribution, Nåsell (1996 and 1999) approximations and the Binomial distribution. The total variation distance for the

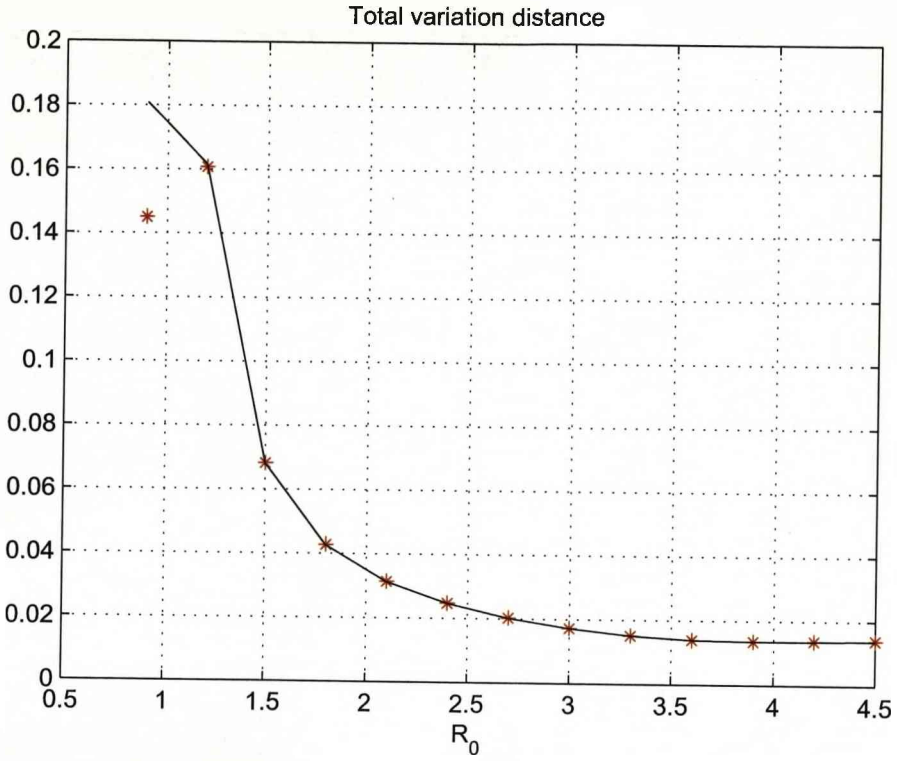

Figure 3.7: The total variation distance is calculated for $N = 200$ and different values of R_0 (R_0 from 0.9 to 4.5 in step size of 0.3). The black solid line represents the total variation distance of Nåsell (1996) approximation from the quasi-stationary distribution. The red asterisks represent the total variation distance of Nåsell (1999) approximation from the quasi-stationary distribution. This graph shows the behaviour of each approximation as R_0 grows from 0.9 to 4.

Binomial distribution goes up and down. This is due to the error caused by rounding n to the nearest whole number. In the Binomial we approximate p and n with n rounded to the nearest whole number. The Log-normal distribution also give good approximations but the Poisson distribution is not good.

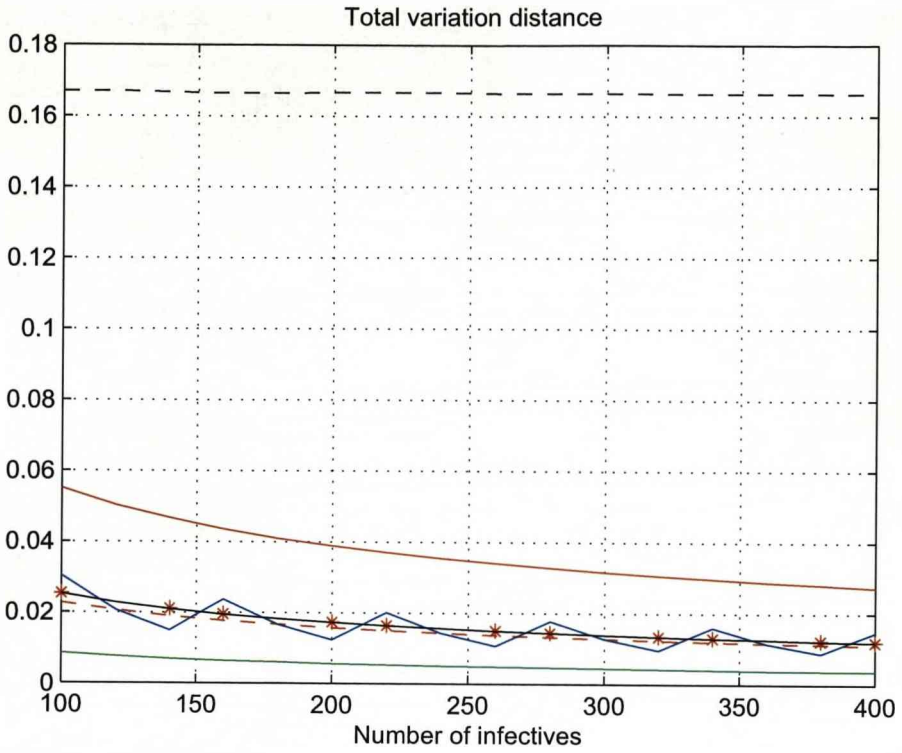

Figure 3.8: The total variation distance is calculated for $R_0 = 3$ and different values of N (N grows from 100 to 400 with step size of 20). The green solid line represents the total variation distance of the Beta-binomial distribution from the quasi-stationary distribution. The red broken line represents the total variation distance of the normal distribution from the quasi-stationary distribution, the red solid line the Log-normal distribution from the quasi-stationary distribution. The blue line represents the total variation distance of the binomial distribution from the quasi-stationary distribution. The red asterisks represent the total variation distance of Nåsell (1996) approximation from the quasi-stationary distribution. The black line represents the total variation distance of Nåsell (1999) approximation from the quasi-stationary distribution. The black broken line represents the total variation distance of the Poisson distribution from the quasi-stationary distribution.

3.9 Moment closure for $q_1 \neq 0$

With $q_1 \neq 0$, that is $R_0 < 1$, we have one more unknown to deal with in equations (3.13)-(3.15). So we have more unknowns than equations. To solve this problem we substitute the parameters for each approximating distribution into the equations. Here we will approximate the quasi-stationary distribution by the Poisson and the geometric distribution.

3.9.1 Poisson distribution

Suppose the quasi-stationary distribution is $I \sim \text{Poisson}(\lambda) + 1$. Then

$$P(I = i) = \frac{e^{-\lambda}\lambda^{i-1}}{(i-1)!},$$

so $\quad q_1 = P(I = 1) = e^{-\lambda}, \quad k_1 = \lambda + 1 \quad$ and $\quad k_2 = \lambda.$

Take first the equation (3.13), giving

$$\frac{\gamma R_0}{N}\left[\left(\left(\frac{R_0 - 1}{R_0}\right)N - k_1\right)k_1 - k_2\right] + \gamma q_1 k_1 = 0. \tag{3.23}$$

Substituting for k_1, k_2 and q_1 in terms of λ into equation (3.23) we have

$$\frac{\gamma R_0}{N}\left[\left(\frac{R_0 - 1}{R_0}\right)N(\lambda + 1) - (\lambda + 1)^2 - \lambda\right] + \gamma(\lambda + 1)e^{-\lambda} = 0$$

$$\Rightarrow \quad (R_0 - 1)(\lambda + 1) + (\lambda + 1)e^{-\lambda} = \frac{R_0}{N}\left((\lambda + 1)^2 + \lambda\right)$$

$$\Rightarrow \quad (R_0 - 1) + e^{-\lambda} = \frac{R_0}{N}\left(\frac{\lambda}{\lambda + 1} + \lambda + 1\right).$$

As $N \to \infty$, below threshold we expect $\lambda = O(1)$, so the right hand side is $O\left(\frac{1}{N}\right)$, so in the limit,

$$\begin{aligned}(R_0 - 1) + e^{-\lambda} &= 0,\\ e^{-\lambda} &= 1 - R_0,\\ \lambda &= -\ln(1 - R_0)\end{aligned}$$

So below threshold ($R_0 < 1$), we approximate the quasi-stationary distribution by $1 + \text{Poisson}\left(\ln\left(\frac{1}{1-R_0}\right)\right)$.

3.9.2 Geometric distribution

Suppose the quasi-stationary distribution is $I \sim \text{Geometric}(p)$. That is,

$$P(I = i) = (1-p)^{i-1}p \qquad i = 1, 2, \ldots$$

Then $q_1 = P(I = 1) = p, \qquad k_1 = \frac{1}{p}, \qquad$ and $\qquad k_2 = \frac{1-p}{p^2}$.
Now substituting the above into equation (3.23) gives

$$\frac{\gamma R_0}{N}\left[\left(\left(\frac{R_0 - 1}{R_0}\right)N - \frac{1}{p}\right)\frac{1}{p} - \frac{1-p}{p^2}\right] + \gamma p\frac{1}{p} = 0,$$

$$\left(\left(\frac{R_0 - 1}{R_0}\right)N - \frac{1}{p}\right)\frac{1}{p} - \frac{1-p}{p^2} + \frac{N}{R_0} = 0.$$

Multiplying through by p^2,

$$p\left(\frac{R_0 - 1}{R_0}\right)N - 1 - 1 + p + \frac{Np^2}{R_0} = 0,$$

$$(R_0 - 1)p + p^2 - \frac{R_0}{N} - \frac{R_0(1-p)}{N} = 0,$$

$$p^2 + \left(R_0 - 1 + \frac{R_0}{N}\right)p - \frac{2R_0}{N} = 0,$$

$$\begin{aligned} p &= \frac{-\left(R_0 - 1 + \frac{R_0}{N}\right) \pm \sqrt{\left(R_0 - 1 + \frac{R_0}{N}\right)^2 + \frac{8R_0}{N}}}{2} \\ &= \frac{1}{2}\left(1 - R_0 - \frac{R_0}{N}\right) \pm \frac{1}{2}\left(R_0 - 1 + \frac{R_0}{N}\right)\sqrt{1 + \frac{8R_0}{N\left(R_0 - 1 + \frac{R_0}{N}\right)^2}}. \end{aligned}$$

Taking two terms approximation of the square root as $N \to \infty$ leads to

$$\begin{aligned} p &= \frac{1}{2}\left(1 - R_0 - \frac{R_0}{N}\right) \pm \frac{1}{2}\left(R_0 - 1 + \frac{R_0}{N}\right)\left(1 + \frac{4R_0}{N\left(R_0 - 1 + \frac{R_0}{N}\right)^2}\right), \\ p &= \frac{1}{2}\left(1 - R_0 - \frac{R_0}{N}\right) \pm \left[\frac{1}{2}\left(R_0 - 1 + \frac{R_0}{N}\right) + \frac{2R_0}{N\left(R_0 - 1 + \frac{R_0}{N}\right)}\right]. \end{aligned}$$

So below threshold ($R_0 < 1$), we approximate the quasi-stationary distribution by a Geometric $\left(1 - R_0 - \frac{R_0}{N} - \frac{2R_0}{N\left(R_0 - 1 + \frac{R_0}{N}\right)}\right)$.

3.9.3 Numerical analysis

Figures 3.9 and 3.10 show the Geometric and Poisson approximations compared with the true quasi-stationary distribution for $R_0 = 0.43$ and $R_0 = 0.71$ respectively. Several other values of R_0 (less than 1) were also tried. These figures are included to demonstrate that the Geometric distribution is a very good approximation for the quasi-stationary distribution for $R_0 < 1$. The Poisson on the other hand, is only a good approximation for R_0 values less than 0.45.

For a better understanding of the performance of these approximating distributions, we worked out the total variation distances and results are plotted in Figure 3.11. It can be seen that total variation distance for the Poisson approximations grows with R_0 while for the Geometric approximation is approximately 0 for values of R_0 less than 0.6 and then grows as R_0 tends to 1, especially for $0.9 < R_0 < 1$. Nåsell's (1996 and 1999) approximations seem to do very well for R_0 values less than 0.8. So the Geometric approximation appears to be the best approximation of the quasi-stationary distribution for $R_0 < 1$.

3.10 Conclusion

In this chapter we analysed the SIS model with a constant population size. We have shown using the Ornstein-Uhlenbeck diffusion approximation that the quasi-stationary distribution can be approximated by a Normal distribution when $R_0 > 1$ and N is sufficiently large. This result was confirmed by the results of the moment closure applied on the cumulant equations for q_1 approximately zero. This was studied by Nåsell (2003). For Nåsell the cumulant approximations derived from the moment closure method are indeed asymptotic approximations of the quasi-stationary distribution cumulants. He showed using the moment closure method (which was presented here) that the quasi-stationary distribution can be approximated by the Normal, Binomial, Poisson and Log-normal distributions. Here we extended that to the Beta-binomial. Nåsell mainly focused on deriving approximations for the first few cumulants of the quasi-stationary distribution without commenting on how well the various approximating distributions perform. Here we commented on how well the various approximations performed, based mainly upon

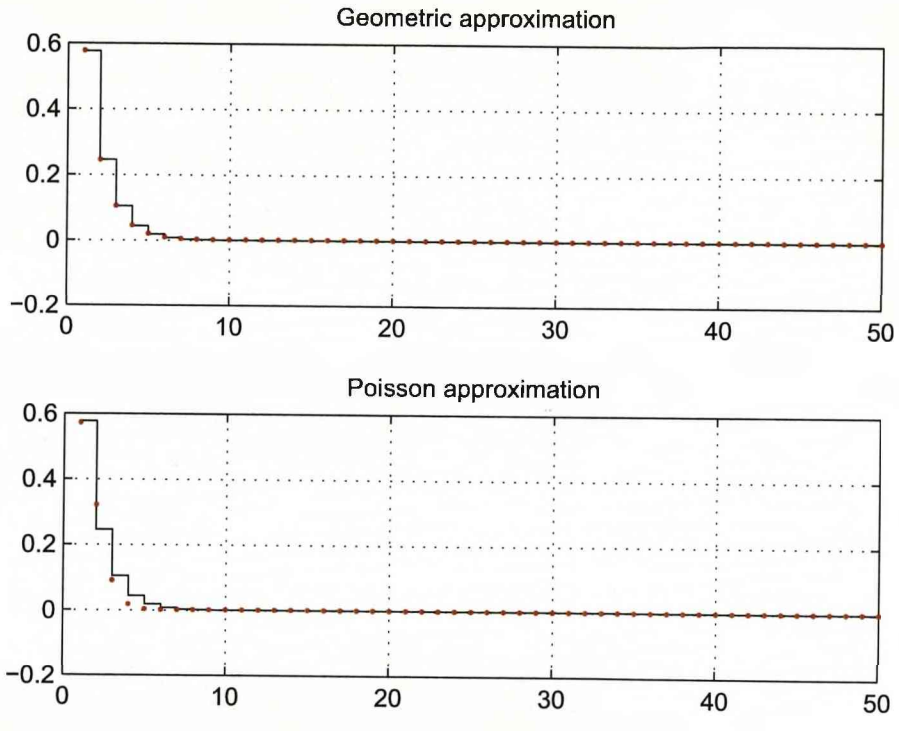

Figure 3.9: Geometric and Poisson approximations of the quasi-stationary distribution using moment closure. The black solid line represents the quasi-stationary distribution and the red dots represent the fitted approximating distribution. The parameter values are $N = 200$, $\beta = 0.7$ and $\gamma = 0.3$ (so $R_0 = 0.43$).

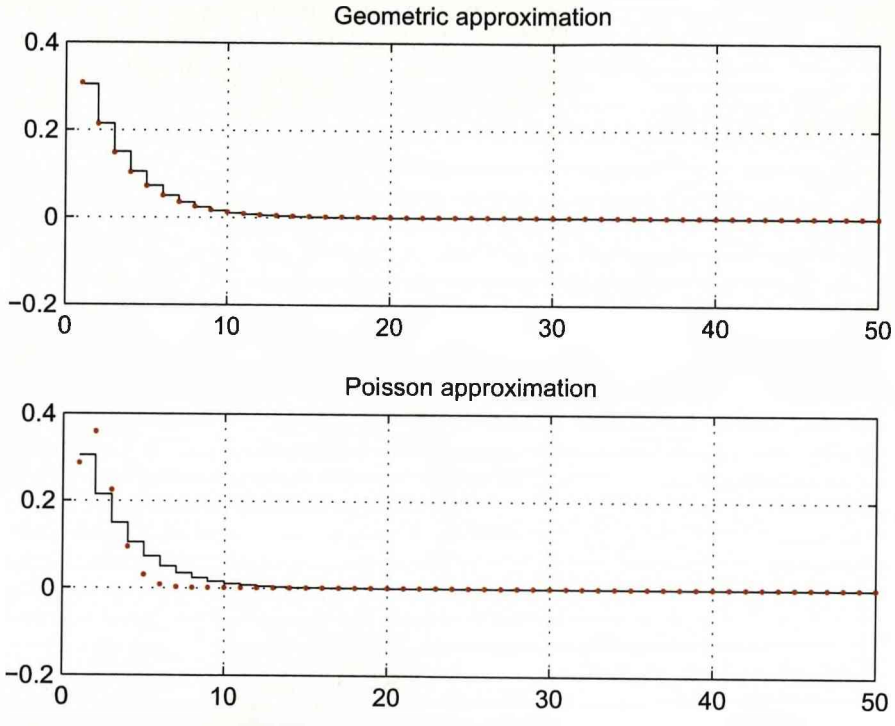

Figure 3.10: Geometric and Poisson approximations of the quasi-stationary distribution using moment closure. The black solid line represents the quasi-stationary distribution and the red dots represent the fitted approximating distribution. The parameter values are $N = 200$, $\beta = 0.7$ and $\gamma = 0.5$ (so $R_0 = 0.71$).

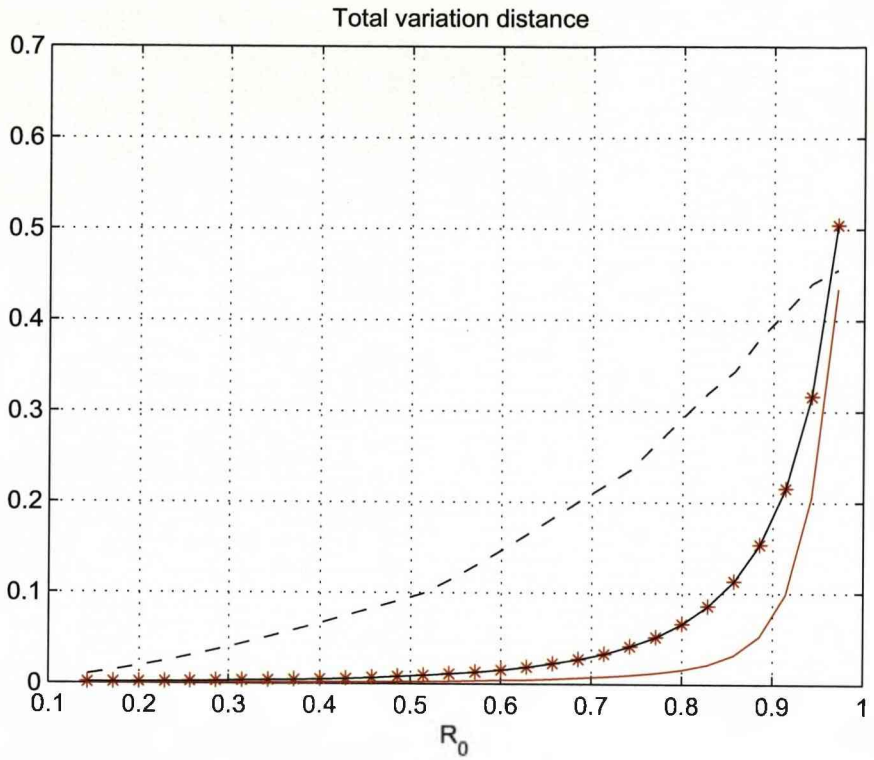

Figure 3.11: The total variation distance is calculated for $N = 200$ and different values of R_0 (R_0 from 0.1 to 1 in step size of 0.05). The red solid line represents the total variation distance of Geometric approximation from the quasi-stationary distribution. The black broken line represents the total variation distance of Poisson approximation from the quasi-stationary distribution. The black solid line represents the total variation distance of Nåsell's (1996) approximation from the quasi-stationary distribution.The asterisks represents the total variation distance of Nåsells' (1999) approximation from the quasi-stationary distribution.This graph shows the behaviour of each approximation as R_0 grows from 0.1 to 1

visual inspection of plots showing both the true quasi-stationary distribution and the approximating distribution under consideration, for a few particular values of the parameters N and R_0. We saw that although all the approximating distributions give very good approximations of the expected number of infected individuals at quasi-stationarity, fitting these distributions on the quasi-stationary distribution showed that the Poisson distribution doesn't give a good fit as illustrated in Figure 3.3. We also attempted to measure goodness of fit in order to decide on which approximating distribution fits best for any given values of (N, R_0) for $R_0 > 1$. We used total variation distance to measure the discrepancy between the approximating distribution and the exact quasi-stationary distribution. It was seen from this measure of goodness of fit that the Beta-binomial provided the best approximation. It also confirmed that although the Poisson distribution gave a good approximation of the expected number of infected individuals at quasi-stationarity, it does not provide a good fit. For comparison, we also compute the total variation distance away from the true quasi-stationary distribution of the asymptotic approximations of Nåsell (1996, 1999). It was seen that the asymptotic approximations of Nåsell (1996, 1999) are very good approximations of the quasi-stationary distribution for $R_0 > 1$. We showed that the Poisson is a better approximation for the number of susceptibles at quasi-stationarity since at quasi-stationarity the mean number of susceptibles is equal to its variance.

For $R_0 < 1$ and $q_1 \neq 0$, we approximated the quasi-stationary distribution by Poisson and Geometric distributions. It was seen that the Poisson only performed well for values of R_0 less than 0.45. The Geometric on the other hand, is a very good approximation of the quasi-stationary distribution for R_0 values less that 0.9. This confirms Nåsell's (1996, 1999) conclusion that the quasi-stationary distribution is well approximated by a Geometric distribution when R_0 is distinctly below 1.

Chapter 4

Two population SIS model without demography

When modelling the spread of a disease in a human population, it is sometimes useful to take into account the formation of small social groups such as households, schools, work places etc. The reason for this is that the spread of infection is usually greatly facilitated among such groups where there is a high level of mixing. Here we study an SIS epidemiological model of individuals partitioned into two separate populations. Each population is divided into susceptibles and infectives. Individuals within a population are more likely to interact with each other, but there are occasional interactions between groups as well. So infection takes place either within or between populations, the latter generally happening much less frequently.

There has been a lot of interest in models for the spread of an epidemic among a population of individuals divided into households. Most of these studies (Ball 1991, Clancy 1994, Becker and Dietz 1995 and 1996, Ball and Lyne 2001, Ball and Neal 2002, etc.), however, have been concerned with SIR epidemics and, therefore, endemic behaviour is not possible. Ball (1999) considered the SIS household-structure model in which the population is partitioned into m households with N members in each household. He determined a threshold R_*. It was shown that for the deterministic model, for households with 2 members, if $R_* \leq 1$ then the epidemic dies out, whilst if $R_* > 1$ the epidemic settles down to an endemic equilibrium. For him the usual basic reproductive ratio R_0 does not provide a good indicator for the behaviour of these household epidemic models unless the household size N is large. Like Ball, Arrigoni and Pugliese (2002) looked at a stochastic SIS model for the spread of

epidemics among a population partitioned into m sites, each containing N individuals; epidemic spread occurs through within-site ('local') contact and global contacts. They analysed the limit behaviour of the system as m and N increase to ∞. Two limit procedures were considered, according to the order in which m and N go to ∞. They showed that the infected distribution converges, as time goes to infinity, to a Dirac measure, centred at an endemic state x^*, if the threshold condition $R_0 > 1$ holds; centred at 0, below the threshold. Neal (2006) also proved the existence of an endemic equilibrium for the epidemic if and only if the threshold parameter R_0 is greater than 1. For the stochastic model, he proved a law of large numbers result for the convergence, to the deterministic limit, of the mean number of infectives per household. We will follow a similar route by approximating the stochastic epidemic model for the spread of an epidemic in a population partitioned into two groups by a deterministic model and deriving a Gaussian approximation process for the fluctuation of the epidemic model about the deterministic equilibrium.

Ghoshal, Sander and Sokolov (2004), in a different approach, analysed the SIS household epidemic using methods from statistical physics, namely self-consistent field methods. The analysis was essentially deterministic, and self-consistent field theory was utilised to consider the individual household epidemics as independent epidemics, subject to a mean-field global infection.

Here we use a diffusion approximation (Ornstein-Uhlenbeck process) to study the long time behaviour of the model. A system of ordinary differential equations describing the cumulants of numbers of infectious individuals per population is derived. This system of equations is then truncated using the moment-closure method used by Nåsell (2005) to derive the steady state distribution of the process. The results of these two approximations are then compared with the exact quasi-stationary distribution.

In section 4.1 we shall define the two-group epidemic model. Then in section 4.2 we will analyse the deterministic approximation of the stochastic model. Our deterministic model is a special case of the model of Lajmanovich and Yorke (1976); the stochastic model has not previously been studied, so far as we are aware. In section 4.3 we will then analyse the process conditioned on non-extinction. A diffusion approximation of the quasi-stationary distribution is given in section 4.4. This

approximation is only valid when R_0 is distinctly larger than one and N is large. Finally we derive cumulant equations in section 4.5 and use them to approximate the quasi-stationary distribution and compare the results with the results obtained from the diffusion approximation.

4.1 Model formulation

Let there be N_1 individuals in population 1 of whom m are initially infectives and N_2 in population 2 of whom n are infectives. Here, we assume that the population sizes are equal and constant ($N_1 = N_2 = N$). The infectious periods of different infectives are independent and identically distributed according to a random variable I which is exponentially distributed with intensity γ. During his or her infectious period, a given infective makes contact with a given individual within his or her population at rate β and a given individual from the other population at rate λ. If the contacted individual is susceptible then he or she becomes infected and is immediately able to infect other individuals. After the infectious period the individual recovers and becomes susceptible to re-infection. We thus assume that the within population infection rates, cross population infection rates and the recovery rates for both populations are equal.

This is a two dimensional Markovian model. The Markov chain $(I_1(t), I_2(t))$ describing the number of infected individuals at time t, takes values in the state space $=\{0, 1, \ldots, N_1\} \times \{0, 1, \ldots, N_2\}$. The only non-zero transition rates are given in Table 4.1 below.

Table 4.1: The transition rates for the model are given as:

Event	State Transition	Transition Rate
Infection in Pop 1	$(i_1, i_2) \to (i_1 + 1, i_2)$	$\beta_{1(i_1,i_2)} + \lambda_{2(i_1,i_2)} = \beta\frac{i_1}{N}(N - i_1) + \lambda\frac{i_2}{N}(N - i_1)$
Infection in Pop 2	$(i_1, i_2) \to (i_1, i_2 + 1)$	$\beta_{2(i_1,i_2)} + \lambda_{1(i_1,i_2)} = \beta\frac{i_2}{N}(N - i_2) + \lambda\frac{i_1}{N}(N - i_2)$
Recovery in Pop 1	$(i_1, i_2) \to (i_1 - 1, i_2)$	$\gamma_{1(i_1,i_2)} = \gamma i_1$
Recovery in Pop 2	$(i_1, i_2) \to (i_1, i_2 - 1)$	$\gamma_{2(i_1,i_2)} = \gamma i_2$

Therefore the Kolmogorov forward equations for the state probabilities $p_{i_1,i_2}(t)$

are

$$\begin{aligned}\frac{dp_{i_1,i_2}}{dt} &= \beta_{1(i_1-1,i_2)}p_{i_1-1,i_2}(t) + \gamma_{1(i_1+1,i_2)}p_{i_1+1,i_2}(t) + \beta_{2(i_1,i_2-1)}p_{i_1,i_2-1}(t) \\ &+\gamma_{2(i_1,i_2+1)}p_{i_1,i_2+1}(t) + \lambda_{2(i_1-1,i_2)}p_{i_1-1,i_2}(t) + \lambda_{1(i_1,i_2-1)}p_{i_1,i_2-1}(t) \\ &-\beta_{1(i_1,i_2)}p_{i_1,i_2}(t) - \beta_{2(i_1,i_2)}p_{i_1,i_2}(t) - \gamma_{1(i_1,i_2)}p_{i_1,i_2}(t) \\ &-\gamma_{2(i_1,i_2)}p_{i_1,i_2}(t) - \lambda_{1(i_1,i_2)}p_{i_1,i_2}(t) - \lambda_{2(i_1,i_2)}p_{i_1,i_2}(t) \qquad (4.1)\end{aligned}$$

for $i_1 = 0, 1, 2, \ldots, N$ and $i_2 = 0, 1, 2, \ldots, N$ and where $p_{-1,i_2}(t) = p_{i_1,-1}(t) = p_{i_1,N+1}(t) = p_{N+1,i_2}(t) = 0$.

4.2 Deterministic model

As $N \to \infty$, the process describing the density of infectives in each population $\{(N^{-1}(I_1, I_2)); \quad t \geq 0\}$ can be approximated by a deterministic model described by the following differential equations

$$\begin{aligned}\frac{di_1}{dt} &= \beta i_1(1-i_1) + \lambda i_2(1-i_1) - \gamma i_1, \\ \frac{di_2}{dt} &= \beta i_2(1-i_2) + \lambda i_1(1-i_2) - \gamma i_2.\end{aligned}$$

The basic reproduction number is

$$R_0 = \frac{\beta + \lambda}{\gamma}. \qquad (4.2)$$

We also introduce a new parameter α_1,

$$\alpha_1 = \frac{\beta}{\gamma}. \qquad (4.3)$$

This is the ratio of within population infection rate to the recovery rate.

4.2.1 Equilibrium

At equilibrium,

$$\begin{aligned}\beta i_1(1-i_1) + \lambda i_2(1-i_1) - \gamma i_1 &= 0, \\ \beta i_2(1-i_2) + \lambda i_1(1-i_2) - \gamma i_2 &= 0.\end{aligned}$$

Solving these equations using Maple gives four possible solutions:

1. $i_1 = 0$, $i_2 = 0$. This point corresponds to the absence of infection in both populations.

2. $i_1^* = 1 - \frac{1}{R_0}$, $i_2^* = 1 - \frac{1}{R_0}$. This corresponds to an endemic infection level. (i_1^*, i_2^*) is only feasible if $R_0 > 1$.

3. i_1 and i_2 equal $\frac{(\beta-\lambda)^2-\gamma(\beta-\lambda)\pm\sqrt{((\beta-\lambda)^2-\gamma(\beta-\lambda))((\beta+\lambda)^2-\gamma(\beta-\lambda))}}{2\beta(\beta-\lambda)}$ respectively.

4. i_1 and i_2 equal $\frac{(\beta-\lambda)^2-\gamma(\beta-\lambda)\mp\sqrt{((\beta-\lambda)^2-\gamma(\beta-\lambda))((\beta+\lambda)^2-\gamma(\beta-\lambda))}}{2\beta(\beta-\lambda)}$ respectively.

To analyse the feasibility of (3) and (4) we let $K = (\beta - \lambda)^2 - \gamma(\beta - \lambda)$ and $L = (\beta + \lambda)^2 - \gamma(\beta - \lambda)$, and so $L > K$. Therefore (3) and (4) can be written as $\frac{K\pm\sqrt{KL}}{2\beta(\beta-\lambda)}$ and $\frac{K\mp\sqrt{KL}}{2\beta(\beta-\lambda)}$ respectively. It is important to note that the equilibrium is feasible if both roots are real and positive and ≤ 1. Analysing the roots $\frac{K\pm\sqrt{KL}}{2\beta(\beta-\lambda)}$ it can be seen that

- If $KL < 0$, then we have complex roots and these are not feasible.

- If $KL > 0$ and $K > 0$, then $K < L$ which implies

$$K^2 < KL$$

$$\Rightarrow K < \sqrt{KL}$$

$$\Rightarrow K - \sqrt{KL} < 0 \qquad \text{whereas} \qquad K + \sqrt{KL} > 0.$$

  So whatever the sign of $\beta - \lambda$, we have roots of opposite signs and therefore not feasible.

- If $KL > 0$ and $K < 0$, then $K - \sqrt{KL} < 0$. But $K < 0$ implies that

$$(\beta - \lambda)^2 - \gamma(\beta - \lambda) < 0$$

$$\Rightarrow (\beta - \lambda)^2 < \gamma(\beta - \lambda)$$

$$\Rightarrow (\beta - \lambda) > 0$$

  So $\frac{K-\sqrt{KL}}{2\beta(\beta-\lambda)} < 0$ and therefore not feasible.

- If $K = 0$ then roots 3 and 4 are equal to root 1.

- If $L = 0$ then $\gamma(\beta - \lambda) = (\beta + \lambda)^2 > 0$ so $\beta > \lambda$ and $K = (\beta - \lambda)^2 - (\beta + \lambda)^2$. Thus roots 3 and 4 equal $\frac{-4\beta\lambda}{2\beta(\beta-\lambda)} = \frac{-2\lambda}{(\beta-\lambda)}$. This is negative since $\beta > \lambda$.

Therefore we reject equilibrium points (3) and (4) as unfeasible.

4.2.2 Stability of equilibria

Our 2-group deterministic model is a special case of the model of Lajmanovich and Yorke (1976). From their Theorem 3.1 we therefore see that for $R_0 \leq 1$, the disease-free equilibrium at $(i_1, i_2) = (0, 0)$ is globally asymptotically stable within the feasible region $[0, 1]^2$, while for $R_0 > 1$ the endemic equilibrium (i_1^*, i_2^*) is globally asymptotically stable in $[0, 1]^2 \setminus (0, 0)$.

For $R_0 > 1$, we can conclude that if the process $(I_1(t), I_2(t))$ is initially close to $N(i_1^*, i_2^*)$ then it will tend to stay close to $N(i_1^*, i_2^*)$ for a considerable time, subject to small random fluctuations.

4.3 Conditioning on non-extinction

Quasi-stationarity is defined by conditioning on non-extinction. The state probabilities conditioned on not being absorbed are denoted by $q_{i_1,i_2}(t)$. They can be determined from the unconditioned probabilities $p_{i_1,i_2}(t)$ via the relation

$$\begin{aligned} q_{i_1,i_2}(t) &= P((I_1(t), I_2(t)) = (i_1, i_2) | (I_1(t), I_2(t)) \neq (0, 0)) \\ &= \frac{p_{i_1,i_2}(t)}{1 - p_{0,0}(t)}, \end{aligned} \tag{4.4}$$

for $i_1 = 0, 1, 2, \ldots, N$ and $i_2 = 0, 1, 2, \ldots, N$. Differentiating (4.4) and using the equation

$$\dot{p}_{0,0}(t) = \gamma p_{0,1}(t) + \gamma p_{1,0}(t), \tag{4.5}$$

which is obtained by putting $i_1 = i_2 = 0$ in equation (4.1), gives

$$\dot{q}_{i_1,i_2}(t) = \frac{\dot{p}_{i_1,i_2}(t)}{1 - p_{0,0}(t)} + \gamma(q_{0,1}(t) + q_{1,0}(t))\frac{p_{i_1,i_2}(t)}{1 - p_{0,0}(t)}. \tag{4.6}$$

The Kolmogorov forward equations (4.1) for the state probabilities $p_{i_1,i_2}(t)$ can be used to derive the differential equations for the conditional state probabilities $q_{i_1,i_2}(t)$

$$\begin{aligned} \frac{dq_{i_1,i_2}}{dt} &= \beta_{1(i_1-1,i_2)} q_{i_1-1,i_2}(t) + \gamma_{1(i_1+1,i_2)} q_{i_1+1,i_2}(t) + \beta_{2(i_1,i_2-1)} q_{i_1,i_2-1}(t) \\ &\quad + \gamma_{2(i_1,i_2+1)} q_{i_1,i_2+1}(t) + \lambda_{2(i_1-1,i_2)} q_{i_1-1,i_2}(t) + \lambda_{1(i_1,i_2-1)} q_{i_1,i_2-1}(t) \\ &\quad - \beta_{1(i_1,i_2)} q_{i_1,i_2}(t) - \beta_{2(i_1,i_2)} q_{i_1,i_2}(t) - \gamma_{1(i_1,i_2)} q_{i_1,i_2}(t) - \gamma_{2(i_1,i_2)} q_{i_1,i_2}(t) \\ &\quad - \lambda_{1(i_1,i_2)} q_{i_1,i_2}(t) - \lambda_{2(i_1,i_2)} q_{i_1,i_2}(t) + (\gamma q_{0,1}(t) + \gamma q_{1,0}(t)) q_{i_1,i_2}(t), \end{aligned} \tag{4.7}$$

for $i_1 = 0, 1, 2 \ldots, N$, $i_2 = 0, 1, 2, \ldots, N$ and $(i_1, i_2) \neq (0, 0)$. The quasi-stationary distribution q_{i_1,i_2} is the stationary solution of this system of differential equations. Analytic solutions are not possible so approximations are sought. We will derive a bivariate normal distribution approximation of the joint distribution of I_1 and I_2 in quasi-stationarity. This normal approximation is only valid if $R_0 > 1$ and N large.

4.4 Diffusion approximation

We now derive the diffusion approximation of the quasi-stationary distribution. The diffusion approximation has a continuous state space, in contrast with the discrete state space of the original process. The approximation is based on the restriction that R_0 is strictly larger than 1 and N is large. Here we approximate the quasi-stationary distribution by a bivariate normal distribution.

If we consider the scaled (i_1, i_2), the change s in the scaled state variables i_1 and i_2 during the time interval $[t, t + \delta t]$ are denoted by δi_1 and δi_2: $\delta i_j = i_j(t + \delta t) - i_j(t)$, $j = 1, 2$. From the transition rates given we can determine the mean and the covariance of the vector with components δi_1 and δi_2. For the mean we have

$$E\begin{pmatrix} \delta i_1 \\ \delta i_2 \end{pmatrix} = \begin{pmatrix} \beta i_1(1 - i_1) + \lambda i_2(1 - i_1) - \gamma i_1 \\ \beta i_2(1 - i_2) + \lambda i_1(1 - i_2) - \gamma i_2 \end{pmatrix} \delta t + o(\delta t).$$

The Jacobian matrix is given by

$$\mathbf{J}(i_1, i_2) = \begin{pmatrix} \frac{\partial}{\partial i_1}\left(\frac{di_1}{dt}\right) & \frac{\partial}{\partial i_2}\left(\frac{di_1}{dt}\right) \\ \frac{\partial}{\partial i_1}\left(\frac{di_2}{dt}\right) & \frac{\partial}{\partial i_2}\left(\frac{di_2}{dt}\right) \end{pmatrix}.$$

That is, at the endemic equilibrium,

$$\mathbf{J}(i_1^*, i_2^*) = \begin{pmatrix} \beta - 2\beta i_1^* - \lambda i_2^* - \gamma & \lambda(1 - i_1^*) \\ \lambda(1 - i_2^*) & \beta - 2\beta i_2^* - \lambda i_1^* - \gamma \end{pmatrix}.$$

Moving on to the covariance matrix of the vector of changes in the state variables during the time interval $[t, t + \delta t]$.

$$\begin{aligned} \mathrm{Cov}\begin{pmatrix} \delta i_1 \\ \delta i_2 \end{pmatrix} &= \begin{pmatrix} \beta i_1(1 - i_1) + \lambda i_2(1 - i_1) + \gamma i_1 & 0 \\ 0 & \beta i_2(1 - i_2) + \lambda i_1(1 - i_2) + \gamma i_2 \end{pmatrix} \delta t + o(\delta t) \\ &= \mathbf{G}(i_1, i_2)\delta t + o(\delta t). \end{aligned}$$

Since we are interested in the behaviour of the process around (i_1^*, i_2^*), we evaluate matrix $\mathbf{G}(i_1, i_2)$ at the point (i_1^*, i_2^*). Therefore

$$\mathbf{G}(i_1^*, i_2^*) = \begin{pmatrix} \beta i_1^*(1 - i_1^*) + \lambda i_2^*(1 - i_1^*) + \gamma i_1^* & 0 \\ 0 & \beta i_2^*(1 - i_2^*) + \lambda i_1^*(1 - i_2^*) + \gamma i_2^* \end{pmatrix}.$$

The process $\sqrt{N}((i_1(t), i_2(t)) - (i_1^*, i_2^*))$ may be approximated for large N by a two-dimensional Ornstein-Uhlenbeck process (Etheir and Kurtz, (1986)). The Ornstein-Uhlenbeck process has local drift matrix $\mathbf{J}(i_1^*, i_2^*)$ and local covariance matrix $\mathbf{G}(i_1^*, i_2^*)$. The quasi-stationary distribution can be approximated by the stationary distribution of this Ornstein-Uhlenbeck process. The stationary distribution of the Ornstein-Uhlenbeck process is bivariate normal with mean (0,0) and variance matrix Σ, where Σ is determined from the matrices $\mathbf{J}(i_1^*, i_2^*)$ and $\mathbf{G}(i_1^*, i_2^*)$ via the relationship

$$\mathbf{J}(i_1^*, i_2^*)\Sigma + \Sigma\mathbf{J}^T(i_1^*, i_2^*) = -\mathbf{G}(i_1^*, i_2^*). \tag{4.8}$$

This can be written as

$$\begin{pmatrix} J_{11} & J_{12} \\ J_{21} & J_{22} \end{pmatrix}\begin{pmatrix} \Sigma_{11} & \Sigma_{12} \\ \Sigma_{12} & \Sigma_{22} \end{pmatrix} + \begin{pmatrix} \Sigma_{11} & \Sigma_{12} \\ \Sigma_{12} & \Sigma_{22} \end{pmatrix}\begin{pmatrix} J_{11} & J_{21} \\ J_{12} & J_{22} \end{pmatrix} = -\begin{pmatrix} G_{11} & G_{12} \\ G_{12} & G_{22} \end{pmatrix}.$$

$\mathbf{G}$ and Σ are symmetrical. Expanding the above gives

$$\begin{aligned} &\begin{pmatrix} 2(J_{11}\Sigma_{11} + J_{12}\Sigma_{12}) & J_{11}\Sigma_{12} + J_{12}\Sigma_{22} + J_{21}\Sigma_{11} + J_{22}\Sigma_{12} \\ J_{11}\Sigma_{12} + J_{12}\Sigma_{22} + J_{21}\Sigma_{11} + J_{22}\Sigma_{12} & 2(J_{21}\Sigma_{12} + J_{22}\Sigma_{22}) \end{pmatrix} \\ = \; &-\begin{pmatrix} G_{11} & G_{12} \\ G_{12} & G_{22} \end{pmatrix}. \end{aligned}$$

To solve for the components of Σ the above can be written as

$$\begin{pmatrix} 2J_{11} & 2J_{12} & 0 \\ J_{21} & (J_{11} + J_{22}) & J_{12} \\ 0 & 2J_{21} & 2J_{22} \end{pmatrix}\begin{pmatrix} \Sigma_{11} \\ \Sigma_{12} \\ \Sigma_{22} \end{pmatrix} = -\begin{pmatrix} G_{11} \\ G_{12} \\ G_{22} \end{pmatrix}.$$

So

$$\begin{pmatrix} \Sigma_{11} \\ \Sigma_{12} \\ \Sigma_{22} \end{pmatrix} = -\begin{pmatrix} 2J_{11} & 2J_{12} & 0 \\ J_{21} & (J_{11} + J_{22}) & J_{12} \\ 0 & 2J_{21} & 2J_{22} \end{pmatrix}^{-1}\begin{pmatrix} G_{11} \\ G_{12} \\ G_{22} \end{pmatrix}.$$

This is equivalent to

$$\begin{aligned} &\begin{pmatrix} \Sigma_{11} \\ \Sigma_{12} \\ \Sigma_{22} \end{pmatrix} = \\ &-\begin{pmatrix} 2\beta(1-2i_1^*) - 2(\lambda i_2^* + \gamma) & 2\lambda(1-i_1^*) & 0 \\ \lambda(1-i_2^*) & 2(\beta-\gamma) - (\lambda+2\beta)(i_1^* + i_2^*) & \lambda(1-i_1^*) \\ 0 & 2\lambda(1-i_2^*) & 2\beta(1-2i_2^*) - 2(\lambda i_1^* + \gamma) \end{pmatrix}^{-1} \\ &\times \begin{pmatrix} \beta i_1^*(1-i_1^*) + \lambda i_2^*(1-i_1^*) + \gamma i_1^* \\ 0 \\ \beta i_2^*(1-i_2^*) + \lambda i_1^*(1-i_2^*) + \gamma i_2^* \end{pmatrix}, \end{aligned}$$

which yields

$$\Sigma = \frac{\gamma}{\beta+\lambda}\begin{pmatrix} \frac{(\beta^2+2\beta\lambda-\gamma\beta+\lambda^2)}{(\beta^2+2\beta\lambda-\gamma\beta+\gamma\lambda+\lambda^2)} & \frac{\lambda\gamma}{(\beta^2+2\beta\lambda-\gamma\beta+\gamma\lambda+\lambda^2)} \\ \frac{\lambda\gamma}{(\beta^2+2\beta\lambda-\gamma\beta+\gamma\lambda+\lambda^2)} & \frac{(\beta^2+2\beta\lambda-\gamma\beta+\lambda^2)}{(\beta^2+2\beta\lambda-\gamma\beta+\gamma\lambda+\lambda^2)} \end{pmatrix}.$$

The explicit formulae for the elements of Σ were found using Maple. Numerical values can be obtain by inputting the values of the variables in the equation. The equilibrium distribution of the Ornstein-Uhlenbeck process is bivariate normal with mean (0,0) and variance matrix Σ satisfying (4.8). So the quasi-stationary distribution of the disease process $(I_1(t), I_2(t))$ can be approximated by a bivariate normal distribution with mean (Ni_1^*, Ni_2^*) and variance matrix $N\Sigma$. So from above the expressions for the approximate mean and the variance of the marginal distributions in quasi-stationarity for the number of infected individuals in each of the populations are:

$$\mu_{I_1} = N\left(\frac{R_0-1}{R_0}\right), \tag{4.9}$$

$$\sigma^2_{I_1} = N\frac{R_0^2-\alpha_1}{R_0(R_0^2+R_0-2\alpha_1)}, \tag{4.10}$$

$$\mu_{I_2} = N\left(\frac{R_0-1}{R_0}\right), \tag{4.11}$$

$$\sigma^2_{I_2} = N\frac{R_0^2-\alpha_1}{R_0(R_0^2+R_0-2\alpha_1)}, \tag{4.12}$$

with R_0 and α_1 given by (4.2) and (4.3). The covariance of I_1 and I_2 in quasi-stationarity is approximately

$$\sigma_{I_1I_2} = N\frac{R_0-\alpha_1}{R_0(R_0^2+R_0-2\alpha_1)}. \tag{4.13}$$

The approximate normality of the joint quasi-stationary distribution requires that both of the marginal distributions are approximately normal, which in turn leads to the requirements that the ratios $C_{I_1} = \sigma_{I_1}/\mu_{I_1}$ and $C_{I_2} = \sigma_{I_2}/\mu_{I_2}$ of standard deviation to mean in each marginal distribution are small. The ratio is the "coefficient of variation" which is a measure of the spread of the distributions of I_1 and I_2. Since a normally distributed random variable takes values larger than 3 standard deviations below its mean with high probability, we take either C_{I_1} or C_{I_2} as sufficiently small

if the value is smaller than 1/3. By the expressions (4.9)-(4.13) we have

$$\begin{aligned} C_{I_1} = C_{I_2} &= \frac{R_0}{N(R_0-1)}\sqrt{\frac{N(R_0^2-\alpha_1)}{R_0(R_0^2+R_0-2\alpha_1)}} \\ &= \frac{R_0}{(R_0-1)}\sqrt{\frac{(R_0^2-\alpha_1)}{NR_0(R_0^2+R_0-2\alpha_1)}}. \end{aligned} \tag{4.14}$$

This shows that as the population size N increases, variability decreases. Therefore we require

$$\frac{R_0}{(R_0-1)}\sqrt{\frac{(R_0^2-\alpha_1)}{NR_0(R_0^2+R_0-2\alpha_1)}} \leq \frac{1}{3},$$

that is,

$$N \geq \frac{9R_0(R_0^2-\alpha_1)}{(R_0-1)^2(R_0^2+R_0-2\alpha_1)}$$

as well as $R_0 > 1$.

Working out the quasi-stationary distribution using the eigenvector method and plotting it with the Ornstein-Uhlenbeck approximation we see from Figures 4.1 that the Ornstein-Uhlenbeck approximation gives a very good approximation of the quasi-stationary distribution of each population, for the chosen parameter values. Figure 4.2 is the joint probability distribution of the numbers of infected individuals in populations 1 and 2 at quasi-stationarity. It can be seen that their joint distribution is approximately normal. Figure 4.3 is the contour plot of the joint distribution.

