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# ASYMPTOTIC DYNAMICS OF DETERMINISTIC AND STOCHASTIC EPIDEMIC MODELS WITH MULTIPLE PATHOGENS

LINDA J. S. ALLEN AND NADARAJAH KIRUPAHARAN

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**Abstract.** Emerging diseases in animals and plants have led to much research on questions of evolution and persistence of pathogens. In particular, there have been numerous investigations on the evolution of virulence and the dynamics of epidemic models with multiple pathogens. Multiple pathogens are involved in the spread of many human diseases including influenza, HIV-AIDS, malaria, dengue fever, and hantavirus pulmonary syndrome [9, 15, 16, 23, 24, 27]. Understanding the impact of these various pathogens on a population is particularly important for their prevention and control. We summarize some of the results that have appeared in the literature on multiple pathogen models. Then we study the dynamics of a deterministic and a stochastic susceptible-infected epidemic model with two pathogens, where the population is subdivided into susceptible individuals and individuals infected with pathogen $j$ for $j = 1, 2$. The deterministic model is a system of ordinary differential equations, whereas the stochastic model is a system of stochastic differential equations. The models assume total cross immunity and vertical transmission. The conditions on the parameters for coexistence of two pathogens are summarized for the deterministic model. Then we compare the coexistence dynamics of the two models through numerical simulations. We show that the deterministic and stochastic epidemic models differ considerably in predicting coexistence of the two pathogens. The probability of coexistence in the stochastic epidemic model is very small. Stochastic variability results in extinction of at least one of the strains. Our results demonstrate the importance of understanding the dynamics of both the deterministic and stochastic epidemic models.

**Key Words.** Epidemic model, multiple pathogens, stochastic differential equation, vertical transmission, cross immunity

## 1. Introduction

The spread and persistence of an infectious disease depend on a multitude of factors. For example, two important factors are pathogen virulence and transmissibility. Pathogens that are too virulent, that kill their host too quickly before transmission to another host, reduce their chance of survival and ultimately, the

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persistence of the disease. This view has led to what has been called "conventional wisdom." Conventional wisdom asserts that pathogens evolve toward reduced virulence [6]. Some well-known natural experiments and theoretical results support this view. More recent evidence suggests that this view is too simplistic. The evolution of virulence has received much attention in the literature (see, e.g., [18, 19, 21, 48] and references therein). Epidemic models with multiple pathogens have provided an important theoretical tool to investigate how complex interactions between host and pathogen affect pathogen evolution and disease persistence [1, 2, 8, 9, 11, 13, 15, 16, 17, 20, 23, 24, 31, 37, 40, 41, 42, 43, 44, 47].

**1.1. Evolution of Virulence.** A well-known natural experiment that supports conventional wisdom involves the rabbit population in Australia. The European rabbit was introduced into Australia about 1859 and within 20 years, the rabbit population had increased to such high densities that they were a serious problem [25, 26, 37]. Various methods of control were tried but none were very successful until 1950 when the myxoma virus was introduced. Initially, the mortality rate due to myxoma virus was estimated at 99.8% [25, 37]. But over time, the virulence changed. Virulence was graded on a scale from I to V, grade I being the most virulent. It was found in studies by Fenner and Ratcliffe [26] that from 1950 to 1965, the average virulence grade in the rabbit population changed from the most virulent, grade I, to an intermediate level of virulence, grade III (see [6, 25, 37]).

Some theoretical results that also support conventional wisdom come from the study of epidemic models. The basic reproduction number is a well-known threshold parameter in the mathematical epidemiology literature [7, 29, 50]. The basic reproduction number is the number of secondary infections caused by an infected individual in an entirely susceptible population. For a simple epidemic model, this threshold parameter can be defined as the transmission rate (number of adequate contacts per time that result in infection) multiplied by the length of the infectious period. Therefore, the basic reproduction number is

$$\mathcal{R}_0 = \frac{\beta}{d+\alpha}. \tag{1}$$

The parameter $\beta$ is the transmission rate and the fraction $1/(d+\alpha)$ is the length of the infectious period, where $d$ is the natural death rate and $\alpha$ is the disease-related death rate. The parameter $\alpha$ is often used as a measure of the virulence of the disease. Generally, an epidemic occurs when $\mathcal{R}_0 > 1$. When $\mathcal{R}_0 < 1$ the disease does not persist. It can be seen from the definition of $\mathcal{R}_0$ that if the pathogen is highly virulent, as measured by $\alpha$, then $\mathcal{R}_0 < 1$. In this case, the disease and the pathogen do not persist. However, if the virulence is decreased, that is, $\alpha$ is decreased, so that $\mathcal{R}_0 > 1$, then the disease persists in the population. Unfortunately, the relationship between reduced virulence and disease persistence is not quite as simple as this discussion appears (see e.g., [6, 18, 19, 38, 44, 47]). The parameters in the definition of $\mathcal{R}_0$ are generally not independent. In fact, transmission may be correlated with virulence [6]. The evolution of virulence becomes even more complicated when the model includes multiple pathogen strains with differing levels of virulence and transmissibility. The edited volume [21] by Dieckmann, Metz, Sabelis, and Sigmund is a good reference for the current knowledge of evolutionary ecology of infectious diseases and management goals for virulent pathogens.

