DISCRETE AND CONTINUOUS
DYNAMICAL SYSTEMS–SERIES B
Volume **5** , Number **2**, May **2005**

Website: http://AIMsciences.org

pp. **175–188**

COMPETITIVE EXCLUSION IN SIS AND SIR EPIDEMIC MODELS WITH TOTAL CROSS IMMUNITY AND DENSITY-DEPENDENT HOST MORTALITY

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(Communicated by Ruan Shigui)

Abstract. We study SIR and SIS epidemic models with multiple pathogen strains. In our models we assume total cross immunity, standard incidence, and density-dependent host mortality. We derive conditions on the models parameters which guarantee competitive exclusion between the n strains. An example is given to show that if these conditions are not satisfied then coexistence between the strains is possible. Furthermore, numerical results are presented to indicate that our conditions on the parameters are sufficient but not necessary for competitive exclusion.

1. **Introduction.** Epidemic models with multiple pathogen strains have received considerable attention recently because of their importance in the evolution, persistence, and treatment of diseases such as influenza, hantavirus, dengue fever, HIV-AIDS, and other sexually transmitted diseases [3, 5, 7, 9, 10, 11, 16, 17, 22, 26, 27, 34]. There are many factors that contribute to the persistence or exclusion of multiple pathogen strains. It has been shown in epidemic models with partial cross immunity, coinfection, superinfection, and birth or mortality rates dependent on the host population size that coexistence of several strains or exclusion of all but one strain may occur (e.g., [1, 4, 5, 6, 8, 9, 10, 11, 12, 13, 16, 17, 19, 20, 21, 25, 26, 27, 28, 29, 30, 31, 32]).

It is the purpose of this investigation to study the effects of host demography on competitive exclusion and coexistence of multiple pathogen strains and to extend some of the results in [1, 6, 8, 12, 28, 31] to n strains. In [1], we derived conditions for exclusion of all but one strain in an SIR epidemic model with n pathogen strains but we also showed that coexistence of more than one strain is possible. However, the analysis in [1] was restricted to mass action incidence, βSI. Here, we extend the results in [1] to SIS and SIR epidemic models with standard incidence, $\beta SI/N$. It has been argued that standard incidence is more biologically

1991 *Mathematics Subject Classification.* 34D05, 34D23, 92D30.
Key words and phrases. Epidemic models, cross immunity, competitive exclusion.

reasonable than mass action for homogeneously mixing populations [14]. Other forms for the incidence rate are discussed in [15, 23, 24]. In our models, total cross immunity is assumed, that is, infection with one strain confers complete cross protection against infection by another strain. In addition, it is assumed that the host population size satisfies a logistic-type growth function with a mortality rate that depends on the population size. In an SIR epidemic model studied by Bremermann and Thieme [8] with n strains, total cross immunity, and a birth rate dependent on the total population size, coexistence of multiple strains does not occur. In addition, in a two-sex, SIS model for sexually transmitted diseases with multiple pathogen strains and no density-dependent birth or mortality, coexistence was not possible [9]. However, when this model was extended to two genetically different female groups, coexistence may occur [10, 11]. In other models with total cross immunity, if the death rate instead of the birth rate depends on the population size, then coexistence of more than one strain is possible. In the two-strain, SI epidemic model studied by Andreasen and Pugliese [6], total cross immunity and density-dependent mortality are assumed. They showed that coexistence of both strains is possible. In the two-strain, SI epidemic models studied by Pugliese [31], Castillo-Chavez and Velasco-Hernandez [12], and Mena-Lorca, Velasco-Hernandez, and Castillo-Chavez [28], the impact of density-dependent mortality and superinfection on coexistence are studied. In these models, there are cases of competitive exclusion and coexistence.

In the next section, the $n-$strain, SIR and SIS epidemic models are described. In section 3, the competitive exclusion results are verified under some conditions on the model parameters. In section 4, some numerical examples are presented to show that the conditions imposed in section 3 on the model parameters are sufficient but not necessary for competitive exclusion to occur. Furthermore, an example is given where coexistence of more than one strain occurs. Finally, we give some concluding remarks in section 5.

2. **SIS and SIR Epidemic Models.** Two basic epidemic models with n pathogen strains are described. These models are based on a modification and extension of the model described in [1]. In [1] an SIR epidemic model with mass action incidence βSI was considered. Here we assume a standard incidence $\beta SI/N$. In addition, we include models of SIS and SI type, where there is no immunity and possibly no recovery. When the disease is not present the dynamics of the host population are described by the following differential equation:

$$\dot{N}(t) = Nf(N),$$

where $\dot{N}(t) = dN/dt$. We make the same assumptions on $f(N)$ that were used in [1]:

(A1) $f \in C^1[0, \infty)$.
(A2) $0 < f(0) < b$.
(A3) $f(N)$ is decreasing for $N > 0$.
(A4) There exists a constant $K > 0$ such that $f(K) = 0$.

Assumptions (A1)–(A4) lead to logistic-type growth. In the absence of infection, solutions $N(t)$ approach the carrying capacity K.

