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Abstract

We are interested in how the addition of type heterogeneities affects the long time behaviour of endemic diseases. We do this by analysing a two-type version of a model introduced by Bartlett under the restriction of proportionate mixing. This model is used to describe diseases for which individuals switch states according to susceptible $\rightarrow$ infectious $\rightarrow$ recovered and immune, where the immunity is lifelong. We describe an approximation of the distribution of the time to extinction given that the process is started in the quasi-stationary distribution, and we analyse how the variance and the coefficient of variation of the number of infectious individuals depends on the degree of heterogeneity between the two types of individuals. These are then used to derive an approximation of the time to extinction. From this approximation we get that if we increase the difference in infectivity between the two types the expected time to extinction decreases, and if we instead increase the difference in susceptibility the behaviour of the expected time to extinction depends on which part of the parameter space we are in, and we can also obtain non monotonic behaviour. These results are supported by simulations.

KEY WORDS: Stochastic SIR epidemic model, Quasi-stationary distribution, Diffusion approximation, Endemic diseases

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1 Introduction

Diseases that are able to persist in a population for a long time without the need of introducing new infectious individuals from an external population are called endemic, see e.g. pp. 73 in [1]. A question which has received a lot of attention in the literature is the behaviour of an endemic disease after a long time, see e.g. [2] and the references therein, [3], [4], [5]. In the present paper we look at the situation when all individuals in a homogeneously mixing population is classified as one of two types, e.g. children or adults, female or male etc. These types give the individuals different characteristics in terms of their ability to become infected while susceptible, and their ability to infect while infectious. We are interested in how this addition of heterogeneity affects the persistence of an infectious disease. As a measure of persistence we use the additional time to extinction conditioned on that the disease has not gone extinct for a long time. We have used a stochastic epidemic model introduced by Bartlett in [6], and modified it to take types into account. Bartlett proposed a very similar deterministic two-type model in [6], and the model treated in the present paper is a stochastic analogue to this model when Bartlett's deterministic model is suitably parametrized. The definition of Bartlett's original stochastic one-type model which we will use is from ch. VII in [7]. This model is used to describe diseases where individuals switch between the states susceptible, S, infectious, I, and recovered (and immune), R, according to $\mathrm{S} \to \mathrm{I} \to \mathrm{R}$. Henceforth we make no distinction between recovered and immune, and only refer to this state as being recovered. Immunity is here regarded as life-long, hence the state R is absorbing up until death. The big difference between Bartlett's model and the standard SIR epidemic, see e.g. [1] pp. 11, is that it has a simple demographic mechanism. This mechanism is necessary in order for the disease to become endemic. That is, since the model has a recovered state, we need to have some inflow of susceptible individuals in order for this behaviour to appear. Bartlett's model has been widely studied over the years, e.g. [2] and the references therein, and different versions of this model has emerged, see e.g. [8]. A central issue in many of these papers is the behaviour of the epidemic after a long time.

We analyse an extension of this model when two types of individuals are present under the restriction of so-called proportionate mixing, that is when the contact parameter λ_{ij} for a contact between an infected i-individual and a susceptible j-individual, has the form $\lambda_{ij} = \alpha_i\beta_j$ (this is sometimes called separable), where $\{\alpha_i\}$ and $\{\beta_j\}$ are called infectivities and susceptibilities respectively. Under this extra restriction we describe an approximation of the distribution of the time to extinction conditioned on that the disease

has not gone extinct for a long time, i.e. an approximation of the quasi-stationary distribution. We also analyse the variance and the coefficient of variation of the number of infectious individuals under quasi-stationarity. When comparing our analytical approximations with simulations, it is seen that the approximations are not perfect, but that they capture the qualitative behaviour of the epidemic in relevant regions of the parameter space. That is, if we increase the difference in infectivity between the two types the expected time to extinction decreases, and if we instead increase the difference in susceptibility the behaviour of the expected time to extinction depends on which parameter region we are in, and we can in fact observe non monotonic behaviour.

For the disposition of this paper, we define the two-type version of Bartlett's epidemic model and describe our main results in Section 2 and in Section 3 we make some numerical comparisons with simulations. Section 4 is devoted to a closing discussion.

2 Bartlett's epidemic model with two types of individuals

We have an open population without social structures where each individual lives forever and is classified as either a type one or a type two individual, e.g. female or male, young or adult etc., and individuals are not allowed to change type. An alternative interpretation of the model is that individuals never die while susceptible or infectious. This interpretation is realistic when we are interested in childhood diseases, and this is the interpretation we will use henceforth. The population is open in that new susceptible individuals are brought into the population via birth/immigration, or more formally: susceptible individuals of type j are born according to a pure birth process with constant rate, $\mu n_j, j = 1, 2$. Here $1/\mu$ is considered to be of the same order of magnitude as the average life-length of a real-life human, e.g. $1/\mu \approx 70$ years, and where n_j is more or less the average number of type j individuals which are either susceptible or infectious, or if we suppose that type j individuals in R dies at rate μ then $n_j \approx \mathrm{S}_j + \mathrm{I}_j + \mathrm{R}_j$. By introducing new susceptible individuals into the population in this way, we will on average have a proportion $\pi_j = n_j/n, n = n_1 + n_2$, type j individuals in the population which are either susceptible or infectious. Turning to the spread of disease, an infectious i individual stays so for an exponentially distributed infectious period with mean $1/\nu_i = 1/\nu$, where $1/\nu$ is considered small, e.g. $1/\nu$ is about one week for measles (if $1/\mu \approx 70$ then $1/\nu \approx 1/52$), see e.g. pp. 31 in [9]. During this time period, the infectious i individual makes contacts with a given j

individual according to a Poisson process with rate λ_{ij}/n. If a contacted j individual is susceptible at the time of contact then this individual becomes infectious. After the infectious period is over the previously infectious individual recovers and becomes immune, that is, individuals switch between being susceptible, infectious and recovered according to S $\to$ I $\to$ R. Since recovered individuals never again will contribute to the infectious pressure in the population, we only need to keep track of the number of susceptible and infectious individuals at each time point to be able to describe the dynamics of the epidemic. Due to this, we can always interpret the model as if death occurs at rate μ in the recovered state, which is reasonable when talking about childhood diseases. Note, that since susceptible individuals are born at a constant rate there will always be a large number of susceptible individuals present in the population at all time points, hence the epidemic will not go extinct due to lack of susceptible individuals to infect.