In this investigation, we concentrate on the theoretical aspects of virulence evolution. In particular, we study the dynamics of epidemic models with multiple pathogens and determine how the systems evolve over time. We shall refer to the various pathogens as strains. We are interested in the persistence of multiple pathogen strains and the properties of these persistent strains. Virulence and transmissibility are two important factors affecting the evolution but there are many other factors. Before the multiple pathogen epidemic model is introduced, some of the complex relationships between host and pathogen are discussed. We discuss factors that affect disease persistence and are important in virulence management and we provide a brief review of some of the literature.

**1.2. Multiple Pathogen Epidemic Models.** In multiple pathogen epidemic models, there arise many complex relationships between host and pathogen that affect the spread and persistence of a disease. For example, infection by one pathogen strain may result in immunity to infection by another related strain, this is known as cross immunity (see e.g., [9, 20, 24, 31]). Cross immunity may not be complete, there may be only partial immunity so that infection by another strain may still occur. When a host is infected by two or more strains this is referred to as coinfection (see e.g., [5, 41, 43]). Superinfection implies that individuals can be infected by a second strain only after infection by a different strain initially [38, 40, 42, 43, 44]. For example, infection with some types of dengue virus are preceded by infection with another type [23]. Transmission of the disease may occur via direct contact with an infected individual, referred to as horizontal transmission or transmission may occur from mother to offspring, referred to as vertical transmission (see [5, 14, 15, 16, 38, 39, 49]). For example, HIV and hepatitis B and C are horizontally and vertically transmitted. The host birth and death rates affect disease persistence because of their impact on the number of hosts available for infection, especially if they are density-dependent (see e.g., [1, 2, 5, 8, 13, 17, 34, 42, 47]).

We discuss two classical papers on multiple pathogen epidemic models. The paper by Levin and Pimentel [37] was the first one to relate a two-strain epidemic model to virulence evolution. In their model, the population is subdivided into susceptible individuals ($x$), individuals infected by an avirulent strain ($y$), and those infected by both an avirulent and a virulent strain ($z$). They showed that as virulence increases (death rate due to the virulent strain), then the virulent strain $z$ can be replaced by the avirulent strain $y$. Another classical paper on multiple pathogen strain epidemic models is by Bremermann and Thieme [13]. In their model, the host population is subdivided into susceptible individuals, $S$, individuals infected with strain $j$, $I_j$, $j = 1, 2 \ldots, n$, and immune individuals, $R$. The model assumes total cross immunity and a density-dependent birth rate. For this SIR epidemic model, they proved that the pathogen strain whose basic reproduction number is maximal persists in the population. In particular, if $\mathcal{R}_j$ represents the basic reproduction number for each of the strains in isolation and if

$$\mathcal{R}_1 > \max_{j=2,\ldots,n} \{1, \mathcal{R}_j\}, \tag{2}$$

then the subpopulation infected with strain 1 persists. All pathogen strains are excluded except the dominant one. This is referred to as competitive exclusion. Since 1989, there have been a multitude of papers that challenge this competitive exclusion result. Epidemic models with coinfection, superinfection, partial cross

immunity, vertical transmission, and density-dependent mortality have been shown to exhibit coexistence of multiple pathogen strains [1, 2, 5, 8, 9, 15, 16, 17, 20, 23, 24, 31, 34, 40, 41, 42, 43, 44, 47]. Most of these studies have been based on deterministic models, systems of differential equations. There have been few studies where stochastic epidemic models with multiple pathogen strains have been applied [28, 33, 34].

In the next section, we describe a susceptible-infected epidemic model with multiple pathogen strains. The population is subdivided into susceptible individuals and infected individuals. The infected subpopulation is further subdivided into $n$ different types of infection. The dynamics of the deterministic model in the case of coexistence of two strains are summarized. Then a stochastic epidemic model is formulated. The coexistence dynamics of the two models are compared in several numerical examples in Section 3.

## 2. Models

**2.1. Deterministic Epidemic Model.** Let $S$ denote the number of individuals susceptible to infection. Let $I_j$ denote the number of individuals infected by pathogen strain $j$, $j = 1, 2, \ldots, n$. We assume that there is no immunity to infection. The model is referred to as an SI epidemic model. These types of models are applicable, for example, to HIV-AIDS infection in humans [38]. They are also applicable to hantavirus infection in rodent populations; recovery does not occur because infection is generally life-long [5]. In addition, we assume that infection with one strain confers immunity to infection by all other strains, i.e., total cross immunity. The SI epidemic model with $n$ pathogen strains has the following form:

$$\frac{dS}{dt} = S\left(b - d(N) - \sum_{k=1}^{n} \frac{\beta_k I_k}{N}\right) + \sum_{k=1}^{n} b_k I_k, \tag{3}$$

$$\frac{dI_j}{dt} = I_j\left(b - b_j - d(N) - \alpha_j + \frac{\beta_j S}{N}\right), \quad j = 1, 2, \ldots, n, \tag{4}$$

where $S(0) > 0$, $I_j(0) > 0$ for $j = 1, 2, \ldots, n$ and the total population size, $N(t) = S(t) + \sum_{k=1}^{n} I_k(t)$, satisfies

$$\frac{dN}{dt} = N\left(b - d(N)\right) - \sum_{k=1}^{n} \alpha_k I_k. \tag{5}$$