The SIR model consists of susceptible individuals, S, individuals infected with strains 1 through n, I_j, $j = 1, 2, \ldots, n$, and immune or removed individuals, R. There is total cross immunity. Such types of models are applicable to diseases

where infection with one strain confers immunity and protection against infection by another strain. For example, in closely related strains of influenza, infection with one strain may provide immunity to another strain. A compartmental diagram in Figure 1 illustrates the relationship between the susceptible, infected, and removed individuals. The SIR model with standard incidence has the form

$$\begin{aligned}
\dot{S}(t) &= S\left(f(N) - \sum_{k=1}^{n}\beta_k \frac{I_k}{N}\right) + \sum_{k=1}^{n} bI_k + bR \\
\dot{I}_j(t) &= I_j\left(f(N) - b + \beta_j \frac{S}{N} - \gamma_j - \mu_j\right), \quad j = 1, 2, \ldots, n, \\
\dot{R}(t) &= R\,(f(N) - b) + \sum_{k=1}^{n} \gamma_k I_k \\
N &= S + R + \sum_{k=1}^{n} I_k.
\end{aligned} \tag{1}$$

In model (1), b is the per capita birth rate and $f(N)$ is the per capita growth rate. The per capita birth rate is constant but the per capita death rate is density-dependent. If we let $d(N)$ denote the density-dependent death rate, then $f(N) = b - d(N)$ and $-d(N) = f(N) - b$. Births and natural deaths are experienced by all individuals, a reasonable assumption if the disease is prolonged. There is no vertical transmission of the disease; all newborns are susceptible. Therefore, the birth rate into the susceptible class is bN. The parameter β_j denotes the transmission rate for the jth strain, while γ_j is the recovery rate from infection with strain j. Finally, μ_j represents the disease-related death rate for strain j. Note that by adding and subtracting the term bS, the differential equation for S in (1) can be expressed as follows:

$$\dot{S}(t) = S\left(f(N) - b - \sum_{k=1}^{n}\beta_k \frac{I_k}{N}\right) + bN.$$

In an SIS epidemic model, there is no immunity, and therefore, no immune state R. Infected individuals recover and return to the susceptible class at a rate $\gamma_j I_j$ (see Figure 1). SIS epidemic models are applicable to sexually transmitted diseases. An SIS epidemic model with n strains takes the form

$$\begin{aligned}
\dot{S}(t) &= S\left(f(N) - \sum_{k=1}^{n}\beta_k \frac{I_k}{N}\right) + \sum_{k=1}^{N}(b + \gamma_k) I_k \\
\dot{I}_j(t) &= I_j\left(f(N) - b + \beta_j \frac{S}{N} - \gamma_j - \mu_j\right), \quad j = 1, 2, \ldots, n, \\
N &= S + \sum_{k=1}^{n} I_k.
\end{aligned} \tag{2}$$

By adding and subtracting the term bS, the differential equation for S in (2) can be expressed as follows:

$$\dot{S}(t) = S\left(f(N) - b - \sum_{k=1}^{n}\beta_k \frac{I_k}{N}\right) + \sum_{k=1}^{N}\gamma_k I_k + bN.$$

In an SI epidemic model, the differential equations are the same as in (2), except that $\gamma_j = 0$ for $j = 1, 2, \ldots, n$, because there is no recovery from infection. To

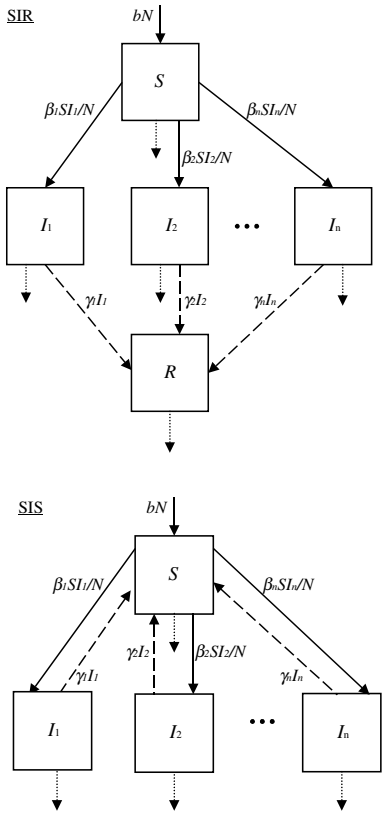

FIGURE 1. Compartmental diagrams of the SIR and SIS epidemic models with n strains. All flow rates are identified in the diagram except for the death rates. The dotted arrows directed downward from each compartment represent the death rates. The death rate for class S is $d(N)S$, the death rate for class I_k is $(d(N) + \mu_k)I_k$, and the death rate for class R is $d(N)R$, where $d(N) = b - f(N)$. All newborns are susceptible.

include SI epidemic models in our analysis, we shall assume $\gamma_j \geq 0$, $j = 1, 2, \ldots, n$ for models (1) and (2). All other parameters are assumed to be positive, b, μ_j, and β_j, $j = 1, 2, \ldots, n$.

