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Global Stability of an Epidemic Model with Super-infection

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Abstract: A two-strain epidemic model is proposed and investigated. The conditions and thresholds to the existence of various equilibria are established. We compute the reproduction number for each strain independently, and show that when both the two reproduction numbers are less than unity, both strains die out. Conditions that guarantee the coexistence of the two strains are obtained. Our analysis shows that coexistence and competitive exclusion are possible due to the interaction between two strains. The asymptotic stability and the regions of stability for the equilibria are discussed. To verify our theoretical results, some numerical simulations are also included.

Keywords: Multiple strains; Strain replacement; Super-infection; Coexistence

1. INTRODUCTION

For many pathogens, they are represented by more than one variant. The importance of including subtypes in modeling the development and evolution of the disease is well recognized. Competitive exclusion and coexistence of strains in gonorrhea and other sexually transmitted diseases are discussed in [1,2]. The re-emergence of tuberculosis and the spread of drug-resistent strains is considered in [3,4]. Dengue is represented by four serotypes and infections by some particular sequences of them can be particularly dangerous as they are believed to lead to the deadly haemorrhagic fever. Dengue models with several serotypes are considered in [5,6]. The virus that causes influenza is so highly mutable that it has promoted scientist to create epidemic models where the infected individuals are continuously structured by the phenotype of the virus [7]. Other multi-strain models of influenza are considered in [8,9]. Epidemic model which investigates multistrain interactions and finds that competitive exclusion is the ultimate outcome is found in [10]. Various mechanisms promote coexistence among the strains. Some of those are super-infection [11,12], mutation [3,4], coinfection [13], cross-immunity [8,5], density-dependent host mortality [14] and vaccination [15].

In [16], the authors proposed and investigated a two-strain influenza epidemic model with isolation and partial cross-immunity, but without super-infection. They established that cross-immunity and host isolation lead to periodic epidemic outbreaks (sustained oscillation) in this multistrain system. Subthreshold coexistence driven by cross-immunity is possible even when the isolated reproduction number of one strain is below 1. Oscillatory coexistence is established via Hopf bifurcation theory.

As we know, super-infection is a mechanism worth consideration, for studies in [17] shows that it is possible for young individuals to become infected with two different strains in one “flu” season. In this paper, we consider a two-strain epidemic model with super-infection. The main focus of this paper is on the identification of competitive outcomes that result from the interactions between two strains. We mainly focus on the disease which have cross-immunity and super-infection, such as tuberculosis, influenza , HIV and others. The presence

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of multiple variants of the pathogen has richer dynamical behaviors, competitive exclusion and coexistence of the two strains can occur.

This paper is structured as follows. Section 2 introduces the general two-strain model; section 3 establishes four thresholds; section 4 carries out the global stability analysis of the disease-free state and the nontrival equilibria; section 5 gives the stability region analysis of different equilibria, some numerical simulations are also included to illustrate our theoretical analysis; section 6 summaries our findings and collects some thoughts.

2. TWO-STRAIN MODEL

In this section, we introduce a two strain epidemic model with super-infection. We consider a population $N(t)$ whose demography is regulated by a constant birth/r-ecruitment rate Λ and a natural mortality rate μ. The susceptible population $S(t)$ can be infected by strain one at a transmission rate β_1 and go to the class of individuals infected by strain one $I(t)$. The infected individuals in class $I(t)$ recover at a rate γ_1 and return to the susceptible class. Alternatively, susceptibles can be infected by strain two at a transmission rate β_2, in which class they go to the class of individuals infected by strain two $J(t)$. Infected individuals with strain two recover at a rate γ_2 and upon recovery return to the susceptible class. We assume that those infected with the second strain can come into a contact with infectious individuals with the first strain and become reinfected with the first strain. This process is referred to as super-infection. The biological difference between the two strains is that strain one $I(t)$ is stronger than strain two $J(t)$, i.e., strain one $I(t)$ can infect individuals already infected by strain two $J(t)$, while strain two $J(t)$ cannot infect individuals already infected by strain one $I(t)$. The transmission coefficient in case of super-infection is $\beta_1\delta$ where δ is the coefficient of reduction or enhancement of infection at reinfection. In particular, if $\delta < 1$ then reinfection is more likely than the regular infection while if $0 < \delta < 1$ then reinfection is less likely than the regular infection. If $\delta = 0$ there is no super-infection. We remark, the influenza virus satisfies the mechanism mentioned above [17], and can be described by the following model (2.1).

