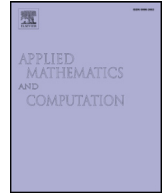
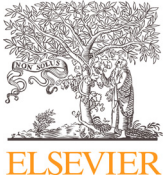




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Infectious diseases spreading on a metapopulation network coupled with its second-neighbor network

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ABSTRACT

Traditional infectious diseases models on metapopulation networks focus on direct transportations (e.g., direct flights), ignoring the effect of indirect transportations. Based on global aviation network, we turn the problem of indirect flights into a question of second neighbors, and propose a susceptible-infectious-susceptible model to study disease transmission on a connected metapopulation network coupled with its second-neighbor network (SNN). We calculate the basic reproduction number, which is independent of human mobility, and we prove the global stability of disease-free and endemic equilibria of the model. Furthermore, the study shows that the behavior that all travelers travel along the SNN may hinder the spread of disease if the SNN is not connected. However, the behavior that individuals travel along the metapopulation network coupled with its SNN contributes to the spread of disease. Thus for an emerging infectious disease, if the real network and its SNN keep the same connectivity, indirect transportations may be a potential threat and need to be controlled. Our work can be generalized to high-speed train and rail networks, which may further promote other research on metapopulation networks.

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1. Introduction

With the rapid development of technology, the rate of globalization has increased, which brings not only opportunities to countries, but also many challenges, such as, the global transmission of infectious diseases. For example, severe acute respiratory syndromes (SARS) [1], originating from Guangdong Province, China, then spread around the world along international air travel routes. Influenza A (H1N1) flu [2] in 2009, which was first reported in Mexico, has become a global issue, which is followed by the emergence of avian influenza [3], Middle East respiratory syndrome coronavirus (MERS-CoV) [4], Ebola virus disease [5], Zika [6]. The outbreak of any infectious disease has a great impact on humans, either physically, mentally, or economically. How to forecast and control the global spread of infectious diseases has always been the focus of research. One of effective methods to address this problem is the introduction of metapopulation networks.

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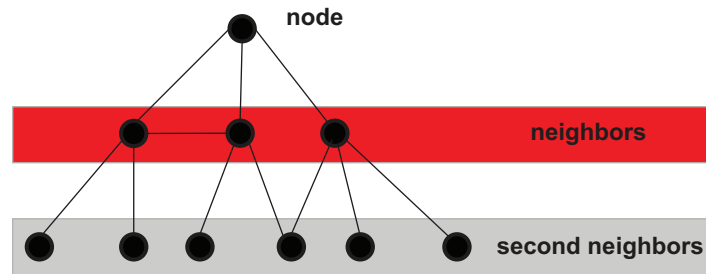


Fig. 1. A schematic depiction of second neighbors of a node.

A metapopulation network is a network, whose nodes (subpopulations) represent well-defined social units, such as countries, cities, towns, villages, with links standing for the mobility of individuals.

Using heterogeneous mean-field (HMF) theory and assuming that subpopulations with the same degree are statistical equivalent, Colizza and Vespignani proposed two models to describe transmission of diseases on heterogeneous metapopulation networks under two different mobility patterns, which sheds light on calculation of global invasion threshold [7]. Next, different network structures, including bipartite metapopulation network [8], time-varying metapopulation network [9], local subpopulation structure [10], interconnected metapopulation network [11], have been found to play an essential role in the global spread of infectious diseases. Furthermore, studies have shown that adaptive behavior of individuals contributes to the global spread of epidemics, contrary to willingness [12–15]. These works mostly focus on large-scale, air-travel-like mobility pattern, without individuals going back to their origins. There are also some studies on recurrent mobility pattern. Balcan and Vespignani investigated invasion threshold on metapopulation network with recurrent mobility pattern [16,17]. Heterogeneous dwelling time in subpopulations was considered in ref. [18].

Nearly all studies above are under the assumption that mobility between two linked subpopulations is based on direct flights or other direct transportations. For aviation networks, sometimes there is no any direct flight when people travel, which makes them have to traverse to other places before reaching their destinations. Even in the case of a direct flight, individuals may have to make two or more stops before reaching their destinations. Actually, these two cases reflect the same problem of individual transfer in a metapopulation network. For an emerging infectious disease, taking transfer once as an example, movement of infectious individuals may result in more susceptible subpopulations being infected, since infectious individuals in an infected subpopulation can arrive not only at its neighbors but also the neighbors of its neighbors. To address this problem, we define second neighbor and second-neighbor network (SNN) on an arbitrary undirected network. Then we investigate the spread of an infectious disease on a connected metapopulation network coupled with its SNN and study how indirect flights affect the global spread of the infectious disease. We show that the behavior that individuals travel along the metapopulation network coupled with its SNN contributes to the spread of disease.