4.5 Cumulant equations

In this section we will derive cumulant equations and use them to approximate the quasi-stationary distribution using the moment closure method of Nåsell (2005). We use the system of equations (4.7) to derive a partial differential equation for the moment generating function M (see Appendix B), defined by

$$M(\theta_1,\theta_2,t) = E[e^{I_1(t)\theta_1+I_2(t)\theta_2}|I_1+I_2>0] = \sum_{\substack{i_1=0\\(i_1,i_2)\neq(0,0)}}^{N}\sum_{i_2=0}^{N} q_{i_1,i_2}(t)e^{i_1\theta_1+i_2\theta_2}$$

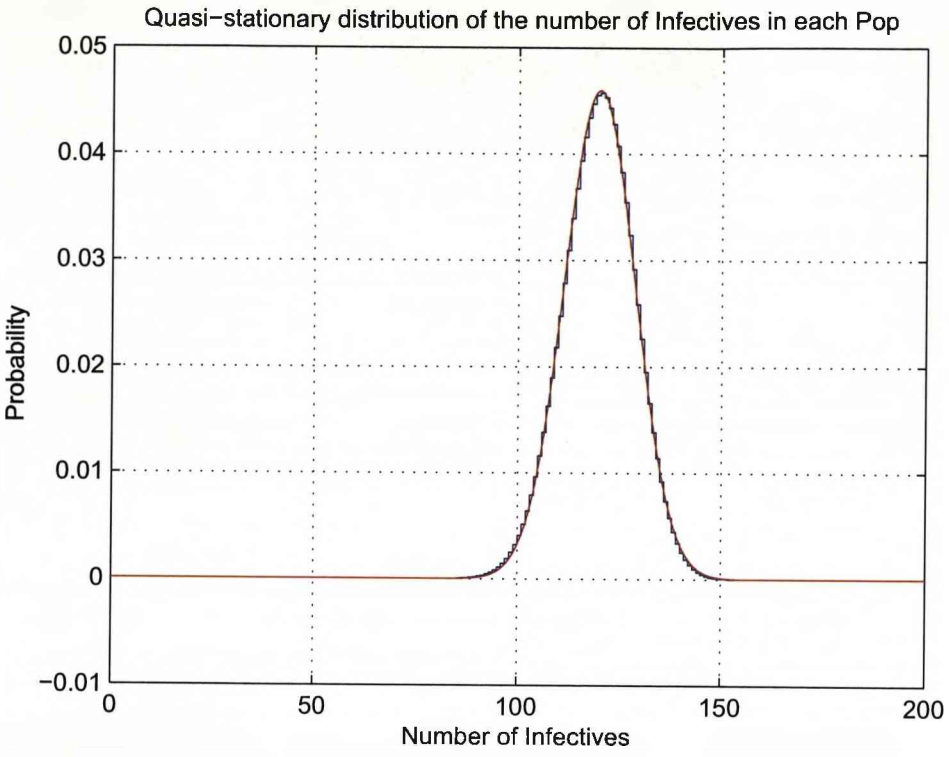

Figure 4.1: Quasi-stationary distribution for the number of infectives in population 1. The blue solid line represents the quasi-stationary distribution for the number of infectives calculated from the truncated transition matrix. The red solid line represents the Ornstein-Uhlenbeck approximation. The parameter values used are $N = 200$, $\gamma = 0.4$, $\beta = 0.9$ and $\lambda = 0.1$. So $R_0 = 2.5$ and $\alpha_1 = 2.25$

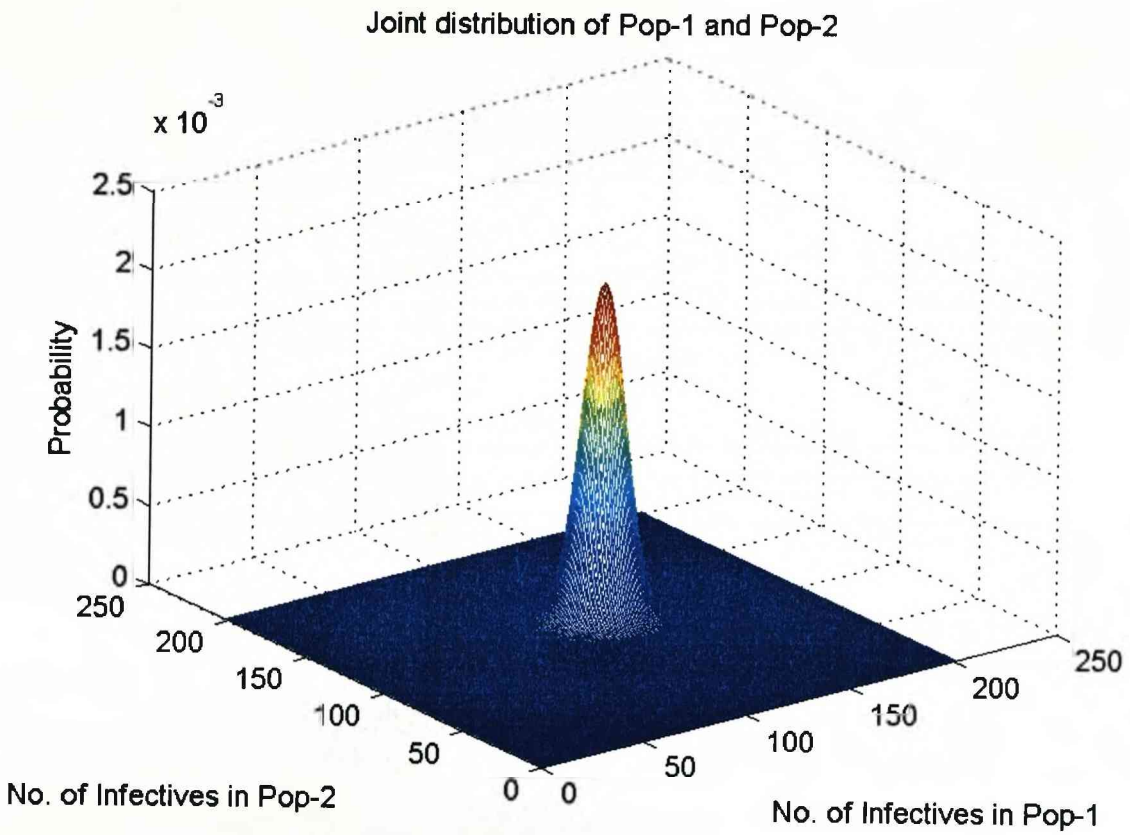

Figure 4.2: The joint distribution of the numbers of infectives in populations 1 and 2. The parameter values used are $N = 200$, $\gamma = 0.4$, $\beta = 0.9$ and $\lambda = 0.1$. So $R_0 = 2.5$ and $\alpha_1 = 2.25$

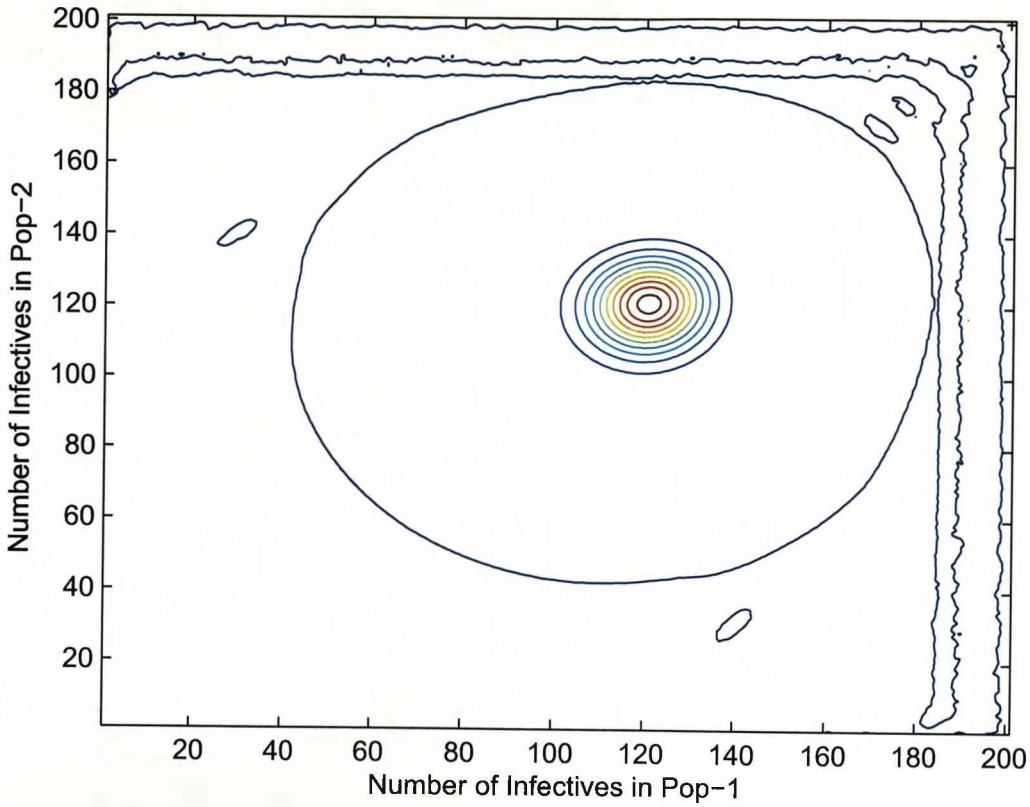

Figure 4.3: The contour plot of the quasi-stationary distribution. The contours are drawn at heights (probability values) of 0.0002, 0.0004, 0.0006, 0.0008, 0.001, 0.0012, 0.0014, 0.0016, 0.0018 and 0.002. The parameter values used are $N = 200$, $\gamma = 0.4$, $\beta = 0.9$ and $\lambda = 0.1$. So $R_0 = 2.5$ and $\alpha_1 = 2.25$

$\theta_1, \theta_2 \in \mathbb{R}$. Thus,

$$\begin{aligned}
\frac{\partial M}{\partial t} &= \beta(e^{\theta_1}-1)\frac{\partial M}{\partial \theta_1} - \frac{\beta}{N}(e^{\theta_1}-1)\frac{\partial^2 M}{\partial \theta_1^2} + \gamma(e^{-\theta_1}-1)\frac{\partial M}{\partial \theta_1} + \beta(e^{\theta_2}-1)\frac{\partial M}{\partial \theta_2} \\
&- \frac{\beta}{N}(e^{\theta_2}-1)\frac{\partial^2 M}{\partial \theta_2^2} + \gamma(e^{-\theta_2}-1)\frac{\partial M}{\partial \theta_2} + \lambda(e^{\theta_1}-1)\frac{\partial M}{\partial \theta_2} - \frac{\lambda}{N}(e^{\theta_1}-1)\frac{\partial^2 M}{\partial \theta_1 \partial \theta_2} \\
&+ \lambda(e^{\theta_2}-1)\frac{\partial M}{\partial \theta_1} - \frac{\lambda}{N}(e^{\theta_2}-1)\frac{\partial^2 M}{\partial \theta_1 \partial \theta_2} + (\gamma q_{0,1}(t) + \gamma q_{1,0}(t))M(\theta_1, \theta_2, t) \\
&- \gamma q_{0,1}(t) - \gamma q_{1,0}(t).
\end{aligned}$$

Using the transformation $K(\theta_1, \theta_2, t) = \log M(\theta_1, \theta_2, t)$ we have the cumulant generating function. $K(\theta_1, \theta_2, t)$ satisfies

$$\begin{aligned}
\frac{\partial K}{\partial t} &= \left(\beta(e^{\theta_1}-1) + \gamma(e^{-\theta_1}-1) + \lambda(e^{\theta_2}-1)\right)\frac{\partial K}{\partial \theta_1} - \frac{\beta}{N}(e^{\theta_1}-1)\left(\frac{\partial^2 K}{\partial \theta_1^2} + \left(\frac{\partial K}{\partial \theta_1}\right)^2\right) \\
&+ \left(\beta(e^{\theta_2}-1) + \gamma(e^{-\theta_2}-1) + \lambda(e^{\theta_1}-1)\right)\frac{\partial K}{\partial \theta_2} - \frac{\beta}{N}(e^{\theta_2}-1)\left(\frac{\partial^2 K}{\partial \theta_2^2} + \left(\frac{\partial K}{\partial \theta_2}\right)^2\right) \\
&- \left(\frac{\lambda}{N}(e^{\theta_1}-1) + \frac{\lambda}{N}(e^{\theta_2}-1)\right)\left(\frac{\partial^2 K}{\partial \theta_1 \partial \theta_2} + \frac{\partial K}{\partial \theta_1}\frac{\partial K}{\partial \theta_2}\right) + \gamma q_{0,1}(t)(1-e^K) \\
&+ \gamma q_{1,0}(t)(1-e^K). \qquad (4.15)
\end{aligned}$$

Using the definition $K(\theta_1\theta_2, t) = \sum_{j\geq 0,\, k\geq 0,\, j+k>0} k_{j,k}(t)\frac{\theta_1^j}{j!}\frac{\theta_2^k}{k!}$ in the partial differential equation (4.15) one can derive ordinary differential equations for the cumulants $k_{j,k}(t)$. The working can be found in Appendix B. The results for the cumulants of order 1 and 2 are as follows:

$$\begin{aligned}
\dot{k}_{1,0} &= (\beta-\gamma)k_{1,0} + \lambda k_{0,1} - \frac{\beta}{N}k_{2,0} - \frac{\beta}{N}k_{1,0}^2 - \frac{\lambda}{N}k_{1,1} - \frac{\lambda}{N}k_{1,0}k_{0,1} \\
&+(\gamma q_{0,1} + \gamma q_{1,0})k_{1,0}, \qquad (4.16)
\end{aligned}$$

$$\begin{aligned}
\dot{k}_{0,1} &= (\beta-\gamma)k_{0,1} + \lambda k_{1,0} - \frac{\beta}{N}k_{0,2} - \frac{\beta}{N}k_{0,1}^2 - \frac{\lambda}{N}k_{1,1} - \frac{\lambda}{N}k_{1,0}k_{0,1} \\
&+(\gamma q_{0,1} + \gamma q_{1,0})k_{0,1}, \qquad (4.17)
\end{aligned}$$

$$\begin{aligned}
\dot{k}_{1,1} &= 2(\beta-\gamma)k_{1,1} + \lambda(k_{2,0}+k_{0,2}) + \frac{\beta}{N}(k_{2,1}+k_{1,2}) - \frac{2\beta}{N}(k_{1,0}k_{1,1} + k_{0,1}k_{1,1}) \\
&-\frac{\lambda}{N}(k_{1,2}+k_{2,1}) - \frac{\lambda}{N}(k_{1,0}k_{1,1} + k_{0,1}k_{1,1}) - \frac{\lambda}{N}(k_{0,1}k_{2,0} + k_{1,0}k_{0,2}) \\
&+(\gamma q_{0,1} + \gamma q_{1,0})(k_{1,1} - k_{1,0}k_{0,1}), \qquad (4.18)
\end{aligned}$$

$$\begin{aligned}\dot{k}_{2,0} &= (\beta+\gamma)k_{1,0} + 2(\beta-\gamma)k_{2,0} - \frac{\beta}{N}(k_{2,0}+2k_{3,0}) + \lambda k_{1,0} + 2\lambda k_{1,1} \\ &\quad -\frac{\beta}{N}k_{1,0}^2 - 4\frac{\beta}{N}k_{1,0}k_{2,0} - \frac{\lambda}{N}(k_{1,0}k_{0,1} + 2k_{1,0}k_{1,1} + k_{0,1}k_{2,0}) \\ &\quad -\frac{\lambda}{N}(k_{1,1}+2k_{2,1}) + (\gamma q_{0,1} + \gamma q_{1,0})(k_{2,0} - k_{1,0}^2), \end{aligned} \tag{4.19}$$

$$\begin{aligned}\dot{k}_{0,2} &= (\beta+\gamma)k_{0,1} + 2(\beta-\gamma)k_{0,2} - \frac{\beta}{N}(k_{0,2}+2k_{0,3}) + \lambda k_{0,1} + 2\lambda k_{1,1} \\ &\quad -\frac{\beta}{N}k_{0,1}^2 - 4\frac{\beta}{N}k_{0,1}k_{0,2} - \frac{\lambda}{N}(k_{1,0}k_{0,1} + 2k_{0,1}k_{1,1} + k_{1,0}k_{0,2}) \\ &\quad -\frac{\lambda}{N}(k_{1,1}+2k_{1,2}) + (\gamma q_{0,1} + \gamma q_{1,0})(k_{0,2}(t) - k_{0,1}^2). \end{aligned} \tag{4.20}$$

These equations are not closed because equations for cumulants of order one contain cumulants of order two, equations for cumulants of order two contain cumulants of order three and so on. In practice, a moment-closure approximation can be used to truncate this system of equations. We will use the moment-closure method used by Nåsell (2005) to determine asymptotic approximations of the stationary solutions to these equations. This is valid in the parameter space where R_0 is distinctly greater than 1. We are mainly interested in the means, variances and covariances, so like Nåsell (2005) we allow $k_{1,2}$, $k_{2,1}$, $k_{0,3}$ and $k_{3,0}$, to grow with N, but not faster than $O(N)$. With this assumption and solving the equations using Maple gives:

$$k_{1,0} = \left(1-\frac{1}{R_0}\right)N - \frac{R_0(\alpha_1+1)-2\alpha_1}{(R_0^2+R_0-2\alpha_1)(R_0-1)} + O\left(\frac{1}{N}\right), \tag{4.21}$$

$$k_{0,1} = \left(1-\frac{1}{R_0}\right)N - \frac{R_0(\alpha_1+1)-2\alpha_1}{(R_0^2+R_0-2\alpha_1)(R_0-1)} + O\left(\frac{1}{N}\right), \tag{4.22}$$

$$k_{1,1} = \frac{R_0-\alpha_1}{R_0(R_0^2+R_0-2\alpha_1)}N + O(1), \tag{4.23}$$

$$k_{2,0} = \frac{R_0^2-\alpha_1}{R_0(R_0^2+R_0-2\alpha_1)}N + O(1), \tag{4.24}$$

$$k_{0,2} = \frac{R_0^2-\alpha_1}{R_0(R_0^2+R_0-2\alpha_1)}N + O(1). \tag{4.25}$$

It can be seen that the variances and covariance of I_1 and I_2 coincide with the approximation derived using the Ornstein-Uhlenbeck approximation given in section 4.4. The approximations for the expectations of I_1 and I_2 have been improved.

4.6 Time to extinction

The time to extinction is a random variable whose distribution depends on the distribution of the initial state. If the process has been going on for a long time and has not gone extinct, then the quasi-stationary distribution can be used as an approximation of the distribution of states (Nåsell (2001)). We can determine the distribution of the time to extinction τ from the probability $p_{0,0}(t)$ since the event $\{\tau \leq t\}$ is equal to the event that $\{I_1(t) = I_2(t) = 0\}$. Therefore

$$P(\tau \leq t) = P((I_1(t), I_2(t)) = (0,0)) = p_{0,0}(t).$$

Assuming that the initial distribution is equal to the quasi-stationary distribution, i.e. $p_{i_1,i_2}(0) = q_{i_1,i_2}$ for $i_1 = 0, 1, 2, \ldots N, i_2 = 0, 1, 2, \ldots N, (i_1, i_2) \neq (0,0)$ and $p_{0,0}(0) = 0$, it can be shown (using the same arguments as Nåsell (1999)) that the time to extinction from the quasi-stationary distribution τ_Q has an exponential distribution with expectation equal to $\frac{1}{\gamma(q_{0,1}+q_{1,0})}$.

4.7 Conclusion

In this chapter we analysed a two group SIS epidemic model with the population size of each group constant. Since explicit solution is not possible, we approximate the quasi-stationary distribution using diffusion approximation and moment closure applied on cumulant equations. The results from both approximations compare very well with each other and with the leading eigenvector of the truncated transition matrix. However, the derivation of cumulant equations is cumbersome and may not be flexible to allow for considerable complications to be added to the model. The diffusion approximation is more flexible but may give rise to complicated solutions when considerable complications are added to the model. This will be seen in a later chapter when demography is added to the model.

Chapter 5

SIS model with demography

Here we consider the SIS model with demography. Nåsell (2004) looked at the SIR model with demography, in which infection is followed by permanent immunity. He derived approximations for the marginal distribution of infected individuals in quasi-stationarity and the time to extinction. He also approximated the quasi-stationary distribution using diffusion approximation and moment closure applied to the cumulant equations. In this chapter we will prove that the process will ultimately be absorbed. We approximate the quasi-stationary distribution of the process using diffusion approximation. Cumulant equations are derived and moment closure applied to them to derive an approximation for the quasi-stationary distribution.

In the first section, we define the model. We then analyse (section 5.2) the deterministic version of the model. In this section we reparametrise the model and work out the equilibrium points. We prove almost sure absorption in section 5.3. In section 5.4 we look at the process conditioned on it not being absorbed. We analyse (section 5.5) diffusion approximation of the process. Using the Ornstein Uhlenbeck process we approximate the fluctuation about the deterministic endemic equilibrium. This provides the approximation for the quasi-stationary distribution. In section 5.6 we derive cumulant differential equations for cumulants up to order 2. We then use a moment closure method to solve these differential equations. The result is compared with the result obtained from the diffusion approximation. In section 5.7 we carry out simulation of the process and use it to validate our result from the diffusion approximation. Our results are then compared with the results obtained by Nåsell (2005) for the SIR model with demography in section 5.8. Concluding remarks on this chapter are given in section 5.9.

5.1 Model

This is a bivariate continuous-time Markov chain. The two state variables used are the number of susceptible individuals $S(t)$ at time t and the number of infectives $I(t)$ at time t. The joint distribution at time t will be denoted by

$$p_{s,i}(t) = P(S(t) = s, I(t) = i)$$

This model has five possible transitions, shown in the table below. Four parameters are used, namely the 'typical' population size N, the death rate per individual μ, the contact rate β, and the recovery rate per individual γ. It is assumed here that there are no deaths due to the disease and no vertical transmission of the disease (all newborns are susceptible), and that $\beta, \gamma, \mu, N > 0$. The state space of the process is $C = \{(s,i) : s = 0,1,2,\ldots, i = 0,1,2,\ldots\}$ and the set of states $A = \{(s,0); s = 0,1,2,\ldots\}$ is an absorbing set.

Table 5.1: The transition rates for the model are given as:

Event	State Transition	Transiton Rate
Immigration of a susceptible individual	$(s,i) \to (s+1,i)$	$\lambda_1(s,i) = \mu N$
Death of a susceptible individual	$(s,i) \to (s-1,i)$	$\mu_1(s,i) = \mu s$
Infection of a susceptible individual	$(s,i) \to (s-1,i+1)$	$\beta_1(s,i) = \frac{\beta}{N} si$
Recovery of an infected individual	$(s,i) \to (s+1,i-1)$	$\gamma_2(s,i) = \gamma i$
Death of an infected	$(s,i) \to (s,i-1)$	$\mu_2(s,i) = \mu i$

With the convention that $p_{s,i}(t) = 0$ for $(s,i) \notin C$, the Kolmogorov forward equations for this process can be written as follows:

$$\begin{aligned} \dot{p}_{s,i}(t) &= \lambda_1(s-1,i)p_{s-1,i}(t) + \mu_1(s+1,i)p_{s+1,i}(t) + \beta_1(s+1,i-1)p_{s+1,i-1}(t) \\ &\quad +\gamma_2(s-1,i+1)p_{s-1,i+1}(t) + \mu_2(s,i+1)p_{s,i+1}(t) \\ &\quad -k(s,i)(t)p_{s,i}(t), \end{aligned} \tag{5.1}$$

for $s = 0,1,2,\ldots$, $i = 0,1,2,\ldots$ and where $k(s,i) = \lambda_1(s,i) + \mu_1(s,i) + \beta_1(s,i) + \gamma_2(s,i) + \mu_2(s,i)$ and we use a dot to represent differentiation with respect to time.

5.2 Deterministic model

We now analyse the deterministic approximation of the stochastic model. For a deterministic approximation we introduce the scaling $s = \frac{S}{N}$ and $i = \frac{I}{N}$. The differential equations for the deterministic version of the model become

$$\frac{ds}{dt} = \mu + \gamma i - \beta si - \mu s, \tag{5.2}$$

$$\frac{di}{dt} = \beta si - (\gamma + \mu)i. \tag{5.3}$$

This version has its threshold at $R_0 = 1$, where $R_0 = \frac{\beta}{\gamma+\mu}$. We also introduce a new parameter α_2 to denote the ratio of the average life length to the average duration of infection:

$$\alpha_2 = \frac{\mu + \gamma}{\mu}.$$

The reparametrised process is:

$$\frac{ds}{dt} = \mu(1 + (\alpha_2 - 1)i - \alpha_2 R_0 si - s), \tag{5.4}$$

$$\frac{di}{dt} = \mu(\alpha_2 R_0 si - \alpha_2 i). \tag{5.5}$$

Adding equations (5.4) and (5.5) gives

$$\frac{ds}{dt} + \frac{di}{dt} = \mu(1 - (s + i)).$$

It follows then that $\lim_{t\to\infty}(s + i) = 1$.

The system of differential equations ((5.4) and (5.5)) has two critical points. One of them is at $(s, i) = (1, 0)$, which corresponds to the disease-free equilibrium. The other critical point corresponds to the endemic infection level and is given as

$$(s^*, i^*) = \left(\frac{1}{R_0}, 1 - \frac{1}{R_0}\right).$$

The equilibrium (s^*, i^*) is feasible if $R_0 > 1$.

5.2.1 Stability of equilibria

Like chapter 4, this is a two dimensional process and the Jacobian matrix will be used to determine the stability of the equilibria. The Jacobian matrix is given by

$$\mathbf{J}(s,i) = \begin{pmatrix} -\mu\alpha_2 R_0 i - \mu & \alpha_2 - 1 - \mu\alpha_2 R_0 s \\ \mu\alpha_2 R_0 i & \mu\alpha_2 R_0 s - \mu\alpha_2 \end{pmatrix}.$$

So at point (1, 0),

$$\mathbf{J}(s,i) = \begin{pmatrix} -\mu & \alpha_2 - 1 - \mu\alpha_2 R_0 \\ 0 & \mu\alpha_2 R_0 - \mu\alpha_2 \end{pmatrix}.$$

The trace is

$$\mathrm{tr}(\mathbf{J}(1,0)) = \mu\alpha_2(R_0 - 1) - \mu, \tag{5.6}$$

and the determinant is

$$\det(\mathbf{J}(0,0)) = -\mu^2\alpha_2(R_0 - 1). \tag{5.7}$$

For stability, we need the trace to be negative and the determinant positive. From equation (5.6) and (5.7), the trace is negative and the determinant positive if and only if $R_0 < 1$. Therefore (1,0) is (locally) stable if $R_0 < 1$. For the endemic equilibrium, (s^*, i^*),

$$\mathbf{J}(s^*,i^*) = \begin{pmatrix} -\mu(\alpha_2(R_0 - 1) + 1) & -\mu \\ \mu\alpha_2(R_0 - 1) & 0 \end{pmatrix}.$$

The trace is $-\mu(\alpha_2(R_0 - 1) + 1)$. This is negative if $R_0 > 1$. The determinant is $\mu^2\alpha_2(R_0 - 1)$, which is positive for $R_0 > 1$. Therefore the endemic equilibrium, (s^*, i^*), is (locally) stable if $R_0 > 1$. The model, therefore, displays a clear threshold at $R_0 = 1$.

Having shown that the endemic equilibrium point (s^*, i^*) is locally stable for $R_0 > 1$, we now show that it is globally stable. For endemic equilibrium, the following equalities hold,

$$\beta s^* i^* = \mu + \gamma i^* - \mu s^* = (\gamma + \mu) i^*. \tag{5.8}$$

at this steady state. To show global stability we shall use the Lyapunov function method. From La Salle and Lefschetz (1961), page 58, we have the following.

Let $V(s,i)$ be a function defined for $s, i > 0$, with continuous partial derivatives, such that

$$\begin{aligned} V(s^*,i^*) &= 0, \\ V(s,i) &> 0 \qquad \forall \quad (s,i) \text{ with } s,i > 0 \text{ such that } (s,i) \neq (s^*,i^*). \end{aligned}$$

For $l > 0$ let Ω_l designate the region where $V(s,i) < l$. Suppose that

$$\frac{dV(s,i)}{dt} \leq 0 \qquad \forall (s,i) \in \Omega_l.$$

Let R be the set of points within Ω_l where $dV/dt = 0$ and let M be the largest invariant set in R. Then every solution in Ω_l tends to M as $t \to \infty$. (See also Barbashin (1970).)

For our process, following Korobeinikov and Wake (2002) we consider a Lyapunov function

$$V(s,i) = s - s^* - s^* \ln \frac{s}{s^*} + \frac{\mu}{\gamma + \mu}\left(i - i^* - i^* \ln \frac{i}{i^*}\right). \tag{5.9}$$

Note that $V(s^*, i^*) = 0$.

The partial derivatives of equation (5.9) are

$$\frac{\partial V(s,i)}{\partial s} = 1 - \frac{s^*}{s} \tag{5.10}$$

and

$$\frac{\partial V(s,i)}{\partial i} = \frac{\mu}{\gamma + \mu}\left(1 - \frac{i^*}{i}\right). \tag{5.11}$$

From (5.10) and (5.11) we see that the only stationary point of $V(s,i)$ occurs at (s^*, i^*). Now from (5.9) it is clear that $V(s,i) \to +\infty$ as $s \to 0$, or $i \to 0$, or $s \to +\infty$, or $i \to +\infty$. Hence $V(s,i) > 0$ for all (s,i) with $s > 0$, $i > 0$ and $(s,i) \neq (s^*, i^*)$.

Now consider the time derivative

$$\frac{dV(s,i)}{dt} = \frac{\partial V(s,i)}{\partial s}\frac{ds}{dt} + \frac{\partial V(s,i)}{\partial i}\frac{di}{dt}. \tag{5.12}$$

Substituting equations (5.2), (5.3), (5.10) and (5.11) into equation (5.12) gives

$$\begin{aligned} \frac{dV(s,i)}{dt} &= \mu + \gamma i - \beta s i - \mu s - \mu\frac{s^*}{s} - \gamma i\frac{s^*}{s} + \beta s^* i + \mu s^* \\ &\quad + \frac{\mu}{\gamma + \mu}(\beta s i - \beta s i^*) - \mu(i - i^*). \end{aligned} \tag{5.13}$$

Using equation (5.8), equation (5.13) can be simplified to

$$\begin{aligned} \frac{dV(s,i)}{dt} &= \mu\left(2 - \frac{s^*}{s} - \frac{s}{s^*}\right) + \gamma i\left(2 - \frac{s^*}{s} - \frac{s}{s^*}\right) \\ &= (\mu + \gamma i)\left(2 - \frac{s^*}{s} - \frac{s}{s^*}\right) \\ &= -(\mu + \gamma i)\frac{s^*}{s}\left(1 - \frac{s}{s^*}\right)^2. \end{aligned}$$

Therefore $\frac{dV(s,i)}{dt} \leq 0$ holds for all $s, i > 0$. The equality $\frac{dV(s,i)}{dt} = 0$ holds only when $s = s^*$ and the point (s^*, i^*) is the only invariant set of the system (5.2)-(5.3) on this line. For any initial point (s, i) of the system with $s, i > 0$, we can choose $l > 0$ such that $(s, i) \in \Omega_l$, and then the solution remains within Ω_l for all $t > 0$, and hence tends to (s^*, i^*) as $t \to \infty$ (La Salle and Lefschetz (1961), page 58). That is, for $R_0 > 1$, the equilibrium (s^*, i^*) is globally asymptotically stable in the positive region $s > 0, i > 0$.

If the initial point has $s = 0$ and $i > 0$, then from (5.4) we see that $ds/dt > 0$ initially, so that the system immediately enters the region with $s > 0$ and from there will converge to (s^*, i^*). If $i = 0$ initially, then there is no infection present in the system, and since there is no mechanism for external introduction of infection the system will converge to the disease-free equilibrium $(s, i) = (1, 0)$.

5.3 Ultimate absorption

To prove ultimate absorption we need to first show that the transition rates matrix $\mathbf{Q}$ is regular. A regular Markov process is a conservative process for which the Kolmogorov forward equations have a unique solution. That is, the transition rates given in Table 5.1 uniquely determine the transition semi-group of the process. We can show that $\mathbf{Q}$ is regular by using the criterion proven by Reuter (1957)(theorem 7); that is a Markov process defined by $\mathbf{Q}$ is regular if, for each $\Lambda > 0$, the equations $(\Lambda + q_m)z_m = \sum_{m \neq n} q_{mn} z_n$ where $0 \leq z_m \leq 1$, have only the trivial solution $z_m = 0$. We shall follow the proof of Theorem 1 of Reuter (1961) to prove the regularity of $\mathbf{Q}$. Writing $z(s, i)$ for z_m,

$$\begin{aligned}(\Lambda + \lambda_1(s,i) + \mu_1(s,i) + \beta_1(s,i) + \gamma_2(s,i) + \mu_2(s,i))z(s,i) \\ = \lambda_1(s,i)z(s+1,i) + \mu_1(s,i)z(s-1,i) + \beta_1(s,i)z(s-1,i+1) \\ +\gamma_2(s,i)z(s+1,i-1) + \mu_2(s,i)z(s,i-1),\end{aligned}$$

for $s \geq 0$ and $i \geq 1$. For $s \geq 0$ and $i = 0$, this immediately gives $\Lambda z_m = 0$. So $z(s, 0) = 0$. Let

$$Z_k = \max\{z(s,i): \quad s \geq 0, \quad i \geq 1, \quad s + i = k\}.$$

If this maximum is attained at (s_k, i_k) then

$$(\Lambda + \lambda_{1_k} + \mu_{1_k} + \beta_{1_k} + \gamma_{2_k} + \mu_{2_k})Z_k \leq \lambda_{1_k} Z_{k+1} + \mu_{1_k} Z_{k-1} + \beta_{1_k} Z_k + \gamma_{2_k} Z_k + \mu_{2_k} Z_{k-1},$$

where $\lambda_{1_k} = \lambda_1(s_k, i_k), \mu_{1_k} = \mu_(s_k, i_k), \beta_{1_k} = \beta_1(s_k, i_k), \gamma_{2_k} = \gamma_2(s_k, i_k), \mu_{2_k} = \mu_2(s_k, i_k)$. Rearranging,

$$\Lambda Z_k + (\mu_{1_k} + \mu_{2_k})(Z_k - Z_{k-1}) \leq \lambda_{1_k}(Z_{k+1} - Z_k),$$

$$(Z_{k+1} - Z_k) \geq \frac{(\mu_{1_k} + \mu_{2_k})}{\lambda_{1_k}}(Z_k - Z_{k-1}) + \frac{\Lambda}{\lambda_{1_k}} Z_k.$$

But $\mu_{1_k} = \mu s_k$, $\mu_{2_k} = \mu i_k$ and $\lambda_{1_k} = \mu N$.

So

$$(Z_{k+1} - Z_k) \geq \frac{\mu k}{\mu N}(Z_k - Z_{k-1}) + \frac{\Lambda}{\mu N} Z_k. \tag{5.14}$$

Following Reuter's (1961) theorem 1, we will show that a sufficient condition for regularity is

$$\sum_{k=1}^{\infty} \left(\frac{1}{\mu N} + \frac{k}{\mu N^2} + \cdots + \frac{k!}{\mu N^k} \right) = \infty. \tag{5.15}$$

Going back to (5.14), if $z(s, i)$ is not identically zero let k_0 be the first k for which $Z_k > 0$. Since Z_k is increasing with k, for $k \geq k_0$

$$(Z_{k+1} - Z_k) \geq \frac{k}{N}(Z_k - Z_{k-1}) + \frac{\Lambda}{\mu N} Z_{k_0},$$

$$(Z_{k+1} - Z_k) \geq \frac{k}{N}\left(\frac{k-1}{N}(Z_{k-1} - Z_{k-2}) + \frac{\Lambda}{\mu N} Z_{k_0} \right) + \frac{\Lambda}{\mu N} Z_{k_0},$$

$$(Z_{k+1} - Z_k) \geq \frac{k(k-1)}{N^2}(Z_{k-1} - Z_{k-2}) + \left(\frac{k}{\mu N^2} + \frac{1}{\mu N} \right) \Lambda Z_{k_0},$$

$$\begin{aligned} (Z_{k+1} - Z_k) \;\geq\; & \left(\frac{1}{\mu N} + \frac{k}{\mu N^2} + \frac{k(k-1)}{\mu N^3} + \cdots + \frac{k(k-1)\ldots(k_0+1)}{\mu N^{k-k_0+1}} \right) \Lambda Z_{k_0} \\ & + \frac{k(k-1)\ldots k_0}{N^{k-k_0+1}}(Z_{k_0} - Z_{k_0-1}). \end{aligned}$$

Let $B = \Lambda Z_{k_0}$. Then

$$(Z_{k+1} - Z_k) \geq B \left(\frac{1}{\mu N} + \frac{k}{\mu N^2} + \frac{k(k-1)}{\mu N^3} + \cdots + \frac{k(k-1)\ldots(k_0+1)}{\mu N^{k-k_0+1}} \right).$$

Summing both sides over all values of k we have

$$\sum_{k=1}^{\infty}(Z_{k+1}-Z_k) \geq B\sum_{k=1}^{\infty}\left(\frac{1}{\mu N}+\frac{k}{\mu N^2}+\frac{k(k-1)}{\mu N^3}+\cdots+\frac{k(k-1)\ldots 2}{\mu N^k}\right).$$

It follows from condition (5.15) above that $\sum_{k=1}^{\infty}(Z_{k+1}-Z_k)$ diverges so that $Z_k \to \infty$, which is contrary to the assumption made earlier that $z(s,i) \leq 1$. Therefore, $z(s,i) = 0$ for all $s \geq 0$, $i \geq 1$ as required. Therefore the Q matrix is regular provided (5.15) holds.

We can show that (5.15) holds by showing that

$$\sum_{k=1}^{\infty}\frac{k!}{\mu N^k} = \infty. \tag{5.16}$$

Equation (5.16) holds because $\frac{k!}{\mu N^k}$ will tend to infinity as $kto\infty$ since μN is constant. Therefore (5.15) holds.

To show ultimate absorption now we apply criterion (C) of Reuter (1961), which can be stated as follows: let D and A respectively denote the sets of non-absorbing and absorbing states: if the process has initial state m ($m = (s,i)$) in D, let α_m be the probability of reaching A and let τ_m be the expected time to reach A: if there exist finite constants $u_n \geq 0$ such that

$$\sum_n q_{mn}u_n + 1 \leq 0, \qquad m \in D, \tag{5.17}$$

then $\alpha_m = 1$ and $0 \leq \tau_m \leq u_m$.

For the SIS model with demography we seek a non-negative solution to the inequality (5.17), which becomes, on writing $u(s,i)$ for u_m, $m = (s,i)$,

$$\Delta u(s,i) \geq 1 \qquad (s,i) \in D \tag{5.18}$$

where

$$\begin{aligned}\Delta u(s,i) &= \mu N[u(s,i)-u(s+1,i)] + \frac{\beta}{N}si[u(s,i)-u(s-1,i+1)] \\ &\quad +\mu s[u(s,i)-u(s-1,i)] + \mu i[u(s,i)-u(s,i-1)] \\ &\quad +\gamma i[u(s,i)-u(s+1,i-1)].\end{aligned}$$

For a trial solution to (5.18) we consider $u = B(s+i)$, where $B > 0$ is a constant.

$$\begin{aligned}\Delta u(s,i) &= B\left[\frac{\beta}{N}si + \mu s - \gamma i - \mu N + \gamma i + \mu i - \frac{\beta}{N}si\right] \\ &= B[\mu s - \mu N + \mu i] \\ &= B\mu[(s+i) - N].\end{aligned}$$

For $s+i \geq N+1$,

$$\Delta u(s,i) = B\mu[s+i-N] \geq B\mu[N+1-N] = B\mu, \tag{5.19}$$

so taking $B > \frac{1}{\mu}$ then $\Delta u(s,i) \geq 1$ for $s+i \geq N+1$.

Suppose that $s+i \leq N$. We have exhibited a function u defined on the state space of the process with $\Delta u(s,i) \geq 1$ for $(s,i) \in D(N) = \{(s,i) \in D : s+i \geq N+1\}$. We now argue as in Clancy, O'Neill and Pollett (2001). That is, by Reuter's Criterion (C) stated earlier, the epidemic process must leave $D(N)$ with probability one, so that it is either ultimately absorbed at $i=0$, or else returns infinitely often to the finite region $D \setminus D(N)$ without being absorbed at $i=0$. However the probability of the latter scenario tends to zero because upon entering $D \setminus D(N)$ the process has a probability of absorption bounded away from zero. Therefore with probability one the process will be absorbed after a finite number of visits to $D \setminus D(N)$. Note that from the above arguments, nothing can be said about expected time to extinction τ_m.

5.4 Conditioning on non-extinction

Having shown that the process will ultimately go extinct, we now consider the process prior to extinction. Quasi-stationarity is defined by conditioning on non-extinction. The state probabilities conditioned on not being absorbed are denoted by $q_{s,i}(t)$. They can be determined from the unconditioned probabilities $p_{s,i}(t)$ via the relation

$$\begin{aligned} q_{s,i}(t) &= P(S(t)=s, I(t)=i | I(t) \neq 0) \\ &= \frac{p_{s,i}(t)}{1-p_{\cdot,0}(t)} \end{aligned} \tag{5.20}$$

where $p_{\cdot,i}(t)$ denotes the marginal distribution of the number of infected individuals at time t,

$$p_{\cdot,i} = \sum_{s=0}^{\infty} p_{s,i}(t) = P(I(t)=i).$$

Taking equation (5.1) and summing for $i=0$ over all s-values we have

$$\dot{p}_{\cdot,0}(t) = (\gamma+\mu)p_{\cdot,1}(t). \tag{5.21}$$

Differentiating equation (5.20) and using (5.21) gives

$$\dot{q}_{s,i}(t) = \frac{\dot{p}_{s,i}(t)}{1 - p_{.,0}(t)} + (\gamma + \mu) q_{.,1} \frac{p_{s,i}(t)}{1 - p_{.,0}(t)},$$

where $q_{.,i}(t) = \sum_{s=1}^{\infty} q_{s,i}(t)$ denotes the marginal distribution of the number of infected individuals at time t conditioned on the process not having been absorbed. Using the Kolmogorov forward equation (5.1) we can derive the following system of differential equations for the conditional state probabilities $q_{s,i}(t)$.

$$\begin{aligned} \dot{q}_{s,i}(t) &= \lambda_1(s-1,i) q_{s-1,i}(t) + \mu_1(s+1,i) q_{s+1,i}(t) + \beta_1(s+1,i-1) q_{s+1,i-1}(t) \\ &\quad + \gamma_2(s-1,i+1) q_{s-1,i+1}(t) + \mu_2(s,i+1) q_{s,i+1}(t) - k(s,i) q_{s,i}(t) \\ &\quad + (\gamma + \mu) q_{.,1} q_{s,i}(t) \end{aligned} \tag{5.22}$$

with $q_{s,i}(t) = 0$ for $(s,i) \notin D$. The quasi-stationary distribution $q_{s,i}$ is the stationary solution of this system of equations.

It can be shown that the time to extinction given that the process is started in the quasi-stationary distribution, T_Q, is exponentially distributed with mean $\frac{1}{(\gamma+\mu)q_{.,1}}$.

5.5 Diffusion approximation

To approximate the quasi-stationary distribution of our process, we use a diffusion approximation. We use the scaled process to derive a diffusion approximation of the stochastic version of the model, valid for $R_0 > 1$. The changes in the scaled state variables $s = S/N$ and $i = I/N$ during a small time interval $[t, t + \delta t]$ will be denoted by δs and δi. From the hypotheses of the original process we can determine the mean and the covariance of the vector of changes in the state variable s (δs) and i (δi). Starting with the mean:

$$\begin{aligned} E[\delta s] &= \mu(1 + (\alpha_2 - 1)i - \alpha_2 R_0 si - s)\delta t + o(\delta t), \\ E[\delta i] &= \mu(\alpha_2 R_0 si - \alpha_2 i)\delta t + o(\delta t). \end{aligned}$$

The Jacobian matrix is defined in section 5.2.1 so we now determine the covariance matrix of the vector of changes in the state variable s and i during the time interval $[t, t + \delta t]$

$$\begin{aligned}\mathbf{Cov}\begin{pmatrix}\delta s\\ \delta i\end{pmatrix} &= \begin{pmatrix}\mu+\mu(\alpha_2-1)i+\mu\alpha_2R_0si+\mu s) & -\mu\alpha_2R_0si-\mu(\alpha_2-1)i\\ -\mu\alpha_2R_0si-\mu(\alpha_2-1)i & \mu\alpha_2R_0si+\mu\alpha_2 i\end{pmatrix}\delta t\\ &\quad +o(\delta t)\\ &= \mathbf{G}(s,i)\delta t+o(\delta t).\end{aligned}$$

The matrix $\mathbf{G}(s,i)$ is approximated by evaluating it at the critical point (s^*,i^*).

$$\mathbf{G}(s^*,i^*) = \frac{\mu}{R_0}\begin{pmatrix}R_0+1+(R_0-1)(2\alpha_2-1) & -(R_0-1)(2\alpha_2-1)\\ -(R_0-1)(2\alpha_2+1) & 2\alpha_2(R_0-1)\end{pmatrix}.$$

Solving equation (4.8) with expressions for $\mathbf{J}(s^*,i^*)$ and $\mathbf{G}(s^*,i^*)$ yields:

$$\Sigma = \begin{pmatrix}\frac{\alpha_2(R_0-1)+2}{R_0(\alpha_2(R_0-1)+1)} & -\frac{1}{R_0}\\ -\frac{1}{R_0} & \frac{R_0(\alpha_2R_0+1)-\alpha_2}{R_0(\alpha_2(R_0-1)+1)}\end{pmatrix}.$$

The quasi-equilibrium distribution of the disease process (S,I) can be approximated by a bivariate normal distribution with mean

$$(Ns^*,Ni^*) = \left(\frac{N}{R_0}, N\left(1-\frac{1}{R_0}\right)\right)$$

and variance matrix

$$N\begin{pmatrix}\frac{\alpha_2(R_0-1)+2}{R_0(\alpha_2(R_0-1)+1)} & -\frac{1}{R_0}\\ -\frac{1}{R_0} & \frac{R_0(\alpha_2R_0+1)-\alpha_2}{R_0(\alpha_2(R_0-1)+1)}\end{pmatrix}.$$

5.6 Cumulant equations

As an alternative to diffusion approximation, a more flexible and more precise approximation method is moment closure. As with the previous chapter, we shall employ a moment closure method based on cumulants, rather than moments. The system of differential equations (5.22) can be used to derive a partial differential equation for the probability generating function M defined by

$$M(\theta_1,\theta_2,t) = E[e^{S\theta_1+I\theta_2}|I>0] = \sum_{s=0}^{\infty}\sum_{i=1}^{\infty}q_{s,i}e^{s\theta_1+i\theta_2} \qquad \theta_1,\theta_2\in\mathbb{R}.$$

Thus,

$$\begin{aligned}\frac{\partial M}{\partial t} &= \mu N(e^{\theta_1}-1)M+\mu(e^{-\theta_1}-1)\frac{\partial M}{\partial\theta_1}+\frac{\beta}{N}(e^{\theta_2-\theta_1}-1)\frac{\partial^2M}{\partial\theta_1\partial\theta_2}\\ &\quad +\mu(e^{-\theta_2}-1)\frac{\partial M}{\partial\theta_2}+\gamma(e^{\theta_1-\theta_2}-1)\frac{\partial M}{\partial\theta_2}+(\gamma+\mu)q_{\cdot1}M\\ &\quad -\gamma e^{\theta_1}q_{\cdot1}\sum_{s=0}^{\infty}q_S(s|1)e^{s\theta_1}-\mu q_{\cdot1}\sum_{s=0}^{\infty}q_S(s|1)e^{s\theta_1}\end{aligned}$$

(see Appendix C) where $q_S(s|1) = \frac{q_{s,1}}{q_{.,1}}$ is the conditional probability that S takes the value s given that $I = 1$ and where $q_{.,1}$ is the marginal probability that I takes the value 1. From this, we derive the partial differential equation for the cumulant generating function using the transformation $K(\theta_1, \theta_2, t) = logM(\theta_1, \theta_2, t)$. We have

$$\begin{aligned}\frac{\partial K}{\partial t} &= \frac{\beta}{N}(e^{\theta_2-\theta_1}-1)\left(\frac{\partial^2 K}{\partial\theta_1\partial\theta_2}+\frac{\partial K}{\partial\theta_1}\frac{\partial K}{\partial\theta_2}\right)+\mu(e^{-\theta_1}-1)\frac{\partial K}{\partial\theta_1}+\mu(e^{-\theta_2}-1)\frac{\partial K}{\partial\theta_2}\\ &+\gamma(e^{\theta_1-\theta_2}-1)\frac{\partial K}{\partial\theta_2}+\mu N(e^{\theta_1}-1)+\gamma q_{.1}\left(1-e^{-K}e^{\theta_1}q_{.1}\sum_{s=0}^{\infty}q_S(s|1)(t)e^{s\theta_1}\right)\\ &+\mu q_{.1}\left(1-e^{-K}q_{.1}\sum_{s=0}^{\infty}q_S(s|1)(t)e^{s\theta_1}\right). \qquad (5.23)\end{aligned}$$

Using the definition of the cumulants $k_{m,n}(t)$ as coefficients of the power series $K(\theta_1,\theta_2,t) = \sum_{m\geq 0,\, n\geq 0,\, m+n>0} k_{m,n}(t)\frac{\theta_1^m}{m!}\frac{\theta_2^n}{n!}$ (for $(m,n)\neq(0,0)$) in the partial differential equation (5.23) one can derive ordinary differential equations for the cumulants $k_{m,n}(t)$. Since we demand less of cumulants of order 3 and higher, we derive only cumulants of order 1 and 2. The results for the cumulants of order 1 and 2 are as follows:

$$\begin{aligned}\dot{k}_{1,0} &= \mu N-\frac{\beta}{N}(k_{1,1}+k_{1,0}k_{0,1})-\mu k_{1,0}+\gamma k_{0,1}-\gamma q_{.,1}\left(1+E[S|I=1]\right)\\ &+(\gamma+\mu)q_{.,1}\left(k_{1,0}-E[S|I=1]\right), \qquad (5.24)\\ \dot{k}_{0,1} &= \frac{\beta}{N}(k_{1,1}+k_{1,0}k_{0,1})-(\mu+\gamma)k_{0,1}-\gamma q_{.,1}+(\gamma+\mu)q_{.,1}k_{0,1}, \qquad (5.25)\\ \dot{k}_{1,1} &= \frac{\beta}{N}(k_{1,0}k_{1,1}-k_{1,1}-k_{1,0}k_{0,1}+k_{2,1}+k_{0,1}k_{2,0}-k_{0,1}k_{1,1}-k_{1,2}\\ &-k_{1,0}k_{0,2})-(2\mu+\gamma)k_{1,1}-\gamma k_{0,1}+\gamma(k_{0,2}+q_{.,1}k_{1,0})\\ &+(\gamma+\mu)q_{.,1}\left(k_{1,1}+k_{0,1}\left(E[S|I=1]-k_{1,0}\right)\right), \qquad (5.26)\\ \dot{k}_{2,0} &= \mu N+\frac{\beta}{N}\left(k_{1,1}+k_{1,0}k_{0,1}-2k_{2,1}-2k_{1,0}k_{1,1}-2k_{0,1}k_{2,0}\right)+\mu k_{1,0}\\ &+\gamma k_{0,1}+2\gamma k_{1,1}-2\mu k_{2,0}+(\gamma+\mu)q_{.,1}\left(k_{2,0}-k_{1,0}^2-E[S^2|I=1]\right)\\ &+\gamma q_{.,1}\left(2k_{1,0}E[S|I=1]-2E[S|I=1]-1-E[S^2|I=1]\right), \qquad (5.27)\\ \dot{k}_{0,2} &= \frac{\beta}{N}\left(k_{1,1}+k_{1,0}k_{0,1}+2k_{1,2}+2k_{0,1}k_{1,1}+2k_{1,0}k_{0,2}\right)-2(\gamma+\mu)k_{0,2}\\ &+(\gamma+\mu)k_{0,1}+(\gamma+\mu)q_{.,1}\left(k_{0,2}-k_{0,1}^2\right). \qquad (5.28)\end{aligned}$$

The equations for the first-order cumulants contain terms with the second order cumulants and equations for the second-order cumulants contain terms with third-order cumulants. The cumulants in equilibrium are related to the moments of the

quasi-stationary distribution as follows: $k_{1,0} \approx E[S]$, $k_{0,1} \approx E[I]$, $k_{1,1} \approx \text{Cov}[S, I]$, $k_{2,0} \approx \text{Var}[S]$ and $k_{0,2} \approx \text{Var}[I]$. See Appendix C for the derivation of the cumulant equations (5.24) - (5.28).

Lloyd (2004) noted for the SIR model that the deterministic system consists of equations (5.24) - (5.25) with $k_{1,0}$ replaced by S, $k_{0,1}$ by I and ignoring second-order terms and terms in $q_{1,.}$ and $q_{.,1}$. So we can say that the deterministic model is obtained as a result of the simplest moment closure technique applied to (5.24) - (5.25) by setting second-order moments and terms involving $q_{.,1}$ to zero.

The differential equations for the cumulants of the unconditioned process can be found by ignoring all the terms containing $q_{.,1}$ in each equation. These can be used to derive asymptotic approximation for the cumulants in quasi-stationarity. This approximation is valid in the case when R_0 is distinctly larger than 1. We shall further assume that cumulants of third-order and higher can be set to zero, equivalent to assuming a bivariate normal distribution for (S, I) in quasi-stationarity. This approximation is again expected to be valid in the case when R_0 is distinctly larger than 1. (Note that following Nåsell (2005) it is actually sufficient to allow $k_{1,2}$, $k_{2,1}$, $k_{0,3}$ and $k_{3,0}$ to grow with N, but not faster then $O(N)$.)

Solving the equilibrium cumulant equations under these assumptions using Maple gives the leading terms in power series for the cumulants as:

$$k_{1,0} = \frac{1}{R_0} N + \frac{1}{R_0 - 1} + O\left(\frac{1}{N}\right), \tag{5.29}$$

$$k_{0,1} = \frac{R_0 - 1}{R_0} N + \frac{1}{1 - R_0} + O\left(\frac{1}{N}\right), \tag{5.30}$$

$$k_{1,1} = -\frac{1}{R_0} N + O(1), \tag{5.31}$$

$$k_{2,0} = \frac{\alpha_2(R_0 - 1) + 2}{R_0(\alpha_2(R_0 - 1) + 1)} N + O(1), \tag{5.32}$$

$$k_{0,2} = \frac{R_0(\alpha_2 R_0 + 1) - \alpha_2}{R_0(\alpha_2(R_0 - 1) + 1)} N + O(1). \tag{5.33}$$

Again, as in chapter 4, it can be seen that the variances and covariance of S and I coincide with the approximation derived using the Ornstein-Uhlenbeck approximation given in section 4.2. The approximations for the expectations of S and I have been improved.

In both the Ornstein-Uhlenbeck approximation and moment closure approxima-

tion, we are approximating a discrete distribution by a continuous distribution. And since we are approximating a discrete distribution by a continuous distribution, then for $(s,i) \in \mathbb{Z}^2$ the probability $P(S=s, I=i)$ in equilibrium can be approximated by integrating the appropriate normal probability function over a unit square centred at (s,i) (Clancy and French(2001)). This can further be approximated by simply evaluating the normal density function at the point (s,i).

5.7 Simulation

We have studied the marginal distribution of the number of infected individuals in quasi-stationary distribution using diffusion approximation and cumulant equation. We now compare these approximations with Monte Carlo simulation to judge the adequacy of these approximations, looking specifically at the marginal distribution of the number of infected individuals. It is impossible work out the exact quasi-stationary distribution (left eigenvector of the reduced transition rate matrix) because the transition rate matrix is infinite and so we run a numerical simulation of the stochastic model. For the simulation, we shall use the same parameter values as Nåsell (2005), that is, $\beta = 750$, $\gamma = 50$, $\mu = 1/70$ and $N = 200,000$. We run $50,000$ simulations, each initiated close to the deterministic endemic equilibrium point and run for 20 time units and the finial number of infectives collected at the end of each simulation. We then plot our results in Figure 5.1.

Figure 5.1 represents the marginal distribution of number of infected individuals at quasi-stationarity. It can be seen from this figure that both the Ornstein-Uhlenbeck approximation and the moment closure approximation give good approximations of the quasi-stationary distribution for these parameter values.

5.8 Comparison of the SIR model and the SIS model

We will now compare our results with the results of Nåsell (2005) for the SIR model with demography. We will start by comparing the deterministic equilibrium results.

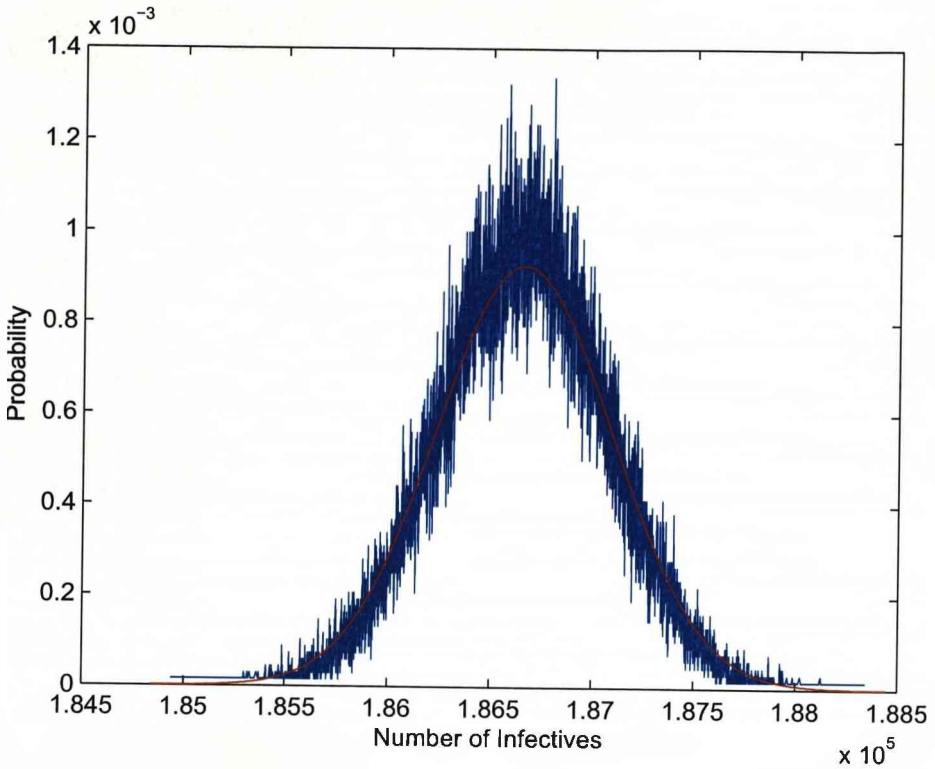

Figure 5.1: The quasi-stationary distribution of the number of infected individuals. The blue solid line is the simulation, based on 50,000 simulation runs, each initiated close to the deterministic endemic equilibrium point and run for 20 time units. The red solid line represents both the moment closure approximation and the Ornstein-Uhlenbeck approximation, which are so close as to be indistinguishable. The parameter values are $N = 200,000$, $\beta = 750$, $\mu = 1/70$ and $\gamma = 50$ (so $R_0 \simeq 15$ and $\alpha_2 = 3501$).