By the assumptions, we can give the model flow diagram.

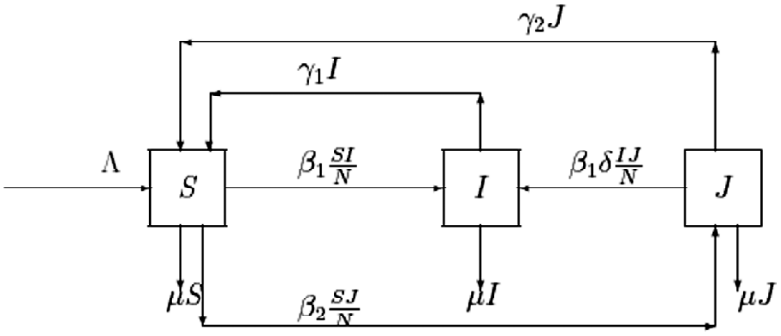

Figure 1: Transmission Diagram of Super-infection

From the transmission diagram, the model takes the form:

$$\begin{cases} \dfrac{dS}{dt} &= \Lambda - \beta_1 \dfrac{SI}{N} - \beta_2 \dfrac{SJ}{N} - \mu S + \gamma_1 I + \gamma_2 J, \\ \dfrac{dI}{dt} &= \beta_1 \dfrac{SI}{N} + \beta_1 \delta \dfrac{IJ}{N} - (\mu + \gamma_1) I, \\ \dfrac{dJ}{dt} &= \beta_2 \dfrac{SJ}{N} - \beta_1 \delta \dfrac{IJ}{N} - (\mu + \gamma_2) J, \end{cases} \tag{2.1}$$

where

$$N(t) = S(t) + I(t) + J(t),$$

and is equipped with the following initial conditions:

$$S(0) = S_0,\ I(0) = I_0,\ J(0) = J0.$$

We first note that this problem has a unique solution in the positive cone $S \geq 0$, $I \geq 0$, $J \geq 0$. Also, summing the equations, we have that the total population $N(t)$ satisfies the differential equation:

$$\frac{dN(t)}{dt} = \Lambda - \mu N(t)$$

whose solution is given by the formula

$$N(t) = N_0 e^{-\mu t} + \frac{\Lambda}{\mu}(1 - e^{-\mu t}).$$

Hence, $N(t) \to \frac{\Lambda}{\mu}$ as $t \to \infty$, and the result in [18] allows us to assume, without loss of generality, that $N(0) = \frac{\Lambda}{\mu}$.

Hence, we set

$$N(t) = S(t) + I(t) + J(t) \equiv \frac{\Lambda}{\mu} \text{ for all } t.$$

If we set

$$s = \frac{S}{N}, \quad i = \frac{I}{N}, \quad j = \frac{J}{N},$$

then $s + i + j = 1$ and system (2.1) becomes:

$$\begin{cases} \dfrac{di}{dt} = \beta_1 i(1 - i - j) + \beta_1 \delta ij - (\mu + \gamma_1) i \triangleq F(i, j), \\ \dfrac{dj}{dt} = \beta_2 j(1 - i - j) - \beta_1 \delta ij - (\mu + \gamma_2) j \triangleq G(i, j). \end{cases} \tag{2.2}$$

Define $D = \{(i, j) \in \mathbb{R}_+^2 : 0 \leq i + j \leq 1\}$, then it is easy to show that D is a positive invariant set with respect to system (2.2).

Theorem 2.1: System (2.2) has no periodic solutions in the interior of D.

Proof: Set Dulac function $B(i, j) = \frac{1}{ij}$, then we have

$$\frac{\partial (FB)}{\partial i} + \frac{\partial (GB)}{\partial j} = -\left(\frac{\beta_1}{j} + \frac{\beta_2}{i} \right) < 0,$$

then by the Bendixson-Daluc criterion, we know there is no closed orbit in the interior of D. This completes the proof.

