State-Dependent Mixing and Sexually Transmitted Disease Dynamics

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Abstract

Non-proportionate mixing among the susceptible and infected class is incorporated into a single-group, SI/SIS model for the spread of a sexually transmitted disease in a single-sex population. State-dependent mixing can result in a wider array of dynamical behavior than proportionate mixing. Examples are given, using particular mixing solutions, of threshold phenomena and multiple stable endemic states.

I. Introduction

Typical models, for example Hethcote and Yorke (1984) and Anderson et al. (1986), for the spread of a sexually transmitted disease (STD) assume proportionate mixing among the susceptible and infected class. It is possible to conjecture situations where this assumption may fail. For instance, if there is some degree of "knowledge" concerning who is and who is not infected, then it is plausible to expect non-proportionate mixing among the epidemiological classes. This "knowledge" may be real or perceived and could come from a variety of sources (external evidence of infection, direct knowledge of infection, questioning of sexual partners about their previous behavior, observed patterns of social behavior, rumors that so-and-so has been doing such-and-such hanging around with you-know-who down here). Another possible justification for non-proportionate mixing between susceptibles and infecteds stems from the realization that infected individuals are infected for a "good" reason, namely, they have had a sexual contact with another infected individual. It is conceivable that subsequent contacts which these individuals engage in may again be with each other or with individuals whom they both know. Similarly, some, although clearly not all, of the susceptible individuals are so because their sexual contacts have been exclusively with other susceptible individuals. Of course, this may be handled through the use of models which explicitly follow the dynamics of pairs (Dietz, 1988; Dietz and Hadeler, 1988). Even then, however, it may be that the process of pair-formation does not occur at random with respect to infectious status.

We incorporate state-dependent mixing into a single-group, single-sex, SI/SIS
model for the spread of a sexually transmitted disease. The general representation of Busenberg and Castillo-Chavez (1991) for mixing among multiple groups is applied to the epidemiological classes within a single-group. Specific examples show that state-dependent mixing can result in a wider array of dynamical behavior than does proportionate mixing. In particular, threshold phenomena and multiple stable endemic states are possible. Our examples suggest several mechanisms for the generation of multiple endemic equilibria in an epidemic model. Finally, certain non-bilinear incidence rates which have been used in epidemic models can be recovered as particular cases of state-dependent mixing. This provides a stronger rationale for the use of such forms in epidemic models.

II. Description of the Epidemic Model

We consider the spread of a sexually transmitted disease in a single-sex population divided into two mutually exclusive epidemiological classes: susceptible and infected; the size of each at time $t$ we denote mnemonically by $S(t)$ and $I(t)$ respectively. Infected individuals are assumed to be infectious. Recruitment into the susceptible class occurs at a constant rate, $\Lambda \geq 0$, per unit time. There is no recruitment into the infected class. Let $\alpha_S(t)$ and $\alpha_I(t)$ be the average number of sexual contacts engaged in per unit time by susceptible and infected individuals respectively and define $p_{SI}(t)$ as the fraction of the susceptible classes sexual contacts which occur with individuals in the infected class. Define $\beta$ as the average probability of transmission of infection given that there is a sexual contact with an infected individual. Let $\mu$ and $\delta$ be the removal rates of susceptibles and infectives respectively. Finally, let $r$ be the rate at which infected individuals recover and return to the susceptible population. The parameters $\beta$, $\mu$, $\delta$, and $r$ are assumed to be constant and nonnegative. Using these definitions our model may be written as

\[
\frac{dS}{dt} = \Lambda - \alpha_S p_{SI} \beta S - \mu S + rI \tag{1}
\]

and

\[
\frac{dI}{dt} = \alpha_S p_{SI} \beta S - \delta I - rI. \tag{2}
\]

Letting $T(t) = S(t) + I(t)$, (1) and (2) may be equivalently written as

\[
\frac{dT}{dt} = \Lambda - \mu (T - I) - \delta I \tag{3}
\]

and

\[
\frac{dI}{dt} = \alpha_S p_{SI} \beta (T - I) - \delta I - rI. \tag{4}
\]
III. State-Dependent Mixing

