J Nonlinear Sci (2013) 23:113–127
DOI 10.1007/s00332-012-9146-1

Journal of Nonlinear Science

Superinfection Behaviors on Scale-Free Networks with Competing Strains

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Received: 21 September 2011 / Accepted: 19 July 2012 / Published online: 31 August 2012

Abstract This paper considers the epidemiology of two strains (I, J) of a disease spreading through a population represented by a scale-free network. The epidemiological model is SIS and the two strains have different reproductive numbers. Superinfection means that strain I can infect individuals already infected with strain J, replacing the strain J infection. Individuals infected with strain I cannot be infected with strain J. The model is set up as a system of ordering differential equations and stability of the disease free, marginal strain I and strain J, and coexistence equilibria are assessed using linear stability analysis, supported by simulations. The main conclusion is that superinfection, as modeled in this paper, can allow strain I to coexist with strain J even when it has a lower basic reproductive number. Most strikingly, it can allow strain I to persist even when its reproductive number is less than 1.

Keywords Complex networks · Epidemic dynamics · Linear stability analysis · Superinfection

Communicated by P. Newton.

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Mathematics Subject Classification 34D20 · 37M20 · 82C22 · 92D30

1 Introduction

The key property of a network is its degree distribution. For any network, the degree distribution $P(k)$ for each $k \geq 1$ is the fraction of nodes with degree k in the population, where $\sum P(k) = 1$. A Scale-free (SF) network (Barabási and Albert 1999) exhibits a power-law degree distribution ($P(k) \propto k^{-\gamma}$ where γ usually ranges between 2 and 3) and provides a more accurate model of real world networks (Small and Tse 2005; Small et al. 2007), such as social networks or the Internet. The epidemic spreading process on SF networks has been widely studied (Pastor-Satorras and Vespignani 2001, 2002; Newman 2005; Wu et al. 2010; Fu et al. 2008).

In this context, the so-called Susceptible-Infected-Susceptible (SIS) model (e.g., Pastor-Satorras and Vespignani 2001) and the Susceptible-Infected-Removed (SIR) (e.g., Madar et al. 2004) are frequently used in epidemiology. The main contribution of Pastor-Satorras and Vespignani (2001) is to identify the conditions beyond which an epidemic spreads and persists in a population by means of a mean-field approach. Although there are some other approaches, e.g., the stochastic process approach (Newman 2005; Wang et al. 2003), the mean-field approach is often used to model the epidemic spreading and analyze its dynamical behaviors (Lou and Ruggeri 2010; Jin et al. 2011). Interestingly, it cannot only be used in the single strain/pathogen, but can also be effective in multiple strains, such as two-strain epidemic models (Masuda and Konno 2006; Ahn et al. 2006).

In the present work, we consider the epidemic propagation dynamics for two competing strains (I, J) in a population represented by a scale-free network and assume that these two strains interact by superinfection. The concept of competing between the two strains of infection (or pathogens) means that two strains from one pathogen cannot co-infect in a single host at any one time. Hence, this concept is referred as a dynamical interaction (Marceau et al. 2011) between two strains/pathogens and is different from model used in Newman (2005). Moreover, superinfection incorporating competing strains means that strain I can infect individuals already infected with strain J, replacing the strain J infection (Nowak and May 1994). Besides the context of epidemiology (Nowak and May 1994; Smith et al. 2005), superinfection between competing strains can be considered as a model of interaction between malicious agents and immunizing agents in the spreading of computing viruses, indicating that the immunizing agent spreads in the whole Internet to seek out and kill the malicious worm (Ahn et al. 2006). Another example is competing ideas/rumor (Wang et al. 2012) and the interaction between aware and unaware agents (Funk et al. 2010), which allows for one idea/rumor/awareness to be replaced by the other one for each individual.

Although the results on superinfection in mixed populations (Nowak and May 1994; Thomasey and Martcheva 2008; NuNo et al. 2005) are abundant, these results cannot be directly and easily extended to the case in a heterogenous population represented by scale-free networks. Recently, Masuda and Konno (2006) studied an SIS

model with competing pathogens and mutation in networks by analyzing the existence of the positive steady state and obtained the impact of mutation rate on epidemic threshold. However, to our knowledge, there has been no further work in this area. In our model, we restrict our attention to the so-called *strain dynamics* including both strain coexistence (the simultaneous propagation of two competing strains) and strain replacement (the strain with the smaller reproductive number can become predominant and another strain with the larger reproductive number will die out) (Thomasey and Martcheva 2008; Cai et al. 2007). In other words, which strain can prevail and persist in a population? To solve this issue, it is necessary to determine the conditions for strain coexistence or strain replacement. We will find that these conditions are not only related with both the reproductive numbers and network structure but also with the associated recovery rate.

For the sake of the following analysis, we firstly present a frequently used lemma.

