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Backwards bifurcations and catastrophe in simple models of fatal diseases

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1 Introduction

In a wide variety of simple disease models, the rate of change in the number of infected people can be written as

$$\dot{I} = \beta \frac{SI}{T} - mI = \left(\beta \frac{S}{T} - m \right) I \,, \tag{1}$$

where I is the number of infected people, S is the number of susceptible people, T is the total number of people in the population, β is the transmission rate of the disease, and m is the rate at which individuals leave the infected group. Here $\dot{I}$ means the derivative of I with respect to time, a convention we will use throughout the paper.

Equation (1) is applicable to a wide variety of one-group models. Following Castillo-Chavez et al. [3], we allow β to be a function of T, allowing a variety of assumptions about mixing. Depending on the type of model, the per-capita removal rate, m, may include the rate of "background" mortality or disease-induced mortality, or transitions to immune, susceptible or quarantined compartments.

Note that the number of infectives will increase when $S/T > m/\beta$ and decrease otherwise. The ratio S/T gives the proportion of susceptibles in a population, and hence the probability that a given contact of infectious individual is with a susceptible individual, under the assumption of homogeneous mixing. This ratio is at a maximum (generally 1) in a population where the disease is absent, and decreases as the disease begins to invade a population. It is this phenomenon of the disease reducing its own

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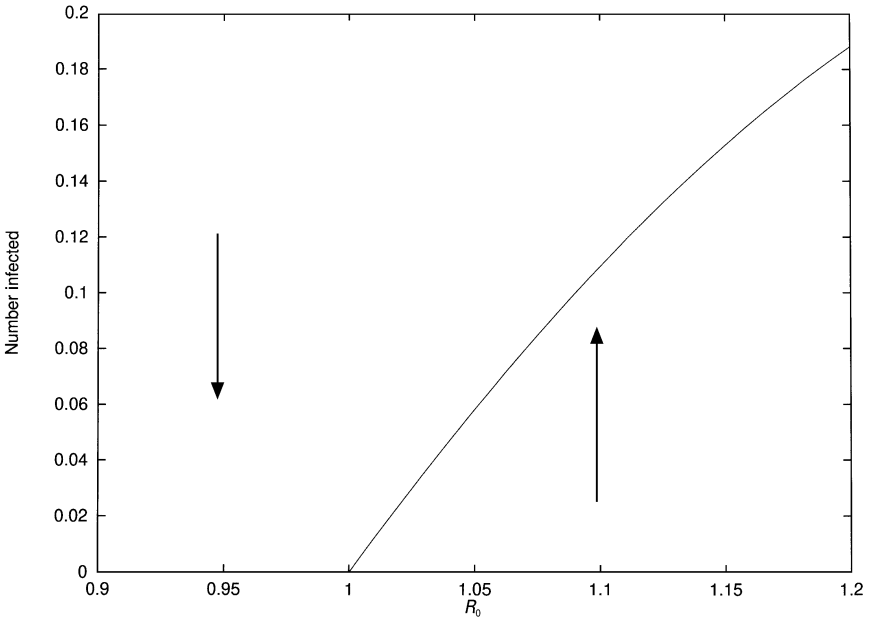

Fig. 1. A forward bifurcation. The curve shows the non-trivial bifurcating equilibrium. The arrows show the direction of flow for the model disease system, after the system reaches the manifold on which slow dynamics occur

reproductive rate by depleting the pool of susceptibles that leads to the ubiquity of the pattern shown in Fig. 1 in simple disease models.

Figure 1 shows a bifurcation diagram for a simple disease model. The x-axis shows R_0, the average number of new infections produced by an infectious individual near the disease-free equilibrium. In (1), if everyone is susceptible at the disease-free equilibrium, R_0 would be β/m. For a given set of parameters, R_0 remains fixed, and the change in the number of infectives is shown by the diagram – in this case when $R_0 < 1$, the number of infectives decreases to zero, while when $R_0 > 1$, the number of infectives will increase or decrease to the curved line that marks the endemic equilibrium.

We will call the type of bifurcation shown in Fig. 1 a "forward bifurcation," with respect to R_0. Characteristics of forward bifurcations include:

1. the absence of positive equilibria near the disease-free equilibrium when $R_0 < 1$ (for simple models, the disease-free equilibrium is often the only equilibrium for $R_0 < 1$); and
2. a low level of endemicity when R_0 is slightly above 1.

This pattern was perhaps first noted by Kermack and McKendrick [14], and can be observed in SI and SIR models which include recruitment and deaths, and in SIS and SIRS models with or without recruitment and deaths (see *e.g.*, [12, 15]).

The forward bifurcation is also commonly found in multi-group models. In many multi-group models, the equation for the number of infectives in group i can be written:

$$\dot{I}_i = \beta \frac{S_i}{T_i} \Lambda_i - m_i I_i \tag{2}$$

Here Λ_i is the "force of infection" as seen by members of group i. Since I_i and Λ_i tend to increase together, a decrease in the proportion of susceptibles will tend to retard disease spread, just as in the one-group case. This leads to forward bifurcations in many cases.

Lajmanovich and Yorke [15] showed that in simple multi-group SIS models with constant population the disease-free equilibrium is globally stable when $R_0 < 1$, and there is a unique, globally stable endemic equilibrium when $R_0 > 1$. In other words, these simple models are completely characterized by a forward bifurcation. Simon and Jacquez [17] extended this work to show similar behavior for a class of models, inspired by HIV/AIDS, which allowed for multiple stages of infection. These models allowed for variation among groups in transmission of the disease, but not in susceptibility to the disease or in rates of progression of the disease.

Some multi-group models, however, exhibit more complicated behaviors, including "backwards bifurcations." In general, when $R_0 = 1$, another equilibrium bifurcates from the disease-free equilibrium. In a forward bifurcation, this bifurcating equilibrium is biologically meaningful (that is, positive) when $R_0 > 1$, and is stable. In a backwards bifurcation, the bifurcating equilibrium is biologically meaningful when $R_0 < 1$, and is unstable (see Fig. 2). As shown in Fig. 2, a backwards bifurcation often implies parameter values for which the disease-free equilibrium and some endemic equilibrium may both be locally stable.

Hadeler and Castillo-Chavez [11] have demonstrated the existence of backward bifurcations in models that include behavioral responses to perceived disease risk. In a particularly striking result, Castillo-Chavez et al. [4, 2, 13] found backwards bifurcations in a multi-group model similar to that of [17], also inspired by HIV/AIDS, including disease-induced mortality and asymmetric transmission.

The possible presence of backwards bifurcations in simple disease models has important qualitative implications. Backwards bifurcations allow multiple stable states with fixed parameters. Further, small changes in parameters can produce large changes in equilibrium behavior. Imagine a population in which the disease is absent and R_0 is changing slowly. In a forward bifurcation, when R_0 first crosses one, the disease can invade to a very low endemic level. If R_0 drops below 1 again, the disease will disappear from the population (see Fig. 1). On the other hand, in a backward bifurcation, once R_0 crosses 1, the disease can invade to a relatively high endemic level. Further, decreasing R_0 to its former level will not necessarily make the disease disappear.