SIR model (Nåsell (2005))	SIS model
$R_0 = \frac{\beta}{\gamma+\mu}$	$R_0 = \frac{\beta}{\gamma+\mu}$
$\alpha = \frac{\gamma+\mu}{\mu}$	$\alpha_2 = \frac{\gamma+\mu}{\mu}$
$s^* = \frac{1}{R_0}$	$s^* = \frac{1}{R_0}$
$i^* = \frac{R_0-1}{\alpha R_0}$	$i^* = \frac{R_0-1}{R_0}$

where $\alpha = \frac{\gamma+\mu}{\mu} > 1$. So i^* (SIR)$< i^*$ (SIS) and s^* (SIR) $= s^*$ (SIS). That is, the SIR and SIS models have the same susceptible population in equilibrium, but the SIS model has a higher infection prevalence. Note that both models have total scaled population size 1 in equilibrium, but for the SIR model there is a third category of individual, the 'Removed' individuals, with equilibrium density $r^* = 1 - s^* - i^*$.

Next, we compare moment closure approximations. Ignoring terms of order $O(1/N)$, we have

SIR model	SIS model
$k_{10} = \frac{N}{R_0} + \frac{\alpha}{R_0-1}$	$k_{10} = \frac{N}{R_0} + \frac{1}{R_0-1}$
$k_{01} = \frac{R_0-1}{\alpha R_0}N - \frac{1}{R_0-1}$	$k_{01} = \frac{R_0-1}{R_0}N - \frac{1}{R_0-1}$

It should be noted that there is a typographic error in Nåsell (2005), where k_{01} is given as $\frac{R_0-1}{\alpha R_0}N + \frac{1}{R_0-1}$ instead of $\frac{R_0-1}{\alpha R_0}N - \frac{1}{R_0-1}$.

See `www.math.kth.se/~ingemar/forsk/endsir/endsir.html`.

In the moment closure approximation it can be seen that the mean number of infective individuals at quasi-stationarity ($k_{0,1}$) in the SIR model is less than in the SIS model, in agreement with the deterministic result. On the other hand, the mean number of susceptible individuals is seen to be slightly greater in the SIR model than the SIS model. Since there are (on average) more infectives present in the SIS model it is not surprising that this higher level of infectivity results in a reduction in the susceptible population size. It is however interesting to note that the effect is sufficiently small not to show up in the deterministic approximation, and requires the greater detail of the moment closure approximation to become apparent.

Looking at total population size, we see that for the SIS model $k_{01} + k_{10} = N$ as expected. For the SIR model we find

$$k_{01} + k_{10} = N\left(\frac{R_0 + \alpha - 1}{\alpha R_0}\right) + \frac{\alpha - 1}{R_0 - 1} < N$$

due to the fact that we have not yet taken into account the 'Removed' category of individuals. The expected number of individual in the removed class at quasi-stationarity is equal to $N\left(\frac{(\alpha-1)(R_0-1)}{\alpha R_0}\right) - \frac{\alpha-1}{R_0-1}$. Adding in this contribution we find that the expected equilibrium total population size for the SIR model is again equal to N.

To compare the variances we can look at their ratio

$$\begin{aligned}\frac{\sigma_S^2(SIR)}{\sigma_S^2(SIS)} &= \frac{\alpha+R_0}{R_0^2}\frac{R_0(\alpha(R_0-1)+1)}{\alpha(R_0-1)+2} \\ &= \frac{\alpha+R_0}{R_0}\frac{\alpha(R_0-1)+1}{\alpha(R_0-1)+2}\end{aligned}$$

Now

$$\begin{aligned}(\alpha+R_0)(\alpha(R_0-1)+1) - R_0(\alpha(R_0-1)+2) &= \alpha^2(R_0-1)+\alpha-R_0 \\ &= \alpha^2(R_0-1)-(R_0-\alpha) > 0\end{aligned}$$

since $\alpha > 1$. Thus,

$$\frac{\alpha+R_0}{R_0}\frac{\alpha(R_0-1)+1}{\alpha(R_0-1)+2} > 1$$

Therefore the variance for the number of susceptible individuals at quasi-stationarity for the SIR model is greater than that of the SIS model.

For the number of infected individuals we have

$$\begin{aligned}\frac{\sigma_I^2(SIR)}{\sigma_I^2(SIS)} &= \frac{\alpha(R_0-1)+R_0^2}{\alpha R_0^2}\frac{R_0(\alpha(R_0-1)+1)}{R_0(\alpha R_0+1)-\alpha} \\ &= \frac{\alpha R_0-\alpha+R_0^2}{R_0(\alpha R_0+1)-\alpha}\frac{\alpha R_0-\alpha+1}{\alpha R_0} \\ &= \frac{R_0(\alpha+R_0)-\alpha}{R_0(\alpha R_0+1)-\alpha}\frac{\alpha R_0-(\alpha-1)}{\alpha R_0} \\ &< \frac{R_0(\alpha+R_0)-\alpha}{R_0(\alpha R_0+1)-\alpha}\end{aligned}$$

since $\alpha > 1$. Now

$$(\alpha R_0+1)-(\alpha+R_0) = (\alpha-1)(R_0-1) > 0.$$

So $(\alpha R_0+1) > (\alpha+R_0)$. Therefore $R_0(\alpha+R_0)-\alpha < R_0(\alpha R_0+1)-\alpha$ and so

$$\frac{R_0(\alpha+R_0)-\alpha}{R_0(\alpha R_0+1)-\alpha} < 1.$$

Therefore the SIS model has a larger variance than the SIR model for the number of infected individuals at quasi-stationarity.

We will now compare the coefficient of variation for the SIS and the SIR models for the number of infected individuals at quasi-stationarity. Coefficient of variation is a statistical measure of dispersion of data around the mean. The higher the coefficient of variation, the greater the dispersion in the data. The coefficient of variation is the ratio of the standard deviation to the mean. For better expressions, we will use their squared coefficient of variation (CV^2).

$$CV^2(SIR) = \frac{\alpha(\alpha(R_0-1)+R_0^2)}{N(R_0-1)^2}$$

and

$$CV^2(SIS) = \frac{R_0(R_0(\alpha R_0+1)-\alpha)}{N(R_0-1)^2(\alpha(R_0-1)+1)}.$$

So

$$\begin{aligned}\frac{CV^2(SIR)}{CV^2(SIS)} &= \frac{\alpha(\alpha(R_0-1)+R_0^2)}{N(R_0-1)^2}\,\frac{N(R_0-1)^2(\alpha(R_0-1)+1)}{R_0(R_0(\alpha R_0+1)-\alpha)} \\ &= \frac{\alpha(\alpha(R_0-1)+R_0^2)(\alpha(R_0-1)+1)}{R_0(R_0(\alpha R_0+1)-\alpha)}.\end{aligned}$$

Now

$$\begin{aligned}&\alpha(\alpha(R_0-1)+R_0^2)(\alpha(R_0-1)+1)-(R_0(R_0(\alpha R_0+1)-\alpha)) \\ &= (\alpha-1)\left(\alpha^2(R_0-1)^2+\alpha R_0(R_0^2-1)+R_0^2\right) > 0\end{aligned}$$

Therefore the SIR model has a larger coefficient of variation than the SIS model.

5.9 Conclusion

In this chapter we showed that the disease will almost surely go extinct from the population. So we studied the distribution of the process prior to extinction after it has been going on for a long time. This stationary distribution conditioned on non-extinction is known as the quasi-stationary distribution. Explicit solution for the quasi-stationary distribution is not possible, so we use a diffusion approximation and moment closure method applied on cumulant equations to approximate it. The results obtained for the quasi-stationary expectation of the number of susceptible and infected individuals from the moment closure method refine the results obtained

from the diffusion approximation. The results for the variances and the covariance are the same for the moment closure approximation and the diffusion approximation. These approximations are only valid for values of $R_0 > 1$ and large N. We showed by comparison with simulation results that these approximations provide very good approximations of the quasi-stationary distribution for these parameter values.

We also compared our results with the results Nåsell (2005) obtained for the SIR model with demography. For the diffusion approximation, the mean number of susceptible individuals at quasi-stationarity is the same for both the SIR and SIS models. In the moment closure approximation, however, the mean number of susceptible individuals at quasi-stationarity in the SIR model is slightly more that those in the SIS model, but the number of infected individuals in the SIS model is more than the SIR model. The variance for the number of susceptible individuals at quasi-stationarity for the SIR model is greater than that of the SIS model but the SIS model has a larger variance than the SIR model for the number of infected individuals. We also showed the SIR model has a larger coefficient of variation than the SIS model which mean that the SIR model has a shorter time to extinction than the SIS model.

It is important to note that the process was simplified and that a few things could have been added. For example, a latent period could have been added or we could have allowed for an infection rate that varies between different stages of infectivity. An age varying infectivity could have also been included. The technical level, however, will be higher under the extended model. Perhaps more important for approaching real life epidemics is to generalise the model by, for example including spatial, social, individual heterogeneities and social effects, which play an important role in the spread of infectious diseases (Anderson & May (1991)). However, we belief that the results obtained here give a good indication of the dynamics of an SIS disease process for the parameters studied.

Chapter 6

Two Population SIS model with demography

In chapter 4 we looked at a two population model with constant population sizes. Now we analyse a two population model with demography. This is a multivariate continuous-time Markov chain. The four state variables used are the number of susceptible individuals in each population $S_1(t)$ and $S_2(t)$ at time t and the number of infectives in each population $I_1(t)$ and $I_2(t)$ at time t. These state variables take values in the state space $\{(s_1, i_1, s_2, i_2) : s_1 = 0, 1, \ldots, i_1 = 0, 1, \ldots, s_2 = 0, 1, \ldots, i_2 = 0, 1, \ldots\}$. The states $(s_1, 0, s_2, 0)$ form the absorbing set A and so communicate with each other, but not with any of the states (s_1, i_1, s_2, i_2) with at least one of i_1 and i_2 greater than 0 which form the transient set D. The joint probability distribution at time t will be denoted by $p_{s_1,i_1,s_2,i_2}(t) = P(S_1(t) = s_1, I_1(t) = i_1, S_2(t) = s_2, I_2(t) = i_2)$. The transition rates to various states are given in Table 6.1. where

$$\lambda_1(s_1, i_1, s_2, i_2) = \mu N, \qquad \mu_1(s_1, i_1, s_2, i_2) = \mu s_1,$$

$$\lambda_2(s_1, i_1, s_2, i_2) = \mu N, \qquad \mu_3(s_1, i_1, s_2, i_2) = \mu s_2,$$

$$\beta_1(s_1, i_1, s_2, i_2) = \frac{\beta}{N} s_1 i_1 + \frac{\lambda}{N} s_1 i_2, \qquad \gamma_1(s_1, i_1, s_2, i_2) = \gamma i_1,$$

$$\beta_2(s_1, i_1, s_2, i_2) = \frac{\beta}{N} s_2 i_2 + \frac{\lambda}{N} s_2 i_1, \qquad \gamma_2(s_1, i_1, s_2, i_2) = \gamma i_2$$

$$\mu_2(s_1, i_1, s_2, i_2) = \mu i_1 \quad \text{and} \quad \mu_4(s_1, i_1, s_2, i_2) = \mu i_2.$$

Table 6.1: The transition rates for the model are given as:

Event	State Transition	Transiton Rate
Immigration of a susceptible in Pop. 1	$(s_1, i_1, s_2, i_2) \to (s_1 + 1, i_1, s_2, i_2)$	$\lambda_1(s_1, i_1, s_2, i_2)$
Death of a susceptible in Pop. 1	$(s_1, i_1, s_2, i_2) \to (s_1 - 1, i_1, s_2, i_2)$	$\mu_1(s_1, i_1, s_2, i_2)$
Infection of a susceptible in Pop. 1	$(s_1, i_1, s_2, i_2) \to (s_1 - 1, i_1 + 1, s_2, i_2)$	$\beta_1(s_1, i_1, s_2, i_2)$
Recovery of an infective in Pop. 1	$(s_1, i_1, s_2, i_2) \to (s_1 + 1, i_1 - 1, s_2, i_2)$	$\gamma_1(s_1, i_1, s_2, i_2)$
Death of an infective in Pop. 1	$(s_1, i_1, s_2, i_2) \to (s_1, i_1 - 1, s_2, i_2)$	$\mu_2(s_1, i_1, s_2, i_2)$
Immigration of a susceptible in Pop. 2	$(s_1, i_1, s_2, i_2) \to (s_1, i_1, s_2 + 1, i_2)$	$\lambda_2(s_1, i_1, s_2, i_2)$
Death of a susceptible in Pop. 2	$(s_1, i_1, s_2, i_2) \to (s_1, i_1, s_2 - 1, i_2)$	$\mu_3(s_1, i_1, s_2, i_2)$
Infection of a susceptible in Pop. 2	$(s_1, i_1, s_2, i_2) \to (s_1, i_1, s_2 - 1, i_2 + 1)$	$\beta_2(s_1, i_1, s_2, i_2)$
Recovery of an infective in Pop. 2	$(s_1, i_1, s_2, i_2) \to (s_1, i_1, s_2 + 1, i_2 - 1)$	$\gamma_2(s_1, i_1, s_2, i_2)$
Death of an infective in Pop. 2	$(s_1, i_1, s_2, i_2) \to (s_1, i_1, s_2, i_2 - 1)$	$\mu_4(s_1, i_1, s_2, i_2)$

The Kolmogorov forward equation for the state probabilities $p_{s_1,i_1,s_2,i_2}(t) = P\{S_1(t) = s_1, I_1(t) = i_1, S_2(t) = s_2, I_2(t) = i_2\}$ can be written as

$$\begin{aligned}
\dot{p}_{s_1,i_1,s_2,i_2}(t) &= \lambda_1(s_1 - 1, i_1, s_2, i_2)p_{s_1-1,i_1,s_2,i_2}(t) + \mu_1(s_1 + 1, i_1, s_2, i_2)p_{s_1+1,i_1,s_2,i_2}(t) \\
&+ \beta_1(s_1 + 1, i_1 - 1, s_2, i_2)p_{s_1+1,i_1-1,s_2,i_2}(t) + \mu_2(s_1, i_1 + 1, s_2, i_2)p_{s_1,i_1+1,s_2,i_2}(t) \\
&+ \gamma_1(s_1 - 1, i_1 + 1, s_2, i_2)p_{s_1-1,i_1+1,s_2,i_2}(t) + \lambda_2(s_1, i_1, s_2 - 1, i_2)p_{s_1,i_1,s_2-1,i_2}(t) \\
&+ \mu_3(s_1, i_1, s_2 + 1, i_2)p_{s_1,i_1,s_2+1,i_2}(t) + \beta_2(s_1, i_1, s_2 + 1, i_2 - 1)p_{s_1,i_1,s_2+1,i_2-1}(t) \\
&+ \gamma_2(s_1, i_1, s_2 - 1, i_2 + 1)p_{s_1,i_1,s_2-1,i_2+1}(t) + \mu_4(s_1, i_1, s_2, i_2 + 1)p_{s_1,i_1,s_2,i_2+1}(t) \\
&- k(s, i)(t)p_{s,i}(t), \qquad (6.1)
\end{aligned}$$

for $s_1 = 0, 1, 2, dots$, $i_1 = 0, 1, 2, \ldots$, $s_2 = 0, 1, 2, dots$, $i_2 = 0, 1, 2, \ldots$ and where $k(s_1, i_1, s_2, i_2) = \lambda_1(s_1, i_1, s_2, i_2) + \mu_1(s_1, i_1, s_2, i_2) + \beta_1(s_1, i_1, s_2, i_2) + \gamma_1(s_1, i_1, s_2, i_2) + \mu_2(s_1, i_1, s_2, i_2) + \lambda_2(s_1, i_1, s_2, i_2) + \mu_3(s_1, i_1, s_2, i_2) + \beta_2(s_1, i_1, s_2, i_2) + \gamma_2(s_1, i_1, s_2, i_2) + \mu_4(s_1, i_1, s_2, i_2)$.

6.1 Deterministic model

As with the previous chapters, we scale the process by introducing the scaling $s_1 = \frac{S_1}{N}$, $i_1 = \frac{I_1}{N}$, $s_2 = \frac{S_2}{N}$ and $i_2 = \frac{I_2}{N}$. The deterministic version of the model is

$$\begin{aligned}
\frac{ds_1}{dt} &= -(\beta i_1 + \lambda i_2)s_1 + \gamma i_1 + \mu - \mu s_1, && (6.2)\\
\frac{di_1}{dt} &= (\beta i_1 + \lambda i_2)s_1 - (\gamma + \mu)i_1, && (6.3)\\
\frac{ds_2}{dt} &= -(\beta i_2 + \lambda i_1)s_2 + \gamma i_2 + \mu - \mu s_2, && (6.4)\\
\frac{di_2}{dt} &= (\beta i_2 + \lambda i_1)s_2 - (\gamma + \mu)i_2. && (6.5)
\end{aligned}$$

The basic reproductive ratio is

$$R_0 = \frac{\beta + \lambda}{\gamma + \mu}.$$

Adding equations (6.2) and (6.3) and equations (6.4) and (6.5), we have

$$\frac{ds_1}{dt} + \frac{di_1}{dt} = \mu(1 - s_1 - i_1), \quad \frac{ds_2}{dt} + \frac{di_2}{dt} = \mu(1 - s_2 - i_2).$$

It follows then that if $s_1(0) + i_1(0) = 1$ then $s_1(t) + i_1(t) = 1$ for all $t \geq 0$, and similarly for $s_2 + i_2$.

The system of equations (6.2) - (6.3) has four critical points. The first, $s_1 = s_2 = 1$ and $i_1 = i_2 = 0$ represents the disease free equilibrium. The second equilibrium which is the endemic equilibrium is $(s_1^*, i_1^*, s_2^*, i_2^*) = (1/R_0, 1 - 1/R_0, 1/R_0, 1 - 1/R_0)$. This is feasible if $R_0 > 1$. The third and fourth are

$$\frac{(\beta-\lambda)^2 - (\beta-\lambda)(\gamma+\mu)) \pm \sqrt{((\beta-\lambda)^2 - (\beta-\lambda)(\gamma+\mu))((\beta+\lambda)^2 - (\gamma+\mu)(\beta-\lambda))}}{2\beta(\beta-\lambda)}$$

and

$$\frac{(\beta-\lambda)^2 - (\beta-\lambda)(\gamma+\mu)) \mp \sqrt{((\beta-\lambda)^2 - (\beta-\lambda)(\gamma+\mu))((\beta+\lambda)^2 - (\gamma+\mu)(\beta-\lambda))}}{2\beta(\beta-\lambda)}.$$

To analyse the feasibility of the third and fourth roots we let $K = (\beta - \lambda)^2 - (\beta - \lambda)(\gamma + \mu)$ and $L = (\beta + \lambda)^2 - (\gamma + \mu)(\beta - \lambda)$, and so $L > K$. Therefore the third and fourth roots can be written as $\frac{K \pm \sqrt{KL}}{2\beta(\beta-\lambda)}$ and $\frac{K \mp \sqrt{KL}}{2\beta((\beta-\lambda)}$ respectively. It is important to note that the equilibrium is feasible if both roots are real and positive and ≤ 1.

Follow similar arguments as in section 4.2.1 and analysing the roots $\frac{K\pm\sqrt{KL}}{2\beta(\beta-\lambda)}$ it can be seen that

- If $KL < 0$, then we have complex roots and these are not feasible.
- If $KL > 0$ and $K > 0$, then $K < L$ which implies

$$K^2 < KL$$

$$\Rightarrow K < \sqrt{KL}$$

$$\Rightarrow K - \sqrt{KL} < 0 \qquad \text{whereas} \qquad K + \sqrt{KL} > 0.$$

  So whatever the sign of $\beta - \lambda$, we have roots of opposite signs and therefore not feasible.

- If $KL > 0$ and $K < 0$, then $K - \sqrt{KL} < 0$. $K < 0$ implies that

$$(\beta - \lambda)^2 - (\beta - \lambda)(\gamma + \mu) < 0$$

$$\Rightarrow (\beta - \lambda)^2 < (\beta - \lambda)(\gamma + \mu)$$

$$\Rightarrow (\beta - \lambda) > 0.$$

  So $\frac{K-\sqrt{KL}}{2\beta(\beta-\lambda)} < 0$ and therefore not feasible.

- If $K = 0$ then roots 3 and 4 are equal to root 1.
- If $L = 0$ then $(\gamma + \mu)(\beta - \lambda) = (\beta + \lambda)^2 > 0$ and so $\beta > \lambda$ and $K = (\beta - \lambda)^2 - (\beta + \lambda)^2$. Thus roots 3 and 4 equal $\frac{-4\beta\lambda}{2\beta(\beta-\lambda)} = \frac{-2\lambda}{(\beta-\lambda)}$. This is negative for $\beta > \lambda$.

Therefore we reject the third and fourth equilibrium points as unfeasible.

Stability

This is a four dimensional process so we use the eigenvalues of the Jacobian matrix to determine the (local) stability of equilibrium points. A point is (locally) stable if all the eigenvalues have negative real parts. The Jacobian matrix is

$$\mathbf{J}(s_1, i_1, s_2, i_2) = \begin{pmatrix} -\beta i_1 - \lambda i_2 - \mu & -\beta s_1 + \gamma & 0 & -\lambda s_1 \\ \beta i_1 + \lambda i_2 & \beta s_1 - (\gamma + \mu) & 0 & \lambda s_1 \\ 0 & -\lambda s_1 & -\beta i_2 - \lambda i_1 - \mu & -\beta s_2 + \gamma \\ 0 & \lambda s_2 & \beta i_2 + \lambda i_1 & \beta s_2 - (\gamma + \mu) \end{pmatrix}.$$

At $(1,0,1,0)$,

$$\mathbf{J}(s_1,i_1,s_2,i_2) = \begin{pmatrix} -\mu & -\beta+\gamma & 0 & -\lambda \\ 0 & \beta-(\gamma+\mu) & 0 & \lambda \\ 0 & -\lambda & -\mu & -\beta+\gamma \\ 0 & \lambda & 0 & \beta-(\gamma+\mu) \end{pmatrix}.$$

Using Maple we find the eigenvalues are $\beta+\lambda-(\gamma+\mu)$, $\beta-(\gamma+\lambda+\mu)$, $-\mu$ and $-\mu$. This is (locally) stable if $(\beta+\lambda)<(\gamma+\mu)$, that is $R_0<1$. In other words, the disease free equilibrium is stable if the endemic equilibrium, $(s_1^*,i_1^*,s_2^*,i_2^*)$, is unfeasible.

At $(s_1^*,i_1^*,s_2^*,i_2^*) = \left(\frac{1}{R_0},\frac{(R_0-1)}{R_0},\frac{1}{R_0},\frac{(R_0-1)}{R_0}\right)$,

$$\mathbf{J}(s_1^*,i_1^*,s_2^*,i_2^*) = \begin{pmatrix} -\frac{(R_0-1)}{R_0}(\beta+\lambda)-\mu & -\frac{\beta}{R_0}+\gamma & 0 & -\frac{\lambda}{R_0} \\ \frac{(R_0-1)}{R_0}(\beta+\lambda) & \frac{\beta}{R_0}-(\gamma+\mu) & 0 & \frac{\lambda}{R_0} \\ 0 & -\frac{\lambda}{R_0} & -\frac{(R_0-1)}{R_0}(\beta+\lambda)-\mu & -\frac{\beta}{R_0}+\gamma \\ 0 & \frac{\lambda}{R_0} & \frac{(R_0-1)}{R_0}(\beta+\lambda) & \frac{\beta}{R_0}-(\gamma+\mu) \end{pmatrix}.$$

Again using Maple gives the eigenvalues as $-\frac{R_0(\mu+\gamma+\lambda+\beta)-2\beta}{R_0}$,$\gamma+\mu-(\beta+\lambda)$,$-\mu$ and $-\mu$. These are all less than 0 if $(\beta+\lambda)>(\gamma+\mu)$, that is $R_0>1$. So the endemic equilibrium is (locally) stable if it is feasible.

For the two-group model without demography, we were able to demonstrate (section 4.2.2) global asymptotic stability of the endemic equilibrium, when $R_0>1$. In this case we have only demonstrated local stability; this is still sufficient to conclude that (for $R_0>1$) if the process $(I_1(t),I_2(t))$ is initially close to $N(i_1^*,i_2^*)$ then it will tend to stay close to $N(i_1^*,i_2^*)$ for a considerable time, subject to small random fluctuations.

6.2 Conditioning on non-extinction

The state probabilities conditioned on not being absorbed (on the states (s_1,i_1,s_2,i_2) with at least one of i_1 and i_2 greater than 0) will be denoted by $q_{s_1,i_1,s_2,i_2}(t)$. They can be determined from the unconditioned probabilities $p_{s_1,i_1,s_2,i_2}(t)$ via the relation

$$\begin{aligned} q_{s_1,i_1,s_2,i_2}(t) &= P((S_1(t),I_1(t),S_2(t),I_2(t))=(s_1,i_1,s_2,i_2)|(I_1(t),I_2(t))\neq(0,0)) \\ &= \frac{p_{s_1,i_1,s_2,i_2}(t)}{1-p_{\cdot,0,\cdot,0}(t)}. \end{aligned} \tag{6.6}$$

where $p_{.,i_1,.,i_2}(t)$ denotes the marginal distribution of the number of infected individuals in population 1 and population 2 at time t.

$$p_{.,i_1,.,i_1} = \sum_{s_1=0}^{\infty}\sum_{s_2=0}^{\infty} p_{s_1,i_1,s_2,i_2}(t) = P(I_1(t) = i_1, I_2(t) = i_2).$$

Differentiating equation (6.6) and using the equation $\dot{p}_{.,0,.,0}(t) = \gamma p_{.,1,.0}(t) + \gamma p_{.0,.,1}(t)$, which is obtained by setting $i_1 = 0$, $i_2 = 0$ in equation (6.1) and summing over all possible values of s_1 and s_2, gives

$$\dot{q}_{s_1,i_1,s_2,i_2}(t) = \frac{\dot{p}_{s_1,i_1,s_2,i_2}(t)}{1 - p_{.,0,.,0}(t)} + \gamma(q_{.,1,.0}(t) + q_{.,0,.,1}(t))\frac{p_i(t)}{1 - p_{.,0,.,0}(t)}.$$

The Kolmogorov forward equation (6.1) for the state probabilities $p_{s_1,i_1,s_2,i_2}(t)$ can be used to derive the differential equations for the conditional state probabilities $q_{s_1,i_1,s_2,i_2}(t)$.

$$\begin{aligned}
\frac{dq_{s_1,i_1,s_2,i_2}}{dt} &= \beta_1(s_1+1, i_1-1, s_2, i_2)q_{s_1+1,i_1-1,s_2,i_2}(t) - \beta_1(s_1, i_1, s_2, i_2)q_{s_1,i_1,s_2,i_2}(t) \\
&+\lambda_1(s_1-1, i_1, s_2, i_2)q_{s_1-1,i_1,s_2,i_2}(t) - \lambda_1(s_1, i_1, s_2, i_2)q_{s_1,i_1,s_2,i_2}(t) \\
&+\mu_1(s_1+1, i_1, s_2, i_2)q_{s_1+1,i_1,s_2,i_2}(t) - \mu_1(s_1, i_1, s_2, i_2)q_{s_1,i_1,s_2,i_2}(t) \\
&+\gamma_1(s_1-1, i_1+1, s_2, i_2)q_{s_1-1,i_1+1,s_2,i_2}(t) - \gamma_1(s_1, i_1, s_2, i_2)q_{s_1,i_1,s_2,i_2}(t) \\
&+\beta_2(s_1, i_1, s_2+1, i_2-1)q_{s_1,i_1,s_2+1,i_2-1}(t) - \beta_2(s_1, i_1, s_2, i_2)q_{s_1,i_1,s_2,i_2}(t) \\
&+\mu_2(s_1, i_1+1, s_2, i_2)q_{s_1,i_1+1,s_2,i_2}(t) - \mu_2(s_1, i_1, s_2, i_2)q_{s_1,i_1,s_2,i_2}(t) \\
&+\lambda_2(s_1, i_1, s_2-1, i_2)q_{s_1,i_1,s_2-1,i_2}(t) - \lambda_2(s_1, i_1, s_2, i_2)q_{s_1,i_1,s_2,i_2}(t) \\
&+\mu_3(s_1, i_1, s_2+1, i_2)q_{s_1,i_1,s_2+1,i_2}(t) - \mu_3(s_1, i_1, s_2, i_2)q_{s_1,i_1,s_2,i_2}(t) \\
&+\gamma_2(s_1, i_1, s_2-1, i_2+1)q_{s_1,i_1,s_2-1,i_2+1}(t) - \gamma_2(s_1, i_1, s_2, i_2)q_{s_1,i_1,s_2,i_2}(t) \\
&+\mu_4(s_1, i_1, s_2, i_2+1)q_{s_1,i_1,s_2,i_2+1}(t) - \mu_4(s_1, i_1, s_2, i_2)q_{s_1,i_1,s_2,i_2}(t) \\
&+(\gamma q_{.,1,.0}(t) + \gamma q_{.,0,.,1}(t))q_{s_1,i_1,s_2,i_2}(t). \qquad (6.7)
\end{aligned}$$

with $q_{s_1,i_1,s_2,i_2} = 0$ for $(s_1, i_1, s_2, i_2) \notin D$ The quasi-stationary distribution q_{s_1,i_1,s_2,i_2} is the stationary solution of this system of differential equations. Analytic solutions are not possible so we will approximate the quasi-stationary distribution using a diffusion approximation.

6.3 Diffusion approximation

Since analytic solution to (6.7) is not available we now derive the diffusion approximation of the quasi-stationary distribution. The diffusion approximation has a continuous state space, in contrast with the discrete state space of the original process. The approximation is based on the restriction that R_0 is strictly larger than 1 and N is large. Here we approximate the quasi-stationary distribution by a multivariate normal distribution.

We study the fluctuation around the endemic deterministic equilibrium. The changes in the scaled state variable s_1, i_1, s_2 and i_2 during a small interval of time $[t, t+\delta t]$ will be denoted by δs_1, δi_1, δs_2 and δi_2 respectively, where $\delta s_1 = s_1(t+\delta t) - s_1(t)$, $\delta i_1 = i_1(t+\delta t) - i_1(t)$, $\delta s_2 = s_2(t+\delta t) - s_2(t)$ and $\delta i_2 = i_2(t+\delta t) - i_2(t)$. We can determine the mean and the covariance of the vector of changes in the state variables from the hypotheses of the original process (Table 6.1). Starting with the mean:

$$\begin{aligned} E\begin{pmatrix} \delta s_1 \\ \delta i_1 \\ \delta s_2 \\ \delta i_2 \end{pmatrix} &= \begin{pmatrix} \mu - (\beta i_1 + \lambda i_2)s_1 + \gamma i_1 - \mu s_1 \\ (\beta i_1 + \lambda i_2)s_1 - (\gamma + \mu)i_1 \\ \mu - (\beta i_2 + \lambda i_1)s_2 + \gamma i_2 - \mu s_2 \\ (\beta i_2 + \lambda i_1)s_2 - (\gamma + \mu)i_1 \end{pmatrix} \delta t + o(\delta t) \\ &= E(s_1, i_1, s_2, i_2)\delta t + o(\delta t). \end{aligned}$$

The Jacobian matrix or local drift matrix of this process evaluated at $(s_1^*, i_1^*, s_2^*, i_2^*)$ is given above (section 6.1) so we move on to define the covariance matrix. The covariance matrix of the vector of changes in the state variables during the time interval $(t, t+\delta)$ is given by

$$\begin{aligned} \mathrm{Cov}\begin{pmatrix} \delta s_1 \\ \delta i_1 \\ \delta s_2 \\ \delta i_2 \end{pmatrix} &= \begin{pmatrix} \mu + (\beta i_1 + \lambda i_2)s_1 + \gamma i_1 + \mu s_1 & -(\beta s_1 + \gamma)i_1 - \lambda i_2 s_1 \\ -(\beta s_1 + \gamma)i_1 - \lambda i_2 s_1 & (\beta i_1 + \lambda i_2)s_1 + (\gamma + \mu)i_1 \\ 0 & 0 \\ 0 & 0 \end{pmatrix} \\ &\quad \begin{pmatrix} 0 & 0 \\ 0 & 0 \\ \mu + (\beta i_2 + \lambda i_1)s_2 + \gamma i_2 + \mu s_2 & -(\beta s_2 + \gamma)i_2 - \lambda i_1 s_2 \\ -(\beta s_2 + \gamma)i_2 - \lambda i_1 s_2 & (\beta i_2 + \lambda i_1)s_2 + (\gamma + \mu)i_2 \end{pmatrix} \delta t + o(\delta t) \\ &= \mathbf{G}(s_1, i_1, s_2, i_2)\delta t + o(\delta t). \end{aligned}$$

We can approximate the $\mathbf{G}(s_1, i_1, s_2, i_2)$ matrix close to the deterministic equi-

librium by evaluating it at the critical point $(s_1^*, i_1^*, s_2^*, i_2^*)$.

The process $\sqrt{N}((s_1(t), i_1(t), s_2(t), i_2(t)) - (s_1^*, i_1^*, s_2^*, i_2^*))$ may be approximated by a four dimensional Ornstein-Uhlenbeck process with local drift matrix $\mathbf{J}(s_1^*, i_1^*, s_2^*, i_2^*)$ and local covariance matrix $\mathbf{G}(s_1^*, i_1^*, s_2^*, i_2^*)$. The quasi-stationary distribution can be approximated by the stationary distribution of this Ornstein-Uhlenbeck process. We can find the covariance matrix, Σ, for the stationary distribution of the Ornstein-Uhlenbeck process by solving (4.8) with expressions for $\mathbf{J}(s_1^*, i_1^*, s_2^*, i_2^*)$ and $\mathbf{G}(s_1^*, i_1^*, s_2^*, i_2^*)$. However, the result is rather messy and not illuminating so we use numerical values to evaluate the result. Using the following parameters: $\mu = 1/70$, $\beta = 15$, $\gamma = 5$, $\lambda = 2$ and $R_0 \approx 3.4$, we have

$$\begin{pmatrix} s_1^* \\ i_1^* \\ s_2^* \\ i_2^* \end{pmatrix} = \begin{pmatrix} 0.294958 \\ 0.705042 \\ 0.294958 \\ 0.705042 \end{pmatrix},$$

$$\Sigma = \begin{pmatrix} 0.2860539 & -0.2409595 & 0.0092552 & -0.0539985 \\ -0.2409595 & 1.1958651 & -0.0539985 & 0.098742 \\ 0.0092552 & -0.0539985 & 0.2860539 & -0.2409595 \\ -0.0539985 & 0.098742 & -0.2409595 & 1.1958651 \end{pmatrix}.$$

This multivariate normal distribution can only provide a reasonable approximation to the quasi-stationary distribution if most of its probability mass is concentrated in the positive quadrant. Since 95% of the probability of a normal distribution lies within two standard deviations of the mean, we require the mean numbers of susceptibles and infectives in each population to be more than two standard deviations for the approximation to be valid. Since the two populations are symmetric we can analyses population one. Using the same parameter values, for susceptibles we require $0.294958N > 2\sqrt{0.2860539N}$, that is, $N > 13$. For infectives, we need $0.705042N > 2\sqrt{1.1958651N}$, that is $N > 9$. So for our normal approximation to be plausible then the expected population size for each population should be greater than 13.

6.4 Numerical results

We now run a numerical simulation of the stochastic model and compare this with the result we obtained from the diffusion approximation. The parameter values used

are $N = 200$, $\beta = 15$, $\lambda = 2$, $\mu = 1/70$, $\gamma = 5$ and $R_0 \approx 3.4$. Figure 6.1 shows the simulation result and the diffusion approximation. It can be seen that the two give similar results for these parameter values.

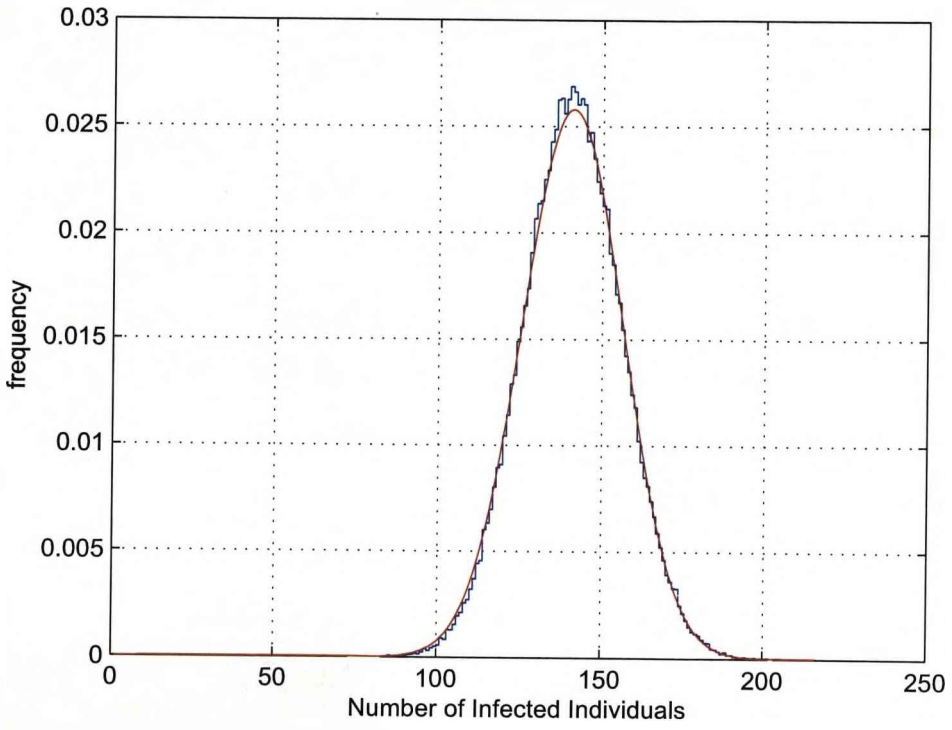

Figure 6.1: The quasi-stationary distribution of the number of infected individuals in each population. The blue solid line is the simulation. The red solid line is the Ornstein Uhlenbeck approximation. The parameter values are $N = 200$, $\beta = 15$, $\lambda = 2$, $\mu = 1/70$, $\gamma = 5$ and $R_0 \approx 3.4$. Simulation is run for 20 time units and for 100,000 iterations.

6.5 Conclusion

In this chapter a two group SIS model with demography is formulated and analysed. Since explicit solution is not possible, we approximate the quasi-stationary distribu-

tion using diffusion approximation. The inclusion of demography makes the model more complicated and leads to complicated results.

First we analysed the deterministic case by working out the equilibrium of the differential equations describing the model. It is shown that these equations have four equilibrium points. One represents the disease free equilibrium, the other an endemic equilibrium and the last two are shown to be unfeasible. The basic reproductive number R_0 determines whether the disease is eliminated or persists. We show that when $R_0 < 1$ the only feasible and stable point is the disease free equilibrium. However, when $R_0 > 1$ the endemic equilibrium is feasible and stable.

The stochastic model is formulated as a Markov process. In this model we expected that when the disease goes extinct from the two populations it will not reoccur unless an infection is reintroduced by immigration of an infective into one of the populations. However, the time to complete fade out can be long so we study the distribution of the process after it has been going on for a long time prior to extinction. In other words, we study the process conditioned on not being absorbed. We use diffusion approximation to derive an approximation for quasi-stationary mean and variance. As stated earlier, the inclusion of demography further complicates the model and therefore complicates the analysis of the diffusion approximation. The result obtained is complicated so numerical values are used. We run a simulation and compare the result with the result obtained from the diffusion approximation. The shape of the quasi-stationary distribution appears to be approximately normal for $R_0 > 1$ and N large.

We did not work out the exact quasi-stationary distribution (left eigenvector of the reduced transition rate matrix) because the transition rate matrix is infinite. We also did not derive cumulant equations and therefore did not use moment closure method because it is very messy and complicated. However, similar methods to those applied to other models should yield corresponding results. We also haven't proved absorption, but similar methods to other chapters (5 and later 7) should work.

Chapter 7

SIRS Model

In this chapter we analyse the SIRS (Susceptible-Infective-Removed-Susceptible) model without demography and the SIRS model with demography. The 'Removed' state describes individuals who have been infected and are now temporarily immune from further infection. Thus the SIRS model describes the situation where immunity is temporary.

For the SIRS model, the population is divided into three classes - susceptibles, infected and recovered (removed), and the numbers of individuals in theses classes are written as S, I and R respectively. The letters S, I, R and S refer to the successive state the individual can be in, i.e., susceptible, infective, recovered and susceptible respectively. The SIRS model without demography may be modelled as 2-dimensional processes, whereas the SIRS model with demography is modelled as a 3-dimensional process, leading to considerably more involved algebra. Here we assume that the rate at which removed individuals lose their immunity and return to the susceptible class is proportional to the number of removed individuals with proportionality constant ν. So the average period of immunity is $1/\nu$. Note that when $\nu = 0$, we get the SIR model and when ν tends to infinity we get the SIS model.

This chapter is divided into three sections. The first section looks at a closed SIRS model without demography. In the second section we analyse the SIRS model with demography. In each of these sections we develop deterministic and stochastic formulations of the model. We first analyse the deterministic model. We then use a diffusion approximation (Ornstein-Uhlenbeck process) to approximate the quasi-stationary distribution of the stochastic model. We then derive cumulant equations

and use a moment closure approximation to work out the means, variances and covariances of the numbers of susceptible, infected and recovered individuals at quasi-stationarity. These approximations are then compared with the results obtained from numerical simulation of the stochastic model. Concluding remarks are given in the final section.

7.1 SIRS model without demography

We formulate the SIRS model first without demography. This model has three variables, namely the number of susceptible individuals $S(t)$, the number of infected individuals $I(t)$ and the number of recovered individuals $R(t)$ at time t. These take values in the state space $\{(s,i,r) : \quad s = 0,1,2,\ldots, \quad i = 0,1,2,\ldots, \quad r = 0,1,2,\ldots, \quad s+r+i = N\}$. The assumption here is that the population size N is constant. Since the population size is constant, we replace $R(t)$ by $N-I(t)-S(t)$ and concentrate on the changes of the numbers of susceptible individuals and infected individuals. Therefore, the stochastic model is a bivariate continuous-time Markov chain with state space $C = \{(s,i) : s = 0,1,2,\ldots,N,\ i = 0,1,2,\ldots,N,\ s+i \leq N\}$. The state probabilities at time t will be denoted as

$$p_{s,i}(t) = P\{S(t) = s, I(t) = i\}.$$

In this model there are three possible transitions, i.e. infection of a susceptible individual, recovery of an infected individual and a recovered individual becoming susceptible again, with rates given in Table 7.1

Table 7.1: The transition rates for the model are given as:

Event	State Transition	Transiton Rate
Infection of a susceptible	$(s,i) \to (s-1, i+1)$	$\beta_1(s,i) = \frac{\beta}{N} si$
Recovery of an infective	$(s,i,r) \to (s, i-1, r+1)$	$\gamma_2(s,i) = \gamma i$
Loss of immunity	$(s,i) \to (s+1, i)$	$\nu_3 = \nu(N-s-i)$

All states where the number of infected individuals is positive are transient, while the set of states $A = \{(s,0) : s = 0,1,2,\ldots,N\}$ forms an absorbing set. Furthermore, once the process enters the set A then the only transitions which can occur are loss of immunity events, and with probability 1 the process will ultimately

be absorbed at the state $(s,i) = (N,0)$. Since the state space is finite, there exists a unique quasi-stationary distribution supported on the set $D = C \setminus A$. Provided that the initial distribution is supported on D then this quasi-stationary distribution is the unique limiting conditional distribution.

The Kolmogorov forward equations for the state probabilities $p_{s,i}(t) = P\{S(t) = s, I(t) = i\}$ can be written as

$$\begin{aligned} \dot{p}_{s,i}(t) &= \beta_1(s+1,i-1)p_{s+1,i-1}(t) + \gamma_2(s,i+1)p_{s,i+1}(t) \\ &\quad +\nu_3(s-1,i)p_{s-1,i}(t) - k(s,i)p_{s,i}(t) \end{aligned} \tag{7.1}$$

for $s = 0,1,2,\ldots,N$, $i = 0,1,2,\ldots,N$, $s+i \leq N$ and where $k(s,i) = \beta_1(s,i) + \gamma_2(s,i) + \nu_3(s,i)$. Since s and i must be non-negative, we define $p_{s,i}(t)$ to be zero if any of s or i is negative.

7.1.1 Deterministic model

To derive a deterministic approximation of the stochastic version of the model, we introduce the scaling $s = \frac{S}{N}$ and $i = \frac{I}{N}$ and reparametrise the model by introducing the following new parameters: R_0, the basic reproduction number defined as the ratio of the contact rate β to the recovery rate γ and η_1, denoting the ratio of the loss of immunity rate ν to the recovery rate γ.

$$R_0 = \frac{\beta}{\gamma},$$

$$\eta_1 = \frac{\nu}{\gamma}.$$

The differential equations for the deterministic version of the model are then

$$\frac{ds}{dt} = \gamma(\eta_1(1-s-i) - R_0 si), \tag{7.2}$$

$$\frac{di}{dt} = \gamma(R_0 s - 1)i. \tag{7.3}$$

This system of equations has two critical points, one at (s,i)=(1,0), which corresponds to the absence of infection. The other critical point corresponds to the endemic infection level and is given by

$$(s^*, i^*) = \left(\frac{1}{R_0}, \frac{\eta_1(R_0-1)}{R_0(1+\eta_1)}\right). \tag{7.4}$$

The equilibrium (s^*, i^*) is feasible if $R_0 > 1$.

When $\nu = 0$ then $\eta_1 = 0$ and therefore

$$(s^*, i^*) = \left(\frac{1}{R_0}, 0\right)$$

which is one of the steady states of the SIR model. Note that the SIR model without demography has equilibrium points at $(s, 0)$ for every $s \in [0, 1]$.

On the other hand, when $\nu \to \infty$ we get

$$(s^*, i^*) = \left(\frac{1}{R_0}, \frac{R_0 - 1}{R_0}\right)$$

the endemic equilibrium of the SIS model without demography.

Thus we see that the introduction of the loss of immunity allows the disease to settle to an endemic equilibrium. However, the number of infected individuals in the endemic equilibrium is less than those in the SIS model. This seems natural since the period of immunity reduces the number of susceptible-infective pairs available, and so infectious contact will occur at a slower rate.

Stability

For (local) stability we use the Jacobian matrix to determine the stability of the equilibrium.

$$\mathbf{J}(s, i) = \begin{pmatrix} -\gamma(\eta_1 + R_0 i) & -\gamma(\eta_1 + R_0 s) \\ \gamma R_0 i & \gamma(R_0 s - 1) \end{pmatrix}.$$

At (1,0)

$$\mathbf{J}(1, 0) = \begin{pmatrix} -\gamma\eta_1 & -\gamma(\eta_1 + R_0) \\ 0 & \gamma(R_0 - 1) \end{pmatrix}.$$

The trace is $\gamma(R_0 - 1 - \eta_1)$. This is less than 0 if $R_0 < 1 + \eta_1$. The determinant is $-\gamma^2\eta_1(R_0 - 1)$, which is less than 0 if $R_0 > 1$. For (local) stability, we need the trace to be negative and the determinant positive. Therefore $(1, 0)$ is unstable for $R_0 > 1$. At $(s^*, i^*) = \left(\frac{1}{R_0}, \frac{\eta_1(R_0-1)}{R_0(1+\eta_1)}\right)$,

$$\mathbf{J}(s^*, i^*) = \begin{pmatrix} -\gamma\left(\eta_1 + \frac{\eta_1(R_0-1)}{(1+\eta_1)}\right) & -\gamma(\eta_1 + 1) \\ \frac{\eta_1(R_0-1)}{\gamma(1+\eta_1)} & 0 \end{pmatrix}.$$

The trace is $-\gamma\eta_1\left(1 + \frac{(R_0-1)}{(1+\eta_1)}\right)$. This is less than 0 if $R_0 > 1$. The determinant is $\eta_1(R_0 - 1)$ which is greater than 0 if $R_0 > 1$. Therefore (s^*, i^*) is (locally) stable if it is feasible.

To prove global stability of the endemic equilibrium of our model (7.1) - (7.2) in the case $R_0 > 1$ we start rewriting the system by substitution $(s, i) \rightarrow (x, i)$, using the transformation $x = s + \frac{\nu}{\beta}$. Therefore, our system (7.1) - (7.2) become

$$\frac{dx}{dt} = \nu(\kappa - x) - \beta x i, \tag{7.5}$$

$$\frac{di}{dt} = \beta x i - \varrho i \tag{7.6}$$

where $\kappa = \frac{\beta+\nu}{\beta}$ and $\varrho = \nu + \gamma$. The new system has endemic equilibrium at

$$x^* = \frac{\kappa}{\hat{R}_0}, \quad i^* = \frac{\nu\kappa}{\varrho}\left(1 - \frac{1}{\hat{R}_0}\right)$$

where $\hat{R}_0 = \frac{\beta\kappa}{\varrho}$. From (7.5) - (7.6) it follows that

$$\beta x^* i^* = \nu(\kappa - x^*) = \varrho i^*. \tag{7.7}$$

at steady state. To show that (x^*, i^*) is globally stable and hence (s^*, i^*) is globally stable we consider the following Lyapunov function

$$V(x, i) = x - x^* - x^* \ln \frac{x}{x^*} + i - i^* - i^* \ln \frac{i}{i^*}. \tag{7.8}$$

The partial derivatives of equation (7.8) are

$$\frac{\partial V(x, i)}{\partial x} = 1 - \frac{x^*}{x} \tag{7.9}$$

and

$$\frac{\partial V(x, i)}{\partial i} = 1 - \frac{i^*}{i}. \tag{7.10}$$

Now

$$\frac{dV(x, i)}{dt} = \frac{\partial V(x, i)}{\partial x}\frac{dx}{dt} + \frac{\partial V(x, i)}{\partial i}\frac{di}{dt} \tag{7.11}$$

and substituting equations (7.5), (7.6), (7.9) and (7.10) into equation (7.11) gives

$$\begin{aligned} \frac{dV(x, i)}{dt} &= \nu\kappa - \nu x - \beta x i - \nu\frac{x^*}{x} + \nu x^* + \beta x^* i \\ &\quad + \beta x i - \beta x i^* - \varrho i + \varrho i^*. \end{aligned} \tag{7.12}$$

Using equation (7.7), equation (7.12) can be simplified to

$$\begin{aligned} \frac{dV(x, i)}{dt} &= \nu\kappa\left(2 - \frac{x^*}{x} - \frac{x}{x^*}\right) \\ &= -\nu\kappa\frac{x^*}{x}\left(1 - \frac{x}{x^*}\right)^2. \end{aligned}$$

Therefore $\frac{dV(x,i)}{dt} \leq 0$ holds for all $x, i > 0$. The equality $\frac{dV(x,i)}{dt} = 0$ holds only when $x = x^*$ and the point (x^*, i^*) is the only invariant set of the system (7.5), (7.6)) on this line. Therefore by asymptotic stability theorem (Barbashin (1970), page 28 or La Salle and Lefschetz (1961), page 58) the equilibrium (s^*, i^*) is globally asymptotically stable in the positive region $s, i > 0$.

7.1.2 Conditioning on non-extinction

We now study the process conditioned on not being absorbed (the number of infectives hitting zero). By conditioning on non-extinction, we can define a new stochastic process that is related, via the extinction process, to the unconditioned process. The state probabilities conditioned on not being absorbed are denoted by $q_{s,i}(t)$. They can be determined from the unconditioned probabilities $p_{s,i}(t)$ via the relation

$$\begin{aligned} q_{s,i}(t) &= P((S(t), I(t)) = (s,i) | I(t) \neq 0) \\ &= \frac{p_{s,i}(t)}{1 - p_{.,0}(t)} \end{aligned} \tag{7.13}$$

where $p_{.,i}(t)$ is the marginal distribution of the number of infected individual at time t and is given by

$$p_{.,i} = \sum_{s=0}^{N-i} p_{s,i}(t) = P(I(t) = i).$$

Taking equation (7.1) and summing for $i = 0$ over all s values we have

$$\dot{p}_{.,0}(t) = \gamma p_{.,1}(t). \tag{7.14}$$

Differentiating equation (7.13) and using (7.14) gives

$$\dot{q}_{s,i_i}(t) = \frac{\dot{p}_{s,i}(t)}{1 - p_{.,0}(t)} + \gamma p_{.,1}(t) \frac{p_i(t)}{(1 - p_{.,0}(t))^2}$$

The Kolmogorov forward equations (7.1) for the state probabilities $p_{s,i}(t)$ can be used to derive the differential equations for the conditional state probabilities $q_{s,i}(t)$,

$$\begin{aligned} \frac{dq_{s,i}}{dt} &= \beta_{1(s+1,i-1)} q_{s+1,i-1}(t) + \gamma_{2(s,i+1)} q_{s,i+1}(t) + \nu_{3(s-1,i)} q_{s-1,i}(t) - \beta_{1(s,i)} q_{s,i}(t) \\ &\quad - \gamma_{2(s,i)} q_{s,i}(t) - \nu_{3(s,i)} q_{i_1,i_2-1}(t) + \gamma q_{.,1} q_{s,i}(t), \end{aligned} \tag{7.15}$$

for $s = 0, 1, \ldots, N, \quad i = 1, 2, \ldots, N - s$. The quasi-stationary distribution $q_{s,i}$ is the stationary solution of this system of differential equations. Since analytic solution of this is not possible, we will use diffusion approximation and cumulant equations to approximate the quasi-stationary distribution.

