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Competitive exclusion and coexistence for pathogens in an epidemic model with variable population size

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Abstract. We study an SIR epidemic model with a variable host population size. We prove that if the model parameters satisfy certain inequalities then competition between n pathogens for a single host leads to exclusion of all pathogens except the one with the largest basic reproduction number. It is shown that a knowledge of the basic reproduction numbers is necessary but not sufficient for determining competitive exclusion. Numerical results illustrate that these inequalities are sufficient but not necessary for competitive exclusion to occur. In addition, an example is given which shows that if such inequalities are not satisfied then coexistence may occur.

1. Introduction

A very important principle in theoretical biology is that of competitive exclusion: *no two species can indefinitely occupy the same ecological niche*. Discussions on the meaning of competitive exclusion and ecological niche have been central to ecology [19,21,25].

The validity of such a principle has been proved for many population models. For example, in [3,26,33] the authors study a competitive Lotka-Volterra system of equations and exhibit a simple algebraic criteria on the parameters which guarantee that all but one of the species are driven to extinction. These results have been extended in [1] to a generalized logistic model. Using the theory of weak convergence of probability measures the authors show that such a principle is valid for the model they investigated. In [2], a predator–prey Lotka-Volterra model composed of many predator–prey subpopulations was studied. Therein, it was shown that all subpopulations die out except for the predator–prey pair that optimizes the growth to mortality ratio. In [31], competitive exclusion is proved for a discrete-time, size-structured, nonlinear matrix model of m competing species in a chemostat. The winner is the population which is able to grow at the lowest nutrient concentration.

Recently, attention has focused on understanding the mechanisms that lead to coexistence, competitive exclusion and coevolution of pathogen strains in infectious diseases. This is especially important for the development of disease management

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strategies. In [6], Anderson and May state that transmission rate and virulence are not independent and that evolution does not necessarily lead to reduced virulence. Levin and Pimentel [20] model two pathogen strains; they show that an excessively virulent pathogen strain can prevail if it can invade a host that harbors the less virulent strain, but not vice versa; such behavior is referred to as superinfection. In [11], Bremermann and Thieme consider an n-pathogen, single host model. They show that pathogen strains with differing levels of virulence die out asymptotically except for those that optimize the basic reproduction number. From these three classical papers, there followed numerous other papers examining the relationships between evolution and virulence or coexistence and competitive exclusion (e.g., [7, 14–18, 22–24, 27, 28, 32]). For example, models with coinfection, where the host harbors multiple infections at one time (e.g., [23, 24, 32]) and models with superinfection, where less virulent strains are replaced by more virulent strains (e.g., [16, 17, 22, 27]), have demonstrated a variety of coexistence and virulence evolution results. In addition, strong density regulation has been shown to result in coexistence of more than one strain [7, 16]. This is due to the different ways in which host density affects the transmission rate and transmission period [7].

The goal of this paper is to study competitive exclusion in an n-pathogen, single host model, where each pathogen may invade the host population. We do not consider coinfection nor superinfection, only density-dependent host regulation. Our model is a generalization of the two-pathogen model studied by Andreasen and Pugliese [7]. It is shown in our model that a knowledge of the basic reproduction numbers is necessary but not sufficient to determine competitive exclusion. The basic reproduction numbers are important in determining successful invasion of a pathogen but are not sufficient to determine extinction of particular strains.

This paper is organized as follows. In Section 2 we describe the model while in Section 3 we prove the competitive exclusion principle. Section 4 is devoted to a numerical example which illustrates that the conditions of Section 3 imposed on the model parameters are sufficient but not necessary for competitive exclusion. While in Section 5 we discuss an example in which survival of strains which do not optimize the reproduction number is possible. In the Appendix, we give a dynamical systems proof for the persistence of the dominant strain.

2. The model

We describe an SIR epidemic model which is based on a modification of the models by Anderson and May [5] and Bremermann and Thieme [11]. In the Anderson and May model exponential growth of the host population is allowed. This is in general not very realistic for a long period of time. In the Bremermann and Thieme model they guarantee limited host populations by assuming that the birth rate is a strictly decreasing function of the total population size. Here we assume that there is a density-dependent death rate, $b - f(N)$, a constant birth rate, b, and a logistic-type population growth rate. 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 assume that $f(N)$ satisfies the following conditions:

(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 $f(K) = 0$.

For example, the following logistic growth rate function satisfies the above conditions: $f(N) = r(1 - N/K)$, where $0 < r < b$. Similar assumptions have been made in other epidemic models (see e.g., [4,7,9,34]).

The model we study is of SIR type, in that the host population consists of susceptibles, S, individuals infected with strains 1 through n, I_j, $j = 1, 2, \ldots, n$, and immune or removed individuals, R. In addition, it is assumed that there is mass action horizontal transmission. The model has the form:

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

In model (1), b is the birth rate, $f(N)$ is the per capita growth rate, and $b - f(N)$ is the natural death rate. Infected individuals may transmit the disease to their offspring–vertical transmission. Hence, the birth rate of the jth infected class is divided into two parts: b_j, denoting those born susceptible, and $b - b_j \geq 0$, denoting those born infected. 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. All of the parameters, b, b_j, μ_j, β_j, and γ_j, $j = 1, 2, \ldots, n$, are assumed to be positive. Models of the type (1) with total cross immunity and no superinfection have been applied to some sexually transmitted diseases (e.g., [14]).