In model (3) and (4), the parameter $b$ is the per capita birth rate and $d(N)$ is the per capita, density-dependent death rate. The per capita birth rate is divided into two parts, $b_j$ and $b - b_j$. Strain $j$ may be passed from mother to offspring. The vertical transmission is represented in the per capita birth rate to the infected class $I_j$, $b - b_j$. If there is no vertical transmission to a newborn, then newborns enter the susceptible class. The per capita birth rate to susceptible class $S$ from class $I_j$ is $b_j$. Parameter $\beta_j$ is the transmission rate and $\alpha_j$ is the disease-related, per capita death rate for individuals infected with strain $j$, $j = 1, 2, \ldots, n$. The parameters $b$, $\alpha_j$, and $\beta_j$, $j = 1, 2, \ldots, n$ are all positive and $b_j$ is nonnegative. We assume that the density-dependent death rate $d(N)$ satisfies the following conditions:

(i) $d \in C^1[0, \infty)$,
(ii) $0 < d(0) < b$,
(iii) $d(N)$ is increasing for $N \in [0, \infty)$,

(iv) there exists a constant $K > 0$ such that $d(K) = b$.

Such types of assumptions have been made in other epidemic models (see [1, 2, 5, 34]). In the absence of infection, conditions (i)–(iv) imply that the total population size $N(t)$ approaches the carrying capacity $K$, $\lim_{t\to\infty} N(t) = K$.

More complex epidemic models than (3) and (4) have been applied to various diseases, models with age and spatial structure, time delays, and additional states. For example, a model referred to as MSEIR includes the additional states $M$, $E$, and $R$. State $M$ is generally included in age-structured models for childhood diseases and refers to infants with passive immunity obtained from the mother. State $E$ is an exposed state; individuals are infected but not yet infectious. State $R$ refers to individuals with immunity to infection; immunity can be temporary or permanent. For simplicity, we consider only two states, $S$ and $I$. The model dynamics are much more complex with age structure, time delays, and additional states (see [12, 29, 30]).

The $n$-strain model (3) and (4) was studied by Ackleh and Allen [2]. They derived sufficient conditions for exclusion of all but one strain. The two-strain model, $n = 2$, was studied by Allen, Langlais, and Phillips [5]. They derived conditions for coexistence of two, exclusion of one, and extinction of both pathogens. Because we are interested in coexistence, the two-strain model will be used to investigate coexistence of pathogen strains, whether vertical transmission has an impact on coexistence, and whether coexistence can be maintained if demographic variability is included. The conditions for coexistence of two pathogens for model (3) and (4) are given in [5]. We show that these conditions can be simplified in some special cases. Then we formulate an analogous stochastic model for (3) and (4) and study the dynamics of the stochastic model under the coexistence conditions. The stochastic model assumes only demographic variability and is formulated as stochastic differential equations. Kirupaharan [33] and Kirupaharan and Allen [34] derived stochastic differential equation models for multiple pathogen epidemics and studied coexistence for two-strains in SIS epidemic models when there is recovery but no vertical transmission. Here we extend the study of SI epidemic models to include vertical transmission.

We consider model (3) and (4) when there are two strains, $n = 2$. Two special cases are considered and these cases will be referred to as cases I and II. In case I, we assume there is no vertical transmission of the disease, $b_j = b$. In case I, the differential equations for the two infected classes are

$$\frac{dI_j}{dt} = I_j\left(-d(N) - \alpha_j + \frac{\beta_j S}{N}\right), \quad j = 1, 2.$$

In case II, we assume that only one of the pathogens is transmitted vertically, pathogen 2, so that $b_1 = b$ and $b_2 = 0$. In this case, the differential equations for the two infected classes are

$$\begin{aligned}\frac{dI_1}{dt} &= I_1\left(-d(N) - \alpha_1 + \frac{\beta_1 S}{N}\right)\\ \frac{dI_2}{dt} &= I_2\left(b - d(N) - \alpha_2 + \frac{\beta_2 S}{N}\right).\end{aligned}$$

The dynamics of model (3) and (4) depend on the basic reproduction numbers. For model (3) and (4), the basic reproduction number for strain $j$ is defined by

$$\mathcal{R}_j = \frac{\beta_j + b - b_j}{b + \alpha_j} = \frac{\beta_j}{b + \alpha_j} + \frac{b - b_j}{b + \alpha_j}, \quad j = 1, 2. \tag{6}$$

Note that the definition for $\mathcal{R}_j$ differs from (1). The basic reproduction number is separated into two ratios. The first ratio represents the contribution due to horizontal transmission of the disease and the second ratio represents the contribution due to vertical transmission. The denominator also differs from (1), where the per capita birth rate $b$ appears, rather than per capita death rate $d$. If $b = d$, then the definitions agree when there is no vertical transmission. If $\mathcal{R}_j > 1$, then pathogen $j$ has a possibility of invading and persisting in the population. It can be shown using techniques in [22, 51] that the basic reproduction number for the $n$-strain model (3) and (4) is

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

This threshold determines whether a pathogen can invade a disease-free population. However, knowledge of $\mathcal{R}_0$ is insufficient to determine the long-term dynamics (see [2, 5]).