Lemma 1 *For the real matrix* $A = [a_{ij}] \in R^{n\times n}$ *where* $a_{ij} = \delta_{ij}\sigma_i + p_i q_j$ $(p_i, q_j \geq 0, i, j = 1, 2, \ldots, n)$ *and* δ_{ij} *is the Kronecker symbol, we have that the determent of* A *is such that*

$$\begin{aligned}\det[A] = {} & \sigma_1\sigma_2\cdots\sigma_n + p_1q_1\sigma_2\cdots\sigma_n + \sigma_1 p_2q_2\sigma_3\cdots\sigma_n \\ & + \cdots + \sigma_1\sigma_2\cdots\sigma_{n-1}p_nq_n.\end{aligned}$$

Specially, if $\sigma_k \neq 0, k = 1, \ldots, n$, *then*

$$\det[A] = \left(1 + \sum_{k=1}^{n} \frac{p_k q_k}{\sigma_k}\right) \prod_{k=1}^{n} \sigma_k;$$

if $\sigma_k = \sigma, k = 1, \ldots, n$, *then*

$$\det[A] = \sigma^{n-1}\left(\sigma + \sum_{k=1}^{n} p_k q_k\right).$$

This lemma is easily proved by the basic determent transformations. We denote, as usual, by $\lambda(A)$ the spectrum of the square matrix A and $\lambda_i(A) \in \lambda(A)$ is an eigenvalue of A. Also, it can be seen that $\det[A - \lambda \mathrm{I}]$ can be directly computed by Lemma 1.

The remainder of this work is presented as follows. Firstly, we study the two-strain epidemic model with superinfection, to obtain threshold conditions of strain coexistence and strain replacement. Next, simulations have been made to verify the obtained results. Finally, conclusions and discussions for our work are given.

2 Model and Analysis

We consider the following dynamical process.

susceptible-infected-susceptible $\beta_1, \beta_2, \gamma_1, \gamma_2$. The epidemic model is SIS (Brauer 2005). SIS models can be adapted for some STDs (such as gonorrhea (Castillo-Chavez et al. 1999)). Note that it may be the case that the two strains have different spreading rates, we let the spreading rates of the strain I and strain J be β_1 and β_2,

respectively. A susceptible individual may become infected owing to contact with other infected ones, and an infected individual may also recover/be treated into the susceptible sate, with the recovery/treatment rates γ_1, γ_2 for strain I and strain J, respectively.

superinfection δ. For those individuals infected with strain J, they may not escape from infection by strain I before recovering to the susceptible state. Hence we introduce the constant transition rate from strain J to strain I, δ, also called the superinfection rate. In addition to superinfection, the model includes components representing "restraint of contact" and "saturated infectivity," which make our model both more reasonable and general.

restraint of contact $\psi(k)$. Recently, Li et al. (2010) studied the relation between the epidemic prevalence and epidemic threshold in networks with effective contact. Perhaps a more plausible scenario is that an infected individual may restrain its behavior such as contact with other friends owing to its physical fitness. Motivated by this, we suppose an individual already infected with strain J potentially decreases contact with its friends infected with strain I. The restraint of contact between infected individuals actually reflects the adjustment of susceptibility (Olinky and Stone 2004) or the effect of individual awareness (Gross et al. 2006; Shaw and Schwartz 2008; Funk et al. 2009). For an individual with connectivity k, we introduce the restraint of contact $\psi(k)$. Obviously, $\psi(k) \leq k$.

saturated infectivity $\varphi(k)$. When considering transmission of a disease in a finite time period, it is natural to suppose that there exists an upper bound on the infectivity of a highly connected individual (Olinky and Stone 2004), instead of the infectivity being equal to the node degree (Pastor-Satorras and Vespignani 2001). For simplicity, we assume that the infectivities of strain I and strain J are the same function of the node degree k, denoted by $\varphi(k)$, which fulfils the three conditions: (i) $\varphi(k) \leq k$; (ii) $\varphi(k)$ is monotonously increasing; (iii) $\lim_{k\to\infty} \varphi(k) = L > 0$.

Recently, Fu et al. (2008) introduced a model of infectivity as a piecewise linear function of node degree. It can be shown that the piecewise linear infectivity is a special case of the saturated infectivity defined above.

We study strain dynamics in scale-free networks by using the mean field approach which proves useful for single strain or multiple strain epidemic systems (Pastor-Satorras and Vespignani 2001; Masuda and Konno 2006). To this end, we divide all the nodes in the network into classes in view of their degrees and their epidemiological states. That is, those nodes with the same number of neighbors and the same states belong to the same class. Let $i_k(t)$ and $j_k(t)$ represent the densities at time t of nodes in class with degree k infected by strain I and strain J respectively. Based on all these assumptions, a general two-strain epidemic model with superinfection can be described by the coupled nonlinear differential equations as

$$\begin{cases} \frac{\mathrm{d}}{\mathrm{d}t} i_k(t) = -\gamma_1 i_k + \beta_1 k(1 - i_k - j_k)\Theta_1(t) + \delta\psi(k) j_k \Theta_1(t) \\ \frac{\mathrm{d}}{\mathrm{d}t} j_k(t) = -\gamma_2 j_k + \beta_2 k(1 - i_k - j_k)\Theta_2(t) - \delta\psi(k) j_k \Theta_1(t) \end{cases} \tag{1}$$

where $\Theta_1(t)$ and $\Theta_2(t)$, called the force of infection (Zou et al. 2011), represent the probabilities that any given link points to a node infected with strain I and strain J respectively. In general, $\Theta_1(t)$ and $\Theta_2(t)$ depend on the node degree (Fu et al. 2008) and can be denoted as $\Theta_1(k,t) = \sum_{k'} P(k'|k)\frac{\varphi(k')}{k'} i_{k'}(t)$ and

$\Theta_2(k,t) = \sum_{k'} P(k'|k)\frac{\varphi(k')}{k'} j_{k'}(t)$, where saturated infectivities are used and $P(k'|k)$ denotes the probability that a randomly selected edge emitting from a node with degree k points to the node with degree k'.