The paper is organized as follows. In Section 2, we introduce second neighbor and give some definitions on SNN of an arbitrary undirected network. Next, an infectious disease model is derived to study how transfer rate affects the global transmission of a disease in Section 3. Further, the basic reproduction number and the stability analysis of model are given in Section 4. Section 5 presents some simulation results. Conclusions are given in Section 6.

2. Second neighbor and SNN

In order to investigate the effect of indirect flights on disease transmission on a metapopulation network, we introduce the concepts of second neighbor and SNN in the following.

Definition 2.1. A second neighbor of node i in a network (undirected) is a node whose distance from i is exactly two.

According to the definition above, j is a second neighbor of i means that there exists(exist) self-avoiding path(s) of length two from i to j . As illustrated in Fig. 1, the number of self-avoiding paths of length two between two nodes may be larger than 1. Since what we focus on is the existence of these paths but not the number, we say these paths are equivalent if the number of self-avoiding paths of length two is larger than 1.

In a similar way, one can define third neighbor and k^{th} neighbor.

Definition 2.2. A third neighbor of node i in a network (undirected) is a node whose distance from i is exactly three.

Definition 2.3. A k^{th} ($k > 3$) neighbor of node i in a network (undirected) is a node whose distance from i is exactly k .

Based on the definitions above, we give the definition of SNN. An SNN for a undirected network is composed by all second neighbors of nodes. In other words, an SNN keep the same nodes with the given network, and there existing a link between two nodes means that one node is a second neighbor of the other. Fig. 2 illustrates a undirected network and its SNN. In panel A, for node 1, for example, its second neighbors are nodes 2 and 6 according to the definition of second

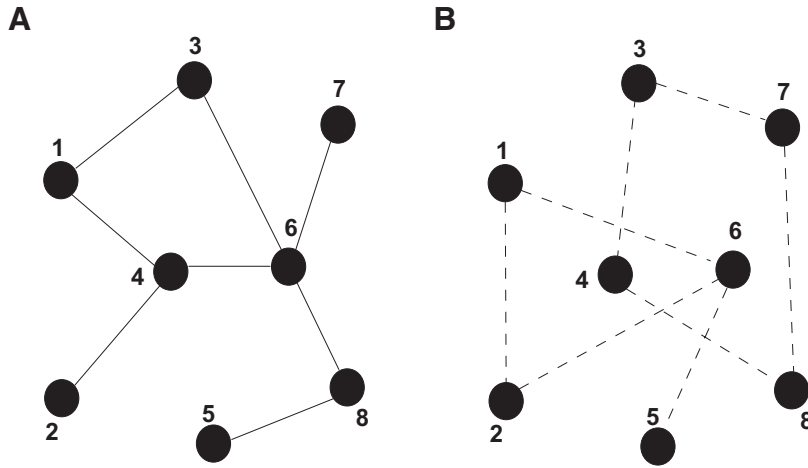


Fig. 2. A schematic depiction of an undirected network and its SNN. The panel A shows a general undirected network. The panel B is an SNN composed by second neighbor(s) of each node in panel A.

neighbor. In the same way, we obtain all second neighbors for each node and construct an SNN (see panel B). Similarly, one can get a third-neighbor network, a fourth-neighbor network, and so on.

Consider a simple undirected network with n nodes and let us label the nodes with integer labels $1, \dots, n$. The adjacency matrix $A = (a_{ij})_{n \times n}$ is a matrix with entries

$$a_{ij} = \begin{cases} 1, & \text{if } i \text{ is adjacent to } j \text{ and } i \neq j, \\ 0, & \text{otherwise,} \end{cases} \quad (2.1)$$

$i, j = 1, \dots, n$. So the degree of node i , denoted by $k_i^{(1)}$, is $k_i^{(1)} = \sum_{j=1}^n a_{ij}$. Meanwhile, we denote $P_k^{(1)}$ the probability distribution of degree k . Then we give the adjacent matrix $B = (b_{ij})_{n \times n}$ of the SNN with entries

$$b_{ij} = \begin{cases} 1, & \text{if } j \text{ is a second neighbor of } i \text{ and } i \neq j, \\ 0, & \text{otherwise.} \end{cases} \quad (2.2)$$

Accordingly, the number of second neighbors of node i , named as next-nearest degree, is $k_i^{(2)} = \sum_{j=1}^n b_{ij}$. Similarly, we use $P_k^{(2)}$ to denote the probability that the number of second neighbors is exactly k .