Model (1) differs from the model of Bremermann and Thieme [11]. In [11], they assume a density-dependent birth rate $g(N)$ instead of a density-dependent death rate. In addition, no density-dependent birth or death rates are assumed in the infected and removed classes and the change in the susceptible subpopulation satisfies

$$\dot{S}(t) = Ng(N) - dS - S\sum_{j=1}^{n} \beta_j I_j,$$

where d is the natural death rate. The example discussed in Section 5 shows that our model exhibits different behavior than their model. In particular, coexistence occurs when there is strong density regulation affecting the death rate.

In the presence of the disease, the population size N in our model is described by the following differential equation:

$$\dot{N}(t) = Nf(N) - \sum_{j=1}^{n} \mu_j I_j. \tag{2}$$

We assume that $S(0) > 0$, $I_j(0) > 0$, $j = 1, 2, \ldots, n$, and $R(0) \geq 0$. Clearly, solutions to (1) 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 $y(t)$ to the differential equation $\dot{y}(t) = yf(y)$ with $y(0) = N(0)$ satisfies $\lim_{t\to\infty} y(t) = K$, it follows by comparison that $\limsup_{t\to\infty} N(t) \leq K$.

The competitive exclusion principle is verified in the next section for the basic model (1).

3. Competitive exclusion

Let $c_j = b_j + \gamma_j + \mu_j > f(0)$. Then the basic reproduction number for strain j is given by

$$\mathcal{R}_{0,j} = \frac{\beta_j}{c_j} K, \qquad j = 1, 2, \ldots, n.$$

We define

$$\mathcal{B}_{0,j} = \frac{\beta_j K}{c_j - f(0)}, \qquad j = 1, 2, \ldots, n,$$

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

$$\mathcal{R}_{0,1} > \mathcal{R}_{0,j} \text{ and } c_j > c_1, \tag{3}$$

or

$$\mathcal{B}_{0,1} > \mathcal{B}_{0,j} \text{ and } \beta_1 > \beta_j. \tag{4}$$

The following stronger conditions imply (3) or (4):

$$\mathcal{R}_{0,1} > \mathcal{R}_{0,j} \text{ and } \mathcal{B}_{0,1} > \mathcal{B}_{0,j}.$$

The conditions in (3) are satisfied for all $j = 2, \ldots, n$, for example, if strain 1 has the largest basic reproduction number $\mathcal{R}_{0,1}$ and the smallest disease-related death rate, recovery rate, and birth rate. The ratio $\mathcal{B}_{0,j}$ can be thought of as a reproduction number also. When $b_j = b$ and $f(0) = r = b - d$, where r is the intrinsic growth rate and d is the density-independent death rate,

$$\mathcal{B}_{0,j} = \frac{\beta_j K}{d + \gamma_j + \mu_j}.$$

In addition, if the total population size is constant, $b = d$, then $\mathcal{B}_{0,j} = \mathcal{R}_{0,j}$. The conditions in (4) are satisfied for all $j = 2, \ldots, n$, for example, if strain 1 has the largest reproduction number $\mathcal{B}_{0,1}$ and the largest transmission rate.

We remark that Bremermann and Thieme [11] only assumed that $\mathcal{R}_{0,1} > \mathcal{R}_{0,j}$ to prove the competitive exclusion principle. The example given in Section 5 shows that this condition alone is not sufficient for competitive exclusion to occur in our model. Our first result in this section is to show that the number of susceptibles, $S(t)$, is bounded below by a positive constant.

Lemma 1. *There exists a constant $\underline{S} > 0$ such that $S(t) \geq \underline{S}$ for $t \in [0, \infty)$.*

Proof. First note that if $N(t) > K$ for all $t \geq 0$ then we have that $\lim_{t\to\infty} N(t) = K$. In this case one can easily show that $S(t) \to K$ as $t \to \infty$ and hence the result follows. To this end, we assume for the rest of the proof that there exists a $t_0 \geq 0$ such that $N(t_0) \leq K$. Then it is clear that $N(t) \leq K$ for all $t \geq t_0$. Now, suppose there does not exist such a constant $\underline{S}$. Then there exist monotone sequences of numbers $\{\epsilon_i\}_{i=1}^{\infty}$ and $\{t_i\}_{i=1}^{\infty}$ satisfying $\lim_{i\to\infty} \epsilon_i = 0$, $t_i \geq t_0$, $i = 1, 2, \ldots$, and $\lim_{i\to\infty} t_i = \infty$ such that $S(t_i) = \epsilon_i > 0$ and $\dot{S}(t_i) \leq 0$.

Hence for sufficiently large t_i we have

$$0 \geq \dot{S}(t_i) = S(t_i) f(N(t_i)) + \sum_{j=1}^{n} I_j(t_i)[b_j - \epsilon_i \beta_j] + bR(t_i)$$

$$\geq \sum_{j=1}^{n} I_j(t_i)[b_j - \epsilon_i \beta_j] > 0,$$

a contradiction. This establishes the result. □

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

Theorem 2. *Assume that for each $j = 2, \ldots, n$, either (3) or (4) holds. Then, for $j = 2, 3, \ldots, n$, $\lim_{t\to\infty} I_j(t) = 0$.*