In the presence of the disease, the population size N in models (1) and (2) is described by the following differential equation:

$$\dot{N}(t) = Nf(N) - \sum_{j=1}^{n} \mu_j I_j. \tag{3}$$

We assume that $S(0) > 0$, $I_j(0) > 0$, $j = 1, 2, \ldots, n$, and for model (1), $R(0) \geq 0$. Clearly, solutions to (1) and (2) exist and are positive for $t > 0$. Furthermore, one can easily deduce that solutions are bounded. In fact,

$$\dot{N}(t) \leq Nf(N),$$

and since the solution $u(t)$ to the differential equation $\dot{u}(t) = uf(u)$ with $u(0) = N(0)$ satisfies $\lim_{t\to\infty} u(t) = K$, it follows by comparison that $\limsup_{t\to\infty} N(t) \leq K$. Therefore, for model (1), $0 \leq \limsup_{t\to\infty}[S(t) + \sum_{k=1}^{n} I_k(t) + R(t)] \leq K$ and for model (2), $\limsup_{t\to\infty}[S(t) + \sum_{k=1}^{n} I_k(t)] \leq K$. We make one more additional assumption on f so that total population extinction does not occur:

(A5) $f(0) > \max_j\{\mu_j\} = \bar{\mu} > 0$.

The competitive exclusion result is verified in the next section for the basic models (1) and (2).

3. **Competitive Exclusion.** Let $c_j = b+\gamma_j+\mu_j > f(0)$ for $j = 1, 2, \ldots, n$. Then the basic reproduction number for strain j is given by

$$\mathcal{R}_j = \frac{\beta_j}{c_j}, \quad j = 1, 2, \ldots, n. \tag{4}$$

We define

$$\mathcal{B}_j = \frac{\beta_j}{c_j - f(0)}, \quad j = 1, 2, \ldots, n. \tag{5}$$

It is straightforward to show that the basic reproduction number for models (1) and (2) with n strains is given by

$$\mathcal{R}_0 = \max_j\{\mathcal{R}_j\}$$

(see e.g., [33]). When $\mathcal{R}_0 < 1$, then the disease-free equilibrium (DFE), where $S = K$, is locally asymptotically stable and when $\mathcal{R}_0 > 1$, the DFE is unstable. The parameter $\mathcal{B}_j$ is related to the basic reproduction number for strain j. Since $f(0) = b - d(0)$, then $c_j - f(0) = d(0) + \gamma_j + \mu_j$ and

$$\mathcal{B}_j = \frac{\beta_j}{d(0) + \mu_j + \gamma_j}.$$

We assume that for each $j = 2, \ldots, n$, one of the following two sets of conditions holds:

$$\mathcal{R}_1 > \mathcal{R}_j \quad \text{and} \quad c_j \geq c_1. \tag{6}$$

$$\mathcal{B}_1 > \mathcal{B}_j \quad \text{and} \quad \beta_1 \geq \beta_j. \tag{7}$$

Assumption (6) and the definition of $\mathcal{R}_0$ implies that $\mathcal{R}_1$ is the basic reproduction number for models (1) and (2).

We begin by defining $s = \frac{S}{N}$, $i_j = \frac{I_j}{N}$, and $r = \frac{R}{N}$. Then the proportional functions s, i_j and r for model (1) satisfy $s + r + \sum_{k=1}^{n} i_k = 1$ and the following system of differential equations:

$$\begin{aligned}
\dot{s} &= s\sum_{k=1}^{n}(\mu_k - \beta_k)i_k + \sum_{k=1}^{n} bi_k + br \\
\dot{i}_j &= i_j\left(\beta_j s + \sum_{k=1}^{n}\mu_k i_k - c_j\right), \quad j = 1, 2, \ldots, n, \\
\dot{r} &= r\left(\sum_{k=1}^{n}\mu_k i_k - b\right) + \sum_{k=1}^{n}\gamma_k i_k.
\end{aligned} \tag{8}$$

For model (2) the differential equations for the proportions satisfy

$$\begin{aligned} \dot{s} &= s\sum_{k=1}^{n}(\mu_k - \beta_k)i_k + \sum_{k=1}^{n}(b+\gamma_k)i_k \\ \dot{i}_j &= i_j\left(\beta_j s + \sum_{k=1}^{n}\mu_k i_k - c_j\right), \quad j = 1,2,\ldots,n, \end{aligned} \tag{9}$$

where $s + \sum_{k=1}^{n} i_k = 1$.

Now we prove that the functions $s(t)$ and $N(t)$ are bounded below by a positive constant for all $t \geq 0$. Hence, complete extinction is not possible.

Lemma 3.1. *Assume (A1)–(A5) hold. Then, in models (1) and (2), there exist positive constants $\underline{s}$ and $\underline{N}$ such that $s(t) \geq \underline{s}$ and $N(t) \geq \underline{N}$ for $t \in [0,\infty)$.*

Proof. Suppose there does not exist such constants $\underline{s}$ and $\underline{N}$. Then there exist monotone sequences of positive numbers $\{\epsilon_l^i\}_{l=1}^{\infty}$ and $\{t_l^i\}_{l=1}^{\infty}$, $i = 1,2$, satisfying $\lim_{l\to\infty}\epsilon_l^i = 0$ and $\lim_{l\to\infty} t_l^i = \infty$ for $i = 1,2$ such that $s(t_l^1) = \epsilon_l^1 > 0$ and $\dot{s}(t_l^1) \leq 0$, $N(t_l^2) = \epsilon_l^2 > 0$ and $\dot{N}(t_l^2) \leq 0$.