3. STEADY STATES

For any equilibrium (i^*, j^*) of system (2.2), if it exists, must be a constant solution of the limiting system associated with (2.2). Thus we have to look for the solution of the following system:

$$\begin{aligned} 0 &= \beta_1 i^*(1-i^*-j^*)+\beta_1\delta i^* j^* -(\mu+\gamma_1)i^*, \\ 0 &= \beta_2 j^*(1-i^*-j^*)-\beta_1\delta i^* j^* -(\mu+\gamma_2)j^*. \end{aligned} \tag{3.1}$$

System (3.1) always has the disease-free equilibrium

$$E_0 = (0, 0), \tag{3.2}$$

while the existence of non-trivial equilibrium will depend on the value of the two parameters.

$$\begin{aligned} R_1 &= \frac{\beta_1}{\mu+\gamma_1}, \\ R_2 &= \frac{\beta_2}{\mu+\gamma_2}, \end{aligned} \tag{3.3}$$

which are the basic reproduction number for strain *I* and strain *J*, respectively, and give the average number of secondary infectious cases produced by an infected individual with strain *I* (respectively, by an infected individual with strain *J*) during the entire infectious period in a purely susceptible population.

Solving system (3.1) we see that, besides E_0, the following one strain exclusion equilibria are feasible, under some conditions on R_1 and R_2. Namely we have

(1) The following strain one exclusive equilibrium exists

$$E_1 = (i_1^*, 0), \quad i_1^* = 1-\frac{1}{R_1}, \tag{3.4}$$

if and only if $R_1 > 1$;

(2) The following strain two exclusive equilibrium exists

$$E_2 = (0, j_2^*), \quad j_2^* = 1-\frac{1}{R_2}, \tag{3.5}$$

if and only if $R_2 > 1$.

Furthermore, the presence of a coexistence equilibrium depends on two other reproduction numbers, namely the invasion reproduction numbers R_{12} and R_{21}. By definition, the invasion reproduction number of the first strain R_{12} gives the number of secondary infections that one infected individual with the first strain will produce in a population in which the second strain *J* is at equilibrium. We refer to [19] for the explanation how these numbers are computed. The invasion reproduction number of the first strain in our case is given by (see(3.5))

$$R_{12} = \frac{R_1}{R_2} + \delta R_1\left(1-\frac{1}{R_2}\right). \tag{3.6}$$

Denote $S_2^+ = \frac{N}{R_2}, J_2^+ = N\left(1-\frac{1}{R_2}\right)$, then $R_{12} = \frac{\beta_1}{\mu+\gamma_1}\frac{S_2^+}{N} + \delta\frac{\beta_1}{\mu+\gamma_1}\frac{J_2^+}{N}$. R_{12} is in fact the result of two additive contributions: $\frac{\beta_1}{\mu+\gamma_1}$ gives the number of secondary cases that a "typical" strain-*I* infected individual will generate in the fully susceptible proportion of the population $\frac{S_2^+}{N}$, while $\delta\frac{\beta_1}{\mu+\gamma_1}$ is the number of secondary cases that a "typical" strain-*I* infected individual will generate in the "super-infection" proportion of the susceptible population $\frac{J_2^+}{N}$.

Analogously, the invasion reproduction number of the second strain R_{21} gives the number of the secondary infections that one infected individual with which the second strain will produce in a population in which the first strain *I* is at equilibrium. The invasion reproduction number of the second strain in our case is given by (see (3.4))

$$R_{21} = \frac{R_2}{R_1} - \frac{\beta_1\delta}{\beta_2}R_2\left(1-\frac{1}{R_1}\right). \tag{3.7}$$

The meaning of R_{21} is similar to that of R_{12}. But since strain *J* is super-infected by strain *I*, then there is a minus sign before the second term in R_{21}.