If we conceive of the parameters that underlie R_0 as changing slowly compared to the dynamics of the disease, backwards bifurcations allow the

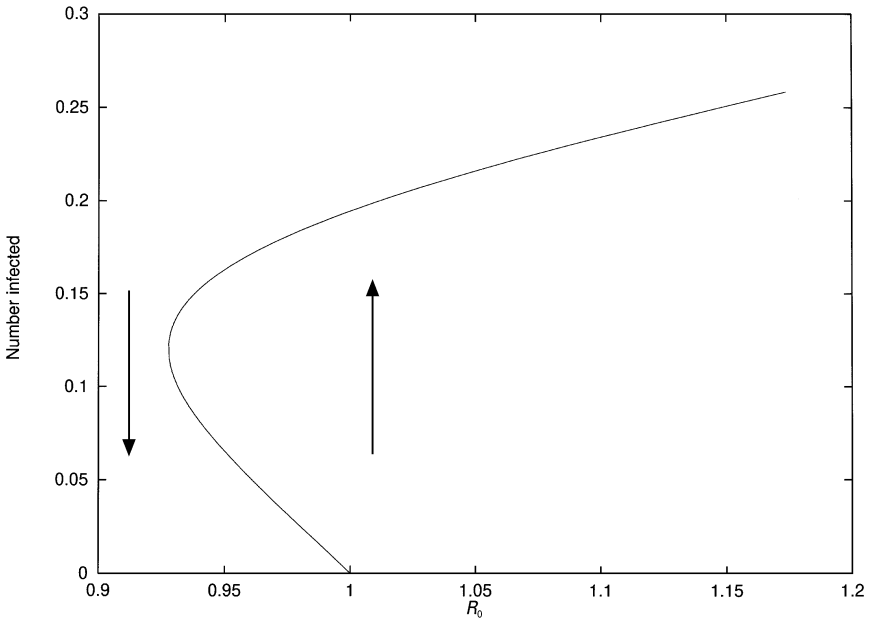

Fig. 2. A forward bifurcation. The curve shows the non-trivial bifurcating equilibrium. The arrows show the direction of flow for the model disease system, after the system reaches the manifold on which slow dynamics occur. Note that the upper branch of (stable) equilibria need not exist in all disease systems with backwards bifurcations. This picture represents the simplest possibility for global behavior with a backwards bifurcation, but not the only possibility (see text)

possibility of slow change punctuated by much more rapid changes when the disease-free equilibrium becomes unstable or when the endemic equilibrium ceases to exist. This sort of behavior is known as "catastrophe" and was first introduced in ecology by Ludwig et al. [16] in a paper discussing outbreaks of the spruce budworm.

It is important to note that Fig. 2 represents only one possibility for the global bifurcation diagram in the case of a backward bifurcation – the simplest one. The backwards bifurcation implies non-local behavior, and therefore a non-local attractor, for R_0 slightly above 1. Although we cannot prove that this picture always holds for our model, this is the picture we have found for specific parameter values leading to a backwards bifurcation. This is also the picture found by [11] and [7] in other disease models which can give rise to backwards bifurcations.

This paper attempts to provide a general framework for the mechanisms behind backwards bifurcations in simple disease models. We discuss the biological interpretation of the features of the model that produce these bifurcations. We also simplify and discuss the criterion developed by Huang et al. [13] for establishing the sign of a bifurcation.

2 A practical criterion for backwards bifurcations

As a disease invades it reduces the number of susceptible individuals in the population, which tends to reduce its reproductive rate. For a backward bifurcation to occur, other factors must outweigh this tendency, so that as the disease invades its reproductive rate *increases*. If a disease lowers its reproductive rate by invading, it would be expected that when $R_0 < 1$ and it cannot invade a naive population, it could never persist at all. Further when R_0 is slightly above 1, the disease would be expected to reach a low endemic level, because of this negative feedback.

On the other hand, a disease that increases its reproductive rate by invading may be able to survive when established in a population, even when $R_0 < 1$ and it cannot invade. Similarly when R_0 is even very slightly above 1, the positive feedback between increase of the disease and rate of spread may lead to a relatively high endemic rate of infection.

In particular, when R_0 is precisely 1, each infection exactly replaces itself in the linear approximation. Hence, whether the disease will invade when $R_0 = 1$ will be determined by whether the reproductive rate increases or decreases as the disease increases along the center manifold. Hence, we would expect the disease to be able to invade at $R_0 = 1$ in the case of a backward bifurcation, but not in the case of a forward bifurcation. This is the behavior implied by the bifurcation diagrams (Figs. 1 and 2). A simple criterion for a backwards bifurcation, then, is one in which the disease can invade when $R_0 = 1$.

Figure 3 shows a projection of the phase plane of a simple disease model. In Fig. 3a, the parameters are such that the disease cannot invade when $R_0 = 1$ (middle panel). If we decrease R_0 slightly, we create a small, linear "pull" toward the disease-free equilibrium. This would not be expected to affect the qualitative dynamics (top panel). If we increase R_0 slightly, we create a small, linear "push" away from the disease-free equilibrium (bottom panel). Although the push is small, because it is linear it will be dominant in some small neighborhood of the disease-free equilibrium. As can be seen from the figure, the properties of a forward bifurcation – the absence of a low-level unstable equilbrium when $R_0 < 1$ and a stable equilibrium bifurcating from the disease-free equilibrium when $R_0 > 1$ – arise naturally when the disease does not invade when $R_0 = 1$.

Figure 3b shows a phase plane for a system in which the disease does invade when $R_0 = 1$ (middle panel). In this case, increasing R_0 to provide a push does not change the qualitative dynamics (bottom panel), while decreasing R_0 to provide a linear pull towards the disease-free equilibrium creates a zone where the disease goes extinct (top panel). Here we have the properties of a backward bifurcation – an unstable equilibrium bifurcating from the disease-free equilibrium when $R_0 < 1$, giving rise to multiple stable states.

Formally, the bifurcation of the disease-free equilibrium will have the topological properties shown in Fig. 3b whenever the bifurcation at $R_0 = 1$ is a transcritical bifurcation (see [10, Chap. 3]), which is generally the case for

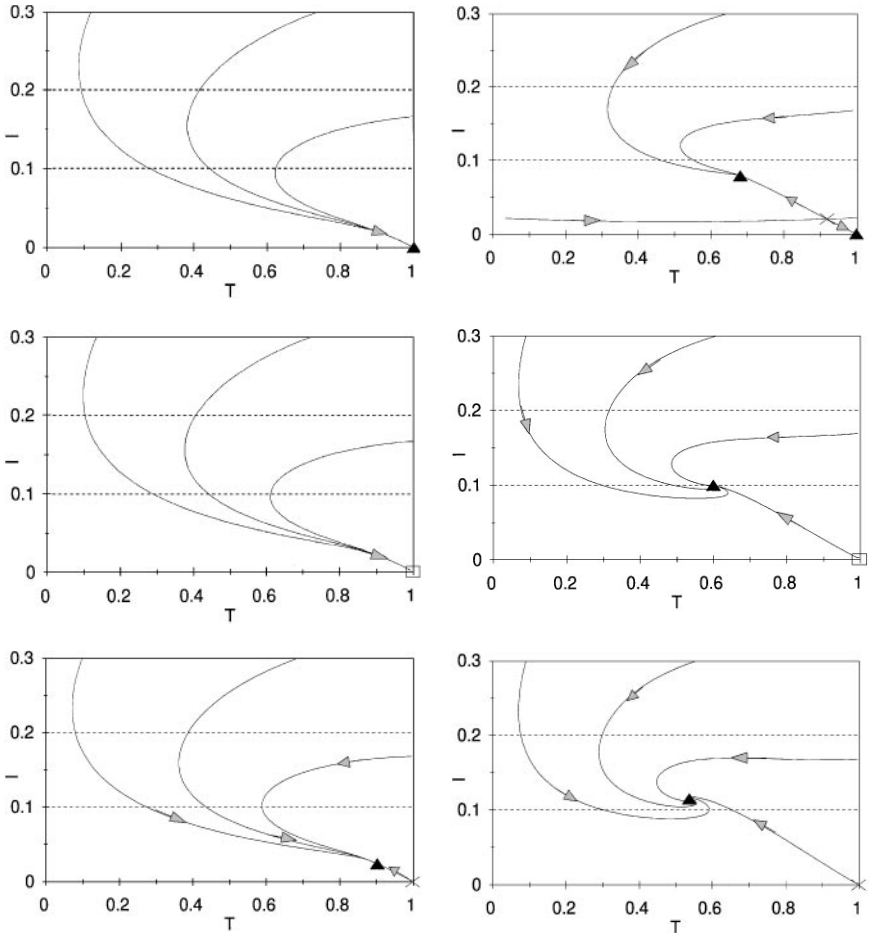

Fig. 3. Phase space diagrams for different parameter values in the neighborhood of two different types of bifurcation points. A triangle indicates an asymptotically stable equilibrium point, a cross a saddle point, and a square an 'indeterminate' (non-hyperbolic) equilibrium

simple disease models. The global behaviors shown hold for many simple models, but a wide range of global behaviors is possible.