For sufficiently large t_l^1 we have from (8)

$$0 \geq \dot{s}(t_l^1) \geq \sum_{k=1}^{n}(b - \beta_k s(t_l^1))i_k(t_l^1) = \sum_{k=1}^{n} i_k(t_l^1)[b - \epsilon_l^1\beta_k] > 0,$$

and from (9)

$$0 \geq \dot{s}(t_l^1) \geq \sum_{k=1}^{n} i_k(t_l^1)[b + \gamma_k - \epsilon_l^1\beta_k] > 0,$$

a contradiction. This establishes the result for s.

For sufficiently large t_l^2, applying assumption (A5), we have

$$0 \geq \dot{N}(t_l^2) = \epsilon_l^2\left(f(\epsilon_l^2) - \sum_{k=1}^{n}\mu_k i_k(t_l^2)\right) \geq \epsilon_l^2(f(\epsilon_l^2) - \bar{\mu}) > 0,$$

a contradiction. □

It follows from Lemma 3.1 that for sufficiently large time t, there exists an $\epsilon > 0$ such that

$$0 < \underline{N} - \epsilon < N(t) < K + \epsilon.$$

Next we show that all of the strains, except possibly one, die out.

Theorem 3.1. *Assume (A1)–(A5) hold. In addition, assume that for each $j = 2,\ldots,n$, either the condition (6) or (7) holds. Then, in models (1) and (2),*

$$\lim_{t\to\infty} I_j(t) = 0 \text{ for } j = 2,3,\ldots,n.$$

Proof. Choose a $j \in \{2, \dots, n\}$ and suppose that condition (6) holds for this j. Define $\Gamma_1(t) = \frac{i_j^{\frac{1}{c_j}}}{i_1^{\frac{1}{c_1}}}$. Then, for $t > 0$

$$\begin{aligned}
\frac{d}{dt}\Gamma_1(t) &= \frac{\frac{1}{c_j} i_j^{\frac{1}{c_j}} \left(\beta_j s + \sum_{k=1}^{n} \mu_k i_k - c_j\right) i_1^{\frac{1}{c_1}} - \frac{1}{c_1} i_1^{\frac{1}{c_1}} \left(\beta_1 s + \sum_{k=1}^{n} \mu_k i_k - c_1\right) i_j^{\frac{1}{c_j}}}{i_1^{\frac{2}{c_1}}} \\
&= \frac{1}{c_j}\Gamma_1(t)\left(\beta_j s + \sum_{k=1}^{n} \mu_k i_k - c_j\right) - \frac{1}{c_1}\Gamma_1(t)\left(\beta_1 s + \sum_{k=1}^{n} \mu_k i_k - c_1\right) \\
&= \Gamma_1(t)\left(\frac{\sum_{k=1}^{n} \mu_k i_k}{c_j} - \frac{\sum_{k=1}^{n} \mu_k i_k}{c_1} + \left(\frac{\beta_j}{c_j} - \frac{\beta_1}{c_1}\right) s\right) \\
&\leq \Gamma_1(t)\left(\frac{\beta_j}{c_j} - \frac{\beta_1}{c_1}\right) \underline{s}.
\end{aligned}$$

This latter inequality implies that

$$\Gamma_1(t) \leq \Gamma_1(0) e^{\left(\frac{\beta_j}{c_j} - \frac{\beta_1}{c_1}\right) \underline{s}\, t}.$$

Thus,

$$i_j^{\frac{1}{c_j}}(t) \leq i_1^{\frac{1}{c_1}}(t)\Gamma_1(0) e^{\left(\frac{\beta_j}{c_j} - \frac{\beta_1}{c_1}\right) \underline{s}\, t}.$$

Since i_1 is bounded, $\underline{s} > 0$, and $\left(\frac{\beta_j}{c_j} - \frac{\beta_1}{c_1}\right) < 0$ we have $\lim_{t\to\infty} i_j(t) = 0$. Because $I_j(t) = i_j(t)N(t) \leq i_j(t)(K+\epsilon)$ for t sufficiently large it follows that $\lim_{t\to\infty} I_j(t) = 0$. Note that we did not use assumption (A5).

Now suppose that for the same j, condition (7) holds. Define $\Gamma_2(t) = \frac{I_j^{\frac{1}{\beta_j}}}{I_1^{\frac{1}{\beta_1}}}$. Using assumption (A3) and a similar technique as in [1] we show that for all $t > 0$

$$\begin{aligned}
\frac{d}{dt}\Gamma_2(t) &= \Gamma_2(t)\left(\frac{f(N)}{\beta_j} - \frac{f(N)}{\beta_1} + \left(\frac{c_1}{\beta_1} - \frac{c_j}{\beta_j}\right)\right) \\
&\leq \Gamma_2(t)\left(\frac{c_1 - f\,(0)}{\beta_1} - \frac{c_j - f\,(0)}{\beta_j}\right).
\end{aligned}$$

Hence, using (7) we get $\lim_{t\to\infty} I_j(t) = 0$. By (A5) and Lemma 3.1, $I_j(t) = i_j(t)N(t) \geq i_j(t)(\underline{N} - \epsilon) > 0$, so that for t sufficiently large, $\lim_{t\to\infty} i_j(t) = 0$. □

We have proved that under the conditions (6) or (7) the pathogen strains with suboptimal reproduction numbers $\mathcal{R}_j$ or $\mathcal{B}_j$, $j = 2, 3, \dots, n$ die out, but we did not show whether the disease persists. This will depend on the reproduction number $\mathcal{R}_1$. The next result proves that if $\mathcal{R}_1 > 1$, then the disease persists.