The force of infection, defined as the average number of new infections per unit time, in a single-group model for the spread of a sexually transmitted disease in a single-sex population is generally written as

\[ B(t) = \alpha(t) \frac{I(t)}{S(t)+I(t)} \beta S(t). \]  

(5)

Here, each susceptible individual has an average of \( \alpha(t) \) sexual contacts per unit time and

\[ p_{SI}(t) = \frac{I(t)}{S(t)+I(t)} \]  

(6)

is the proportion of the population which is infected at time \( t \). We generalize this to allow for non-proportionate mixing among the susceptible and infected classes.

Recall the definition of \( p_{SI}(t) \) and let \( p_{SS}(t) \), \( p_{IS}(t) \), and \( p_{II}(t) \) be similarly defined. Hence, at time \( t \), there are \( \alpha_S(t)S(t) \) total sexual contacts per unit time involving a susceptible individual; \( p_{SS}(t) \) is the fraction which involve two susceptible individuals and \( p_{SI}(t) \) is the fraction which involve one susceptible and one infected individual. Similarly, at time \( t \), infected individuals engage in \( \alpha_I(t)I(t) \) total sexual contacts per unit time; \( p_{II}(t) \) is the fraction which involve two infected individuals and \( p_{IS}(t) \) is the fraction which involve one infected and one susceptible individual. Clearly the set

\[ P(t) = \{ p_{SS}(t), p_{SI}(t), p_{IS}(t), p_{II}(t) \} \]  

(7)

must satisfy

\[ 0 \leq p_{SS}(t), p_{SI}(t), p_{IS}(t), p_{II}(t) \leq 1 \]  

(i)

\[ p_{SS}(t) + p_{SI}(t) = 1 \quad \text{and} \quad p_{IS}(t) + p_{II}(t) = 1 \]  

(ii)

\[ \alpha_S(t)S(t)p_{SI}(t) = \alpha_I(t)I(t)p_{IS}(t) \]  

(iii)

and

\[ \alpha_S(t)S(t) = 0 \rightarrow p_{IS}(t) = 0 \quad \text{and} \quad \alpha_I(t)I(t) = 0 \rightarrow p_{SI}(t) = 0 \]  

(iv)
for all time $t$. The problem described by (i)-(iv) represents a new application of sexual mixing among two interacting groups in a single-sex population. Applying the results of Busenberg and Castillo-Chavez (1991), we may express $p_{SI}(t)$ in its general form as

$$p_{SI}(t) = \bar{p}_I(t) \left[ \frac{R_S(t)R_I(t)}{V(t)} + \phi_{SI}(t) \right].$$

(8)

Here,

$$\bar{p}_S(t) = \frac{\alpha_S(t)S(t)}{\alpha_S(t)S(t) + \alpha_I(t)I(t)},$$

(9)

$$\bar{p}_I(t) = \frac{\alpha_I(t)I(t)}{\alpha_S(t)S(t) + \alpha_I(t)I(t)},$$

(10)

$$R_S(t) = 1 - \bar{p}_S(t)\phi_{SS}(t) - \bar{p}_I(t)\phi_{SI}(t),$$

(11)

$$R_I(t) = 1 - \bar{p}_S\phi_{IS} - \bar{p}_I\phi_{II},$$

(12)

$$V(t) = \bar{p}_S(t)R_S(t) + \bar{p}_I(t)R_I(t),$$

(13)

and

$$\phi(t) = \begin{bmatrix} \phi_{SS}(t) & \phi_{SI}(t) \\ \phi_{IS}(t) & \phi_{II}(t) \end{bmatrix}$$

(14)

is symmetric, $\phi_{SI}(t) = \phi_{IS}(t)$. Blythe et al. (1991) gives a detailed discussion of the application and interpretation of this representation for mixing among multiple subgroups in a population.