In this work, we suppose that the connectivity of nodes is uncorrelated. For more realistic correlated cases, the discussion is similar to that below, but the expressions are much more complicated. In degree-uncorrelated networks, we have $P(k'|k) = k'P(k')/\langle k\rangle$ where the mean degree $\langle k\rangle = \sum_s sP(s)$. Using this condition, $\Theta_1(t)$ and $\Theta_1(t)$ are not related with k and become more simple as follows:

$$\Theta_1(t) = \frac{\sum_{k'} \varphi(k')P(k')i_{k'}(t)}{\langle k\rangle}, \qquad \Theta_2(t) = \frac{\sum_{k'} \varphi(k')P(k')j_{k'}(t)}{\langle k\rangle}. \tag{2}$$

It can be seen that system (1) has five parameters, i.e., $\beta_1, \beta_2, \gamma_1, \gamma_2, \delta$, which can be reduced to four by using a typical time-scale transformation. Hence, both γ_1 and γ_2 can not simultaneously be set to 1. However, this case is always ignored in the literature (Masuda and Konno 2006). In the following analysis, we will see that the recovery rates play an important role on the epidemic dynamics. So we still keep the number of parameters in system (1). In addition, it will be found that the composed parameters $\tau_i = \frac{\beta_i}{\gamma_i}$, $i = 1, 2$ are important to analyze the epidemic dynamics, and they are referred to as the effective spreading rates for strain I and strain J, respectively. Using these two composed parameters, we introduce two parameters

$$\mathcal{R}_1 = \frac{\tau_1\langle k\varphi(k)\rangle}{\langle k\rangle}, \qquad \mathcal{R}_2 = \frac{\tau_2\langle k\varphi(k)\rangle}{\langle k\rangle}, \tag{3}$$

where $\langle k\varphi(k)\rangle = \sum_s s\varphi(s)P(s)$ follows as the usual meaning of $\langle\cdot\rangle$. They are just the effective reproductive numbers (Olinky and Stone 2004) for strain I and strain J, respectively, when there is only one strain epidemic through the network. The effective reproductive number characterizes the level of epidemic outbreak (Olinky and Stone 2004) and represents the average number of new infections an infection causes early in an outbreak (Miller 2007). Also, it is easy to see that the two reproductive numbers are related to the effective spreading rates. If $\tau_1 = \tau_2$, then $\mathcal{R}_1 = \mathcal{R}_2$. Otherwise, they are not identical to each other.

Before we study the model (1) more deeply, it is interesting to consider some reduced forms of it.

Reduced Model I: $\delta = 0$. In this case, the model is

$$\begin{cases} \frac{\mathrm{d}}{\mathrm{d}t} i_k(t) = -\gamma_1 i_k + \beta_1 k(1 - i_k - j_k)\Theta_1(t) \\ \frac{\mathrm{d}}{\mathrm{d}t} j_k(t) = -\gamma_2 j_k + \beta_2 k(1 - i_k - j_k)\Theta_2(t). \end{cases} \tag{4}$$

This model (when $\varphi(k) = k$), which we studied in Wu et al. (2011), accounts for the pure competition between two strains in the same network. Our results indicate the existence of a simple competing-exclusion, i.e., only the strain with a higher reproductive number can prevail and persist for ever in the population. We will see that this nature can be kept in the general model (1) when the superinfection rate δ is sufficiently small.

Reduced Model II: $\beta_1 = \beta_2 = \beta$, $\gamma_1 = \gamma_2 = \gamma$. Let $\rho_k = i_k + j_k$ for each k, then the model (1) can be reduced into

$$\frac{\mathrm{d}}{\mathrm{d}t}\rho_k(t) = -\gamma\rho_k + \beta k(1 - \rho_k)\Theta(t), \tag{5}$$

where $\Theta(t) = \Theta_1(t) + \Theta_2(t)$. This model is the standard networked SIS model (Pastor-Satorras and Vespignani 2001). Hence, when $\mathcal{R}_1 = \mathcal{R}_2 = \mathcal{R} \leq 1$, both strains dies out; when $\mathcal{R} > 1$, strain I or strain J prevails eventually. What is more, we can show that only strain J can persist in the network.

2.1 Stability of the Disease-Free Equilibrium (DFE)

It is easy to see that there is always a DFE $E_0 : i_k^* = 0, j_k^* = 0, k = 1, \ldots, n$ for system (1), where $*$ stands for the steady state. Omitting the high order terms in Eqs. (1), it is easily deduced that E_0 is locally stable when $\mathcal{R}_1 \leq 1, \mathcal{R}_2 \leq 1$ (Wu et al. 2011).

In addition to the trivial disease-free equilibrium, the model (1) may also have nontrivial equilibria: the boundary equilibria $E_I : i_k^* > 0, j_k^* = 0, k = 1, \ldots, n$ and $E_J : i_k^* = 0, j_k^* > 0, k = 1, \ldots, n$, and the positive/endemic equilibrium $E_* : i_k^* > 0, j_k^* > 0, k = 1, \ldots, n$.