7.1.3 Diffusion approximation

The changes in the scaled state variables s and i during the time interval from t to $t+\delta t$ are denoted by δs and δi, where $\delta s = s(t+\delta t) - s(t)$ and $\delta i = i(t+\delta t) - i(t)$. From the original process we can determine the mean and the covariance with components δs and δi. For the mean:

$$\begin{aligned} E\begin{pmatrix} \delta s \\ \delta i \end{pmatrix} &= \begin{pmatrix} \gamma(\eta_1(1-s-i) - R_0 si) \\ \gamma(R_0 si - i) \end{pmatrix} \delta t + o(\delta t) \\ &= E(s,i)\delta t + o(\delta t). \end{aligned}$$

The Jacobian matrix $\mathbf{J}(s,i)$ is defined above so we move on to define the covariance matrix. The covariance matrix of the vector of changes in the state variables during the time interval $(t, t+\delta)$ is given by

$$\begin{aligned} Cov\begin{pmatrix} \delta s \\ \delta i \end{pmatrix} &= \begin{pmatrix} \gamma(\eta_1(1-s-i) + R_0 si) & -\gamma R_0 si \\ -\gamma R_0 si & \gamma(R_0 si + i) \end{pmatrix} \delta t + o(\delta t) \\ &= \mathbf{G}(s,i)\delta t + o(\delta t). \end{aligned}$$

We can approximate the $\mathbf{G}(s,i)$ matrix close to the deterministic equilibrium by evaluating it at the critical point (s^*, i^*).

$$\mathbf{G}(s^*, i^*) = \frac{\gamma(R_0 - 1)\eta_1}{R_0(1+\eta_1)} \begin{pmatrix} 2 & -1 \\ -1 & 2 \end{pmatrix}.$$

We find the covariance matrix Σ by solving (4.8) with expressions for $\mathbf{J}(s^*, i^*)$ and $\mathbf{G}(s^*, i^*)$, yielding

$$\Sigma = \begin{pmatrix} \frac{\eta_1(R_0-1)+(1+\eta_1)^2}{\eta_1(R_0+\eta_1)R_0} & -\frac{1}{R_0} \\ -\frac{1}{R_0} & \frac{\eta_1(R_0+\eta_1)^2+(\eta_1+1)(R_0-1)}{(1+\eta_1)^2(R_0+\eta_1)R_0} \end{pmatrix}.$$

Therefore for $R_0 > 1$ and N sufficiently large, the distributions of the numbers of susceptible and infected individuals in quasi-stationarity is approximately bivariate normal with mean (μ_S, μ_I) and variances

$$\begin{pmatrix} \sigma_S^2 & \sigma_{SI} \\ \sigma_{SI} & \sigma_I^2 \end{pmatrix},$$

where

$$\mu_S = \frac{N}{R_0}, \tag{7.16}$$

$$\sigma_S^2 = \frac{N((\eta_1(R_0-1)+(1+\eta_1)^2))}{\eta_1(R_0+\eta_1)R_0}, \tag{7.17}$$

$$\mu_I = \frac{\eta_1(R_0-1)N}{R_0(1+\eta_1)}, \tag{7.18}$$

$$\sigma_I^2 = \frac{N(\eta_1(R_0+\eta_1)^2+(\eta_1+1)(R_0-1))}{(1+\eta_1)^2(R_0+\eta_1)R_0}. \tag{7.19}$$

$$\sigma_{SI} = \frac{-N}{R_0}. \tag{7.20}$$

7.2 Time to extinction

We have already seen from expression (7.4) that an increase in the average immune period (decrease in η_1), with R_0 held fixed, leads to lower equilibrium infection prevalence. Using the diffusion approximation we can now study the effect of the immune period upon time to fade-out of infection. More precisely, the time to absorption at A starting from quasi-stationarity, is exponentially distributed with mean $(\gamma q_{\cdot,1})^{-1}$, since at quasi-stationarity this is the (constant) hazard rate of absorption at A. Thus an increase in $q_{\cdot,1}$, the quasi-stationary marginal probability that $I = 1$, corresponds to a decrease in the mean time to extinction or more rapid fade-out of infection. For $R_0 > 1$, when the marginal quasi-stationary distribution of I is approximately normal, an increase in $q_{\cdot,1}$ roughly corresponds to an increase in the coefficient of variation of this marginal distribution. Thus, we will use the coefficient of variation (CV_I) to analyse the prevalence of the disease. A large coefficient of variation can give rise to a high probability of low prevalence. In other words, when the coefficient of variation is large we expect a rapid extinction of the disease process. This can happen if the immune period is long, which means η_1 is small. We will start by analysing the change in expected number of infectives with respect to η_1.

From (7.18),

$$\frac{d\mu_I}{d\eta_1} = \frac{(R_0-1)N}{R_0(1+\eta_1)^2}.$$

This is greater than zero for $R_0 > 1$. This means that if the immune period is short (η_1 is high) then there is a high average prevalence (μ_I is high). Now

$$CV_I = \frac{\sigma_I}{\mu_I}.$$

Due to the complicated nature of CV_I because of the square root of the variance we will work with CV_I^2. We find from the expressions (7.18) and (7.19) that

$$\begin{aligned} CV_I^2 &= \frac{NR_0^2(1+\eta_1)^2(\eta_1(R_0+\eta_1)^2+(\eta_1+1)(R_0-1))}{\eta_1^2(R_0-1)^2N^2(1+\eta_1)^2(R_0+\eta_1)R_0} \\ &= \frac{R_0(\eta_1(R_0+\eta_1)^2+(\eta_1+1)(R_0-1))}{N\eta_1^2(R_0-1)^2(R_0+\eta_1)}, \end{aligned}$$

so that

$$\frac{d}{d\eta_1}(CV_I^2) = -\frac{R_0[2(R_0-1)(R_0+\eta_1+\eta_1^2)+\eta_1(R_0^2(R_0+1)-1)\eta_1^2R_0(2R_0+\eta_1)]}{N\eta_1^3(R_0-1)^2(R_0+\eta_1)^2}$$

This is less than 0 for $R_0 > 1$, which implies that the probability I is close to zero decreases as η_1 increases. That is, any decrease in average immune period, for fixed $R_0 > 1$, corresponds to an increase in expected time to extinction of infection from the population.

7.2.1 Cumulant equations

We now derive differential equations for the cumulant. The system of differential equations (7.15) can be used to derive a partial differential equation for the moment generating function M defined by

$$M(\theta_1,\theta_2,t) = E[e^{S\theta_1+I\theta_2}|I>0] = \sum_{s=0}^{N}\sum_{i=1}^{N-s} q_{s,i}e^{s\theta_1+i\theta_2} \qquad \theta_1,\theta_2 \in \mathbb{R}.$$

Multiplying equations (7.15) by $\exp(s\theta_1 + i\theta_2)$ and taking the sum $s = 0, 1, 2, \ldots N$ and $i = 1, 2, \ldots N - s$ and simplifying (see Appendix D) we have

$$\begin{aligned} \frac{\partial M}{\partial t} &= \frac{\beta}{N}(e^{\theta_2-\theta_1}-1)\frac{\partial^2 M}{\partial\theta_1\partial\theta_2} + \gamma(e^{-\theta_2}-1)\frac{\partial M}{\partial\theta_2} - \gamma q_{\cdot,1}\sum_{s=0}^{N} q_S(s|1)(t)e^{s\theta_1} \\ &\quad +\nu N(e^{\theta_1}-1)M - \nu(e^{\theta_1}-1)\frac{\partial M}{\partial\theta_1} - \nu(e^{\theta_1}-1)\frac{\partial M}{\partial\theta_2} + \gamma q_{\cdot,1}M \end{aligned}$$

where $q_S(s|1) = \frac{q_{s,1}}{q_{\cdot,1}}$ is the conditional probability that S takes the value s given that $I = 1$. In terms of the cumulant generating function $K(\theta_1,\theta_2,t) = logM(\theta_1,\theta_2,t)$ this becomes

$$\begin{aligned} \frac{\partial K}{\partial t} &= \frac{\beta}{N}(e^{\theta_2-\theta_1}-1)\left(\frac{\partial^2 K}{\partial\theta_1\partial\theta_2} + \frac{\partial K}{\partial\theta_1}\frac{\partial K}{\partial\theta_2}\right) + \gamma(e^{-\theta_2}-1)\frac{\partial K}{\partial\theta_2} \\ &\quad +\nu N(e^{\theta_1}-1) - \nu(e^{\theta_1}-1)\frac{\partial K}{\partial\theta_1} - \nu(e^{\theta_1}-1)\frac{\partial K}{\partial\theta_2} \\ &\quad -\gamma e^{-K}q_{\cdot,1}\sum_{s=0}^{N} q_S(s|1)(t)e^{s\theta_1} + \gamma q_{\cdot,1}. \end{aligned} \tag{7.21}$$

Using the definition $K(\theta_1, \theta_2, t) = \sum_{m\geq 0,\, n\geq 0,\, m+n>0} k_{m,n}(t)\ \theta_1^m\ \theta_2^n/m!\ n!$ where $k_{m,n}(t)$ denotes the (m,n)th cumulant function we derive the cumulant equations by expanding equation (7.21) in powers of θ_1 and θ_2 and equating coefficients. We only wish to consider cumulants of order up to two, but note that the expansion can be taken to higher and higher orders of cumulants. The equations for cumulants of order up to two are as follows:

$$\begin{aligned}
\dot{k}_{1,0} &= \nu N - \frac{\beta}{N}(k_{1,1} + k_{1,0}k_{0,1}) - \nu(k_{1,0} + k_{0,1}) \\
&\quad +\gamma q_{.,1}\left(k_{1,0} - E[S|I=1]\right), && (7.22)\\
\dot{k}_{0,1} &= \frac{\beta}{N}(k_{1,1} + k_{1,0}k_{0,1}) - \gamma k_{0,1} + \gamma q_{.,1} k_{0,1}, && (7.23)\\
\dot{k}_{1,1} &= \frac{\beta}{N}\left(k_{1,0}k_{1,1} - k_{1,1} - k_{1,0}k_{0,1} + k_{2,1} + k_{0,1}k_{2,0} - k_{0,1}k_{1,1} - k_{1,2} - k_{1,0}k_{0,2}\right) \\
&\quad -(\nu+\gamma)k_{1,1} + \nu k_{0,2} + \gamma q_{.,1}\left(k_{1,1} - k_{1,0}k_{0,1} + k_{0,1}E[S|I=1]\right), && (7.24)\\
\dot{k}_{2,0} &= \nu N + \frac{\beta}{N}\left(k_{1,1} + k_{1,0}k_{0,1} - 2k_{2,1} - 2k_{1,0}k_{1,1} - 2k_{0,1}k_{2,0}\right) \\
&\quad -\nu(k_{1,0} + k_{0,1} + 2k_{2,0} + 2k_{1,1}) \\
&\quad +\gamma q_{.,1}\left(k_{2,0} - k_{1,0}^2 - E[S^2|I=1] + 2k_{1,0}E[S|I=1]\right), && (7.25)\\
\dot{k}_{0,2} &= \frac{\beta}{N}\left(k_{1,1} + k_{1,0}k_{0,1} + 2k_{1,2} + 2k_{0,1}k_{1,1} + 2k_{1,0}k_{0,2}\right) + \gamma(k_{0,1} - 2k_{0,2}) \\
&\quad +\gamma q_{.,1}\left(k_{0,2} - k_{0,1}^2\right). && (7.26)
\end{aligned}$$

As in section 4.5 we allow $k_{1,2}$, $k_{2,1}$, $k_{0,3}$ and $k_{3,0}$ to grow with N, but not faster than N. With this assumption and solving the equations using Maple gives

$$\begin{aligned}
k_{1,0} &= \frac{1}{R_0}\,N + \frac{1+\eta_1}{\eta_1(R_0-1)} + O\left(\frac{1}{N}\right), && (7.27)\\
k_{0,1} &= \frac{(R_0-1)\eta_1}{R_0(1+\eta_1)}\,N - \frac{1}{R_0-1} + O\left(\frac{1}{N}\right), && (7.28)\\
k_{1,1} &= -\frac{1}{R_0}\,N + O(1), && (7.29)\\
k_{2,0} &= \frac{(R_0-1)\eta_1 + (1+\eta_1)^2}{\eta_1(R_0+\eta_1)R_0}\,N + O(1), && (7.30)\\
k_{0,2} &= \frac{\eta_1(R_0+\eta_1)^2 + (\eta_1+1)(R_0-1)}{(1+\eta_1)^2(R_0+\eta_1)R_0}\,N + O(1). && (7.31)
\end{aligned}$$

Again the variances and covariance match those calculated using the Ornstein-Uhlenbeck process, while the mean approximations are refined.

7.2.2 Numerical results

Although this model has a finite population size, it was not possible to work out the exact quasi-stationary distribution (left eigenvector of the reduced transition rate matrix) because the transition rate matrix is too large ($200000^2 \times 200000^2$). Matlab had no sufficient memory to work out the left eigenvector of the reduced transition rate matrix. So we now run a numerical simulation of the stochastic model and compare this with the results from the Ornstein-Uhlenbeck process approximation and the moment closure method applied on the cumulant equations. It can be seen from Figure 7.1 that both the Ornstein-Uhlenbeck approximation and the moment closure approximation give very good approximations of the quasi-stationary distribution for these parameter values.

7.3 SIRS model with demography

Here we study the SIRS model with demography. Like the other models, the transitions are only allowed to neighbouring states. In this model there are seven triggering events, i.e. immigration of a susceptible individual, infection of a susceptible individual, death of a susceptible individual, recovery of an infected individual, death of an infected individual, death of a recovered individual and a recovered individual becoming susceptible again. The immigration rate is taken as μN and the per-capita death rate as μ, hence the average individual lifespan is $1/\mu$ while the typical population size is N. The per-capita recovery rate is γ and so the average duration of infectiousness is $1/(\gamma + \mu)$. The loss of immunity rate is ν, so the average period of immunity is $1/(\nu + \mu)$. Finally, the transmission rate is taken to be $\beta si/N$.

The various transitions and their rates are given in Table 7.2.

Here five parameters are used, namely the typical population size N, the death rate per individual μ, the contact rate β, the recovery rate per infected individual γ and loss of immunity rate per immune individual ν. All these parameters are assumed to be strictly positive. We assume that $\gamma + \mu > 0$, which means that there must be some flow out of the infective class and $\mu + \nu > 0$ means that there must be some flow into the susceptible class.

The state space C may be partitioned as $C = A \cup D$ where the set of states

Table 7.2: The transition rates for the model are given as:

Event	State Transition	Transiton Rate
Immigration of a susceptible	$(s,i,r) \to (s+1,i,r)$	$\lambda_1(s,i,r) = \mu N$
Death of a susceptible	$(s,i,r) \to (s-1,i,r)$	$\mu_1(s,i,r) = \mu s$
Infection of a susceptible	$(s,i,r) \to (s-1,i+1,r)$	$\beta_1(s,i,r) = \frac{\beta}{N} si$
Death of an infective	$(s,i,r) \to (s,i-1,r)$	$\mu_2(s,i,r) = \mu i$
Recovery of an infective	$(s,i,r) \to (s,i-1,r+1)$	$\gamma_2(s,i,r) = \gamma i$
Death of a recovered individual	$(s,i,r) \to (s,i,r-1)$	$\mu_3(s,i,r) = \mu r$
Recovered individual becomes susceptible	$(s,i,r) \to (s+1,i,r-1)$	$\nu_3(s,i,r) = \nu r$

$A = \{(s,0,r) : s \geq 0, r \geq 0\}$ is absorbing while $D = \{(s,i,r) : s \geq 0, r \geq 0, i \geq 1\}$ is transient. If the process ever reaches A then it will be further absorbed into $A_2 = \{(s,0,0) : s \geq 0\} \subset A$, after which the population consists entirely of susceptible individuals and population size evolves according to a birth-and-death process with constant birth rate μN and linear death rate μs.

Denoting the state probabilities as $p_{s,i,r}(t) = P\{S(t) = s, I(t) = i, R(t) = r\}$, the Kolmogorov forward equations for this model can be written as

$$\begin{aligned} \dot{p}_{s,i,r}(t) &= \lambda_1(s-1,i,r)p_{s-1,i,r}(t) + \beta_1(s+1,i-1,r)p_{s+1,i-1,r}(t) \\ &\quad +\mu_1(s+1,i,r)p_{s+1,i,r}(t) + \mu_2(s,i+1,r)p_{s,i+1,r}(t) \\ &\quad +\gamma_2(s,i+1,r-1)p_{s,i+1,r-1}(t) + \mu_3(s,i,r+1)p_{s,i,r+1}(t) \\ &\quad +\nu_3(s-1,i,r+1)p_{s-1,i,r+1}(t) - k(s,i,r)p_{s,i,r}(t) \end{aligned} \tag{7.32}$$

where $k(s,i,r) = \lambda_1(s,i,r)+\mu_1(s,i,r)+\beta_1(s,i,r)+\mu_2(s,i,r)+\gamma_2(s,i,r)+\mu_3(s,i,r)+\nu_3(s,i,r)$ and $p_{s,i,r}(t) = 0$ for $(s,i,r) \notin C$.

7.3.1 Deterministic model

As in section 5.2 we derive the deterministic approximation of the stochastic version of the model by introduce the scaling $s = \frac{S}{N}$, $i = \frac{I}{N}$ and $r = \frac{R}{N}$. We reparametrise the model by introducing R_0 to denote the reproduction number defined as the ratio of the contact rate β to the sum of the recovery rate γ and the death rate μ. We also introduce η_2 to denote the ratio of the sum of the recovery rate γ and the death rate μ to the death rate μ. Finally, we introduce η_3 to denote the ratio of the sum

of the loss of immunity rate ν and the death rate μ to the death rate μ.

$$R_0 = \frac{\beta}{\gamma + \mu},$$
$$\eta_2 = \frac{\gamma + \mu}{\mu},$$
$$\eta_3 = \frac{\mu + \nu}{\mu}.$$

The differential equations for the deterministic version of the model become

$$\frac{ds}{dt} = \mu(1 + (\eta_3 - 1)r - R_0\eta_2 si - s), \tag{7.33}$$
$$\frac{di}{dt} = \mu\eta_2(R_0 si - i), \tag{7.34}$$
$$\frac{dr}{dt} = \mu((\eta_2 - 1)i - \eta_3 r). \tag{7.35}$$

Summing up the three equations (7.33) - (7.35), we have

$$\frac{ds}{dt} + \frac{di}{dt} + \frac{dr}{dt} = \mu(1 - s - i - r).$$

It follows then that

$$\lim_{t\to\infty} s + i + r = 1.$$

This system of equations (7.33) - (7.35) has two critical points, one at $(s,i,r) = (1,0,0)$, which corresponds to the absence of infection. The other critical point corresponds to the endemic infection level and is given by

$$(s^*, i^*, r^*) = \left(\frac{1}{R_0}, \frac{\eta_3(R_0 - 1)}{R_0(\eta_3 + \eta_2 - 1)}, \frac{(\eta_2 - 1)(R_0 - 1)}{R_0(\eta_3 + \eta_2 - 1)}\right).$$

The equilibrium point at (s^*, i^*, r^*) is feasible if $R_0 > 1$.

When $\nu = 0$ then $\eta_3 = 1$ and we find $(s^*, i^*) = \left(1/R_0, \frac{(R_0-1)}{R_0\eta_2}\right)$ which is the endemic equilibrium of the SIR model with demography.

On the other hand, when $\nu \to \infty$ we get $(s^*, i^*) = (1/R_0, (R_0 - 1)/R_0)$, the endemic equilibrium of the SIS model with demography.

It is important to note that the number of infected individuals in endemic equilibrium of the SIRS model is more than in the SIR model but less than in the SIS model. The introduction of loss of immunity allows for more susceptibles into the susceptible stream thus increasing susceptible-infective pairs available compared to the SIR, and so infectious contacts will occur at a faster overall rate. On the other hand, the period of immunity reduces the number of susceptible-infective pairs available compared to the SIS.

Stability

For stability of each of the critical points we analyse the eigenvalues of the Jacobian matrix evaluated at each critical point. The point is stable if the eigenvalues have negative real parts.

The Jacobian matrix is

$$\mathbf{J}(s,i,r) = \begin{pmatrix} -\mu(R_0\eta_2 i + 1) & -\mu R_0\eta_2 s & \mu(\eta_3 - 1) \\ \mu R_0\eta_2 i & \mu\eta_2(R_0 s - 1) & 0 \\ 0 & \mu(\eta_2 - 1) & -\mu\eta_3 \end{pmatrix}.$$

At $(1,0,0)$

$$\mathbf{J}(s,i,r) = \begin{pmatrix} -\mu & -\mu R_0\eta_2 & \mu(\eta_3 - 1) \\ 0 & \mu\eta_2(R_0 - 1) & 0 \\ 0 & \mu(\eta_2 - 1) & -\mu\eta_3 \end{pmatrix}.$$

The eigenvalues are $-\mu$, $\mu\eta_2(R_0 - 1)$, $-\mu\eta_3$. This is stable if $R_0 < 1$, that is, if (s^*, i^*, r^*) is unfeasible.

At $(s^*, i^*, r^*) = \left(\frac{1}{R_0}, \frac{\eta_2(R_0-1)}{R_0(\eta_3+\eta_2-1)}, \frac{(\eta_2-1)(R_0-1)}{R_0(\eta_3+\eta_2-1)}\right)$,

$$\mathbf{J}(s^*,i^*,r^*) = \begin{pmatrix} -\mu(\eta_2\frac{\eta_2(R_0-1)}{(\eta_3+\eta_2-1)} + 1) & -\mu\eta_2 & \mu(\eta_3 - 1) \\ \mu\eta_2\frac{\eta_2(R_0-1)}{(\eta_3+\eta_2-1)} & 0 & 0 \\ 0 & \mu(\eta_2 - 1) & -\mu\eta_3 \end{pmatrix}.$$

Using Maple gives one of the eigenvalues as $-\mu$. The other two are complicated but evaluating them using numerical values shows that they are negative when $R_0 > 1$ and complex when $R_0 < 1$. Therefore, it seems that the endemic equilibrium is (locally) stable when $R_0 > 1$. The question of global stability remains open.

7.3.2 Ultimate absorption

Like in section 5.3, to prove ultimate absorption, we will first prove that the $\mathbf{Q}$ matrix is regular.

Regularity

We shall now show that $\mathbf{Q}$ is regular by using the criterion proven by Reuter (1957) (theorem 6) which is stated in section 5.3. We shall follow the proof of Theorem 1 of Reuter (1961) to prove the regularity of $\mathbf{Q}$. Writing $z(s,i,r)$ for z_m as in section

5.3,

$$(\Lambda + \lambda_1(s,i,r) + \mu_1(s,i,r) + \beta_1(s,i,r) + \gamma_2(s,i,r) + \mu_2(s,i,r) + \nu_3(s,i,r)$$
$$+\mu_3(s,i,r))z(s,i,r,)$$
$$= \lambda_1(s,i,r)z(s+1,i,r) + \mu_1(s,i,r)z(s-1,i,r) + \beta_1(s,i,r)z(s-1,i+1,r)$$
$$+\gamma_2(s,i,r)z(s,i-1,r+1) + \mu_2(s,i,r)z(s,i-1,r))$$
$$+\nu_3(s,i,r)z(s+1,i,r-1) + \mu_3(s,i,r)z(s,i,r-1),$$

for $s \geq 0$, $i \geq 1$ and $r \geq 0$. We modify the process by setting $q_m = 0$ for states $m = (s,0,r)$ since when i hits zero the disease fades out of the population unless it is reintroduced. This immediately gives $\Lambda z_m = 0$ for $m = (s,0,r)$. So $z(s,0,r) = 0$. Let

$$Z_k = \max\{z(s,i,r): \quad s \geq 0, \quad i \geq 1, \quad r \geq 0, \quad s+i+r = k\}.$$

If this maximum is attained at (s_k, i_k, r_k) then

$$\begin{aligned}(\Lambda + \lambda_{1_k} + \mu_{1_k} + \beta_{1_k} + \gamma_{2_k} + \mu_{2_k} + \nu_{3_k} + \mu_{3_k})Z_k \;&\leq\; \lambda_{1_k}Z_{k+1} + \mu_{1_k}Z_{k-1} + \beta_{1_k}Z_k \\ &+\; \gamma_{2_k}Z_k + \mu_{2_k}Z_{k-1} + \nu_{3_k}Z_k \\ &+\; \mu_{3_k}Z_{k-1},\end{aligned}$$

where $\lambda_{1_k} = \lambda_1(s_k,i_k,r_k)$, $\mu_{1_k} = \mu_(s_k,i_k,r_k)$, $\beta_{1_k} = \beta_1(s_k,i_k,r_k)$, $\gamma_{2_k} = \gamma_2(s_k,i_k,r_k)$, $\mu_{2_k} = \mu_2(s_k,i_k,r_k)$, $\mu_{3_k} = \mu_3(s_k,i_k,r_k)$, $\mu_{3_k} = \mu_3(s_k,i_k,r_k)$. Rearranging we have ,

$$(Z_{k+1} - Z_k) \geq \frac{(\mu_{1_k} + \mu_{2_k} + \mu_{3_k})}{\lambda_{1_k}}(Z_k - Z_{k-1}) + \frac{\Lambda}{\lambda_{1_k}}Z_k.$$

But $\mu_{1_k} = \mu s_k$, $\mu_{2_k} = \mu i_k$, $\mu_{3_k} = \mu r_k$ and $\lambda_{1_k} = \mu N$.

So

$$(Z_{k+1} - Z_k) \geq \frac{\mu k}{\mu N}(Z_k - Z_{k-1}) + \frac{\Lambda}{\mu N}Z_k. \tag{7.36}$$

For regularity, following Reuter's (1961) theorem 1, we need

$$\sum_{k=1}^{\infty}\left(\frac{1}{\mu N} + \frac{k}{\mu N^2} + \cdots + \frac{k!}{\mu N^k}\right) = \infty. \tag{7.37}$$

So if $z(s,i,r)$ is not identically zero let k_0 be the first k for which $Z_k > 0$. Since Z_k is increasing with k, for $k \geq k_0$,

$$(Z_{k+1} - Z_k) \geq \frac{k}{N}(Z_k - Z_{k-1}) + \frac{\Lambda}{\mu N}Z_{k_0},$$

$$(Z_{k+1} - Z_k) \geq \left(\frac{1}{\mu N} + \frac{k}{\mu N^2} + \frac{k(k-1)}{\mu N^3} + \cdots + \frac{k(k-1)\ldots(k_0+1)}{\mu N^{k-k_0+1}}\right) \Lambda Z_{k_0} + \frac{k(k-1)\ldots k_0}{N^{k-k_0+1}}(Z_{k_0} - Z_{k_0-1}).$$

Let $B = \Lambda Z_{k_0}$. Then

$$(Z_{k+1} - Z_k) \geq B\left(\frac{1}{\mu N} + \frac{k}{\mu N^2} + \frac{k(k-1)}{\mu N^3} + \cdots + \frac{k(k-1)\ldots(k_0+1)}{\mu N^{k-k_0+1}}\right).$$

Summing both sides over all values of k we have

$$\sum_{k=1}^{\infty}(Z_{k+1} - Z_k) \geq B\sum_{k=1}^{\infty}\left(\frac{1}{\mu N} + \frac{k}{\mu N^2} + \frac{k(k-1)}{\mu N^3} + \cdots + \frac{k(k-1)\ldots 2}{\mu N^k}\right).$$

It follows from condition (7.37) above that $\sum_{k=1}^{\infty}(Z_{k+1} - Z_k)$ diverges so that $Z_k \to \infty$, which is contrary to the assumption made earlier in section 5.3 that $z(s,i,r) \leq 1$. Therefore, $z(s,i,r) = 0$ for all $s \geq 0$, $i \geq 1$ and $r \geq 0$ as required. Therefore the Q matrix is regular provided (7.37) holds.

(7.37) holds if

$$\sum_{k=1}^{\infty}\frac{k!}{\mu N^k} = \infty. \tag{7.38}$$

Equation (7.38) holds because $\frac{k!}{\mu N^k}$ tends to infinity as $k \to \infty$ since μN is constant. Therefore (7.37) holds.

Absolute absorption

To prove absolute absorption, we apply criterion (C) of Reuter (1961), which can be stated as follows: let D and A respectively denote the sets of non-absorbing and absorbing states: if the process has initial state m ($m = (s,i,r)$) in D, let α_m be the probability of reaching A and let τ_m be the expected time to reach A: if there exist finite constants $u_n \geq 0$ such that

$$\sum_n q_{mn}u_n + 1 \leq 0, \qquad m \in D, \tag{7.39}$$

then $\alpha_m = 1$ and $0 \leq \tau_m \leq u_m$.

For the SIRS model with demography we seek a non-negative solution to the inequality (7.39), which becomes, on writing $u(s,i,r)$ for u_m, $m = (s,i,r)$,

$$\Delta u(s,i,r) \geq 1 \qquad (s,i,r) \in D \tag{7.40}$$

where

$$\begin{aligned}\Delta u(s,i,r) &= \mu N[u(s,i,r)-u(s+1,i,r)]+\frac{\beta}{N}si[u(s,i,r)-u(s-1,i+1,r)]\\ &\quad +\mu s[u(s,i,r)-u(s-1,i,r)]+\mu i[u(s,i,r)-u(s,i-1,r)]\\ &\quad +\gamma i[u(s,i,r)-u(s,i-1,r+1)]+\mu r[u(s,i,r)-u(s,i,r-1)]\\ &\quad +\nu r[u(s,i,r)-u(s+1,i,r-1)].\end{aligned}$$

For a trial solution to (2) we consider $u = B(s+i+r)$, where $B > 0$ is a constant.

$$\begin{aligned}\Delta u(s,i,r) &= B[\mu s-\mu N+\mu i+\mu r]\\ &= B\mu[(s+i+r)-N].\end{aligned}$$

For $s+i+r \geq N+1$,

$$\Delta u(s,i) = B\mu[s+i+r-N] \geq B\mu[N+1-N] = B\mu, \tag{7.41}$$

so taking $B > \frac{1}{\mu}$ then $\Delta u \geq 1$ for $s+i \geq N+1$.

Suppose that $s+i+r < N$. We have exhibited a function u defined on the state space of the process with $\Delta u(s,i) \geq 1$ for $(s,i,r) \in D(N) = \{(s,i,r) \in D : s+i+r \geq N+1\}$. Like in Section 5.3 we can conclude that the epidemic process must leave $D(N)$ with probability one, so that it is either ultimately absorbed at $i = 0$, or else returns infinitely often to the finite region $D \setminus D(N)$ without being absorbed at $i = 0$. However the probability of the latter scenario tends to zero because upon entering $D \setminus D(N)$ the process has a probability of absorption bounded away from zero. Therefore with probability one the process will be absorbed after a finite number of visits to $D \setminus D(N)$. Note that as in section 5.3, the above arguments do not allow us to say anything about the expected time to extinction τ_m.

7.3.3 Conditioning on non-extinction

We have shown that the disease will fade out of of the population. This occurs when the number of infectives falls to zero and this happens if there is a single infected individual in the population who recovers or dies before passing on the disease. We now study the process conditioned on non-extinction. We determine the state probabilities conditioned on not being absorbed denoted by $q_{s,i,r}(t)$ from

the unconditioned probabilities $p_{s,i}(t)$ via the relation

$$\begin{aligned} q_{s,i,r}(t) &= P((S(t), I(t)R(t)) = (s,i,r)|I(t) \neq 0) \\ &= \frac{p_{s,i}(t)}{1 - p_{.,0,.}(t)} \end{aligned} \tag{7.42}$$

where $p_{.,i,.}(t)$ is the marginal distribution of the number of infected individuals at time t and is given by

$$p_{.,i,.} = \sum_{s=0}^{\infty} \sum_{r=0}^{\infty} p_{s,i,r}(t) = P(I(t) = i).$$

Taking equation (7.32) and summing for $i = 0$ over all s and r values we have

$$\dot{p}_{.,0.}(t) = (\gamma + \mu) p_{.,1,.}(t). \tag{7.43}$$

Differentiating (7.42) and using (7.43) and the Kolmogorov forward equations (7.32) we derive the system of differential equations for conditional state probabilities $q_{s,i,r}(t)$.

$$\begin{aligned} \dot{q}_{s,i,r}(t) &= \lambda_1(s-1,i,r) q_{s-1,i,r}(t) + \beta_1(s+1,i-1,r) q_{s+1,i-1,r}(t) \\ &\quad + \mu_1(s+1,i,r) q_{s+1,i,r}(t) + \mu_2(s,i+1,r) q_{s,i+1,r}(t) \\ &\quad + \gamma_2(s,i+1,r-1) q_{s,i+1,r-1}(t) + \mu_3(s,i,r+1) q_{s,i,r+1}(t) \\ &\quad + \nu_3(s-1,i,r+1) q_{s-1,i,r+1}(t) - k(s,i,r) q_{s,i,r}(t) \\ &\quad + (\gamma + \mu) q_{.,1.}(t) q_{s,i,r}(t), \end{aligned} \tag{7.44}$$

where $q_{.,1,.}(t) = \sum_{s,r} q_{s,1,r}(t)$ and $q_{s,i,r}(t) = 0$ for $(s,i,r) \notin D$

One of the differences between these equations and (7.32) is the inclusion of an additional term in each one to account for the rate at which the infection goes extinct. This extra term further complicates the analysis of this set of equations. As a result approximations are sought.

7.3.4 Diffusion approximation

From the original process we can determine the mean and the covariance with components δs, δi and δr. For the mean:

$$\begin{aligned} E\begin{pmatrix} \delta s \\ \delta i \\ \delta r \end{pmatrix} &= \begin{pmatrix} \mu(1 + (\eta_3 - 1)r - R_0\eta_2 si - s) \\ \mu\eta_2(R_0 si - i) \\ \mu((\eta_2 - 1)i - \eta_3 r) \end{pmatrix} \delta t + o(\delta t) \\ &= E(s,i,r)\delta t + o(\delta t). \end{aligned}$$

The Jacobian matrix of the mean vector $E(s,i,r)$ is given above.

The covariance matrix of the vector of change in the state variables during the time interval $(t, t+\Delta)$ is given by

$$Cov\begin{pmatrix}\delta s\\ \delta i\\ \delta r\end{pmatrix} = \begin{pmatrix}\mu(1+(\eta_3-1)r+R_0\eta_2 si+s) & -\mu R_0\eta_2 si & -\mu(\eta_3-1)r\\ -\mu R_0\eta_2 si & \mu\eta_2(R_0 si+i) & -\mu(\eta_2-1)i\\ -\mu(\eta_3-1)r & -\mu(\eta_2-1)i & \mu((\eta_2-1)i+\eta_3 r)\end{pmatrix}\delta t$$
$$+o(\delta t) = G(s,i,r)\delta t + o(\delta t).$$

We can approximate the $\mathbf{G}(s,i,r)$ matrix by evaluating it at the critical point (s^*, i^*, r^*).

As in section 7.1.3 we find the covariance matrix Σ by solving (4.8) with expressions for $\mathbf{J}(s^*,i^*,r^*)$ and $\mathbf{G}(s^*,i^*,r^*)$. However, the result for this model is complicated so we use numerical value to evaluate it and compare the result with simulation. The parameter values used are $N = 200,000$, $\beta = 750$, $\mu = 1/70$, $\gamma = 50$ and $\nu = 1$ as before (section 5.7).

It can seen from Figure 7.2 that the diffusion approximation gives a very good approximation of the quasi-stationary distribution, for these parameter values.

7.3.5 Cumulant equations

The system of differential equations (7.44) can be used to derive a partial differential equation for the moment generating function M defined by

$$M(\theta_1,\theta_2,\theta_3,t) = E[e^{S\theta_1+I\theta_2+R\theta_3}|I>0] = \sum_{s=0}^{\infty}\sum_{i=1}^{\infty}\sum_{r=0}^{\infty} q_{s,i,r}e^{s\theta_1+i\theta_2+r\theta_3},$$

$\theta_1,\theta_2,\theta_3 \in \mathbb{R}$. Multiplying equations (7.44) by $e^{s\theta_1+i\theta_2+r\theta_2}$ and summing over all values of s,i,r and simplifying (see Appendix E) we have

$$\begin{aligned}\frac{\partial M}{\partial t} &= \mu N(e^{\theta_1}-1)M + \mu(e^{-\theta_1}-1)\frac{\partial M}{\partial \theta_1} + \frac{\beta}{N}(e^{\theta_2-\theta_1}-1)\frac{\partial^2 M}{\partial\theta_1\partial\theta_2}\\ &+\mu(e^{-\theta_2}-1)\frac{\partial M}{\partial\theta_2} + \gamma(e^{\theta_1-\theta_2}-1)\frac{\partial M}{\partial\theta_2} + \mu(e^{-\theta_3}-1)\frac{\partial M}{\partial\theta_3}\\ &+\nu(e^{\theta_1-\theta_3}-1)\frac{\partial M}{\partial\theta_3} - \mu q_{\cdot,1,\cdot}\sum_{s=0}^{\infty}\sum_{r=0}^{\infty} q_{S,R}(s,r|1)(t)e^{s\theta_1+r\theta_3}\\ &-\gamma q_{\cdot,1,\cdot}e^{\theta_1}\sum_{s=0}^{\infty}\sum_{r=0}^{\infty} q_{S,R}(s,r|1)(t)e^{s\theta_1+r\theta_3} + (\gamma+\mu)q_{\cdot,1,\cdot}M, \qquad (7.45)\end{aligned}$$

where $q_{S,R}(s,r|1)(t) = \frac{q_{s,1,r}}{q_{.,1,.}}$ is the conditional probability that S takes the value s and R takes the value r given that $I = 1$. Using the transformation $K(\theta_1, \theta_2, \theta_3, t) = logM(\theta_1, \theta_2, \theta_3, t)$ we have

$$\begin{aligned}
\frac{\partial K}{\partial t} &= \frac{\beta}{N}(e^{\theta_2-\theta_1}-1)\left(\frac{\partial^2 K}{\partial\theta_1\partial\theta_2}+\frac{\partial K}{\partial\theta_1}\frac{\partial K}{\partial\theta_2}\right)+\mu N(e^{\theta_1}-1)+\mu(e^{-\theta_1}-1)\frac{\partial K}{\partial\theta_1} \\
&+\mu(e^{-\theta_2}-1)\frac{\partial K}{\partial\theta_2}+\gamma(e^{\theta_3-\theta_2}-1)\frac{\partial K}{\partial\theta_2}+\mu(e^{-\theta_3}-1)\frac{\partial K}{\partial\theta_3} \\
&+\nu(e^{\theta_1-\theta_3}-1)\frac{\partial K}{\partial\theta_3}+\mu q_{.,1,.}\left(1-e^{-K}\sum_{s=0}^{\infty}\sum_{r=0}^{\infty}q_{S,R}(s,r|1)(t)e^{s\theta_1+r\theta_3}\right) \\
&+\gamma q_{.,1,.}\left(1-e^{\theta_3}e^{-K}\sum_{s=0}^{\infty}\sum_{r=0}^{\infty}q_{S,R}(s,r|1)(t)e^{s\theta_1+r\theta_3}\right). \qquad (7.46)
\end{aligned}$$

Using the definition $K(\theta_1,\theta_2,\theta_2,t) = \sum_{x\geq 0,\, y\geq 0,\, z\geq 0,\, x+y+z>0} k_{x,y,z}(t)\ \theta_1^x\ \theta_2^y\ \theta_2^z/x!\ y!\ z!$ where $k_{x,y,z}(t)$ denotes the (x,y,z)th cumulant function - for $(x,y,z) \neq (0,0,0)$, we derive the following cumulant equations.

$$\begin{aligned}
\dot{k}_{1,0,0}(t) &= \mu N - \frac{\beta}{N}\Big(k_{1,1,0}(t)+k_{1,0,0}(t)k_{0,1,0}(t)\Big)-\mu k_{1,0,0}(t)+\nu k_{0,0,1}(t) \\
&+(\gamma+\mu)q_{.,1,.}(t)\left(k_{1,0,0}(t)-E[S|I=1]\right), \qquad (7.47) \\
\dot{k}_{0,1,0}(t) &= \frac{\beta}{N}\Big(k_{1,1,0}(t)+k_{1,0,0}(t)k_{0,1,0}(t)\Big)-(\mu+\gamma)k_{0,1,0}(t) \\
&+(\gamma+\mu)q_{.,1,.}(t)k_{0,1,0}(t), \qquad (7.48) \\
\dot{k}_{0,0,1}(t) &= \gamma k_{0,1,0}(t)-\mu k_{0,0,1}(t)-\nu k_{0,0,1}(t))-\gamma q_{.,1,.}(t)(1+E[R|I=1]) \\
&+(\mu+\gamma)q_{.,1,.}(k_{0,0,1}(t)+E[R|I=1])-\gamma q_{.,1,.}(t), \qquad (7.49) \\
\dot{k}_{1,1,0}(t) &= \frac{\beta}{N}\Big[k_{1,0,0}(t)k_{1,1,0}(t)-k_{1,1,0}(t)-k_{1,0,0}(t)k_{0,1,0}(t)+k_{2,1,0}(t) \\
&+k_{0,1,0}(t)k_{2,0,0}(t)-k_{0,1,0}(t)k_{1,1,0}(t)-k_{1,2,0}(t)-k_{1,0,0}(t)k_{0,2,0}(t)\Big] \\
&-(2\mu+\gamma)k_{1,1,0}(t)-\nu k_{0,1,1}(t)+(\gamma+\mu)q_{.,1,.}(t)[k_{1,1,0}(t) \\
&+k_{0,1,0}(t)E[S|I=1]-k_{1,0,0}(t)k_{0,1,0}(t)], \qquad (7.50) \\
\dot{k}_{1,0,1}(t) &= -\frac{\beta}{N}\Big(k_{1,1,1}+k_{1,0,0}(t)k_{0,1,1}(t)+k_{1,0,1}(t)k_{0,1,0}(t)\Big)-2\mu k_{1,0,1}(t) \\
&+\gamma k_{1,1,0}(t)-\nu(k_{0,0,1}(t)+k_{1,0,1}(t)-k_{0,0,2}(t))+(\gamma+\mu)q_{.,1,.}(t)[k_{1,0,1}(t) \\
&+k_{1,0,0}(t)E[R|I=1]+k_{0,0,1}(t)E[S|I=1]+E[SR|I=1] \\
&-k_{1,0,0}(t)k_{0,1,0}(t)]-\gamma q_{.,1,.}(t)(E[SR|I=1]+E[S|I=1]), \qquad (7.51)
\end{aligned}$$

$$
\begin{aligned}
\dot{k}_{0,1,1}(t) &= \frac{\beta}{N}\Big(k_{1,1,1}(t) + k_{1,0,0}(t)k_{0,1,1}(t) + k_{0,1,0}(t)k_{1,0,1}(t) \Big) - 2\mu k_{0,1,1}(t) \\
&\quad +\gamma(k_{0,2,0}(t) - k_{0,1,1}(t) - k_{0,1,0}(t)) - \nu k_{0,1,1}(t) + \gamma q_{\cdot,1,\cdot}(t)k_{0,1,0}(t) \\
&\quad +(\gamma+\mu)q_{\cdot,1,\cdot}(t)\left(k_{0,1,1}(t) - k_{0,1,0}(t)k_{0,0,1}(t)\right), \qquad (7.52) \\
\dot{k}_{2,0,0}(t) &= \frac{\beta}{N}\Big(k_{1,1,0}(t) + k_{1,0,0}(t)k_{0,1,0}(t) - 2k_{2,1,0}(t) - 2k_{1,0,0}(t)k_{1,1,0}(t) \\
&\quad -2k_{0,1,0}(t)k_{2,0,0}(t) \Big) + \mu N + \mu k_{1,0,0}(t) + \nu k_{0,0,1}(t) + 2\nu k_{1,0,1}(t) \\
&\quad -2\mu k_{2,0,0}(t) + (\gamma+\mu)q_{\cdot,1,\cdot}(t)\left(k_{2,0,0}(t) - k_{1,0,0}(t)^2 - E[S^2|I=1]\right. \\
&\quad \left.+2k_{1,0,0}(t)E[S|I=1]\right), \qquad (7.53) \\
\dot{k}_{0,2,0}(t) &= \frac{\beta}{N}\Big(k_{1,1,0}(t) + k_{1,0,0}(t)k_{0,1,0}(t) + 2k_{1,2,0}(t) + 2k_{0,1,0}(t)k_{1,1,0}(t) \\
&\quad +2k_{1,0,0}(t)k_{0,2,0}(t) \Big) + (\gamma+\mu)(k_{0,1,0}(t) - 2k_{0,2,0}(t)) \\
&\quad +(\gamma+\mu)q_{\cdot,1,\cdot}(t)\left(k_{0,2,0}(t) - k_{0,1,0}(t)^2\right), \qquad (7.54) \\
\dot{k}_{0,0,2}(t) &= \gamma(k_{0,1,0}(t) + 2k_{0,1,1}(t)) + \mu(k_{0,0,1}(t) - 2k_{0,0,2}(t)) + \nu(k_{0,0,1}(t) \\
&\quad -2k_{0,0,2}(t)) - \gamma q_{\cdot,1,\cdot}(t)\left(1 + 2E[R|I=1] - E[R^2|I=1]\right) \\
&\quad +(\gamma+\mu)q_{\cdot,1,\cdot}(t)\left(k_{0,0,2}(t)E[R^2|I=1] - k_{0,0,1}(t)^2\right). \qquad (7.55)
\end{aligned}
$$

We let all cumulants of order greater than two grow with N, but not faster than N. With this assumption and solving the equations using Maple we find that the following are the only cumulants that are simple to write down.

$$
\begin{aligned}
k_{1,0,0} &= \frac{1}{R_0}N + \frac{\eta_3+\eta_2-1}{\eta_3(R_0-1)} + O\left(\frac{1}{N}\right), \qquad (7.56) \\
k_{0,1,0} &= \frac{\eta_3(R_0-1)}{R_0(\eta_3+\eta_2-1)}N - \frac{1}{R_0-1} + O\left(\frac{1}{N}\right), \qquad (7.57) \\
k_{0,0,1} &= \frac{(\eta_2-1)(R_0-1)}{R_0(\eta_3+\eta_2-1)}N - \frac{\eta_2-1}{\eta_3(R_0-1)} + O\left(\frac{1}{N}\right), \qquad (7.58) \\
k_{1,1,0} &= -\frac{1}{R_0}N + O(1). \qquad (7.59)
\end{aligned}
$$

The other covariances and variances are too complicated so we use numerical values to evaluate them and compare the results with simulation.

Neglecting terms of order $O(1/N)$ we see that $k_{1,0,0} + k_{0,1,0} + k_{0,0,1} = N$, as expected. Further, the leading term in $k_{0,1,0}$ is increasing in η_3 (for fixed R_0 and η_2), meaning that any increase in mean immune period corresponds to a decrease in the mean number of infectives present in quasi-stationarity. The leading term of $k_{1,0,0}$ is unaffected by η_2, η_3, while the second order term is decreasing in η_3 (for

fixed R_0, η_2). Any increase in mean immune period corresponds to a small increase in mean number of susceptibles in quasi-stationarity.

7.3.6 Numerical results

The parameter values used are $N = 200,000$, $\beta = 750$, $\mu = 1/70$, $\gamma = 50$, $\nu = 1$, $R_0 \approx 15$, $\eta_2 = 3501$ and $\eta_3 = 71$. It can be seen from Figure 7.2 that the diffusion approximation and moment closure method both give very good approximation of the quasi-stationary distribution, for these parameter values.

7.3.7 Time to extinction

Like in section 7.2, we will use the diffusion approximation to study the effect of the immune period upon the time to fade-out of infection. The time to extinction starting from quasi-stationarity is exponentially distributed with mean $((\gamma + \mu)q_{\cdot,1,\cdot})^{-1}$. Therefore, an increase in $q_{\cdot,1,\cdot}$, the quasi-stationary marginal probability that $I = 1$, corresponds to more rapid fade-out of infection. We have already seen that when $R_0 > 1$, the marginal distribution at quasi-stationarity is approximately normal. Thus an increase in $q_{\cdot,1,\cdot}$ corresponds to an increase in the coefficient of variation of the marginal distribution of the number infectives in quasi-stationarity.

Since the variance of this model is complicated, the expression for the coefficient of variation is very messy to be of any use analytically, so we carry out numerical analysis. Using Maple, we tried various values of $R_0 > 1$ (see Table 7.3) and it can be seen that $\frac{d}{d\eta_3}(CV_I^2)$ (see Appendix F for the expression for $\frac{d}{d\eta_3}(CV_I^2)$) is less than 0 for all these values which implies that the probability I is close to zero decreases as η_3 increases.

Table 7.3: $\frac{d}{d\eta_3}(CV_I^2)$ for various values of $R_0 > 1$

R_0	1.2	1.5	2	3	6	10	15
$\frac{dCV_I^2}{d\eta_3}$	-0.001812	-0.000710	-0.000355	-0.000179	-0.000074	-0.000043	-0.000029

Using Matlab, we plot η_3 against the coefficient of variation and from Figure 7.3 it can be seen that the coefficient of variation decreases as η_3 increases which confirms

the Maple results. Thus, any decrease in the average immune period, for fixed $R_0 > 1$, corresponds to an increase in the expected time to extinction of infection.

7.3.8 Conclusion

In this chapter we analysed the SIRS model with and without demography. In both cases we studied the distribution of the process prior to extinction after it has been going on for a long time. We used a diffusion approximation to derive expressions for the quasi-stationary expectations of the numbers of susceptible, infected and recovered individuals. The results obtained for the variances and covariances are complicated and so numerical values are used to evaluate them. Cumulant equations are derived and an extension of the moment closure method applied on these cumulant equations to obtain expressions for expected numbers of susceptible, infected and recovered individuals at quasi-stationarity. These results refine the results obtained from the diffusion approximation. The results for the variances and covariances are the same as those obtained from the diffusion approximation. We carry out simulations and compare the results from both the diffusion approximation and the moment closure approximation. Comparison with simulation results shows that both the diffusion approximation and the moment closure approximation provide very good approximations of the quasi-stationary distribution for parameter values in the region $R_0 > 1$.

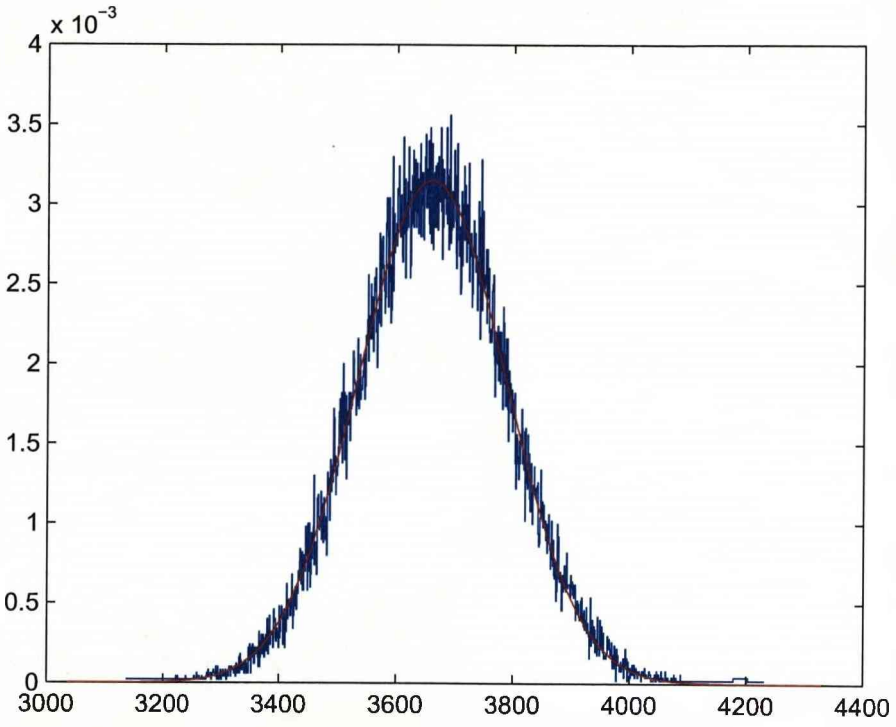

Figure 7.1: The quasi-stationary distribution of the number of infected individuals. The blue solid line is the simulation, based on 50,000 simulation runs, each allowed to run for 20 time units. The red solid line represents both the moment closure approximation and the Ornstein-Uhlenbeck approximation, which are so close as to be indistinguishable. Parameter values are $N = 200,000$, $\beta = 750$, $\nu = 1$ and $\gamma = 50$ (so $R_0 \simeq 15$, $\alpha_2 = 0.02$).

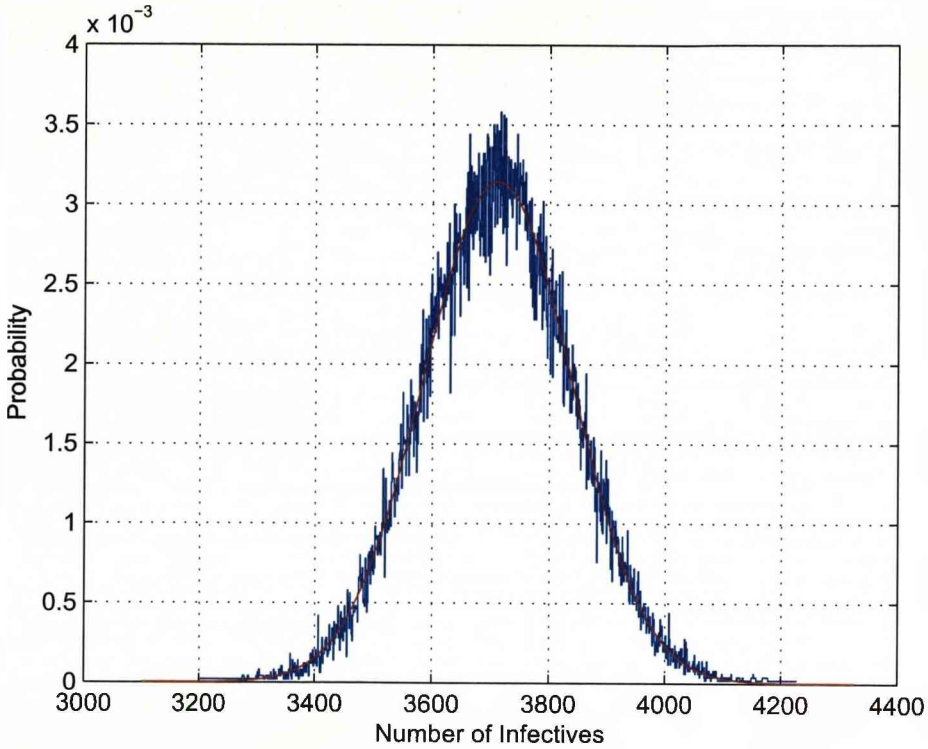

Figure 7.2: The quasi-stationary distribution of the number of infected individuals. The blue solid line is the simulation results, based on 50,000 simulation runs, each allowed to run for 20 time units. The red solid line represents both the moment closure approximation and the Ornstein-Uhlenbeck approximation, which are so close as to be indistinguishable. Parameter values are $N = 200,000$, $\beta = 750$, $\mu = 1/70$, $\gamma = 50$ and $\nu = 1$ (so $R_0 \approx 15$, $\alpha_1 = 3501$, $\alpha_3 = 71$).