We examine the role of state-dependent mixing on the dynamical behavior of (3) and (4) using some particular choices for $\phi(t)$ and assuming that

$$\alpha_S(t) = \alpha_I(t) = \alpha(t) = \alpha;$$

(15)

the contacts rates of susceptible and infected individuals are constant and not state-dependent. At equilibria (3) and (4) must satisfy
\[ \Lambda - \mu(\hat{T} - \hat{I}) - \delta \hat{I} = 0 \quad (16) \]

and

\[ \alpha \hat{P}_{SI} \beta(\hat{T} - \hat{I}) - (\delta + r)\hat{I} = 0. \quad (17) \]

For \( \hat{T} \neq 0 \) we may divide (16) and (17) by \( \hat{T} \) obtaining

\[ \frac{\Lambda}{\hat{T}} - \frac{\mu(\hat{T} - \hat{I})}{\hat{T}} - \frac{\delta \hat{I}}{\hat{T}} = 0 \quad (18) \]

and

\[ \frac{\alpha \beta \hat{P}_{SI}(\hat{T} - \hat{I})}{\hat{T}} - \frac{(\delta + r)\hat{I}}{\hat{T}} = 0. \quad (19) \]

Recall from (8) that

\[ \psi = \frac{R_{SI}}{V} + \phi_{SI} \quad (21) \]

and define

\[ \zeta = \frac{\hat{I}}{\hat{T}}. \quad (22) \]

Using these, (18) and (19) become

\[ \frac{\Lambda}{\hat{T}} - \mu(1 - \zeta) - \delta \zeta = 0 \quad (23) \]

and

\[ \alpha \beta \psi(1 - \zeta) - (\delta + r)\zeta = 0. \quad (24) \]

Solving (23) for \( \hat{T} \) we obtain

\[ \hat{T} = \frac{\Lambda}{\mu + (\delta - \mu)\zeta} \quad (25) \]

which is positive since \( \mu \) and \( \delta \) are positive and \( 0 \leq \zeta \leq 1. \) Now from (24) we obtain

\[ \zeta [ \alpha \beta \psi(1 - \zeta) - (\delta + r) ] = 0 \quad (26) \]

which has solutions

\[ \zeta = 0, \text{ (the disease-free state)}, \quad (27) \]

and
\( \alpha \beta \hat{\phi}(1 - \hat{c}) - (\delta + \tau) = 0 \) (the endemic states). \hfill (28)

Thus, the system (3) and (4) always has a disease-free equilibrium

\[
\hat{I} = \frac{A}{\mu} \hfill (29)
\]

and

\[
\hat{I} = 0 . \hfill (30)
\]

Furthermore, if \( \phi(t) \) is not explicitly time-dependent but depends on \( \bar{p}_S \) and \( \bar{p}_I \) only, then (28) becomes a function of \( \zeta \) and the solutions which lie in \((0,1)\) represent endemic equilibria. Defining

\[
F(\zeta) \equiv (1 - \zeta)\psi \hfill (31)
\]

and

\[
R_0^P = \frac{\alpha \beta}{\delta + \tau} , \hfill (32)
\]

the endemic equilibria are given by the intersection(s) in \( 0 < \zeta \leq 1 \) of \( F(\zeta) \) with the horizontal line \( 1/R_0^P \). Here, \( R_0^P \) is the basic reproductive number, interpreted as the expected number of new cases generated by a typical infectious individual in a completely susceptible population, for the epidemic with proportionate mixing. Clearly, if \( F(\zeta) \) is strictly monotone, there exists at most one endemic equilibrium. Also, if \( \psi \) is continuous, then \( F(\zeta) \) is continuous and has a maximum on \([0,1]\), say \( F_m(\zeta_m) \). Then for

\[
R_0^P > \frac{1}{F_m(\zeta_m)} \hfill (33)
\]

there will be no endemic equilibria. We now consider the local stability of the disease-free state and the behavior of \( F(\zeta) \) for some particular mixing solutions.