Proof. We divide the proof into two cases. First assume that the conditions in (3) hold for a fixed $j \in \{2, \ldots, n\}$ and define $\Gamma_1(t) = \dfrac{I_j^{\frac{1}{c_j}}}{I_1^{\frac{1}{c_1}}}$. Using the assumptions on f, the previous Lemma, and the fact that $\limsup_{t\to\infty} N(t) \leq K$ we can choose $\bar{t}$ large enough such that $f(N(t))(\frac{1}{c_j} - \frac{1}{c_1}) \leq \frac{1}{2}\left(\frac{\beta_1}{c_1} - \frac{\beta_j}{c_j}\right)\underline{S}$ for all $t \geq \bar{t}$. Hence, for any $t \geq \bar{t}$

$$\frac{d}{dt}\Gamma_1(t) = \frac{\frac{1}{c_j} I_j^{\frac{1}{c_j}} (f(N) + \beta_j S - c_j) I_1^{\frac{1}{c_1}} - \frac{1}{c_1} I_1^{\frac{1}{c_1}} (f(N) + \beta_1 S - c_1) I_j^{\frac{1}{c_j}}}{I_1^{\frac{2}{c_1}}}$$

$$= \frac{1}{c_j}\Gamma_1(t)(f(N) + \beta_j S - c_j) - \frac{1}{c_1}\Gamma_1(t)(f(N) + \beta_1 S - c_1)$$

$$= \Gamma_1(t)\left(\frac{f(N)}{c_j} - \frac{f(N)}{c_1} + \left(\frac{\beta_j}{c_j} - \frac{\beta_1}{c_1}\right) S\right)$$
$$\leq \frac{1}{2}\Gamma_1(t)\left(\frac{\beta_j}{c_j} - \frac{\beta_1}{c_1}\right)\underline{S}.$$

Expressed in terms of logarithms,

$$\frac{d\ln\Gamma_1(t)}{dt} \leq \frac{1}{2}\left(\frac{\beta_j}{c_j} - \frac{\beta_1}{c_1}\right)\underline{S}.$$

This latter inequality implies that

$$\Gamma_1(t) \leq \Gamma_1(0)e^{\frac{1}{2}\left(\frac{\beta_j}{c_j} - \frac{\beta_1}{c_1}\right)\underline{S}\,t}.$$

Thus,

$$I_j^{\frac{1}{c_j}}(t) \leq I_1^{\frac{1}{c_1}}(t)\Gamma_1(0)e^{\frac{1}{2}\left(\frac{\beta_j}{c_j} - \frac{\beta_1}{c_1}\right)\underline{S}\,t}.$$

Since I_1 is bounded, $\underline{S} > 0$, and $\left(\frac{\beta_j}{c_j} - \frac{\beta_1}{c_1}\right) < 0$ we have $\lim_{t\to\infty} I_j(t) = 0$.

Now suppose that for the same j condition (4) holds and define $\Gamma_2(t) = \frac{I_j^{\frac{1}{\beta_j}}}{I_1^{\frac{1}{\beta_1}}}$. Using assumption (A3) we see that for all $t > 0$

$$\frac{d}{dt}\Gamma_2(t) = \Gamma_2(t)\left(\frac{f(N)}{\beta_j} - \frac{f(N)}{\beta_1} + \left(\frac{c_1}{\beta_1} - \frac{c_j}{\beta_j}\right)\right)$$
$$\leq \Gamma_2(t)\left(f(0)\left(\frac{1}{\beta_j} - \frac{1}{\beta_1}\right) + \left(\frac{c_1}{\beta_1} - \frac{c_j}{\beta_j}\right)\right)$$
$$= \Gamma_2(t)\left(\frac{c_1 - f\,(0)}{\beta_1} - \frac{c_j - f\,(0)}{\beta_j}\right).$$

Hence, using (4) and arguing as before we get $\lim_{t\to\infty} I_j(t) = 0$.

Since j was arbitrary, we have $\lim_{t\to\infty} I_j(t) = 0$ for $j = 2, \ldots, n$. □

We have so far proved that under the conditions (3) or (4) the pathogen strains with suboptimal reproduction numbers $\mathcal{R}_{0,j}$ or $\mathcal{B}_{0,j}$, $j = 2, 3, \ldots, n$, die out, but we did not show whether the disease persists. This will depend on the reproduction number $\mathcal{R}_{0,1}$. The next result proves that if $\mathcal{R}_{0,1} > 1$, then the disease persists.

Theorem 3. *Assume that for each $j = 2, \ldots, n$, either (3) or (4) holds and $\mathcal{R}_{0,1} > 1$, then* $\liminf_{t\to\infty} I_1(t) > 0$.

Proof. Assume that $I_1(t) \to 0$ as $t \to \infty$. Since $N(t) \geq S(t) \geq \underline{S} > 0$ then it follows from Theorem 2 that for $j = 1, 2, \ldots, n$, $\frac{I_j(t)}{N(t)} \to 0$ as $t \to \infty$. Hence, we have $\sum_{j=1}^{n} \mu_j \frac{I_j(t)}{N(t)} \to 0$ as $t \to \infty$. From this one can verify that $N(t) \to K$ as $t \to \infty$. This implies that $f\,(N(t)) \to 0$ and hence $R(t) \to 0$ as $t \to \infty$. Thus

$S(t) \to K$ as $t \to \infty$. From the I_1 equation in (1) we see that $\frac{\dot{I}_1(t)}{I_1(t)} \to \beta_1 K - c_1 > 0$ which says that I_1 grows exponentially as $t \to \infty$. This contradiction implies that

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

Now assume that $\liminf_{t\to\infty} I_1(t) = 0$. Then for any $0 < \epsilon < \bar{\epsilon}$ there exists two sequences $t_m, s_m \to \infty$ as $m \to \infty$ such that $t_1 < s_1 < t_2 < s_2 < \cdots < t_m < s_m < \cdots$ and

$$I_1(t_m) = \epsilon, \quad I_1(s_m) = \frac{\epsilon}{m}, \quad \frac{\epsilon}{m} \leq I_1(t) \leq \epsilon \quad t_m \leq t \leq s_m.$$

From the I_1 equation in (1) we get that there exists a positive constant A such that

$$\frac{\dot{I}_1}{I_1} \geq -A.$$

Integrating from t_m to s_m we obtain

$$\ln \frac{1}{m} \geq -A(s_m - t_m).$$

Letting $m \to \infty$ we obtain that $s_m - t_m \to \infty$. Let $\tau_m = s_m - t_m$. Then clearly $\tau_m \to \infty$.