3 A simple multi-group model

Our model is a simplified version of the one developed for AIDS by Huang et al. [13]. The model is a multi-group SI model with disease-induced mortality. In general, we can write:

$$\begin{aligned} \dot{I}_i &= B_i - \mu_i(\sigma_i + 1)I_i \\ \dot{S}_i &= \Lambda_i - B_i - \mu_i S_i \end{aligned} \tag{3}$$

Here I_i and S_i are the number of infectives and susceptibles, respectively, in group i. Individuals are recruited into the susceptible pool at rate Λ_i, and contract the disease at rate B_i. Both Λ_i and B_i can be functions of any or all of the dynamic variables. Susceptible individuals die at rate μ_i, while infected individuals experience disease-induced mortality at a rate that is σ_i times as great, as well as mortality from other sources at the rate μ_i.

Since B_i is often the most complicated term in such a model, we simplify the treatment by rewriting (3) in terms of I_i and T_i, where $T_i = S_i + I_i$ is the total number of people in group i:

$$\begin{aligned} \dot{I}_i &= B_i - \mu_i(\sigma_i + 1)I_i \\ \dot{T}_i &= \Lambda_i - \mu_i T_i - \mu_i \sigma_i I_i \end{aligned} \tag{4}$$

We simplify this general model by assuming proportional mixing, and by assuming that the mixing rate for each group, the probability of transmission between any two groups and the rate of recruitment into each group remain fixed. If the mixing rate of group i is c_i, then the total mixing activity is $\sum_j c_j T_j$, and the proportion of group i's contacts that are with members of group j is $c_j T_j / \sum_k c_k T_k$. Let λ_{ij} be the fraction of contacts between group i susceptibles and group j infectives which lead to infection. Since the proportion of group j that is infected is I_j/T_j, and the total number of contacts made by group i susceptibles is $c_i S_i$, the rate at which group i susceptibles become infected is:

$$B_i = c_i S_i \frac{\sum_j c_j \lambda_{ij} I_j}{\sum_j c_j T_j} \tag{5}$$

For convenience of notation, define the total mixing activity, $N(T) = \sum_j c_j T_j$, the transmission rate from group j to group i, $l_{ij} = c_i c_j \lambda_{ij}$ and the total death rate of infectives, $m_i = \mu_i(\sigma_i + 1)$. Then (4) becomes:

$$\begin{aligned} \dot{I}_i &= \frac{S_i}{N(T)} \sum_j l_{ij} I_j - m_i I_i \\ \dot{T}_i &= \Lambda_i - \mu_i T_i - \mu_i \sigma_i I_i \end{aligned} \tag{6}$$

We assume that the mixing rates c_i remain constant as subgroup sizes change. This assumption is an important part of the reason why backwards bifurcations are observed. Under the common assumption of bilinearity (where the transmission term is given by $S_i I_j$, rather than $S_i I_j / N(T)$), mixing rates increase linearly with subgroup sizes and backwards bifurcations do not occur in this model. It is commonly thought that real mixing patterns lie somewhere between these two extremes. See [18] for a discussion of the importance of the relationship between population sizes and mixing rates on disease dynamics. For the sake of mathematical simplicity, we will also assume that all of the l_{ij} are positive, and hence that every subgroup has at least some transmission of the disease to every other subgroup.

4 Determining the sign of a bifurcation

Huang et al. [13] have analyzed the bifurcations of this model, using μ as a bifurcation parameter. We are going to take a different approach. We define R_0 formally as the dominant eigenvalue of the 'next-generation' matrix (see [6]). Thus we know that a bifurcation point (that is, a point where the leading eigenvalue of the Jacobian matrix at the disease-free equilibrium is zero) will occur whenever $R_0 = 1$. We analyze the sign of the bifurcation in the neigborhood of a particular bifurcation point by analyzing whether the disease can invade at the bifurcation point. Appendix 2 shows formally that this calculation determines the sign of the bifurcation with respect to a change in parameters that increases the leading eigenvalue in the neighborhood of zero, and thus that increases R_0 in the neighborhood of 1.

At the bifurcation point, the dominant eigenvalue of the Jacobian matrix, zero, is associated with a unique right eigenvector, which we will call the dominant eigenvector. This eigenvector gives the distribution of infected individuals in different groups in the direction in which the disease initially spreads. In the case where the disease does not spread, the dominant eigenvector gives the asymptotic distribution of infecteds in different groups as the disease dies out.

The Jacobian matrix also has a dominant left eigenvector, corresponding to the zero eigenvalue. Caswell [5, Chap. 4] has provided a biological interpretation of dominant left eigenvectors. The left eigenvector gives the projection of a vector onto the dominant eigenvector in the eigenvector basis. The dominant eigenvector component in turn determines the long-term dynamics of the system. Hence the dominant left eigenvector reflects how much an infected individual in each subgroup contributes to the spread of the disease, as it begins to invade.

Intuitively speaking, we are going to develop a criterion for whether the disease can invade when $R_0 = 1$ by assuming that the disease invades a small amount along the dominant eigenvector, calculating the vector field at a point along the dominant eigenvector near the disease-free equilibrium, and multiplying by the dominant left eigenvector to find out if the component of the vector field in the direction of the dominant eigenvector is positive or negative.

More formally, let $V = (I, T)$ be the vector of dynamical variables and $\hat{V} = (0, \hat{T})$, $\hat{T} = (\Lambda_1/\mu_1, \ldots, \Lambda_n/\mu_n)^T$ be the disease-free equilibrium. Then we can write (6) in vector form as:

$$\dot{V} = H(V)(V - \hat{V}) \tag{7}$$

Here

$$H(V) = \begin{pmatrix} F(V) & 0 \\ -\operatorname{diag}\{\mu_i \sigma_i\} & -\operatorname{diag}\{\mu_i\} \end{pmatrix}$$

and

$$F(V) = \left[\frac{T_i - I_i}{N(T)} l_{ij} \right] - \operatorname{diag}\{\mu_i\}$$

Let $\hat{N} = \sum_j c_j \hat{T}_j$ be $N(T)$ evaluated at the disease-free equilibrium and let

$$\hat{F} = F(\hat{V}) = \left[\frac{\hat{T}_i}{\hat{N}} l_{ij}\right] - \text{diag}\{\mu_i\}$$

be the matrix F evaluated at the disease-free equilibrium. Then we can write the Jacobian matrix (H evaluated at the disease-free equilibrium) as:

$$\hat{H} = \begin{pmatrix} \hat{F} & 0 \\ -\text{diag}\{\mu_i \sigma_i\} & -\text{diag}\{\mu_i\} \end{pmatrix}$$

Since we have assumed that the dominant eigenvalue of $\hat{H}$ is zero, it follows that the dominant eigenvalue of $\hat{F}$ is zero. Furthermore, since the off-diagonal entries of $\hat{F}$ are positive, the dominant eigenvalue, zero, must be a simple eigenvalue and the dominant eigenvector $I^0 = (I_i^0)$ is strictly positive [9, Chap. 12].