Theorem 3.2. *Assume (A1)–(A5) hold. In addition, assume that for each $j = 2, \dots, n$, either (6) or (7) holds and $\mathcal{R}_1 > 1$. Then, in models (1) and (2),*

$$\liminf_{t\to\infty} I_1(t) > 0.$$

Proof. Assume that $I_1(t) \to 0$ as $t \to \infty$. Then $\lim_{t\to\infty} i_1(t) = 0$ and using the previous result we have that $\sum_{k=1}^{n} \mu_k i_k(t) \to 0$. Hence, $\lim_{t\to\infty} N(t) = K$. Also, in model (1), $\lim_{t\to\infty} R(t) = 0$ and $\lim_{t\to\infty} s(t) = 1$. From the i_1 equation in (8)

or (9) it follows that $\frac{\dot{i}_1(t)}{i_1(t)} \to \beta_1 - c_1 > 0$ which says that $i_1(t)$ grows exponentially as $t \to \infty$. This contradiction implies

$$\limsup_{t\to\infty} I_1(t) \geq \bar{\epsilon} > 0.$$

Now assume that $\liminf_{t\to\infty} I_1(t) = 0$. This implies $\liminf_{t\to\infty} i_1(t) = 0$. Then for any $0 < \epsilon < \bar{\epsilon}$ there exists two increasing sequences $t_m, \tau_m \to \infty$ as $m \to \infty$ such that

$$i_1(t_m) = \epsilon, \quad i_1(t_m + \tau_m) = \frac{\epsilon}{m}, \quad \frac{\epsilon}{m} \leq i_1(t) \leq \epsilon, \quad t_m \leq t \leq t_m + \tau_m.$$

For any $0 < \delta < 1$ we can choose $\epsilon > 0$ small enough such that the following two inequalities hold for $t_m \leq t \leq t_m + \tau_m$ and m sufficiently large:

$$\sum_{k=1}^{n} i_k(t) \quad \leq \quad \delta \tag{10}$$

$$\delta\left(\sum_{k=1}^{n} \mu_k i_k(t) - b\right) + \sum_{k=1}^{n} \gamma_k i_k(t) \quad \leq \quad -\frac{b\delta}{2}. \tag{11}$$

These inequalities are a consequence of the choice of ϵ, where on the subintervals, $[t_m, t_m + \tau_m]$, the summations with $i_k(t)$ are sufficiently small.

Define

$$\tau = \frac{2(1-\delta)}{b\delta}. \tag{12}$$

Then choose m large enough so that $\tau_m > \tau$ and the inequalities (10) and (11) are satisfied. We will now show that

$$r(t) \leq \delta, \quad t_m + \tau \leq t \leq t_m + \tau_m. \tag{13}$$

Note that $\sum_{k=1}^{n} \mu_k i_k(t) - b \leq -b/2$ from inequality (11). Therefore, from the r equation in (8) and inequality (11) we have for any $t_m < t \leq t_m + \tau_m$ satisfying $r(t) \geq \delta$,

$$\dot{r}(t) \leq -\frac{b\delta}{2}. \tag{14}$$

If $r(t_m) \leq \delta$, then $r(t) \leq \delta$ for $t_m \leq t \leq t_m + \tau_m$. If not, there exists a time $t_m < \tau_1 \leq t_m + \tau_m$ such that $r(\tau_1) > \delta$ and $\dot{r}(\tau_1) > 0$ which contradicts (14). Suppose that $r(t_m) > \delta$. Then using (14) there exists a $\tau_2 > t_m$ such that $r(t) > \delta$ for all $t \in (t_m, \tau_2)$ and $r(\tau_2) = \delta$. Consider the differential equation

$$\begin{aligned} \dot{z}(t) &= -\frac{b\delta}{2}, \qquad t > t_m \\ z(t_m) &= 1. \end{aligned}$$

Integrating this differential equation we get $z(t) = 1 - b\delta(t - t_m)/2$. Therefore, for τ defined by (12), $z(t_m + \tau) = \delta$. Because r satisfies (14) and $r(t_m) \leq 1$ it follows that $\tau_2 \leq \tau$. Using the facts that $r(\tau_2) = \delta$ and $\tau_2 \leq \tau$ and applying the previous argument, we get that $r(t) \leq \delta$ for all $t_m + \tau \leq t \leq t_m + \tau_m$. This proves (13).