The two invasion reproduction numbers determine the occurrence of one coexistence equilibrium. In fact, solving (3.1) for non-trivial i^* and j^* we see that it there exists the endemic equilibrium

$$E^* = (i^*, j^*)$$

where

$$\begin{aligned} i^* &= \frac{1}{\beta_1\delta}\left[\frac{\beta_2(\beta_1\delta+\gamma_2-\gamma_1)}{\beta_1\delta+\beta_2-\beta_1} - (\mu+\gamma_2)\right], \\ j^* &= \frac{1}{\beta_1\delta}\left[\mu+\gamma_1 - \frac{\beta_1(\beta_1\delta+\gamma_2-\gamma_1)}{\beta_1\delta+\beta_2-\beta_1}\right]. \end{aligned} \tag{3.8}$$

that is feasible if and only if the following condition is satisfied

$$\frac{1}{R_2} < \frac{\beta_1\delta+\gamma_2-\gamma_1}{\beta_1\delta+\beta_2-\beta_1} < \frac{1}{R_1}, \tag{3.9}$$

Thus we have

(3) If $\beta_1\delta+\gamma_2-\gamma_1 > 0$, then E_* exists if and only if the two invasion reproduction numbers are both greater than one, that is

$$R_{12} > 1, R_{21} > 1. \tag{3.10}$$

In fact, we can check that the upper inequality in (3.9) is equivalent to the inequality $R_{21} > 1$, while the lower inequality is equivalent to the inequality $R_{12} >$.

(4) If $\beta_1\delta + \gamma_2 - \gamma_1 < 0$, then E_* exists if and only if the two invasion reproduction numbers are both less than one, that is

$$R_{12} < 1, R_{21} < 1. \tag{3.11}$$

We note that feasibility implies $R_1 < R_2$.

We summarize the issues above in the following theorem:

Theorem 3.1: Let R_1, R_2, R_{12}, R_{21} be the reproduction number respectively defined in (3.3), (3.6), (3.7). Then

(i) The disease-free equilibrium E_0 given in (3.2) exists for all values of the parameters.

(ii) The strain one exclusive equilibrium E_1 given in (3.4) exists if and only if $R_1 > 1$.

(iii) The strain two exclusive equilibrium E_2 given in (3.5) exists if and only if $R_2 > 1$.

(iv) If $\beta_1\delta + \gamma_2 - \gamma_1 > 0$, the coexistence equilibrium E_* given in (3.8) exists if and only if $R_{12} > 1$ and $R_{21} > 1$.

(v) If $\beta_1\delta + \gamma_2 - \gamma_1 < 0$, the coexistence equilibrium E_* given in (3.8) exists if and only if $R_{12} < 1$ and $R_{21} < 1$.

We see that though condition (3.9) shows a rather complicated dependence of coexistence from the parameters, nevertheless there is a simple description in terms of significant parameters such as reproduction numbers and invasion numbers.

4. STABILITY ANALYSIS

In this section we investigate the stability properties of the equilibria whose existence has been stated in the previous analysis. Denote $R_0 = \max\{R_1, R_2\}$. Then we start with the trivial disease free equilibrium.

Theorem 4.1: If $R_0 < 1$, then the disease free equilibrium E_0 is globally asymptotically stable, if $R_0 > 1$, then E_0 is unstable.

Proof: Taking the linearization of system (2.2) at the point E_0, we get the following characteristic equation

$$[\lambda - (R_1 - 1)(\mu + \gamma_1)][\lambda - (R_2 - 1)(\mu + \gamma_2)] = 0.$$

The eigenvalues are $\lambda_1 - (R_1 - 1)(\mu + \gamma_1)][\lambda_2 - (R_2 - 1)(\mu + \gamma_2)$, we see if $R_0 > 1$ then $R_1 > 1$ or $R_2 > 1$, then at least one solution of this equation is positive, so E_0 is unstable. If $R_0 < 1$, then $R_1 < 1$ and $R_2 < 1$, then $\gamma_1 < 0$, and $\gamma_2 < 0$, thus E_0 is locally asymptotically stable. Next we show the global attractiveness of E_0 when $R_0 < 1$. Set

$$V(t) = i + j$$

calculating the derivative of $V(t)$ along the system (2.2), we obtain

$$\frac{dV}{dt} = \frac{di}{dt} + \frac{dj}{dt}$$

$$= (\beta_1 i + \beta_2 j)(1 - i - j) - (\mu + \gamma_1)i - (\mu + \gamma_2)j$$

$$= (\mu + \gamma_1)(R_1 - 1)i + (\mu + \gamma_2)(R_2 - 1)j - (\beta_1 i + \beta_2 j)(i + j) \le 0.$$