Notice that

$$A^2 = (a_{ij}^{(2)})_{n \times n},$$

where $a_{ij}^{(2)} (\geq 0)$ is the number of paths with length two between nodes i and j . With the definition of second neighbor, B can be uniquely expressed by A and A^2 with

$$b_{ij} = \begin{cases} 1, & \text{if } a_{ij} = 0, a_{ij}^{(2)} > 0 \text{ and } i \neq j, \\ 0, & \text{otherwise.} \end{cases} \quad (2.3)$$

Remark 2.1. The matrix B is symmetric due to the fact that the matrix A is symmetric.

Remark 2.2. For complete graphs and networks with all nodes' degrees being 0 or 1, $B = \mathbf{0}$, that is, B is a zero matrix.

3. Infectious disease modeling on a metapopulation network and its SNN

For an aviation network, more common is indirect flights with one stop except for direct flights, which is due to the fact that people are rarely willing to have more than one stop during their journey. Actually, the network constructed by all these indirect flights is exactly the SNN of the aviation network. Thus, to solve the problem of these indirect flights is equivalent to fixing the problem of the SNN for a metapopulation network.

Consider a connected and undirected metapopulation network with n subpopulations coupled with its SNN, and an acute infectious disease (such as, influenza) with a susceptible-infectious-susceptible (SIS) transmission process intra subpopulation. As illustrated in Fig. 3, each node represents a population in which individuals with different disease states (blue circle for susceptible individuals, red pentagram for infectious individuals) are well-mixed, while links represent that there exists individuals' mobility between two nodes. Here dashed links represent the second neighbor relationship.

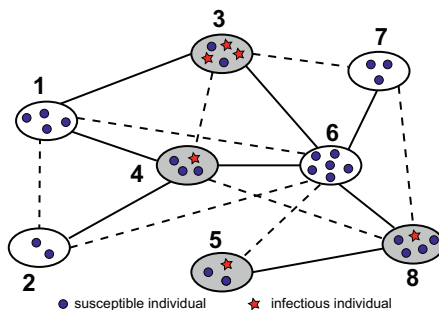


Fig. 3. A connected metapopulation network coupled with its SNN. The SNN is connected by dashed links. In each node, blue circles stand for susceptible individuals, and red pentagrams represent infectious individuals.

On the other hand, metapopulation networks are weighted, which measures traffic flows between two linked subpopulations. For node i , let the weight of a link be defined as the probability at which individuals in node i travel along the link. In consideration of a general form, weight matrix for a metapopulation network is of the form

$$W^{(1)} = (a_{ij}w_{ij}^{(1)})_{n \times n},$$

here $w_{ij}^{(1)} \geq 0$ ($i, j = 1, \dots, n$) and equality holds when $a_{ij} = 0$. In addition, the matrix $W^{(1)}$ satisfies the condition that each row sum equals one, that is, $\sum_{j=1}^n a_{ij}w_{ij}^{(1)} = 1$.

In the same way, weight matrix for its SNN takes the form

$$W^{(2)} = (b_{ij}w_{ij}^{(2)})_{n \times n},$$

where $w_{ij}^{(2)} \geq 0$ and equality holds when $b_{ij} = 0$. For node i , if $k_i^{(2)} = 0$, that is, its next-nearest degree equals to 0, then $\sum_{j=1}^n b_{ij}w_{ij}^{(2)} = 0$; otherwise, $\sum_{j=1}^n b_{ij}w_{ij}^{(2)} = 1$.

Furthermore, for disease spreading process intra subpopulation, let β denote transmission rate, and γ denote recovery rate of an infectious individual. Referring to mobility process inter subpopulations, mobility rate at which an individual leaves a given subpopulation to its neighbors or second neighbors is denoted by δ . To depict the case of individuals transfer, we denote transfer rate by q , the rate at which an individual leaves a given subpopulation to its second neighbors, so the rate of an individual leaving a given subpopulation to its neighbors is $1 - q$. We note that $q = 0$ when $k_i^{(2)} = 0$. We assume that these rates keep the same for all subpopulations and that these rates are all at unit time: per day.