From (10)–(13) it follows that s in (8) satisfies

$$s(t) = 1 - r(t) - \sum_{k=1}^{n} i_k(t) \geq 1 - 2\delta, \quad t_m + \tau \leq t \leq t_m + \tau_m$$

and s in (9) satisfies

$$s(t) = 1 - \sum_{k=1}^{n} i_k(t) \geq 1 - \delta > 1 - 2\delta, \quad t_m + \tau \leq t \leq t_m + \tau_m.$$

Now, choose $\delta > 0$ small enough such that

$$\beta_1(1 - 2\delta) - c_1 = \eta > 0. \tag{15}$$

Note that the expression on the left-hand side of (15) is positive because it can be made sufficiently close to $\beta_1 - c_1 > 0$. Then from the i_1 equation in (8) or (9) we get

$$\begin{aligned}\epsilon \geq i_1(t_m + \tau_m) &= i_1(t_m) e^{\int_{t_m}^{t_m+\tau} \left(\beta_1 s + \sum_{k=1}^{n} \mu_k i_k - c_1\right) dt} e^{\int_{t_m+\tau}^{t_m+\tau_m} \left(\beta_1 s + \sum_{k=1}^{n} \mu_k i_k - c_1\right) dt} \\ &\geq i_1(t_m) e^{-c_1 \tau} e^{\eta(\tau_m - \tau)},\end{aligned}$$

a contradiction, since $\tau_m \to \infty$. □

The next result shows that if for each $j = 2, \ldots, n$, either (6) or (7) are satisfied but $\mathcal{R}_1 < 1$, then solutions approach the DFE; the DFE is globally asymptotically stable.

Theorem 3.3. *Assume (A1)–(A5) hold. In addition, assume that for each $j = 2, \ldots, n$, either the condition (6) or (7) holds and $\mathcal{R}_1 < 1$. Then, in models (1) and (2),*

$$\lim_{t \to \infty} (S(t), \sum_{j=1}^{n} I_j(t)) = (K, 0).$$

Proof. From the i_1 equation in (8) we have

$$\dot{i_1} = i_1 \left(\beta_1 s - c_1 + \mu_1 i_1 + \sum_{k=2}^{n} \mu_k i_k \right). \tag{16}$$

Note that since $s(t) \geq \underline{s}$, then there exists a $\delta > 0$ such that $0 < i_1(t) \leq 1 - \delta$. Hence, it follows in a similar manner as the proof of Theorem 4 in [1] that $\lim_{t \to \infty} i_1(t) = 0$. Because $I_1(t) \leq i_1(t)(K + \epsilon)$ for t sufficiently large, it follows that $\lim_{t \to \infty} I_1(t) = 0$. Thus, in model (1), $\lim_{t \to \infty} R(t) = 0$, and in models (1) and (2), $\lim_{t \to \infty} S(t) = K$. □

The condition (A5) that prevents total population extinction can be weakened for some special cases of Theorems 3.2 and 3.3 as follows:

(A5)′ $f(0) > \mu_1$.

If the assumptions (A1)–(A4) are satisfied, and the condition (6) holds for $j = 2, \ldots, n$, then it follows from Theorem 3.1 that $\lim_{t \to \infty} i_j(t) = 0$ for $j = 2, \ldots, n$. In this case assumption (A5) is not needed and we obtain the following result.

Corollary 3.1. *Assume (A1)–(A4) hold.*

(i) *If condition (6) holds for $j = 2, \ldots, n$ and $\mathcal{R}_1 < 1$. Then, in models (1) and (2), $\lim_{t \to \infty} (S(t), \sum_{j=1}^{n} I_j(t)) = (K, 0)$.*
(ii) *If (A5)′ holds, the condition (6) is satisfied for $j = 2, \ldots, n$, and $\mathcal{R}_1 > 1$. Then, in models (1) and (2), $\liminf_{t \to \infty} I_1(t) > 0$.*

Proof. Under the assumptions in part (i), the proofs of Theorems 3.1 and 3.3 show that

$$\lim_{t\to\infty} \sum_{j=1}^{n} \mu_j i_j(t) = 0.$$

Then, for any $\epsilon > 0$, there exists a time T such that for $t > T$

$$N(f(N) - \epsilon) \leq \dot{N} \leq Nf(N).$$

By comparison, it follows that $\lim_{t\to\infty} N(t) = K$ and the conclusion of part (i) follows.

To prove part (ii), it is necessary to show that total population extinction cannot occur. Because $\lim_{t\to\infty} i_j(t) = 0$ for $j = 2, \ldots, n$ (Theorem 3.1), choose ϵ sufficiently small and T sufficiently large such that for $t > T$,

$$\sum_{j=2}^{n} \mu_j i_j(t) < \epsilon < f(0) - \mu_1.$$

Then for $t > T$,

$$\dot{N} \geq N(f(N) - \mu_1 - \epsilon).$$

It follows as in the proof of Lemma 3.1 that there exists $\underline{N} > 0$ such that $N(t) > \underline{N}$ for all $t \geq 0$. Now the proof of part (ii) follows directly from the proof of Theorem 3.2. □