We summarize the results for coexistence of two strains for model (3) and (4). First, some additional notation and parameters are introduced. Let the coexistence equilibrium for model (3) and (4) be denoted as $E = (\bar{S}, \bar{I}_1, \bar{I}_2)$, where $\bar{S} > 0$, $\bar{I}_1 > 0$, $\bar{I}_2 > 0$, and $\bar{N} = \bar{S} + \bar{I}_1 + \bar{I}_2$. Let

$$\rho_{11} = \frac{\beta_1 - b_1 - \alpha_1}{\beta_1 - \alpha_1}, \quad \rho_{12} = \frac{\beta_1 - b_1 - \alpha_1}{\beta_1 - \alpha_2},$$

$$\rho_{21} = \frac{\beta_2 - b_2 - \alpha_2}{\beta_2 - \alpha_1}, \quad \text{and} \quad \rho_{22} = \frac{\beta_2 - b_2 - \alpha_2}{\beta_2 - \alpha_2}.$$

The parameters $\rho_{jj}$ represent proportional equilibrium values for strain $j$, $j = 1, 2$, that is, $\rho_{11} = \bar{I}_1/\bar{N}$, where $\bar{I}_1$ is the equilibrium value for strain 1 when $I_2 \equiv 0$. We assume that the parameters $\rho_{ij}$ are well defined and nonzero (denominators and numerators $\neq 0$); they can be either positive or negative. In addition, the results in [5] assume there cannot be 100% vertical transmission of both strains, $b_1 + b_2 > 0$. We relax this assumption in the numerical examples.

Allen, Langlais, and Phillips [5] made the additional assumption:

(v) $b > d(0) + \alpha_1 \dfrac{\bar{I}_1}{\bar{N}} + \alpha_2 \dfrac{\bar{I}_2}{\bar{N}}$.

Assumption (v) requires apriori knowledge of the equilibrium coordinates of $E$. Another stronger condition, but much simpler condition was assumed by Ackleh and Allen [2]. This simpler condition does not require knowledge of $E$. We refer to this condition as (v)$'$:

(v)$'$ $b > d(0) + \max\{\alpha_1, \alpha_2\}$.

Conditions (v) or (v)$'$ prevent complete population extinction because the birth rate exceeds the death rate (natural and disease-related) when population sizes are small. Coexistence when $n = 2$ in cases I and II means stability of the equilibrium $E$; there are no periodic or chaotic solutions in these two cases. However, if both strains are transmitted vertically, we give a numerical example that shows a much different type of solution behavior. Theorem 1 states conditions for coexistence, $\lim_{t\to\infty} I_j(t) = \bar{I}_j > 0$, $j = 1, 2$. A proof of Theorem 1 can be found in [5].

**Theorem 1.** *Suppose conditions (i)–(v) hold for model (3) and (4) with* $n = 2$. *Then equilibrium* $E$ *is globally asymptotically stable if*

(a) $\mathcal{R}_1 > 1$, $\mathcal{R}_2 < 1$, *and* $0 < \rho_{21} < \rho_{11}$, *or*
(b) $\mathcal{R}_1 < 1$, $\mathcal{R}_2 > 1$, *and* $0 < \rho_{12} < \rho_{22}$, *or*
(c) $\mathcal{R}_1 > 1$, $\mathcal{R}_2 > 1$, *and if any one of the three additional sets of conditions hold:*

$$0 < \rho_{11} < \rho_{21} \quad \text{and} \quad 0 < \rho_{22} < \rho_{12}, \tag{7}$$

$$0 < \rho_{11} < \rho_{21} \quad \text{and} \quad \rho_{12} < 0, \tag{8}$$

$$0 < \rho_{22} < \rho_{12} \quad \text{and} \quad \rho_{21} < 0. \tag{9}$$

The conditions in Theorem 1 are stated as sufficient conditions for global stability of $E$. However, when assumptions (i)–(v) hold, the conditions in (a), (b), and (c) are necessary and sufficient conditions for coexistence provided all of the inequalities in Theorem 1 are strict. When the conditions of Theorem 1 are not satisfied, i.e. some of the inequalities are reversed, then there is either extinction of one or both of the strains. Notice that the conditions require at least one of the basic reproduction numbers to exceed unity. Even for $n$ pathogen strains, at least one reproduction number must be greater than unity for disease persistence. If all of the basic reproduction numbers are less than one, then generally disease extinction occurs, i.e., $\lim_{t\to\infty} I_j(t) = 0$, $j = 1, 2, \ldots, n$ [2].

There appears to be many possible cases for coexistence outlined in Theorem 1. But under the simpler condition (v)$'$, we find that most of these cases do not occur. Corollary 1 summarizes the coexistence cases in the two special cases, I: $b_j = b$ for $j = 1, 2$ and II: $b_1 = b$ and $b_2 = 0$.

**Corollary 1.** *Suppose conditions (i)–(iv) and (v)$'$ hold for model (3) and (4). Then equilibrium* $E$ *is globally asymptotically stable for cases I and II under the following restrictions:*

I: *conditions (c) and (7) of Theorem 1 hold.*
II: *condition (a) of Theorem 1 holds.*

The proof of Corollary 1 is based on the fact that condition (v)$'$ contradicts some of the coexistence conditions in Theorem 1.

*Proof of Corollary 1.* The inequalities in case I, where $b_j = b$ for $j = 1, 2$, show that condition (a) and conditions (c) and (9) in Theorem 1 imply $b + \alpha_2 < \alpha_1$ which contradicts (v)$'$. Condition (b) and conditions (c) and (8) imply $b + \alpha_1 < \alpha_2$ which again contradicts (v)$'$.