Set H = $\{(i, j) : \frac{dV}{dt} = 0\}$, then (0, 0) is the largest set in H which is invariant with respect to system (2.2). Then by Lyapunov-LaSalle invariant principle [20], we see E_0 is globally attractive. From the above, we see E_0 is globally asymptotically stable when $R_0 < 1$. Then the proof of Theorem 4.1 is completed.

The theorem below says that each strain can dominate if its reproduction number is larger than one and the other strain cannot invade its equilibrium.

Theorem 4.2: The one strain exclusive equilibria satisfy:

(i) If $R_1 > 1$, the boundary equilibrium E_1 is stable for $R_{21} < 1$ and unstable for $R_{21} > 1$.

(ii) If $R_2 > 1$, the boundary equilibrium E_2 is stable for $R_{12} < 1$ and unstable for $R_{12} > 1$.

Proof: Let $R_1 > 1$, then the equilibrium E_1 exists and the linearization of (2.2) at E_1 gives the following characteristic equation:

$$\left[\lambda - \beta_1\left(\frac{1}{R_1} - 1\right)\right][\lambda - (\mu + \gamma_2)(R_{21} - 1)] = 0.$$

Then the two eigenvalues are $\lambda - \beta_1\left(\frac{1}{R_1} - 1\right) < 0$, $\lambda_2 = (\mu + \gamma_2)(R_{21} - 1)$. Hence if $R_{21} > 1$, $\lambda_2 > 0$, then E_1 is unstable. If $R_{21} < 1$, $\lambda_2 < 0$, then E_1 is stable. This completes (i). Part (ii) can be proved in the same way as we proved part (i). This completes the proof of Theorem 4.2.

Denote $D_1 = \{(i, j) \in D : i \neq 0\}$, $D_2 = \{(i, j) \in D : j \neq 0\}$, $D_3 = \{(i, j) \in D : ij \neq 0\}$.

Theorem 4.3: If $\beta_1\delta + \gamma_2 - \gamma_1 > 0$, $R_{21} > 1$, $R_{21} > 1$, then E_* is globally asymptotically stable on D_3.

Proof: From Theorem 3.1, we know E_* exists under the condition given in Theorem 4.3. By $\beta_1\delta + \gamma_2 - \gamma_1 < 0$, $R_{21} > 1$we get $\beta_1\delta + \beta_2 - \beta_1 > 0$. The linearization of (2.2) at E_* gives the following characteristic equation:

$$\lambda^2 + (\beta_1 i^* + \beta_2 j^*)\lambda + (\beta_1\delta + \beta_2 - \beta_1)i^* j^* \beta_1 \delta = 0 \tag{4.2}$$

Obviously, (4.2) has no root with nonnegative real part, then E_* is locally asymptotically. Since $R_{12} > 1$ and $R_{21} > 1$, by Theorem 3.1 and 4.2, we obtain that E_1 (E_2) does not exist or is unstable (if exists). If $R_1 \le 1$ and $R_2 \le 1$, the by (3.9) we have $R_1 < R_2$ thus $R_{12} = \frac{R_1}{R_2} + \delta R_1(1 - \frac{1}{R_2}) \le \frac{R_1}{R_2} < 1$, which is a contradiction. Then E_0 is unstable. Hence by Theorem 2.1, we get E_* is globally asymptotically stable on D_3. This completes the proof.

Corollary 4.1: If , $\beta_1\delta + \gamma_2 - \gamma_1 < 0$, $R_{12} < 1$, $R_{21} < 1$, then E_* is unstable.

Proof. From Theorem 3.1, we know E_* exists under the condition given in Corollary 4.1, and we have $\beta_1\delta + \beta_2 - \beta_1 < 0$. Then (4.2) has one positive root. Thus E_* is unstable. Completing the proof.

Corollary 4.2: If $R_1 > 1$ and $R_2 \le 1$, then E_1 is globally asymptotically sable on D_1.