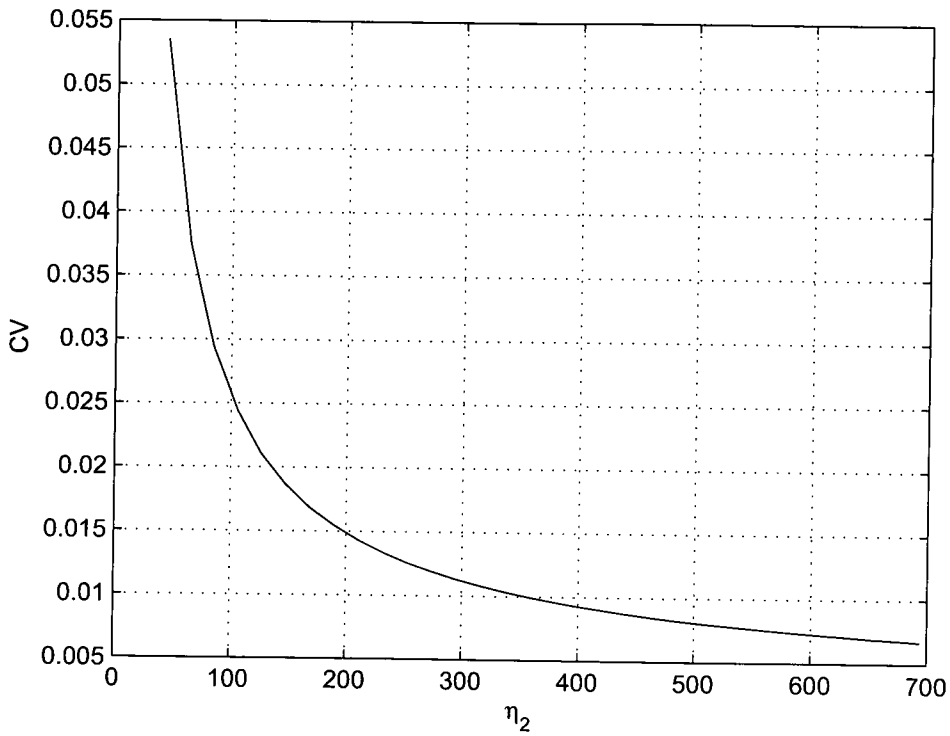

Figure 7.3: A plot of η_3 against the coefficient of variation with varying values of ν. ν varies from 0.6 to 10 in step size of 0.3. The other parameter values are $N = 200,000$, $\beta = 750$, $\mu = 1/70$, $\gamma = 50$ and $R_0 \approx 15$.

Chapter 8

Conclusion

We have formulated and analysed deterministic and stochastic models for six different models: SIS model without demography, SIS model with demography, two-group SIS model without demography, two-group SIS model with demography, SIRS model without demography and SIRS model with demography.

For the deterministic cases, we showed that the basic reproductive number R_0 determines whether the disease is eliminated quickly or persists. It was shown that when $R_0 < 1$, then the disease free equilibrium is stable and the disease cannot invade the population. However, when $R_0 > 1$ then the disease free equilibrium is unstable and the endemic equilibrium is stable. That is, the disease can invade a completely susceptible population if and only if $R_0 > 1$.

For the stochastic cases, all the models studied here have degenerate stationary distributions with all probability at the absorbing states, independent of the value of the basic reproductive number. However, the expected time until extinction can be long. When this is the case, interest focuses upon the long-term behaviour of the disease process prior to extinction, which is described by the quasi-stationary distribution. The main goal of this thesis was to analyse the quasi-stationary distributions of stochastic epidemic models. Pursuing this goal led to difficult mathematical problems. Exact solutions could not be found so approximations were used. We approximated the fully stochastic models using diffusion approximation and moment closure methods applied to cumulant equations. The diffusion approximation has a continuous state space, in contrast with the discrete state space of the original process. The diffusion approximation is only valid when R_0, the basic reproductive number, is distinctly larger than one and N is large. In all the models considered

here except for the two-group model with demography, the cumulant equations were derived, and a moment closure method (used by Nåsell (2005)) was applied to these equations when R_0 is distinctly larger than 1. It was shown that the results for the expected number of susceptible individuals, infected individuals and removed individuals (in the case of the SIRS model with demography) refined the results obtained in the diffusion approximation. Furthermore, the same results for variances and covariance were obtained for both the moment closure method and the diffusion approximation. Comparison with simulation results showed that these approximations provided good approximations for the quasi-stationary distribution when R_0 is distinctly larger than one.

In chapter 3 we analysed the simple SIS epidemic model with a constant population size. We showed using the Ornstein-Uhlenbeck diffusion approximation that the quasi-stationary distribution can be approximated by a Normal distribution when $R_0 > 1$ and N is sufficiently large. This result was confirmed by the results of the moment closure applied on the cumulant equations for q_1 (the probability the number of infectives at quasi-stationarity is equal to one) approximately zero. The cumulant approximations derived from the moment closure method are indeed asymptotic approximations of the quasi-stationary distribution cumulants (Nåsell (2003)). Nåsell (2003) showed using the moment closure method that the quasi-stationary distribution can be approximated by the Normal, Binomial, Poison, Log-normal distributions. We extended that to the Beta-binomial. We saw for the moment closure method that all the above distributions give very good approximations of the expected number of infected individuals at quasi-stationarity. However, plotting these distributions against the true quasi-stationary distribution showed that the Poisson distribution doesn't give a good fit as illustrated in Figure 3.3. The total variation distances of these distributions from the quasi-stationary distribution were calculated and it was seen that the Beta-binomial provided the best approximation. It also confirmed that although the Poisson distribution gave a good approximation of the expected number of infected individuals at quasi-stationarity, it does not provide a good fit. We showed, in Figure 3.5, that the Poisson is a better approximation for the number of susceptibles at quasi-stationarity since at quasi-stationarity the mean number of susceptibles is equal to its variance.

In chapter 4 we analysed a two group SIS epidemic model with the population size of each group constant. We derived an approximation for the quasi-stationary distribution using diffusion approximation and moment closure applied on cumulant equations. The results from both approximations compared very well with each other and with the leading eigenvector of the truncated transition matrix (the exact quasi-stationary distribution).

In chapter 5 we analysed the SIS model with demography. First we showed that the disease will almost surely go extinct from the population irrespective of the parameter values. However, for large N and R_0 distinctly larger than one the process will settle to some form of equilibrium prior to extinction. The number of infected individuals increases to a long-lived quasi-stationary state, the mean of which is close to the deterministic endemic level. We derived approximation for the means and variances of the number of infected and susceptibles in quasi-stationarity. We used a diffusion approximation and moment closure method applied on cumulant equations to approximate the quasi-stationary distribution. The results obtained for the quasi-stationary expectation of the number of susceptible and infected individuals from the moment closure method refined the results obtained from the diffusion approximation. The results for the variances and the covariance are the same for the moment closure approximation and the diffusion approximation. We showed by comparison with simulation results that these approximations provided very good approximations of the quasi-stationary distribution for these parameter values. Nåsell (2005) analysed the SIR model with demography in detail. In chapter 5 we compared our results with the results he obtained for the SIR model with demography. For the diffusion approximation, the mean number of susceptible individuals at quasi-stationarity is the same for both the SIR and SIS models. In the moment closure approximation, however, the mean number of susceptible individuals at quasi-stationarity in the SIR model is slightly more that those in the SIS model, but the number of infected individuals in the SIS model is more than the SIR model. The variance for the number of susceptible individuals at quasi-stationarity for the SIR model is greater than that of the SIS model but the SIS model has a larger variance than the SIR model for the number of infected individuals. We also showed the SIR model has a larger coefficient of variation than the SIS model which means that the SIR model has a shorter time to extinction than the SIS model.

In chapter 6 a two group SIS epidemic model with demography was formulated and analysed. The inclusion of demography made the model more complicated and led to complicated results. First we analysed the deterministic case by working out the equilibrium of the differential equations describing the model. It was shown that these equations have four equilibrium points. One represents the disease free equilibrium, the other an endemic equilibrium and the last two are complicated and not feasible. The stochastic model is formulated as a Markov process. We used a diffusion approximation to derive an approximation for the quasi-stationary mean and variance. As stated earlier, the inclusion of demography further complicated the model and therefore complicated the analysis of the diffusion approximation. The result obtained was complicated so numerical values were used. We ran a simulation and compared the result with the result obtained from the diffusion approximation. The shape of the quasi-stationary distribution appeared to be approximately normal for $R_0 > 1$ and N large.

In chapter 7 we analysed the SIRS model with and without demography. In both cases we studied the distribution of the process prior to extinction after it has been going on for a long time. We derived expressions for the quasi-stationary expectations of the numbers of susceptible, infected and recovered individuals using diffusion approximations. The results obtained for the variances and covariances for the SIRS model with demography were messy and so numerical values were used to evaluate them. Cumulant equations were derived and an extension of the moment closure method (Nåsell (2005)) applied on these cumulant equations when R_0 is distinctly larger than one. This led to expressions for the quasi-stationary expectation of the number of susceptible, infected and recovered individuals. These results refined the results obtained from the diffusion approximation. The results for the variances and covariances are the same as those obtained from the diffusion approximation. Comparison with simulation results showed that both the diffusion approximation and the moment closure approximation provide very good approximations of the quasi-stationary distribution for parameter values in the region $R_0 > 1$. It was shown that when the loss of immunity rate $\nu = 0$ then we get an SIR model and when $\nu \to \infty$ we get the SIS model. Thus, the introduction of loss of immunity allows the disease to settle to an endemic equilibrium for the SIRS model without demography, but the number of infected individuals in endemic equilibrium for both the model with

and without demography is less than in the SIS model. Further, we have been able to conclude that a longer period of immunity results in a shorter persistence time for infection in the population, for infections well above threshold. Specifically, we showed in section 7.2 that for a model without demography, any increase in mean immune period results in a corresponding decrease in expected persistence time. For the full SIRS model with demography, we would expect a corresponding result, that any increase in mean immune period leads to a decrease in time to fade-out of infection. However, for this model the algebra becomes considerably less tractable. Numerical results, however, suggest that the result does indeed remain true. This confirms the conclusion that the SIR model has a shorter time to extinction than the SIS model.

It is important to note that the processes studied here were simplified. For example, they assume that the population is uniform and homogeneously mixing, whereas it is known that mixing depends on many factors including age (children usually have more adequate contacts per day that adults) (Hethcote (2000)). Moreover, different geographic and social groups have different contact rates. So a few other things could have been added. For example, a latent period could have been added or we could have allowed for an infection rate that varies between different stages of infectivity. An age varying infectivity could have also been included. The technical level, however, will be higher under the extended models. For example, the models discussed here (SIR, SIS and SIRS) make the assumption that individuals immediately become infectious upon contracting the infection. In reality, there is usually a latent period between acquisition of infection and the start of infectiousness. This can be accounted for within the model by allowing newly infected individuals to enter an exposed class where they remain for an average time length $1/\vartheta$, say, before moving into the infectious class. The duration of the latent period is thus exponentially distributed and the number of exposed individuals can be written as E. Therefore the models become SEIR, SEIS and SEIRS. Individuals, therefore, move from exposed to infectious class at a rate of ϑE. Note that the SIR, SIS and SIRS models are recovered when $\vartheta \to \infty$. The addition of this extra class makes analysis more complicated but the models more realistic. Another thing that could have been considered is the case when $R_0 < 1$ for two-group models, the SIRS models and the SIS model with demography. These cases are complicated and have

been left for future research. Note that for $R_0 < 1$, although the quasi-stationary distribution can still be defined, disease is likely to die out before quasi-stationary behaviour is observed in practice.

Perhaps more important for approaching real life epidemic is to generalise the model to include for example, spatial, social, individual heterogeneities and social effects, which play an important role in the spread of infectious diseases (Anderson & May (1991)). These are things that can be explored in the future. However, we believe that the results obtained here give a good indication of the dynamics of disease processes for the parameters studied.

Appendix A

Cumulant equations for a closed SIS model

The Kolmogorov forward equation for the state probabilities conditioned on non-extinction $q_i(t)$ can be written as

$$\frac{dq_i}{dt} = \beta_{i-1}q_{i-1} + \gamma_{i+1}q_{i+1} - (\beta_i + \gamma_i)q_i + \gamma q_1 q_i \tag{A.1}$$

for $i = 1, 2, 3, \ldots$. Multiplying equation (A.1) by $e^{i\theta}$, $\theta \in \mathbb{R}$, and summing over all values of i gives

$$\sum_{i=1}^{N} \frac{dq_i}{dt} e^{i\theta} = \sum_{i=2}^{N} \beta_{i-1}q_{i-1}e^{i\theta} - \sum_{i=1}^{N-1} \beta_i q_i e^{i\theta} + \sum_{i=1}^{N-1} \gamma_{i+1}q_{i+1}e^{i\theta} - \sum_{i=1}^{N} \gamma_i q_i e^{i\theta} + \sum_{i=1}^{N} \gamma q_1 q_i e^{i\theta}$$

since $\gamma_0 = \beta_0 = \beta_N = 0$.

$$\begin{aligned}\sum_{i=1}^{N} \frac{dq_i}{dt} e^{i\theta} &= \sum_{i=1}^{N-1} \beta_i q_i e^{\theta(i+1)} - \sum_{i=1}^{N-1} \beta_i q_i e^{i\theta} + \sum_{i=2}^{N} \gamma_i q_i e^{\theta(i-1)} - \sum_{i=2}^{N} \gamma_i q_i e^{i\theta} - \gamma q_1 e^{\theta} \\ &\quad + \sum_{i=1}^{N} \gamma q_1 q_i e^{i\theta}\end{aligned}$$

$$\sum_{i=1}^{N} \frac{dq_i}{dt} e^{i\theta} = (e^{\theta} - 1) \sum_{i=1}^{N-1} \beta_i q_i e^{i\theta} + (e^{-\theta} - 1) \sum_{i=2}^{N} \gamma_i q_i e^{i\theta} - \gamma q_1 e^{\theta} + \sum_{i=1}^{N} \gamma q_1 q_i e^{i\theta}$$

$$\begin{aligned}\sum_{i=1}^{N} \frac{dq_i}{dt} e^{i\theta} &= (e^{\theta} - 1) \sum_{i=1}^{N-1} \beta \frac{i}{N}(N - i) q_i e^{i\theta} + (e^{-\theta} - 1) \sum_{i=2}^{N} \gamma i q_i e^{i\theta} - \gamma q_1 e^{\theta} \\ &\quad + \sum_{i=1}^{N} \gamma q_1 q_i e^{i\theta}\end{aligned}$$

$$\sum_{i=1}^{N} \frac{dq_i}{dt} e^{i\theta} = \left(\beta(e^{\theta}-1)\right) \sum_{i=1}^{N-1} i q_i e^{i\theta} - \frac{\beta}{N}(e^{\theta}-1) \sum_{i=1}^{N-1} i^2 q_i e^{i\theta} + \left(\gamma(e^{-\theta}-1)\right) \sum_{i=2}^{N} i q_i e^{i\theta}$$
$$-\gamma q_1 e^{\theta} + \sum_{i=1}^{N} \gamma q_1 q_i e^{i\theta}. \tag{A.2}$$

Using $M(\theta,t) = E[e^{I\theta} \mid I > 0] = \sum_{i=1}^{N} q_i e^{i\theta}$, $\theta \in \mathbb{R}$,

$$\frac{\partial M(\theta,t)}{\partial \theta} = \sum_{i=1}^{N} i q_i e^{i\theta}$$

and

$$\frac{\partial^2 M(\theta,t)}{\partial \theta^2} = \sum_{i=1}^{N} i^2 q_i e^{i\theta} = \sum_{i=1}^{N-1} i^2 q_i e^{i\theta} + N^2 q_N e^{N\theta}$$

equation (A.2) becomes

$$\frac{\partial M}{\partial t} = \left(\beta(e^{\theta}-1)\right)\left(\frac{\partial M}{\partial \theta} - N q_N e^{N\theta}\right) - \frac{\beta}{N}\left(e^{\theta}-1\right)\left(\frac{\partial^2 M}{\partial \theta^2} - N^2 q_N e^{N\theta}\right)$$
$$+ \left(\gamma(e^{-\theta}-1)\right)\frac{\partial M}{\partial \theta} - \gamma(e^{-\theta}-1) q_1 e^{\theta} + \gamma q_1 M(\theta,t) - \gamma q_1 e^{\theta},$$

$$\frac{\partial M}{\partial t} = \left[\beta(e^{\theta}-1) + \gamma(e^{-\theta}-1)\right]\frac{\partial M}{\partial \theta} - \frac{\beta}{N}\left(e^{\theta}-1\right)\frac{\partial^2 M}{\partial \theta^2} + \gamma q_1 (M(\theta,t)-1).$$

Using the transformation $K(\theta,t) = log M(\theta,t)$ gives

$$e^K \frac{\partial K}{\partial t} = \left[\beta(e^{\theta}-1) + \gamma(e^{-\theta}-1)\right] e^K \frac{\partial K}{\partial \theta} - \frac{\beta}{N}\left(e^{\theta}-1\right)\left[e^K \frac{\partial^2 K}{\partial \theta^2} + e^K \left(\frac{\partial K}{\partial \theta}\right)^2\right]$$
$$+\gamma q_1 (e^K - 1)$$
$$\frac{\partial K}{\partial t} = \left[\beta(e^{\theta}-1) + \gamma(e^{-\theta}-1)\right]\frac{\partial K}{\partial \theta} - \frac{\beta}{N}\left(e^{\theta}-1\right)\left[\frac{\partial^2 K}{\partial \theta^2} + \left(\frac{\partial K}{\partial \theta}\right)^2\right]$$
$$+\gamma q_1 (1 - e^{-K})$$
$$\frac{\partial K}{\partial t} = \left[\beta\left(\theta + \frac{\theta^2}{2!} + \frac{\theta^3}{3!} + \cdots\right) + \gamma\left(-\theta + \frac{\theta^2}{2!} - \frac{\theta^3}{3!} + \cdots\right)\right]\frac{\partial K}{\partial \theta}$$
$$-\frac{\beta}{N}\left(\theta + \frac{\theta^2}{2!} + \frac{\theta^3}{3!} + \cdots\right)\left[\frac{\partial^2 K}{\partial \theta^2} + \left(\frac{\partial K}{\partial \theta}\right)^2\right]$$
$$+\gamma q_1 \left(K - \frac{K^2}{2!} + \frac{K^3}{3!} - \cdots\right). \tag{A.3}$$

Using the definition $K(\theta,t) = \sum_{i=1}^{\infty} k_i(t)\frac{\theta^i}{i!}$ where $k_i(t)$ denotes the ith cumulant function,

$$\begin{aligned}
K(\theta,t) &= k_1(t)\theta + k_2(t)\frac{\theta^2}{2!} + k_3(t)\frac{\theta^3}{3!} + \cdots, \\
\frac{\partial K}{\partial t} &= \dot{k}_1(t)\theta + \dot{k}_2(t)\frac{\theta^2}{2!} + \dot{k}_3(t)\frac{\theta^3}{3!} + \cdots, \\
\frac{\partial K}{\partial \theta} &= k_1(t) + k_2(t)\theta + k_3(t)\frac{\theta^2}{2!} + \cdots, \\
\frac{\partial^2 K}{\partial \theta^2} &= k_2(t) + k_3(t)\theta + k_4(t)\frac{\theta^2}{2!} + \cdots, \\
\left(\frac{\partial K}{\partial \theta}\right)^2 &= \left(k_1(t) + k_2(t)\theta + k_3(t)\frac{\theta^2}{2!} + \cdots\right)\left((k_1(t) + k_2(t)\theta + k_3(t)\frac{\theta^2}{2!} + \cdots\right) \\
&= (k_1(t))^2 + 2\theta k_1(t)k_2(t) + \theta^2(k_1(t)k_3(t) + (k_2(t))^2) \\
&\quad +\theta^3\left(\frac{1}{3}(k_1(t)k_4(t) + (k_2(t)k_3(t)\right) + \cdots.
\end{aligned}$$

Substituting these into equation (A.3) we have

$$\begin{aligned}
&\dot{k}_1(t)\theta + \dot{k}_2(t)\frac{\theta^2}{2!} + \dot{k}_3(t)\frac{\theta^3}{3!} + \cdots = \\
&\left[\beta\left(\theta + \frac{\theta^2}{2!} + \frac{\theta^3}{3!} + \cdots\right) + \gamma\left(-\theta + \frac{\theta^2}{2!} - \frac{\theta^3}{3!} + \cdots\right)\right]\left(k_1(t) + k_2(t)\theta + k_3(t)\frac{\theta^2}{2!} + \cdots\right) \\
&-\frac{\beta}{N}\left(\theta + \frac{\theta^2}{2!} + \frac{\theta^3}{3!} + \cdots\right) \\
&\left((k_1(t))^2 + k_2(t) + \theta(2k_1(t)k_2(t) + k_3(t)) + \theta^2\left(k_1(t)k_3(t) + (k_2(t))^2 + \frac{1}{2}k_4(t)\right) + \cdots\right) \\
&+\gamma q_1\left(k_1(t)\theta + k_2(t)\frac{\theta^2}{2!} + k_3(t)\frac{\theta^3}{3!} - (k_1(t))^2\frac{\theta^2}{2!} - k_1k_2\frac{\theta^3}{2!} + (k_1(t))^3\frac{\theta^3}{3!} + \cdots\right).
\end{aligned}$$

Equating the coefficients of θ

$$\begin{aligned}
\dot{k}_1(t) &= (\beta-\gamma)k_1(t) - \frac{\beta}{N}(k_1(t))^2 - \frac{\beta}{N}k_2(t) + \gamma q_1 k_1(t) \\
&= k_1(t)((\beta-\gamma) - \frac{\beta}{N}k_1(t)) - \frac{\beta}{N}k_2(t) + \gamma q_1 k_1(t) \\
&= \frac{\beta}{N}\left[k_1(t)\left(\frac{N(\beta-\gamma)}{\beta} - k_1(t)\right) - k_2(t)\right] + \gamma q_1 k_1(t)
\end{aligned}$$

$$\dot{k}_1(t) = \frac{\gamma R_0}{N}\left[\left(N\left(1-\frac{1}{R_0}\right) - k_1(t)\right)k_1(t) - k_2(t)\right] + \gamma q_1 k_1(t). \quad \text{(A.4)}$$

Taking the coefficients of θ^2

$$\begin{aligned}
\frac{1}{2}\dot{k}_2(t) &= \frac{\beta}{2}k_1(t) + \frac{\gamma}{2}k_1(t) + (\beta-\gamma)k_2(t) - \frac{\beta}{2N}(k_1(t))^2 - \frac{\beta}{2N}k_2(t) - \frac{\beta}{N}k_3(t) \\
&\quad -\frac{2\beta}{N}k_1(t)k_2(t) + \frac{1}{2}\gamma q_1(k_2(t) - (k_1(t))^2) \\
&= \frac{1}{2}(\beta+\alpha)k_1(t) - \frac{\beta}{2N}(k_1(t))^2 + \left((\beta-\gamma) - \frac{\beta}{2N}\right)k_2(t) - \frac{\beta}{N}k_3(t) \\
&\quad -2\frac{\beta}{N}k_1(t)k_2(t) + \gamma q_1(k_2(t) - (k_1(t))^2) \\
&= \frac{\beta}{N}\left[\left(\frac{N(\beta-\gamma)}{\beta} - k_1(t)\right)\frac{1}{2}k_1(t) + \left(N - \frac{N\gamma}{\beta} - \frac{1}{2}\right)k_2(t) - 2k_1(t)k_2(t) - k_3(t)\right] \\
&\quad +\gamma q_1(k_2(t) - (k_1(t))^2),
\end{aligned}$$

$$\begin{aligned}
\dot{k}_2(t) &= \frac{\gamma R_0}{N}\left[\left(N\left(1+\frac{1}{R_0}\right) - k_1(t)\right)k_1(t) + \left(2N\left(1-\frac{1}{R_0}\right) - 1\right)k_2(t)\right. \\
&\quad \left. -4k_1(t)k_2(t) - 2k_3(t)\right] + \gamma q_1(k_2(t) - (k_1(t))^2). \qquad \text{(A.5)}
\end{aligned}$$

Taking the coefficients of θ^3

$$\begin{aligned}
\frac{1}{6}\dot{k}_3(t) &= \frac{1}{2}(\beta-\gamma)k_1(t) + \frac{1}{2}(\beta+\gamma)K_2(t) - \frac{\beta}{6N}(k_1(t))^2 - \frac{\beta}{6N}k_2(t) - \frac{\beta}{2N}k_3(t) \\
&\quad -\frac{\beta}{N}k_1(t)k_2(t) - \frac{\beta}{N}k_1(t)k_3(t) - \frac{\beta}{N}(k_2(t))^2 - \frac{\beta}{2N}k_4(t) \\
&\quad +\gamma q_1\left(\frac{k_1(t)}{3!} - \frac{k_1(t)k_2(t)}{2!} + \frac{k_3(t)}{3!}\right),
\end{aligned}$$

$$\begin{aligned}
\dot{k}_3(t) &= \frac{\gamma R_0}{N}\left[\left(N\left(1-\frac{1}{R_0}\right) - k_1(t)\right)k_1(t) - 6k_1(t)k_2(t) - 6k_1(t)k_3(t) - 6(k_2(t))^2\right. \\
&\quad \left. -\left(3N\left(1+\frac{1}{R_0}\right) - 1\right)k_2(t) + 3\left(N\left(1-\frac{1}{R_0}\right) - 1\right)k_3(t) - 3k_4(t)\right] \\
&\quad +\gamma q_1(k_1(t) - 3k_1(t)k_2(t) + k_3(t)). \qquad \text{(A.6)}
\end{aligned}$$

Appendix B

Cumulant equations for a closed Two-group SIS model

The Kolmogorov forward equations for the state probabilities conditioned on non-extinction $q_{i_1,i_2}(t)$ can be written as

$$\begin{aligned}\frac{dq_{i_1,i_2}}{dt} &= \beta_{1(i_1-1,i_2)}q_{i_1-1,i_2}(t) + \gamma_{1(i_1+1,i_2)}q_{i_1+1,i_2}(t) + \beta_{2(i_1,i_2-1)}q_{i_1,i_2-1}(t) \\ &+\gamma_{2(i_1,i_2+1)}q_{i_1,i_2+1}(t) + \lambda_{2(i_1-1,i_2)}q_{i_1-1,i_2}(t) + \lambda_{1(i_1,i_2-1)}q_{i_1,i_2-1}(t) \\ &-\beta_{1(i_1,i_2)}q_{i_1,i_2}(t) - \beta_{2(i_1,i_2)}q_{i_1,i_2}(t) - \gamma_{1(i_1,i_2)}q_{i_1,i_2}(t) - \gamma_{2(i_1,i_2)}q_{i_1,i_2}(t) \\ &-\lambda_{1(i_1,i_2)}q_{i_1,i_2}(t) - \lambda_{2(i_1,i_2)}q_{i_1,i_2}(t) + (\gamma q_{0,1}(t) + \gamma q_{1,0}(t))q_{i_1,i_2}(t),\end{aligned}$$

for $i_1 = 0, 1, 2 \ldots, N$, $i_2 = 0, 1, 2, \ldots, N$ and $(i_1, i_2) \neq (0, 0)$. Multiplying this system of equations by $e^{i_1\theta_1+i_2\theta_2}$, $\theta_1, \theta_2 \in \mathbb{R}$, and summing over all values of i_1, i_2 gives

$$
\begin{aligned}
\sum_{\substack{i_1=0\\(i_1,i_2)\neq(0,0)}}^{N}\sum_{i_2=0}^{N}\frac{dq_{i_1,i_2}}{dt}e^{i_1\theta_1+i_2\theta_2} &= \sum_{i_1=2}^{N}\sum_{i_2=0}^{N}\beta_{1(i_1-1,i_2)}q_{i_1-1,i_2}(t)e^{i_1\theta_1+i_2\theta_2}\\
&+ \sum_{i_1=0}^{N-1}\sum_{i_2=0}^{N}\gamma_{1(i_1+1,i_2)}q_{i_1+1,i_2}(t)e^{i_1\theta_1+i_2\theta_2}\\
&+ \sum_{i_1=0}^{N}\sum_{i_2=2}^{N}\beta_{2(i_1,i_2-1)}q_{i_1,i_2-1}(t)e^{i_1\theta_1+i_2\theta_2}\\
&+ \sum_{i_1=0}^{N}\sum_{i_2=0}^{N-1}\gamma_{2(i_1,i_2+1)}q_{i_1,i_2+1}(t)e^{i_1\theta_1+i_2\theta_2}\\
&+ \sum_{i_1=1}^{N}\sum_{i_2=1}^{N}\lambda_{2(i_1-1,i_2)}q_{i_1-1,i_2}(t)e^{i_1\theta_1+i_2\theta_2}\\
&+ \sum_{i_1=1}^{N}\sum_{i_2=1}^{N}\lambda_{1(i_1,i_2-1)}q_{i_1,i_2-1}(t)e^{i_1\theta_1+i_2\theta_2}\\
&- \sum_{i_1=1}^{N-1}\sum_{i_2=0}^{N}\beta_{1(i_1,i_2)}q_{i_1,i_2}(t)e^{i_1\theta_1+i_2\theta_2}\\
&- \sum_{i_1=0}^{N}\sum_{i_2=1}^{N-1}\beta_{2(i_1,i_2)}q_{i_1,i_2}(t)e^{i_1\theta_1+i_2\theta_2}\\
&- \sum_{i_1=1}^{N}\sum_{i_2=0}^{N}\gamma_{1(i_1,i_2)}q_{i_1,i_2}(t)e^{i_1\theta_1+i_2\theta_2}\\
&- \sum_{i_1=0}^{N}\sum_{i_2=1}^{N}\gamma_{2(i_1,i_2)}q_{i_1,i_2}(t)e^{i_1\theta_1+i_2\theta_2}\\
&- \sum_{i_1=1}^{N}\sum_{i_2=0}^{N-1}\lambda_{1(i_1,i_2)}q_{i_1,i_2}(t)e^{i_1\theta_1+i_2\theta_2}\\
&- \sum_{i_1=0}^{N-1}\sum_{i_2=1}^{N}\lambda_{2(i_1,i_2)}q_{i_1,i_2}(t)e^{i_1\theta_1+i_2\theta_2}\\
&+ \left(\gamma q_{0,1}(t)+\gamma q_{1,0}(t)\right)\sum_{i_1=0}^{N}\sum_{i_2=0}^{N}q_{i_1,i_2}(t)e^{i_1\theta_1+i_2\theta_2},
\end{aligned}
$$

$$
\begin{aligned}
\sum_{i_1=0}^{N}\sum_{i_2=0}^{N}\frac{dq_{i_1,i_2}}{dt}e^{i_1\theta_1+i_2\theta_2} &= \sum_{i_1=1}^{N-1}\sum_{i_2=0}^{N}\beta_{1(i_1,i_2)}q_{i_1,i_2}(t)e^{\theta_1(i_1+1)+i_2\theta_2} \\
&- \sum_{i_1=1}^{N-1}\sum_{i_2=0}^{N}\beta_{1(i_1,i_2)}q_{i_1,i_2}(t)e^{i_1\theta_1+i_2\theta_2} \\
&+ \sum_{i_1=1}^{N}\sum_{i_2=0}^{N}\gamma_{1(i_1,i_2)}q_{i_1,i_2}(t)e^{\theta_1(i_1-1)+i_2\theta_2} \\
&- \sum_{i_1=1}^{N}\sum_{i_2=0}^{N}\gamma_{1(i_1,i_2)}q_{i_1,i_2}(t)e^{i_1\theta_1+i_2\theta_2} \\
&+ \sum_{i_1=0}^{N}\sum_{i_2=1}^{N-1}\beta_{2(i_1,i_2)}q_{i_1,i_2}(t)e^{i_1\theta_1+\theta_2(i_2+1)} \\
&- \sum_{i_1=0}^{N}\sum_{i_2=1}^{N-1}\beta_{2(i_1,i_2)}q_{i_1,i_2}(t)e^{i_1\theta_1+i_2\theta_2} \\
&+ \sum_{i_1=0}^{N}\sum_{i_2=1}^{N}\gamma_{2(i_1,i_2)}q_{i_1,i_2}(t)e^{i_1\theta_1+\theta_2(i_2-1)} \\
&- \sum_{i_1=0}^{N}\sum_{i_2=1}^{N}\gamma_{2(i_1,i_2)}q_{i_1,i_2}(t)e^{i_1\theta_1+i_2\theta_2} \\
&+ \sum_{i_1=0}^{N-1}\sum_{i_2=1}^{N}\lambda_{2(i_1,i_2)}q_{i_1,i_2}(t)e^{\theta_1(i_1+1)+i_2\theta_2} \\
&- \sum_{i_1=0}^{N-1}\sum_{i_2=1}^{N}\lambda_{2(i_1,i_2)}q_{i_1,i_2}(t)e^{i_1\theta_1+i_2\theta_2} \\
&+ \sum_{i_1=1}^{N}\sum_{i_2=0}^{N-1}\lambda_{1(i_1,i_2)}q_{i_1,i_2}(t)e^{i_1\theta_1+\theta_2(i_2+1)} \\
&- \sum_{i_1=1}^{N}\sum_{i_2=0}^{N-1}\lambda_{1(i_1,i_2)}q_{i_1,i_2}(t)e^{i_1\theta_1+i_2\theta_2} \\
&+ (\gamma q_{0,1}(t)+\gamma q_{1,0}(t))\sum_{i_1=0}^{N}\sum_{i_2=0}^{N}q_{i_1,i_2}(t)e^{i_1\theta_1+i_2\theta_2} \\
&- \gamma q_{0,1}(t)-\gamma q_{1,0}(t).
\end{aligned}
$$

$$
\begin{aligned}
\sum_{i_1=0}^{N}\sum_{i_2=0}^{N}\frac{dq_{i_1,i_2}}{dt}e^{i_1\theta_1+i_2\theta_2} &= (e^{\theta_1}-1)\sum_{i_1=1}^{N-1}\sum_{i_2=0}^{N}\beta_{1(i_1,i_2)}q_{i_1,i_2}(t)e^{i_1\theta_1+i_2\theta_2} \\
&\quad +(e^{-\theta_1}-1)\sum_{i_1=1}^{N}\sum_{i_2=0}^{N}\gamma_{1(i_1,i_2)}q_{i_1,i_2}(t)e^{i_1\theta_1+i_2\theta_2} \\
&\quad +(e^{\theta_2}-1)\sum_{i_1=0}^{N}\sum_{i_2=1}^{N-1}\beta_{2(i_1,i_2)}q_{i_1,i_2}(t)e^{i_1\theta_1+i_2\theta_2} \\
&\quad +(e^{-\theta_2}-1)\sum_{i_1=0}^{N}\sum_{i_2=1}^{N}\gamma_{2(i_1,i_2)}q_{i_1,i_2}(t)e^{i_1\theta_1+i_2\theta_2} \\
&\quad +(e^{\theta_1}-1)\sum_{i_1=0}^{N-1}\sum_{i_2=1}^{N}\lambda_{2(i_1,i_2)}q_{i_1,i_2}(t)e^{i_1\theta_1+i_2\theta_2} \\
&\quad +(e^{\theta_2}-1)\sum_{i_1=1}^{N}\sum_{i_2=0}^{N-1}\lambda_{1(i_1,i_2)}q_{i_1,i_2}(t)e^{i_1\theta_1+i_2\theta_2} \\
&\quad +(\gamma q_{0,1}(t)+\gamma q_{1,0}(t))\sum_{i_1=0}^{N}\sum_{i_2=0}^{N}q_{i_1,i_2}(t)e^{i_1\theta_1+i_2\theta_2} \\
&\quad -\gamma q_{0,1}(t)-\gamma q_{1,0}(t),
\end{aligned}
$$

but

$$
\begin{aligned}
\beta_{1(i_1,i_2)} &= \beta\frac{i_1}{N}(N-i_1), \qquad & \beta_{2(i_1,i_2)} &= \beta\frac{i_2}{N}(N-i_2), \\
\lambda_{1(i_1,i_2)} &= \lambda\frac{i_2}{N}(N-i_1), \qquad & \lambda_{2(i_1,i_2)} &= \lambda\frac{i_1}{N}(N-i_2), \\
\gamma_{1(i_1,i_2)} &= \gamma i_1, \qquad & \gamma_{2(i_1,i_2)} &= \gamma i_2,
\end{aligned}
$$

SO

$$\begin{aligned}
\sum_{i_1=0}^{N}\sum_{i_2=0}^{N}\frac{dq_{i_1,i_2}}{dt}e^{i_1\theta_1+i_2\theta_2} &= (e^{\theta_1}-1)\sum_{i_1=1}^{N-1}\sum_{i_2=0}^{N}\beta\frac{i_1}{N}(N-i_1)q_{i_1,i_2}(t)e^{i_1\theta_1+i_2\theta_2} \\
&+(e^{-\theta_1}-1)\sum_{i_1=1}^{N}\sum_{i_2=0}^{N}\gamma i_1 q_{i_1,i_2}(t)e^{i_1\theta_1+i_2\theta_2} \\
&+(e^{\theta_2}-1)\sum_{i_1=0}^{N}\sum_{i_2=1}^{N-1}\beta\frac{i_2}{N}(N-i_2)q_{i_1,i_2}(t)e^{i_1\theta_1+i_2\theta_2} \\
&+(e^{-\theta_2}-1)\sum_{i_1=0}^{N}\sum_{i_2=1}^{N}\gamma i_2 q_{i_1,i_2}(t)e^{i_1\theta_1+i_2\theta_2} \\
&+(e^{\theta_1}-1)\sum_{i_1=0}^{N-1}\sum_{i_2=1}^{N}\lambda\frac{i_2}{N}(N-i_1)q_{i_1,i_2}(t)e^{i_1\theta_1+i_2\theta_2} \\
&+(e^{\theta_2}-1)\sum_{i_1=1}^{N}\sum_{i_2=0}^{N-1}\lambda\frac{i_1}{N}(N-i_2)q_{i_1,i_2}(t)e^{i_1\theta_1+i_2\theta_2} \\
&+(\gamma q_{0,1}(t)+\gamma q_{1,0}(t))\sum_{i_1=0}^{N}\sum_{i_2=0}^{N}q_{i_1,i_2}(t)e^{i_1\theta_1+i_2\theta_2} \\
&-\gamma q_{0,1}(t)-\gamma q_{1,0}(t).
\end{aligned}$$

$$
\begin{aligned}
\sum_{i_1=0}^{N}\sum_{i_2=0}^{N}\frac{dq_{i_1,i_2}}{dt}e^{i_1\theta_1+i_2\theta_2} &= \beta(e^{\theta_1}-1)\sum_{i_1=1}^{N-1}\sum_{i_2=0}^{N} i_1 q_{i_1,i_2}(t)e^{i_1\theta_1+i_2\theta_2} \\
&- \frac{\beta}{N}(e^{\theta_1}-1)\sum_{i_1=1}^{N-1}\sum_{i_2=0}^{N} i_1^2 q_{i_1,i_2}(t)e^{i_1\theta_1+i_2\theta_2} \\
&+ \gamma(e^{-\theta_1}-1)\sum_{i_1=1}^{N}\sum_{i_2=0}^{N} i_1 q_{i_1,i_2}(t)e^{i_1\theta_1+i_2\theta_2} \\
&+ \beta(e^{\theta_2}-1)\sum_{i_1=0}^{N}\sum_{i_2=1}^{N-1} i_2 q_{i_1,i_2}(t)e^{i_1\theta_1+i_2\theta_2} \\
&- \frac{\beta}{N}(e^{\theta_2}-1)\sum_{i_1=0}^{N}\sum_{i_2=1}^{N-1} i_2^2 q_{i_1,i_2}(t)e^{i_1\theta_1+i_2\theta_2} \\
&+ \gamma(e^{-\theta_2}-1)\sum_{i_1=0}^{N}\sum_{i_2=1}^{N} i_2 q_{i_1,i_2}(t)e^{i_1\theta_1+i_2\theta_2} \\
&+ \lambda(e^{\theta_1}-1)\sum_{i_1=0}^{N-1}\sum_{i_2=1}^{N} i_2 q_{i_1,i_2}(t)e^{i_1\theta_1+i_2\theta_2} \\
&- \frac{\lambda}{N}(e^{\theta_1}-1)\sum_{i_1=0}^{N-1}\sum_{i_2=1}^{N} i_1 i_2 q_{i_1,i_2}(t)e^{i_1\theta_1+i_2\theta_2} \\
&+ \lambda(e^{\theta_2}-1)\sum_{i_1=1}^{N}\sum_{i_2=0}^{N-1} i_1 q_{i_1,i_2}(t)e^{i_1\theta_1+i_2\theta_2} \\
&- \frac{\lambda}{N}(e^{\theta_2}-1)\sum_{i_1=1}^{N}\sum_{i_2=0}^{N-1} i_1 i_2 q_{i_1,i_2}(t)e^{i_1\theta_1+i_2\theta_2} \\
&+ (\gamma q_{0,1}(t)+\gamma q_{1,0}(t))\sum_{i_1=0}^{N}\sum_{i_2=0}^{N} q_{i_1,i_2}(t)e^{i_1\theta_1+i_2\theta_2} \\
&- \gamma q_{0,1}(t)-\gamma q_{1,0}(t).
\end{aligned}
$$

Using

$$
M(\theta_1,\theta_2,t)=E[e^{I_1\theta_1+I_2\theta_2}\mid I_1+I_2>0]=\sum_{i_1=0}^{N}\sum_{i_2=0}^{N} q_{i_1,i_2}e^{i_1\theta_1+i_2\theta_2}
$$

for $(i_1,i_2)\neq(0,0)$, then

$$
\frac{\partial M(\theta_1\theta_2,t)}{\partial\theta_1}=\sum_{i_1=0}^{N}\sum_{i_2=0}^{N} i_1 q_{i_1,i_2}e^{i_1\theta_1+i_2\theta_2},
$$

$$\frac{\partial M(\theta_1\theta_2,t)}{\partial\theta_2}=\sum_{i_1=0}^{N}\sum_{i_2=0}^{N}i_2q_{i_1,i_2}e^{i_1\theta_1+i_2\theta_2},$$

$$\frac{\partial^2 M(\theta_1\theta_2,t)}{\partial\theta_1^2}=\sum_{i_1=0}^{N}\sum_{i_2=0}^{N}i_1^2q_{i_1,i_2}e^{i_1\theta_1+i_2\theta_2},$$

$$\frac{\partial^2 M(\theta_1\theta_2,t)}{\partial\theta_2^2}=\sum_{i_1=0}^{N}\sum_{i_2=0}^{N}i_2^2q_{i_1,i_2}e^{i_1\theta_1+i_2\theta_2},$$

and

$$\frac{\partial^2 M(\theta_1\theta_2,t)}{\partial\theta_1\partial\theta_2}=\sum_{i_1=0}^{N}\sum_{i_2=0}^{N}i_1i_2q_{i_1,i_2}e^{i_1\theta_1+i_2\theta_2},$$

so that

$$\begin{aligned}
\frac{\partial M}{\partial t} &= \beta(e^{\theta_1}-1)\left(\frac{\partial M}{\partial\theta_1}-Ne^{N\theta_1}\sum_{i_2=0}^{N}q_{N,i_2}e^{i_2\theta_2}\right)\\
&\quad-\frac{\beta}{N}(e^{\theta_1}-1)\left(\frac{\partial^2 M}{\partial\theta_1^2}-N^2e^{N\theta_1}\sum_{i_2=0}^{N}q_{N,i_2}e^{i_2\theta_2}\right)\\
&\quad+\beta(e^{\theta_2}-1)\left(\frac{\partial M}{\partial\theta_2}-Ne^{N\theta_2}\sum_{i_1=0}^{N}q_{i_1,N}e^{i_1\theta_1}\right)\\
&\quad-\frac{\beta}{N}(e^{\theta_2}-1)\left(\frac{\partial^2 M}{\partial\theta_2^2}-N^2e^{N\theta_2}\sum_{i_1=0}^{N}q_{i_1,N}e^{i_1\theta_1}\right)\\
&\quad+\gamma(e^{-\theta_2}-1)\frac{\partial M}{\partial\theta_2}+\lambda(e^{\theta_1}-1)\left(\frac{\partial M}{\partial\theta_2}-e^{N\theta_1}\sum_{i_2=1}^{N}i_2q_{N,i_2}e^{i_2\theta_2}\right)\\
&\quad+\gamma(e^{-\theta_1}-1)\frac{\partial M}{\partial\theta_1}-\frac{\lambda}{N}(e^{\theta_1}-1)\left(\frac{\partial^2 M}{\partial\theta_1\partial\theta_2}-Ne^{N\theta_1}\sum_{i_2=1}^{N}i_2q_{N,i_2}e^{i_2\theta_2}\right)\\
&\quad+\lambda(e^{\theta_2}-1)\left(\frac{\partial M}{\partial\theta_1}-e^{N\theta_2}\sum_{i_1=1}^{N}i_1q_{i_1,N}e^{i_1\theta_1}\right)\\
&\quad-\frac{\lambda}{N}(e^{\theta_2}-1)\left(\frac{\partial^2 M}{\partial\theta_1\partial\theta_2}-Ne^{N\theta_2}\sum_{i_1=1}^{N}i_1q_{i_1,N}e^{i_1\theta_1}\right)\\
&\quad+(\gamma q_{0,1}(t)+\gamma q_{1,0}(t))M(\theta_1,\theta_2,t)-\gamma q_{0,1}(t)-\gamma q_{1,0}(t).
\end{aligned}$$

$$\begin{aligned}
\frac{\partial M}{\partial t} &= \beta(e^{\theta_1}-1)\frac{\partial M}{\partial \theta_1} - \frac{\beta}{N}(e^{\theta_1}-1)\frac{\partial^2 M}{\partial \theta_1^2} + \gamma(e^{-\theta_1}-1)\frac{\partial M}{\partial \theta_1} + \beta(e^{\theta_2}-1)\frac{\partial M}{\partial \theta_2} \\
&- \frac{\beta}{N}(e^{\theta_2}-1)\frac{\partial^2 M}{\partial \theta_2^2} + \gamma(e^{-\theta_2}-1)\frac{\partial M}{\partial \theta_2} + \lambda(e^{\theta_1}-1)\frac{\partial M}{\partial \theta_2} - \frac{\lambda}{N}(e^{\theta_1}-1)\frac{\partial^2 M}{\partial \theta_1 \partial \theta_2} \\
&+ \lambda(e^{\theta_2}-1)\frac{\partial M}{\partial \theta_1} - \frac{\lambda}{N}(e^{\theta_2}-1)\frac{\partial^2 M}{\partial \theta_1 \partial \theta_2} + (\gamma q_{0,1}(t) + \gamma q_{1,0}(t))M(\theta_1,\theta_2,t) \\
&- \gamma q_{0,1}(t) - \gamma q_{1,0}(t).
\end{aligned}$$

Using the transformation $K(\theta_1,\theta_2,t) = logM(\theta_1,\theta_2,t)$ we have

$$\begin{aligned}
\frac{\partial K}{\partial t} &= \beta(e^{\theta_1}-1)\frac{\partial K}{\partial \theta_1} - \frac{\beta}{N}(e^{\theta_1}-1)\left(\frac{\partial^2 K}{\partial \theta_1^2} + \left(\frac{\partial K}{\partial \theta_1}\right)^2\right) + \gamma(e^{-\theta_1}-1)\frac{\partial K}{\partial \theta_1} \\
&+ \beta(e^{\theta_2}-1)\frac{\partial K}{\partial \theta_2} - \frac{\beta}{N}(e^{\theta_2}-1)\left(\frac{\partial^2 K}{\partial \theta_2^2} + \left(\frac{\partial K}{\partial \theta_2}\right)^2\right) + \gamma(e^{-\theta_2}-1)\frac{\partial K}{\partial \theta_2} \\
&+ \lambda(e^{\theta_1}-1)\frac{\partial K}{\partial \theta_2} - \frac{\lambda}{N}(e^{\theta_1}-1)\left(\frac{\partial^2 K}{\partial \theta_1 \partial \theta_2} + \frac{\partial K}{\partial \theta_1}\frac{\partial K}{\partial \theta_2}\right) + \lambda(e^{\theta_2}-1)\frac{\partial K}{\partial \theta_1} \\
&- \frac{\lambda}{N}(e^{\theta_2}-1)\left(\frac{\partial^2 K}{\partial \theta_1 \partial \theta_2} + \frac{\partial K}{\partial \theta_1}\frac{\partial K}{\partial \theta_2}\right) + \gamma q_{0,1}(t)(1-e^K) + \gamma q_{1,0}(t)(1-e^K)
\end{aligned}$$

$$\begin{aligned}
\frac{\partial K}{\partial t} &= \left(\beta(e^{\theta_1}-1) + \gamma(e^{-\theta_1}-1) + \lambda(e^{\theta_2}-1)\right)\frac{\partial K}{\partial \theta_1} - \frac{\beta}{N}(e^{\theta_1}-1)\left(\frac{\partial^2 K}{\partial \theta_1^2} + \left(\frac{\partial K}{\partial \theta_1}\right)^2\right) \\
&+ \left(\beta(e^{\theta_2}-1) + \gamma(e^{-\theta_2}-1) + \lambda(e^{\theta_1}-1)\right)\frac{\partial K}{\partial \theta_2} - \frac{\beta}{N}(e^{\theta_2}-1)\left(\frac{\partial^2 K}{\partial \theta_2^2} + \left(\frac{\partial K}{\partial \theta_2}\right)^2\right) \\
&- \left(\frac{\lambda}{N}(e^{\theta_1}-1) + \frac{\lambda}{N}(e^{\theta_2}-1)\right)\left(\frac{\partial^2 K}{\partial \theta_1 \partial \theta_2} + \frac{\partial K}{\partial \theta_1}\frac{\partial K}{\partial \theta_2}\right) + \gamma q_{0,1}(t)(1-e^K) \\
&+ \gamma q_{1,0}(t)(1-e^K)
\end{aligned}$$

$$
\begin{aligned}
\frac{\partial K}{\partial t} &= \left[\beta\left(\theta_1+\frac{\theta_1^2}{2!}+\cdots\right)+\gamma\left(-\theta_1+\frac{\theta_1^2}{2!}+\cdots\right)+\lambda\left(\theta_2+\frac{\theta_2^2}{2!}+\cdots\right)\right]\frac{\partial K}{\partial \theta_1} \\
&+ \left[\beta\left(\theta_2+\frac{\theta_2^2}{2!}+\cdots\right)+\gamma\left(-\theta_2+\frac{\theta_2^2}{2!}+\cdots\right)+\lambda\left(\theta_1+\frac{\theta_1^2}{2!}+\cdots\right)\right]\frac{\partial K}{\partial \theta_2} \\
&- \frac{\beta}{N}\left(\theta_1+\frac{\theta_1^2}{2!}+\frac{\theta_1^3}{3!}+\cdots\right)\left(\frac{\partial^2 K}{\partial \theta_1^2}+\left(\frac{\partial K}{\partial \theta_1}\right)^2\right) \\
&- \frac{\beta}{N}\left(\theta_2+\frac{\theta_2^2}{2!}+\cdots\right)\left(\frac{\partial^2 K}{\partial \theta_2^2}+\left(\frac{\partial K}{\partial \theta_2}\right)^2\right) \\
&- \left(\frac{\lambda}{N}\left(\theta_1+\frac{\theta_1^2}{2!}+\cdots\right)+\frac{\lambda}{N}\left(\theta_2+\frac{\theta_2^2}{2!}+\cdots\right)\right)\left(\frac{\partial^2 K}{\partial \theta_1 \partial \theta_2}+\frac{\partial K}{\partial \theta_1}\frac{\partial K}{\partial \theta_2}\right) \\
&+ \gamma q_{0,1}(t)(1-e^K)+\gamma q_{1,0}(t)(1-e^K). \qquad \text{(B.1)}
\end{aligned}
$$