**Example 1:** If

\[
\text{DET } \phi(t) - \text{TR } \phi(t) - 2\phi_{SI}(t) = 0 \hfill (34)
\]

for all time \( t \), then

\[
\bar{p}_{SI} = \bar{p}_I = \frac{1}{\hat{I}} \hfill (35)
\]
and (3) and (4) becomes the classical single-group model for the spread of a sexually transmitted disease among two proportionately mixing epidemiological classes in a single-sex population. The disease-free state is locally asymptotically stable if $R_0^p \leq 1$ and is unstable if $R_0^p > 1$. $F(\zeta)$ is monotone decreasing. There is no endemic equilibrium when $R_0^p \leq 1$ and for $R_0^p > 1$ there is a unique endemic state. This model has been widely studied and for $R_0^p \leq 1$ the disease-free state is globally asymptotically stable; for $R_0^p > 1$ the disease-free state is unstable and a unique endemic equilibrium is persistent (Simon and Jacquez, 1991). We reiterate these results as a point of reference for our subsequent examples.

**Example 2:** Let $\phi_{SS}$, $\phi_{SP}$, $\phi_{IS}$, and $\phi_{II}$ each be constants in $[0,1]$. This is a sufficient, although not necessary, condition for (8) to satisfy the axioms (i)-(iv). For $\phi_{SS} \neq 1$, the conditions for local stability of the disease-free state are the same as for proportionate mixing. For $\phi_{SS} = 1$, the disease-free state is locally asymptotically stable if

$$Q_o = \frac{\alpha \beta}{\gamma + \gamma} \left( \frac{\phi_{SI} + 1}{2} \right) = R_0^p \left( \frac{\phi_{SI} + 1}{2} \right) \leq 1$$

and is unstable if $Q_o > 1$. In either case, $F(\zeta)$ is monotone decreasing. For $\phi_{SS} \neq 1$, there is a unique endemic equilibrium when $R_0^p > 1$ and no endemic state for $R_0^p \leq 1$. For $\phi_{SS} = 1$, there is a unique endemic state when $Q_o > 1$ and there are no endemic equilibria when $Q_o \leq 1$.

**Example 3:** Let

$$\phi = \begin{bmatrix} 0 & b \\ b & 0 \end{bmatrix},$$

where $b$ is a constant in $[-2,2]$. This choice of $\phi$ gives a one-parameter family of mixing solutions which satisfies axioms (i)-(iv). The condition for local stability of the disease-free state is the same as for proportionate mixing, however,

$$F(\zeta) = (1 - \zeta) \left[ \frac{(1 - b) + b^2(1 - \zeta)\zeta}{1 - 2b(1 - \zeta)\zeta} + b \right]$$

is not monotone for $b < -1$ or $b > 2$. For $R_0^p > 1$, there may be either 1 or 3 endemic equilibria. Two examples of $F(\zeta)$ and the corresponding phase plot for the model, with $R_0^p$ appropriately chosen to lie within the region where multiple endemic equilibria
exist, are illustrated in Figure 1. In both cases, there is a stable endemic state at a low level of infection and another stable endemic state at a high level of infection. The intermediate endemic equilibrium is unstable and serves as a threshold level of infection between the two stable equilibria. The solution curves lie sufficiently close to one another so that a change in the level of infection in the population (say by an influx or efflux of infected individuals) could result in a dramatic change in the endemic level of infection in the population.

Example 4: Preferred mixing (Nold, 1980; Hethcote and Yorke, 1984; Jacquez et al., 1988) can be represented by taking

$$\phi = \begin{bmatrix} \frac{a}{P_S} & 0 \\ 0 & \frac{b}{P_I} \end{bmatrix}, \quad (39)$$

where a and b are constants in [0,1]. The interpretation of this solution is that susceptible individuals always reserve a fixed fraction a of their sexual contacts for other susceptible individuals and infected individuals reserve of fixed fraction b of their sexual contacts for other infected individuals. Each class's remaining sexual contacts are distributed among susceptible and infected individuals at random. The disease-free state is locally asymptotically stable for

$$Q_0 = \frac{\alpha \beta}{\delta + \gamma} (1 - b) \leq 1 \quad (40)$$

and is unstable for $$Q_0 > 1$$. F(\(\zeta\)) is monotone decreasing, hence, for $$Q_0 > 1$$ there is a unique endemic equilibrium.