2.2 Stability of E_I

We next examine the local stability of E_I. To this end, perturbing the stationary state $(i_k^*, 0)_{k\geq 1}$ so that $i_k = \varepsilon_k + i_k^*$ and $j_k = \eta_k$. Upon omitting higher powers of ε_k, η_k, we can get the linear differential equations

$$\begin{cases} \frac{\mathrm{d}}{\mathrm{d}t}\varepsilon_k(t) = -(\gamma_1 + \beta_1 k\Theta_1^*)\varepsilon_k + \beta_1 k(1 - i_k^*)\Theta_1 \\ \frac{\mathrm{d}}{\mathrm{d}t}\eta_k(t) = -[\gamma_2 - \delta\psi(k)\Theta_1^*]\eta_k + \beta_2 k(1 - i_k^*)\Theta_2. \end{cases} \tag{6}$$

The Jacobi matrix determining the stable state thus can be described as

$$A = \begin{pmatrix} A_1 & A_2 \\ 0 & A_3 \end{pmatrix}.$$

Since $\lambda(A) = \lambda(A_1) \cup \lambda(A_3)$, it is required to determine the eigenvalues of matrix A_1 and A_3 respectively. In order to assess the eigenvalues of matrix A_1 by Lemma 1, we denote the entry of matrix $A_1 - \lambda \mathrm{I}$ be $a_{rs} = \delta_{rs}\sigma_r + p_r q_s$, where $p_r = \beta_1 r(1 - i_r^*), q_s = \langle k\rangle^{-1}\varphi(s)P(s)$ and $\sigma_r = -\gamma_1 - \beta_1 r\Theta_1^* - \lambda$. According to the first equality in Lemma 1, $\sigma_r \neq 0$ for each r, otherwise there exists two different r values such that $\sigma_r = 0$ (this is impossible in view of the expression for σ_r). With the second equality in Lemma 1, $\det[A_1 - \lambda \mathrm{I}] = 0$ is equivalent to

$$1 + \sum_{k=1}^{n} \frac{p_k q_k}{\sigma_k} = 0 \Longleftrightarrow \beta_1 \langle k\rangle^{-1} \sum_k \frac{k\varphi(k)P(k)}{\Delta(k)} = 1 \tag{7}$$

where $\Delta(k) = \frac{\gamma_1 + \lambda + \beta_1 k\Theta_1^*}{1 - i_k^*}$.

Since $1 - i_k^* = \frac{\gamma_1 i_k^*}{\beta_1 k\Theta_1^*}$, (7) becomes the following equality

$$\sum_k \frac{\varphi(k)P(k)i_k^*}{\gamma_1 + \lambda + \beta_1 k\Theta_1^*} = \sum_k \frac{\varphi(k)P(k)i_k^*}{\gamma_1}, \tag{8}$$

which establishes n complex roots, $\lambda_i, i = 1, \ldots, n$. Upon substituting each root $\lambda_s = a_s + b_s i$ into (8), we obtain

$$\sum_k \frac{\varphi(k)P(k)i_k^*(\gamma_1 + a_s + \beta_1 k\Theta_1^*)}{(\gamma_1 + a_s + \beta_1 k\Theta_1^*)^2 + b_s^2} = \sum_k \frac{\varphi(k)P(k)i_k^*}{\gamma_1}, \tag{9}$$

and

$$-b_s \sum_k \frac{\varphi(k)P(k)i_k^*}{(\gamma_1 + a_s + \beta_1 k\Theta_1^*)^2 + b_s^2} i = 0. \tag{10}$$

The second equation (10) implies that $b_s = 0$. Hence, the eigenvalues $\lambda_s = a_s$ are all real numbers. From (8), one can get that all eigenvalues of matrix A_1 are negative, that is, $\lambda_s < 0, s = 1, \ldots, n$.

On the other hand, by solving the equation $\det[A_3 - \lambda \mathrm{I}] = 0$ we obtain the maximum eigenvalue of A_3

$$\lambda_{\max}(A_3) = \frac{1}{\beta_1}(\beta_2\gamma_1 - \beta_1\gamma_2) - \delta\langle k\rangle^{-1} \sum_{k=1}^{n} \varphi(k)\psi(k)P(k)i_k^*.$$

In order to make sure of the stability of E_I, it is necessary that $\lambda_{\max}(A_3) < 0$, that is,

$$\delta \geq \delta_c = \frac{\beta_2\gamma_1 - \beta_1\gamma_2}{\beta_1\langle k\rangle^{-1} \sum_{k=1}^{n} \varphi(k)\psi(k)P(k)i_k^*}.$$

In the special case, when the effectively uniform contact $\psi(k) = l$ is assumed (Li et al. 2010), we have

$$\delta_c = \frac{\beta_2\gamma_1 - \beta_1\gamma_2}{\beta_1 l\Theta_1^*}, \tag{11}$$

where Θ_1^* satisfies

$$1 = \frac{\tau_1}{\langle k\rangle} \sum_{k'} \frac{k'\varphi(k')P(k')}{1 + \tau_1 k'\Theta_1^*}. \tag{12}$$

According to the expression of δ_c, it is easy to see that E_I is always stable if $\mathcal{R}_1 \geq \mathcal{R}_2$ regardless of δ because $\delta_c \leq 0$ at this case. That is to say, the superinfection has no remarkable effect on the epidemic development under this condition. So in the present work, we mainly focus on the assumption: (H) $\mathcal{R}_1 < \mathcal{R}_2$.