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

$$f(K - \delta) - \sum_{j=1}^{n} \mu_j \frac{I_j(t)}{N(t)} > 0, \tag{5}$$

$$\delta(f(K - \delta) - b) + \sum_{j=1}^{n} \gamma_j I_j(t) < 0, \tag{6}$$

$$\sum_{j=1}^{n} I_j(t) \leq \delta. \tag{7}$$

These inequalities are a consequence of the choice of ϵ and $0 < f(K - \delta) < b$, where on the subintervals, $[t_m, t_m + \tau_m]$, the summations with $I_j(t)$ are sufficiently small. Since, $\limsup_{t\to\infty} N(t) \leq K$, then for any sufficiently large m we have that

$$N(t) \leq K + \delta, \quad t_m \leq t \leq t_m + \tau_m.$$

Furthermore, using (2) and (5) we see that there exists a $\bar{\tau}$ such that

$$N(t) \geq K - \delta, \quad t_m + \bar{\tau} \leq t \leq t_m + \tau_m. \tag{8}$$

From the R equation in (1) and (6), we obtain

$$R(t) \leq \delta, \quad t_m + \tau \leq t \leq t_m + \tau_m, \tag{9}$$

provided we choose $\tau(>\bar{\tau})$ large enough. Hence, it follows from (7)–(9) that

$$S(t) = N(t) - R(t) - \sum_{j=1}^{n} I_j(t) \geq K - 3\delta, \quad t_m + \tau \leq t \leq t_m + \tau_m.$$

Now, choose $0 < \delta < K$ small enough such that

$$f(K+\delta) + \beta_1(K - 3\delta) - c_1 = \eta > 0. \tag{10}$$

Note that the expression on the left-hand side of (10) is positive because it can be made sufficiently close to $\beta_1 K - c_1 > 0$. Then from the I_1 equation in (1) we get

$$\begin{aligned}\epsilon \geq I_1(t_m + \tau_m) &= I_1(t_m) e^{\int_{t_m}^{t_m+\tau} (f(N)+\beta_1 S - c_1)dt} e^{\int_{t_m+\tau}^{t_m+\tau_m} (f(N)+\beta_1 S - c_1)dt} \\ &\geq I_1(t_m) e^{(f(K+\delta)-c_1)\tau} e^{\eta(\tau_m - \tau)}.\end{aligned}$$

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

The next result shows that if for each $j = 2, \ldots, n$, either (3) or (4) are satisfied but $\mathcal{R}_{0,1} < 1$, then solutions approach the disease-free equilibrium.

Theorem 4. *Assume that for each $j = 2, \ldots, n$, either (3) or (4) holds and $\mathcal{R}_{0,1} < 1$, then*

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

Proof. Define $u = I_1/N$. Then

$$\dot{u} = u\left(\beta_1 S - c_1 + \mu_1 u + \sum_{j=2}^{n} \mu_j i_j\right), \tag{11}$$

where $i_j = I_j/N$, $j = 2, \ldots, n$. Note that since $S(t) \geq \underline{S}$, then there exists a $\delta > 0$ such that $0 < u(t) \leq 1 - \delta$.

If the inequality

$$\beta_1 K - c_1 + \mu_1 < 0 \tag{12}$$

is satisfied, choose a positive constant ϵ_1 sufficiently small such that

$$a_1 = \beta_1(K + \epsilon_1) - c_1 + \mu_1 + \epsilon_1 < 0.$$

For such a choice of ϵ_1 choose T_1 large enough such that for $t \geq T_1$,

$$N(t) \leq K + \epsilon_1, \qquad \sum_{j=2}^{n} \mu_j i_j(t) < \epsilon_1. \tag{13}$$

From (11) and (13) it follows that $\dot{u} \leq a_1 u$ for $t \geq T_1$. Hence, $\lim_{t\to\infty} u(t) = 0$.

Suppose (12) does not hold; that is,

$$\beta_1 K - c_1 + \mu_1 \geq 0.$$

Let

$$r_1 = \frac{c_1 - \beta_1(K + \epsilon_1) - \epsilon_1}{\mu_1} = \frac{c_1 - \beta_1 K}{\mu_1} - \tilde{\epsilon}_1 \leq 1,$$

where $\tilde{\epsilon}_1 = (\beta_1\epsilon_1 + \epsilon_1)/\mu_1 > 0$. Clearly ϵ_1 can be chosen sufficiently small (and T_1 sufficiently large) such that

$$r_1 > \max\{0, 1 - \beta_1 K/\mu_1\}. \tag{14}$$

Hence, for $t \geq T_1$,

$$\dot{u} \leq \mu_1 u(-r_1 + u).$$

If for any time $T > T_1$, $u(T) < r_1$, then $\lim_{t\to\infty} u(t) = 0$. But if $u(t) \geq r_1$ for $t > T_1$, then we obtain the following upper bound for $S(t)$:

$$S(t) < N(t) - I_1(t) \leq N(t)(1 - r_1).$$

Next, if the following inequality holds:

$$\beta_1(1 - r_1)K - c_1 + \mu_1 < 0, \tag{15}$$

choose a positive constant $\epsilon_2 < \epsilon_1$ sufficiently small and $T_2 > T_1$ sufficiently large such that

$$a_2 = \beta_1(1 - r_1)(K + \epsilon_2) - c_1 + \mu_1 + \epsilon_2 < 0,$$

and for $t \geq T_2$,

$$N(t) \leq K + \epsilon_2, \qquad \sum_{j=2}^{n} \mu_j i_j(t) < \epsilon_2.$$

Hence, for $t \geq T_2$ it follows that $\dot{u} \leq a_2 u$, and $\lim_{t\to\infty} u(t) = 0$.