Example 5: Consider

$$\phi = \begin{bmatrix} 1 & 2a-1 \\ 2a-1 & 1 \end{bmatrix}; \quad (41)$$

then

$$P = \begin{bmatrix} P_{SS} & P_{SI} \\ P_{IS} & P_{II} \end{bmatrix} = \begin{bmatrix} 1-aP_I aP_S \\ aP_S 1-aP_S \end{bmatrix} \quad (42)$$
is a valid mixing solution for

\[ 0 \leq a \leq \min\{ \frac{1}{p_S}, \frac{1}{p_I} \}. \]  \hspace{1cm} (43)

The force of infection is then given by

\[ B = \alpha \beta S a \frac{p_I}{T} = \alpha \beta S a \left( \frac{1}{T} \right). \]  \hspace{1cm} (44)

If \( a \) is a constant in \([0,1]\) then this example reduces to a special case of preferred mixing where susceptibles and infecteds both reserve the same fraction for intraclass interactions. A more interesting case of (44) is to set

\[ a \equiv (\frac{p_I}{T})^b \]  \hspace{1cm} (45)

where \( b \geq 0 \).

Then the force of infection becomes

\[ B = \alpha \beta S \left( \frac{1}{T} \right)^{1+b}. \]  \hspace{1cm} (46)

In this case, the disease-free state is always locally asymptotically stable. Here,

\[ F(\zeta) = (1 - \zeta)\zeta^b \]  \hspace{1cm} (47)

which is clearly not monotone for \( b > 0 \). For \( R_0^P \) satisfying (33), there are two endemic equilibria, a low infection state and a high infection state. Numerical simulation of the model suggests that the low infection state is an unstable threshold between the disease-free state and the stable high infection state. An example is shown in Figure 2.

IV. Discussion

Traditional models for the spread of a sexually transmitted disease in a single-group, single-sex population assume proportionate mixing among the epidemiological classes (REFS). The dynamical behavior of such models is typically robust; the disease-free state loses stability as a critical parameter combination (usually the basic reproductive number) exceeds unity giving rise to a unique, stable, endemic equilibrium. We have applied the mixing representation developed by Busenberg and Castillo-Chavez (1991) to the epidemiological classes, susceptible and infected, in a
single-group, single-sex, SI/SIS model for the spread of a sexually transmitted disease. This allows us to introduce non-proportionate mixing among the susceptible and infected classes. Several examples of particular mixing solutions are used to show that state-dependent mixing can result in a “richer” dynamical behavior than does proportionate mixing.

With the exception of example 5, the behavior of the disease-free state is typical, an exchange of stability giving rise to an endemic equilibrium as a particular parameter combination exceeds unity. Some of our examples show that this condition may be less stringent than it is in the proportionate mixing model. For instance, if $R_b^0 = 2$, the disease-free state is unstable for proportionate mixing but is locally stable for preferred mixing with $b < 1/2$. An extreme case occurs in example 5 where the disease-free state is identically stable.

Examples 1, 2, and 4 are all “typical” with respect to the endemic equilibrium as well, a unique endemic state exists when the disease-free state is unstable. More interestingly, examples 3 and 5 show that state-dependent mixing may result in more complex dynamical behavior for the model, namely, multiple endemic equilibria and threshold phenomena. In example 3, as $R_b^0$ increases through one the disease-free state loses stability and gives rise to a unique endemic equilibrium. As $R_b^0$ continues to increase three endemic states are possible. Numerical simulations of the model in this region suggest that the low and high infection states are stable and that the medium infection state serves as a threshold between them. As $R_b^0$ increases further the low and medium infection level endemic states disappear and there is again a unique endemic equilibrium at a high level of infection. In example 5, the disease-free state is always stable and for $R_b^0$ large enough we enter a region of two endemic equilibria. Numerical simulations here suggest that the lower infection level state is an unstable threshold between the stable disease-free state and the stable high infection equilibrium. We have constructed a single example which exhibits the same range of dynamical behaviors as is contained in examples 3 and 5. Choosing