2.3 Stability of E_J

Herein, we discuss conditions for the stability of E_J, i.e., $i_k^* = 0$, $j_k^* > 0, k = 1, \ldots, n$ (here, $\mathcal{R}_2 > 1$). Using the method similar to the above subsection, we get the condition of this issue such that

$$\frac{1}{\beta_2}(\beta_1\gamma_2 - \beta_2\gamma_1) + \delta\langle k\rangle^{-1} \sum_{k=1}^{n} \varphi(k)\psi(k)P(k)j_k^* < 0.$$

This leads to

$$\delta \leq \delta_c' = \frac{\beta_2\gamma_1 - \beta_1\gamma_2}{\beta_2\langle k\rangle^{-1} \sum_{k=1}^{n} \varphi(k)\psi(k)P(k)j_k^*}.$$

Specifically, when $\psi(k) = l$, we have

$$\delta_c' = \frac{\beta_2\gamma_1 - \beta_1\gamma_2}{\beta_2 l \Theta_2^*}, \tag{13}$$

where Θ_2^* satisfies

$$1 = \frac{\tau_2}{\langle k\rangle}\sum_{k'}\frac{k'\varphi(k')P(k')}{1+\tau_2 k'\Theta_2^*}.$$

2.4 Main Theoretical Results

For the model (1), it seems to be difficult to obtain sufficient conditions for the positive equilibrium E_*. However, it is helpful to note that the dynamical behaviors in the case $\delta = 0$. Actually, this case corresponds to the most basic and simplest competing model. Since (H) is assumed, E_J is stable and only strain J prevails in the network (Wu et al. 2011). With the order parameter δ increasing, we can investigate the impact of superinfection on the epidemic transmission. In the following analysis, we use a novel quantity, the ratio of δ_c and δ_c',

$$\Lambda = \frac{\delta_c'}{\delta_c} = \frac{\beta_1\sum_{k=1}^n \varphi(k)\psi(k)P(k)i_k^*}{\beta_2\sum_{k=1}^n \varphi(k)\psi(k)P(k)j_k^*}.$$

Based on the knowledge of equilibria E_0, E_I, and E_J, we have the following analysis and conclusions under the assumption (H).

Case I: $\mathcal{R}_1 \le 1 < \mathcal{R}_2$. In this case, E_I does not exist, but E_J exists. Note that $\mathcal{R}_2 > 1$, we have E_0 is unstable (Wu et al. 2011). If $\delta > \delta_c'$, then E_J is unstable too. In a single strain model, the condition of an epidemic outbreak is always established according to the local stability of a DFE (Allen Linda and van den Driessche 2008). Similarly, in our two-strain model if $\delta > \delta_c'$, then both the boundary equilibrium and the DFE are unstable and further two competing strains can co-exist. If $\delta \le \delta_c'$, only strain J dominates the prevalence. (This is based on the assumption that the local stability of the positive equilibrium E_* excludes the local stability of the boundary equilibrium E_J. The following analysis also uses this. These judgments will be backed up by simulations later.) So if $\delta_c' < 1$, then two strains can coexist in a population if $\delta > \delta_c'$ and strain replacement cannot emerge.

Case II: $1 < \mathcal{R}_1 < \mathcal{R}_2$. This case is more complicated and can be further classified into three cases:

(1) $\Lambda < 1$ (that is, $\delta_c' < \delta_c$). If $\delta \le \delta_c'$, only strain J prevails. If $\delta \ge \delta_c$, only strain I prevails. If $\delta_c' < \delta < \delta_c$, we can see that both strain I and strain J can coexist since E_0, E_I and E_J are all unstable. In conclusion, under the assumption that $\delta_c < 1$, strain coexistence occurs if $\delta \in (\delta_c', \delta_c)$ and then strain replacement emerges if $\delta \ge \delta_c$ with the superinfection rate δ increasing from zero to 1.

(2) $\Lambda > 1$ (that is, $\delta_c' > \delta_c$). Since E_I is stable if and only if $\delta \ge \delta_c$ and E_J is stable if and only if $\delta \le \delta_c'$. So we have following conclusions. If $\delta < \delta_c$, only strain I spreads eventually; if $\delta \in [\delta_c, \delta_c']$, both E_I and E_J are stable which corresponds to a bistable phenomenon and the steady state is related to the initial infection distribution; if $\delta > \delta_c'$, only strain I transmits in the network and strain replacement occurs since

the reproductive number of strain I is smaller than strain J. For simplicity, we call δ_c coexistence threshold and δ_c' replacement threshold.

It is noteworthy to remark that this case possibly exists. Since i_k^*, j_k^* only depend on τ_1, τ_2, respectively, if $\tau_1 \approx \tau_2$, it is easy to adjust β_1/β_2 and let Λ be larger than unity.

(3) $\Lambda = 1$. This is the critical case. At this case, if $\delta < \delta_c = \delta_c'$, E_J is stable; otherwise, E_I is stable. The threshold δ_c is the critical point of the on-off phenomenon between strain I or strain J prevails.