Upon these bases, we consider the following model

$$S'_i = -\beta \frac{S_i I_i}{N_i} + \gamma I_i - \delta S_i + \delta(1-q) \sum_{j=1}^n a_{ji}w_{ji}^{(1)} S_j + \delta q \sum_{j=1}^n b_{ji}w_{ji}^{(2)} S_j, \quad (3.1a)$$

$$I'_i = \beta \frac{S_i I_i}{N_i} - \gamma I_i - \delta I_i + \delta(1-q) \sum_{j=1}^n a_{ji}w_{ji}^{(1)} I_j + \delta q \sum_{j=1}^n b_{ji}w_{ji}^{(2)} I_j, \quad (3.1b)$$

$$i = 1, \dots, n.$$

For Eq. (3.1a), the first and the second terms represent disease transmission and recovery processes in a given subpopulation i , respectively. Meanwhile, the latter three terms express the mobility process inter subpopulations. In detail, the fourth term is on behalf of the case that individuals arrive at subpopulation i from its neighbors, and the fifth term shows the case of individuals traveling along SNN. The process of individuals in subpopulation i traveling to other subpopulations, including neighbors and second neighbors, is described by the third term, which is equivalent to the expression

$$\delta S_i = \delta(1-q) \sum_{j=1}^n a_{ij}w_{ij}^{(1)} S_i + \delta q \sum_{j=1}^n b_{ij}w_{ij}^{(2)} S_i.$$

Similar expressions hold for I'_i , forming Eq. (3.1b).

Notice that, in model (3.1), transfer rate q measures the level of indirect flights.

Remark 3.1. $q = 0$ depicts the case of individuals traveling along a metapopulation network. At this point, system (3.1) becomes

$$S'_i = -\beta \frac{S_i I_i}{N_i} + \gamma I_i - \delta S_i + \delta \sum_{j=1}^n a_{ji}w_{ji}^{(1)} S_j, \quad (3.2a)$$

$$I'_i = \beta \frac{S_i I_i}{N_i} - \gamma I_i - \delta I_i + \delta \sum_{j=1}^n a_{ji} w_{ji}^{(1)} I_j, \quad (3.2b)$$

$$i = 1, \dots, n.$$

This model is the traditional metapopulation network model [19].

Remark 3.2. $q = 1$ portrays the case that all individuals travel along the SNN of the metapopulation network, which corresponds to the situation that governments prohibit direct flights when an infectious disease occurs or the case in areas with underdeveloped economy and poor traffic, and it is expressed by

$$S'_i = -\beta \frac{S_i I_i}{N_i} + \gamma I_i - \delta S_i + \delta \sum_{j=1}^n b_{ji} w_{ji}^{(2)} S_j, \quad (3.3a)$$

$$I'_i = \beta \frac{S_i I_i}{N_i} - \gamma I_i - \delta I_i + \delta \sum_{j=1}^n b_{ji} w_{ji}^{(2)} I_j, \quad (3.3b)$$

$$i = 1, \dots, n.$$

Remark 3.3. For the metapopulation network, assuming that subpopulations with the same degree and next-nearest degree are statistically equivalent and that link weights depend on degree (for the metapopulation network) and next-nearest degree (for the SNN) of nodes, according to ref. [20], we obtain an equivalent mean-field model

$$S'_{k^{(1)}, k^{(2)}} = -\beta \frac{S_{k^{(1)}, k^{(2)}} I_{k^{(1)}, k^{(2)}}}{N_{k^{(1)}, k^{(2)}}} + \gamma I_{k^{(1)}, k^{(2)}} - \delta S_{k^{(1)}, k^{(2)}} + \delta (1 - q) k^{(1)} \sum_{l^{(1)}} \sum_{l^{(2)}} P^{(1)}(l^{(1)} | k^{(1)}) w_{l^{(1)} k^{(1)}}^{(1)} S_{l^{(1)}, l^{(2)}} \\ + \delta q k^{(2)} \sum_{l^{(2)}} \sum_{l^{(1)}} P^{(2)}(l^{(2)} | k^{(2)}) w_{l^{(2)} k^{(2)}}^{(2)} S_{l^{(1)}, l^{(2)}}, \quad (3.4a)$$