Proof: From the conditions in Corollary 4.2, we have E_0 is unstable E_2, does not exist. Since $R_{21} = \frac{R_2}{R_1} - \frac{\beta_1\delta}{\beta_2}(1 - \frac{1}{R_1})R_2 \le \frac{R_2}{R_1} < 1$, then by Theorem 3.1 and Corollary 4.1, we get E_* does not exist or is unstable (if exists). Then by Theorem 2.1 and Theorem 4.2, we obtain that E_1 is globally asymptotically sable on D_1. Which completes the proof.

Corollary 4.3: If $R_2 > 1$, $R_1 \le 1$, and $R_{12} < 1$, then E_2 is globally asymptotically sable on D_2.

Proof: From the conditions in Corollary 4.3, Theorem 3.1 and Theorem 4.1, we have E_0 is unstable E_1 does not exist. By Theorem 3.1 and Corollary 4.1, we get E_* does not exist or is unstable (if exists). Then by Theorem 2.1 and Theorem 4.2, we obtain that E_1 is globally asymptotically sable on D_2. The proof of Corollary 4.3 is completed.

From theorems and corollaries above, we see the disease is extinct when $R_0 < 1$, while when $R_0 > 1$, the disease may persist.

5. STABILITY REGION OF TWO-STRAIN

In section 3, we know there are four critical curves $R_1 = 1$, $R_2 = 1$, $R_{12} = 1$, $R_{21} = 1$, which determine the stability of the four equilibria. Functions R_{12} and R_{21} help in the characterization of the stability and coexistence regions for strain 1 and 2. Changes in the regions of stability for either a single or for both strains can be illustrated as the coefficient of super-infection are varied. In this section, we investigate the stability region of the nontrivial equilibria and the change of the region.

First we consider the two curves R_{12} and $R_{21} = 1$.

By $R_{12} = 1$ we obtain L1:

$$R_2 = \frac{R_1(1-\delta)}{1-\delta R_1} \quad \text{and} \quad \frac{dR_2}{dR_1} = \frac{1-\delta}{(1-\delta R_1)^2};$$

By R_{21} we obtain L2:

$$R_2 = \frac{R_1}{1-\beta_1\delta\beta_2(R_1-1)} \quad \text{and} \quad \frac{dR_2}{dR_1} = \frac{1+\dfrac{\beta_1\delta}{\beta_2}}{(1-\dfrac{\beta_1\delta}{\beta_2}(R_1-1))^2}.$$

We suppose $\beta_1\delta + \gamma_2 - \gamma_1 > 0$, then there are three cases to consider:

(1) $0 < \delta < 1$.

Figure 2(a) and (b) gives the bifurcation diagram in the (R_1, R_2)-plane. The curves $R_{12} = 1$ and $R_{21} = 1$ divide the region $\mathbb{R}^2_+ - \{(R_1, R_2) \mid R_1 < 1, R_2 < 1\}$ into three subregions: I, II, III. When the parameters are in region I (II) only strain 1 (strain 2) will be maintained (a globally stable boundary equilibrium). In Figure 2(a), region III,