$$\psi = \frac{44x^2}{33} - \frac{13x}{33} + \frac{1}{22}$$  \(48\)

we obtain $F(\zeta)$ as depicted in Figure 3. Numerical simulations of this example for various choices of $R_b^0$ are shown in Figure 4. As $R_b^0$ increases the behavior changes initially from a stable disease-free equilibrium only to a region where the disease-free state is still stable and there are two endemic equilibria, a low level threshold and a stable high level endemic state as in example 5. Further increasing $R_b^0$ the disease-free
state becomes unstable and gives rise to a stable low level endemic state. Finally, as $R_0^P$ continues to increase we return to a region with only the high level endemic equilibrium in existence.

Since our main point in this paper has been to introduce state-dependent mixing into the model and to examine the possibilities for non-traditional dynamical behaviors we have made no attempt to rationalize the particular mixing solutions which we have used for our examples. Given the difficulty in obtaining data for sexual interactions among multiple subgroups in a population (REFS) it seems reasonable to expect that data on mixing patterns between susceptible and infected individuals will also be difficult to obtain. Furthermore, although there has been some exciting work on procedures for estimating the mixing parameters from survey data (Blythe et al. 1991; Rubin et al. 1991), these techniques are as yet not sufficiently developed to the point where they may be practically employed. We are, however, working on the specification of particular mixing solutions which are generated from some simple rule based mechanism for behavior in the population. One such idea is to assume that all individuals are aware of their infection status and that susceptible individuals always ask their potential partners about their status of infection. We then suppose that infected individuals are truthful a certain percentage of the time and try to develop the particular mixing solution corresponding with this behavior.

Another idea which we have hinted at but not explored in this paper is the notion that sexual contact rates may be state-dependent as well, $\alpha_S$ may not be equal to $\alpha_I$. One case which we have begun to examine assumes that $\alpha_S S + \alpha_I I = \alpha T$ for all time $t$ and that $\alpha_I I = F(I,T)\alpha T$, the average per capita contact rate of the population is $\alpha$ and F(I,T) is the fraction of the total contacts which involve an infected individual given that there are I infected individuals in a population of size T. Clearly, $F(0,T) = 0$, $F(T,T) = 1$, and $0 \leq F(I,T) \leq 1$. If we now assume proportionate mixing among the epidemiological classes, the force of infection becomes

$$B = \alpha\beta T (1 - F) F . \quad (49)$$

Assuming that $F_T = 0$ at the disease-free state and that $F_I$ evaluated at the disease-free state is finite and positive, the condition for stability of the disease-free state becomes

$$Q_0 = R_0^P \frac{A}{\mu} F_I(0) \leq 1 . \quad (50)$$

We are currently investigating plausible forms for $F(I,T)$ and their effects on the
dynamical behavior of our model with and without the assumption of proportionate mixing.

The majority of epidemic models exhibit "classical" dynamics, a transcritical bifurcation of the disease-free state giving rise to a unique endemic equilibrium. It is generally recognized that in certain situations and for certain diseases such models may not always be applicable. Broadly speaking, there have been two approaches to extending these models, the introduction of multi-group models to explicitly exploit particular aspects of population heterogeneity and the introduction of more general incidence terms in single-group models. Castillo-Chavez et al. (1989b) and Lin (1991) give examples of multiple endemic equilibria in a multi-group epidemic model for the spread of AIDS with proportionate mixing among the groups and asymmetric transmission probabilities. Our model may also be interpreted as a proportionate mixing model with a frequency-dependent transmission probability given by $\beta\psi(\zeta)$. Castillo-Chavez et al. (1989a) consider a single-group model for the spread of AIDS where the number of contacts per individual per unit time is a nondecreasing function of the total population size, $\alpha = \alpha(T)$, and the per capita contact rate $\alpha(T)/T$ is nonincreasing. This model exhibits classical dynamical behavior. Our state-dependent-mixing model can be interpreted as proportionate mixing with a frequency-dependent contact rate $\alpha = \alpha(\zeta)$. Thus, when the contact rate depends on the level of infection in the population, $I/T$, non-classical dynamics are possible. Liu et al. (1986, 1987) have illustrated a wide range of dynamical behaviors in epidemic models with where the incidence rate is of the form $\lambda(1-\zeta)^p\zeta^q$ where $p$, $q$ are positive. They discuss several plausible mechanisms underlying the assumption of a nonbilinear incidence rate. We may recover this particular form for the incidence using (39) and taking