Using the definition $K(\theta_1\theta_2,t)=\sum_{i_1=0}^{\infty}\sum_{i_2=0}^{\infty}k_{i_1,i_2}(t)\frac{\theta_1^{i_1}}{i_1!}\frac{\theta_2^{i_2}}{i_1!}$ where $k_{i_1,i_2}(t)$ denotes the (i_1,i_2)th cumulant function - for $(i_1,i_2)\neq(0,0)$,

$$
\begin{aligned}
K(\theta_1,\theta_2,t) &= k_{0,1}(t)\theta_2+k_{1,0}(t)\theta_1+k_{1,1}(t)\theta_1\theta_2+k_{2,0}(t)\frac{\theta_1^2}{2!}+k_{0,2}(t)\frac{\theta_2^2}{2!}+k_{1,2}(t)\frac{\theta_1\theta_2^2}{2!} \\
&+ k_{2,1}(t)\frac{\theta_1^2\theta_2}{2!}+k_{2,2}(t)\frac{\theta_1^2\theta_2^2}{2!2!}+\cdots \\
\frac{\partial K}{\partial t} &= \dot{k}_{0,1}(t)\theta_2+\dot{k}_{1,0}(t)\theta_1+\dot{k}_{1,1}(t)\theta_1\theta_2+\dot{k}_{2,0}(t)\frac{\theta_1^2}{2!}+\dot{k}_{0,2}(t)\frac{\theta_2^2}{2!}+\dot{k}_{1,2}(t)\frac{\theta_1\theta_2^2}{2!} \\
&+ \dot{k}_{2,1}(t)\frac{\theta_1^2\theta_2}{2!}+\dot{k}_{2,2}(t)\frac{\theta_1^2\theta_2^2}{2!2!}+\cdots
\end{aligned}
$$

$$
\begin{aligned}
\frac{\partial K}{\partial \theta_1} &= k_{1,0}(t) + k_{1,1}(t)\theta_2 + k_{2,0}(t)\theta_1 + k_{1,2}(t)\frac{\theta_2^2}{2!} + k_{2,1}(t)\theta_1\theta_2 + k_{2,2}(t)\frac{\theta_1\theta_2^2}{2!} + \cdots \\
\frac{\partial K}{\partial \theta_2} &= k_{0,1}(t) + k_{1,1}(t)\theta_1 + k_{0,2}(t)\theta_2 + k_{2,1}(t)\frac{\theta_2^2}{2!} + k_{1,2}(t)\theta_1\theta_2 + k_{2,2}(t)\frac{\theta_1^2\theta_2}{2!} + \cdots \\
\frac{\partial^2 K}{\partial \theta_1^2} &= k_{2,0}(t) + k_{2,1}(t)\theta_2 + k_{2,2}(t)\frac{\theta_1^2}{2!} + k_{3,0}\theta_1 + \cdots \\
\frac{\partial^2 K}{\partial \theta_2^2} &= k_{0,2}(t) + k_{1,2}(t)\theta_1 + k_{2,2}(t)\frac{\theta_2^2}{2!} + k_{3,0}\theta_2 + \cdots \\
\frac{\partial^2 K}{\partial \theta_1 \partial \theta_2} &= k_{1,1}(t) + k_{2,1}(t)\theta_1 + k_{1,2}(t)\theta_2 + k_{2,2}(t)\theta_1\theta_2 + \cdots \\
\left(\frac{\partial K}{\partial \theta_1}\right)^2 &= \left(k_{1,0}(t) + k_{1,1}(t)\theta_2 + k_{2,0}(t)\theta_1 + k_{1,2}(t)\frac{\theta_2^2}{2!} + k_{2,1}(t)\theta_1\theta_2 + k_{2,2}(t)\frac{\theta_1\theta_2^2}{2!} + \cdots\right)^2 \\
&= k_{1,0}^2(t) + 2k_{1,0}(t)k_{1,1}(t)\theta_2 + 2k_{1,0}(t)k_{2,0}(t)\theta_1 + k_{1,0}(t)k_{1,2}(t)\theta_2^2 \\
&\quad + 2k_{1,0}(t)k_{2,1}(t)\theta_1\theta_2 + \cdots \\
\left(\frac{\partial K}{\partial \theta_2}\right)^2 &= \left(k_{0,1}(t) + k_{1,1}(t)\theta_1 + k_{0,2}(t)\theta_2 + k_{2,1}(t)\frac{\theta_1^2}{2!} + k_{1,2}(t)\theta_1\theta_2 + k_{2,2}(t)\frac{\theta_1\theta_2^2}{2!} + \cdots\right)^2 \\
&= k_{0,1}^2(t) + 2k_{0,1}(t)k_{1,1}(t)\theta_1 + 2k_{0,1}(t)k_{0,2}(t)\theta_2 + k_{0,1}(t)k_{2,1}(t)\theta_1^2 \\
&\quad + 2k_{0,1}(t)k_{2,1}(t)\theta_1\theta_2 + \cdots
\end{aligned}
$$

$$
\begin{aligned}
\frac{\partial K}{\partial \theta_1}\frac{\partial K}{\partial \theta_2} &= \left(k_{1,0}(t) + k_{1,1}(t)\theta_2 + k_{2,0}(t)\theta_1 + k_{1,2}(t)\frac{\theta_2^2}{2!} + k_{2,1}(t)\theta_1\theta_2 + k_{2,2}(t)\frac{\theta_1\theta_2^2}{2!} + \cdots\right) \\
&\quad \left(k_{0,1}(t) + k_{1,1}(t)\theta_1 + k_{0,2}(t)\theta_2 + k_{2,1}(t)\frac{\theta_2^2}{2!} + k_{1,2}(t)\theta_1\theta_2 + k_{2,2}(t)\frac{\theta_1^2\theta_2}{2!} + \cdots\right) \\
&= k_{1,0}(t)k_{0,1}(t) + k_{1,0}(t)k_{1,1}(t)\theta_1 + k_{0,1}(t)k_{1,1}(t)\theta_2 + k_{1,1}(t)^2\theta_1\theta_2 + k_{1,0}(t)k_{0,2}(t)\theta_2 \\
&+ k_{0,1}(t)k_{2,0}(t)\theta_1 + +k_{1,1}(t)k_{2,0}(t)\theta_1^2 + k_{1,1}(t)k_{0,2}(t)\theta_2^2 + k_{1,0}(t)k_{1,2}(t)\theta_1\theta_2 \\
&+ k_{0,1}(t)k_{1,2}(t)\theta_1\theta_2 + k_{0,1}(t)k_{1,2}(t)\frac{\theta_2^2}{2!} + k_{1,0}(t)k_{1,2}(t)\frac{\theta_1^2}{2!} + \cdots
\end{aligned}
$$

Substituting these into equation (B.1) gives

$$\dot{k}_{0,1}(t)\theta_2 + \dot{k}_{1,0}(t)\theta_1 + \dot{k}_{1,1}(t)\theta_1\theta_2 + \dot{k}_{2,0}(t)\frac{\theta_1^2}{2!} + \dot{k}_{0,2}(t)\frac{\theta_2^2}{2!} + \cdots =$$
$$\left[\beta\left(\theta_1 + \frac{\theta_1^2}{2!} + \cdots\right) + \gamma\left(-\theta_1 + \frac{\theta_1^2}{2!} + \cdots\right) + \lambda\left(\theta_2 + \frac{\theta_2^2}{2!} + \cdots\right)\right]$$
$$\left(k_{1,0}(t) + k_{1,1}(t)\theta_2 + k_{2,0}(t)\theta_1 + k_{1,2}(t)\frac{\theta_2^2}{2!} + k_{2,1}(t)\theta_1\theta_2 + \cdots\right)$$
$$+\left[\beta\left(\theta_2 + \frac{\theta_2^2}{2!} + \cdots\right) + \gamma\left(-\theta_2 + \frac{\theta_2^2}{2!} + \cdots\right) + \lambda\left(\theta_1 + \frac{\theta_1^2}{2!} + \cdots\right)\right]$$
$$\left(k_{0,1}(t) + k_{1,1}(t)\theta_1 + k_{0,2}(t)\theta_2 + k_{2,1}(t)\frac{\theta_2^2}{2!} + k_{1,2}(t)\theta_1\theta_2 + \cdots\right)$$
$$-\frac{\beta}{N}\left(\theta_1 + \frac{\theta_1^2}{2!} + \cdots\right)\left(k_{2,0}(t) + k_{2,1}(t)\theta_2 + k_{2,2}(t)\frac{\theta_1^2}{2!} + k_{3,0}\theta_1 + k_{1,0}^2(t)\right.$$
$$\left.+2k_{1,0}(t)k_{1,1}(t)\theta_2 + 2k_{1,0}(t)k_{2,0}(t)\theta_1 + k_{1,0}(t)k_{1,2}(t)\theta_2^2 + 2k_{1,0}(t)k_{2,1}(t)\theta_1\theta_2 + \cdots\right)$$
$$-\frac{\beta}{N}\left(\theta_2 + \frac{\theta_2^2}{2!} + \cdots\right)\left(k_{0,2}(t) + k_{1,2}(t)\theta_1 + k_{2,2}(t)\frac{\theta_2^2}{2!} + k_{0,3}\theta_2 + k_{0,1}^2(t)\right.$$
$$\left.+2k_{0,1}(t)k_{1,1}(t)\theta_1 2k_{0,1}(t)k_{0,2}(t)\theta_2 + k_{0,1}(t)k_{2,1}(t)\theta_1^2 + 2k_{0,1}(t)k_{2,1}(t)\theta_1\theta_2 + \cdots\right)$$
$$-\left(\frac{\lambda}{N}\left(\theta_1 + \frac{\theta_1^2}{2!} + \cdots\right) + \frac{\lambda}{N}\left(\theta_2 + \frac{\theta_2^2}{2!} + \cdots\right)\right)$$
$$\left(k_{1,1}(t) + k_{2,1}(t)\theta_1 + k_{1,2}(t)\theta_2 + k_{2,2}(t)\theta_1\theta_2 + k_{1,0}(t)k_{0,1}(t) + k_{1,0}(t)k_{1,1}(t)\theta_1\right.$$
$$+k_{0,1}(t)k_{1,1}(t)\theta_2 + k_{1,1}^2(t)\theta_1\theta_2 + k_{1,0}(t)k_{0,2}(t)\theta_2 + k_{0,1}(t)k_{2,0}(t)\theta_1 + k_{1,1}(t)k_{2,0}(t)\theta_1^2$$
$$+k_{1,1}(t)k_{0,2}(t)\theta_2^2 + k_{1,0}(t)k_{1,2}(t)\theta_1\theta_2 + k_{0,1}(t)k_{1,2}(t)\theta_1\theta_2 + k_{0,1}(t)k_{1,2}(t)\frac{\theta_2^2}{2!}$$
$$\left.+k_{1,0}(t)k_{1,2}(t)\frac{\theta_1^2}{2!} + \cdots\right) + \gamma q_{0,1}(t) + \gamma q_{1,0}(t),$$

$$\dot{k}_{0,1}(t)\theta_2 + \dot{k}_{1,0}(t)\theta_1 + \dot{k}_{1,1}(t)\theta_1\theta_2 + \dot{k}_{2,0}(t)\frac{\theta_1^2}{2!} + \dot{k}_{0,2}(t)\frac{\theta_2^2}{2!} + \cdots =$$
$$\left[\beta\left(\theta_1 + \frac{\theta_1^2}{2!} + \cdots\right) + \gamma\left(-\theta_1 + \frac{\theta_1^2}{2!} - \frac{\theta_1^3}{3!} + \cdots\right) + \lambda\left(\theta_2 + \frac{\theta_2^2}{2!} + \cdots\right)\right]$$
$$\left(k_{1,0}(t) + k_{1,1}(t)\theta_2 + k_{2,0}(t)\theta_1 + k_{1,2}(t)\frac{\theta_2^2}{2!} + k_{2,1}(t)\theta_1\theta_2 + \cdots\right)$$
$$+\left[\beta\left(\theta_2 + \frac{\theta_2^2}{2!} + \cdots\right) + \gamma\left(-\theta_2 + \frac{\theta_2^2}{2!} + \cdots\right) + \lambda\left(\theta_1 + \frac{\theta_1^2}{2!} + \cdots\right)\right]$$
$$\left(k_{0,1}(t) + k_{1,1}(t)\theta_1 + k_{0,2}(t)\theta_2 + k_{2,1}(t)\frac{\theta_2^2}{2!} + k_{1,2}(t)\theta_1\theta_2 + \cdots\right)$$
$$-\frac{\beta}{N}\left(\theta_1 + \frac{\theta_1^2}{2!} + \cdots\right)\left(k_{2,0}(t) + k_{2,1}(t)\theta_2 + k_{2,2}(t)\frac{\theta_1^2}{2!} + k_{3,0}\theta_1 + k_{1,0}^2(t)\right.$$
$$\left.+2k_{1,0}(t)k_{1,1}(t)\theta_2 + 2k_{1,0}(t)k_{2,0}(t)\theta_1 + k_{1,0}(t)k_{1,2}(t)\theta_2^2 + 2k_{1,0}(t)k_{2,1}(t)\theta_1\theta_2 + \cdots\right)$$
$$-\frac{\beta}{N}\left(\theta_2 + \frac{\theta_2^2}{2!} + \cdots\right)\left(k_{0,2}(t) + k_{1,2}(t)\theta_1 + k_{2,2}(t)\frac{\theta_2^2}{2!} + k_{0,3}\theta_2 + k_{0,1}^2(t)\right.$$
$$\left.+2k_{0,1}(t)k_{1,1}(t)\theta_1 + 2k_{0,1}(t)k_{0,2}(t)\theta_2 + k_{0,1}(t)k_{2,1}(t)\theta_1^2 + 2k_{0,1}(t)k_{2,1}(t)\theta_1\theta_2 + \cdots\right)$$
$$-\left(\frac{\lambda}{N}\left(\theta_1 + \frac{\theta_1^2}{2!} + \cdots\right) + \frac{\lambda}{N}\left(\theta_2 + \frac{\theta_2^2}{2!} + \cdots\right)\right)$$
$$\left(k_{1,1}(t) + k_{2,1}(t)\theta_1 + k_{1,2}(t)\theta_2 + k_{2,2}(t)\theta_1\theta_2 + k_{1,0}(t)k_{0,1}(t) + k_{1,0}(t)k_{1,1}(t)\theta_1\right.$$
$$+k_{0,1}(t)k_{1,1}(t)\theta_2 + k_{1,1}^2(t)\theta_1\theta_2 + k_{1,0}(t)k_{0,2}(t)\theta_2 + k_{0,1}(t)k_{2,0}(t)\theta_1 + k_{1,1}(t)k_{2,0}(t)\theta_1^2$$
$$+k_{1,1}(t)k_{0,2}(t)\theta_2^2 + k_{1,0}(t)k_{1,2}(t)\theta_1\theta_2 + k_{0,1}(t)k_{1,2}(t)\theta_1\theta_2 + k_{0,1}(t)k_{1,2}(t)\frac{\theta_2^2}{2!}$$
$$\left.+k_{1,0}(t)k_{1,2}(t)\frac{\theta_1^2}{2!} + \cdots\right) + \left(\gamma q_{0,1}(t) + \gamma q_{1,0}(t)\right)\left(k_{0,1}(t)\theta_2 + k_{1,0}(t)\theta_1 + k_{1,1}(t)\theta_1\theta_2\right.$$
$$\left.+k_{2,0}(t)\frac{\theta_1^2}{2!} + k_{0,2}(t)\frac{\theta_2^2}{2!} - k_{0,1}^2(t)\frac{\theta_2^2}{2!} - k_{1,0}^2(t)\frac{\theta_1^2}{2!} - k_{1,0}(t)k_{0,1}(t)\theta_1\theta_2 + \cdots\right).$$

Equating coefficients of $\theta_1, \theta_2, \theta_1\theta_2, \theta_1^2, \theta_2^2$ respectively, on the left hand side of the

pde with the corresponding coefficients on the right hand side we have

$$\begin{aligned}
\dot{k}_{1,0} &= (\beta-\gamma)k_{1,0} + \lambda k_{0,1} - \frac{\beta}{N}k_{2,0} - \frac{\beta}{N}k_{1,0}^2 - \frac{\lambda}{N}k_{1,1} - \frac{\lambda}{N}k_{1,0}k_{0,1} \\
&\quad +(\gamma q_{0,1} + \gamma q_{1,0})k_{1,0}, \qquad \text{(B.2)} \\
\dot{k}_{0,1} &= (\beta-\gamma)k_{0,1} + \lambda k_{1,0} - \frac{\beta}{N}k_{0,2} - \frac{\beta}{N}k_{0,1}^2 - \frac{\lambda}{N}k_{1,1} - \frac{\lambda}{N}k_{1,0}k_{0,1} \\
&\quad +(\gamma q_{0,1} + \gamma q_{1,0})k_{0,1}, \qquad \text{(B.3)} \\
\dot{k}_{1,1} &= 2(\beta-\gamma)k_{1,1} + \lambda(k_{2,0}+k_{0,2}) + \frac{\beta}{N}(k_{2,1}+k_{1,2}) - \frac{2\beta}{N}(k_{1,0}k_{1,1}+k_{0,1}k_{1,1}) \\
&\quad -\frac{\lambda}{N}(k_{1,2}+k_{2,1}) - \frac{\lambda}{N}(k_{1,0}k_{1,1}+k_{0,1}k_{1,1}) - \frac{\lambda}{N}(k_{0,1}k_{2,0}+k_{1,0}k_{0,2}) \\
&\quad +(\gamma q_{0,1} + \gamma q_{1,0})(k_{1,1} - k_{1,0}k_{0,1}), \qquad \text{(B.4)} \\
\dot{k}_{2,0} &= (\beta+\gamma)k_{1,0} + 2(\beta-\gamma)k_{2,0} - \frac{\beta}{N}(k_{2,0}+2k_{3,0}) + \lambda k_{1,0} + 2\lambda k_{1,1} \\
&\quad -\frac{\beta}{N}k_{1,0}^2 - 4\frac{\beta}{N}k_{1,0}k_{2,0} - \frac{\lambda}{N}(k_{1,0}k_{0,1} + 2k_{1,0}k_{1,1} + k_{0,1}k_{2,0}) \\
&\quad -\frac{\lambda}{N}(k_{1,1}+2k_{2,1}) + (\gamma q_{0,1} + \gamma q_{1,0})(k_{2,0} - k_{1,0}^2), \qquad \text{(B.5)} \\
\dot{k}_{0,2} &= (\beta+\gamma)k_{0,1} + 2(\beta-\gamma)k_{0,2} - \frac{\beta}{N}(k_{0,2}+2k_{0,3}) + \lambda k_{0,1} + 2\lambda k_{1,1} \\
&\quad -\frac{\beta}{N}k_{0,1}^2 - 4\frac{\beta}{N}k_{0,1}k_{0,2} - \frac{\lambda}{N}(k_{1,0}k_{0,1} + 2k_{0,1}k_{1,1} + k_{1,0}k_{0,2}) \\
&\quad -\frac{\lambda}{N}(k_{1,1}+2k_{1,2}) + (\gamma q_{0,1} + \gamma q_{1,0})(k_{0,2}(t) - k_{0,1}^2). \qquad \text{(B.6)}
\end{aligned}$$

Appendix C

Cumulant equations for the SIS model with demography

The Kolmogorov forward equations for the state probability conditioned on not being absorbed, $q_{s,i}(t)$, can be written as.

$$\begin{aligned}\frac{dq_{s,i}}{dt} &= \lambda_1(s-1,i)q_{s-1,i}(t) + \mu_1(s+1,i)q_{s+1,i}(t) + \beta_1(s+1,i-1)p_{s+1,i-1}(t) \\ &+\gamma_2(s-1,i+1)q_{s-1,i+1}(t) + \mu_2(s,i+1)q_{s,i+1}(t) - \lambda_1(s,i)q_{s,i}(t) \\ &-\mu_1(s,i)q_{s,i}(t) - \beta_1(s,i)q_{s,i}(t) - \gamma_2(s,i)q_{s,i}(t) - \mu_2(s,i)q_{s,i}(t) \\ &+(\gamma+\mu)q_{.,1}q_{s,i}(t),\end{aligned}$$

for $s = 0, 1, 2 \ldots$, $i = 1, 2, \ldots$. Multiplying this system of equations by $e^{s\theta_1 + i\theta_2}$,$\theta_1, \theta_2 \in \mathbb{R}$, and summing over all values of s, i gives

$$\begin{aligned}
\sum_{s=0}^{\infty}\sum_{i=1}^{\infty}\frac{dq_{s,i}}{dt}e^{s\theta_1+i\theta_2} &= \sum_{s=1}^{\infty}\sum_{i=1}^{\infty}\lambda_1(s-1,i)q_{s-1,i}(t)e^{s\theta_1+i\theta_2} \\
&+ \sum_{s=0}^{\infty}\sum_{i=2}^{\infty}\beta_1(s+1,i-1)q_{s+1,i-1}(t)e^{s\theta_1+i\theta_2} \\
&+ \sum_{s=1}^{\infty}\sum_{i=1}^{\infty}\gamma_2(s-1,i+1)q_{s-1,i+1}(t)e^{s\theta_1+i\theta_2} \\
&+ \sum_{s=0}^{\infty}\sum_{i=1}^{\infty}\mu_1(s+1,i)q_{s+1,i}(t)e^{s\theta_1+i\theta_2} \\
&+ \sum_{s=0}^{\infty}\sum_{i=1}^{\infty}\mu_2(s,i+1)q_{s,i+1}(t)e^{s\theta_1+i\theta_2} \\
&- \sum_{s=0}^{\infty}\sum_{i=1}^{\infty}\lambda_1(s,i)q_{s,i}(t)e^{s\theta_1+i\theta_2} - \sum_{s=1}^{\infty}\sum_{i=1}^{\infty}\mu_1(s,i)q_{s,i}(t)e^{s\theta_1+i\theta_2} \\
&- \sum_{s=1}^{\infty}\sum_{i=1}^{\infty}\beta_1(s,i)q_{s,i}(t)e^{s\theta_1+i\theta_2} - \sum_{s=0}^{\infty}\sum_{i=1}^{\infty}\gamma_2(s,i)q_{s,i}(t)e^{s\theta_1+i\theta_2} \\
&- \sum_{s=0}^{\infty}\sum_{i=1}^{\infty}\mu_2(s,i)q_{s,i}(t)e^{s\theta_1+i\theta_2} + (\gamma+\mu)q_{\cdot,1}\sum_{s=0}^{\infty}\sum_{i=1}^{\infty}q_{s,i}(t)e^{s\theta_1+i\theta_2}
\end{aligned}$$

$$\begin{aligned}
\sum_{s=0}^{\infty}\sum_{i=1}^{\infty}q'_{s,i}(t)e^{s\theta_1+i\theta_2} &= \sum_{s=0}^{\infty}\sum_{i=1}^{\infty}\lambda_1(s,i)q_{s,i}(t)e^{(s+1)\theta_1+i\theta_2} - \sum_{s=0}^{\infty}\sum_{i=1}^{\infty}\lambda_1(s,i)q_{s,i}(t)e^{s\theta_1+i\theta_2} \\
&+ \sum_{s=1}^{\infty}\sum_{i=1}^{\infty}\mu_1(s,i)q_{s,i}(t)e^{(s-1)\theta_1+i\theta_2} - \sum_{s=1}^{\infty}\sum_{i=1}^{\infty}\mu_1(s,i)q_{s,i}(t)e^{s\theta_1+i\theta_2} \\
&+ \sum_{s=1}^{\infty}\sum_{i=1}^{\infty}\beta_1(s,i)q_{s,i}(t)e^{(s-1)\theta_1+(i+1)\theta_2} - \sum_{s=1}^{\infty}\sum_{i=1}^{\infty}\beta_1(s,i)q_{s,i}(t)e^{s\theta_1+i\theta_2} \\
&+ \sum_{s=0}^{\infty}\sum_{i=2}^{\infty}\gamma_2(s,i)q_{s,i}(t)e^{(s+1)\theta_1+(i-1)\theta_2} - \sum_{s=0}^{\infty}\sum_{i=1}^{\infty}\gamma_2(s,i)q_{s,i}(t)e^{s\theta_1+i\theta_2} \\
&+ \sum_{s=0}^{\infty}\sum_{i=2}^{\infty}\mu_2(s,i)q_{s,i}(t)e^{s\theta_1+(i-1)\theta_2} - \sum_{s=0}^{\infty}\sum_{i=1}^{\infty}\mu_2(s,i)q_{s,i}(t)e^{s\theta_1+i\theta_2} \\
&+ (\gamma+\mu)q_{\cdot,1}\sum_{s=0}^{\infty}\sum_{i=1}^{\infty}q_{s,i}(t)e^{s\theta_1+i\theta_2}
\end{aligned}$$

$$\begin{aligned}
\sum_{s=0}^{\infty}\sum_{i=1}^{\infty} q'_{s,i}(t)e^{s\theta_1+i\theta_2} &= (e^{\theta_1}-1)\sum_{s=0}^{\infty}\sum_{i=1}^{\infty}\lambda_1(s,i)q_{s,i}(t)e^{s\theta_1+i\theta_2} \\
&\quad +(e^{-\theta_1}-1)\sum_{s=1}^{\infty}\sum_{i=1}^{\infty}\mu_1(s,i)q_{s,i}(t)e^{s\theta_1+i\theta_2} \\
&\quad +(e^{\theta_2-\theta_1}-1)\sum_{s=1}^{\infty}\sum_{i=1}^{\infty}\beta_1(s,i)q_{s,i}(t)e^{s\theta_1+i\theta_2} \\
&\quad +(e^{\theta_1-\theta_2}-1)\sum_{s=0}^{\infty}\sum_{i=2}^{\infty}\gamma_2(s,i)q_{s,i}(t)e^{s\theta_1+i\theta_2} \\
&\quad +(e^{-\theta_2}-1)\sum_{s=0}^{\infty}\sum_{i=2}^{\infty}\mu_2(s,i)q_{s,i}(t)e^{s\theta_1+i\theta_2} \\
&\quad -\sum_{s=0}^{\infty}\gamma_2(s,1)q_{s,1}(t)e^{s\theta_1+\theta_2}-\sum_{s=0}^{\infty}\mu_2(s,1)q_{s,1}(t)e^{s\theta_1+\theta_2} \\
&\quad +(\gamma+\mu)q_{\cdot,1}\sum_{s=0}^{\infty}\sum_{i=1}^{\infty}q_{s,i}(t)e^{s\theta_1+i\theta_2}.
\end{aligned}$$

But

$$\lambda_1(s,i)=\mu N,\quad \mu_1(s,i)=\mu s,\quad \beta_1(s,i)=\frac{\beta}{N}si,\quad \gamma_2(s,i)=\gamma i,\quad \mu_2(s,i)=\mu i,$$

so

$$\begin{aligned}
\sum_{s=0}^{\infty}\sum_{i=1}^{\infty} q'_{s,i}(t)e^{s\theta_1+i\theta_2} &= (e^{\theta_1}-1)\mu N\sum_{s=0}^{\infty}\sum_{i=1}^{\infty}q_{s,i}(t)e^{s\theta_1+i\theta_2} \\
&\quad +(e^{-\theta_1}-1)\mu\sum_{s=1}^{\infty}\sum_{i=1}^{\infty}sq_{s,i}(t)e^{s\theta_1+i\theta_2} \\
&\quad +(e^{\theta_2-\theta_1}-1)\frac{\beta}{N}\sum_{s=1}^{\infty}\sum_{i=1}^{\infty}siq_{s,i}(t)e^{s\theta_1+i\theta_2} \\
&\quad +(e^{\theta_1-\theta_2}-1)\gamma\sum_{s=0}^{\infty}\sum_{i=2}^{\infty}iq_{s,i}(t)e^{s\theta_1+i\theta_2} \\
&\quad -\sum_{s=0}^{\infty}\gamma_2(s,1)q_{s,1}(t)e^{s\theta_1+\theta_2}-\sum_{s=0}^{\infty}\mu_2(s,1)q_{s,1}(t)e^{s\theta_1+\theta_2} \\
&\quad +(e^{-\theta_2}-1)\mu\sum_{s=0}^{\infty}\sum_{i=2}^{\infty}iq_{s,i}(t)e^{s\theta_1+i\theta_2} \\
&\quad +(\gamma+\mu)q_{\cdot,1}\sum_{s=0}^{\infty}\sum_{i=1}^{\infty}q_{s,i}(t)e^{s\theta_1+i\theta_2}.
\end{aligned}$$

Using

$$M(\theta_1,\theta_2,t) = E[e^{S\theta_1+I\theta_2} \mid I>0] = \sum_{s=0}^{\infty}\sum_{i=1}^{\infty} q_{s,i}(t)e^{s\theta_1+i\theta_2}$$

$$\frac{\partial M(\theta_1\theta_2,t)}{\partial\theta_1} = \sum_{s=0}^{\infty}\sum_{i=1}^{\infty} sq_{s,i}(t)e^{s\theta_1+i\theta_2},$$

$$\frac{\partial M(\theta_1\theta_2,t)}{\partial\theta_2} = \sum_{s=0}^{\infty}\sum_{i=1}^{\infty} iq_{s,i}(t)e^{s\theta_1+i\theta_2},$$

and

$$\frac{\partial^2 M(\theta_1\theta_2,t)}{\partial\theta_1\partial\theta_2} = \sum_{s=0}^{\infty}\sum_{i=1}^{\infty} siq_{s,i}(t)e^{s\theta_1+i\theta_2}$$

gives

$$\begin{aligned}\frac{\partial M}{\partial t} &= \mu N(e^{\theta_1}-1)+\mu(e^{-\theta_1}-1)\frac{\partial M}{\partial\theta_1}+\frac{\beta}{N}(e^{\theta_2-\theta_1}-1)\frac{\partial^2 M}{\partial\theta_1\partial\theta_2}\\ &+\mu(e^{-\theta_2}-1)\left(\frac{\partial M}{\partial\theta_2}-\sum_{s=0}^{\infty}q_{s,1}(t)e^{s\theta_1+\theta_2}\right)\\ &+\gamma(e^{\theta_1-\theta_2}-1)\left(\frac{\partial M}{\partial\theta_2}-\sum_{s=0}^{\infty}q_{s,1}(t)e^{s\theta_1+\theta_2}\right)-\mu e^{\theta_2}\sum_{s=0}^{\infty}q_{s,1}(t)e^{s\theta_1}\\ &-\gamma e^{\theta_2}\sum_{s=0}^{\infty}q_{s,1}(t)e^{s\theta_1}+(\gamma+\mu)q_{.,1}M.\end{aligned}$$

$$\begin{aligned}\frac{\partial M}{\partial t} &= \mu N(e^{\theta_1}-1)M+\mu(e^{-\theta_1}-1)\frac{\partial M}{\partial\theta_1}+\frac{\beta}{N}(e^{\theta_2-\theta_1}-1)\frac{\partial^2 M}{\partial\theta_1\partial\theta_2}\\ &+\mu(e^{-\theta_2}-1)\frac{\partial M}{\partial\theta_2}+\gamma(e^{\theta_1-\theta_2}-1)\frac{\partial M}{\partial\theta_2}-\mu\sum_{s=0}^{\infty}q_{s,1}(t)e^{s\theta_1}\\ &-\gamma e^{\theta_1}\sum_{s=0}^{\infty}q_{s,1}(t)e^{s\theta_1}+(\gamma+\mu)q_{.,1}M\end{aligned}$$

$$\begin{aligned}\frac{\partial M}{\partial t} &= \mu NM(e^{\theta_1}-1)+\mu(e^{-\theta_1}-1)\frac{\partial M}{\partial\theta_1}+\frac{\beta}{N}(e^{\theta_2-\theta_1}-1)\frac{\partial^2 M}{\partial\theta_1\partial\theta_2}\\ &+\mu(e^{-\theta_2}-1)\frac{\partial M}{\partial\theta_2}+\gamma(e^{\theta_1-\theta_2}-1)\frac{\partial M}{\partial\theta_2}-\mu q_{.,1}\sum_{s=0}^{\infty}q_S(s|1)(t)e^{s\theta_1}\\ &-\gamma q_{.,1}e^{\theta_1}\sum_{s=0}^{\infty}q_S(s|1)(t)e^{s\theta_1}+(\gamma+\mu)q_{.,1}M\end{aligned}$$

where $q_S(s|1)(t) = \frac{q_{s,1}}{q_{.1}}$ is the conditional probability that S takes the value s given that $I = 1$. Using the transformation $K(\theta_1, \theta_2, t) = logM(\theta_1, \theta_2, t)$ we have

$$\begin{aligned}
\frac{\partial K}{\partial t} &= \frac{\beta}{N}(e^{\theta_2-\theta_1}-1)\left(\frac{\partial^2 K}{\partial\theta_1\partial\theta_2}+\frac{\partial K}{\partial\theta_1}\frac{\partial K}{\partial\theta_2}\right)+\mu N(e^{\theta_1}-1)+\mu(e^{-\theta_1}-1)\frac{\partial K}{\partial\theta_1} \\
&+\mu(e^{-\theta_2}-1)\frac{\partial K}{\partial\theta_2}+\gamma(e^{\theta_1-\theta_2}-1)\frac{\partial K}{\partial\theta_2}+\mu q_{.,1}\left(1-e^{-K}\sum_{s=0}^{\infty}q_S(s|1)(t)e^{s\theta_1}\right) \\
&+\gamma q_{.,1}\left(1-e^{\theta_1}e^{-K}\sum_{s=0}^{\infty}q_S(s|1)(t)e^{s\theta_1}\right).
\end{aligned}$$

$$\begin{aligned}
\frac{\partial K}{\partial t} &= \frac{\beta}{N}\left(\theta_2-\theta_1-\theta_1\theta_2+\frac{1}{2}\theta_1^2+\frac{1}{2}\theta_2^2+\frac{1}{2}\theta_2\theta_1^2-\frac{1}{2}\theta_1\theta_2^2+\cdots\right)\left(\frac{\partial^2 K}{\partial\theta_1\partial\theta_2}+\frac{\partial K}{\partial\theta_1}\frac{\partial K}{\partial\theta_2}\right) \\
&+\mu N\left(\theta_1+\frac{\theta_1^2}{2!}+\cdots\right)+\mu\left(-\theta_1+\frac{\theta_1^2}{2!}+\cdots\right)\frac{\partial K}{\partial\theta_1}+\mu\left(-\theta_2+\frac{\theta_2^2}{2!}+\cdots\right)\frac{\partial K}{\partial\theta_2} \\
&+\gamma\left(\theta_1-\theta_2-\theta_1\theta_2+\frac{1}{2}\theta_1^2+\frac{1}{2}\theta_2^2+\frac{1}{2}\theta_1\theta_2^2-\frac{1}{2}\theta_2\theta_1^2+\frac{1}{4}\theta_1^2\theta_2^2+\cdots\right)\frac{\partial K}{\partial\theta_2} \\
&+\mu q_{.,1}\left(1-e^{-K}\sum_{s=0}^{\infty}q_S(s|1)(t)\left(1+s\theta_1+\frac{s^2\theta_1^2}{2}+\cdots\right)\right) \\
&+\gamma q_{.,1}\left(1-\left(1+\theta_1+\frac{\theta_1^2}{2!}+\cdots\right)e^{-K}\sum_{s=0}^{\infty}q_S(s|1)(t)\left(1+s\theta_1+\frac{s^2\theta_1^2}{2}\right.\right. \\
&\left.\left.+\cdots\right)\right) \qquad \text{(C.1)}
\end{aligned}$$

Using the definition $K(\theta_1\theta_2,t) = \sum_{s=0}^{\infty}\sum_{i=0}^{\infty} k_{s,i}(t)\frac{\theta_1^s}{s!}\frac{\theta_2^i}{i!}$ where $k_{s,i}(t)$ denotes the (s,i)th cumulant function - for $(s,i) \neq (0,0)$ we have

$$
\begin{aligned}
K(\theta_1,\theta_2,t) &= k_{0,1}(t)\theta_2 + k_{1,0}(t)\theta_1 + k_{1,1}(t)\theta_1\theta_2 + k_{2,0}(t)\frac{\theta_1^2}{2!} + k_{0,2}(t)\frac{\theta_2^2}{2!} + k_{1,2}(t)\frac{\theta_1\theta_2^2}{2!} \\
&+ k_{2,1}(t)\frac{\theta_1^2\theta_2}{2!} + k_{2,2}(t)\frac{\theta_1^2\theta_2^2}{2!2!} + \cdots, \\
\frac{\partial K}{\partial t} &= \dot{k}_{0,1}(t)\theta_2 + \dot{k}_{1,0}(t)\theta_1 + \dot{k}_{1,1}(t)\theta_1\theta_2 + \dot{k}_{2,0}(t)\frac{\theta_1^2}{2!} + \dot{k}_{0,2}(t)\frac{\theta_2^2}{2!} + \dot{k}_{1,2}(t)\frac{\theta_1\theta_2^2}{2!} \\
&+ \dot{k}_{2,1}(t)\frac{\theta_1^2\theta_2}{2!} + \dot{k}_{2,2}(t)\frac{\theta_1^2\theta_2^2}{2!2!} + \cdots, \\
\frac{\partial K}{\partial \theta_1} &= k_{1,0}(t) + k_{1,1}(t)\theta_2 + k_{2,0}(t)\theta_1 + k_{1,2}(t)\frac{\theta_2^2}{2!} + k_{2,1}(t)\theta_1\theta_2 \\
&+ k_{2,2}(t)\frac{\theta_1\theta_2^2}{2!} + \cdots, \\
\frac{\partial K}{\partial \theta_2} &= k_{0,1}(t) + k_{1,1}(t)\theta_1 + k_{0,2}(t)\theta_2 + k_{2,1}(t)\frac{\theta_2^2}{2!} + k_{1,2}(t)\theta_1\theta_2 \\
&+ k_{2,2}(t)\frac{\theta_1^2\theta_2}{2!} + \cdots, \\
\frac{\partial^2 K}{\partial\theta_1\partial\theta_2} &= k_{1,1}(t) + k_{2,1}(t)\theta_1 + k_{1,2}(t)\theta_2 + k_{2,2}(t)\theta_1\theta_2 + \cdots, \\
\frac{\partial K}{\partial\theta_1}\frac{\partial K}{\partial\theta_2} &= \left(k_{1,0}(t) + k_{1,1}(t)\theta_2 + k_{2,0}(t)\theta_1 + k_{1,2}(t)\frac{\theta_2^2}{2!} + k_{2,1}(t)\theta_1\theta_2\right. \\
&\left. + k_{2,2}(t)\frac{\theta_1\theta_2^2}{2!} + \cdots\right) \\
&\left(k_{0,1}(t) + k_{1,1}(t)\theta_1 + k_{0,2}(t)\theta_2 + k_{2,1}(t)\frac{\theta_2^2}{2!}\right. \\
&\left. + k_{1,2}(t)\theta_1\theta_2 + k_{2,2}(t)\frac{\theta_1^2\theta_2}{2!} + \cdots\right) \\
&= k_{1,0}(t)k_{0,1}(t) + k_{1,0}(t)k_{1,1}(t)\theta_1 + k_{0,1}(t)k_{1,1}(t)\theta_2 + k_{1,1}(t)^2\theta_1\theta_2 \\
&+ k_{1,0}(t)k_{0,2}(t)\theta_2 + k_{0,1}(t)k_{2,0}(t)\theta_1 + k_{1,1}(t)k_{2,0}(t)\theta_1^2 + k_{1,1}(t)k_{0,2}(t)\theta_2^2 \\
&+ k_{1,0}(t)k_{1,2}(t)\theta_1\theta_2 + k_{0,1}(t)k_{1,2}(t)\theta_1\theta_2 + k_{0,1}(t)k_{1,2}(t)\frac{\theta_2^2}{2!} \\
&+ k_{1,0}(t)k_{1,2}(t)\frac{\theta_1^2}{2!} + \cdots.
\end{aligned}
$$

Substituting these into equation (C.1) the above gives

$$\dot{k}_{0,1}(t)\theta_2 + \dot{k}_{1,0}(t)\theta_1 + \dot{k}_{1,1}(t)\theta_1\theta_2 + \dot{k}_{2,0}(t)\frac{\theta_1^2}{2!} + \dot{k}_{0,2}(t)\frac{\theta_2^2}{2!} + \cdots =$$
$$\frac{\beta}{N}\left(\theta_2 - \theta_1 - \theta_1\theta_2 + \frac{1}{2}\theta_1^2 + \frac{1}{2}\theta_2^2 + \frac{1}{2}\theta_2\theta_1^2 - \frac{1}{2}\theta_1\theta_2^2 + \frac{1}{4}\theta_1^2\theta_2^2 + \cdots\right)$$
$$\Big(\, k_{1,1}(t) + k_{2,1}(t)\theta_1 + k_{1,2}(t)\theta_2 + k_{2,2}(t)\theta_1\theta_2 + k_{1,0}(t)k_{0,1}(t) + k_{1,1}^2(t)\theta_1\theta_2$$
$$+k_{1,0}(t)k_{1,1}(t)\theta_1 + k_{0,1}(t)k_{1,1}(t)\theta_2 + k_{1,0}(t)k_{0,2}(t)\theta_2 + k_{0,1}(t)k_{2,0}(t)\theta_1$$
$$+k_{1,1}(t)k_{2,0}(t)\theta_1^2 + k_{1,1}(t)k_{0,2}(t)\theta_2^2 + k_{1,0}(t)k_{1,2}(t)\theta_1\theta_2 + k_{0,1}(t)k_{1,2}(t)\theta_1\theta_2$$
$$+k_{0,1}(t)k_{1,2}(t)\frac{\theta_2^2}{2!} + k_{1,0}(t)k_{1,2}(t)\frac{\theta_1^2}{2!} + \cdots\Big) + \mu N\left(\theta_1 + \frac{\theta_1^2}{2!} + \cdots\right)$$
$$+\mu\left(-\theta_1 + \frac{\theta_1^2}{2!} + \cdots\right)\left(k_{1,0}(t) + k_{1,1}(t)\theta_2 + k_{2,0}(t)\theta_1 + k_{1,2}(t)\frac{\theta_2^2}{2!} + k_{2,1}(t)\theta_1\theta_2 + \cdots\right)$$
$$+\mu\left(-\theta_2 + \frac{\theta_2^2}{2!} + \cdots\right)\left(k_{0,1}(t) + k_{1,1}(t)\theta_1 + k_{0,2}(t)\theta_2 + k_{2,1}(t)\frac{\theta_2^2}{2!} + k_{1,2}(t)\theta_1\theta_2 + \cdots\right)$$
$$+\gamma\left(\theta_1 - \theta_2 - \theta_1\theta_2 + \frac{1}{2}\theta_1^2 + \frac{1}{2}\theta_2^2 + \frac{1}{2}\theta_1\theta_2^2 - \frac{1}{2}\theta_2\theta_1^2 + \frac{1}{4}\theta_1^2\theta_2^2 + \cdots\right)$$
$$\left(k_{0,1}(t) + k_{1,1}(t)\theta_1 + k_{0,2}(t)\theta_2 + k_{2,1}(t)\frac{\theta_2^2}{2!} + k_{1,2}(t)\theta_1\theta_2 + \cdots\right)$$
$$+\gamma q_{\cdot,1}(t)\left[\left(1 - \left(1 + \theta_1 + \frac{\theta_1^2}{2!} + \cdots\right)\Big(\, 1 - k_{0,1}(t)\theta_2 - k_{1,0}(t)\theta_1 - k_{1,1}(t)\theta_1\theta_2\right.\right.$$
$$\left.\left.-k_{2,0}(t)\frac{\theta_1^2}{2!} - k_{0,2}(t)\frac{\theta_2^2}{2!} + k_{0,1}^2(t)\frac{\theta_2^2}{2} + k_{1,0}^2(t)\frac{\theta_1^2}{2} + k_{0,1}(t)k_{1,0}(t)\theta_1\theta_2 + \cdots\Big)\right)$$
$$\sum_{i_1=0}^{N} q_S(s|1)(t)\left(1 + s\theta_1 + \frac{s^2\theta_1^2}{2} + \cdots\right)\Bigg] + \mu q_{\cdot,1}(t)\Big[\,\Big(\, 1 - \Big(\, 1 - k_{0,1}(t)\theta_2$$
$$-k_{1,0}(t)\theta_1 - k_{1,1}(t)\theta_1\theta_2 - k_{2,0}(t)\frac{\theta_1^2}{2!} - k_{0,2}(t)\frac{\theta_2^2}{2!} + k_{0,1}^2(t)\frac{\theta_2^2}{2} + k_{1,0}^2(t)\frac{\theta_1^2}{2}$$
$$+k_{0,1}(t)k_{1,0}(t)\theta_1\theta_2 + \cdots\Big)\Big)\sum_{i_2=0}^{N} q_S(s|1)(t)\left(1 + s\theta_1 + \frac{s^2\theta_1^2}{2} + \cdots\right)\Bigg]$$

$$\dot{k}_{0,1}(t)\theta_2 + \dot{k}_{1,0}(t)\theta_1 + \dot{k}_{1,1}(t)\theta_1\theta_2 + \dot{k}_{2,0}(t)\frac{\theta_1^2}{2!} + \dot{k}_{0,2}(t)\frac{\theta_2^2}{2!} + \cdots =$$
$$\frac{\beta}{N}\left(\theta_2 - \theta_1 - \theta_1\theta_2 + \frac{1}{2}\theta_1^2 + \frac{1}{2}\theta_2^2 + \frac{1}{2}\theta_2\theta_1^2 - \frac{1}{2}\theta_1\theta_2^2 + \frac{1}{4}\theta_1^2\theta_2^2 + \cdots\right)$$
$$\Big(k_{1,1}(t) + k_{2,1}(t)\theta_1 + k_{1,2}(t)\theta_2 + k_{2,2}(t)\theta_1\theta_2 + k_{1,0}(t)k_{0,1}(t) + k_{1,0}(t)k_{1,1}(t)\theta_1$$
$$+k_{0,1}(t)k_{1,1}(t)\theta_2 + k_{1,1}^2(t)\theta_1\theta_2 + k_{1,0}(t)k_{0,2}(t)\theta_2 + k_{0,1}(t)k_{2,0}(t)\theta_1 + k_{1,1}(t)k_{2,0}(t)\theta_1^2$$
$$+k_{1,1}(t)k_{0,2}(t)\theta_2^2 + k_{1,0}(t)k_{1,2}(t)\theta_1\theta_2 + k_{0,1}(t)k_{1,2}(t)\theta_1\theta_2 + k_{0,1}(t)k_{1,2}(t)\frac{\theta_2^2}{2!}$$
$$+k_{1,0}(t)k_{1,2}(t)\frac{\theta_1^2}{2!} + \cdots\Big) + \mu N\left(\theta_1 + \frac{\theta_1^2}{2!} + \cdots\right) + \mu\left(-\theta_1 + \frac{\theta_1^2}{2!} + \cdots\right)$$
$$\left(k_{1,0}(t) + k_{1,1}(t)\theta_2 + k_{2,0}(t)\theta_1 + k_{1,2}(t)\frac{\theta_2^2}{2!} + k_{2,1}(t)\theta_1\theta_2 + \cdots\right)$$
$$+\mu\left(-\theta_2 + \frac{\theta_2^2}{2!} + \cdots\right)\left(k_{0,1}(t) + k_{1,1}(t)\theta_1 + k_{0,2}(t)\theta_2 + k_{2,1}(t)\frac{\theta_2^2}{2!} + k_{1,2}(t)\theta_1\theta_2 + \cdots\right)$$
$$+\gamma\left(\theta_1 - \theta_2 - \theta_1\theta_2 + \frac{1}{2}\theta_1^2 + \frac{1}{2}\theta_2^2 + \frac{1}{2}\theta_1\theta_2^2 - \frac{1}{2}\theta_2\theta_1^2 + \frac{1}{4}\theta_1^2\theta_2^2 + \cdots\right)$$
$$\left(k_{0,1}(t) + k_{1,1}(t)\theta_1 + k_{0,2}(t)\theta_2 + k_{2,1}(t)\frac{\theta_2^2}{2!} + k_{1,2}(t)\theta_1\theta_2 + \cdots\right) + \gamma q_{.,1}(t)$$
$$\Bigg[\left(1 - \left(1 + \theta_2 + \frac{\theta_2^2}{2!} + \cdots\right)\left(1 - k_{0,1}(t)\theta_2 - k_{1,0}(t)\theta_1 - k_{1,1}(t)\theta_1\theta_2 - k_{2,0}(t)\frac{\theta_1^2}{2!}\right.\right.$$
$$\left.\left.-k_{0,2}(t)\frac{\theta_2^2}{2!} + k_{0,1}^2(t)\frac{\theta_2^2}{2} + k_{1,0}^2(t)\frac{\theta_1^2}{2} + k_{0,1}(t)k_{1,0}(t)\theta_1\theta_2 + \cdots\right)\right)\left(1 + \theta_1 E[S|I=1]\right.$$
$$\left.+\frac{\theta_1^2}{2}E[S^2|I=1] + \cdots\right)\Bigg] + \mu q_{.,1}(t)\left[\left(1 - \left(1 - k_{0,1}(t)\theta_2 - k_{1,0}(t)\theta_1\right.\right.\right.$$
$$\left.\left.\left.-k_{1,1}(t)\theta_1\theta_2 - k_{2,0}(t)\frac{\theta_1^2}{2!} - k_{0,2}(t)\frac{\theta_2^2}{2!} + k_{0,1}^2(t)\frac{\theta_2^2}{2} + k_{1,0}^2(t)\frac{\theta_1^2}{2} + k_{0,1}(t)k_{1,0}(t)\theta_1\theta_2 + \cdots\right)\right)$$
$$\left(1 + \theta_1 E[S|I=1] + \frac{\theta_1^2}{2}E[S^2|I=1] + \cdots\right)\Bigg].$$

Equating coefficients of $\theta_1, \theta_2, \theta_1\theta_2, \theta_1^2, \theta_2^2$ respectively, on the left hand side of the pde with the corresponding coefficients on the right hand side gives

$$\begin{aligned}
\dot{k}_{1,0} &= \mu N - \frac{\beta}{N}(k_{1,1} + k_{1,0}k_{0,1}) - \mu k_{1,0} + \gamma k_{0,1} - \gamma q_{.,1}\left(1 + E[S|I=1]\right) \\
&+ (\gamma + \mu)q_{.,1}\left(k_{1,0} - E[S|I=1]\right) \qquad \text{(C.2)} \\
\dot{k}_{0,1} &= \frac{\beta}{N}(k_{1,1} + k_{1,0}k_{0,1}) - (\mu + \gamma)k_{0,1} - \gamma q_{.,1} + (\gamma + \mu)q_{.,1}k_{0,1}, \qquad \text{(C.3)} \\
\dot{k}_{1,1} &= \frac{\beta}{N}(k_{1,0}k_{1,1} - k_{1,1} - k_{1,0}k_{0,1} + k_{2,1} + k_{0,1}k_{2,0} - k_{0,1}k_{1,1} - k_{1,2} \\
&- k_{1,0}k_{0,2}) - (2\mu + \gamma)k_{1,1} - \gamma k_{0,1} + \gamma(k_{0,2} + q_{.,1}k_{1,0}) \\
&+ (\gamma + \mu)q_{.,1}\left(k_{1,1} + k_{0,1}\left(E[S|I=1] - k_{1,0}\right)\right), \qquad \text{(C.4)} \\
\dot{k}_{2,0} &= \mu N + \frac{\beta}{N}\left(k_{1,1} + k_{1,0}k_{0,1} - 2k_{2,1} - 2k_{1,0}k_{1,1} - 2k_{0,1}k_{2,0}\right) + \mu k_{1,0} \\
&+ \gamma k_{0,1} + 2\gamma k_{1,1} - 2\mu k_{2,0} + (\gamma + \mu)q_{.,1}\left(k_{2,0} - k_{1,0}^2 - E[S^2|I=1]\right) \\
&+ \gamma q_{.,1}\left(2k_{1,0}E[S|I=1] - 2E[S|I=1] - 1 - E[S^2|I=1]\right), \qquad \text{(C.5)} \\
\dot{k}_{0,2} &= \frac{\beta}{N}\left(k_{1,1} + k_{1,0}k_{0,1} + 2k_{1,2} + 2k_{0,1}k_{1,1} + 2k_{1,0}k_{0,2}\right) - 2(\gamma + \mu)k_{0,2} \\
&+ (\gamma + \mu)k_{0,1} + (\gamma + \mu)q_{.,1}\left(k_{0,2} - k_{0,1}^2\right). \qquad \text{(C.6)}
\end{aligned}$$

Appendix D

Cumulant equations for the SIRS model without demography

The Kolmogorov forward equations for the state probabilities conditioned on non-extinction, $q_{s,i}(t)$, can be written as

$$\begin{aligned}\frac{dq_{s,i}}{dt} &= \beta_{1(s+1,i-1)}q_{s+1,i-1}(t) + \gamma_{2(s,i+1)}q_{s,i+1}(t) + \nu_{3(s-1,i)}q_{s-1,i}(t) - \beta_{1(s,i)}q_{s,i}(t) \\ &\quad -\gamma_{2(s,i)}q_{s,i}(t) - \nu_{3(s,i)}q_{i_1,i_2-1}(t) + \gamma q_{.,1}q_{s,i}(t),\end{aligned}$$

for $s = 0, 1, 2 \ldots, N$, $i = 1, 2, N-s$. Multiplying this system of equations by $e^{s\theta_1+i\theta_2}$, $\theta_1, \theta_2 \in \mathbb{R}$, and summing over all values of s, i gives

$$\begin{aligned}\sum_{s=0}^{N-1}\sum_{i=1}^{N-s}\frac{dq_{s,i}}{dt}e^{s\theta_1+i\theta_2} &= \sum_{s=0}^{N}\sum_{i=2}^{N-s}\beta_{1(s+1,i-1)}q_{s+1,i-1}(t)e^{s\theta_1+i\theta_2} - \sum_{s=1}^{N}\sum_{i=1}^{N-s}\beta_{1(s,i)}q_{s,i}(t)e^{s\theta_1+i\theta_2} \\ &\quad + \sum_{s=0}^{N}\sum_{i=1}^{N-s-1}\gamma_{2(s,i+1)}q_{s,i+1}(t)e^{s\theta_1+i\theta_2} - \sum_{s=0}^{N}\sum_{i=1}^{N-s}\gamma_{2(s,i)}q_{s,i}(t)e^{s\theta_1+i\theta_2} \\ &\quad + \sum_{s=1}^{N}\sum_{i=1}^{N-s}\nu_{3(s-1,i)}q_{s-1,i}(t)e^{s\theta_1+i\theta_2} - \sum_{s=0}^{N-1}\sum_{i=1}^{N-s}\nu_{3(s,i)}q_{s,i}(t)e^{s\theta_1+i\theta_2} \\ &\quad + \sum_{s=0}^{N}\sum_{i=1}^{N-s}\gamma q_{.,1}q_{s,i}(t)e^{s\theta_1+i\theta_2}.\end{aligned}$$

$$\begin{aligned}\sum_{s=0}^{N}\sum_{i=1}^{N-s}\frac{dq_{s,i}}{dt}e^{s\theta_1+i\theta_2} &= \sum_{s=1}^{N}\sum_{i=1}^{N-s}\beta_{1(s,i)}q_{s,i}(t)e^{(s-1)\theta_1+(i+1)\theta_2}-\sum_{s=1}^{N}\sum_{i=1}^{N-s}\beta_{1(s,i)}q_{s,i}(t)e^{s\theta_1+i\theta_2}\\ &+\sum_{s=0}^{N}\sum_{i=2}^{N-s}\gamma_{2(s,i)}q_{s,i}(t)e^{s\theta_1+(i-1)\theta_2}-\sum_{s=0}^{N}\sum_{i=1}^{N-s}\gamma_{2(s,i)}q_{s,i}(t)e^{s\theta_1+i\theta_2}\\ &+\sum_{s=0}^{N-1}\sum_{i=1}^{N-s}\nu_{3(s,i)}q_{s,i}(t)e^{(s+1)\theta_1+i\theta_2}-\sum_{s=0}^{N-1}\sum_{i=1}^{N-s}\nu_{3(s,i)}q_{s,i}(t)e^{s\theta_1+i\theta_2}\\ &+\sum_{s=0}^{N}\sum_{i=1}^{N-s}\gamma q_{.,1}q_{s,i}(t)e^{s\theta_1+i\theta_2}\end{aligned}$$

$$\begin{aligned}\sum_{s=0}^{N}\sum_{i=1}^{N-s}\frac{dq_{s,i}}{dt}e^{s\theta_1+i\theta_2} &= (e^{\theta_2-\theta_1}-1)\sum_{s=1}^{N}\sum_{i=1}^{N-s}\beta_{1(s,i)}q_{s,i}(t)e^{s\theta_1+i\theta_2}\\ &+(e^{-\theta_2}-1)\sum_{s=0}^{N}\sum_{i=2}^{N-s}\gamma_{2(s,i)}q_{s,i}(t)e^{s\theta_1+i\theta_2}-\sum_{s=0}^{N}\gamma_{2(s,1)}q_{s,1}(t)e^{s\theta_1+\theta_2}\\ &+(e^{\theta_1}-1)\sum_{s=0}^{N-1}\sum_{i=1}^{N-s}\nu_{3(s,i)}q_{s,i}(t)e^{s\theta_1+i\theta_2}+\sum_{s=0}^{N}\sum_{i=1}^{N-s}\gamma q_{.,1}q_{s,i}(t)e^{s\theta_1+i\theta_2}\end{aligned}$$

But

$$\beta_{1(s,i)}=\frac{\beta}{N}si,\quad \gamma_{2(s,i)}=\gamma i \quad\text{and}\quad \nu_{3(s,i)}=\nu(N-s-i),$$

so

$$\begin{aligned}\sum_{s=0}^{N}\sum_{i=1}^{N-s}\frac{dq_{s,i}}{dt}e^{s\theta_1+i\theta_2} &= \frac{\beta}{N}(e^{\theta_2-\theta_1}-1)\sum_{s=1}^{N}\sum_{i=1}^{N-s}siq_{s,i}(t)e^{s\theta_1+i\theta_2}\\ &+\gamma(e^{-\theta_2}-1)\sum_{s=0}^{N}\sum_{i=2}^{N-s}iq_{s,i}(t)e^{s\theta_1+i\theta_2}-\gamma e^{\theta_2}\sum_{s=0}^{N}q_{s,1}(t)e^{s\theta_1}\\ &+\nu(e^{\theta_1}-1)\sum_{s=0}^{N-1}\sum_{i=1}^{N-s}(N-s-i)q_{s,i}(t)e^{s\theta_1+i\theta_2}\\ &+\gamma q_{.,1}\sum_{s=0}^{N}\sum_{i=1}^{N-s}q_{s,i}(t)e^{s\theta_1+i\theta_2}.\end{aligned}$$

Using

$$M(\theta_1,\theta_2,t)=E[e^{S\theta_1+I\theta_2}\mid I>0]=\sum_{s=0}^{N}\sum_{i=1}^{N-s}q_{s,i}e^{s\theta_1+i\theta_2}$$

$$\frac{\partial M(\theta_1,\theta_2,t)}{\partial \theta_1} = \sum_{s=0}^{N}\sum_{i=1}^{N-s} s q_{s,i} e^{s\theta_1+i\theta_2},$$

$$\frac{\partial M(\theta_1,\theta_2,t)}{\partial \theta_2} = \sum_{s=0}^{N}\sum_{i=1}^{N-s} i q_{s,i} e^{s\theta_1+i\theta_2},$$

$$\frac{\partial^2 M(\theta_1,\theta_2,t)}{\partial \theta_1^2} = \sum_{s=0}^{N}\sum_{i=1}^{N-s} s^2 q_{s,i} e^{s\theta_1+i\theta_2},$$

$$\frac{\partial^2 M(\theta_1,\theta_2,t)}{\partial \theta_2^2} = \sum_{s=0}^{N}\sum_{i=1}^{N-s} i^2 q_{s,i} e^{s\theta_1+i\theta_2},$$

and

$$\frac{\partial^2 M(\theta_1,\theta_2,t)}{\partial \theta_1 \partial \theta_2} = \sum_{s=0}^{N}\sum_{i=1}^{N-s} si q_{s,i} e^{s\theta_1+i\theta_2}$$

$$\begin{aligned}\frac{\partial M}{\partial t} &= \frac{\beta}{N}(e^{\theta_2-\theta_1}-1)\frac{\partial^2 M}{\partial\theta_1\partial\theta_2} + \gamma(e^{-\theta_2}-1)\left(\frac{\partial M}{\partial\theta_2} - \sum_{s=0}^{N} q_{s,1}(t)e^{s\theta_1+\theta_2}\right)\\ &-\gamma\sum_{s=0}^{N} q_{s,1}(t)e^{s\theta_1+\theta_2} + \nu N(e^{\theta_1}-1)M - \nu(e^{\theta_1}-1)\frac{\partial M}{\partial\theta_1} - \nu(e^{\theta_1}-1)\frac{\partial M}{\partial\theta_2}\\ &+\gamma q_{.,1}M.\end{aligned}$$

$$\begin{aligned}\frac{\partial M}{\partial t} &= \frac{\beta}{N}(e^{\theta_2-\theta_1}-1)\frac{\partial^2 M}{\partial\theta_1\partial\theta_2} + \gamma(e^{-\theta_2}-1)\frac{\partial M}{\partial\theta_2} - \gamma\sum_{s=0}^{N} q_{s,1}(t)e^{s\theta_1}\\ &+\nu N(e^{\theta_1}-1)M - \nu(e^{\theta_1}-1)\frac{\partial M}{\partial\theta_1} - \nu(e^{\theta_1}-1)\frac{\partial M}{\partial\theta_2} + \gamma q_{.,1}M.\end{aligned}$$

$$\begin{aligned}\frac{\partial M}{\partial t} &= \frac{\beta}{N}(e^{\theta_2-\theta_1}-1)\frac{\partial^2 M}{\partial\theta_1\partial\theta_2} + \gamma(e^{-\theta_2}-1)\frac{\partial M}{\partial\theta_2} - \gamma q_{.,1}\sum_{s=0}^{N} q_S(s|1)(t)e^{s\theta_1}\\ &+\nu N(e^{\theta_1}-1)M - \nu(e^{\theta_1}-1)\frac{\partial M}{\partial\theta_1} - \nu(e^{\theta_1}-1)\frac{\partial M}{\partial\theta_2} + \gamma q_{.,1}M,\end{aligned}$$

where $q_S(s|1) = \frac{q_{(s,1)}}{q_{.,1}}$ is the conditional probability that S takes the value s given that $I = 1$.