$$I'_{k^{(1)}, k^{(2)}} = \beta \frac{S_{k^{(1)}, k^{(2)}} I_{k^{(1)}, k^{(2)}}}{N_{k^{(1)}, k^{(2)}}} - \gamma I_{k^{(1)}, k^{(2)}} - \delta I_{k^{(1)}, k^{(2)}} + \delta (1 - q) k^{(1)} \sum_{l^{(1)}} \sum_{l^{(2)}} P^{(1)}(l^{(1)} | k^{(1)}) w_{l^{(1)} k^{(1)}}^{(1)} I_{l^{(1)}, l^{(2)}} \\ + \delta q k^{(2)} \sum_{l^{(2)}} \sum_{l^{(1)}} P^{(2)}(l^{(2)} | k^{(2)}) w_{l^{(2)} k^{(2)}}^{(2)} I_{l^{(1)}, l^{(2)}}, \quad (3.4b)$$

here subscripts are degree $k^{(1)}$ and next-nearest degree $k^{(2)}$, respectively. $N_{k^{(1)}, k^{(2)}}$ is the average population of subpopulations with the same degree $k^{(1)}$ and the same next-nearest degree $k^{(2)}$, and definitions of $S_{k^{(1)}, k^{(2)}}$ and $I_{k^{(1)}, k^{(2)}}$ are similar. $P^{(1)}(l^{(1)} | k^{(1)})$ denotes the conditional probability that a subpopulation with degree $k^{(1)}$ is connected to a subpopulation of degree $l^{(1)}$, and $P^{(2)}(l^{(2)} | k^{(2)})$ is a similar definition on SNN to $P^{(1)}(l^{(1)} | k^{(1)})$.

Summing Eqs. (3.1a) and (3.1b) gives

$$N'_i = -\delta N_i + \delta (1 - q) \sum_{j=1}^n a_{ji} w_{ji}^{(1)} N_j + \delta q \sum_{j=1}^n b_{ji} w_{ji}^{(2)} N_j, \quad i = 1, \dots, n. \quad (3.5)$$

Define $C = (c_{ij})_{n \times n}$ with entries

$$c_{ij} = (1 - q) a_{ij} w_{ij}^{(1)} + q b_{ij} w_{ij}^{(2)}.$$

With $\mathbb{N} = [N_1, \dots, N_n]^T$, Eq. (3.5) can be rewritten as

$$\mathbb{N}' = M\mathbb{N}, \quad (3.6)$$

where $M = \delta C^T - \text{diag}(\delta)$. Note that each column sum of $-M$ is zero, i.e., $\mathbb{1}_n^T (-M) = 0$, where the $1 \times n$ vector $\mathbb{1}_n^T = [1, \dots, 1]$. Thus, $(-M)$ is a singular M-matrix. From (3.6), letting $N = \sum_{i=1}^n N_i$, we obtain that the total population N is constant (because $N' = 0$). Subject to this constraint, by Theorem 3.3 in [21], we show that (3.6) has a unique positive equilibrium $N_i = N_i^*$, which is globally asymptotically stable.

Since we are only interested in the asymptotic dynamics of the global transmission of disease on the metapopulation network coupled with its SNN, we will study the limiting system of (3.1)

$$I'_i = -\beta \frac{I_i^2}{N_i^*} + \beta I_i - \gamma I_i - \delta I_i + \delta \sum_{j=1}^n c_{ji} I_j, \quad i = 1, \dots, n. \quad (3.7)$$

4. Stability analysis

In this section, we calculate the basic reproduction number, and prove the existence and stability of disease-free equilibrium (DFE) and endemic equilibrium (EE).

4.1. Basic reproduction number and global stability of DFE

Before studying the global stability of DFE, we calculate the basic reproduction number following the approach of van den Driessche and Watmough [22]. Obviously, there exists a unique DFE $E^0 = (0, \dots, 0)$ for system (3.7). According to Eq. (3.7), the rate of appearance of new infections F and the rate of transfer of individuals out of the compartments V in the E^0 are given by

$$F = \text{diag}(\beta)$$

and

$$V = \text{diag}(\gamma + \delta) - \delta C^T,$$

here F and V are $n \times n$ matrices. Using the next-generation matrix theory [22], the basic reproduction number is $R_0 = \rho(FV^{-1})$, where ρ is the spectral radius of the matrix FV^{-1} .

In the following, we calculate the basic reproduction number R_0 . Note that the sum of each column of matrix V is γ and the matrix V is column diagonally dominant. So V is an irreducible nonsingular M-matrix. Thus V^{-1} is a positive matrix.