In the final part, we would like to prove the conclusions about two reduced models. For the reduced model I, we conclude that the feature of a simple competing-exclusion can be kept when δ is sufficiently small. In fact, without loss of generality, we assume that $\mathcal{R}_1, \mathcal{R}_2 > 1$. When $\mathcal{R}_1 > \mathcal{R}_2$ we have that $\delta_c, \delta_c' < 0$, so E_I is always stable and E_J is always unstable. When $\mathcal{R}_1 < \mathcal{R}_2$, we have that $\delta_c, \delta_c' > 0$. If we take δ such that $\delta < \min\{\delta_c, \delta_c'\}$, then only E_J is stable.

For the reduced model II, we can analyze its stability (when $\mathcal{R} > 1$) to determine which strain can prevail. In this model, $\beta_1 = \beta_2$ and $\gamma_1 = \gamma_2$. Upon substituting these conditions to the expressions of δ_c and δ_c', we have that $\delta_c = \delta_c' = 0$. So the superinfection rate δ is always larger than δ_c, which indicates that only strain I can persist. Compared to the model (1), we can not observe the phenomenon of strain coexistence or strain replacement in this model. So strain dynamics are not only related to the superinfection rate, but also to the difference of two strains in the epidemiology.

3 Simulations

In Sect. 2, we obtained conditions for strain coexistence and strain replacement. We know that the superinfection rate plays an important role in determining which strain can cause an epidemic. On the other hand, these conditions are obtained by linear stability analysis. In this section, these theoretical results will be supported by numerical simulations. It is worth noting that the simulations are a numerical integration of the deterministic ordinary differential equations (1) and (2) with respect to time.

The underlying network is a Barabási–Albert (BA) scale-free network (Barabási and Albert 1999) with the degree distribution $P(k) \sim k^{-3}\theta(k_c - k)$ (where $\theta(x)$ is the Heaviside step function, and $k_c = 83$ is a hard cutoff due to the network size (Pastor-Satorras and Vespignani 2002)), the average degree $\langle k \rangle = 6$, and the network size $N = 1000$. In all simulations, we take $\psi(k) = 1$ and $\varphi(k)$ is of piecewise linear form (Fu et al. 2008):

$$\varphi(k) = \min\{k, 20\}.$$

In order to investigate the epidemic spreading behavior, densities of nodes infected with strain I and J, denoted by $\rho_i(t) = \sum_s P(s) i_s(t)$ and $\rho_j(t) = \sum_s P(s) j_s(t)$ respectively, are frequently used in epidemiology. We denote by $\rho_i(\infty)$ and $\rho_j(\infty)$ the steady state (asymptotic) values of infection density for strain I and strain J, respectively. In our simulations, we will inspect the impact of the superinfection rate on these two steady state values.

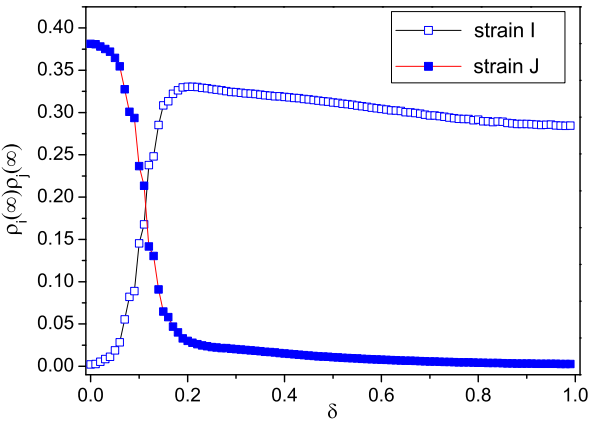

Fig. 1 Densities of infected nodes by strain I and J with respect to superinfection rate δ for given parameters $\beta_1 = 0.0008, \beta_2 = 0.3, \gamma_1 = 0.01, \gamma_2 = 1$

We firstly consider the case $\mathcal{R}_1 < 1$. According to the conclusions obtained in Sect. 2.4, we mainly justify strain coexistence. In order to do this, we must make sure that $\delta_c' < 1$. Note that

$$\delta_c' = \frac{\beta_2\gamma_1 - \beta_1\gamma_2}{\beta_2\Theta_2^*} \tag{14}$$

and Θ_2^* is a function of R_2 for given $\varphi(k)$ and $P(k)$, so Eq. (14) can be written as

$$\frac{\delta_c'}{\gamma_1} = \frac{\mathcal{R}_2 - \mathcal{R}_1}{\mathcal{R}_2\Theta_2^*(\mathcal{R}_2)}, \tag{15}$$

which indicates that δ_c' is related with γ_1 (or say the average infection period $\frac{1}{\gamma_1}$) under the fixed $\mathcal{R}_1$ and $\mathcal{R}_2$. This tell us that δ_c' can be made smaller by adjusting the associated recovery rate γ_1. In simulations, we set $\beta_1 = 0.0008, \beta_2 = 0.3, \gamma_1 = 0.01, \gamma_2 = 1$. In the light of $\mathcal{R}_1 = \tau_1 \frac{\langle k\varphi(k)\rangle}{\langle k\rangle}$ and the formula (see (9) in Fu et al. 2008), we have $(\frac{\langle k\varphi(k)\rangle}{\langle k\rangle})^{-1} = 0.11$ (of course approximately). So $\tau_1 = 0.08 < 0.11$ (i.e., $\mathcal{R}_1 < 1$) and $\tau_2 = 0.3$ (i.e., $\mathcal{R}_2 > 1$). According to (14) and $\Theta_2^* \cong 0.43$ (using *matlab software*), we have $\delta_c' \cong 0.0171$.