Using the transformation $K(\theta_1,\theta_2,t) = logM(\theta_1,\theta_2,t)$ we have

$$\begin{aligned}\frac{\partial K}{\partial t} &= \frac{\beta}{N}(e^{\theta_2-\theta_1}-1)\left(\frac{\partial^2 K}{\partial\theta_1\partial\theta_2}+\frac{\partial K}{\partial\theta_1}\frac{\partial K}{\partial\theta_2}\right)+\gamma(e^{-\theta_2}-1)\frac{\partial M}{\partial\theta_2}\\ &\quad +\nu N(e^{\theta_1}-1)-\nu(e^{\theta_1}-1)\frac{\partial K}{\partial\theta_1}-\nu(e^{\theta_1}-1)\frac{\partial K}{\partial\theta_2}\\ &\quad -\gamma e^{-K}q_{.,1}\sum_{s=0}^{N}q_S(s|1)(t)e^{s\theta_1}+\gamma q_{.,1}\end{aligned}$$

$$\begin{aligned}\frac{\partial K}{\partial t} &= \frac{\beta}{N}\left(\theta_2-\theta_1-\theta_1\theta_2+\frac{1}{2}\theta_1^2+\frac{1}{2}\theta_2^2+\frac{1}{2}\theta_2\theta_1^2-\frac{1}{2}\theta_1\theta_2^2+\frac{1}{4}\theta_1^2\theta_2^2+\cdots\right)\\ &\quad \left(\frac{\partial^2 K}{\partial\theta_1\partial\theta_2}+\frac{\partial K}{\partial\theta_1}\frac{\partial K}{\partial\theta_2}\right)+\gamma\left(-\theta_2+\frac{\theta_2^2}{2!}+\cdots\right)\frac{\partial M}{\partial\theta_2}+\nu N\left(\theta_1+\frac{\theta_1^2}{2!}+\cdots\right)\\ &\quad -\nu\left(\theta_1+\frac{\theta_1^2}{2!}+\cdots\right)\frac{\partial K}{\partial\theta_1}-\nu\left(\theta_1+\frac{\theta_1^2}{2!}+\cdots\right)\frac{\partial K}{\partial\theta_2}\\ &\quad -\gamma q_{.,1}e^{-K}\sum_{s=0}^{N}q_S(s|1)(t)\left(1+s\theta_1+\frac{s^2\theta_1^2}{2}+\cdots\right)+\gamma q_{.,1}. \qquad \text{(D.1)}\end{aligned}$$

Using the definition $K(\theta_1\theta_2,t)=\sum_{s=0}^{\infty}\sum_{i=0}^{\infty}k_{s,i}(t)\frac{\theta_1^s}{s!}\frac{\theta_2^i}{i!}$ where $k_{s,i}(t)$ denotes the (s,i)th cumulant function - for $(s,i)\neq(0,0)$ we have

$$
\begin{aligned}
K(\theta_1,\theta_2,t) &= k_{0,1}(t)\theta_2 + k_{1,0}(t)\theta_1 + k_{1,1}(t)\theta_1\theta_2 + k_{2,0}(t)\frac{\theta_1^2}{2!} + k_{0,2}(t)\frac{\theta_2^2}{2!} \\
&\quad + k_{1,2}(t)\frac{\theta_1\theta_2^2}{2!} + k_{2,1}(t)\frac{\theta_1^2\theta_2}{2!} + k_{2,2}(t)\frac{\theta_1^2\theta_2^2}{2!2!} + \cdots \\
\frac{\partial K}{\partial t} &= \dot{k}_{0,1}(t)\theta_2 + \dot{k}_{1,0}(t)\theta_1 + \dot{k}_{1,1}(t)\theta_1\theta_2 + \dot{k}_{2,0}(t)\frac{\theta_1^2}{2!} + \dot{k}_{0,2}(t)\frac{\theta_2^2}{2!} \\
&\quad + \dot{k}_{1,2}(t)\frac{\theta_1\theta_2^2}{2!} + \dot{k}_{2,1}(t)\frac{\theta_1^2\theta_2}{2!} + \dot{k}_{2,2}(t)\frac{\theta_1^2\theta_2^2}{2!2!} + \cdots \\
\frac{\partial K}{\partial \theta_1} &= k_{1,0}(t) + k_{1,1}(t)\theta_2 + k_{2,0}(t)\theta_1 + k_{1,2}(t)\frac{\theta_2^2}{2!} + k_{2,1}(t)\theta_1\theta_2 \\
&\quad + k_{2,2}(t)\frac{\theta_1\theta_2^2}{2!} + \cdots \\
\frac{\partial K}{\partial \theta_2} &= k_{0,1}(t) + k_{1,1}(t)\theta_1 + k_{0,2}(t)\theta_2 + k_{2,1}(t)\frac{\theta_2^2}{2!} + k_{1,2}(t)\theta_1\theta_2 \\
&\quad + k_{2,2}(t)\frac{\theta_1^2\theta_2}{2!} + \cdots \\
\frac{\partial^2 K}{\partial \theta_1 \partial \theta_2} &= k_{1,1}(t) + k_{2,1}(t)\theta_1 + k_{1,2}(t)\theta_2 + k_{2,2}(t)\theta_1\theta_2 + \cdots \\
\frac{\partial K}{\partial \theta_1}\frac{\partial K}{\partial \theta_2} &= \left(k_{1,0}(t) + k_{1,1}(t)\theta_2 + k_{2,0}(t)\theta_1 + k_{1,2}(t)\frac{\theta_2^2}{2!} + k_{2,1}(t)\theta_1\theta_2\right. \\
&\quad \left. + k_{2,2}(t)\frac{\theta_1\theta_2^2}{2!} + \cdots\right)\left(k_{0,1}(t) + k_{1,1}(t)\theta_1 + k_{0,2}(t)\theta_2 + k_{2,1}(t)\frac{\theta_2^2}{2!}\right. \\
&\quad \left. + k_{1,2}(t)\theta_1\theta_2 + k_{2,2}(t)\frac{\theta_1^2\theta_2}{2!} + \cdots\right) \\
&= k_{1,0}(t)k_{0,1}(t) + k_{1,0}(t)k_{1,1}(t)\theta_1 + k_{0,1}(t)k_{1,1}(t)\theta_2 + k_{1,1}(t)^2\theta_1\theta_2 \\
&\quad + k_{1,0}(t)k_{0,2}(t)\theta_2 + k_{0,1}(t)k_{2,0}(t)\theta_1 + + k_{1,1}(t)k_{2,0}(t)\theta_1^2 \\
&\quad + k_{1,1}(t)k_{0,2}(t)\theta_2^2 + k_{1,0}(t)k_{1,2}(t)\theta_1\theta_2 + k_{0,1}(t)k_{1,2}(t)\theta_1\theta_2 \\
&\quad + k_{0,1}(t)k_{1,2}(t)\frac{\theta_2^2}{2!} + k_{1,0}(t)k_{1,2}(t)\frac{\theta_1^2}{2!} + \cdots
\end{aligned}
$$

Substituting these into equation (D.1) gives

$$\dot{k}_{0,1}(t)\theta_2 + \dot{k}_{1,0}(t)\theta_1 + \dot{k}_{1,1}(t)\theta_1\theta_2 + \dot{k}_{2,0}(t)\frac{\theta_1^2}{2!} + \dot{k}_{0,2}(t)\frac{\theta_2^2}{2!} + \cdots =$$
$$\frac{\beta}{N}\left(\theta_2 - \theta_1 - \theta_1\theta_2 + \frac{1}{2}\theta_1^2 + \frac{1}{2}\theta_2^2 + \frac{1}{2}\theta_2\theta_1^2 - \frac{1}{2}\theta_1\theta_2^2 + \frac{1}{4}\theta_1^2\theta_2^2 + \cdots\right)$$
$$\Big(k_{1,1}(t) + k_{2,1}(t)\theta_1 + k_{1,2}(t)\theta_2 + k_{2,2}(t)\theta_1\theta_2 + k_{1,0}(t)k_{0,1}(t) + k_{1,0}(t)k_{1,1}(t)\theta_1$$
$$+k_{0,1}(t)k_{1,1}(t)\theta_2 + k_{1,1}^2(t)\theta_1\theta_2 + k_{1,0}(t)k_{0,2}(t)\theta_2 + k_{0,1}(t)k_{2,0}(t)\theta_1 + k_{1,1}(t)k_{2,0}(t)\theta_1^2$$
$$+k_{1,1}(t)k_{0,2}(t)\theta_2^2 + k_{1,0}(t)k_{1,2}(t)\theta_1\theta_2 + k_{0,1}(t)k_{1,2}(t)\theta_1\theta_2 + k_{0,1}(t)k_{1,2}(t)\frac{\theta_2^2}{2!}$$
$$+k_{1,0}(t)k_{1,2}(t)\frac{\theta_1^2}{2!} + \cdots\Big) + \gamma\left(-\theta_2 + \frac{\theta_2^2}{2!} + \cdots\right)\Big(k_{0,1}(t) + k_{1,1}(t)\theta_1 + k_{0,2}(t)\theta_2$$
$$+k_{2,1}(t)\frac{\theta_2^2}{2!} + k_{1,2}(t)\theta_1\theta_2 + \cdots\Big) + \nu N\left(\theta_1 + \frac{\theta_1^2}{2!} + \cdots\right) - \nu\left(\theta_1 + \frac{\theta_1^2}{2!} + \cdots\right)$$
$$\left(k_{1,0}(t) + k_{1,1}(t)\theta_2 + k_{2,0}(t)\theta_1 + k_{1,2}(t)\frac{\theta_2^2}{2!} + k_{2,1}(t)\theta_1\theta_2 + \cdots\right)$$
$$-\nu\left(\theta_1 + \frac{\theta_1^2}{2!} + \cdots\right)\left(k_{0,1}(t) + k_{1,1}(t)\theta_1 + k_{0,2}(t)\theta_2 + k_{2,1}(t)\frac{\theta_2^2}{2!} + k_{1,2}(t)\theta_1\theta_2 + \cdots\right)$$
$$-\gamma q_{\cdot,1}\Big(1 - k_{0,1}(t)\theta_2 - k_{1,0}(t)\theta_1 - k_{1,1}(t)\theta_1\theta_2 - k_{2,0}(t)\frac{\theta_1^2}{2!} - k_{0,2}(t)\frac{\theta_2^2}{2!}$$
$$+k_{0,1}^2(t)\frac{\theta_2^2}{2} + k_{1,0}^2(t)\frac{\theta_1^2}{2} + k_{0,1}(t)k_{1,0}(t)\theta_1\theta_2 + \cdots\Big)\sum_{s=0}^{N} q_S(s|1)(t)\left(1 + s\theta_1 + \frac{s^2\theta_1^2}{2} + \cdots\right)$$
$$+\gamma q_{\cdot,1}.$$

$$
\begin{aligned}
&\dot{k}_{0,1}(t)\theta_2 + \dot{k}_{1,0}(t)\theta_1 + \dot{k}_{1,1}(t)\theta_1\theta_2 + \dot{k}_{2,0}(t)\frac{\theta_1^2}{2!} + \dot{k}_{0,2}(t)\frac{\theta_2^2}{2!} + \cdots = \\
&\frac{\beta}{N}\left(\theta_2 - \theta_1 - \theta_1\theta_2 + \frac{1}{2}\theta_1^2 + \frac{1}{2}\theta_2^2 + \frac{1}{2}\theta_2\theta_1^2 - \frac{1}{2}\theta_1\theta_2^2 + \frac{1}{4}\theta_1^2\theta_2^2 + \cdots\right) \\
&\Big(k_{1,1}(t) + k_{2,1}(t)\theta_1 + k_{1,2}(t)\theta_2 + k_{2,2}(t)\theta_1\theta_2 + k_{1,0}(t)k_{0,1}(t) + k_{1,0}(t)k_{1,1}(t)\theta_1 \\
&+k_{0,1}(t)k_{1,1}(t)\theta_2 + k_{1,1}^2(t)\theta_1\theta_2 + k_{1,0}(t)k_{0,2}(t)\theta_2 + k_{0,1}(t)k_{2,0}(t)\theta_1 + k_{1,1}(t)k_{2,0}(t)\theta_1^2 \\
&+k_{1,1}(t)k_{0,2}(t)\theta_2^2 + k_{1,0}(t)k_{1,2}(t)\theta_1\theta_2 + k_{0,1}(t)k_{1,2}(t)\theta_1\theta_2 + k_{0,1}(t)k_{1,2}(t)\frac{\theta_2^2}{2!} \\
&+k_{1,0}(t)k_{1,2}(t)\frac{\theta_1^2}{2!} + \cdots\Big) + \gamma\left(-\theta_2 + \frac{\theta_2^2}{2!} + \cdots\right)\Big(k_{0,1}(t) + k_{1,1}(t)\theta_1 + k_{0,2}(t)\theta_2 \\
&+k_{2,1}(t)\frac{\theta_2^2}{2!} + k_{1,2}(t)\theta_1\theta_2 + \cdots\Big) + \nu N\left(\theta_1 + \frac{\theta_1^2}{2!} + \cdots\right) - \nu\left(\theta_1 + \frac{\theta_1^2}{2!} + \cdots\right) \\
&\left(k_{1,0}(t) + k_{1,1}(t)\theta_2 + k_{2,0}(t)\theta_1 + k_{1,2}(t)\frac{\theta_2^2}{2!} + k_{2,1}(t)\theta_1\theta_2 + \cdots\right) \\
&-\nu\left(\theta_1 + \frac{\theta_1^2}{2!} + \cdots\right)\left(k_{0,1}(t) + k_{1,1}(t)\theta_1 + k_{0,2}(t)\theta_2 + k_{2,1}(t)\frac{\theta_2^2}{2!} + k_{1,2}(t)\theta_1\theta_2 + \cdots\right) \\
&-\gamma q_{.,1}\Big(1 - k_{0,1}(t)\theta_2 - k_{1,0}(t)\theta_1 - k_{1,1}(t)\theta_1\theta_2 - k_{2,0}(t)\frac{\theta_1^2}{2!} - k_{0,2}(t)\frac{\theta_2^2}{2!} + k_{0,1}^2(t)\frac{\theta_2^2}{2} \\
&+k_{1,0}^2(t)\frac{\theta_1^2}{2} + k_{0,1}(t)k_{1,0}(t)\theta_1\theta_2 + \cdots\Big)\left(1 + \theta_1 E[S|I=1] + \frac{\theta_1^2}{2}E[S^2|I=1] + \cdots\right) \\
&+\gamma q_{.,1}.
\end{aligned}
$$

Equating coefficients of $\theta_1, \theta_2, \theta_1\theta_2, \theta_1^2, \theta_2^2$ respectively, on the left hand side of the pde with the corresponding coefficients on the right hand side gives

$$
\begin{aligned}
\dot{k}_{1,0} &= \nu N - \frac{\beta}{N}(k_{1,1} + k_{1,0}k_{0,1}) - \nu(k_{1,0} + k_{0,1}) \\
&\quad +\gamma q_{.,1}\left(k_{1,0} - E[S|I=1]\right), && \text{(D.2)} \\
\dot{k}_{0,1} &= \frac{\beta}{N}(k_{1,1} + k_{1,0}k_{0,1}) - \gamma k_{0,1} + \gamma q_{.,1}k_{0,1}, && \text{(D.3)} \\
\dot{k}_{1,1} &= \frac{\beta}{N}\left(k_{1,0}k_{1,1} - k_{1,1} - k_{1,0}k_{0,1} + k_{2,1} + k_{0,1}k_{2,0} - k_{0,1}k_{1,1} - k_{1,2} - k_{1,0}k_{0,2}\right) \\
&\quad - (\nu + \gamma)k_{1,1} + \nu k_{0,2} + \gamma q_{.,1}\left(k_{1,1} - k_{1,0}k_{0,1} + k_{0,1}E[S|I=1]\right), && \text{(D.4)} \\
\dot{k}_{2,0} &= \nu N + \frac{\beta}{N}\left(k_{1,1} + k_{1,0}k_{0,1} - 2k_{2,1} - 2k_{1,0}k_{1,1} - 2k_{0,1}k_{2,0}\right) \\
&\quad - \nu(k_{1,0} + k_{0,1} + 2k_{2,0} + 2k_{1,1}) \\
&\quad + \gamma q_{.,1}\left(k_{2,0} - k_{1,0}^2 - E[S^2|I=1] + 2k_{1,0}E[S|I=1]\right), && \text{(D.5)} \\
\dot{k}_{0,2} &= \frac{\beta}{N}\left(k_{1,1} + k_{1,0}k_{0,1} + 2k_{1,2} + 2k_{0,1}k_{1,1} + 2k_{1,0}k_{0,2}\right) + \gamma(k_{0,1} - 2k_{0,2}) \\
&\quad + \gamma q_{.,1}\left(k_{0,2} - k_{0,1}^2\right). && \text{(D.6)}
\end{aligned}
$$

Appendix E

Cumulant equations for the SIRS model with demography

The Kolmogorov forward equations for the state probabilities conditioned on non-extinction, $q_{s,i,r}(t)$, can be written as

$$\begin{aligned} q'_{s,i,r}(t) &= \lambda_1(s-1,i,r)q_{s-1,i,r}(t) + \mu_1(s+1,i,r)q_{s+1,i,r}(t) \\ &+\beta_1(s+1,i-1,r)p_{s+1,i-1,r}(t) + \gamma_2(s,i+1,r-1)q_{s,i+1,r-1}(t) \\ &+\mu_2(s,i+1,r)q_{s,i+1,r}(t) + \mu_3(s,i,r+1)q_{s,i,r+1}(t) \\ &+\nu_3(s-1,i,r+1)q_{s-1,i,r+1}(t) - \lambda_1(s,i,r)q_{s,i,r}(t) - \mu_1(s,i,r)q_{s,i,r}(t) \\ &-\beta_1(s,i,r)q_{s,i,r}(t) - \gamma_2(s,i,r)q_{s,i,r}(t) - \mu_2(s,i,r)q_{s,i,r}(t) \\ &-\mu_3(s,i,r)q_{s,i,r}(t) - \nu_3(s,i,r)q_{s,i,r}(t) + (\gamma+\mu)q_{.,1,.}q_{s,i,r}(t), \end{aligned}$$

for $s = 0, 1, 2\ldots$, $i = 1, 2, \ldots$ and $r = 0, 1, 2, \ldots$. Multiplying this system of equations by $e^{s\theta_1+i\theta_2+r\theta_3}$, $\theta_1, \theta_2, \theta_3 \in \mathbb{R}$ and summing over all values of s, i, r gives

$$\begin{aligned}
\sum_{s=0}^{\infty}\sum_{i=1}^{\infty}\sum_{r=0}^{\infty}\frac{dq_{s,i,r}}{dt}e^{s\theta_1+i\theta_2+r\theta_3} &= \sum_{s=1}^{\infty}\sum_{i=1}^{\infty}\sum_{r=0}^{\infty}\lambda_1(s-1,i,r)q_{s-1,i,r}(t)e^{s\theta_1+i\theta_2+r\theta_3} \\
&+\sum_{s=0}^{\infty}\sum_{i=1}^{\infty}\sum_{r=0}^{\infty}\mu_1(s+1,i,r)q_{s+1,i,r}(t)e^{s\theta_1+i\theta_2+r\theta_3} \\
&+\sum_{s=0}^{\infty}\sum_{i=2}^{\infty}\sum_{r=0}^{\infty}\beta_1(s+1,i-1,r)q_{s+1,i-1,r}(t)e^{s\theta_1+i\theta_2+r\theta_3} \\
&+\sum_{s=0}^{\infty}\sum_{i=1}^{\infty}\sum_{r=1}^{\infty}\gamma_2(s,i+1,r-1)q_{s,i+1,r-1}(t)e^{s\theta_1+i\theta_2+r\theta_3} \\
&+\sum_{s=0}^{\infty}\sum_{i=1}^{\infty}\sum_{r=0}^{\infty}\mu_2(s,i+1,r)q_{s,i+1,r}(t)e^{s\theta_1+i\theta_2+r\theta_3} \\
&+\sum_{s=0}^{\infty}\sum_{i=1}^{\infty}\sum_{r=0}^{\infty}\mu_3(s,i,r+1)q_{s,i,r+1}(t)e^{s\theta_1+i\theta_2+r\theta_3} \\
&+\sum_{s=1}^{\infty}\sum_{i=1}^{\infty}\sum_{r=0}^{\infty}\nu_3(s-1,i,r+1)q_{s-1,i,r+1}(t)e^{s\theta_1+i\theta_2+r\theta_3} \\
&-\sum_{s=0}^{\infty}\sum_{i=1}^{\infty}\sum_{r=0}^{\infty}\lambda_1(s,i,r)q_{s,i,r}(t)e^{s\theta_1+i\theta_2+r\theta_3} \\
&-\sum_{s=1}^{\infty}\sum_{i=1}^{\infty}\sum_{r=0}^{\infty}\mu_1(s,i,r)q_{s,i,r}(t)e^{s\theta_1+i\theta_2+r\theta_3} \\
&-\sum_{s=1}^{\infty}\sum_{i=1}^{\infty}\sum_{r=0}^{\infty}\beta_1(s,i,r)q_{s,i,r}(t)e^{s\theta_1+i\theta_2+r\theta_3} \\
&-\sum_{s=0}^{\infty}\sum_{i=1}^{\infty}\sum_{r=0}^{\infty}\gamma_2(s,i,r)q_{s,i,r}(t)e^{s\theta_1+i\theta_2+r\theta_3} \\
&-\sum_{s=0}^{\infty}\sum_{i=1}^{\infty}\sum_{r=0}^{\infty}\mu_2(s,i,r)q_{s,i,r}(t)e^{s\theta_1+i\theta_2+r\theta_3} \\
&-\sum_{s=0}^{\infty}\sum_{i=1}^{\infty}\sum_{r=1}^{\infty}\mu_3(s,i,r)q_{s,i,r}(t)e^{s\theta_1+i\theta_2+r\theta_3} \\
&-\sum_{s=0}^{\infty}\sum_{i=1}^{\infty}\sum_{r=1}^{\infty}\nu_3(s,i,r)q_{s,i,r}(t)e^{s\theta_1+i\theta_2+r\theta_3} \\
&+(\gamma+\mu)q_{\cdot,1,\cdot}\sum_{s=0}^{\infty}\sum_{i=1}^{\infty}\sum_{r=0}^{\infty}q_{s,i,r}(t)e^{s\theta_1+i\theta_2+r\theta_3}
\end{aligned}$$

$$
\begin{aligned}
\sum_{s=0}^{\infty}\sum_{i=1}^{\infty}\sum_{r=0}^{\infty}\frac{dq_{s,i,r}}{dt}e^{s\theta_1+i\theta_2+r\theta_3} &= \sum_{s=0}^{\infty}\sum_{i=1}^{\infty}\sum_{r=0}^{\infty}\lambda_1(s,i,r)q_{s,i,r}(t)e^{(s+1)\theta_1+i\theta_2+r\theta_3} \\
&+\sum_{s=1}^{\infty}\sum_{i=1}^{\infty}\sum_{r=0}^{\infty}\mu_1(s,i,r)q_{s,i,r}(t)e^{(s-1)\theta_1+i\theta_2+r\theta_3} \\
&+\sum_{s=1}^{\infty}\sum_{i=1}^{\infty}\sum_{r=0}^{\infty}\beta_1(s,i,r)q_{s,i,r}(t)e^{(s-1)\theta_1+(i+1)\theta_2+r\theta_3} \\
&+\sum_{s=0}^{\infty}\sum_{i=2}^{\infty}\sum_{r=0}^{\infty}\gamma_2(s,i,r)q_{s,i,r}(t)e^{s\theta_1+(i-1)\theta_2+(r+1)\theta_3} \\
&+\sum_{s=0}^{\infty}\sum_{i=2}^{\infty}\sum_{r=0}^{\infty}\mu_2(s,i,r)q_{s,i,r}(t)e^{s\theta_1+(i-1)\theta_2+r\theta_3} \\
&+\sum_{s=0}^{\infty}\sum_{i=1}^{\infty}\sum_{r=1}^{\infty}\mu_3(s,i,r)q_{s,i,r}(t)e^{s\theta_1+i\theta_2+(r-1)\theta_3} \\
&+\sum_{s=0}^{\infty}\sum_{i=1}^{\infty}\sum_{r=1}^{\infty}\nu_3(s,i,r)q_{s,i,r}(t)e^{(s+1)\theta_1+(i-1)\theta_2+r\theta_3} \\
&-\sum_{s=0}^{\infty}\sum_{i=1}^{\infty}\sum_{r=0}^{\infty}\lambda_1(s,i,r)q_{s,i,r}(t)e^{s\theta_1+i\theta_2+r\theta_3} \\
&-\sum_{s=1}^{\infty}\sum_{i=1}^{\infty}\sum_{r=0}^{\infty}\mu_1(s,i,r)q_{s,i,r}(t)e^{s\theta_1+i\theta_2+r\theta_3} \\
&-\sum_{s=1}^{\infty}\sum_{i=1}^{\infty}\sum_{r=0}^{\infty}\beta_1(s,i,r)q_{s,i,r}(t)e^{s\theta_1+i\theta_2+r\theta_3} \\
&-\sum_{s=0}^{\infty}\sum_{i=1}^{\infty}\sum_{r=0}^{\infty}\gamma_2(s,i,r)q_{s,i,r}(t)e^{s\theta_1+i\theta_2+r\theta_3} \\
&-\sum_{s=0}^{\infty}\sum_{i=1}^{\infty}\sum_{r=0}^{\infty}\mu_2(s,i,r)q_{s,i,r}(t)e^{s\theta_1+i\theta_2+r\theta_3} \\
&-\sum_{s=0}^{\infty}\sum_{i=1}^{\infty}\sum_{r=1}^{\infty}\mu_3(s,i,r)q_{s,i,r}(t)e^{s\theta_1+i\theta_2+r\theta_3} \\
&-\sum_{s=0}^{\infty}\sum_{i=1}^{\infty}\sum_{r=1}^{\infty}\nu_3(s,i,r)q_{s,i,r}(t)e^{s\theta_1+i\theta_2+r\theta_3} \\
&+(\gamma+\mu)q_{\cdot,1,\cdot}\sum_{s=0}^{\infty}\sum_{i=1}^{\infty}\sum_{r=0}^{\infty}q_{s,i,r}(t)e^{s\theta_1+i\theta_2+r\theta_3}
\end{aligned}
$$

$$
\begin{aligned}
\sum_{s=0}^{\infty}\sum_{i=1}^{\infty}\sum_{r=0}^{\infty}\frac{dq_{s,i,r}}{dt}e^{s\theta_1+i\theta_2+r\theta_3} &= (e^{\theta_1}-1)\sum_{s=0}^{\infty}\sum_{i=1}^{\infty}\sum_{r=0}^{\infty}\lambda_1(s,i,r)q_{s,i,r}(t)e^{s\theta_1+i\theta_2+r\theta_3} \\
&+(e^{-\theta_1}-1)\sum_{s=1}^{\infty}\sum_{i=1}^{\infty}\sum_{r=0}^{\infty}\mu_1(s,i,r)q_{s,i,r}(t)e^{s\theta_1+i\theta_2+r\theta_3} \\
&+(e^{\theta_2-\theta_1}-1)\sum_{s=1}^{\infty}\sum_{i=1}^{\infty}\sum_{r=0}^{\infty}\beta_1(s,i,r)q_{s,i,r}(t)e^{s\theta_1+i\theta_2+r\theta_3} \\
&+(e^{\theta_3-\theta_2}-1)\sum_{s=0}^{\infty}\sum_{i=2}^{\infty}\sum_{r=0}^{\infty}\gamma_2(s,i,r)q_{s,i,r}(t)e^{s\theta_1+i\theta_2+r\theta_3} \\
&-\sum_{s=0}^{\infty}\sum_{r=0}^{\infty}\gamma_2(s,1,r)q_{s,1,r}(t)e^{s\theta_1+\theta_2+r\theta_3} \\
&+(e^{-\theta_2}-1)\sum_{s=0}^{\infty}\sum_{i=2}^{\infty}\sum_{r=0}^{\infty}\mu_2(s,i,r)q_{s,i,r}(t)e^{s\theta_1+i\theta_2+r\theta_3} \\
&-\sum_{s=0}^{\infty}\sum_{r=0}^{\infty}\mu_2(s,1,r)q_{s,1,r}(t)e^{s\theta_1+\theta_2+r\theta_3} \\
&+(e^{-\theta_3}-1)\sum_{s=0}^{\infty}\sum_{i=1}^{\infty}\sum_{r=1}^{\infty}\mu_3(s,i,r)q_{s,i,r}(t)e^{s\theta_1+i\theta_2+r\theta_3} \\
&+(e^{\theta_1-\theta_3}-1)\sum_{s=0}^{\infty}\sum_{i=1}^{\infty}\sum_{r=1}^{\infty}\nu_3(s,i,r)q_{s,i,r}(t)e^{s\theta_1+i\theta_2+r\theta_3} \\
&+(\gamma+\mu)q_{\cdot,1,\cdot}\sum_{s=0}^{\infty}\sum_{i=1}^{\infty}\sum_{r=0}^{\infty}q_{s,i,r}(t)e^{s\theta_1+i\theta_2+r\theta_3}.
\end{aligned}
$$

From the definition of $\lambda_1(s,i,r)$, $\mu_1(s,i,r)$, $\beta_1(s,i,r)$, $\gamma_2(s,i,r)$, $\mu_2(s,i,r)$, $\mu_3(s,i,r)$

and $\nu_3(s,i,r)$ in Table 7.2 we have

$$\begin{aligned}
\sum_{s=0}^{\infty}\sum_{i=1}^{\infty}\sum_{r=0}^{\infty}\frac{dq_{s,i,r}}{dt}e^{s\theta_1+i\theta_2+r\theta_3} &= (e^{\theta_1}-1)\mu N\sum_{s=0}^{\infty}\sum_{i=1}^{\infty}\sum_{r=0}^{\infty}q_{s,i,r}(t)e^{s\theta_1+i\theta_2+r\theta_3}\\
&+(e^{-\theta_1}-1)\mu\sum_{s=1}^{\infty}\sum_{i=1}^{\infty}\sum_{r=0}^{\infty}sq_{s,i,r}(t)e^{s\theta_1+i\theta_2+r\theta_3}\\
&+(e^{\theta_2-\theta_1}-1)\frac{\beta}{N}\sum_{s=1}^{\infty}\sum_{i=1}^{\infty}\sum_{r=0}^{\infty}siq_{s,i,r}(t)e^{s\theta_1+i\theta_2+r\theta_3}\\
&+(e^{\theta_3-\theta_2}-1)\gamma\sum_{s=0}^{\infty}\sum_{i=2}^{\infty}\sum_{r=0}^{\infty}iq_{s,i,r}(t)e^{s\theta_1+i\theta_2+r\theta_3}\\
&-\gamma e^{\theta_2}\sum_{s=0}^{\infty}\sum_{r=0}^{\infty}q_{s,1,r}(t)e^{s\theta_1+r\theta_3}\\
&+(e^{-\theta_2}-1)\mu\sum_{s=0}^{\infty}\sum_{i=2}^{\infty}\sum_{r=0}^{\infty}iq_{s,i,r}(t)e^{s\theta_1+i\theta_2+r\theta_3}\\
&-\mu e^{\theta_2}\sum_{s=0}^{\infty}\sum_{r=0}^{\infty}q_{s,1,r}(t)e^{s\theta_1+r\theta_3}\\
&+(e^{-\theta_3}-1)\mu\sum_{s=0}^{\infty}\sum_{i=1}^{\infty}\sum_{r=1}^{\infty}rq_{s,i,r}(t)e^{s\theta_1+i\theta_2+r\theta_3}\\
&+(e^{\theta_1-\theta_3}-1)\nu\sum_{s=0}^{\infty}\sum_{i=1}^{\infty}\sum_{r=1}^{\infty}rq_{s,i,r}(t)e^{s\theta_1+i\theta_2+r\theta_3}\\
&+(\gamma+\mu)q_{\cdot,1,\cdot}\sum_{s=0}^{\infty}\sum_{i=1}^{\infty}\sum_{r=0}^{\infty}q_{s,i,r}(t)e^{s\theta_1+i\theta_2+r\theta_3}.
\end{aligned}$$

Using

$$M(\theta_1,\theta_2,\theta_3,t)=E[e^{S\theta_1+I\theta_2+R\theta_3}\mid I>0]=\sum_{s=0}^{\infty}\sum_{i=1}^{\infty}\sum_{r=0}^{\infty}q_{s,i}(t)e^{s\theta_1+i\theta_2+r\theta_3}$$

$$\begin{aligned}
\frac{\partial M(\theta_1,\theta_2,\theta_3,t)}{\partial\theta_1}&=\sum_{s=0}^{\infty}\sum_{i=1}^{\infty}\sum_{r=0}^{\infty}sq_{s,i}(t)e^{s\theta_1+i\theta_2+r\theta_3},\\
\frac{\partial M(\theta_1\theta_2,\theta_3,t)}{\partial\theta_2}&=\sum_{s=0}^{\infty}\sum_{i=1}^{\infty}\sum_{r=0}^{\infty}iq_{s,i}(t)e^{s\theta_1+i\theta_2+r\theta_3},\\
\frac{\partial M(\theta_1\theta_2,\theta_3,t)}{\partial\theta_3}&=\sum_{s=0}^{\infty}\sum_{i=1}^{\infty}\sum_{r=0}^{\infty}rq_{s,i}(t)e^{s\theta_1+i\theta_2+r\theta_3},
\end{aligned}$$

and

$$\frac{\partial^2 M(\theta_1,\theta_2,\theta_3,t)}{\partial\theta_1\partial\theta_2}=\sum_{s=0}^{\infty}\sum_{i=1}^{\infty}\sum_{r=0}^{\infty}siq_{s,i}(t)e^{s\theta_1+i\theta_2+r\theta_3}$$

$$\begin{aligned}
\frac{\partial M}{\partial t} &= \mu N(e^{\theta_1}-1)+\mu(e^{-\theta_1}-1)\frac{\partial M}{\partial \theta_1}+\frac{\beta}{N}(e^{\theta_2-\theta_1}-1)\frac{\partial^2 M}{\partial\theta_1\partial\theta_2} \\
&+\mu(e^{-\theta_2}-1)\left(\frac{\partial M}{\partial\theta_2}-\sum_{s=0}^{\infty}\sum_{r=0}^{\infty}q_{s,1,r}(t)e^{s\theta_1+\theta_2+r\theta_3}\right) \\
&+\gamma(e^{\theta_3-\theta_2}-1)\left(\frac{\partial M}{\partial\theta_2}-\sum_{s=0}^{\infty}\sum_{r=0}^{\infty}q_{s,1,r}(t)e^{s\theta_1+\theta_2+r\theta_3}\right) \\
&-\mu e^{\theta_2}\sum_{s=0}^{\infty}\sum_{r=0}^{\infty}q_{s,1,r}(t)e^{s\theta_1+r\theta_3}-\gamma e^{\theta_2}\sum_{s=0}^{\infty}\sum_{r=0}^{\infty}q_{s,1,r}(t)e^{s\theta_1+r\theta_3} \\
&+\mu(e^{-\theta_3}-1)\frac{\partial M}{\partial\theta_3}+\nu(e^{\theta_1-\theta_3}-1)\frac{\partial M}{\partial\theta_3}+(\gamma+\mu)q_{.,1,.}M.
\end{aligned}$$

$$\begin{aligned}
\frac{\partial M}{\partial t} &= \mu N(e^{\theta_1}-1)M+\mu(e^{-\theta_1}-1)\frac{\partial M}{\partial \theta_1}+\frac{\beta}{N}(e^{\theta_2-\theta_1}-1)\frac{\partial^2 M}{\partial\theta_1\partial\theta_2} \\
&+\mu(e^{-\theta_2}-1)\frac{\partial M}{\partial\theta_2}+\gamma(e^{\theta_1-\theta_2}-1)\frac{\partial M}{\partial\theta_2}+\mu(e^{-\theta_3}-1)\frac{\partial M}{\partial\theta_3} \\
&+\nu(e^{\theta_1-\theta_3}-1)\frac{\partial M}{\partial\theta_3}-\mu\sum_{s=0}^{\infty}\sum_{r=0}^{\infty}q_{s,1}(t)e^{s\theta_1+r\theta_3} \\
&-\gamma e^{\theta_3}\sum_{s=0}^{\infty}\sum_{r=0}^{\infty}q_{s,1}(t)e^{s\theta_1+r\theta_3}+(\gamma+\mu)q_{.,1,.}M.
\end{aligned}$$

$$\begin{aligned}
\frac{\partial M}{\partial t} &= \mu N(e^{\theta_1}-1)M+\mu(e^{-\theta_1}-1)\frac{\partial M}{\partial \theta_1}+\frac{\beta}{N}(e^{\theta_2-\theta_1}-1)\frac{\partial^2 M}{\partial\theta_1\partial\theta_2} \\
&+\mu(e^{-\theta_2}-1)\frac{\partial M}{\partial\theta_2}+\gamma(e^{\theta_1-\theta_2}-1)\frac{\partial M}{\partial\theta_2}+\mu(e^{-\theta_3}-1)\frac{\partial M}{\partial\theta_3} \\
&+\nu(e^{\theta_1-\theta_3}-1)\frac{\partial M}{\partial\theta_3}-\mu q_{.,1,.}\sum_{s=0}^{\infty}\sum_{r=0}^{\infty}q_{S,R}(s,r|1)(t)e^{s\theta_1+r\theta_3} \\
&-\gamma q_{.,1,.}e^{\theta_1}\sum_{s=0}^{\infty}\sum_{r=0}^{\infty}q_{S,R}(s,r|1)(t)e^{s\theta_1+r\theta_3}+(\gamma+\mu)q_{.,1,.}M
\end{aligned}$$

where $q_{S,R}(s,r|1)(t)=\frac{q_{s,1,r}}{q_{.,1,.}}$ is the conditional probability that S takes the value s and R takes the value r given that $I=1$. Using the transformation $K(\theta_1,\theta_2,\theta_3,t)=logM(\theta_1,\theta_2,\theta_3,t)$ we have

$$\begin{aligned}\frac{\partial K}{\partial t} &= \frac{\beta}{N}(e^{\theta_2-\theta_1}-1)\left(\frac{\partial^2 K}{\partial\theta_1\partial\theta_2}+\frac{\partial K}{\partial\theta_1}\frac{\partial K}{\partial\theta_2}\right)+\mu N(e^{\theta_1}-1)+\mu(e^{-\theta_1}-1)\frac{\partial K}{\partial\theta_1}\\ &+\mu(e^{-\theta_2}-1)\frac{\partial K}{\partial\theta_2}+\gamma(e^{\theta_3-\theta_2}-1)\frac{\partial K}{\partial\theta_2}+\mu(e^{-\theta_3}-1)\frac{\partial K}{\partial\theta_3}\\ &+\nu(e^{\theta_1-\theta_3}-1)\frac{\partial K}{\partial\theta_3}+\mu q_{\cdot,1,\cdot}\left(1-e^{-K}\sum_{s=0}^{\infty}\sum_{r=0}^{\infty}q_{S,R}(s,r|1)(t)e^{s\theta_1+r\theta_3}\right)\\ &+\gamma q_{\cdot,1,\cdot}\left(1-e^{\theta_3}e^{-K}\sum_{s=0}^{\infty}\sum_{r=0}^{\infty}q_{S,R}(s,r|1)(t)e^{s\theta_1+r\theta_3}\right).\end{aligned}$$

$$\begin{aligned}\frac{\partial K}{\partial t} &= \frac{\beta}{N}\left(\theta_2-\theta_1-\theta_1\theta_2+\frac{1}{2}\theta_1^2+\frac{1}{2}\theta_2^2+\frac{1}{2}\theta_2\theta_1^2-\frac{1}{2}\theta_1\theta_2^2+\frac{1}{4}\theta_1^2\theta_2^2+\cdots\right)\\ &\left(\frac{\partial^2 K}{\partial\theta_1\partial\theta_2}+\frac{\partial K}{\partial\theta_1}\frac{\partial K}{\partial\theta_2}\right)+\mu N\left(\theta_1+\frac{\theta_1^2}{2!}+\cdots\right)+\mu\left(-\theta_1+\frac{\theta_1^2}{2!}+\cdots\right)\frac{\partial K}{\partial\theta_1}\\ &+\gamma\left(\theta_3-\theta_2-\theta_3\theta_2+\frac{1}{2}\theta_3^2+\frac{1}{2}\theta_2^2+\frac{1}{2}\theta_3\theta_2^2-\frac{1}{2}\theta_2\theta_3^2+\frac{1}{4}\theta_3^2\theta_2^2+\cdots\right)\frac{\partial K}{\partial\theta_2}\\ &+\mu\left(-\theta_2+\frac{\theta_2^2}{2!}+\cdots\right)\frac{\partial K}{\partial\theta_2}+\mu\left(-\theta_3+\frac{\theta_3^2}{2!}+\cdots\right)\frac{\partial K}{\partial\theta_3}\\ &+\nu\left(\theta_1-\theta_3-\theta_1\theta_3+\frac{1}{2}\theta_1^2+\frac{1}{2}\theta_3^2+\frac{1}{2}\theta_1\theta_2^2-\frac{1}{2}\theta_3\theta_1^2+\frac{1}{4}\theta_1^2\theta_3^2+\cdots\right)\frac{\partial K}{\partial\theta_3}\\ &+\mu q_{\cdot,1}\left(1-e^{-K}\sum_{s=0}^{\infty}\sum_{r=0}^{\infty}q_S(s|1)(t)\left(1+s\theta_1+r\theta_3+\frac{s^2\theta_1^2}{2}+\frac{r^2\theta_3^2}{2}\right.\right.\\ &\left.\left.+sr\theta_1\theta_3+\cdots\right)\right)+\gamma q_{\cdot,1}\left(1-\left(1+\theta_3+\frac{\theta_3^2}{2!}+\cdots\right)e^{-K}\sum_{s=0}^{\infty}\sum_{r=0}^{\infty}q_S(s|1)(t)\right.\\ &\left.\left(1+s\theta_1+r\theta_3+\frac{s^2\theta_1^2}{2}+\frac{r^2\theta_3^2}{2}+sr\theta_1\theta_3+\cdots\right)\right). \qquad \text{(E.1)}\end{aligned}$$

Using the definition $K(\theta_1,\theta_2,\theta_3,t)=\sum_{x=0}^{\infty}\sum_{y=0}^{\infty}\sum_{z=0}^{\infty}k_{x,y,z}(t)\frac{\theta_1^x}{x!}\frac{\theta_2^y}{y!}\frac{\theta_2^z}{z!}$ where $k_{x,y,z}(t)$ denotes the (x,y,z)th cumulant function - for $(x,y,z)\neq(0,0,0)$ we have

$$
\begin{aligned}
K(\theta_1,\theta_2,\theta_3,t) &= k_{0,1,0}(t)\theta_2 + k_{1,0,0}(t)\theta_1 + k_{0,0,1}(t)\theta_3 + k_{1,1,0}(t)\theta_1\theta_2 \\
&\quad + k_{1,0,1}(t)\theta_1\theta_3 + k_{0,1,1}(t)\theta_2\theta_3 + k_{2,0,0}(t)\frac{\theta_1^2}{2!} + k_{0,2,0}(t)\frac{\theta_2^2}{2!} \\
&\quad + k_{0,0,2}(t)\frac{\theta_3^2}{2!} + k_{1,1,1}(t)\theta_1\theta_2\theta_3 + k_{1,2,0}(t)\frac{\theta_1\theta_2^2}{2!} + k_{2,1,0}(t)\frac{\theta_1^2\theta_2}{2!} \\
&\quad + k_{2,0,1}(t)\frac{\theta_1^2\theta_3}{2!} + k_{0,2,1}(t)\frac{\theta_3\theta_2^2}{2!} + k_{1,0,2}(t)\frac{\theta_1\theta_3^2}{2!} + k_{0,1,2}(t)\frac{\theta_2\theta_3^2}{2!} \\
&\quad + k_{2,1,1}(t)\frac{\theta_1^2\theta_2\theta_3}{2!} + k_{1,2,1}(t)\frac{\theta_1\theta_2^2\theta_3}{2!} + k_{1,1,2}(t)\frac{\theta_1\theta_2\theta_3^2}{2!} + \cdots
\end{aligned}
$$

$$
\begin{aligned}
\frac{\partial K}{\partial t} &= \dot{k}_{0,1,0}(t)\theta_2 + \dot{k}_{1,0,0}(t)\theta_1 + \dot{k}_{0,0,1}(t)\theta_3 + \dot{k}_{1,1,0}(t)\theta_1\theta_2 + \dot{k}_{1,0,1}(t)\theta_1\theta_3 \\
&\quad + \dot{k}_{0,1,1}(t)\theta_2\theta_3 + \dot{k}_{2,0,0}(t)\frac{\theta_1^2}{2!} + \dot{k}_{0,2,0}(t)\frac{\theta_2^2}{2!} + \dot{k}_{0,0,2}(t)\frac{\theta_2^2}{2!} + \dot{k}_{1,1,1}(t)\theta_1\theta_2\theta_3 \\
&\quad + \dot{k}_{1,2,0}(t)\frac{\theta_1\theta_2^2}{2!} + \dot{k}_{2,1,0}(t)\frac{\theta_1^2\theta_2}{2!} + \dot{k}_{2,0,1}(t)\frac{\theta_1^2\theta_3}{2!} + \dot{k}_{0,2,1}(t)\frac{\theta_3\theta_2^2}{2!} + \dot{k}_{1,0,2}(t)\frac{\theta_1\theta_3^2}{2!} \\
&\quad + \dot{k}_{0,1,2}(t)\frac{\theta_2\theta_3^2}{2!} + \dot{k}_{2,1,1}(t)\frac{\theta_1^2\theta_2\theta_3}{2!} + \dot{k}_{1,2,1}(t)\frac{\theta_1\theta_2^2\theta_3}{2!} + \dot{k}_{1,1,2}(t)\frac{\theta_1\theta_2\theta_3^2}{2!} + \cdots \\
\frac{\partial K}{\partial \theta_1} &= k_{1,0,0}(t) + k_{1,1,0}(t)\theta_2 + k_{1,0,1}(t)\theta_3 + k_{2,0,0}(t)\theta_1 + k_{1,1,1}(t)\theta_2\theta_3 \\
&\quad + k_{1,2,0}(t)\frac{\theta_2^2}{2!} + k_{2,1,0}(t)\theta_1\theta_2 + k_{2,0,1}(t)\theta_1\theta_3 + k_{1,0,2}(t)\frac{\theta_3^2}{2!} + k_{2,1,1}(t)\theta_1\theta_2\theta_3 \\
&\quad + k_{1,2,1}(t)\frac{\theta_2^2\theta_3}{2!} + k_{1,1,2}(t)\frac{\theta_2\theta_3^2}{2!} + \cdots \\
\frac{\partial K}{\partial \theta_2} &= k_{0,1,0}(t) + k_{1,1,0}(t)\theta_1 + k_{0,1,1}(t)\theta_3 + k_{0,2,0}(t)\theta_2 + k_{1,1,1}(t)\theta_1\theta_3 \\
&\quad + k_{1,2,0}(t)\theta_1\theta_2 + k_{2,1,0}(t)\frac{\theta_1^2}{2!} + k_{0,2,1}(t)\theta_3\theta_2 + k_{0,1,2}(t)\frac{\theta_3^2}{2!} + k_{2,1,1}(t)\frac{\theta_1^2\theta_3}{2!} \\
&\quad + k_{1,2,1}(t)\theta_1\theta_2\theta_3 + k_{1,1,2}(t)\frac{\theta_1\theta_3^2}{2!} + \cdots \\
\frac{\partial K}{\partial \theta_3} &= k_{0,0,1}(t) + k_{1,0,1}(t)\theta_1 + k_{0,1,1}(t)\theta_2 + k_{0,0,2}(t)\theta_3 + k_{1,1,1}(t)\theta_1\theta_2 \\
&\quad + k_{2,0,1}(t)\frac{\theta_1^2}{2!} + k_{0,2,1}(t)\frac{\theta_2^2}{2!} + k_{1,0,2}(t)\theta_1\theta_3 + k_{0,1,2}(t)\theta_2\theta_3 + k_{2,1,1}(t)\frac{\theta_1^2\theta_2}{2!} \\
&\quad + k_{1,2,1}(t)\frac{\theta_1\theta_2^2}{2!} + k_{1,1,2}(t)\theta_1\theta_2\theta_3^2 + \cdots \\
\frac{\partial^2 K}{\partial \theta_1 \partial \theta_2} &= k_{1,1,0}(t) + k_{1,1,1}(t)\theta_3 + k_{1,2,0}(t)\theta_2 + k_{2,1,0}(t)\theta_1 + k_{2,1,1}(t)\theta_1\theta_3 \\
&\quad + k_{1,2,1}(t)\theta_2\theta_3 + k_{1,1,2}(t)\frac{\theta_3^2}{2!} + \cdots
\end{aligned}
$$

$$
\begin{aligned}
\frac{\partial K}{\partial \theta_1}\frac{\partial K}{\partial \theta_2} &= (k_{1,0,0}(t) + k_{1,1,0}(t)\theta_2 + k_{1,0,1}(t)\theta_3 + k_{2,0,0}(t)\theta_1 + k_{1,1,1}(t)\theta_2\theta_3 \\
&\quad + k_{1,2,0}(t)\frac{\theta_2^2}{2!} + k_{2,1,0}(t)\theta_1\theta_2 + k_{2,0,1}(t)\theta_1\theta_3 + k_{1,0,2}(t)\frac{\theta_3^2}{2!} + k_{2,1,1}(t)\theta_1\theta_2\theta_3 \\
&\quad + k_{1,2,1}(t)\frac{\theta_2^2\theta_3}{2!} + k_{1,1,2}(t)\frac{\theta_2\theta_3^2}{2!} + \cdots\Big) \\
&\quad (k_{0,1,0}(t) + k_{1,1,0}(t)\theta_1 + k_{0,1,1}(t)\theta_3 + k_{0,2,0}(t)\theta_2 + k_{1,1,1}(t)\theta_1\theta_3 \\
&\quad + k_{1,2,0}(t)\theta_1\theta_2 + k_{2,1,0}(t)\frac{\theta_1^2}{2!} + k_{0,2,1}(t)\theta_3\theta_2 + k_{0,1,2}(t)\frac{\theta_3^2}{2!} + k_{2,1,1}(t)\frac{\theta_1^2\theta_3}{2!} \\
&\quad + k_{1,2,1}(t)\theta_1\theta_2\theta_3 + k_{1,1,2}(t)\frac{\theta_1\theta_3^2}{2!} + \cdots\Big) \\
&= k_{1,0,0}(t)k_{0,1,0}(t) + k_{1,0,0}(t)k_{1,1,0}(t)\theta_1 + k_{0,1,0}(t)k_{1,1,0}(t)\theta_2 \\
&\quad + k_{1,0,0}(t)k_{0,1,1}(t)\theta_3 + k_{0,1,0}(t)k_{1,0,1}(t)\theta_3 + k_{0,1,0}(t)k_{2,0,0}(t)\theta_1 \\
&\quad + k_{1,0,0}(t)k_{0,2,0}(t)\theta_2 + k_{0,1,0}(t)k_{1,1,1}(t)\theta_2\theta_3 + k_{1,0,0}(t)k_{1,1,1}(t)\theta_1\theta_3 + \\
&\quad k_{0,1,0}(t)k_{2,1,0}(t)\theta_1\theta_2 + k_{1,0,0}(t)k_{1,2,0}(t)\theta_1\theta_2 + k_{0,1,0}(t)k_{2,0,1}(t)\theta_1\theta_3 \\
&\quad + k_{1,0,0}(t)k_{0,2,1}(t)\theta_2\theta_3 + k_{1,1,0}(t)^2\theta_1\theta_2 + k_{1,1,0}(t)k_{0,1,1}(t)\theta_2\theta_3 \\
&\quad + k_{1,1,0}(t)k_{1,0,1}(t)\theta_1\theta_3 + k_{1,1,0}(t)k_{0,2,0}(t)\theta_2^2 + k_{1,1,0}(t)k_{2,0,0}(t)\theta_1^2 \\
&\quad + 2k_{1,1,0}(t)k_{1,1,1}(t)\theta_1\theta_2\theta_3 + k_{1,1,0}(t)k_{1,2,0}(t)\theta_1\theta_2^2 + k_{1,1,0}(t)k_{2,1,0}(t)\theta_1^2\theta_2 \\
&\quad + k_{1,1,0}(t)k_{2,0,1}(t)\theta_1^2\theta_3 + k_{1,1,0}(t)k_{0,2,1}(t)\theta_2^2\theta_3 + k_{1,0,1}(t)k_{0,1,1}(t)\theta_3^2 \\
&\quad + k_{1,0,1}(t)k_{0,2,0}(t)\theta_2\theta_3 + k_{0,1,1}(t)k_{2,0,0}(t)\theta_1\theta_3 + k_{1,0,1}(t)k_{1,1,1}(t)\theta_1\theta_3^2 \\
&\quad + k_{0,1,1}(t)k_{1,1,1}(t)\theta_2\theta_3^2 + k_{0,1,1}(t)k_{2,1,0}(t)\theta_1\theta_2\theta_3 + k_{1,0,1}(t)k_{1,2,0}(t)\theta_1\theta_2\theta_3 \\
&\quad + k_{0,1,1}(t)k_{2,0,1}(t)\theta_1\theta_3^2 + k_{1,0,1}(t)k_{0,2,1}(t)\theta_2\theta_3^2 + k_{0,1,0}(t)k_{1,2,0}(t)\frac{\theta_2^2}{2!} \\
&\quad + k_{1,0,0}(t)k_{2,1,0}(t)\frac{\theta_1^2}{2!} + k_{1,0,0}(t)k_{0,1,2}(t)\frac{\theta_3^2}{2!} + k_{0,1,0}(t)k_{1,0,2}(t)\frac{\theta_3^2}{2!} + \cdots
\end{aligned}
$$