In the present paper we will use this model under the extra restriction of proportionate mixing, which is the situation when λ_{ij} can be written as $\lambda_{ij} = \alpha_i\beta_j$ where $\{\alpha_i\}$ and $\{\beta_j\}$ are called infectivities and susceptibilities respectively. Let $(\mathbf{X}(t), \mathbf{Y}(t)) = (X_1(t), X_2(t), Y_1(t), Y_2(t))$ denote the process of number of susceptible and infectious individuals of the two types at t. Rates for all possible transitions are defined in Table 1. From these rates we also see that the disease-free set of states is absorbing. Denote this set by $\mathcal{S}_{\text{abs}}$, where

$$\mathcal{S}_{\text{abs}} = \{(\mathbf{x}, \mathbf{y}); \mathbf{x} \in \mathbb{N} \times \mathbb{N}, \mathbf{y} = \mathbf{0}\} \tag{1}$$

where $\mathbb{N} = \{0, 1, 2, \ldots\}$. If we instead look at the process of proportions, $(\mathbf{X}(t)/n, \mathbf{Y}(t)/n)$, where $n = n_1 + n_2$, then its deterministic counterpart is described by the following system of differential equations:

$$\begin{cases} x_j'(t) &= \mu\pi_j - \beta_j x_j(t)\left(\alpha_1 y_1(t) + \alpha_2 y_2(t)\right) \\ y_j'(t) &= \beta_j x_j(t)\left(\alpha_1 y_1(t) + \alpha_2 y_2(t)\right) - \nu y_j(t) \end{cases} \tag{2}$$

where $\pi_j = n_j/n,\ j = 1, 2$. An important epidemiological quantity is R_0, the so-called basic reproduction number. For general multi-type epidemic models R_0 is defined as the largest eigenvalue of the mean offspring matrix $\{\lambda_{ij}\pi_j/\nu\}$, see pp. 51-61 in [1]. For Bartlett's model with two types of individuals, under the restriction of proportionate mixing, the mean offspring matrix becomes $\{\alpha_i\beta_j\pi_j/\nu\}$, and we get that

$$R_0 = \frac{\alpha_1\beta_1\pi_1 + \alpha_2\beta_2\pi_2}{\nu}. \tag{3}$$

In general, for a disease to be able to become endemic R_0 must be strictly above one, see e.g. ch. 8 in [1]. This is however *not* the case for Bartlett's

model, which can become endemic for *any* $R_0 > 0$. That is, regardless of the value of $R_0 > 0$, the epidemic process has always a positive probability of stabilising around some equilibrium.

That a disease becomes endemic is the same as to say that it has been able to persist in the population for a long but finite time. In the present paper we use the additional time to extinction conditioned on that the process has not gone extinct for a long but finite time, as a measure of persistence. If the process has not gone extinct after a long time it is likely to have stabilised, making small fluctuations, around the endemic level. The endemic level is obtained by finding the stationary points to the system of differential equations defined in (2). For this particular model we get one stationary point

$$(\hat{x}_j, \hat{y}_j) = \left(\frac{\pi_j \mu \gamma}{\alpha_\pi \beta_j}, \frac{\pi_j}{\gamma} \right), \ j = 1, 2 \tag{4}$$

where $\alpha_\pi = \alpha_1 \pi_1 + \alpha_2 \pi_2$, $\beta_j > 0, j = 1, 2$, and $\gamma = \nu/\mu$. Here γ denotes the ratio of average lifetime and average infectious period. Note that as discussed above, the stationary point from (4) will always exist as soon as $R_0 > 0$. Under these circumstances it is natural to look at the quasi-stationary distribution of the epidemic process denoted Q, i.e. the distribution conditioned on that the epidemic has not died out by time t when we let t tend to infinity. Hence, we are interested in T_Q, the time to extinction given that the process is started in the quasi-stationary distribution. Regardless of whether or not we *know* the quasi-stationary distribution, we can still say something about T_Q:

$$\begin{aligned} P(T_Q > t + s \mid T_Q > t, \ (\mathbf{X}(0), \mathbf{Y}(0)) \sim Q) &= \\ &= P(T_Q > t + s \mid T_Q > t, \ (\mathbf{X}(t), \mathbf{Y}(t)) \sim Q) \\ &= P(T_Q > s \mid (\mathbf{X}(0), \mathbf{Y}(0)) \sim Q) \end{aligned}$$

i.e. T_Q has the lack of memory property which implies that T_Q is exponentially distributed. This follows the same reasoning as in [3]. To determine this exponential distribution completely we need to know its mean. Following the lines of [2] for Bartlett's original model, we know that $P(T_Q \leq t) = P(\mathbf{Y}(t) = \mathbf{0})$, and by defining the Kolmogorov forward equations for $P(\mathbf{Y}(t) = \mathbf{i})$ one can show that $E(T_Q) = \tau_Q = 1/\mu\gamma q_{\bullet,1}$. Here $q_{\bullet,1} = \sum_{\mathbf{x}} (q_{\mathbf{x},\mathbf{e}_1} + q_{\mathbf{x},\mathbf{e}_2})$, where $\mathbf{e}_j$ is the j'th unit vector. Thus, the distribution of T_Q will depend on the rate with which $(\mathbf{X}(t), \mathbf{Y}(t))$ enters the set of absorbing states, $\mathcal{S}_{\text{abs}}$ from (1). We state this more precisely in the following proposition:

Table 1: Bartlett's model with two types of individuals, possible transitions for individuals of type $j = 1, 2$. Here s_j and i_j denote the number of susceptible and infectious type j individuals at a certain time point. Note that if a change of state occurs for the type 1 individuals, the state of the type 2 individuals remains unchanged, and vice versa.

From	To	Rate
(s_j, i_j)	$(s_j + 1, i_j)$	μn_j
(s_j, i_j)	$(s_j - 1, i_j + 1)$	$\frac{\beta_j}{n} s_j(\alpha_1 i_1 + \alpha_2 i_2)$
(s_j, i_j)	$(s_j, i_j - 1)$	νi_j

Proposition 1 *The time to extinction given that the process is started in the quasi-stationary distribution, T_Q, is exponentially distributed with mean*

$$\tau_Q = \frac{1}{\mu\gamma q_{\bullet,1}} \tag{5}$$

where

$$q_{\bullet,1} = \sum_{\mathbf{x} \geq \mathbf{0}} (q_{\mathbf{x},\mathbf{e}_1} + q_{\mathbf{x},\mathbf{e}_2}) \tag{6}$$

and where $\mathbf{e}_j$ is the j'th unit vector.

A way of approximating the quasi-stationary distribution, $q_{\bullet,k}$, is via a diffusion approximation. Introduce the scaled and centred process

$$(\widetilde{\mathbf{X}}_n(t), \widetilde{\mathbf{Y}}_n(t)) = \sqrt{n}\left(\frac{\mathbf{X}(t)}{n} - \hat{\mathbf{x}}, \frac{\mathbf{Y}(t)}{n} - \hat{\mathbf{y}}\right) \tag{7}$$

where $(\hat{\mathbf{x}}, \hat{\mathbf{y}})$ corresponds to the endemic level of infection. From the theory of diffusion processes it is known that this process converges weakly to an Ornstein-Uhlenbeck process, $(\widetilde{\mathbf{X}}(t), \widetilde{\mathbf{Y}}(t))$, as n tends to infinity, see e.g. ch. 11 in [10]. Since the limiting process is of Ornstein-Uhlenbeck type, it has a *stationary* Gaussian distribution with mean $\mathbf{0}$ and covariance matrix $\hat{\mathbf{\Sigma}} = \{\hat{\sigma}_{ij}\}$, which is the solution to the following equation

$$\hat{\mathbf{B}}\hat{\mathbf{\Sigma}} + \hat{\mathbf{\Sigma}}\hat{\mathbf{B}}^{\mathrm{T}} = -\hat{\mathbf{S}}, \tag{8}$$

see e.g. pp. 357 in [11]. Here $\mathbf{B}$ and $\mathbf{S}$ are the local drift and covariance matrices of $(\widetilde{\mathbf{X}}(t), \widetilde{\mathbf{Y}}(t))$. The local drift matrix is the Jacobian of the first