In Fig. 1, we draw the change of $\rho_i(\infty)$ and $\rho_j(\infty)$ with the superinfection rate δ increasing. This plot shows that the theoretical value of δ_c' is very close to the simulation value. Although strain replacement cannot occur when $\mathcal{R}_1 < 1$, an interesting phenomenon similar to strain replacement is that strain I spreads at high level and strain J spreads at low level when the superinfection rate δ is enough large.

Next, we investigate the case $\mathcal{R}_1 > 1$. We take $\beta_1 = 0.2, \beta_2 = 0.3$, and unit recovery rates $\gamma_1 = \gamma_2 = 1$. By approximate relations ($\Theta_1^* \cong 0.264$ and $\Theta_2^* \cong 0.43041$), we have $\delta_c \cong 1.8939 > 1$ and $\delta_c' \cong 0.7752 < 1$. Hence, strain coexistence can emerge while strain replacement can not occur, which can be seen in Fig. 2.

However, we can find strain replacement by slightly adjusting parameters. In Fig. 3, we take $\beta_1 = 0.25$ and leave the other parameters as used in Fig. 2. By the computation method above, we get $\delta_c \cong 0.5574 < 1$ and $\delta_c' \cong 0.3872 < 1$, which establishes the three intervals of parameter δ. These threshold values agree with the simulation results in Fig. 3. From this, it can be seen that strain replacement occurs

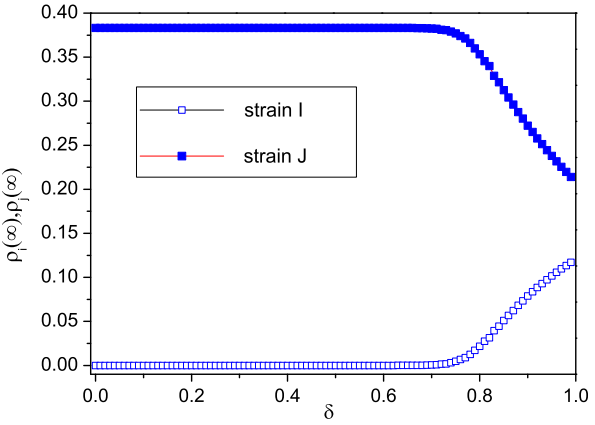

Fig. 2 Densities of infected nodes by strain I and J with respect to superinfection rate δ for given parameters $\beta_1 = 0.2, \beta_2 = 0.3, \gamma_1 = \gamma_2 = 1$

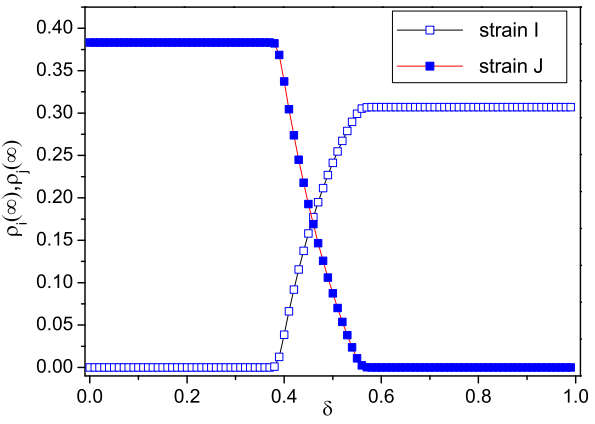

Fig. 3 Densities of infected nodes by strain I and J with respect to superinfection rate δ for given parameters $\beta_1 = 0.25, \beta_2 = 0.3$, $\gamma_1 = \gamma_2 = 1$

after strain coexistence by enhancing parameter δ. Meanwhile, the superinfection mechanism potentially generates strain coexistence in competing strains whenever $\mathcal{R}_1 \leq 1$ or $\mathcal{R}_1 > 1$.

According to the formula (11) and (13), an interesting phenomenon has also been found, that is, the values of δ_c and δ_c' are closely related with the recovery rate γ_1 even if both $\mathcal{R}_1$ and $\mathcal{R}_2$ are unchanged. Consequently, we rewrite these thresholds as functions of γ_1, $\delta_c = \delta_c(\gamma_1)$ and $\delta_c' = \delta_c'(\gamma_1)$. It then follows from (11) and (13) that both the rates of change $\partial\delta_c'/\partial\gamma_1$ and $\partial\delta_c/\partial\gamma_1$ are larger than zero. What is more, it can be seen that the former change is linear in the parameter γ_1, while the latter one is nonlinear in the same parameter. These features can be easily observed in the parametric plot (Fig. 4).