However, if the inequality (15) does not hold; that is,

$$\beta_1(1 - r_1)K - c_1 + \mu_1 \geq 0.$$

Then, using similar arguments as above, we define

$$r_2 = \frac{c_1 - \beta_1(1 - r_1)(K + \epsilon_2) - \epsilon_2}{\mu_1} = \frac{c_1 - \beta_1(1 - r_1)K}{\mu_1} - \tilde{\epsilon}_2 \leq 1,$$

where $\tilde{\epsilon}_2 = [\beta_1(1 - r_1)\epsilon_2 + \epsilon_2]/\mu_1 > 0$. In addition,

$$r_2 = \frac{c_1 - \beta_1 K}{\mu_1} + \frac{\beta_1 K}{\mu_1} r_1 - \tilde{\epsilon}_2 > r_1 + \frac{\beta_1 K}{\mu_1} r_1 = r_1\left(1 + \frac{\beta_1 K}{\mu_1}\right) = r_1(1 + \tilde{\beta}),$$

where $\tilde{\beta} = \beta_1 K/\mu_1$. Because $\dot{u} \leq \mu_1 u(-r_2 + u)$ for $t \geq T_2$, if for any time $T > T_2$, $u(T) < r_2$, we have $\lim_{t\to\infty} u(t) = 0$. But if $u(t) \geq r_2$ for $t \geq T_2$, then $S(t) \leq N(t)(1 - r_2)$. We can choose a positive constant $\epsilon_3 < \epsilon_2$ sufficiently small and $T_3 > T_2$ sufficiently large such that

$$a_3 = \beta_1(K + \epsilon_3)(1 - r_2) - c_2 + \mu_1 + \epsilon_3 < 0,$$

and for $t \geq T_3$, $N(t) \leq K + \epsilon_3$, and $\sum_{j=2}^{n} \mu_j i_j(t) \leq \epsilon_3$.

Again, we have two cases. If

$$\beta_1(1 - r_2)K - c_1 + \mu_1 < 0,$$

then, in a manner similar to the preceding arguments, it can be shown that $\lim_{t\to\infty} u(t) = 0$. But if

$$\beta_1(1 - r_2)K - c_1 + \mu_1 \geq 0,$$

we define

$$r_3 = \frac{c_1 - \beta_1(1 - r_2)(K + \epsilon_3) - \epsilon_3}{\mu_1} = \frac{c_1 - \beta_1(1 - r_2)K}{\mu_1} - \tilde{\epsilon}_3 \leq 1,$$

where

$$r_3 > r_1 + \tilde{\beta} r_2 > r_1 + \tilde{\beta} r_1(1 + \tilde{\beta}) = r_1(1 + \tilde{\beta} + \tilde{\beta}^2).$$

We continue in this manner, obtaining a monotone sequence bounded above by one, $0 < r_1 < r_2 < \cdots < r_n \leq 1$, and having the property that

$$r_n > r_1 \sum_{k=0}^{n-1} \tilde{\beta}^k.$$

If $\tilde{\beta} = \beta_1 K/\mu_1 \geq 1$, then $\lim_{n\to\infty} r_n = \infty$ and if $\tilde{\beta} < 1$, then by choice of r_1 (see (14)),

$$\lim_{n\to\infty} r_n \geq \frac{r_1}{1 - \tilde{\beta}} = \frac{r_1}{1 - \beta_1 K/\mu_1} > 1.$$

Therefore, there must exist an integer m with $r_m > 1 - \delta \geq u(t)$ such that

$$\dot{u} \leq \mu_1 u(-r_m + u).$$

It follows that $\lim_{t\to\infty} u(t) = 0$. Thus, $\lim_{t\to\infty} \sum_{j=1}^{n} I_j(t) = 0$, and as shown in the proof of Theorem 3, $\lim_{t\to\infty} N(t) = K$, $\lim_{t\to\infty} R(t) = 0$, and $\lim_{t\to\infty} S(t) = K$. This establishes the desired result. □

4. Numerical results for competitive exclusion

In this section, we consider the logistic function $f(N) = r(1 - N/K)$, where $0 < r < b$. We assume that the carrying capacity is $K = 100$, the birth rate is $b = b_j = 1$, and the intrinsic growth rate is $r = 0.7$. Furthermore, we let the recovery rate be $\gamma_j = 0.5$. If the time unit is years, then the average length of infection is about one year. We assume that the transmission rate β_j depends on the virulence or disease-related death rate μ_j (see, e.g. [10,11,22–24,27]). In particular, we let

$$\beta_j = \frac{a\mu_j}{c + \mu_j}.$$

Let $a = 0.075$, $c = 0.2$, and $\mu_j \in [0.1, 1]$. Then

$$\mathcal{R}_{0,j} = \frac{7.5\mu_j}{(0.2 + \mu_j)(1.5 + \mu_j)} \text{ and } \mathcal{B}_{0,j} = \frac{7.5\mu_j}{(0.2 + \mu_j)(0.8 + \mu_j)}.$$