order infinitesimal moment of $(\widetilde{\mathbf{X}}_n, \widetilde{\mathbf{Y}}_n)$ and the local covariance matrix is the infinitesimal covariance matrix of $(\widetilde{\mathbf{X}}_n, \widetilde{\mathbf{Y}}_n)$. We are interested in the behaviour of the epidemic process close to the endemic level, and we therefore approximate $\mathbf{B}$ and $\mathbf{S}$ at the endemic level, denoted $\widehat{\mathbf{B}}$ and $\widehat{\mathbf{S}}$. We can now conclude the following: after a long but finite time the process is likely to have stabilised around the stationary point (4), and then $\mathbf{Y}(t) \approx \sqrt{n}\widetilde{\mathbf{Y}}(t) + n\hat{\mathbf{y}}$ implying that $\mathbf{Y}(t) \sim apprN(n\hat{\mathbf{y}}, nCov(\widetilde{\mathbf{Y}}))$. In particular we have that $Y_1(t) + Y_2(t) \sim apprN(\mu_Y, \sigma_Y^2)$, where

$$\begin{aligned} \mu_Y &= E(Y_1 + Y_1) = n(\hat{y}_1 + \hat{y}_2) \\ \sigma_Y^2 &= Var(Y_1 + Y_2) = n(\hat{\sigma}_{11}^2 + \hat{\sigma}_{22}^2 + 2\hat{\sigma}_{12}) \end{aligned} . \tag{9}$$

This, however, contradicts our original definition of the process $\mathbf{Y}(t)$ which is non-negative and integer valued, since we can not have a negative number of individuals, whereas the approximate distribution of the total number of infected individuals after a long time is defined on $\mathbb{R}$. But, if we truncate this distribution at 0 (or at 0.5 using continuity correction) we get an approximation of the the probability that $Y_1(t) + Y_2(t) = k$, i.e. $q_{\bullet,k}$:

$$q_{\bullet,k} \approx \frac{1}{\sigma_Y} \frac{\varphi((k - \mu_Y)/\sigma_Y)}{\Phi((\mu_Y - 0.5)/\sigma_Y)}, \ k \geq 0 \tag{10}$$

where $\Phi(\cdot)$ and $\varphi(\cdot)$ are the standard normal distribution and density functions, and μ_Y and σ_Y are from (9). By using $q_{\bullet,1}$ from (10) together with Proposition 1 the distribution of T_Q is determined. This is analogous to what Nåsell did for Bartlett's original model in [2].

In Appendix A we derive $\widehat{\mathbf{B}}$ and $\widehat{\mathbf{S}}$ for Bartlett's model with two types, with which we can find a solution to equation (8). This amounts to solving a ten dimensional equation system, and for this task we have used the symbolic software `MAPLE`. Unfortunately the closed expression for $\widehat{\Sigma}$ is lengthy and not easy to grasp, and is hence omitted. We can, however, calculate μ_Y and σ_Y^2 from (9). Calculating μ_Y gives us

$$\mu_Y = \frac{n}{\gamma}. \tag{11}$$

A general expression for σ_Y^2 turns out to be long and not illuminating, but if we either set $\alpha_1 = \alpha_2 = \alpha$ and vary β_1 and β_2, or set $\beta_1 = \beta_2 = \beta$ and vary α_1 and α_2, we can simplify σ_Y^2 quite a lot.

If we set $\alpha_1 = \alpha_2 = \alpha$ we get that

$$\sigma_{Y,\beta}^2 = \frac{n}{\gamma} + n\frac{\mu\gamma}{\alpha} \frac{\beta_1^2\pi_2 + \beta_2^2\pi_1 + \beta_1\beta_2 + (\beta_1\pi_1 + \beta_2\pi_2)\frac{\mu\gamma^2}{\alpha}}{\beta_1^2\left(\beta_2 + \frac{\mu\gamma^2}{\alpha}\pi_1\right) + \beta_2^2\left(\beta_1 + \frac{\mu\gamma^2}{\alpha}\pi_2\right)} \tag{12}$$

and if we instead set $\beta_1 = \beta_2 = \beta$ we get

$$\sigma^2_{Y,\alpha} = \frac{n}{\gamma} + n\frac{\mu\gamma}{\alpha_\pi}\frac{2\beta + ((\alpha_1+\alpha_2)\alpha_\pi - \alpha_1\alpha_2)\,\frac{\mu\gamma^2}{\alpha_\pi^3}}{2\beta + \frac{\mu\gamma^2}{\alpha_\pi}} \tag{13}$$

where $\alpha_\pi = \alpha_1\pi_1 + \alpha_2\pi_2$. Our particular interest is to analyse the effect of the heterogeneity caused by including types into the model, and this we would do by looking at the α's and β's separately, i.e. $\lambda_{ij} = \alpha\beta_j$ or $\lambda_{ij} = \alpha_i\beta$, so from this point of view we have not limited ourselves. A measure used to get an idea of how far the process is from extinction, is the coefficient of variation, CV_Y, defined as

$$CV_Y = \frac{\sigma_Y}{\mu_Y} \tag{14}$$

but, since μ_Y from (11) is independent of all α's and β's, we can analyse σ^2_Y as a function of either the α's or β's instead. That it is enough to analyse σ^2_Y, and no higher order moments, is due to that we approximate the quasi-stationary distribution with a truncated normal distribution, i.e. the approximating distribution lacks skewness. Intuitively, as σ^2_Y increases, we are more likely to make larger fluctuations around the endemic level, and are hence more likely to hit $\mathcal{S}_{\text{abs}}$, the disease-free set of states. Thus, increasing the variance ought to shorten the expected time to extinction, and vice versa.

2.1 Analysing $\sigma^2_{Y,\beta}(\delta)$: the effect of difference in susceptibility between the two types

To be able to compare our results with those for Bartlett's original one-type model, we parametrize β_1 and β_2 according to

$$\begin{cases}\beta_1 = \beta(1-\delta) \\ \beta_2 = \beta(1+\frac{\pi_1}{\pi_2}\delta)\end{cases}, \ \delta \in [0,1] \tag{15}$$

where δ correspond to the degree of heterogeneity between the two types. By using this parametrization we get that $R_0 = \alpha\beta/\gamma$, hence independent of δ and thus compatible with R_0 for the original Bartlett model. Note that the limits for δ are chosen so that both β_1 and β_2 will remain positive, and due to symmetry we only look at $\delta \in [0,1]$, since we do not gain any extra information by including $\delta \in [-\pi_2/\pi_1, 0)$. Further, since R_0 is independent of δ and we are interested in the heterogeneity caused by differences in the susceptibilities, we can set $\alpha_1 = \alpha_2 = 1$, because we can always scale the β's

such that the α's can be set to unity. When parametrizing the β's in this way and setting $\pi_1 = 1-\pi$ and $\pi_2 = \pi$ then $\sigma^2_{Y,\beta}$ from (12) can be written as

$$\sigma^2_{Y,\beta}(\delta) = \frac{n}{\gamma} + n\frac{f(\delta)}{\mu\gamma R_0 f(\delta) + g(\delta)}\mu\gamma \tag{16}$$

where

$$\begin{aligned} f(\delta) &= \beta(2\beta + \mu\gamma^2)\pi^2 + 3\beta^2(1-2\pi)\pi\delta + \beta^2(1-2\pi)^2\delta^2 = \\ &= R_0(\mu\gamma)^2(2R_0+\gamma)\pi^2 + 3(R_0\mu\gamma)^2(1-2\pi)\pi\delta + (R_0\mu\gamma)^2(1-2\pi)^2\delta^2 \\ &= a_1 + a_2\delta + a_3\delta^2 \qquad (17) \\ g(\delta) &= \beta^2(\mu\gamma^2 - 2\beta)\pi(1-\pi)\delta^2 - \beta^3(1-\pi)(1-2\pi)\delta^3 \\ &= R_0^3(\mu\gamma)^4(\gamma - 2R_0)\pi(1-\pi)\delta^2 - (R_0\mu\gamma)^3(1-\pi)(1-2\pi)\delta^3 \\ &= a_4\delta^2 + a_5\delta^3 \qquad (18) \end{aligned}$$