In Fig. 4, the solid line (i.e., the nonlinear curve in inset plot) stands for $\delta_c(\gamma_1)$ and the dash one represents $\delta_c'(\gamma_1)$ (i.e., the straight line in inset plot). Apparently, these two curves split the whole region into three parts: conventional phase (A, bottom), coexistence phase (B, middle), and replacement phase (C, upper). The conventional phase refers to the one where the strain with a higher reproductive number can prevail and persist for ever in competing dynamics (Wu et al. 2011). It can be found from

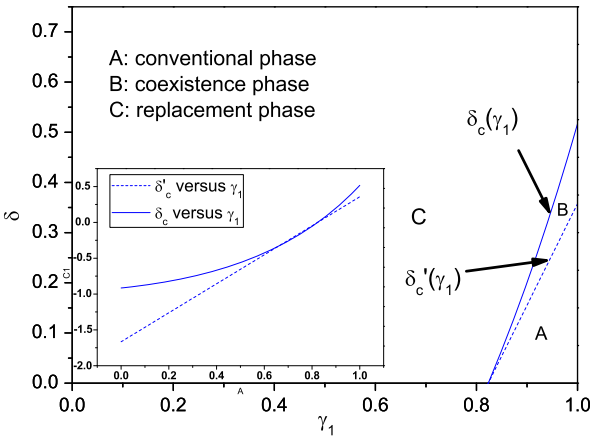

Fig. 4 Parametric plot of the superinfection rate δ and the recovery rate γ_1. Parameter values used in this plot: $\beta_1 = 0.25$, $\beta_2 = 0.3$, and $\gamma_2 = 1$. The two threshold lines in the plot are numerically solved in (11) and (13), respectively. *Inset*: a perfect plot of the original parametric plot

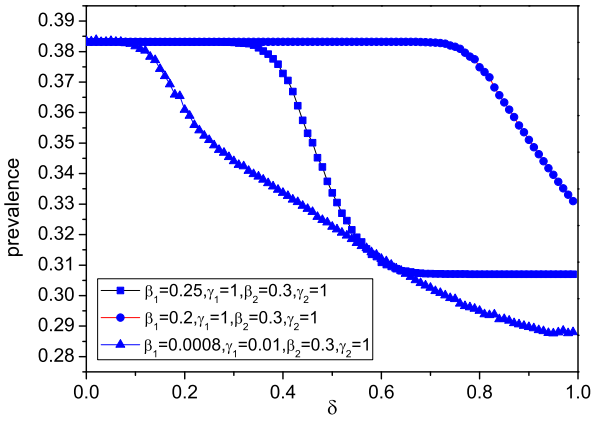

Fig. 5 The prevalence with respect to the superinfection rate δ. Simulations indicate that superinfection can inhibit the epidemic spreading

this figure that the conventional phase can be transitioned into the other phases by two routes: one is to raise the value of δ and the other is to decrease the value of γ_1. This phenomenon may be of relevance for vaccination programmes (Thomasey and Martcheva 2008).

Superinfection is known to facilitate the coexistence of several pathogen strains in a host population (Boldin and Diekmann 2008), which can be seen in Fig. 4. Additionally, we investigate the impact of δ on the epidemic prevalence in Fig. 5. We illustrate the total infection density $\rho = \rho_i(\infty) + \rho_j(\infty)$ in view of the superinfection rate δ under the different parameter cases. With δ increasing, it can be seen that ρ decreases with δ, which implies that the epidemic disease can be inhibited by superinfection (superinfection is directed from the higher reproductive number to the lower reproductive number). Although this has not been rigorously justified in theory, it is interesting to uncover the biological implication of superinfection in diseases such as gonorrhea.

4 Conclusions and Discussions

The study of a superinfection process in networked epidemic systems has implications concerning our understanding of worldwide virus diversity, individual immunity (Pastor-Satorras and Vespignani 2002) and disease progression, and vaccine development. For many diseases whose causative agents are represented by multiple strains, the protection offered by a vaccine is only partial and may be only effective against some strains (Thomasey and Martcheva 2008). Hence, whether the vaccine preventable strains spread is an important issue. In this work, we investigate the role of the superinfection rate δ on the epidemic spreading, particularly for two forms of strain dynamical behaviors: strain coexistence and strain replacement.

Based on the knowledge of two competing strains we proposed and studied mathematical models of the dynamical behavior of such systems. The mathematical models are a set of ordinary differential equations (Masuda and Konno 2006). Under the assumption (H), we not only determine the positive coexistence threshold δ_c' above which the two strains can coexist, but also establish the positive replacement threshold δ_c which may be larger than δ_c' (see Fig. 3). According to the parameter classifications in Sect. 2, we can find that strain I can coexist with strain J even if it has a lower basic reproductive number (i.e., $\mathcal{R}_1 < \mathcal{R}_2$). Most strikingly, it can allow strain I to persist even when its reproductive number is less than 1 (i.e., $\mathcal{R}_1 < 1 < \mathcal{R}_2$) (Vasco et al. 2007). These mathematical results have been justified by extensive simulations in Sect. 3. In addition, we have confirmed the potential existence of the bi-stable state in theory.

In this theoretical analysis, we adopted the linear stability analysis of all simple equilibria (including E_0, E_I and E_J) to study the conditions of strain coexistence and strain replacement. As stressed by Masuda and Konno (2006), it is a vital problem to give the rigorous proof of the global stability of the steady states, especially the endemic equilibrium. However, it seems difficult to solve by current methods (d'Onofrio 2008; Wang and Dai 2008). So future work is still needed to rigorously establish these results. Moreover, we did not consider the coinfection between two strains which allows two strains to coexist in the same host. The previous results have shown that coinfection can induce complex dynamic behavior, such as oscillations and chaotic attractors (Kamo and Sasaki 2002). Recently, a generalized framework of modeling interaction dynamics between two strains in a single host population has been developed (Vasco et al. 2007; Shrestha et al. 2011). Based on these work, our results may be extended to these complex dynamical cases.

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