$$a = b = 1 - \frac{1}{T} (\bar{\beta}_S)^{p-1} (\bar{\beta}_T)^{q-1}$$

which is a particular example of state-dependent mixing.

Clearly, the form of the incidence rate plays a critical role in governing the dynamical behavior of epidemiological models. State-dependent mixing is a means of introducing a fairly general nonlinear incidence rate which is subject to an interpretable set of axioms. Such formulations can result in nonclassical dynamics and may provide an additional rationale for the study and interpretation of certain nonlinear incidence rates which have been used in epidemic models.
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References


Figure Captions

Figure 1: State-dependent mixing can result in multiple stable endemic equilibria. In (a) and (b) we plot $F(\zeta)$ given by (38) in the text with $b = -1.9$ and $b = 1.9$ respectively; the intersection(s) of $F(\zeta)$ with the horizontal line $1/R_0^P$ where $R_0^P$ is given by (32) represent endemic equilibria of the model. Corresponding phase plots for case (a) and (b) above, with $R_0^P = 25$ ($\alpha = 5, \beta = 0.5, \delta = 0.1, r = 0$) and $R_0^P = 1.1$ ($\alpha = 5, \beta = 0.5, \delta = 0.1, r = 2.1727273$) respectively, are given in (c) and (d). From an initial population size of 20,000 the trajectories approach one of two endemic equilibria depending on the initial level of infection in the population.

Figure 2: State-dependent mixing can result in threshold behavior. In (a) we plot $F(\zeta)$ given by (47) in the text; the intersection(s) of $F(\zeta)$ with the horizontal line $1/R_0^P$ where $R_0^P$ is given by (32) represent endemic equilibria of the model. The corresponding phase plot for $b = 0.5$ and $R_0^P = 4$ ($\alpha = 5, \beta = 0.5, \delta = 0.1, r = 0.7333$) is given in (b). From an initial population size of 20,000 the trajectories approach either the disease-free state or the endemic equilibrium depending on the initial level of infection in the population.

Figure 3: An single example with both multiple stable endemic equilibria and threshold behavior. In (a) we plot $F(\zeta)$ with $\varphi(\zeta)$ given by (48) in the text; the intersection(s) of $F(\zeta)$ with the horizontal line $1/R_0^P$ where $R_0^P$ is given by (32) represent endemic equilibria of the model. Corresponding phase plots with $R_0^P = 100$ ($\alpha = 20, \beta = 0.5, \delta = 0.1, r = 0$), 50 ($\alpha = 10, \beta = 0.5, \delta = 0.1, r = 0$), and 10 ($\alpha = 2, \beta = 0.5, \delta = 0.1, r = 0$) are shown in (b), (c), and (d) respectively.
Figure 1a
Figure 1b
Figure 1c
Figure 1d
Figure 2a.

The diagram shows plots for different values of $b$:

- $b = 0.5$
- $b = 1.0$
- $b = 1.5$

Vertical axis: $F(t)$
Horizontal axis: $t$
Figure 2b

PHASE PLOT

Even Components $\rightarrow$

I(t)

Odd Components $\rightarrow$

T(t)
Figure 3a
Figure 3b
Figure 3c
Figure 3d
Notes and Unfinished Suggestions

1. General conditions for stability of the disease-free state: the various partial derivatives of (3) and (4) are given by

\[ T_T = -\mu \]
\[ T_I = \mu - \delta \]
\[ I_T = \alpha \beta \frac{I}{T}[\psi + (T - 1)\psi_T] + \psi(T - 1)(-\alpha \beta \frac{I}{T^2}) \]
\[ I_I = \alpha \beta \frac{I}{T}[\psi + (T - 1)\psi_T] + \psi(T - 1)\frac{\alpha \beta}{T} - (\delta + r) \]