Analysing $\sigma^2_{Y,\beta}(\delta)$ at its end points gives us

$$\sigma^2_{Y,\beta}(\delta) = \begin{cases} \frac{n}{\gamma} + \frac{n}{R_0} & \text{if } \delta = 0 \\ \frac{n}{\gamma\pi} + n\frac{\pi}{R_0} & \text{if } \delta = 1 \end{cases} \tag{19}$$

so that if $\pi = R_0/\gamma$ then $\sigma^2_{Y,\beta}(0) = \sigma^2_{Y,\beta}(1)$. Setting $\pi = R_0/\gamma$, then straightforward calculations gives us that $\sigma^2_{Y,\beta}(\delta)$ is *not* independent of δ, hence $\sigma^2_{Y,\beta}(\delta)$ is *not* monotone for all choices of parameters. We also see that when $\pi \geq R_0/\gamma$ then $\sigma^2_{Y,\beta}(0) \geq \sigma^2_{Y,\beta}(1)$, and that when $\pi < R_0/\gamma$ then $\sigma^2_{Y,\beta}(0) < \sigma^2_{Y,\beta}(1)$. Note that if $\delta = 1$ then $\beta_1 = 0$, thus, susceptible type one individuals can never become infectious and $X_1(t)$ is a strictly *growing* process. This gives us that $X_1(t)$ does not have an endemic level and from (2) we see that the only stable point for $Y_1(t)$ is 0. Hence, $\sigma^2_{Y,\beta}(1)$ only describes the variation among infectious type two individuals. From (16) together with (17) and (18) we see that $\sigma^2_{Y,\beta}(\delta)$ depends on δ in a non-trivial way, that is, if we change δ in $0 \leq \delta \leq 1$ we can not tell whether $\sigma^2_{Y,\beta}(\delta)$ increases or decreases for arbitrary choices of R_0, γ, μ and π. In order to find the extreme points of $\sigma^2_{Y,\beta}(\delta)$ we equate the first derivative of $\sigma^2_{Y,\beta}(\delta)$ to 0, which immediately gives us that $\delta_0 = 0$ is a root, and if we calculate the second derivative of $\sigma^2_{Y,\beta}(\delta)$ in the point 0 we get

$$\frac{d^2}{d\delta^2}\sigma^2_{Y,\beta}(0) = n\frac{2}{(\mu\gamma)^2 R_0^3}\frac{2R_0 - \gamma}{2R_0 + \gamma}\frac{1-\pi}{\pi} \tag{20}$$

so that $\sigma^2_{Y,\beta}(0)$ is a local maximum if $0 < R_0 < \gamma/2$ and a local minimum if $R_0 > \gamma/2$. Note that for all practical purposes 0 will be a local maximum to

$\sigma^2_{Y,\beta}$, since typical values of R_0 and γ for diseases like measles are $R_0 \approx 10-15$ and $\gamma \approx 1800-3500$, see e.g. pp. 31 and 70 in [9]. The remaining three roots can be solved explicitly by using Cardano's formula, see e.g. pp. 65 in [12], and this is done in Appendix B. Using these roots together with the values of $\sigma^2_{Y,\beta}(\delta)$ in the end points of the interval $\delta \in [0,1]$ we can determine the functional form of $\sigma^2_{Y,\beta}(\delta)$.

2.2 Analysing $\sigma^2_{Y,\alpha}(\delta)$: the effect of difference in infectivity between the two types

If we instead set $\beta_1 = \beta_2 = 1$ and parametrize α_1 and α_2 analogously to (15), then $\sigma^2_{Y,\alpha}$ from (13) simplifies to

$$\sigma^2_{Y,\alpha}(\delta) = \frac{n}{\gamma} + \frac{n}{R_0}\frac{2R_0 + \gamma + \gamma\frac{1-\pi}{\pi}\delta^2}{2R_0+\gamma} \tag{21}$$

which increases monotonically as δ increases, such that

$$\sigma^2_{Y,\alpha}(\delta) = \begin{cases} \frac{n}{\gamma} + \frac{n}{R_0} & \text{if } \delta = 0 \\ \frac{n}{\gamma} + \frac{n}{R_0}\frac{2R_0+\frac{\gamma}{\pi}}{2R_0+\gamma} & \text{if } \delta = 1 \end{cases} \tag{22}$$

Worth noticing is that if we set $\delta = 1$, we have moved the *entire* infectious pressure to the type two individuals, and the only way that a susceptible individual may become infected is via an infectious type two individual. To see that this only corresponds to a shift in the infectious pressure, we can look at the endemic level from (4) which is unchanged.

2.3 The effect of type heterogeneities on τ_Q

Using the approximations $\sigma^2_{Y,\beta}(\delta)$ and $\sigma^2_{Y,\alpha}(\delta)$ from Eqs. (16) and (21) respectively, together with Proposition 1 gives us approximations $\tau_{Q,\beta}(\delta)$ and $\tau_{Q,\alpha}(\delta)$, the expected time to extinction when the epidemic process is started at quasi-stationarity as a function of the degree of heterogeneity in terms of susceptibility or infectivity. We will in the remainder of this exposition sometimes use the notation $\tau_{Q,\cdot}$ and $\sigma^2_{Y,\cdot}$ when we do not want to stress the effect of neither varying susceptibility nor infectivity.

From the definitions of μ_Y and $\sigma_{Y,\cdot}(\delta)$ we know that for large enough n the relation $\mu_Y > \sigma_{Y,\cdot}(\delta)$ holds for all δ, i.e. $\mu_Y/\sigma_{Y,\cdot}(\delta) > 1$ for all δ. If we

see to $q_{\bullet,1}$ from (10) we can write it as

$$q_{\bullet,1}(\delta) \approx \frac{1}{\sigma_{Y,\cdot}(\delta)} \frac{\varphi\left(\frac{1-\mu_Y}{\sigma_{Y,\cdot}(\delta)}\right)}{\Phi\left(\frac{\mu_Y-0.5}{\sigma_{Y,\cdot}(\delta)}\right)} \approx \frac{1}{\sigma_{Y,\cdot}(\delta)} \frac{\varphi\left(\frac{\mu_Y}{\sigma_{Y,\cdot}(\delta)}\right)}{\Phi\left(\frac{\mu_Y}{\sigma_{Y,\cdot}(\delta)}\right)} = \frac{1}{\mu_Y} \frac{\mu_Y}{\sigma_{Y,\cdot}(\delta)} \frac{\varphi\left(\frac{\mu_Y}{\sigma_{Y,\cdot}(\delta)}\right)}{\Phi\left(\frac{\mu_Y}{\sigma_{Y,\cdot}(\delta)}\right)} \tag{23}$$

$$= \frac{1}{\mu_Y} \frac{u\varphi(u)}{\Phi(u)} = \frac{1}{\mu_Y} g(u) > 0. \tag{24}$$