In case II, $b_1 = b$ and $b_2 = 0$, so that $\rho_{22} = 1$. Conditions (b) and (c) imply $b + \alpha_1 < \alpha_2$, a contradiction to (v)$'$. □

Corollary 1 excludes the cases $b + \alpha_i < \alpha_j$, $i, j = 1, 2$, $i \neq j$. For highly virulent diseases, when $\alpha_j$ is large, these cases may occur. Then Theorem 1 must be applied to check for coexistence. According to Corollary 1, when there is no vertical transmission of either strain, both basic reproduction numbers must be greater than unity for coexistence. When one of the strains is transmitted vertically, then for coexistence to occur, the vertically transmitted strain must have a basic reproduction number less than unity and the other one must have a basic reproduction

number greater than unity. Both basic reproduction numbers cannot be less than unity because, in this case, both infected classes approach zero [5]. In case II, if the vertically transmitted strain 2 has a basic reproduction number greater than unity, then it will outcompete the other strain; strain 1 dies out and strain 2 persists. Thus, coexistence requires a compromise between the two strains.

Another interesting case is when both strains are transmitted vertically, $b_j = 0$ for $j = 1, 2$. We shall refer to this case as case III. In case III, the differential equations for the two infected classes are

$$\frac{dI_j}{dt} = I_j \left( b - d(N) - \alpha_j + \frac{\beta_j S}{N} \right), \quad j = 1, 2.$$

However, Theorem 1 does not apply to case III because $b_1 + b_2 = 0$. The positive equilibrium may not be globally asymptotically stable. The dynamics in this case are illustrated in the numerical examples. It should be noted that this case may be more theoretically interesting than biologically realistic. There are few diseases where both strains have 100% vertical transmission, i.e., where all newborns are born infected. This can be said about case II also. If vertical transmission occurs, it may be more often the case that it is not 100%, $b_j > 0$, so that a proportion $b_j/b$ of newborns are born infected and a proportion $(b - b_j)/b$ are not infected. However, case II is useful to compare the dynamics of vertical and horizontal transmission.

**2.2. Stochastic Epidemic Model.** We formulate a stochastic differential equation (SDE) model with demographic stochasticity for model (3) and (4). Let the script letters $\mathcal{S}$ and $\mathcal{I}_j$ for $j = 1, \ldots, n$, denote continuous random variables for susceptible and infected individuals, respectively. We assume that $\mathcal{S}$ and $\mathcal{I}_j$ take on values in $[0, 2K]$ such that $\mathcal{S} + \sum_{k=1}^{n} \mathcal{I}_k = \mathcal{N} \in [0, 2K]$. A system of Itô SDEs for the stochastic epidemic model can be formulated as follows [3, 33, 34]:

$$\frac{d\mathcal{S}}{dt} = \mathcal{S} \left( b - d(\mathcal{N}) - \sum_{k=1}^{n} \frac{\beta_k \mathcal{I}_k}{\mathcal{N}} \right) + \sum_{k=1}^{n} b_k I_k + \sum_{k=1}^{n+1} B_{1k} \frac{dW_k}{dt}, \tag{10}$$

$$\frac{d\mathcal{I}_j}{dt} = \mathcal{I}_j \left( b - b_j - d(\mathcal{N}) - \alpha_j + \frac{\beta_j \mathcal{S}}{\mathcal{N}} \right) + \sum_{k=1}^{n+1} B_{j+1,k} \frac{dW_k}{dt}, \tag{11}$$

$j = 1, \ldots, n$, where $W_k(t)$ are $n+1$ independent Wiener processes, $k = 1, 2, \ldots, n+1$, and $B = \sqrt{C}$. Matrix $C$ is an $(n+1) \times (n+1)$ symmetric, positive definite matrix satisfying

$$C = \begin{pmatrix} 0 & \sigma_{12} & \cdots & \sigma_{1,n+1} \\ \sigma_{21} & 0 & \cdots & 0 \\ \vdots & \vdots & \vdots & \vdots \\ \sigma_{n+1,1} & 0 & \cdots & 0 \end{pmatrix} + \operatorname{diag}(\sigma_{11}, \sigma_{22} \ldots, \sigma_{n+1,n+1}),$$

where

$$\begin{aligned}
\sigma_{11} &= \mathcal{S}\left(b + d(\mathcal{N}) + \sum_{k=1}^{n} \beta_k \frac{\mathcal{I}_k}{\mathcal{N}}\right) + \sum_{k=1}^{n} b_k I_k \\
\sigma_{jj} &= I_j\left(b - b_j + d(\mathcal{N}) + \alpha_j + \beta_j \frac{S}{N}\right), \quad j = 2, \ldots, n+1, \\
\sigma_{1,j+1} &= -\beta_j \frac{\mathcal{S}\mathcal{I}_j}{N} = \sigma_{j+1,1}, \quad j = 1, 2, \ldots, n
\end{aligned}$$

Matrix $C$ is the covariance matrix for the change in the population sizes. The nonzero elements $\sigma_{1,j+1}$ and $\sigma_{j+1,1}$ in $C$ are due to the interactions between $S$ and $I_j$. There are no interactions between $I_j$ and $I_k$ for $j \neq k$ because of cross immunity, so the terms $\sigma_{jk}$ and $\sigma_{kj}$ are zero in matrix $C$. Matrix $C$ is positive definite, and therefore, it has a unique positive definite square root matrix $B$ [34, 45]. The numerical computations for the stochastic model are performed using an an explicit Taylor method of strong order of convergence 0.5 [35, 36]. In addition, an implicit Taylor method for stochastic differential equations was used to check the results [35, 36]. The stochastic sample paths of (10) and (11) are compared to the solution of the deterministic model (3) and (4).