By inspection, it can be seen that the dominant eigenvector of $\hat{H}$ is $V^0 = (I^0, T^0)$, with $T^0 = (-\sigma_1 I_1^0, \ldots, -\sigma_n I_n^0)^T$. Hence, as the disease invades along the dominant eigenvector, people in subgroup i die from the disease at a rate σ_i times as fast as the rate that the number of infectives increases. This may seem surprising, since we may suppose that the disease would invade on a faster time scale than it would cause mortality. This is true in general, but here we have chosen the parameters such that we are at a bifurcation point, and hence the linear rate of increase of the disease is zero.

Similarly, $\hat{F}$ has a strictly positive dominant left eigenvector, which we will call I^*. Then, by inspection, $V^* = (I^*, 0)$ is the dominant left eigenvector of $\hat{H}$, which we will choose so that $V^* \cdot V^0 = 1$. Since V^* gives the projection of the vector field onto the dominant eigenvector, we conclude that this projection is determined by the I components, and not the T components, of the vector field.

In Appendix 1, we show that as the disease initially invades along the dominant eigenvector, the component along the eigenvector is governed by the equation

$$\dot{\alpha} = h\alpha^2 + O(\alpha^3)\,, \tag{8}$$

where

$$h = V^* \cdot H' V^0$$

is the projection of the initial direction of the vector field onto the dominant eigenvector, and

$$H' = \frac{d}{d\alpha} H(\hat{V} + \alpha V^0)|_{\alpha=0}$$

is the initial rate of change of the matrix H as the disease invades. The disease can invade when $R_0 = 1$, and hence we have a backward bifurcation, when $h > 0$.

Also in Appendix 1, we calculate h for the system (6) and show that:

$$h = \frac{1}{\hat{N}} \sum_i m_i I_i^* I_i^0 \left(\sum_k c_k \sigma_k I_k^0 - \frac{\hat{N}}{\hat{T}_i} (\sigma_i + 1) I_i^0 \right). \tag{9}$$

As the corollary in Appendix 2 shows, when $h < 0$, changing the parameters slightly to make R_0 slightly greater than one will yield a positive (biologically meaningful) branching equilibrium, while making R_0 slightly less than one will not. This is the pattern for a forward bifurcation. Similarly, when $h > 0$, the branching equilibrium is positive when R_0 is slightly less than 1, giving a backwards bifurcation.

Now let $J^0 = (1/\sum_j m_j I_j^* I_j^0) I^*$. Like I^*, J^0 is a dominant left eigenvector, giving the relative weights of the various groups in spreading the disease. Our condition for a backward bifurcation (9) becomes:

$$\sum_i c_i \sigma_i I_i^0 > \sum_i m_i I_i^0 J_i^0 \frac{I_i^0}{\hat{T}_i} \hat{N} (\sigma_i + 1) \tag{10}$$

If we further let $w_i = c_i \hat{T}_i / \sum_j c_j \hat{T}_j$ be the proportion of total mixing activity accounted for by group i, then (10) becomes:

$$\sum_i w_i \frac{I_i^0}{\hat{T}_i} \sigma_i > \sum_i m_i I_i^0 J_i^0 \frac{I_i^0}{\hat{T}_i} (\sigma_i + 1) \tag{11}$$

5 Interpreting the backwards bifurcation

The criterion (11) allows an intuitive explanation of how backwards bifurcations can occur in this simple model. Since

$$\sum_i w_i = \sum_i m_i I_i^0 J_i^0 = 1$$

both sides of the inequality can be interpreted as weighted averages. The right-hand side is a weighted average of the relative rate at which people contract the disease and leave the susceptible pool. The reduction in the number of susceptibles tends to reduce the reproductive rate of the disease. The left-hand side is a weighted average of the rate at which people leave the mixing population due to the disease. Because we have assumed that mixing rates remain the same as population sizes get smaller, decreasing population size alone tends to increase the disease reproductive rate, after the negative effect of reducing the pool of susceptibles is taken into account. When the disease is invading, the population is initially entirely susceptible. Hence the rate at which individuals leave the mixing population entirely must be less than the rate at which the leave the susceptible pool.

Although the left-hand side is an average of a smaller quantity than the right-hand side, if the weights are suitably skewed it is possible for the left-hand side to be larger and for a backwards bifurcation to occur. The

weights on the left-hand side simply reflect the proportion of mixing activity in the population due to each subgroup. The weights on the right-hand side are a measure of the effect of the disease on the subpopulation, since they combine a measure of how quickly the population is getting (and spreading) the disease with a measure of how quickly individuals in the subpopulation die once they have the disease.

For the disease to invade when $R_0 = 1$, the right-hand side must be relatively small, implying a negative relationship between J_i^0, the effect of infectives of group i on the spread of the disease, and $I_i^0(\sigma_i + 1)$, the effect of the disease on the subgroup. Note that J_i^0 gives the per-case contribution of group i to the dominant eigenvector, and hence to the spread of the disease. Hence, for the disease to invade there must be groups that are strongly affected by the disease but less important in spreading it (which we will call 'victim' groups) and groups that are more important in spreading the disease but are less affected by it (which we will call 'core' groups).

For a disease to invade at a neutrally stable equilibrium, the depletion of susceptibles must be counteracted by a change in population structure that favors the disease. This requires that the disease be fatal (or at least debilitating) so that it can change the overall structure of the mixing population. It also requires that the subgroups most important in spreading the disease be different from those most affected by it, so that the population composition changes favor the disease. Finally, it requires that a reduction in the size of the mixing population increase the amount of contact between those individuals who remain. Here we have assumed that $\beta(T) = b$, a constant. If we had assumed instead that $\beta(T) = bT$, then reducing the pool of susceptibles could only have a negative effect. If we had assumed an intermediate form for β (see [18] for a brief review) then backwards bifurcations would still be possible, but less likely.

6 A two-group example

A simple example will perhaps help to clarify the mechanism of backwards bifurcations. To understand the behavior in a region of parameter space near a given bifurcation point we study the bifurcation point itself. A simple set of parameters that correspond to a backwards bifurcation point is:

$$c_i = 1; \quad \mu_i = 0.5; \quad \sigma_i = 15; \quad \Lambda_i = 1; \quad (l_{ij}) = \begin{pmatrix} 12 & 1 \\ 40 & 6 \end{pmatrix} \tag{12}$$

For simplicity, we have chosen all the parameters except the transmission rates (l_{ij}) symmetrically for the two groups. In fact, interactions between transmission, mixing and disease-induced mortality can be important in backwards bifurcations, as we will discuss below.

With the set of parameters (12) we can calculate:

$$F = \begin{pmatrix} -2 & 1/2 \\ 20 & -5 \end{pmatrix}$$

and hence $I^0 = (1, 4)^T$ and $J^0 = (10, 1)^T/112$ (the 112 is chosen to satisfy our assumption that $\sum_i m_i I_i^0 J_i^0 = 1$). Hence the first group is more important in allowing the disease to spread, but people in the second group get sick more as the disease spreads (and hence die more, since σ is constant). This is the sort of phenomenon that can lead to a backwards bifurcation.