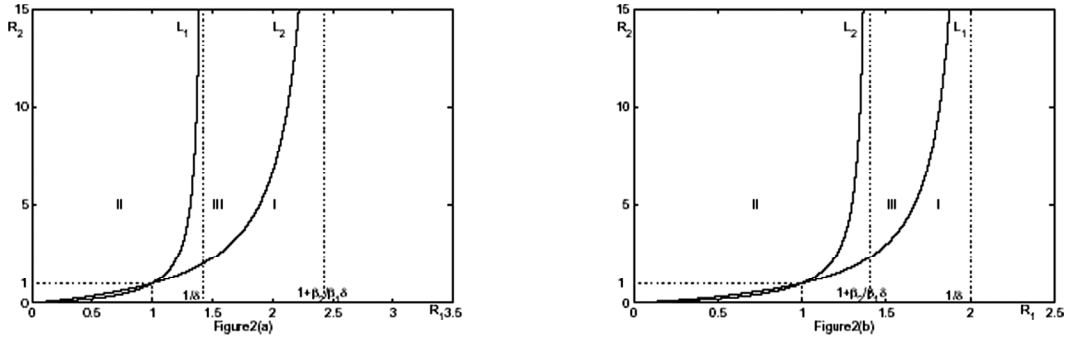

Figure 2: The Figures Show when $0 < \delta < 1$, the Stability Regions of Different Nontrivial Equilibria in the (R_1, R_2)-plane. The Curves $R_{12} = 1$and $R_{21} = 1$ Divide the Region $\mathbb{R}^2_+ - \{(R_1, R_2) \mid R_1 < 1, R_2 < 1\}$ into Three Subregions: I, II, III

both strains will be maintained (a globally stable positive equilibrium). In Figure 2(b), region III, the two strain does not coexistence, but two boundary equilibrium are stable.

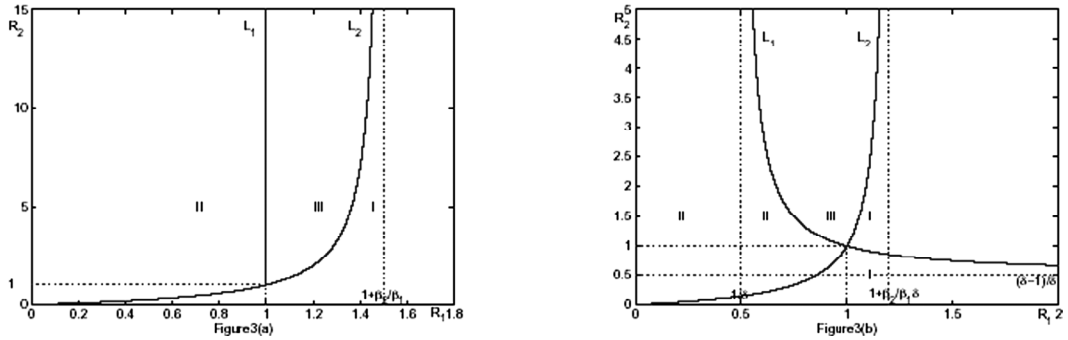

Figure 3: The Figures Show the Bifurcation Diagram of δ = 1and δ > 1 in the (R_1, R_2)-plane, Respectively. The Meanings of these Regions are the Same as Those of Figure 1(a)

Figure 3(a), (b) gives the bifurcation diagrams of δ = 1 and δ > 1, respectively. The curves $R_{12} = 1$ and $R_{21} = 1$ divide the region $\mathbb{R}^2_+ - \{(R_1, R_2) \mid R_1 < 1, R_2 < 1\}$ into three subregions: I, II, III. The meanings of these regions are the same as those in Figure 2(a).

From Figure 2(a), we see, $R_{21} < 1$ is a necessary condition for the stability of strain 1. Hence, E_1 is unstable when $R_{21} > 1$. Similarly, E_2 is unstable when $R_{12} > 1$. Hence, coexistence is expected when $R_{12} > 1$ and $R_{21} > 1$.

From Figure 2 and Figure 3, we see the stability region for strain 1 (I) may be significantly larger than that of strain 2 (II) with the increase of δ. The changes in the relative sizes of these stability regions seem to cause strong super-infection when strain *J* is infected by strain *I*.

The possibility that strain *J* may become established under these conditions can be small. Likewise, weaker levels of super-infection to strain *J* after an infection with strain *I* (δ↓ 0) will support relatively larger regions of stability for strain *J*.

The stability region for strain 1(I) and strain 2(II) in the (R_1, R_2)-plane ($0 < \delta < 1$, $\delta = 1$, $\delta > 1$) are illustrated in Figure 2 and Figure 3. We show that as the levels of super-infection increase, that is, as the values of get bigger, the region of stability corresponding to strain 1 (region (I)) is increased significantly. Simultaneously, an increase in the region of multiple strain coexistence (if E_* exists) can be observed as super-infection is increased (see Fig.4(a)-(d)). It seems that as strains become antigenically distinct, that is, when super-infection is strong, coexistence is more likely. Weak levels super-infection support the survival of a single strain, that is, in this case competition for susceptibles between strains is "fierce"("competition exclusion"). The strain with the highest ability to invade the host is the most likely to become established (driving the other strain to extinction).