Evaluating at the disease-free state these become

\[ T_T = -\mu \]
\[ T_I = \mu - \delta \]
\[ I_T = \alpha \beta \frac{I}{T}(T - 1)\psi_T \]
\[ I_I = \alpha \beta \frac{I}{T}(T - 1)\psi_T + \psi(T - 1)\frac{\alpha \beta}{T} - (\delta + r) \]

Hence, assuming that \( \psi_T \) and \( \psi_I \) evaluated at the disease-free state are finite the condition for stability of the disease-free state becomes

\[ \frac{\alpha \beta}{\delta + r} \psi(0) \leq 1 \]

where \( \psi(0) \) is the value of \( \psi \) at the disease-free state.

2. Is \( Q_0 \) equivalent to the basic reproductive number for the model?

3. If we assume that \( \delta = \mu \), (i.e. there is no disease-induced mortality), then (3) and (4) reduce to

\[ \frac{dT}{dt} = \Lambda - \mu T \]
\[ \frac{dI}{dt} = \alpha_S \beta p_{SI}(T - I) - (\mu + r)I \]

which can be reduced to a single equation in I. In particular, at equilibrium \( T = \lambda/\mu \) and the theory of limiting equations may become useful.

4. Could try to apply the Bendixon-DuLac Criterion to (3) and (4) and show that there are no closed trajectories. It would be nice to show this in general (or to determine sufficient conditions on \( \psi \) to assure this), otherwise, this could be attempted for each of the individual examples we have used. What is the right function to multiply the right hand side of the derivative by?

5. Is there any value in extending the model to cover the SIR case where R is recovered and immune?

6. Necessary conditions for the existence of multiple endemic equilibria: recall that

\[ F(\zeta) = (1 - \zeta)\psi \]

Then

\[ \frac{dF}{d\zeta} = (1 - \zeta)\psi - \psi. \]

If \( \psi_\zeta \) is identically negative the \( F_\zeta \) is always negative and \( F(\zeta) \) will be monotone decreasing and hence there will be at most a unique endemic equilibrium. For multiple endemic states to exist it is necessary that \( \psi_\zeta \) be positive for some interval of \( \zeta \). This implies that \( \psi \) must increase over some range of values of \( \zeta \). In other words, for multiple endemic states to exist the mixing among susceptible and infected individuals (or alternatively the transmission probability \( \beta \psi \) or the average contact rate \( \alpha \psi \)) must become less assortative (increase) as the level of infection increases.

7. Possible "forms" for \( F(\zeta) \). Since \( \psi(1) \) is finite we always have \( F(1) = 0 \). Thus, \( F(\zeta) \) can only take certain general forms. For instance, \( F(\zeta) \) cannot be constant (unless it is identically equal to zero which is a very boring case) and it cannot be monotone increasing. \( F(\zeta) \) may be monotone decreasing (it does not need to be strictly decreasing however). If \( F(\zeta) \) has a single interior critical point then it must be a maximum. If \( F(\zeta) \)
has two interior critical points then the first must be a local minimum and the second a local maximum. Thus, it may be possible to outline the possible dynamical behavior of the model by obtaining bounds on $F(\zeta)$, (from the bounds on $\psi$), and then constructing diagrams of the possible shapes of $F(\zeta)$ within those bounds.

  - Brauer (1990)
  - Pugliese (1990)

Comparison with two strain models: Pimentel (Am. Nat.), Nitechi and Levin (1986) Myxamatosis

State-dependent mixing may be applicable as a rationale for the introduction of a nonbilinear incidence rate in an epidemic model (first attributable to Ross?) ... applications to general epidemic modelling (removal of homogeneous mixing assumption)? and to vector transmitted disease models?