Differentiating $g(u)$ w.r.t. u and using that $\Phi'(u) = \varphi(u)$ and $\varphi'(u) = -u\varphi(u)$ we get that

$$g'(u) = \frac{g(u)}{u}(1 - u^2 - g(u)). \tag{25}$$

This together with that $g(u)/u > 0$ for all $u > 0$ gives us that $g'(u) < 0$ for $u \geq 1$, i.e. $g(u)$ decreases monotonically when $u \geq 1$. Thus for $u \geq 1$ all non monotonic behaviour of $q_{\bullet,1}$ is a result of the non monotonic behaviour of $\sigma_{Y,\cdot}(\delta)$. We will henceforth only consider this situation. Using the relation that $\mu_Y/\sigma_{Y,\cdot}(\delta) \geq 1$ we can get bounds on n for this to hold, and these bounds on n are needed in the next section when we compare our analytical results with simulations. If we see to $\sigma_{Y,\beta}(\delta)$ we know 1) that when $\pi \geq R_0/\gamma$ then $\sigma^2_{Y,\beta}(0) \geq \sigma^2_{Y,\beta}(1)$ and 2) that when $\pi < R_0/\gamma$ then $\sigma^2_{Y,\beta}(0) < \sigma^2_{Y,\beta}(1)$. If we start with 1) and assume that $\sigma_{Y,\beta}(0)$ is the largest value of $\sigma_{Y,\beta}(\delta)$ for $\delta \in [0, 1]$, we get that

$$\frac{\mu_Y}{\sigma_{Y,\beta}(\delta)} \geq \frac{\mu_Y}{\sigma_{Y,\beta}(0)} \geq 1 \tag{26}$$

$$\Rightarrow \frac{n}{\gamma} = \mu_Y \geq \sigma_{Y,\beta}(0) = \sqrt{\frac{n}{\gamma} + \frac{n}{R_0}} \tag{27}$$

which gives us the following lower bound on n

$$n_\beta \geq \gamma^2 \left(\frac{1}{\gamma} + \frac{1}{R_0}\right). \tag{28}$$

Likewise for 2) we get that

$$\frac{\mu_Y}{\sigma_{Y,\beta}(\delta)} \geq \frac{\mu_Y}{\sigma_{Y,\beta}(1)} \geq 1 \tag{29}$$

which gives us

$$\Rightarrow n_\beta \geq \gamma^2 \left(\frac{1}{\gamma\pi} + \frac{\pi}{R_0}\right). \tag{30}$$

Note that for almost all practical situations $\pi \geq R_0/\gamma$ will hold, since typical values of $R_0 \approx 10 - 15$ and $\gamma \approx 1800 - 3500$, see pp. 31 and 70 in [9].

In the same way we get a lower bound on n for $\sigma_{Y,\alpha}(\delta)$, which becomes

$$n_\alpha \geq \gamma^2 \left(\frac{1}{\gamma} + \frac{2R_0 + \frac{\gamma}{\pi}}{2R_0 + \gamma} \right). \tag{31}$$

Note that n_α is very sensitive to the choice of π.

Returning to the effect of type heterogeneities on $\tau_{Q,\cdot}(\delta)$, we have that if we are in the situation when $\mu_Y/\sigma_{Y,\cdot}(\delta) \geq 1$ holds for all $\delta \in [0,1]$, then an increase in $\sigma_{Y,\cdot}(\delta)$ leads to an increase in $q_{\bullet,1}(\delta)$ that, in turn, leads to a decrease in $\tau_{Q,\cdot}(\delta)$. Thus, we have a more formal statement supporting the heuristic arguments that was made when the coefficient of variation was introduced above.

To conclude, an increase of the difference in infectivity between the two types ought to decrease the expected time to extinction, where as it is a more complicated situation when the difference in susceptibility between the two types are changed, and non monotonic behaviour may occur.

3 Examples

In this section we compare the analytical approximations for $\tau_{Q,\cdot}(\delta)$ with simulations. We give some examples where we apart from varying δ, focus on varying π for different values of n when keeping R_0, μ and γ fix. When comparing the analytical approximations with simulations it is seen that they are not perfect, but that they capture the qualitative behaviour of the underlying epidemic.

All simulations have been performed using Monte Carlo simulation, and all the routines are written in the `C` programming language. The graphical presentation has been done using `Matlab`. The quasi-stationary behaviour of the epidemic has been approximated by simulating 1000 epidemics, and when the first 800 had gone extinct, we restarted the clock for the remaining 200 and kept them as our sample from the quasi-stationary distribution.

We have concentrated on the following parameter values: $R_0 = 10, \mu = 1$ (when $\mu = 1$ time is measured in units of life-lengths) and $\nu = 500$. The reason for choosing $\nu = 500$ instead of $\nu \approx 1800 - 3500$, which is typical for childhood diseases and which are the values we have been referring to in the previous sections, is of practical nature. That is, for the concept of quasi-stationarity to have any meaning, the expected time to extinction should be at least 5-10 years, which in turn corresponds to that we roughly have at least 10 infected individuals at the endemic level of infection, but when

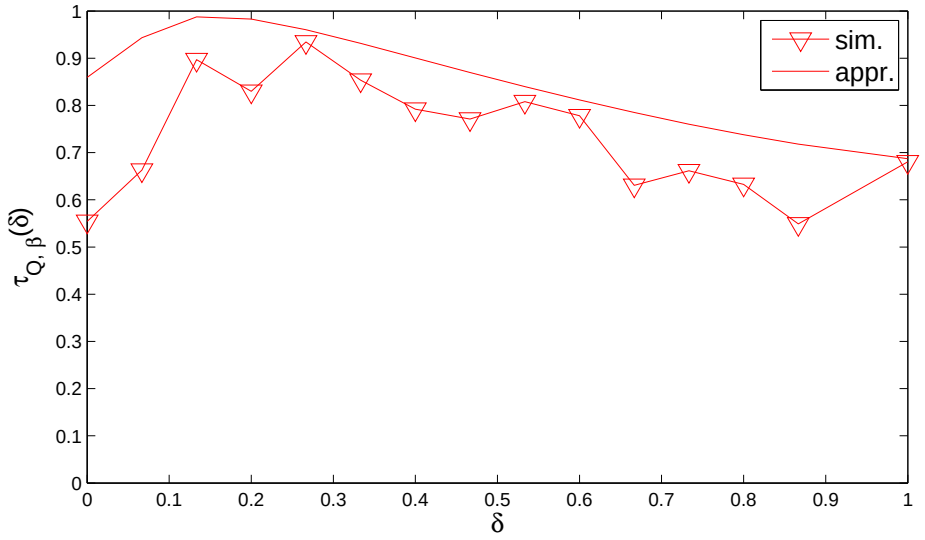

Figure 1: The expected time to extinction as a function of the difference in susceptibility between the two types ($\alpha_1 = \alpha_2 = 1$) when $R_0 = 10, \mu = 1, \nu = 500, n = 50,000$ and $\pi = 1/100$.