In fact, if we evaluate the criterion (11) we see:

$$\sum_i w_i \frac{I_i^0}{\hat{T}_i} \sigma_i = \frac{1}{2} \cdot \frac{15}{2} + \frac{1}{2} \cdot 30 = \frac{75}{4} = 18.75$$

$$\sum_i m_i I_i^0 J_i^0 \frac{I_i^0}{\hat{T}_i} (\sigma_i + 1) = \frac{5}{7} \cdot 8 + \frac{2}{7} \cdot 32 = \frac{104}{7} \approx 14.86$$

Hence (11) holds and (12) describes a backwards bifurcation point.

When $R_0 < 1$ close enough to a backward bifurcation point, we expect to see multiple stable equilibria. Figures 4 and 5 illustrate the behavior of this system when $\mu = 0.52$. Figure 4 shows the behavior of the system if we start with $T_i = \hat{T}_i$, the population levels at the disease-free equilibrium – and $I_i = T_i/100$ – that is, one percent of the population in each group is infected initially. Initially the level of disease in the victim group increases. This is due to the fact that infection in the core group tends to give rise to higher levels of the disease in the victim group. However, once the number of infected in the victim group rises high enough above the level of the core group, the number of infected in both groups decreases to zero, because $R_0 < 1$ and the disease cannot be sustained.

Figure 5 shows the same system, but where the initial number of infected in each group is 10 percent of the total. Again the number of infected in the victim group initially rises, after which the number infected in both groups decreases. In this case, however, the disease has a dramatic effect on the population of the victim group, and changes the relative proportions of core and victim groups enough that it is able to persist. Note also the damped oscillations in the ratio of number of infected individuals in the two groups.

7 Separable transmission

Although our criterion (11) gives some insight into the causes of backwards bifurcations, the dependence of the eigenvectors I^0 and J^0 on the parameters is somewhat difficult to interpret. In this section we evaluate the criterion in the special case where transmission is separable to examine some of the tradeoffs that might lead to backwards bifurcations.

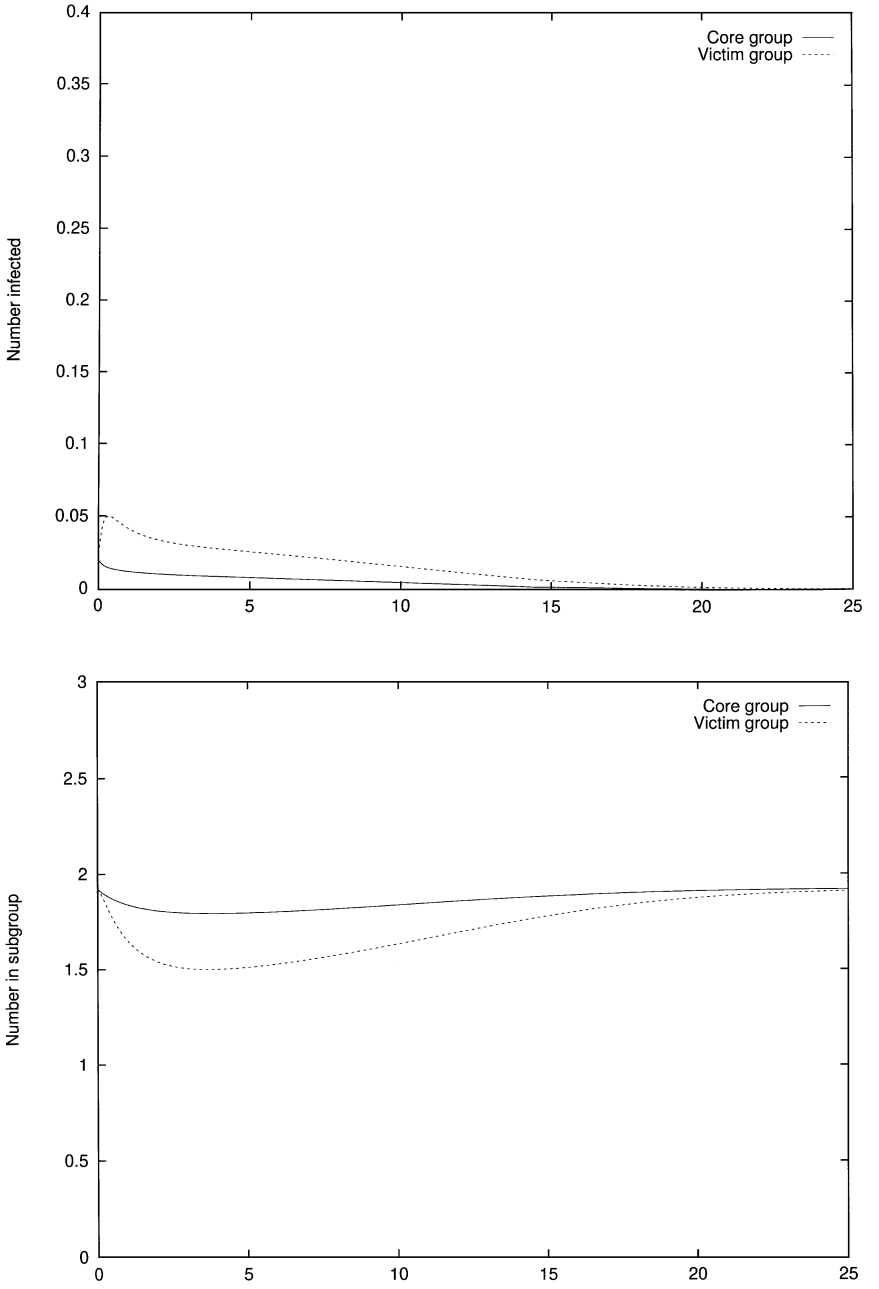

Fig. 4. The time course of the model when $R_0 < 1$, near a backward bifurcation point, with 1% of the population initially infected