If the μ_j are restricted to $[0.1, 0.4]$, then condition (4) is satisfied for all $j = 2, \ldots, n$ and the dominant strain is the one with the largest disease-related death rate. This strain also has the highest transmission rate. However, if the μ_j are restricted to $[0.55, 1]$, then condition (3) is satisfied for all $j = 2, \ldots, n$ and the dominant strain is the one with the smallest disease-related death rate. If there are strains whose disease-related death rates are in the interval $[0.1, 1]$, then it may be the case that conditions (3) and (4) are not satisfied. For example, suppose there are five strains satisfying $\mu_j = 0.05j + 0.35$, $j = 1, 2, 3, 4, 5$. In this example, conditions (3) and (4) are not satisfied but the third strain, where $\mu_3 = 0.5$, appears to be the dominant strain. For the initial conditions $I_j(0) = 1$, $j = 1, 2, 3, 4, 5$, $S(0) = 1$, and $R(0) = 0$, solutions to this five strain model are graphed in Figure 1. It is clear from this figure that competitive exclusion occurs. This five strain example shows that the conditions (3) and (4) are sufficient but not necessary conditions for competitive exclusion to occur.

In the next section, we give an example where the conditions of Theorem 3 are not satisfied, but where coexistence occurs.

5. A coexistence case

In this section we consider the following case with two strains, i.e., $n = 2$. Let $f(N) = r(1 - N/K)$, where the carrying capacity is $K = 100$ and intrinsic growth rate is $r = 4$. Suppose the birth rate $b = b_j = 6$ and the transmission rates and recovery rates for the two strains are $\beta_1 = 2$, $\beta_2 = 1$, and $\gamma_1 = 1 = \gamma_2$, respectively. Suppose strain 1 with the largest transmission rate also has the highest virulence or disease-related death rate, $\mu_1 = 10$ and $\mu_2 = 3$. Clearly in this case the reproduction number $\mathcal{R}_{0,1} = 11.765 > 10 = \mathcal{R}_{0,2}$ but $c_1 = 17 > 10 = c_2$. However, $\mathcal{B}_{0,1} = 15.385 < 16.667 = \mathcal{B}_{0,2}$ but $\beta_1 > \beta_2$. Hence, neither conditions (3) nor (4) are satisfied. Simple computations show that a positive steady state exists for this case and is given by:

$$S = 7,\ I_1 = 4.929,\ I_2 = 8.571,\ \text{and}\ R = 4.5.$$

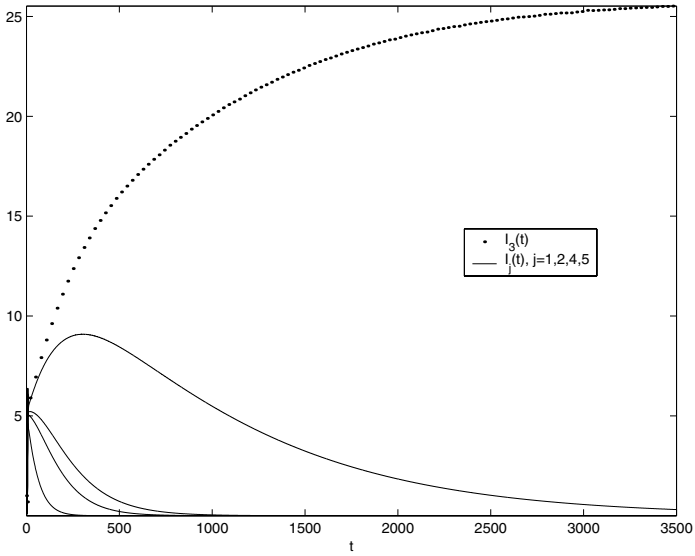

Fig. 1. Competitive exclusion when conditions (3) and (4) are not satisfied.

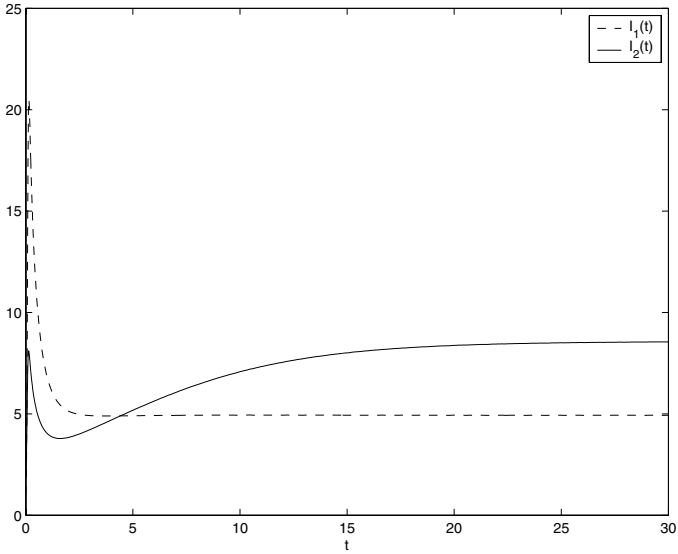

Fig. 2. Coexistence of the strains $I_1(t)$ and $I_2(t)$.

Furthermore, local stability analysis proves that this positive steady state is locally asymptotically stable. In particular, the Jacobian matrix has eigenvalues given by

$$\lambda_1 = -8.657 + 6.338i,\ \lambda_2 = -8.657 - 6.338i,\ \lambda_3 = -1.899,\ \text{and}\ \lambda_4 = -0.216.$$

Our numerical results indicate that this equilibrium is indeed globally asymptotically stable. In Figure 2 we present the two coexisting strains.