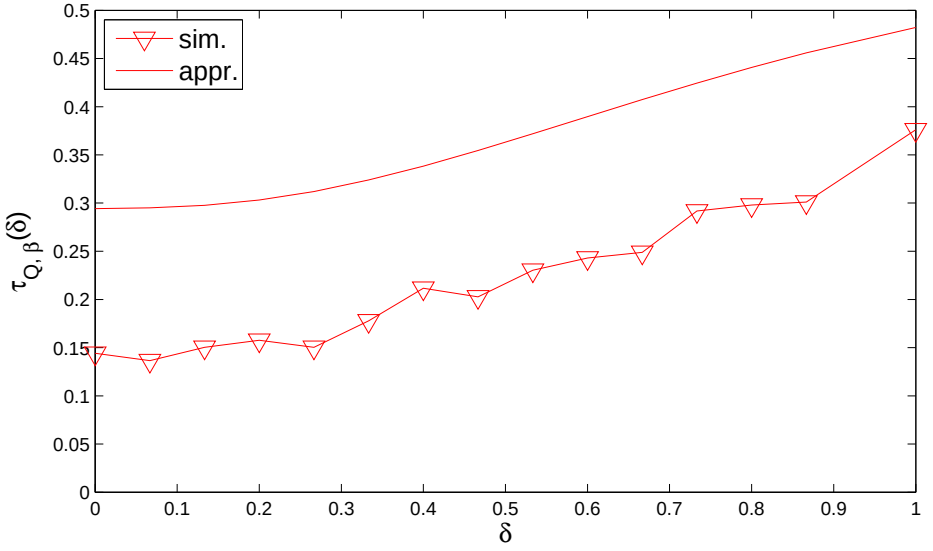

Figure 2: The expected time to extinction as a function of the difference in susceptibility between the two types ($\alpha_1 = \alpha_2 = 1$) when $R_0 = 10, \mu = 1, \nu = 500, n = 22,000$ and $\pi = 1/11$.

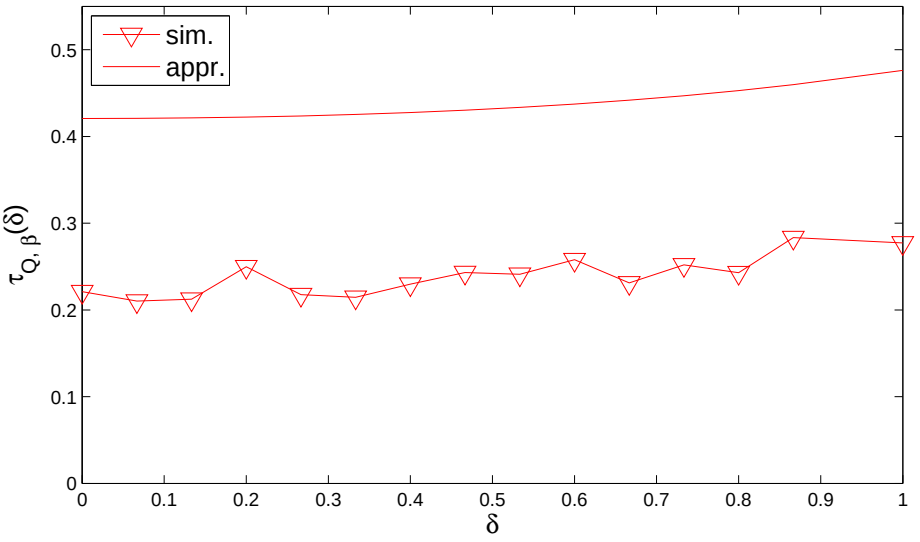

Figure 3: The expected time to extinction as a function of the difference in susceptibility between the two types ($\alpha_1 = \alpha_2 = 1$) when $R_0 = 10, \mu = 1, \nu = 500, n = 30,000$ and $\pi = 2/3$.

$\nu \approx 1800 - 3500$ we need to have a very large population or that $\pi \approx 1/2$, see Eq. (4), which is very time consuming to simulate. Thus, if we decrease ν we can still have a long expected time to extinction (the process is close to quasi-stationary) with a much smaller population, and the theory from the previous sections does not give any support to that $\nu = 500$ should not be regarded as an arbitrary parameter choice.

For the parameters chosen above $\tau_{Q,\beta}(\delta)$ gives a good description of the qualitative behaviour of the underlying epidemic already for small values of n (e.g. $n \approx n_\beta \approx 25,500$ where n_β is from (28)), see Figs. 1-4. From the previous section the analysis of $\sigma^2_{Y,\beta}(\delta)$ showed that it under certain conditions was not increasing/decreasing monotonically in δ which indicated a non monotonic behaviour of $\tau_{Q,\beta}(\delta)$. This behaviour can be seen from simulations, see e.g. Fig. 1, but note that $\pi = 1/100$ so it can not be regarded as a typical value of π. The behaviour of $\tau_{Q,\alpha}(\delta)$ is more sensitive to the choices of n, and it is especially important that n_2 is large. The reason for this is that the infectious pressure gets more and more shifted to the type two individuals as δ tends to α, so it becomes more and more important that the size of n_2 yields a sufficient number of infected type two individuals in order for the process to reach quasi-stationarity. Simulations indicate that if $n \approx n_\alpha$, where n_α is from (30), then $\tau_{Q,\alpha}(\delta)$ captures the qualitative

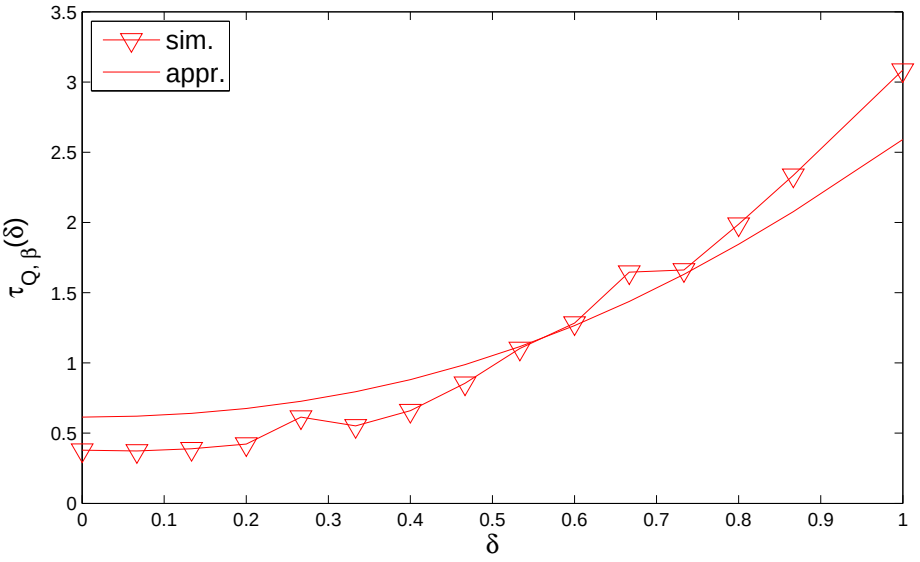

Figure 4: The expected time to extinction as a function of the difference in susceptibility between the two types ($\alpha_1 = \alpha_2 = 1$) when $R_0 = 10, \mu = 1, \nu = 500, n = 40,000$ and $\pi = 1/8$.

behaviour of the underlying population, but note that we need a much larger n, see Figs. 5.