Matrix V has column sum γ , i.e., $\mathbb{1}_n^T V = \gamma \mathbb{1}_n^T$. Hence $\mathbb{1}_n^T V^{-1} = 1/\gamma \mathbb{1}_n^T$. Therefore, $\mathbb{1}_n^T FV^{-1} = \beta/\gamma \mathbb{1}_n^T$, that is, matrix FV^{-1} has column sum β/γ . By Theorem 1.1 in chapter 2 in ref. [23], the basic reproduction number is

$$R_0 = \frac{\beta}{\gamma}.$$

Remark 4.1. The threshold value R_0 depends only on disease parameters β and γ but not on mobility rate δ or transfer rate q , thus, mobility of individuals has no impact on the basic reproduction number. However, movements of individuals between subpopulations accelerates the global spread of infectious diseases on metapopulation networks [24].

Notice that if $R_0 < 1$, then E^0 is locally asymptotically stable; while $R_0 > 1$, E^0 is unstable. In fact, we can further prove the global stability of E^0 . We give the following lemma first.

Lemma 4.1. Define $\Omega_n = \prod_{i=1}^n [0, N_i^*]$. The set Ω_n is positively invariant for system (3.7).

Proof. First, we will show that $I_i(t) > 0$ for any $t > 0$ and $i = 1, \dots, n$ and initial value $I(0) \in \Omega_n$. Otherwise assume that there exist an $i_0 \in \{1, \dots, n\}$ and $t_0 > 0$, such that $I_{i_0}(t_0) = 0$. Letting $t^* = \inf\{t > 0, I_{i_0}(t) = 0\}$, we have

$$I'_{i_0}(t^*) = \delta \sum_{j=1}^n c_{ji_0} I_j,$$

then $I'_{i_0}(t^*) > 0$, but the definition of t^* implies $I'_{i_0}(t^*) \leq 0$, which is a contradiction.

Second, we show that for any $t \geq 0$, $I_i(t) \leq N_i^*$ and $i = 1, \dots, n$.

For any initial value $I(0) \in \Omega_n$, let $x_i(t) = N_i^* - I_i(t)$. According to (3.7), we have the following system:

$$x'_i = \beta \frac{(N_i^* - x_i)^2}{N_i^*} - \beta(N_i^* - x_i) + \gamma(N_i^* - x_i) + \delta(N_i^* - x_i) - \delta \sum_{j=1}^n c_{ji}(N_j^* - x_j).$$

We will show that for any $t > 0$, $x_i(t) > 0$. If this is not true, there exist an $i_0 (1 \leq i_0 \leq n)$ and $t_0 > 0$, such that $x_{i_0}(t_0) = 0$. Letting $t^{**} = \inf\{t > 0, x_{i_0}(t) = 0\}$, we have

$$x'_{i_0}(t^{**}) = \gamma N_{i_0}^* + \delta N_{i_0}^* - \delta \sum_{j=1}^n c_{ji_0}(N_j^* - x_j).$$

Since $x_j > 0$ for all $j \neq i_0$ and $N_i^* = \sum_{j=1}^n c_{ji} N_j^*$, $x'_{i_0}(t^{**}) > 0$. But the definition of t^{**} implies $x'_{i_0}(t^{**}) \leq 0$. Obviously, this is also a contradiction. Thus $I_{i_0}(t) \leq N_{i_0}^*$. \square

Theorem 4.1. If $R_0 < 1$, then E^0 of system (3.7) is globally asymptotically stable.

Proof. To complete the proof, we need only to show that E^0 is globally attractive. It is sufficient to show that

$$\lim_{t \rightarrow +\infty} I_i = 0, \quad i = 1, \dots, n.$$

For system (3.7), the following inequalities hold

$$I'_i \leq \beta I_i - \gamma I_i - \delta I_i + \delta \sum_{j=1}^n c_{ji} I_j, \quad i = 1, \dots, n.$$

Define an auxiliary linear system, namely,

$$I_i' = \beta I_i - \gamma I_i - \delta I_i + \delta \sum_{j=1}^n c_{ji} I_j, \quad i = 1, \dots, n. \quad (4.1)$$

The right side of (4.1) has coefficient matrix $F - V$. For $R_0 = \rho(FV^{-1}) < 1$, each eigenvalue of $F - V$ lies in the left half plane. Thus each non-negative solution of (4.1) satisfies

$$\lim_{t \rightarrow +\infty} I_i = 0, \quad i = 1, \dots, n.$$

Since (4.1) is a linear system, the DFE of this system is globally asymptotically stable. By the comparison principle, each non-negative solution of (3.7) satisfies

$$\lim_{t \rightarrow +\infty} I_i = 0, \quad i = 1, \dots, n.$$

Notice that E^0 is locally asymptotically stable, thus E^0 is globally asymptotically stable. \square

4.2. The existence and stability of EE

Next, we study the existence and global stability of EE to system (3.7).