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Appendix: A dynamical systems proof of theorem 3

To show $\liminf_{t\to\infty} I_1(t) > 0$ if for each $j = 2, \ldots, n$, either (3) or (4) holds and $\mathcal{R}_{0,1} > 1$, we apply dynamical systems theory (see e.g., [12,13,30]). To this end, note that the system of $n+2$ differential equations has only two equilibria points satisfying $\bar{I}_j = 0$ for $j = 1, 2, \ldots, n$. One equilibrium is the extinction equilibrium, $E_0 = (0, 0, \ldots, 0)$, where $\bar{N} = 0$ and the other one is the disease-free equilibrium, $E_1 = (K, 0, 0, \ldots, 0)$, where $\bar{S} = K = \bar{N}$.

The Jacobian matrix or variational matrix at the extinction equilibrium E_0 satisfies

$$V_0 = \begin{pmatrix} f(0) & b & b & \cdots & b \\ 0 & f(0)-c_1 & 0 & \cdots & 0 \\ 0 & 0 & f(0)-c_2 & \cdots & 0 \\ \vdots & \vdots & \vdots & \ddots & \vdots \\ 0 & \gamma_1 & \gamma_2 & \cdots & f(0)-b \end{pmatrix}.$$

Clearly there is one positive eigenvalue, $f(0)$, with corresponding eigenvector $(1, 0, 0, \ldots, 0)^t$ and the remaining eigenvalues are negative: $f(0) - c_j < 0$, $j = 1, 2, \ldots, n$, and $f(0)-b < 0$ with corresponding eigenvector $(1, 0, 0, \ldots, -1)^t$. The direction of flow in the S-R phase plane is shown in Figure 3.

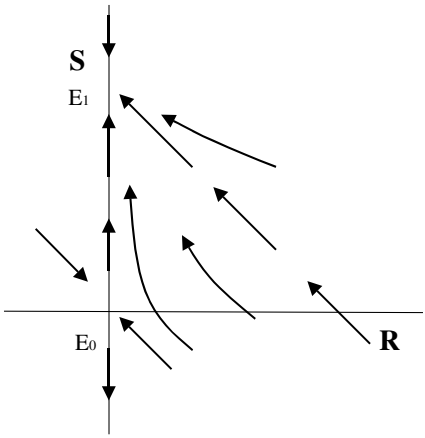

Fig. 3. S-R phase plane.

The variational matrix at the disease-free equilibrium E_1 satisfies

$$V_1 = \begin{pmatrix} Kf'(K) & K(f'(K)-\beta_1)+b & K(f'(K)-\beta_2)+b & \cdots & Kf'(K)+b \\ 0 & \beta_1 K - c_1 & 0 & \cdots & 0 \\ 0 & 0 & \beta_2 K - c_2 & \cdots & 0 \\ \vdots & \vdots & \vdots & \ddots & \vdots \\ 0 & \gamma_1 & \gamma_2 & \cdots & -b \end{pmatrix}.$$

If $\mathcal{R}_{0,j} < 1$ for $j = 1, 2, \ldots, n$, then all of the eigenvalues are negative and the disease-free equilibrium is locally asymptotically stable. However, if $\mathcal{R}_{0,1} > 1$, then there is at least one positive eigenvalue. The eigenvalues are $Kf'(K)$ with corresponding eigenvector $(1, 0, 0, \ldots, 0)^t$, $\beta_j K - c_j$, $j = 1, 2, \ldots, n$, and $-b$ with corresponding eigenvector $(1, 0, 0, \ldots, -1)^t$. These facts will be used below to show that $\liminf_{t\to\infty} I_1(t) > 0$ if $\mathcal{R}_{0,1} > 1$.

Suppose there exists a solution with $\liminf_{t\to\infty} I_1(t) = 0$. Denote the positive orbit as $\Gamma(X_0, t)$, where X_0 is the vector of initial conditions, $S(0) > 0$, $I_j(0) > 0$, $j = 1, 2, \ldots, n$, and $R(0) \geq 0$. Since $\lim_{t\to\infty} I_j(t) = 0$ for $j > 1$, the omega-limit set $\omega(X_0)$ of $\Gamma(X_0, t)$ must intersect the positive quadrant of the S-R plane, $\Omega_{SR} = \{(S, 0, 0, \ldots, R) | S \geq 0, R \geq 0\}$, in a nontrivial point. The omega-limit set cannot equal E_1 because then $\lim_{t\to\infty} I_j(t) = 0$, $j = 1, 2, \ldots, n$, and $\lim_{t\to\infty} N(t) = K = \lim_{t\to\infty} S(t)$. However, from the I_1 differential equation in (1) it follows that $\dot{I}_1(t) > I_1(t)(\beta_1 K - c_1 - \epsilon) > 0$ for $t > T$ sufficiently large and ϵ sufficiently small which contradicts the fact that $I_1(t)$ approaches zero. Thus, the omega-limit set must intersect Ω_{SR} in a point P different from E_0 and E_1. Because $\omega(X_0)$ is closed and invariant, it must contain the entire orbit containing P that lies in Ω_{SR}; this means $E_1 \in \omega(X_0)$.

If P lies on the S-axis, $P \neq E_0$ and $P \neq E_1$, then either the orbit along the S-axis which is above or below E_1 belongs to $\omega(X_0)$. Either case is impossible because if the orbit on the S-axis, below E_1, lies in $\omega(X_0)$, so does the origin and if the orbit along the S-axis, above E_1, lies in $\omega(X_0)$, then solutions are unbounded.

If P lies in the interior of Ω_{SR} or on the R-axis, then the orbit containing P is unbounded, again a contradiction. In all cases, there is a contradiction; hence, it is impossible for $\omega(X_0)$ to contain a point $P \neq E_0$, $P \neq E_1$, $P \in \Omega_{SR}$. Thus, $\liminf_{t\to\infty} I_1(t) > 0$.