To conclude, as long as $n \approx n_\alpha$, from (28) or (29), or $n \approx n_\beta$, from (30), depending on the situation, our approximations captures the qualitative behaviour of the epidemic.

4 Discussion

Bartlett's two-type epidemic model which has been analysed in the present paper is perhaps not the most realistic model, but we still believe that it captures some of the relevant behaviour which would appear in more complex models. A more realistic model which would be interesting to analyse in a two-type version is the so-called SIR model with demography which in its one-type version has been thoroughly analysed by Nåsell in [2]. A two-type version of this model is however much harder to analyse and obtain explicit expressions for. It would also be of interest to extend Bartlett's model to k types, which could be done using similar methodology as we have used in the present paper.

From a more general point it is always of interest to try and relax the

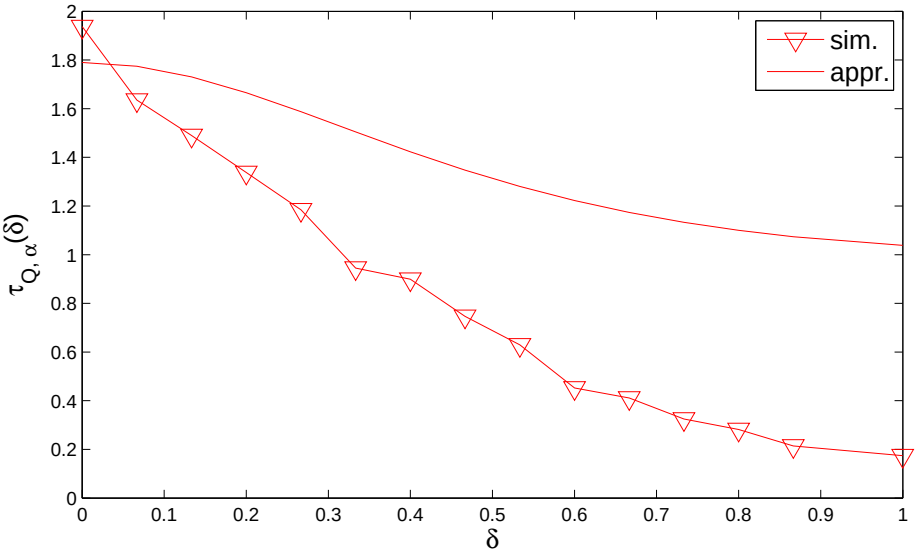

Figure 5: The expected time to extinction as a function of the difference in infectivity between the two types ($\beta_1 = \beta_2 = 1$) when $R_0 = 10, \mu = 1, \nu = 500, n = 75,000$ and $\pi = 1/3$.

assumption of exponentially distributed infectious periods, life-lengths and to include latency periods, see e.g. [3]. Another interesting extension could be to add some structure to the population, see e.g. [13] and [5], and it would also be of interest to analyse seasonal effects in a two-type setting, see e.g. [14] and [15].

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A Appendix

Here we derive the local drift and covariance matrices, $\mathbf{B}$ and $\mathbf{S}$ respectively, for $(\widetilde{\mathbf{X}}(t), \widetilde{\mathbf{X}}(t))$ from (7). To start, set $\widetilde{\mathbf{Z}}(t) = (\widetilde{X}_1(t), \widetilde{Y}_1(t), \widetilde{X}_2(t), \widetilde{Y}_2(t))^{\mathrm{T}}$ to simplify the notation, and let $\mathcal{F}_t$ denote the σ-algebra generated by the process $\widetilde{\mathbf{Z}}(t)$ up to time t. The infinitesimal first moment and covariance is

then defined as:

$$E_t\left[\Delta\widetilde{Z}_j\right] = \frac{1}{h}E\left[\widetilde{Z}_j(t+h) - \widetilde{Z}_j(t) \;\middle|\; \mathcal{F}_t\right] \tag{32}$$

and

$$Cov_t\left(\Delta\widetilde{Z}_i, \Delta\widetilde{Z}_j\right) = E_t\left[\Delta\widetilde{Z}_i\Delta\widetilde{Z}_j\right] - E_t\left[\Delta\widetilde{Z}_i\right]E_t\left[\Delta\widetilde{Z}_j\right] = E_t\left[\Delta\widetilde{Z}_i\Delta\widetilde{Z}_j\right] \tag{33}$$

where $i, j = 1, \ldots, 4$ and h is small. The matrices $\mathbf{B}$ and $\mathbf{S}$ are then defined as

$$\{\mathbf{B}\}_{ij} = \frac{\partial}{\partial\widetilde{Z}_j}E_t\left[\Delta\widetilde{Z}_i\right] \tag{34}$$

and

$$\{\mathbf{S}\}_{ij} = Cov_t\left(\Delta\widetilde{Z}_i, \Delta\widetilde{Z}_j\right) \tag{35}$$

where $i, j = 1, \ldots, 4$. For relief of notation we use the shorthand x_j and y_j for $x_j(t)$ and $y_j(t)$ respectively. For the two-type version of Bartlett's model treated here we get

$$\mathbf{B} = \begin{pmatrix} -\beta_1(\alpha_1 y_1 + \alpha_2 y_2) & -\beta_1\alpha_1 x_1 & 0 & -\beta_1\alpha_2 x_1 \\ \beta_1(\alpha_1 y_1 + \alpha_2 y_2) & \beta_1\alpha_1 x_1 - \mu\gamma & 0 & \beta_1\alpha_2 x_1 \\ 0 & -\beta_2\alpha_1 x_2 & -\beta_2(\alpha_1 y_1 + \alpha_2 y_2) & -\beta_2\alpha_2 x_2 \\ 0 & \beta_2\alpha_1 x_2 & \beta_2(\alpha_1 y_1 + \alpha_2 y_2) & \beta_2\alpha_2 x_2 - \mu\gamma \end{pmatrix} \tag{36}$$

and

$$\mathbf{S}_j = \begin{pmatrix} \mu\pi_j + \beta_j x_j(\alpha_1 y_1 + \alpha_2 y_2) & -\beta_j x_j(\alpha_1 y_1 + \alpha_2 y_2) \\ -\beta_j x_j(\alpha_1 y_1 + \alpha_2 y_2) & \beta_j x_j(\alpha_1 y_1 + \alpha_2 y_2) - \mu\gamma y_j \end{pmatrix},\ j = 1, 2 \tag{37}$$

such that

$$\mathbf{S} = \begin{pmatrix} \mathbf{S}_1 & \mathbf{0} \\ \mathbf{0} & \mathbf{S}_2 \end{pmatrix} \tag{38}$$

Evaluating these matrices at the endemic level yields

$$\widehat{\mathbf{B}} = \begin{pmatrix} -\frac{\alpha_\pi\beta_1}{\gamma} & -\frac{\alpha_1\pi_1\mu\gamma}{\alpha_\pi} & 0 & -\frac{\alpha_2\pi_1\mu\gamma}{\alpha_\pi} \\ \frac{\alpha_\pi\beta_1}{\gamma} & \mu\gamma\left(\frac{\alpha_1\pi_1}{\alpha_\pi} - 1\right) & 0 & \frac{\alpha_2\pi_1\mu\gamma}{\alpha_\pi} \\ 0 & -\frac{\alpha_1\pi_2\mu\gamma}{\alpha_\pi} & -\frac{\alpha_\pi\beta_2}{\gamma} & -\frac{\alpha_2\pi_2\mu\gamma}{\alpha_\pi} \\ 0 & \frac{\alpha_1\pi_2\mu\gamma}{\alpha_\pi} & \frac{\alpha_\pi\beta_2}{\gamma} & \mu\gamma\left(\frac{\alpha_2\pi_2}{\alpha_\pi} - 1\right) \end{pmatrix} \tag{39}$$

and

$$\widehat{\mathbf{S}} = \mu \begin{pmatrix} 2\pi_1 & -\pi_1 & 0 & 0 \\ -\pi_1 & 2\pi_1 & 0 & 0 \\ 0 & 0 & 2\pi_2 & -\pi_2 \\ 0 & 0 & -\pi_2 & 2\pi_2 \end{pmatrix} \tag{40}$$

with which we can find a solution $\widehat{\mathbf{\Sigma}} = \{\hat{\sigma}_{ij}\},\ i, j = 1, \ldots, 4$.