4. **Numerical Examples.** We consider two strains, $n = 2$. The initial conditions $S(0) = 1$, $I_j(0) = 1$, $R(0) = 0$ are used in all the figures presented in this section. The first example demonstrates that if neither conditions (6) nor (7) are satisfied, there may be coexistence of both strains. We make some hypothetical but reasonable assumptions regarding the model parameters. Let $f(N) = r(1 - N/K)$, where the carrying capacity is $K = 100$ and intrinsic growth rate is $r = 5$. Suppose the birth rate $b = 6$ and the transmission, recovery, and disease-related death rates for the two strains are $\beta_1 = 30$, $\beta_2 = 15$, $\gamma_1 = 6$, $\gamma_2 = 1$, $\mu_1 = 4$, and $\mu_2 = 1.4$. Because of the high birth rate, the time unit for the progression of human diseases (e.g., sexually transmitted disease) may be decades. However, for animal diseases (e.g., hantavirus in rodents), the time unit may be years. Both strains are easily transmissible (large β_j) but the first strain has a greater transmission, recovery, and death rate than the second strain. Assumptions (A1)–(A5) hold. In this example, the reproduction number $\mathcal{R}_1 = 1.875 > 1.786 = \mathcal{R}_2$ but $c_1 = 16 > 8.4 = c_2$. Because $\mathcal{R}_j > 1$, $j = 1, 2$, a single strain could persist in the population in the absence of other competing strains. The parameters $\mathcal{B}_1 = 2.727 < 4.412 = \mathcal{B}_2$ but $\beta_1 > \beta_2$. Neither conditions (6) nor (7) are satisfied. In model (1), there is a locally stable coexistence equilibrium at $\bar{I}_1 = 12.605$ and $\bar{I}_2 = 11.986$ (Figure 2 (a)). In model (2), there is a locally stable coexistence equilibrium at $\bar{I}_1 = 3.532$ and $\bar{I}_2 = 37.908$ (Figure 2 (b)).

Suppose strain 2 becomes more virulent, so that the disease-related death rate due to strain 2 increases to $\mu_2 = 2.2$. All of the other parameters remain the same as in Figure 2. In this case, the equilibrium with strain 1 positive and strain 2 zero changes from unstable to stable in models (1) and (2) (see Figure 3). Eventually there are no individuals infected with strain 2; strain 1 is dominant. Now, suppose strain 2 becomes less virulent, so that the disease-related death rate due to strain 2 decreases to $\mu_2 = 1.1$. Then the equilibrium with strain 2 positive and strain 1 zero changes from unstable to stable in models (1) and (2). Eventually, there

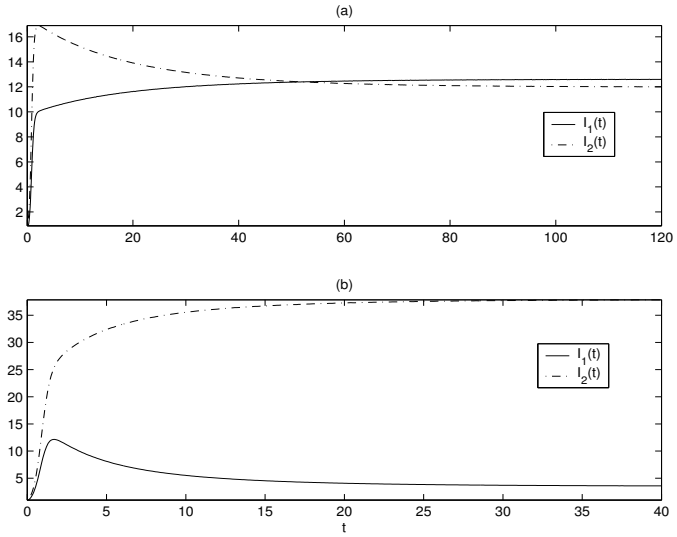

FIGURE 2. Coexistence in models (1) and (2) when conditions (6) and (7) are not satisfied. Figure (a) represents the results of model (1) while figure (b) represents the results of model (2).

are no individuals infected with strain 1; strain 2 is dominant. The numerical simulations indicate that the equilibria in these latter two examples are globally stable; coexistence does not occur. It is interesting to note that in these examples $\mathcal{R}_1 > \mathcal{R}_2 > 1$ but neither conditions (6) nor (7) are satisfied. Therefore, conditions (6) or (7) are sufficient but not necessary for competitive exclusion to occur.

Epidemic models with standard incidence can result in total population extinction, $N(t) \to 0$ (see e.g., [2]). Suppose the two strains have transmission, recovery, and disease-related death rates similar in magnitude to the previous examples, that is, $\beta_1 = 30$, $\beta_2 = 15$, $\gamma_1 = 2$, $\gamma_2 = 1$, $\mu_1 = 5$, and $\mu_2 = 2$. The first strain has higher transmission, recovery, and disease-related death rates than the second strain. We assume that the birth rate b is the same as in the previous examples, $b = 6$. However, the natural death rate, $b - f(N)$, is much greater, $f(N) = r(1 - N/K)$, where $r = 2$ and $K = 100$. In this example, condition (7) is satisfied, but not condition (6), $\mathcal{B}_1 = 2.727 > 2.143 = \mathcal{B}_2$ and $\beta_1 = 30 > 15 = \beta_2$; $\mathcal{R}_1 = 2.308 > 1.667 = \mathcal{R}_2$ and $c_2 = 9 < 13 = c_1$. In addition, neither conditions (A5) nor (A5)$'$ are satisfied. For these parameter values, occurrence of an epidemic causes total population extinction. The growth rate $f(0) = r = 2$ is too small to sustain the population at low population levels when the disease-related death rate is large, $\mu_1 = 5$. However, it is interesting to note that the infected proportion i_1 persists but not i_2; $i_1(t) \to 0.4208$ and $i_2(t) \to 0$ in model (1) while in model (2) $i_1(t) \to 0.6461$ and $i_2(t) \to 0$ (see Figure 4).