6. DISCUSSIONS

In this paper, we consider the development and evolution of a disease represented by two strains. The focus of this paper is on the interaction of two strains. We have assumed that the first pathogen can infect individuals already infected by the second, a process called super-infection, while the other way around has such a small incidence that it can be neglected. Altogether, this makes the first strain stronger. Thus, if $R_1 > R_2$ the first strain dominates. The outcome of the competition between the two strains when $R_1 < R_2$ depends on the two invasion reproduction numbers: the invasion reproduction number of the first strain at equilibrium of the second R_{12} and

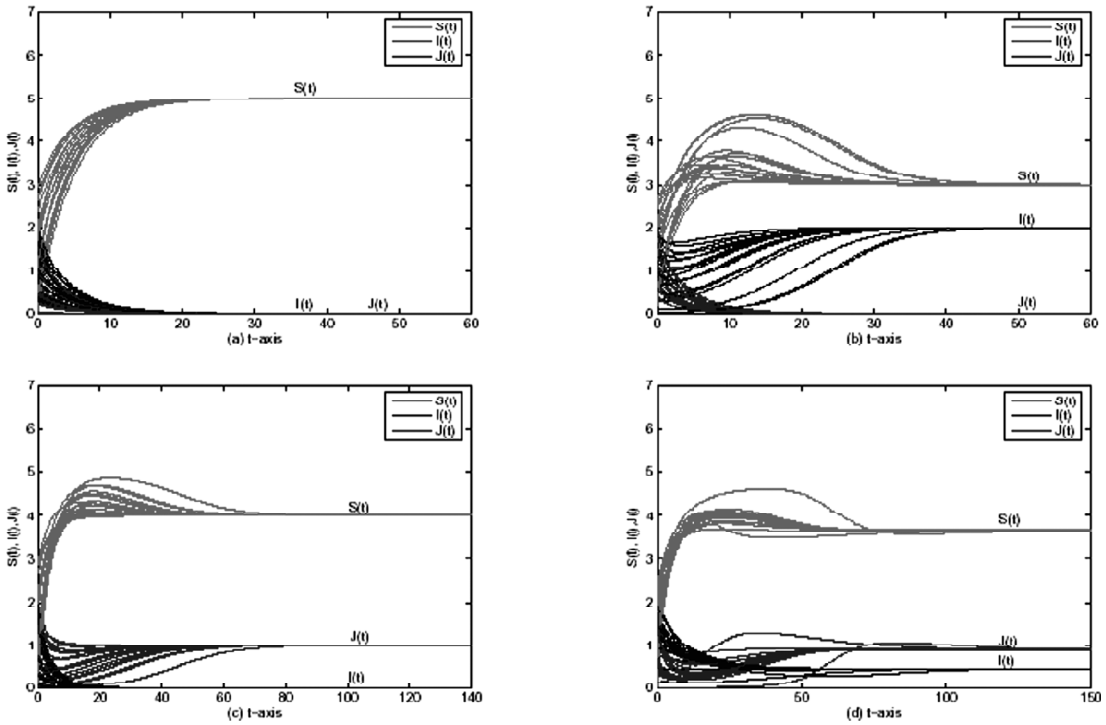

Figure 4: The Figures (a)-(d) Show as the Super-infection Coefficient δ is Increased (in Figure 4 (a)-(d), δ = 0.1, δ = 0.1, δ = 0.1, and δ = 1.5, Respectively), the Two Strains can Coexist more likely

invasion reproduction number of the second strain in the equilibrium of the first R_{21}. If $R_{21} < 1$ then strain one dominates, if $R_{12} < 1$ then strain two dominates, if both invasion reproduction number are larger than one, then the two strains coexist. Our results show that multiple strain coexistence is highly likely for antigenically distinct (strong super-infection) strains and not for antigenically similar strains. However, more understanding of the evolutionary implications that result from human host and virus interactions may require the study of systems that incorporate additional mechanisms such as infection-age structure, isolation, individual differences in susceptibility or infectiousness, and the possibility of coinfections.

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