B Appendix

Here we derive the local min/max points of $\sigma^2_{Y,\beta}(\delta)$ from Section 2. The local extreme points are found by locating points δ_0 such that $\frac{d}{d\delta}\sigma^2_{Y,\beta}(\delta_0) = 0$. From (16) we have that $\sigma^2_{Y,\beta}(\delta)$ can be written on the following form:

$$\sigma^2_{Y,\beta}(\delta) \sim \frac{f(\delta)}{\mu\gamma R_0 f(\delta) + g(\delta)}, \tag{41}$$

where $f(\cdot)$ and $g(\cdot)$ are two polynomials of order two and three respectively defined as

$$\begin{aligned} f(\delta) &= R_0(\mu\gamma)^2(2R_0 + \gamma)\pi^2 + 3(R_0\mu\gamma)^2(1-2\pi)\pi\delta + (R_0\mu\gamma)^2(1-2\pi)^2\delta^2 && (42)\\ &= a_1 + a_2\delta + a_3\delta^2 && (43)\\ g(\delta) &= R_0^3(\mu\gamma)^4(\gamma - 2R_0)\pi(1-\pi)\delta^2 - (R_0\mu\gamma)^3(1-\pi)(1-2\pi)\delta^3 \\ &= a_4\delta^2 + a_5\delta^3 && (44) \end{aligned}$$

Equating the first derivative w.r.t. δ of $\sigma^2_{Y,\beta}(\delta)$ to 0 gives us

$$\begin{aligned} &\frac{d}{d\delta}\sigma^2_{Y,\beta}(\delta) = f'(\delta)g(\delta) - f(\delta)g'(\delta) = 0 && (45)\\ \Rightarrow &(a_2 + 2a_3\delta)(a_4\delta^2 + a_5\delta^3) - (a_1 + a_2\delta + a_3\delta^2)(2a_4\delta + 3a_5\delta^2) = 0 && (46) \end{aligned}$$

from which it follows that $\delta_0 = 0$ is a root. Continuing, we can simplify further which gives us

$$a_3a_5\delta^3 + 2a_2a_5\delta^2 + 2a_1a_4 = 0 \tag{47}$$

and in order to solve this polynomial of order three we use the substitution $\delta = x - a_2/3a_1 = x - b_0$. After some further simplifications we will get a new polynomial:

$$x^3 + b_1x + b_2 = 0 \tag{48}$$

where

$$b_1 = \frac{1}{a_1}\left(a_3 - \frac{a_2^2}{3a_1}\right) \tag{49}$$

$$b_2 = \frac{1}{a_1}\left(a_4 + \frac{2a_2^3}{27a_1^2} - \frac{a_2 a_3}{3a_1}\right) \tag{50}$$

Introduce D defined as

$$D = \left(\frac{b_1}{3}\right)^3 + \left(\frac{b_2}{2}\right)^2 \tag{51}$$

By using Cardano's formula, see e.g. pp. 65 in [12], we get that if $D > 0$ there exist one real root, if $D = 0$ there exist three real roots where at least two are equal, and if $D < 0$ there exist three distinct real roots, and the roots of (47) are given by

$$\delta_1 = \sqrt[3]{-\frac{b_2}{2} + \sqrt[2]{D}} + \sqrt[3]{-\frac{b_2}{2} - \sqrt[2]{D}} - b_0 \tag{52}$$

$$\delta_{2,3} = -\frac{\sqrt[3]{-\frac{b_2}{2} + \sqrt[2]{D}} + \sqrt[3]{-\frac{b_2}{2} - \sqrt[2]{D}}}{2} - b_0 \pm \frac{\sqrt[3]{-\frac{b_2}{2} + \sqrt[2]{D}} + \sqrt[3]{-\frac{b_2}{2} - \sqrt[2]{D}}}{2} i\sqrt{3} \tag{53}$$

References

[1] H. Andersson, T. Britton, Stochastic Epidemic Models and Their Statistical Analysis, Lecture Notes in Statistics 151, Springer-Verlag, New York, 2000.

[2] I. Nåsell, On the time to extinction in recurrent epidemics, Journal of the Royal Statistical Society Series B 61 Part 2 (1999) 309-330.

[3] H. Andersson, T. Britton, Stochastic epidemics in dynamic populations: quasi-stationarity and extinction, Journal of Mathematical Biology 41 (2000) 559-580.

[4] I. Nåsell, Stochastic models of some endemic infections, Mathematical Biosciences, 179 (2002) 1-19.

[5] T.J. Hagenaars, C.A. Donnelly, N.M. Ferguson, Spatial heterogeneity and the persistence of infectious diseases, Journal of Theoretical Biology, 229 (2004) 349-359.

[6] M.S. Bartlett, Deterministic and stochastic models for recurrent epidemics, in: J. Neyman, (Ed.), Proceedings of the third Berkeley symposium on mathematical statistics and probability vol IV, University of California Press, 1956, pp. 81-109.

[7] M.S. Bartlett, Stochastic Population Models in Ecology & Epidemiology, London, Methuen, 1960.

[8] D. Clancy, P.D. O'Neill, P.K. Pollett, Approximations for the Long-Term Behaviour of an Open-Population Epidemic Model, Methodology and Computing in Applied Probability, 3 (2001) 75-95.

[9] R.M. Anderson, R.M. May, Infectious Diseases of Humans - Dynamics and Control, Oxford University Press, 1991.

[10] S.N. Ethier, T.G. Kurtz, Markov processes - Characterization and Convergence, Wiley, New York, 1986.

[11] I. Karatzas, S.E. Shreve, Brownian Motion and Stochastic Calculus, 2 ed. , Graduate Texts in Mathematics 113, Springer-Verlag, New York, 1991.

[12] L. Råde, B. Westergren, Mathematics handbook for engineers and Science, 4 ed. , Studentlitteratur, Lund, 1998.

[13] J.S. Koopman, S.E. Chick, C.P. Simon, C.S. Riolo, G. Jacquez, Stochastic effects on endemic infection levels of disseminating versus local contacts, Mathematical Biosciences 180 (2002) 49-71.

[14] R. Kuske, L.F. Gordillo, P. Greenwood, Sustained oscillations via coherence resonance in SIR, Journal of Theoretical Biology (2006) doi:10.1016/j.jtbi.2006.10.029

[15] L. Stone, R. Olinky, A. Huppert, Seasonal dynamics of recurrent epidemics, Nature, 446 (2007) doi:10.1038/nature05638