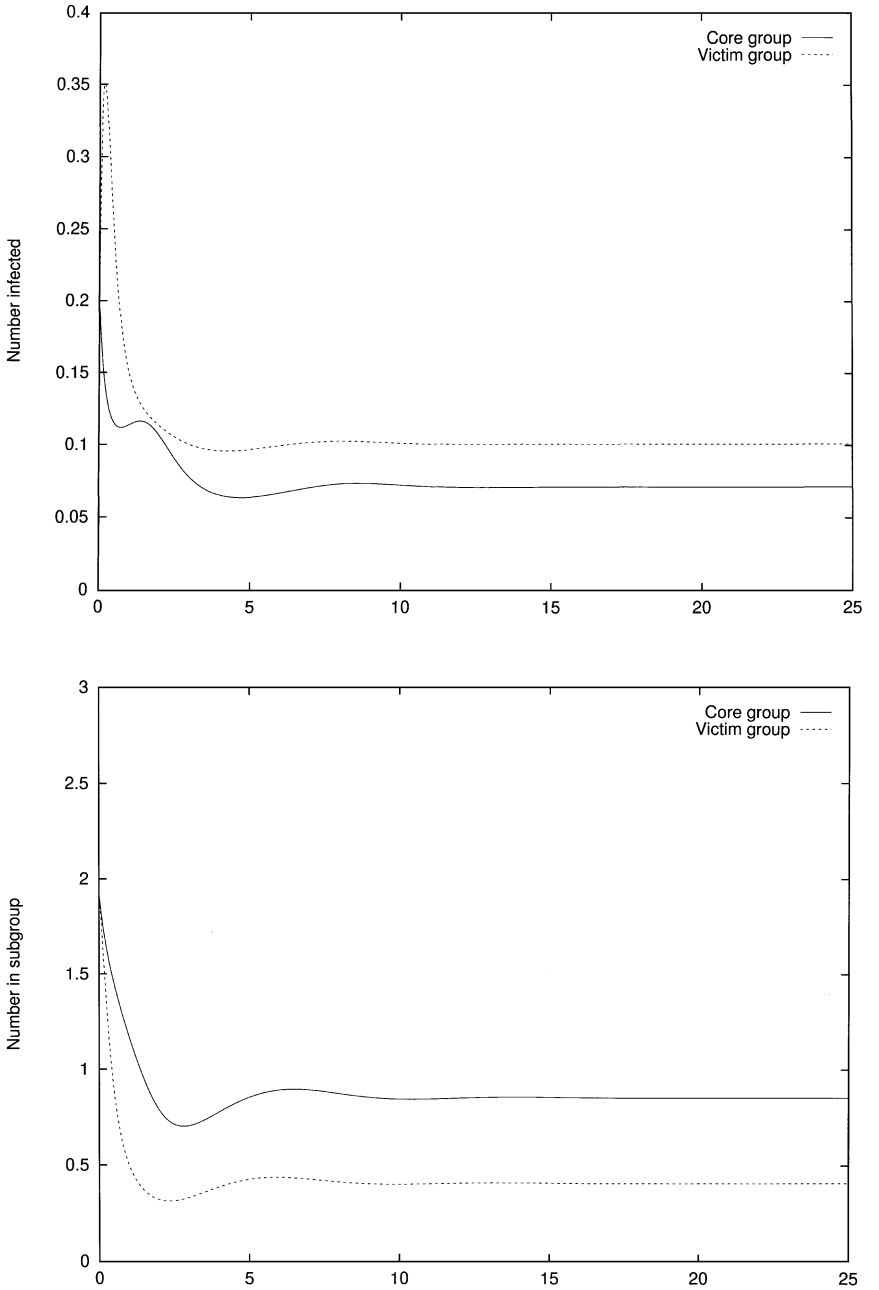

Fig. 5. The time course of the model when $R_0 < 1$, near a backward bifurcation point, with 1% of the population initially infected

Recall that $l_{ij} = c_i c_j \lambda_{ij}$. We assume that $\lambda_{ij} = v_i \beta_j$ where v_i measures the susceptibility of a member of group i and β_j measures the tendency of a member of group j to transmit the disease. To help clarify interpretation, we will also assume that the death rate of susceptibles is a constant, μ.

With these assumptions, the expression for the change in the number of infectives becomes (from (6)):

$$\dot{I}_i = \frac{S_i}{N} \sum_j c_i c_j v_i \beta_j I_j - m_i I_i$$

The linearized equation for the change in the number of infectives is thus:

$$\dot{I}_i = \frac{\hat{T}_i}{\hat{N}} \sum_j c_i c_j v_i \beta_j I_j - m_i I_i \tag{13}$$

Hence the linearized transmission matrix $\hat{F}$ can be written:

$$\hat{F} = K - \text{diag}\{m_i\}$$

where K is the separable matrix given by:

$$K_{ij} = \frac{\hat{T}_i c_i v_i}{\hat{N}} c_j \beta_j = w_i v_i c_j \beta_j$$

At a bifurcation point, if $I = I^0$ – the dominant eigenvector – the disease should neither increase nor decrease in the linearized model. Hence $\hat{F} I^0 = 0$ which implies $K I^0 = (m_i I_i^0)^T$ or

$$w_i v_i \sum_j c_j \beta_j I_j^0 = m_i I_i^0 \tag{14}$$

Since $\sum_j c_j \beta_j I_j^0$ is the same for all values of i, we can write I^0 as $(w_i v_i / m_i)^T$. In other words, the number of cases in group i as the disease begins to spread is proportional to the proportion of mixing contributed by members of group i and their susceptibility to the disease, and inversely proportional to the rate at which infected members of the group leave the mixing population.

For (14) to hold, we must have:

$$R_0 \equiv \sum_j c_j \beta_j I_j^0 = \sum_j c_j \beta_j w_j v_j / m_j = 1 \tag{15}$$

This is the condition that the parameters in fact constitute a bifurcation point. We omit the proof that R_0 is in fact the basic reproductive model for this model, as defined by Diekmann et al. [6].

We can similarly calculate the distribution of the left eigenvector J^0. We know $J^0 F = 0$, hence $J^0 K = (m_i J_i^0)$, or

$$c_i \beta_i \sum_j w_j v_j J_j^0 = m_i J_i^0$$

and $J_0 = (c_i\beta_i/m_i)$. In other words, the contribution of an infectious individual in group i to the spread of the disease is proportional to the mixing rate and the transmission coefficient of group i, and again inversely proportional to the 'death' rate.

Note that, fortuitously, these unscaled values for I^0 and J^0 yield

$$\sum_i m_i I_i^0 J_i^0 = R_0 = 1 \ ,$$

satisfying the assumptions of (11).

Hence we can write (11), the criterion for a backwards bifurcation, in the case of separable mixing as:

$$\sum_i w_i \frac{w_i v_i}{m_i \hat{T}_i} \sigma_i > \sum_i c_i \beta_i \frac{w_i v_i}{m_i} \frac{w_i v_i}{m_i \hat{T}_i} (\sigma_i + 1)$$

Multiplying both sides by $\hat{N}$ and recalling that $w_i = c_i \hat{T}_i / \hat{N}_i$, we obtain:

$$\sum_i w_i \frac{c_i v_i}{m_i} \sigma_i > \sum_i c_i \beta_i \frac{w_i v_i}{m_i} \frac{c_i v_i}{m_i} (\sigma_i + 1) \tag{16}$$

Note that

$$\sum_i w_i = \sum_i c_i \beta_i w_i v_i / m_i = 1 \ .$$

Hence, as in (11), we can interpret the left-hand side as a weighted average of the rate at which people die of the disease, and the right-hand side as a weighted average of the (higher) rate at which people contract the disease. Now recall that $m_i = \mu(\sigma_i + 1)$, and multiply both sides of (16) by μ to obtain:

$$\sum_i w_i c_i v_i \frac{\sigma_i}{\sigma_i + 1} > \sum_i c_i \beta_i \frac{w_i v_i}{\mu(\sigma_i + 1)} c_i v_i \ .$$

Here the left-hand side is a weighted average of $c_i v_i$, the mixing rate times the susceptibility rate, multiplied by a 'discounting factor' of $\sigma/(\sigma + 1)$, while the right-hand side is a weighted average of $c_i v_i$. The weighting factors differ by a multiple of

$$c_i v_i \frac{\beta_i}{\sigma_i + 1}$$

(ignoring the constant μ). For a backwards bifurcation, we require a negative association between the weighting factor and $c_i v_i$ strong enough to overcome the 'discounting factor', despite the fact that $c_i v_i$ is itself a factor of the weighting factor. Thus, as $c_i v_i$ increases, $\beta_i/(\sigma_i + 1)$ must decrease sharply enough that the product of the two terms, which yields the weight, decreases.

In this simplified separable model there are four tradeoffs which can lead to backwards bifurcations. Groups with a higher mixing rate c could have sharply lower transmission rates or sharply higher disease-induced death rates. Or more susceptible groups might display either of those characteristics. Interestingly, there are two tradeoffs – that between transmission rate and

disease-induced death rate, and that between mixing rate and susceptibility – which *cannot* produce backward bifurcations.

8 Discussion

Our purpose in writing this paper was to provide an intuitive explanation of the mechanisms that drive backwards bifurcations in some simple disease models, and thus to make it possible to explore in what circumstances such bifurcations might occur in more realistic disease models and hence in what circumstances we should look for the dynamical signature of the backwards bifurcations – breakpoints above which the disease can persist for certain values of R_0, and the possibility of 'catastrophic' fast dynamics as underlying parameters change slowly – in real-world disease systems.