Substituting these into equation (E.1) gives

$$\dot{k}_{0,1,0}(t)\theta_2 + \dot{k}_{1,0,0}(t)\theta_1 + \dot{k}_{0,0,1}(t)\theta_3 + \dot{k}_{1,1,0}(t)\theta_1\theta_2 + \dot{k}_{1,0,1}(t)\theta_1\theta_3$$
$$+\dot{k}_{0,1,1}(t)\theta_2\theta_3 + \dot{k}_{2,0,0}(t)\frac{\theta_1^2}{2!} + \dot{k}_{0,2,0}(t)\frac{\theta_2^2}{2!} + \dot{k}_{0,0,2}(t)\frac{\theta_2^2}{2!} + \cdots =$$
$$\frac{\beta}{N}\left(\theta_2 - \theta_1 - \theta_1\theta_2 + \frac{1}{2}\theta_1^2 + \frac{1}{2}\theta_2^2 + \frac{1}{2}\theta_2\theta_1^2 - \frac{1}{2}\theta_1\theta_2^2 + \frac{1}{4}\theta_1^2\theta_2^2 + \cdots\right)$$
$$\Big(k_{1,1,0}(t) + k_{1,1,1}(t)\theta_3 + k_{1,2,0}(t)\theta_2 + k_{2,1,0}(t)\theta_1 + k_{2,1,1}(t)\theta_1\theta_3 + k_{1,2,1}(t)\theta_2\theta_3$$
$$+k_{1,1,2}(t)\frac{\theta_3^2}{2!} + k_{1,0,0}(t)k_{0,1,0}(t) + k_{1,0,0}(t)k_{1,1,0}(t)\theta_1 + k_{0,1,0}(t)k_{1,1,0}(t)\theta_2 +$$
$$k_{1,0,0}(t)k_{0,1,1}(t)\theta_3 + k_{0,1,0}(t)k_{1,0,1}(t)\theta_3 + k_{0,1,0}(t)k_{2,0,0}(t)\theta_1 + k_{1,0,0}(t)k_{0,2,0}(t)\theta_2$$
$$+k_{0,1,0}(t)k_{1,1,1}(t)\theta_2\theta_3 + k_{1,0,0}(t)k_{1,1,1}(t)\theta_1\theta_3 + k_{0,1,0}(t)k_{2,1,0}(t)\theta_1\theta_2$$
$$+k_{1,0,0}(t)k_{1,2,0}(t)\theta_1\theta_2 + k_{0,1,0}(t)k_{2,0,1}(t)\theta_1\theta_3 + k_{1,0,0}(t)k_{0,2,1}(t)\theta_2\theta_3$$
$$+k_{1,1,0}(t)^2\theta_1\theta_2 + k_{1,1,0}(t)k_{0,1,1}(t)\theta_2\theta_3 + k_{1,1,0}(t)k_{1,0,1}(t)\theta_1\theta_3$$
$$+k_{1,1,0}(t)k_{0,2,0}(t)\theta_2^2 + k_{1,1,0}(t)k_{2,0,0}(t)\theta_1^2 + 2k_{1,1,0}(t)k_{1,1,1}(t)\theta_1\theta_2\theta_3$$
$$+k_{1,1,0}(t)k_{1,2,0}(t)\theta_1\theta_2^2 + k_{1,1,0}(t)k_{2,1,0}(t)\theta_1^2\theta_2 + k_{1,1,0}(t)k_{2,0,1}(t)\theta_1^2\theta_3$$
$$+k_{1,1,0}(t)k_{0,2,1}(t)\theta_2^2\theta_3 + k_{1,0,1}(t)k_{0,1,1}(t)\theta_3^2 + k_{1,0,1}(t)k_{0,2,0}(t)\theta_2\theta_3$$
$$+k_{0,1,1}(t)k_{2,0,0}(t)\theta_1\theta_3 + k_{1,0,1}(t)k_{1,1,1}(t)\theta_1\theta_3^2 + k_{0,1,1}(t)k_{1,1,1}(t)\theta_2\theta_3^2$$
$$+k_{0,1,0}(t)k_{1,2,0}(t)\frac{\theta_2^2}{2!} + k_{0,1,1}(t)k_{2,0,1}(t)\theta_1\theta_3^2 + k_{1,0,1}(t)k_{0,2,1}(t)\theta_2\theta_3^2$$
$$+k_{1,0,0}(t)k_{2,1,0}(t)\frac{\theta_1^2}{2!} + k_{1,0,0}(t)k_{0,1,2}(t)\frac{\theta_3^2}{2!} + k_{0,1,1}(t)k_{2,1,0}(t)\theta_1\theta_2\theta_3$$
$$+k_{1,0,1}(t)k_{1,2,0}(t)\theta_1\theta_2\theta_3 + k_{0,1,0}(t)k_{1,0,2}(t)\frac{\theta_3^2}{2!} + \cdots\Big)$$
$$+\mu N\left(\theta_1 + \frac{\theta_1^2}{2!} + \cdots\right) + \mu\left(-\theta_1 + \frac{\theta_1^2}{2!} + \cdots\right)\Big(k_{1,0,0}(t) + k_{1,1,0}(t)\theta_2$$
$$+k_{1,0,1}(t)\theta_3 + k_{2,0,0}(t)\theta_1 + k_{1,1,1}(t)\theta_2\theta_3 + k_{1,2,0}(t)\frac{\theta_2^2}{2!} + k_{2,1,0}(t)\theta_1\theta_2$$
$$+k_{2,0,1}(t)\theta_1\theta_3 + k_{1,0,2}(t)\frac{\theta_3^2}{2!} + k_{2,1,1}(t)\theta_1\theta_2\theta_3 + k_{1,2,1}(t)\frac{\theta_2^2\theta_3}{2!} + k_{1,1,2}(t)\frac{\theta_2\theta_3^2}{2!} + \cdots\Big)$$
$$+\mu\left(-\theta_2 + \frac{\theta_2^2}{2!} + \cdots\right)\Big(k_{0,1,0}(t) + k_{1,1,0}(t)\theta_1 + k_{0,1,1}(t)\theta_3 + k_{0,2,0}(t)\theta_2$$
$$+k_{1,1,1}(t)\theta_1\theta_3 + k_{1,2,0}(t)\theta_1\theta_2 + k_{2,1,0}(t)\frac{\theta_1^2}{2!} + k_{0,2,1}(t)\theta_3\theta_2 + k_{0,1,2}(t)\frac{\theta_3^2}{2!}$$
$$+k_{2,1,1}(t)\frac{\theta_1^2\theta_3}{2!} + k_{1,2,1}(t)\theta_1\theta_2\theta_3 + k_{1,1,2}(t)\frac{\theta_1\theta_3^2}{2!} + \cdots\Big).$$

$$+\gamma\left(\theta_3-\theta_2-\theta_3\theta_2+\frac{1}{2}\theta_3^2+\frac{1}{2}\theta_2^2+\frac{1}{2}\theta_3\theta_2^2-\frac{1}{2}\theta_2\theta_3^2+\frac{1}{4}\theta_3^2\theta_2^2+\cdots\right)$$
$$(k_{0,1,0}(t)+k_{1,1,0}(t)\theta_1+k_{0,1,1}(t)\theta_3+k_{0,2,0}(t)\theta_2+k_{1,1,1}(t)\theta_1\theta_3+k_{1,2,0}(t)\theta_1\theta_2$$
$$+k_{2,1,0}(t)\frac{\theta_1^2}{2!}+k_{0,2,1}(t)\theta_3\theta_2+k_{0,1,2}(t)\frac{\theta_3^2}{2!}+k_{2,1,1}(t)\frac{\theta_1^2\theta_3}{2!}+k_{1,2,1}(t)\theta_1\theta_2\theta_3$$
$$+k_{1,1,2}(t)\frac{\theta_1\theta_3^2}{2!}+\cdots\Bigg)+\mu\left(-\theta_3+\frac{\theta_3^2}{2!}+\cdots\right)(k_{0,0,1}(t)+k_{1,0,1}(t)\theta_1+k_{0,1,1}(t)\theta_2$$
$$+k_{0,0,2}(t)\theta_3+k_{2,0,1}(t)\frac{\theta_1^2}{2!}+k_{1,1,1}(t)\theta_1\theta_2$$
$$+k_{0,2,1}(t)\frac{\theta_2^2}{2!}+k_{1,0,2}(t)\theta_1\theta_3+k_{0,1,2}(t)\theta_2\theta_3+k_{1,1,2}(t)\theta_1\theta_2\theta_3+k_{2,1,1}(t)\frac{\theta_1^2\theta_2}{2!}$$
$$+k_{1,2,1}(t)\frac{\theta_1\theta_2^2}{2!}+\cdots\Bigg)$$
$$+\nu\left(\theta_1-\theta_3-\theta_1\theta_3+\frac{1}{2}\theta_1^2+\frac{1}{2}\theta_3^2+\frac{1}{2}\theta_1\theta_2^2-\frac{1}{2}\theta_3\theta_1^2+\frac{1}{4}\theta_1^2\theta_3^2+\cdots\right)$$
$$\Bigg(k_{0,0,1}(t)+k_{1,0,1}(t)\theta_1+k_{0,1,1}(t)\theta_2+k_{0,0,2}(t)\theta_3+k_{1,1,1}(t)\theta_1\theta_2+k_{2,0,1}(t)\frac{\theta_1^2}{2!}$$
$$+k_{0,2,1}(t)\frac{\theta_2^2}{2!}+k_{1,0,2}(t)\theta_1\theta_3+k_{0,1,2}(t)\theta_2\theta_3+k_{2,1,1}(t)\frac{\theta_1^2\theta_2}{2!}+k_{1,2,1}(t)\frac{\theta_1\theta_2^2}{2!}$$
$$+k_{1,1,2}(t)\theta_1\theta_2\theta_3^2+\cdots\Bigg)+\gamma q_{\cdot,1,\cdot}(t)\Bigg[\Bigg(1-\left(1+\theta_3+\frac{\theta_3^2}{2!}+\cdots\right)\Bigg(1-k_{0,1,0}(t)\theta_2$$
$$-k_{1,0,0}(t)\theta_1-k_{0,0,1}(t)\theta_3-k_{1,1,0}(t)\theta_1\theta_2-k_{1,0,1}(t)\theta_1\theta_3-k_{0,1,1}(t)\theta_2\theta_3$$
$$-k_{2,0,0}(t)\frac{\theta_1^2}{2!}-k_{0,2,0}(t)\frac{\theta_2^2}{2!}-k_{0,0,2}(t)\frac{\theta_3^2}{2!}-k_{1,1,1}(t)\theta_1\theta_2\theta_3+k_{0,1,0}^2(t)\frac{\theta_2^2}{2}$$
$$+k_{1,0,0}^2(t)\frac{\theta_1^2}{2}+k_{0,1,0}(t)k_{1,0,0}(t)\theta_1\theta_2+k_{0,0,1}(t)k_{1,0,0}(t)\theta_1\theta_3+k_{0,1,0}(t)k_{0,0,1}(t)\theta_2\theta_3$$
$$+k_{0,0,1}^2(t)\frac{\theta_3^2}{2}+\cdots\Bigg)\Bigg)\sum_{i_1=0}^{N}q_S(s|1)(t)\left(1+s\theta_1+r\theta_3+\frac{s^2\theta_1^2}{2}+\frac{r^2\theta_3^2}{2}+sr\theta_1\theta_3+\cdots\right)\Bigg]$$
$$+\mu q_{\cdot,1,\cdot}(t)\Bigg[\Bigg(1-\Bigg(1-k_{0,1,0}(t)\theta_2-k_{1,0,0}(t)\theta_1-k_{0,0,1}(t)\theta_3-k_{1,1,0}(t)\theta_1\theta_2-k_{2,0,0}(t)\frac{\theta_1^2}{2!}$$
$$-k_{0,1,1}(t)\theta_2\theta_3-k_{1,0,1}(t)\theta_1\theta_3-k_{0,2,0}(t)\frac{\theta_2^2}{2!}-k_{0,0,2}(t)\frac{\theta_3^2}{2!}-k_{1,1,1}(t)\theta_1\theta_2\theta_3+k_{0,1,0}^2(t)\frac{\theta_2^2}{2}$$
$$+k_{1,0,0}^2(t)\frac{\theta_1^2}{2}+k_{0,1,0}(t)k_{1,0,0}(t)\theta_1\theta_2+k_{0,0,1}(t)k_{1,0,0}(t)\theta_1\theta_3+k_{0,1,0}(t)k_{0,0,1}(t)\theta_2\theta_3$$
$$+k_{0,0,1}^2(t)\frac{\theta_3^2}{2}+\cdots\Bigg)\Bigg)\sum_{i_2=0}^{N}q_S(s|1)(t)\left(1+s\theta_1+r\theta_3+\frac{s^2\theta_1^2}{2}+\frac{r^2\theta_3^2}{2}+sr\theta_1\theta_3+\cdots\right)\Bigg]$$

$$\dot{k}_{0,1,0}(t)\theta_2 + \dot{k}_{1,0,0}(t)\theta_1 + \dot{k}_{0,0,1}(t)\theta_3 + \dot{k}_{1,1,0}(t)\theta_1\theta_2 + \dot{k}_{1,0,1}(t)\theta_1\theta_3$$
$$+\dot{k}_{0,1,1}(t)\theta_2\theta_3 + \dot{k}_{2,0,0}(t)\frac{\theta_1^2}{2!} + \dot{k}_{0,2,0}(t)\frac{\theta_2^2}{2!} + \dot{k}_{0,0,2}(t)\frac{\theta_2^2}{2!} + \cdots =$$
$$\frac{\beta}{N}\left(\theta_2 - \theta_1 - \theta_1\theta_2 + \frac{1}{2}\theta_1^2 + \frac{1}{2}\theta_2^2 + \frac{1}{2}\theta_2\theta_1^2 - \frac{1}{2}\theta_1\theta_2^2 + \frac{1}{4}\theta_1^2\theta_2^2 + \cdots\right)$$
$$(k_{1,1,0}(t) + k_{1,1,1}(t)\theta_3 + k_{1,2,0}(t)\theta_2 + k_{2,1,0}(t)\theta_1 + k_{2,1,1}(t)\theta_1\theta_3 + k_{1,2,1}(t)\theta_2\theta_3$$
$$+k_{1,1,2}(t)\frac{\theta_3^2}{2!} + k_{1,0,0}(t)k_{0,1,0}(t) + k_{1,0,0}(t)k_{1,1,0}(t)\theta_1 + k_{0,1,0}(t)k_{1,1,0}(t)\theta_2 +$$
$$k_{1,0,0}(t)k_{0,1,1}(t)\theta_3 + k_{0,1,0}(t)k_{1,0,1}(t)\theta_3 + k_{0,1,0}(t)k_{2,0,0}(t)\theta_1 + k_{1,0,0}(t)k_{0,2,0}(t)\theta_2$$
$$+k_{0,1,0}(t)k_{1,1,1}(t)\theta_2\theta_3 + k_{1,0,0}(t)k_{1,1,1}(t)\theta_1\theta_3 + k_{0,1,0}(t)k_{2,1,0}(t)\theta_1\theta_2$$
$$+k_{1,0,0}(t)k_{1,2,0}(t)\theta_1\theta_2 + k_{0,1,0}(t)k_{2,0,1}(t)\theta_1\theta_3 + k_{1,0,0}(t)k_{0,2,1}(t)\theta_2\theta_3 + k_{1,1,0}(t)^2\theta_1\theta_2$$
$$+k_{1,1,0}(t)k_{0,1,1}(t)\theta_2\theta_3 + k_{1,1,0}(t)k_{1,0,1}(t)\theta_1\theta_3 + k_{1,1,0}(t)k_{0,2,0}(t)\theta_2^2 + k_{1,1,0}(t)k_{2,0,0}(t)\theta_1^2$$
$$+2k_{1,1,0}(t)k_{1,1,1}(t)\theta_1\theta_2\theta_3 + k_{1,1,0}(t)k_{1,2,0}(t)\theta_1\theta_2^2 + k_{1,1,0}(t)k_{2,1,0}(t)\theta_1^2\theta_2$$
$$+k_{1,1,0}(t)k_{2,0,1}(t)\theta_1^2\theta_3 + k_{1,1,0}(t)k_{0,2,1}(t)\theta_2^2\theta_3 + k_{1,0,1}(t)k_{0,1,1}(t)\theta_3^2 + k_{1,0,1}(t)k_{0,2,0}(t)\theta_2\theta_3$$
$$+k_{0,1,1}(t)k_{2,0,0}(t)\theta_1\theta_3 + k_{1,0,1}(t)k_{1,1,1}(t)\theta_1\theta_3^2 + k_{0,1,1}(t)k_{1,1,1}(t)\theta_2\theta_3^2 + k_{0,1,0}(t)k_{1,2,0}(t)\frac{\theta_2^2}{2!}$$
$$+k_{0,1,1}(t)k_{2,0,1}(t)\theta_1\theta_3^2 + k_{1,0,1}(t)k_{0,2,1}(t)\theta_2\theta_3^2 + k_{1,0,0}(t)k_{2,1,0}(t)\frac{\theta_1^2}{2!} + k_{1,0,0}(t)k_{0,1,2}(t)\frac{\theta_3^2}{2!}$$
$$+k_{0,1,1}(t)k_{2,1,0}(t)\theta_1\theta_2\theta_3 + k_{1,0,1}(t)k_{1,2,0}(t)\theta_1\theta_2\theta_3 + k_{0,1,0}(t)k_{1,0,2}(t)\frac{\theta_3^2}{2!} + \cdots\Big)$$
$$+\mu N\left(\theta_1 + \frac{\theta_1^2}{2!} + \cdots\right) + \mu\left(-\theta_1 + \frac{\theta_1^2}{2!} + \cdots\right)$$
$$\Big(k_{1,0,0}(t) + k_{1,1,0}(t)\theta_2 + k_{1,0,1}(t)\theta_3 + k_{2,0,0}(t)\theta_1 + k_{1,1,1}(t)\theta_2\theta_3 + k_{1,2,0}(t)\frac{\theta_2^2}{2!} + k_{2,1,0}(t)\theta_1\theta_2$$
$$+k_{2,0,1}(t)\theta_1\theta_3 + k_{1,0,2}(t)\frac{\theta_3^2}{2!} + k_{2,1,1}(t)\theta_1\theta_2\theta_3 + k_{1,2,1}(t)\frac{\theta_2^2\theta_3}{2!} + k_{1,1,2}(t)\frac{\theta_2\theta_3^2}{2!} + \cdots\Big)$$
$$+\mu\left(-\theta_2 + \frac{\theta_2^2}{2!} + \cdots\right)(k_{0,1,0}(t) + k_{1,1,0}(t)\theta_1 + k_{0,1,1}(t)\theta_3 + k_{0,2,0}(t)\theta_2 + k_{1,1,1}(t)\theta_1\theta_3$$
$$+k_{1,2,0}(t)\theta_1\theta_2 + k_{2,1,0}(t)\frac{\theta_1^2}{2!} + k_{0,2,1}(t)\theta_3\theta_2 + k_{0,1,2}(t)\frac{\theta_3^2}{2!} + k_{2,1,1}(t)\frac{\theta_1^2\theta_3}{2!}$$
$$+k_{1,2,1}(t)\theta_1\theta_2\theta_3 + k_{1,1,2}(t)\frac{\theta_1\theta_3^2}{2!} + \cdots\Big)$$

$$+\gamma\left(\theta_3-\theta_2-\theta_3\theta_2+\frac{1}{2}\theta_3^2+\frac{1}{2}\theta_2^2+\frac{1}{2}\theta_3\theta_2^2-\frac{1}{2}\theta_2\theta_3^2+\frac{1}{4}\theta_3^2\theta_2^2+\cdots\right)$$
$$\left(k_{0,1,0}(t)+k_{1,1,0}(t)\theta_1+k_{0,1,1}(t)\theta_3+k_{0,2,0}(t)\theta_2+k_{1,1,1}(t)\theta_1\theta_3+k_{2,1,0}(t)\frac{\theta_1^2}{2!}\right.$$
$$+k_{0,2,1}(t)\theta_3\theta_2+k_{1,2,0}(t)\theta_1\theta_2+k_{0,1,2}(t)\frac{\theta_3^2}{2!}+k_{2,1,1}(t)\frac{\theta_1^2\theta_3}{2!}$$
$$\left.+k_{1,2,1}(t)\theta_1\theta_2\theta_3+k_{1,1,2}(t)\frac{\theta_1\theta_3^2}{2!}+\cdots\right)+\mu\left(-\theta_3+\frac{\theta_3^2}{2!}+\cdots\right)\left(k_{2,0,1}(t)\frac{\theta_1^2}{2!}\right.$$
$$+k_{0,0,1}(t)+k_{1,0,1}(t)\theta_1+k_{0,1,1}(t)\theta_2+k_{0,0,2}(t)\theta_3+k_{1,1,1}(t)\theta_1\theta_2+k_{0,2,1}(t)\frac{\theta_2^2}{2!}$$
$$\left.+k_{1,0,2}(t)\theta_1\theta_3+k_{0,1,2}(t)\theta_2\theta_3+k_{1,1,2}(t)\theta_1\theta_2\theta_3+k_{2,1,1}(t)\frac{\theta_1^2\theta_2}{2!}+k_{1,2,1}(t)\frac{\theta_1\theta_2^2}{2!}+\cdots\right)$$
$$+\nu\left(\theta_1-\theta_3-\theta_1\theta_3+\frac{1}{2}\theta_1^2+\frac{1}{2}\theta_3^2+\frac{1}{2}\theta_1\theta_2^2-\frac{1}{2}\theta_3\theta_1^2+\frac{1}{4}\theta_1^2\theta_3^2+\cdots\right)$$
$$\left(k_{0,0,1}(t)+k_{1,0,1}(t)\theta_1+k_{0,1,1}(t)\theta_2+k_{0,0,2}(t)\theta_3+k_{1,1,1}(t)\theta_1\theta_2+k_{2,0,1}(t)\frac{\theta_1^2}{2!}\right.$$
$$+k_{0,2,1}(t)\frac{\theta_2^2}{2!}+k_{1,0,2}(t)\theta_1\theta_3+k_{0,1,2}(t)\theta_2\theta_3+k_{2,1,1}(t)\frac{\theta_1^2\theta_2}{2!}+k_{1,1,2}(t)\theta_1\theta_2\theta_3^2$$
$$\left.+k_{1,2,1}(t)\frac{\theta_1\theta_2^2}{2!}+\cdots\right)+\gamma q_{\cdot,1,\cdot}(t)\left[\left(1-\left(1+\theta_3+\frac{\theta_3^2}{2!}+\cdots\right)(1-k_{0,1,0}(t)\theta_2\right.\right.$$
$$-k_{1,0,0}(t)\theta_1-k_{0,0,1}(t)\theta_3-k_{1,1,0}(t)\theta_1\theta_2-k_{1,0,1}(t)\theta_1\theta_3-k_{0,1,1}(t)\theta_2\theta_3$$
$$-k_{2,0,0}(t)\frac{\theta_1^2}{2!}-k_{0,2,0}(t)\frac{\theta_2^2}{2!}-k_{0,0,2}(t)\frac{\theta_3^2}{2!}-k_{1,1,1}(t)\theta_1\theta_2\theta_3+k_{0,1,0}^2(t)\frac{\theta_2^2}{2}+k_{1,0,0}^2(t)\frac{\theta_1^2}{2}$$
$$+k_{0,1,0}(t)k_{1,0,0}(t)\theta_1\theta_2+k_{0,0,1}(t)k_{1,0,0}(t)\theta_1\theta_3+k_{0,1,0}(t)k_{0,0,1}(t)\theta_2\theta_3$$
$$\left.\left.+k_{0,0,1}^2(t)\frac{\theta_3^2}{2}+\cdots\right)\right)\left(1+\theta_1E[S|I=1]+\theta_3E[R|I=1]+\frac{\theta_1^2}{2}E[S^2|I=1]\right.$$
$$\left.+\frac{\theta_3^2}{2}E[R^2|I=1]+E[SR|I=1]\theta_1\theta_3+\cdots\right)\Bigg]$$
$$+\mu q_{\cdot,1,\cdot}(t)\left[\left(1-\left(1-k_{0,1,0}(t)\theta_2-k_{1,0,0}(t)\theta_1-k_{0,0,1}(t)\theta_3-k_{1,1,0}(t)\theta_1\theta_2-k_{2,0,0}(t)\frac{\theta_1^2}{2!}\right.\right.\right.$$
$$-k_{0,1,1}(t)\theta_2\theta_3-k_{1,0,1}(t)\theta_1\theta_3-k_{0,2,0}(t)\frac{\theta_2^2}{2!}-k_{0,0,2}(t)\frac{\theta_3^2}{2!}-k_{1,1,1}(t)\theta_1\theta_2\theta_3+k_{0,1,0}^2(t)\frac{\theta_2^2}{2}$$
$$+k_{1,0,0}^2(t)\frac{\theta_1^2}{2}+k_{0,1,0}(t)k_{1,0,0}(t)\theta_1\theta_2+k_{0,0,1}(t)k_{1,0,0}(t)\theta_1\theta_3+k_{0,1,0}(t)k_{0,0,1}(t)\theta_2\theta_3$$
$$\left.\left.\left.+k_{0,0,1}^2(t)\frac{\theta_3^2}{2}+\cdots\right)\right)\left(1+\theta_1E[S|I=1]+\theta_3E[R|I=1]+\frac{\theta_1^2}{2}E[S^2|I=1]\right.\right.$$
$$\left.\left.+\frac{\theta_3^2}{2}E[R^2|I=1]+E[SR|I=1]\theta_1\theta_3+\cdots\right)\right].$$

Equating the corresponding coefficients of $\theta_1, \theta_2, \theta_1\theta_2, \theta_1^2, \theta_2^2$ gives,

$$\begin{aligned}
\dot{k}_{1,0,0}(t) &= \mu N - \frac{\beta}{N}(k_{1,1,0}(t) + k_{1,0,0}(t)k_{0,1,0}(t)) - \mu k_{1,0,0}(t) + \nu k_{0,0,1}(t) \\
&\quad +(\gamma+\mu)q_{.,1,.}(t)\left(k_{1,0,0}(t) - E[S|I=1]\right) && \text{(E.2)} \\
\dot{k}_{0,1,0}(t) &= \frac{\beta}{N}(k_{1,1,0}(t) + k_{1,0,0}(t)k_{0,1,0}(t)) - (\mu+\gamma)k_{0,1,0}(t) \\
&\quad +(\gamma+\mu)q_{.,1,.}(t)k_{0,1,0}(t) && \text{(E.3)} \\
\dot{k}_{0,0,1}(t) &= \gamma k_{0,1,0}(t) - \mu k_{0,0,1}(t) - \nu k_{0,0,1}(t)) - \gamma q_{.,1,.}(t)(1 + E[R|I=1]) \\
&\quad +(\mu+\gamma)q_{.,1,.}(k_{0,0,1}(t) + E[R|I=1]) - \gamma q_{.,1,.}(t) && \text{(E.4)} \\
\dot{k}_{1,1,0}(t) &= \frac{\beta}{N}[k_{1,0,0}(t)k_{1,1,0}(t) - k_{1,1,0}(t) - k_{1,0,0}(t)k_{0,1,0}(t) + k_{2,1,0}(t) \\
&\quad +k_{0,1,0}(t)k_{2,0,0}(t) - k_{0,1,0}(t)k_{1,1,0}(t) - k_{1,2,0}(t) - k_{1,0,0}(t)k_{0,2,0}(t)] \\
&\quad -(2\mu+\gamma)k_{1,1,0}(t) - \nu k_{0,1,1}(t) + (\gamma+\mu)q_{.,1,.}(t)[k_{1,1,0}(t) \\
&\quad +k_{0,1,0}(t)E[S|I=1] - k_{1,0,0}(t)k_{0,1,0}(t)] && \text{(E.5)} \\
\dot{k}_{1,0,1}(t) &= -\frac{\beta}{N}\left(k_{1,1,1} + k_{1,0,0}(t)k_{0,1,1}(t) + k_{1,0,1}(t)k_{0,1,0}(t)\right) - 2\mu k_{1,0,1}(t) \\
&\quad +\gamma k_{1,1,0}(t) - \nu(k_{0,0,1}(t) + k_{1,0,1}(t) - k_{0,0,2}(t)) \\
&\quad +(\gamma+\mu)q_{.,1,.}(t)[k_{1,0,1}(t) + k_{1,0,0}(t)E[R|I=1] + k_{0,0,1}(t)E[S|I=1] \\
&\quad +(\gamma+\mu)q_{.,1,.}(t)[E[SR|I=1] - k_{1,0,0}(t)k_{0,1,0}(t)] \\
&\quad -\gamma q_{.,1,.}(t)(E[SR|I=1] + E[S|I=1]) && \text{(E.6)} \\
\dot{k}_{0,1,1}(t) &= \frac{\beta}{N}\left(k_{1,1,1}(t) + k_{1,0,0}(t)k_{0,1,1}(t) + k_{0,1,0}(t)k_{1,0,1}(t)\right) - 2\mu k_{0,1,1}(t) \\
&\quad +\gamma(k_{0,2,0}(t) - k_{0,1,1}(t) - k_{0,1,0}(t)) - \nu k_{0,1,1}(t) \\
&\quad +(\gamma+\mu)q_{.,1,.}(t)\left(k_{0,1,1}(t) - k_{0,1,0}(t)k_{0,0,1}(t)\right) + \gamma q_{.,1,.}(t)k_{0,1,0}(t) && \text{(E.7)} \\
\dot{k}_{2,0,0}(t) &= \frac{\beta}{N}\left(k_{1,1,0}(t) + k_{1,0,0}(t)k_{0,1,0}(t) - 2k_{2,1,0}(t) - 2k_{1,0,0}(t)k_{1,1,0}(t)\right) \\
&\quad -2\frac{\beta}{N}k_{0,1,0}(t)k_{2,0,0}(t) + \mu N + \mu k_{1,0,0}(t) + \nu k_{0,0,1}(t) + 2\nu k_{1,0,1}(t) \\
&\quad -2\mu k_{2,0,0}(t) + (\gamma+\mu)q_{.,1,.}(t)\left(k_{2,0,0}(t) - k_{1,0,0}(t)^2\right) \\
&\quad +(\gamma+\mu)q_{.,1,.}(t)\left(2k_{1,0,0}(t)E[S|I=1] - E[S^2|I=1]\right) && \text{(E.8)} \\
\dot{k}_{0,2,0}(t) &= \frac{\beta}{N}\left(k_{1,1,0}(t) + k_{1,0,0}(t)k_{0,1,0}(t) + 2k_{1,2,0}(t) + 2k_{0,1,0}(t)k_{1,1,0}(t)\right) \\
&\quad +2\frac{\beta}{N}k_{1,0,0}(t)k_{0,2,0}(t) + (\gamma+\mu)(k_{0,1,0}(t) - 2k_{0,2,0}(t)) \\
&\quad +(\gamma+\mu)q_{.,1,.}(t)\left(k_{0,2,0}(t) - k_{0,1,0}(t)^2\right) && \text{(E.9)} \\
\dot{k}_{0,0,2}(t) &= \gamma(k_{0,1,0}(t) + 2k_{0,1,1}(t)) + \mu(k_{0,0,1}(t) - 2k_{0,0,2}(t)) + \nu(k_{0,0,1}(t) - 2k_{0,0,2}(t)) \\
&\quad -\gamma q_{.,1,.}(t)\left(1 + 2E[R|I=1] - E[R^2|I=1]\right) \\
&\quad +(\gamma+\mu)q_{.,1,.}(t)\left(k_{0,0,2}(t)E[R^2|I=1] - k_{0,0,1}(t)^2\right) && \text{(E.10)}
\end{aligned}$$

Appendix F

The derivative of the squared coefficient of variation with respect to η_3

$$\frac{d}{d\eta_3}(CV_I^2) = 1/N(-1R_0 - 2\eta_3 - 8\eta_2 + \eta_2^4 R_0 + \eta_2^4 R_0^2 + 2R_0^3\eta_2^2\eta_3 + 6\eta_2\eta_3 - 26\eta_2\eta_3 R_0 - 9\eta_3^2 + 4\eta_2^2 + 24\eta_3^2\eta_2 - 8\eta_2^2 R_0 + 8\eta_2 R_0 + 28\eta_2^2\eta_3 R_0 + 4\eta_2^2\eta_3 + 14\eta_2\eta_3 R_0^2 - 3\eta_2^2\eta_3^2 R_0^3 + 3\eta_2^3 - 10\eta_2^3\eta_3 + 8\eta_2^2\eta_3^3 - 20\eta_2\eta_3^3 - 21\eta_3^2\eta_2^2 + 2R_0\eta_3 + 3R_0\eta_3^2 - 6\eta_2^3\eta_3^2 R_0^2 + 18\eta_2^2\eta_3^2 R_0^2 - 16\eta_2^2\eta_3^3 R_0 + 24\eta_2\eta_3^3 R_0 + 10\eta_2^3\eta_3 R_0^2 - 6\eta_2^3\eta_3^2 R_0 + 6\eta_2^2\eta_3^2 R_0 + 8\eta_3^3 - 6\eta_2\eta_3^2 R_0 + 6\eta_2^3\eta_3^2 + 4\eta_2^2 R_0^2 - 2\eta_2^3 R_0^2 - 2\eta_2^4 - 4R_0^2\eta_3^3\eta_2 - 28\eta_2^2\eta_3 R_0^2 + 4\eta_2^4\eta_3 + 6\eta_2^3\eta_3^2 R_0^3 + 8\eta_2^2\eta_3^3 R_0^2 - 8\eta_2^4\eta_3 R_0 + 4\eta_2^4\eta_3 R_0^2 - 4R_0\eta_3^3 - 9\eta_2\eta_3^2 R_0^2 + 3 - 3R_0^2\eta_2)/(\eta_3 + 5\eta_2 - 6\eta_2\eta_3 + 4\eta_2\eta_3 R_0 + \eta_3^2 - 6\eta_2^2 - 2\eta_3^2\eta_2 + \eta_2^2 R_0 - 1\eta_2 R_0 - 8\eta_2^2\eta_3 R_0 + 7\eta_2^2\eta_3 + 2\eta_2^3 - 2\eta_2^3\eta_3 - 2\eta_2^2\eta_3^3 + 3\eta_2\eta_3^3 + \eta_3^2\eta_2^2 + 2\eta_2^3\eta_3^2 R_0^2 - 1\eta_2^2\eta_3^2 R_0^2 + 3\eta_2^3\eta_3 R_0 + 2\eta_2^2\eta_3^3 R_0 - 1\eta_2\eta_3^3 R_0 + \eta_2^3\eta_3 R_0^2 - 2\eta_2^3\eta_3^2 R_0 + 4\eta_2^2\eta_3^2 R_0 - 1\eta_3^3 - 2\eta_2\eta_3^2 R_0 - 1)R_0/(\eta_3 + \eta_2 - 1)/\eta_3^2/(R_0 - 1)^2(\eta_3 + \eta_2 - 1)^2 - 1/N(3\eta_3 + 2\eta_2 - 8\eta_2\eta_3 + 8\eta_2\eta_3 R_0 - 1\eta_3^2 - 1\eta_2^2 + 3\eta_3^2\eta_2 - 2\eta_2^2 R_0 + \eta_2 R_0 - 8\eta_2^2\eta_3 R_0 + 4\eta_2^2\eta_3 - 3\eta_2\eta_3 R_0^2 + \eta_2^2\eta_3^2 R_0^3 + \eta_2^3 R_0 + 3\eta_2^3\eta_3 - 7\eta_2^2\eta_3^3 + 8\eta_2\eta_3^3 + 2\eta_3^2\eta_2^2 - 1R_0\eta_3 + R_0\eta_3^2 + 5\eta_2^3\eta_3^2 R_0^2 - 14\eta_2^2\eta_3^2 R_0^2 + 2\eta_2^2\eta_3^3 R_0 - 2\eta_2\eta_3^3 R_0 - 2\eta_2^3\eta_3 R_0^2 + 14\eta_2^2\eta_3^2 R_0 - 3\eta_3^3 - 13\eta_2\eta_3^2 R_0 - 5\eta_2^3\eta_3^2 - 3R_0^2\eta_3^3\eta_2 + 2\eta_3^4 + 4\eta_2^2\eta_3 R_0^2 + 2\eta_2^4\eta_3^2 + 2\eta_2^2\eta_3^4 + 2\eta_2^3\eta_3^3 - 5\eta_2\eta_3^4 - 2\eta_2^4\eta_3 - 4\eta_2^4\eta_3^2 R_0 - 4\eta_2^2\eta_3^4 R_0 - 2\eta_2^3\eta_3^3 R_0 + 2\eta_2^3\eta_3^3 R_0^3 + 2\eta_2^4\eta_3^2 R_0^2 + 2\eta_2^2\eta_3^4 R_0^2 + 6\eta_2\eta_3^4 R_0 - 2\eta_2^3\eta_3^3 R_0^2 + 6\eta_2^2\eta_3^3 R_0^2 + \eta_2^4\eta_3 R_0 + \eta_2^4\eta_3 R_0^2 + R_0\eta_3^3 + 7\eta_2\eta_3^2 R_0^2 - 1\eta_3^4 R_0 - 1 - \eta_2\eta_3^4 R_0^2 - 1\eta_2^2\eta_3^3 R_0^3)/(\eta_3 + 5\eta_2 - 6\eta_2\eta_3 + 4\eta_2\eta_3 R_0 + \eta_3^2 - 6\eta_2^2 - 2\eta_3^2\eta_2 + \eta_2^2 R_0 - 1\eta_2 R_0 - 8\eta_2^2\eta_3 R_0 + 7\eta_2^2\eta_3 + 2\eta_2^3 - 2\eta_2^3\eta_3 - 2\eta_2^2\eta_3^3 + 3\eta_2\eta_3^3 + \eta_3^2\eta_2^2 + 2\eta_2^3\eta_3^2 R_0^2 - \eta_2^2\eta_3^2 R_0^2 + 3\eta_2^3\eta_3 R_0 + 2\eta_2^2\eta_3^3 R_0 - 1\eta_2\eta_3^3 R_0 + \eta_2^3\eta_3 R_0^2 - 2\eta_2^3\eta_3^2 R_0 + 4\eta_2^2\eta_3^2 R_0 - 1\eta_3^3 - 2\eta_2\eta_3^2 R_0 - 1)^2 R_0/(\eta_3 + \eta_2 - 1)/\eta_3^2/(R_0 - 1)^2(\eta_3 + \eta_2 - 1)^2(1 - 6\eta_2 + 4\eta_2 R_0 + 2\eta_3 - 4\eta_2\eta_3 - 8\eta_2^2 R_0 + 7\eta_2^2 - 2\eta_2^3 - 6\eta_3^2\eta_2^2 + 9\eta_3^2\eta_2 + 2\eta_2^2\eta_3 + 4\eta_2^3\eta_3 R_0^2 - 2\eta_2^2\eta_3 R_0^2 + 3\eta_2^3 R_0 + 6\eta_2^2\eta_3^2 R_0 - 3\eta_2\eta_3^2 R_0 + \eta_3^2 R_0^2 - 4\eta_2^3\eta_3 R_0 + 8\eta_2^2\eta_3 R_0 - 3\eta_3^2 - 4\eta_2\eta_3 R_0) - 1/N(3\eta_3 + 2\eta_2 - 8\eta_2\eta_3 + 8\eta_2\eta_3 R_0 - 1\eta_3^2 - 1\eta_2^2 +$$

$$3\eta_3^2\eta_2 - 2\eta_2^2 R_0 + \eta_2 R_0 - 8\eta_2^2\eta_3 R_0 + 4\eta_2^2\eta_3 - 3\eta_2\eta_3 R_0^2 + \eta_2^2\eta_3^2 R_0^3 + \eta_2^3 R_0 + 3\eta_2^3\eta_3 - 7\eta_2^2\eta_3^3 +$$
$$8\eta_2\eta_3^3 + 2\eta_3^2\eta_2^2 - 1R_0\eta_3 + R_0\eta_3^2 + 5\eta_2^3\eta_3^2 R_0^2 - 14\eta_2^2\eta_3^2 R_0^2 + 2\eta_2^2\eta_3^3 R_0 - 2\eta_2\eta_3^3 R_0 - 2\eta_2^3\eta_3 R_0^2 +$$
$$14\eta_2^2\eta_3^2 R_0 - 3\eta_3^3 - 13\eta_2\eta_3^2 R_0 - 5\eta_2^3\eta_3^2 - 3R_0^2\eta_3^3\eta_2 + 2\eta_3^4 + 4\eta_2^2\eta_3 R_0^2 + 2\eta_2^4\eta_3^2 + 2\eta_2^2\eta_3^4 +$$
$$2\eta_2^3\eta_3^3 - 5\eta_2\eta_3^4 - 2\eta_2^4\eta_3 - 4\eta_2^4\eta_3^2 R_0 - 4\eta_2^2\eta_3^4 R_0 - 2\eta_2^3\eta_3^3 R_0 + 2\eta_2^3\eta_3^3 R_0^3 + 2\eta_2^4\eta_3^2 R_0^2 + 2\eta_2^2\eta_3^4 R_0^2 +$$
$$6\eta_2\eta_3^4 R_0 - 2\eta_2^3\eta_3^3 R_0^2 + 6\eta_2^2\eta_3^3 R_0^2 + \eta_2^4\eta_3 R_0 + \eta_2^4\eta_3 R_0^2 + R_0\eta_3^3 + 7\eta_2\eta_3^2 R_0^2 - 1\eta_3^4 R_0 - 1 -$$
$$\eta_2\eta_3^4 R_0^2 - 1\eta_2^2\eta_3^3 R_0^3)/(\eta_3 + 5\eta_2 - 6\eta_2\eta_3 + 4\eta_2\eta_3 R_0 + \eta_3^2 - 6\eta_2^2 - 2\eta_3^2\eta_2 + \eta_2^2 R_0 - 1\eta_2 R_0 -$$
$$8\eta_2^2\eta_3 R_0 + 7\eta_2^2\eta_3 + 2\eta_2^3 - 2\eta_2^3\eta_3 - 2\eta_2^2\eta_3^3 + 3\eta_2\eta_3^3 + \eta_3^2\eta_2^2 + 2\eta_2^3\eta_3^2 R_0^2 - 1\eta_2^2\eta_3^2 R_0^2 + 3\eta_2^3\eta_3 R_0 +$$
$$2\eta_2^2\eta_3^3 R_0 - 1\eta_2\eta_3^3 R_0 + \eta_2^3\eta_3 R_0^2 - 2\eta_2^3\eta_3^2 R_0 + 4\eta_2^2\eta_3^2 R_0 - 1\eta_3^3 - 2\eta_2\eta_3^2 R_0 - 1)R_0/(\eta_3 + \eta_2 -$$
$$1)^2/\eta_3^2/(R_0 - 1)^2(\eta_3 + \eta_2 - 1)^2 - 2/N(3\eta_3 + 2\eta_2 - 8\eta_2\eta_3 + 8\eta_2\eta_3 R_0 - 1\eta_3^2 - 1\eta_2^2 + 3\eta_3^2\eta_2 -$$
$$2\eta_2^2 R_0 + \eta_2 R_0 - 8\eta_2^2\eta_3 R_0 + 4\eta_2^2\eta_3 - 3\eta_2\eta_3 R_0^2 + \eta_2^2\eta_3^2 R_0^3 + \eta_2^3 R_0 + 3\eta_2^3\eta_3 - 7\eta_2^2\eta_3^3 + 8\eta_2\eta_3^3 +$$
$$2\eta_3^2\eta_2^2 - 1R_0\eta_3 + R_0\eta_3^2 + 5\eta_2^3\eta_3^2 R_0^2 - 14\eta_2^2\eta_3^2 R_0^2 2\eta_2^2\eta_3^3 R_0 - 2\eta_2\eta_3^3 R_0 - 2\eta_2^3\eta_3 R_0^2 + 14\eta_2^2\eta_3^2 R_0 -$$
$$3\eta_3^3 - 13\eta_2\eta_3^2 R_0 - 5\eta_2^3\eta_3^2 - 3R_0^2\eta_3^3\eta_2 + 2\eta_3^4 + 4\eta_2^2\eta_3 R_0^2 + 2\eta_2^4\eta_3^2 + 2\eta_2^2\eta_3^4 + 2\eta_2^3\eta_3^3 - 5\eta_2\eta_3^4 -$$
$$2\eta_2^4\eta_3 - 4\eta_2^4\eta_3^2 R_0 - 4\eta_2^2\eta_3^4 R_0 - 2\eta_2^3\eta_3^3 R_0 + 2\eta_2^3\eta_3^3 R_0^3 + 2\eta_2^4\eta_3^2 R_0^2 + 2\eta_2^2\eta_3^4 R_0^2 + 6\eta_2\eta_3^4 R_0 -$$
$$2\eta_2^3\eta_3^3 R_0^2 + 6\eta_2^2\eta_3^3 R_0^2 + \eta_2^4\eta_3 R_0 + \eta_2^4\eta_3 R_0^2 + R_0\eta_3^3 + 7\eta_2\eta_3^2 R_0^2 - 1\eta_3^4 R_0 - 1 - 1\eta_2\eta_3^4 R_0^2 -$$
$$1\eta_2^2\eta_3^3 R_0^3)/(\eta_3 + 5\eta_2 - 6\eta_2\eta_3 + 4\eta_2\eta_3 R_0 + \eta_3^2 - 6\eta_2^2 - 2\eta_3^2\eta_2 + \eta_2^2 R_0 - 1\eta_2 R_0 - 8\eta_2^2\eta_3 R_0 +$$
$$7\eta_2^2\eta_3 + 2\eta_2^3 - 2\eta_2^3\eta_3 - 2\eta_2^2\eta_3^3 + 3\eta_2\eta_3^3 + \eta_3^2\eta_2^2 + 2\eta_2^3\eta_3^2 R_0^2 - \eta_2^2\eta_3^2 R_0^2 + 3\eta_2^3\eta_3 R_0 + 2\eta_2^2\eta_3^3 R_0 -$$
$$\eta_2\eta_3^3 R_0 + \eta_2^3\eta_3 R_0^2 - 2\eta_2^3\eta_3^2 R_0 + 4\eta_2^2\eta_3^2 R_0 - 1\eta_3^3 - 2\eta_2\eta_3^2 R_0 - 1)R_0/(\eta_3 + \eta_2 - 1)/\eta_3^3/(R_0 -$$
$$1)^2(\eta_3\eta_2 - 1)^2 + 2/N(3\eta_3 + 2\eta_2 - 8\eta_2\eta_3 + 8\eta_2\eta_3 R_0 - 1\eta_3^2 - 1\eta_2^2 + 3\eta_3^2\eta_2 - 2\eta_2^2 R_0 +$$
$$\eta_2 R_0 - 8\eta_2^2\eta_3 R_0 + 4\eta_2^2\eta_3 - 3\eta_2\eta_3 R_0^2 + \eta_2^2\eta_3^2 R_0^3 + \eta_2^3 R_0 + 3\eta_2^3\eta_3 - 7\eta_2^2\eta_3^3 + 8\eta_2\eta_3^3 + 2\eta_3^2\eta_2^2 -$$
$$R_0\eta_3 + R_0\eta_3^2 + 5\eta_2^3\eta_3^2 R_0^2 - 14\eta_2^2\eta_3^2 R_0^2 + 2\eta_2^2\eta_3^3 R_0 - 2\eta_2\eta_3^3 R_0 - 2\eta_2^3\eta_3 R_0^2 + 14\eta_2^2\eta_3^2 R_0 - 3\eta_3^3 -$$
$$13\eta_2\eta_3^2 R_0 - 5\eta_2^3\eta_3^2 - 3R_0^2\eta_3^3\eta_2 + 2\eta_3^4 + 4\eta_2^2\eta_3 R_0^2 + 2\eta_2^4\eta_3^2 + 2\eta_2^2\eta_3^4 + 2\eta_2^3\eta_3^3 - 5\eta_2\eta_3^4 - 2\eta_2^4\eta_3 -$$
$$4\eta_2^4\eta_3^2 R_0 - 4\eta_2^2\eta_3^4 R_0 - 2\eta_2^3\eta_3^3 R_0 + 2\eta_2^3\eta_3^3 R_0^3 + 2\eta_2^4\eta_3^2 R_0^2 + 2\eta_2^2\eta_3^4 R_0^2 + 6\eta_2\eta_3^4 R_0 - 2\eta_2^3\eta_3^3 R_0^2 +$$
$$6\eta_2^2\eta_3^3 R_0^2 + \eta_2^4\eta_3 R_0 + \eta_2^4\eta_3 R_0^2 + R_0\eta_3^3 + 7\eta_2\eta_3^2 R_0^2 - 1\eta_3^4 R_0 - 1 - \eta_2\eta_3^4 R_0^2 - 1\eta_2^2\eta_3^3 R_0^3)/(\eta_3 +$$
$$5\eta_2 - 6\eta_2\eta_3 + 4\eta_2\eta_3 R_0 + \eta_3^2 - 6\eta_2^2 - 2\eta_3^2\eta_2 + \eta_2^2 R_0 - 1\eta_2 R_0 - 8\eta_2^2\eta_3 R_0 + 7\eta_2^2\eta_3 + 2\eta_2^3 - 2\eta_2^3\eta_3 -$$
$$2\eta_2^2\eta_3^3 + 3\eta_2\eta_3^3 + \eta_3^2\eta_2^2 + 2\eta_2^3\eta_3^2 R_0^2 - 1\eta_2^2\eta_3^2 R_0^2 + 3\eta_2^3\eta_3 R_0 + 2\eta_2^2\eta_3^3 R_0 - 1\eta_2\eta_3^3 R_0 + \eta_2^3\eta_3 R_0^2 -$$
$$2\eta_2^3\eta_3^2 R_0 + 4\eta_2^2\eta_3^2 R_0 - 1\eta_3^3 - 2\eta_2\eta_3^2 R_0 - 1)R_0/(\eta_3 + \eta_2 - 1)/\eta_3^2/(R_0 - 1)^2(\eta_3 + \eta_2 - 1)$$

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