References

[1] Ackleh, A.S., Marshall, D.F., Fitzpatrick, B.G., Heatherly, H.E.: Survival of the fittest in a generalized logistic model. Math. Models Methods Appl. Sci. **9**, 1379–1391 (1999)

[2] Ackleh, A.S., Marshall, D.F., Heatherly, H.E.: Extinction in a generalized Lotka-Volterra predator–prey model. J. Appl. Math. Stochastic Anal. **13**, 287–297 (2000)

[3] Ahmad, S.: Extinction of species in nonautonomous Lotka-Volterra systems. Proc. Amer. Math. Soc. **127**, 2905–2910 (1999)

[4] Allen, L.J.S., Cormier, P.J.: Environmentally driven epizootics. Math. Biosci. **131**, 51–80 (1996)

[5] Anderson, R.M., May, R.M.: Population biology of infectious diseases. Part I. Nature **280**, 361–367 (1979)

[6] Anderson, R.M., May, R.M.: Coevolution of hosts and parasites. Parasitology **85**, 411–426 (1982)
[7] Andreasen, V., Pugliese, A.: Pathogen coexistence induced by density dependent host mortality. J. Theor. Biol. **177**, 159–165 (1995)
[8] Beverton, R.J.H., Holt, S.J.: On the dynamics of exploited fish population. Fishery Investigations Ser. 2, **19**, London: H.M.S.O 1957
[9] Brauer, F.: Models for the spread of universally fatal diseases. J. Math. Biol. **28**, 451–462 (1990)
[10] Bremermann, H.J., Pickering, J.: A game-theoretical model of parasite virulence. J. Theor. Biol. **100**, 411–426 (1983)
[11] Bremermann, H.J., Thieme, H.R.: A competitive exclusion principle for pathogen virulence. J. Math. Biol. **27**, 179–190 (1989)
[12] Butler, G., Freedman, H.I., Waltman, P.: Uniformly persistence systems. Proc. Am. Math. Soc. **96**, 425–430 (1986)
[13] Butler, G., Waltman, P.: Persistence in dynamical systems. J. Differential Eqns. **63**, 255–263 (1986)
[14] Castillo-Chavez, C., Huang, W., Li, J.: Competitive exclusion in gonorrhea models and other sexually transmitted diseases. SIAM J. Appl. Math. **56**, 494–508 (1996)
[15] Castillo-Chavez, C., Huang, W., Li, J.: Competitive exclusion and coexistence of multiple strains in an SIS STD model. SIAM J. Appl. Math. **59**, 1790–1811 (1999)
[16] Castillo-Chavez, C., Velasco-Hernández, J.X.: On the relationship between evolution of virulence and host demography. J. Theor. Biol. **192**, 437–444 (1998)
[17] Feng, Z., Velasco-Hernández, J.X.: Competitve exclusion in a vector–host model for the dengue fever. J. Math. Biol. **35**, 523–544 (1997)
[18] Hochberg, M.E., Holt, R.D.: The coexistence of competing parasites I. The role of cross-species infection. Amer. Nat. **136**, 517–541 (1990)
[19] Levin, S.A.: Community equilibria and stability, and an extension of the competitive exclusion principle. Amer. Nat. **104**, 413–423 (1970)
[20] Levin, S.A., Pimentel, D.: Selection of intermediate rates increase in parasite–host systems. Amer. Nat. **117**, 308–315 (1981)
[21] May, R.M.: Stability and Complexity in Model Ecosystems, Princeton University Press, Princeton, NJ, 1973
[22] May, R.M., Nowak, M.A.: Superinfection, metapopulation dynamics, and the evolution of virulence. J. Theor. Biol. **170**, 95–114 (1994)
[23] May, R.M., Nowak, M.A.: Coinfection and the evolution of parasite virulence. Proc. R. Soc. London B **261**, 209–215 (1995)
[24] Mosquera, J., Adler, F.R.: Evolution of virulence: a unifed framework for coinfection and superinfection. J. Theor. Biol. **195**, 293–313 (1998)
[25] Maynard Smith, J.: The Evolution of Sex. Cambridge University Press, Cambridge, UK, 1978
[26] Montes de Oca, F., Zeeman, M.L.: Extinction in nonautonomous competitive Lotka-Volterra systems. Proc. Amer. Math. Soc. **124**, 3677–3687 (1996)
[27] Nowak, M.A., May, R.M.: Superinfection and the evolution of parasite virulence. Proc. R. Soc. London B **255**, 81–89 (1994)
[28] Pugliese, A.: Population models for diseases with no recovery. J. Math. Biol. **28**, 65–82 (1990)
[29] Ricker, W.E.: Stock and recruitment. J. Fish Res. Bd. Canada **11**, 559–623 (1954)
[30] Smith, H.L., Waltman, P.: The Theory of the Chemostat. Cambridge University Press, Cambridge, UK., 1995
[31] Smith, H.L., Zhao, X.-Q.: Competitive exclusion in a discrete-time, size-structured chemostat model. Discrete Contin. Dyn. Syst. Ser. B **1**, 183–191 (2001)

[32] van Baalen, M., Sabelis, M.W.: The dynamics of multiple infection and the evolution of virulence. Amer. Nat. **146**, 881–910 (1995)
[33] Zeeman, M.L.: Extinction in competitive Lotka-Volterra systems. Proc. Amer. Math. Soc. **123**, 87–96 (1995)
[34] Zhou, J., Hethcote, H.W.: Population size dependent incidence in models for diseases without immunity. J. Math. Biol. **32**, 809–834 (1994)