The original models on which our analysis is based are AIDS models [4, 2, 13]. It is natural to consider the possibility that backwards bifurcations of the type discussed here may occur in AIDS, with men making up the core groups and women the victim groups, since male homosexual transmission is thought to be very important to the spread of AIDS in many places. For this to cause backwards bifurcations, however, AIDS would need to change the population structure in such a way as to increase the proportion of men's sexual contacts that were with other men. This is certainly possible, but does not intuitively seem likely. In general, models of sexual mixing involve complicating social factors beyond the scope of this discussion. An exploration of the possibility of core/victim backwards bifurcations in AIDS would certainly be of interest, however. Another difficulty with AIDS modeling is that, directly contrary to our discussion of slow-changing parameters, it seems likely that behavioral 'parameters' in a disease like AIDS change quickly compared to the time scale of disease spread itself.

For a wide variety of other diseases, it is at least plausible that a 'core' group of healthier, more active people might be both more important than other groups at spreading the disease, and less affected by it. For backwards bifurcations to be caused by the mechanism discussed here, however, it would be necessary for such a disease to cause enough mortality or morbidity to substantially change the structure of the mixing population, which sharply reduces the range of possibilities. It is possible that this mechanism for backwards bifurcations would be more relevant in studies of animal diseases. Studies have demonstrated that diseases like anthrax [1] and myxomatosis [8] have had profound effects on animal populations.

9 Appendix 1

Since the dominant eigenvalue of the Jacobian matrix is zero, it is well known that we can decompose a neighborhood of the disease-free state into a stable manifold W^S and a center manifold W^C (see *e.g.* [10, Sect. 3.2]. In particular,

the dynamical behavior of (7) near the disease-free equilibrium is determined by the flow on the center manifold. Moreover, the fact that zero is a simple eigenvalue implies that W^C is one-dimensional and it is tangential to the eigenvector V^0 at 0, thus the center manifold W^C can be parameterized as

$$W^C = \{\hat{V} + \alpha V^0 + Z(\alpha)\colon V^* \cdot Z(\alpha) = 0, \quad -\alpha_0 \leqq \alpha \leqq \alpha_0\}$$

where $\alpha_0 > 0$ is a constant, and $Z\colon [-\alpha_0, \alpha_0] \to Ran(\hat{H})$ satisfies:

$$Z(0) = \frac{d}{d\alpha} Z(0) = 0 \,.$$

That is, $Z(\alpha) = O(\alpha^2)$.

In other words, α gives the component of the center manifold that lies along the dominant eigenvector, while $Z(\alpha)$ gives the component of the center manifold that does not lie along the dominant eigenvector, in the eigenvector basis. Hence $V^* \cdot Z(\alpha) = 0$. Since the center manifold is tangent to V^0, we have that $Z(\alpha) = O(\alpha^2)$ is small compared to the component along the dominant eigenvector.

To determine the flows on W^C we need to see how α depends on time, t. Let

$$V(t) = \hat{V} + \alpha(t) V^0 + Z(\alpha(t)) \,,$$

since W^C is invariant, from (7) we have

$$\begin{aligned} \dot{\alpha}(t) V^0 + \frac{d}{dt} Z(\alpha(t)) &= \dot{V}(t) \\ &= H(V(t))[V(t) - \hat{V}] \\ &= H(\hat{V} + \alpha(t) V^0 + Z(\alpha(t)))[\alpha(t) V^0 + Z(\alpha(t))] \end{aligned}$$

Multiplying both sides of above equation by V^* and using the fact that

$$V^* \cdot \frac{d}{dt} Z(\alpha(t)) \equiv 0, \quad V^* \hat{H} = 0, \quad V^* \cdot V^0 = 1$$

and $Z(\alpha) = O(\alpha^2)$ we arrive at

$$\begin{aligned} \dot{\alpha} &= V^* \cdot H(\hat{V} + \alpha V^0 + Z(\alpha))[\alpha V^0 + Z(\alpha)] \\ &= V^* \cdot H(\hat{V} + \alpha V^0)[\alpha V^0 + Z(\alpha)] + O(\alpha^3) \\ &= V^* \cdot [H(\hat{V} + \alpha V^0) - \hat{H}][\alpha V^0 + Z(\alpha)] + O(\alpha^3) \end{aligned}$$

Since the difference $[H(\hat{V} + \alpha V^0) - \hat{H}]$ is of order α, its product with $Z(\alpha)$ is $O(\alpha^3)$ and we have:

$$\dot{\alpha} = \alpha V^* \cdot [H(\hat{V} + \alpha V^0) - \hat{H}] V^0 + O(\alpha^3) \tag{17}$$

The sign of this expression for small α is what determines whether the disease can invade at the bifurcation point. In the limit, as α goes to zero, (17) goes to:

$$\dot{\alpha} = V^* \cdot H' V^0 \alpha^2 + O(\alpha^3) , \tag{18}$$

where

$$H' = \left.\frac{dH(\hat{V} + \alpha V^0)}{d\alpha}\right|_{\alpha=0} = \sum_i V_i^0 \left.\frac{\partial H}{\partial V_i}\right|_{V=\hat{V}}$$

gives the rate of change of the vector field as the disease invades. Hence, the number

$$h = V^* H' V^0 \tag{19}$$

determines whether the disease can invade when $R_0 = 1$, and hence gives the sign of the bifurcation.

For our system specifically, we note that, due to the zeroes in H and V^*, we have

$$h = I^* F' I^0,$$

where

$$F' = \left.\frac{dF(\hat{V} + \alpha V^0)}{d\alpha}\right|_{\alpha=0}$$

From the definition of F, and our expression for T^0, it follows (with some calculation) that:

$$F' = \frac{1}{\hat{N}^2}\left[\left(\hat{T}_i\left(\sum_k c_k \sigma_k I_k^0\right) - \hat{N}(\sigma_i + 1) I_i^0\right) l_{ij}\right]_{n \times n} .$$

Hence the direction of change of the vector field is given by:

$$(F' I^0)_i = \frac{1}{\hat{N}^2}\left(\hat{T}_i \sum_k c_k \sigma_k I_k^0 - \hat{N}(\sigma_i + 1) I_i^0\right) \sum_j l_{ij} I_j^0$$

We can simplify this expression by making use of the fact that, since $\hat{F} I^0 = 0$,

$$\frac{\hat{T}_i}{\hat{N}} \sum_j l_{ij} I_j^0 = m_i I_i^0 .$$

Hence:

$$(F' I^0)_i = \frac{1}{\hat{N}} m_i I_i^0 \left(\sum_k c_k \sigma_k I_k^0 - \frac{\hat{N}}{\hat{T}_i}(\sigma_i + 1) I_i^0\right)$$

$$\Rightarrow h = \frac{1}{\hat{N}} \sum_i m_i I_i^* I_i^0 \left(\sum_k c_k \sigma_k I_k^0 - \frac{\hat{N}}{\hat{T}_i}(\sigma_i + 1) I_i^0\right) . \tag{20}$$

10 Appendix 2

In this appendix we present a generic bifurcation theorem.

Let $f: \mathbb{R}^n \times \mathbb{R}^m \to \mathbb{R}^n$ such that

$$f(0, \lambda) \equiv 0, \quad \forall \lambda \in \mathbb{R}^n .$$

Further we suppose that

1. $f(x, \lambda)$ is sufficiently smooth with respect to x, and $D_x f(x, \lambda)$ and $D_x^2 f(x, \lambda)$ are continuous on (x, λ) in a neighborhood $U \times V \subset \mathbb{R}^n \times \mathbb{R}^m$ of $(0, 0)$;
2. $D_x f(0, 0)$ has a simple zero eigenvalue.