5. **Concluding Remarks.** In models (1) and (2), the host population size is regulated by two different factors. When disease is absent, the population size is regulated by natural mortality, $b - f(N)$, which depends on the population size N. When disease is present, there is an additional mortality factor due to disease-related deaths, μ_j, which also depends on the host population size through the

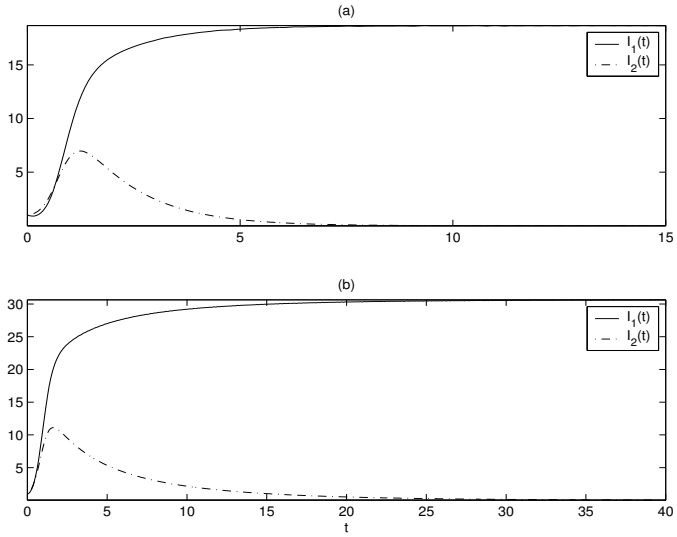

FIGURE 3. Competitive exclusion when conditions (6) and (7) are not satisfied. Figure (a) represents the results of model (1) while figure (b) represents the results of model (2).

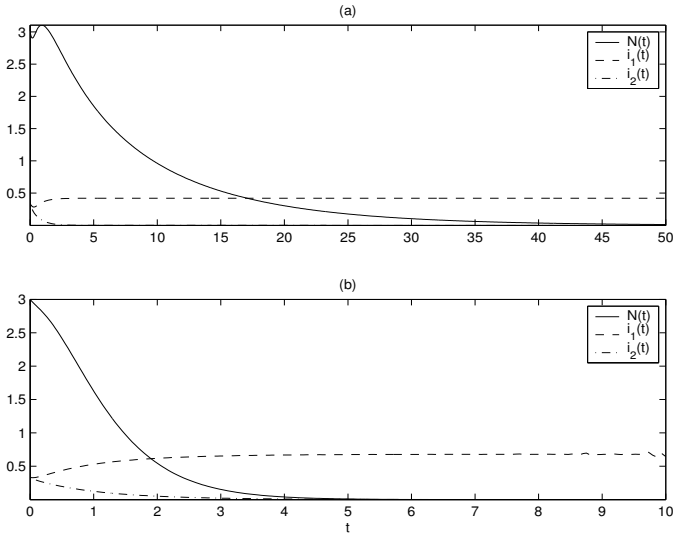

FIGURE 4. Extinction of the total population N when conditions (A5) and (A5)′ are not satisfied. Figure (a) represents the results of model (1) while figure (b) represents the results of model (2).

transmission rate [6, 18]. Because these two mortality factors affect the dynamics of the host population size in different ways, their combination may change the outcome of competition [6]. We have shown in models (1) and (2) and it has been demonstrated in other models with disease-related deaths and density-dependent

natural mortality that there are cases where competitive exclusion of all but one strain or where coexistence of more than one strain may occur [1, 6, 12, 28, 31].

We conclude with two final remarks. First, when $\mathcal{R}_j > 1$, it is straightforward to show that an equilibrium exists with a single strain j in the SIS epidemic model. In fact, the proportional equilibrium values $\bar{s}$ and $\bar{i}_j$ satisfy

$$\bar{s} = \frac{b + \gamma_j}{\beta_j - \mu_j} \quad \text{and} \quad \bar{i}_j = \frac{\beta_j - c_j}{\beta_j - \mu_j}.$$

The equilibrium values $\bar{S} = \bar{s}\bar{N}$ and $\bar{I}_j = \bar{i}_j\bar{N}$, where $\bar{N}$ is the unique solution to $f(\bar{N}) = \mu_j\bar{i}_j$. It is possible that many other equilibria exist with one or more strains present. However, the results of the theorems and the numerical examples show that these various equilibria may not be stable. Second, the theoretical results can be generalized to the case where there is some vertical transmission of strain j as in [1]. If the birth rate of the jth infected class is divided into two parts: $b_j > 0$, denoting those born susceptible, and $b - b_j \geq 0$ denoting those born infected, then the theoretical results apply with $\mathcal{R}_j$ and $\mathcal{B}_j$ given by (4) and (5), respectively. However, with vertical transmission $\mathcal{R}_j$ is not the basic reproduction number for strain j. The basic reproduction number in the case of vertical transmission is given by

$$\frac{\beta_j + b - b_j}{c_j}.$$

An equilibrium stability analysis is presented in [3] for an SIS epidemic model similar to (2) but with two strains, where one strain is transmitted vertically and the other horizontally.

Acknowledgements. A.S. Ackleh was partially supported by the NSF grant # DMS-0311969. L.J.S. Allen was partially supported by the NSF grant # DMS-0201105. We thank Pauline van den Driessche for helpful discussions on the basic reproduction number and two anonymous referees for their useful suggestions.

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Received September 2003; revised August 2004

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