Theorem 4.2. If $R_0 > 1$, system (3.7) admits a unique EE $E^* = (I_1^*, \dots, I_n^*)$, and it is globally asymptotically stable with respect to any initial value $y(0) \in \Omega_n$.

Proof. To prove the existence and global stability of endemic equilibrium, we will use cooperate system theory in Corollary 3.2 in [25].

In fact, let $f: \Omega_n \rightarrow \Omega_n$ be defined by the right-hand side of (3.7), $f = (f_1, \dots, f_n)$. Clearly, f is continuously differentiable, $f(0) = 0$, $f_i(I) \geq 0$ for all $I = (I_1, \dots, I_n) \in \Omega_n$ with $I_i = 0$ and $\partial f_i / \partial I_j \geq 0, i \neq j$ for $I \in \Omega_n$. So f is cooperative. Clearly $Dy = (\partial f_i / \partial I_j)_{1 \leq i, j \leq n}$ is irreducible for every $I \in \Omega_n$.

Note that for $\forall \alpha \in (0, 1)$ and $I_i > 0$,

$$\begin{aligned} f_i(\alpha I) &= \alpha \left\{ -\beta \frac{\alpha I_i^2}{N_i^*} + \beta I_i - \gamma I_i - \delta I_i + \delta \sum_{j=1}^n c_{ji} I_j \right\}, \\ &\geq \alpha \left\{ -\beta \frac{I_i^2}{N_i^*} + \beta I_i - \gamma I_i - \delta I_i + \delta \sum_{j=1}^n c_{ji} I_j \right\}, \\ &= \alpha f_i(I), \end{aligned}$$

thus f is strong sublinear on Ω_n . By Lemma 2 and Corollary 3.2 in [25], we conclude that system (3.7) admits a unique EE $E^* = (I_1^*, \dots, I_n^*)$ which is globally asymptotically stable. \square

5. Simulation results

5.1. The probability distribution of next-nearest degree

Prior to simulating an infectious disease spreading on a metapopulation network coupled with its SNN, it is necessary to make it clear that what network topology is and which distribution the next-nearest degree follows. In [26], Newman derived an expression of probability $P_k^{(2)}$ as follows:

$$P_k^{(2)} = \sum_m P_m \sum_{j_1} \dots \sum_{j_m} \delta(k, \sum_{r=1}^m j_r) \prod_{r=1}^m q_{j_r}.$$

Here q_k means that the probability of excess degree is exactly k , and it is given by $q_k = (k+1)P_{k+1}^{(1)} / \langle k \rangle$. For a network with small size of nodes or simple structures (such as regular network), this probability is easily calculated. While for a general complex network, it is complex to calculate $P_k^{(2)}$ directly. The introduction of generating function makes this problem easier, but extracting explicit probability distribution for next-nearest degrees is quite difficult. In Fig. 4, we illustrate $P_k^{(2)}$ for two kinds of networks with average degree 7: homogeneous networks whose degrees follow a Poisson distribution and heterogeneous networks with degrees power-law distributed, which makes the distribution of next-nearest degrees clearer.

Obviously, heterogeneity of network structures makes a big difference on $P_k^{(2)}$. Referring to degrees of nodes Poisson distributed, the probability distribution of next-nearest degrees is almost symmetric about $k = 49$, the average next-nearest degree (the average number of second neighbors). In contrast, in the case that degrees of nodes follow a power-law distribution, next-nearest degrees present high heterogeneity with k range from 4 to 537. However, there is something in common that $P_k^{(2)}$ keeps relatively bigger when $k \in [45, 50]$.