By the continuity of eigenvalues with respect to the parameter λ we conclude that there exists a neighborhood $\hat{V} \subset V$ of $\lambda = 0$ and a continuous function γ: $\hat{V} \to \mathbb{R}$ such that $\gamma(0) = 0$ and for $\forall \lambda \in \hat{V}$, $\gamma(\lambda)$ is a simple eigenvalue of $D_x f(0, \lambda)$.

Theorem. *Let x_0 and x_0^* be the right and left eigenvectors of $D_x f(0, 0)$ corresponding to the zero eigenvalue with $x_0^T x_0 = x_0^* x_0 = 1$. If*

$$h = x_0^* D_x^2 f(0, 0)\langle x_0, x_0 \rangle \neq 0 ,$$

then there are neighborhoods $\bar{U} \subset \mathbb{R}^n$ of $x = 0$ and $\bar{V} \subset \mathbb{R}^m$ of $\lambda = 0$ such that $\forall \lambda \in \bar{V}$, $f(x, \lambda) = 0$ has a solution $x(\lambda) \in \bar{U} \setminus \{0\}$ if and only if $\gamma(\lambda) \neq 0$.

Proof. For $\lambda \in \hat{V}$, let x_λ^* and x_λ be the left and right eigenvectors of $D_x f(0, \lambda)$ corresponding to the eigenvalue $\gamma(\lambda)$ such that $x_\lambda^T x_\lambda = x_\lambda^* x_\lambda = 1$. Since $\gamma(\lambda)$ is a simple eigenvalue of $D_x f(0, \lambda)$, $\mathbb{R}^n$ can be decomposed as $\mathbb{R}^n = \mathrm{Span}[x_\lambda] \oplus R_\lambda$, where R_λ is the generalized eigenfunction space corresponding to all eigenvalues of $D_x f(0, \lambda)$ other than $\gamma(\lambda)$. Hence for $\forall x \in \mathbb{R}$, there exist unique $\alpha \in \mathbb{R}$ and $y \in R_\lambda$ such that $\alpha = x_\lambda^* x$ and $x = \alpha x_\lambda + y$. By applying the Taylor expansion we have

$$\begin{aligned} f(x, \lambda) &= f(\alpha x_\lambda + y) \\ &= D_x f(0, \lambda)(\alpha x_\lambda + y) + g(\alpha, y, \lambda) \\ &= \alpha D_x f(0, \lambda) x_\lambda + D_x f(0, \lambda) y + g(\alpha, y, \lambda) \\ &= \alpha \gamma(\lambda) x_\lambda + T_\lambda y + g(\alpha, y, \lambda) , \end{aligned} \tag{21}$$

where

$$T_\lambda = D_x f(0, \lambda), \quad g(\alpha, y, \lambda) = \int_0^1 D_x^2 f(\theta(\alpha x_\lambda + y, \lambda))\theta \, d\theta \langle \alpha x_\lambda + y, \alpha x_\lambda + y \rangle .$$

Let $g(\alpha, y, \lambda)$ be decomposed as

$$g(\alpha, y, \lambda) = \beta_\lambda(\alpha, y) x_\lambda + Y_\lambda(\alpha, y) \tag{22}$$

with $\beta_\lambda(\alpha, y) = x_\lambda^* g(\alpha, y, \lambda) \in \mathbb{R}$ and $Y_\lambda(\alpha, y) \in R_\lambda$. By substituting (22) into (21) one sees that for $\alpha \in \mathbb{R}$ and $y \in R_\lambda$, $f(\alpha x_\lambda + y, \lambda) = 0$ if and only if

$$\begin{aligned} \alpha\gamma(\lambda) + \beta_\lambda(\alpha, y) &= 0 \\ \bar{T}_\lambda y + Y_\lambda(\alpha, y) &= 0 \,, \end{aligned} \tag{23}$$

where $\bar{T}_\lambda$ is the restriction of $\bar{T}_\lambda$ on R_λ.

Note that for $\lambda \in \hat{V}$, the linear operator $\bar{T}_\lambda$: $R_\lambda \to R_\lambda$ is invertible. Moreover, following the definition of $Y_\lambda(\alpha, y)$ it is easy to verify that

$$Y_\lambda(0, 0) = 0, \qquad D_y Y_\lambda(0, 0) = 0 \,. \tag{24}$$

Therefore the implicit function theorem implies that there are a neighborhood $O \subset \mathbb{R}$ of 0 and a continuously differentiable function y_λ: $O \to R_\lambda$ such that

$$\bar{T}_\lambda y_\lambda(\alpha) + Y_\lambda(\alpha, y_\lambda(\alpha)) = 0, \quad \forall \alpha \in O \,. \tag{25}$$

As a consequence of (24) and (25) we have

$$y_\lambda(0) = 0, \qquad D_\alpha y_\lambda(0) = 0 \,.$$

Together with the fact that $\bar{T}_\lambda^{-1}$ and partial derivatives of Y_λ with respect to α and y are continous on (λ, α, y) we conclude that $y_\lambda(\alpha) = O(\alpha^2)$ as $\alpha \to 0$ uniformly for $\lambda \in \hat{V}$. Substituting $y = y_\lambda(\alpha)$ into the first equation of (23) we obtain the equation for α as

$$\alpha\gamma(\lambda) + \beta_\lambda(\alpha, y_\lambda(\alpha)) = 0 \,. \tag{26}$$

A straightforward computation from the definition of β_λ shows that

$$\beta_\lambda(\alpha, y_\lambda(\alpha)) = x_\lambda^* D_x^2 f(0, \lambda)\langle x_\lambda, x_\lambda\rangle \alpha^2 + O(\alpha^3) \,.$$

Since $x_\lambda^* D_x^2 f(0, \lambda)\langle x_\lambda, x_\lambda\rangle \to h$ as $\lambda \to 0$, $\operatorname{Sgn}(x_\lambda^* D_x^2 f(0, \lambda)\langle x_\lambda, x_\lambda\rangle) = \operatorname{Sgn}(h)$ if $\lambda \in \bar{V}$ and $\bar{V}$ is a sufficiently small neighborhood of $\lambda = 0$. Since we have assumed $h \neq 0$, we have that the second term of (26) is nonzero $\forall \lambda \in \bar{V}$. Hence the equation (26) has a nonzero solution $\alpha_\lambda \in O$ if and only if $\gamma(\lambda) \neq 0$. And furthermore

$$\alpha_\lambda \approx \frac{-\gamma(\lambda)}{x_\lambda^* D_x^2 f(0, \lambda)\langle x_\lambda, x_\lambda\rangle} \,. \tag{27}$$

Now it is clear that $x = \alpha_\lambda x_\lambda + y_\lambda(\alpha_\lambda))$ gives the unique solution to $f(x, \lambda) = 0$ in a small neighborhood $\bar{U} \setminus \{0\}$ of $x = 0$.

As an immediate consequence of (27) we have:

Corollary. *If the eigenvector x_0 defined in above is strictly positive, then the bifurcating solution $x = \alpha_\lambda x_\lambda + y_\lambda(\alpha_\lambda))$ of $f(x, \lambda) = 0$ is strictly positive if and only if $\gamma(\lambda)h < 0$*

If γ is the dominant eigenvalue of $D_x f(0, 0)$, we know that $\gamma > 0$ precisely when $R_0 > 1$ [6]. Hence the bifurcating solution will be positive (and have biological meaning) for $R_0 > 1$ when $h < 0$ and for $R_0 < 1$ when $h > 0$.

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