## 3. Numerical Examples

We present some numerical examples for the deterministic and stochastic epidemic models in three cases, cases I, II, and III. In all cases, it will be seen that the coexistence dynamics differ between the deterministic and stochastic models.

The initial conditions in the numerical examples are chosen large enough so that if extinction occurs, it does not occur immediately due to the small initial values. For all cases, the initial conditions satisfy

$$S(0) = 50, \quad I_1(0) = 10, \quad \text{and} \quad I_2(0) = 10.$$

The SDE model and the deterministic model have the same initial conditions, $\mathcal{S}(0) = 50, \mathcal{I}_1(0) = 10$, and $\mathcal{I}_2(0) = 10$. In the absence of disease, $I_1(0) = 0 = I_2(0)$, the deterministic population grows logistically to carrying capacity $K = 100$.

For the stochastic model, we define probabilities of extinction and coexistence. Let $p_C(t)$ denote the probability that both strains coexist at time $t$,

$$p_C(t) = \text{Prob}\{\mathcal{I}_1(t) > 0 \text{ and } \mathcal{I}_2(t) > 0\}.$$

The probability of coexistence is computed from the extinction probabilities for strain 1, strain 2, or both strains:

$$p_1(t) = \text{Prob}\{\mathcal{I}_1(t) = 0\}, \quad p_2(t) = \text{Prob}\{\mathcal{I}_2(t) = 0\},$$

and

$$p_b(t) = \text{Prob}\{\mathcal{I}_1(t) = 0 \text{ and } \mathcal{I}_2(t) = 0\}.$$

Then

$$p_C(t) = 1 - [p_1(t) + p_2(t) - p_b(t)].$$

These probabilities are approximated from numerical simulation of 10,000 sample paths of the SDEs.

**3.1. Case 1: No Vertical Transmission.** Suppose neither strain is transmitted vertically, $b_1 = b = b_2$. Let $b = 6$, $\beta_1 = 30$, $\beta_2 = 15$, $\alpha_1 = 8.5$, $\alpha_2 = 3$, and $d(N) = 1 + 5N/100$. The basic reproduction numbers for the two strains are

$$\mathcal{R}_1 = 2.07 \quad \mathcal{R}_2 = 1.67.$$

The conditions of Corollary 1, part I are satisfied. The deterministic solution approaches a globally stable equilibrium,

$$\lim_{t\to\infty} I_1(t) = 8.73 \quad \text{and} \quad \lim_{t\to\infty} I_2(t) = 10.27.$$

Figure 1 shows the graphs of the deterministic solution and two different sample paths of the stochastic model. It can be seen that in one sample path, strain 2 persists but in the other one, neither strain persists. For coexistence in this case, the strain with the highest transmission rate, $\beta_1$, requires a high virulence rate, $\alpha_1$. These large values increase the variability in the stochastic model and increase the chances of extinction. When strain 1 is not present in the population, strain 2 may persist because $\mathcal{R}_2 > 1$. However, when strain 2 is not present in the population, because strain 1 has a high virulence rate it has a small probability of persistence, even though $\mathcal{R}_1 > 1$ (see Figures 1 and 2). The probability of coexistence approaches zero rapidly.

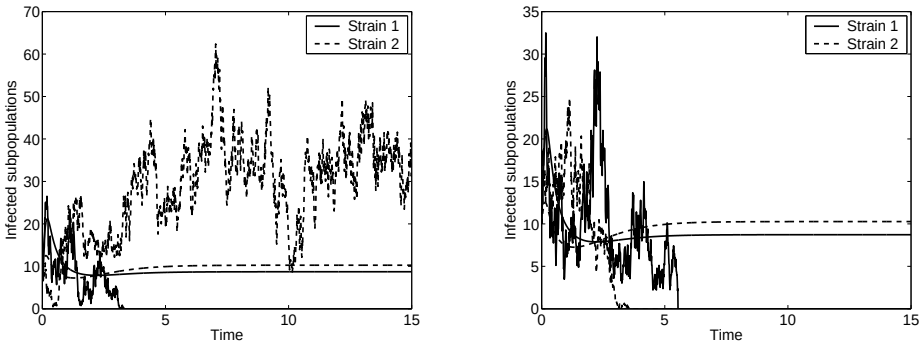


FIGURE 1. The deterministic solution and sample paths of the epidemic model with no vertical transmission. The parameter values are $b = 6$, $b_1 = b = b_2$, $\beta_1 = 30$, $\beta_2 = 15$, $\alpha_1 = 8.5$, $\alpha_2 = 3$, and $d(N) = 1 + 5N/100$.

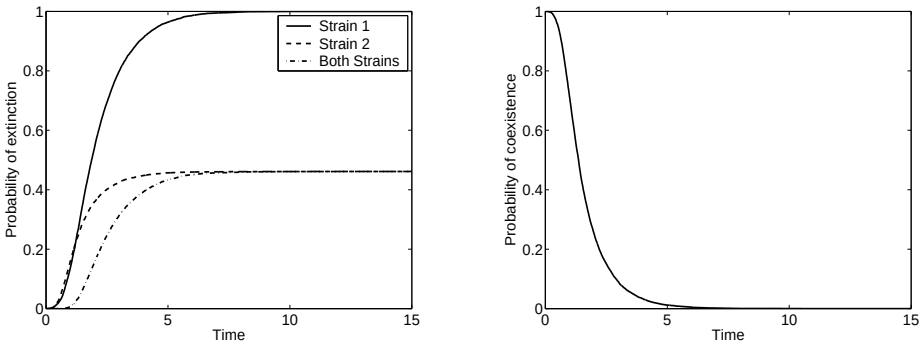


FIGURE 2. Probability of extinction of strain 1, strain 2, and both strains, and probability of coexistence for the stochastic epidemic model with no vertical transmission. The parameter values are the same as in Figure 1.

Similar results were obtained for deterministic and stochastic SIS epidemic models with recovery in [33, 34].

**3.2. Case II: Vertical Transmission of Strain 2.** Suppose $b_2 = 0$ so that the second strain is vertically transmitted. Let $b = 6 = b_1$, $\beta_1 = 15$, $\beta_2 = 1$, $\alpha_1 = 3$, $\alpha_2 = 1.5$, and $d(N) = 1 + 5N/100$. The basic reproduction numbers are

$$\mathcal{R}_1 = 1.67 \quad \text{and} \quad \mathcal{R}_2 = 0.933.$$

The conditions of Corollary 1, part II are satisfied. When both strains are present, the deterministic solution converges to

$$\lim_{t\to\infty} I_1(t) = 14.4 \quad \text{and} \quad \lim_{t\to\infty} I_2(t) = 23.1.$$

The dynamics of the deterministic and stochastic solutions are illustrated in Figure 3. Two sample paths of the stochastic model are compared to the deterministic solution. In the stochastic model, if strain 1 dies out before strain 2, then strain 2 does not persist for a long period of time because $\mathcal{R}_2 < 1$. However, if strain 2 dies out before strain 1, the infected subpopulation with strain 2 may vary for a long period of time around the equilibrium value, $\bar{I}_1 = 35$ (equilibrium in the absence of $I_2$).

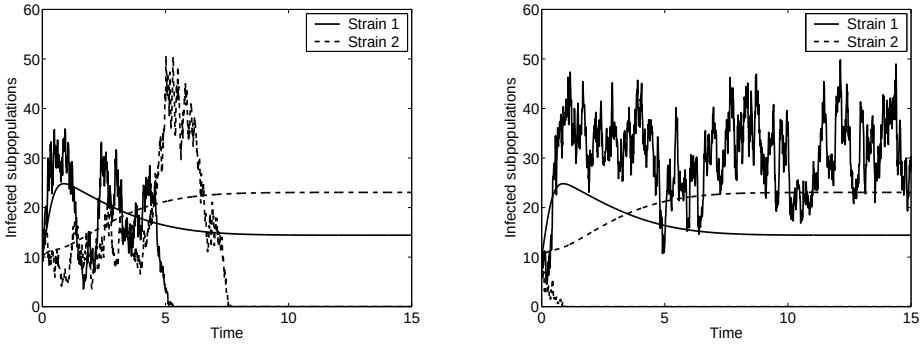


FIGURE 3. The deterministic solution and sample paths of the epidemic model with vertical transmission of strain 2. The parameter values are $b = 6 = b_1$, $b_2 = 0$, $\beta_1 = 15$, $\beta_2 = 1$, $\alpha_1 = 3$, $\alpha_2 = 1.5$, and $d(N) = 1 + 5N/100$.

It can be seen in Figure 4 that there is a high probability at least one strain does not survive. The probability of coexistence approaches zero rapidly.

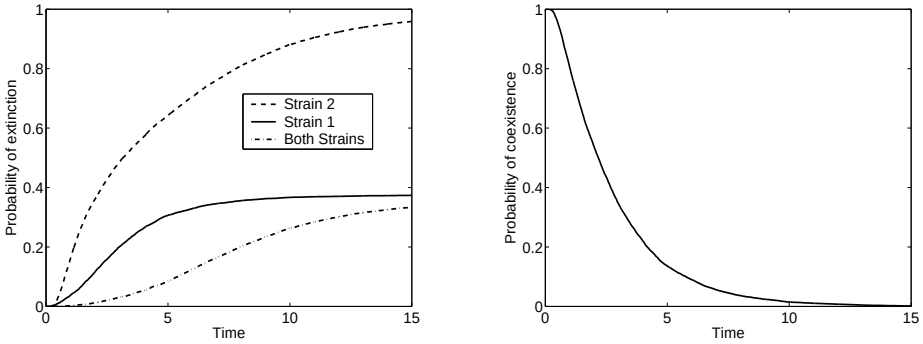


FIGURE 4. Probability of extinction of strain 1, strain 2, and both strains, and probability of coexistence for the stochastic epidemic model with vertical transmission of strain 2. The parameter values are the same as in Figure 3.

**3.3. Case III: Vertical Transmission of Both Strains.** Suppose both strains are transmitted vertically, $b_1 = 0 = b_2$. In this case, Theorem 1 does not apply. The positive equilibrium is not globally asymptotically stable. In fact, it can be shown that linearization of the system about the positive proportional equilibrium $(\bar{I}_1/\bar{N}, \bar{I}_2/\bar{N}) = (\bar{i}_1, \bar{i}_2)$ always leads to pure imaginary complex conjugate eigenvalues for the Jacobian matrix. Let $b = 6$, $\beta_1 = 15$, $\beta_2 = 1$, $\alpha_1 = 2.5$, $\alpha_2 = 2$, and $d(N) = 1 + 5N/100$. The basic reproduction numbers are

$$\mathcal{R}_1 = 2.47 \quad \text{and} \quad \mathcal{R}_2 = 0.875.$$

The deterministic model has a coexistence equilibrium at

$$\bar{S} = 2.17, \quad \bar{I}_1 = 4.34, \quad \text{and} \quad \bar{I}_2 = 54.21.$$

However, this equilibrium is not stable. The deterministic solution cycles closer and closer to each of the equilibria $(100, 0, 0)$, $(0, 40, 0)$, and $(0, 0, 60)$, but spends an increasing amount of time near the equilibrium where $I_2 = 60$. This can be seen in Figure 5. It can be shown that there is a heteroclinic orbit in the $i_1 - i_2$ phase plane, where $(1, 0) \to (0, 1) \to (0, 0) \to (1, 0)$.

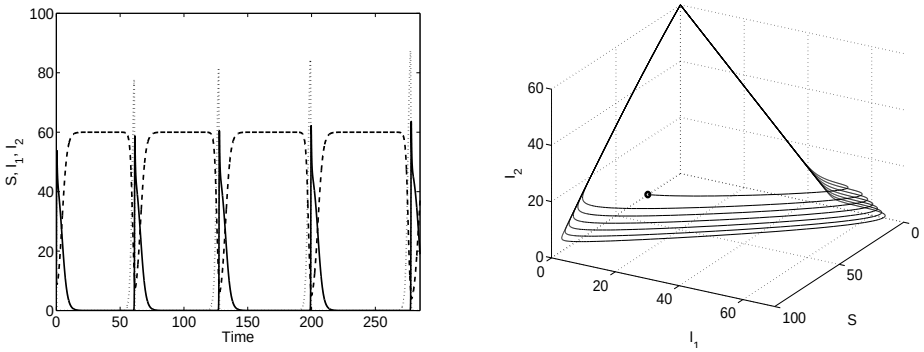


FIGURE 5. The deterministic solution is graphed as a function of time, $t \in [0, 285]$, and in the $S$-$I_1$-$I_2$ phase space, $t \in [0, 500]$. The graph of $S$ is the dotted curve, $I_1$ is the solid curve, and $I_2$ is the dashed curve. The parameter values are $b = 6$, $b_1 = 0 = b_2$, $\beta_1 = 15$, $\beta_2 = 1$, $\alpha_1 = 2.5$, $\alpha_2 = 2$, $d(N) = 1 + 5N/100$.

Because the deterministic solution approaches close to the axes, it is clear that extinction of at least one strain will have a high probability in the stochastic model. Extinction will depend very much on the initial conditions. Therefore, we do not compute the probability of extinction or probability of coexistence. Two sample paths with the deterministic solution are illustrated in Figure 6.

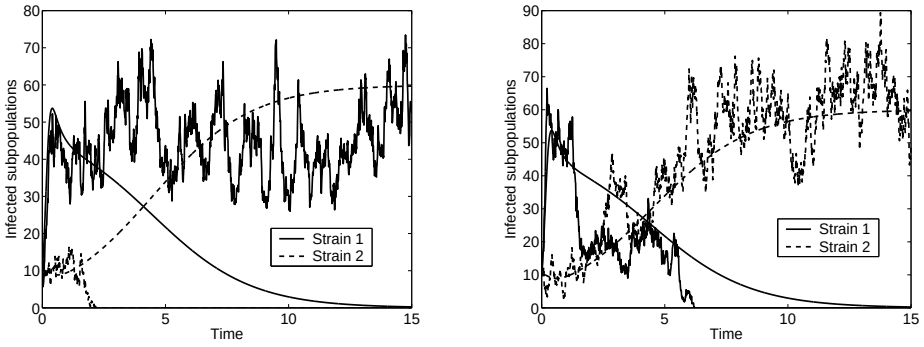


FIGURE 6. The deterministic solution and sample paths of the epidemic model with vertical transmission of both strains. The parameter values are the same as in Figure 5.

These three cases are hypothetical but illustrate some of the differences between horizontal and vertical transmission and between the deterministic and stochastic models.

**3.4. Summary.** A brief review of the literature on evolution of virulence and multiple pathogen strain epidemic models is presented. Then deterministic and stochastic $n$-strain epidemic models are formulated. The two-strain epidemic models are investigated analytically and numerically. The models assume there is total cross immunity and a density-dependent host death rate. In these models, the impact of vertical transmission on the coexistence of two strains is investigated and the coexistence dynamics of the deterministic and stochastic models are compared. The numerical examples show that coexistence in the stochastic models has a very low probability. Generally, only one strain persists resulting in competitive exclusion. Our numerical results emphasize the importance of studying the dynamics of the deterministic and the stochastic epidemic models.

These results have implications for treatment and control strategies that target a specific strain. To prevent an outbreak it may be necessary to reduce the reproduction numbers for all strains to values less than unity. If treatment strategies target only the dominant strain (or the one that persists in the stochastic model), then it is possible for another strain, with a reproduction number greater than unity, to become dominant, resulting in a disease outbreak from this other strain. Treatment strategies, drug resistance, and vaccine development are among the many problems that are being studied in models for HIV-AIDS and other diseases with multiple strains (see e.g., [10, 11, 32, 46]).

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Department of Mathematics and Statistics, Texas Tech University, Lubbock, Texas 79409-1042
*E-mail*: lallen@math.ttu.edu

Department of Mathematics, Borough of Manhattan Community College, 199 Chambers Street, The City University of New York, New York, NY 10007