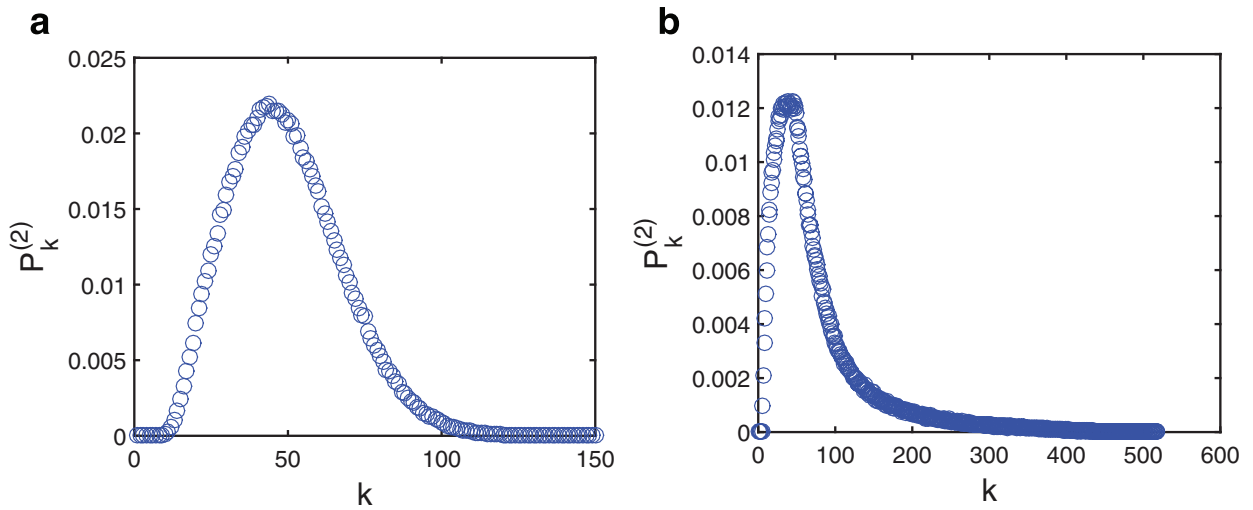


Fig. 4. Probability distribution of next-nearest degrees. Two kinds of different networks containing 2000 nodes are performed: homogeneous networks with $P_k^{(1)} = 7^k \exp(-7)/k!$ (the left panel) and heterogeneous networks with $P_k^{(1)} = k^{-2.1674} / \sum_{k=3}^{44} k^{-2.1674}$ (the right panel). Note that the average degrees $\langle k \rangle$ of these two kinds of networks keep the same. All values are obtained by averaging over 300 stochastic realizations.

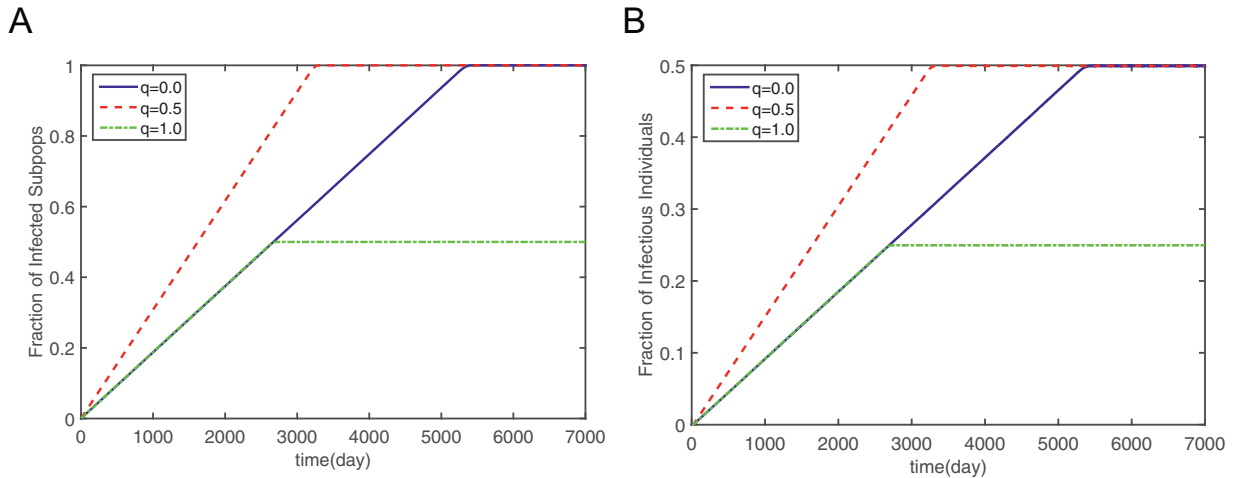


Fig. 5. The time evolution of infected subpopulations and infectious individuals on a linear metapopulation network. Transfer rates are $q = 0$ (blue line), $q = 0.5$ (red dashed line), $q = 1$ (green dot-dashed line), individually. The left panel shows the fraction of infected subpopulations evolving over time, while the right panel is the proportion of infectious individuals. All values are obtained by averaging over 50 stochastic realizations.

5.2. The effect of transfer rate on disease transmission

In Section 4, we calculate R_0 , which is independent of transfer rate, meaning that transfer rate has little impact on the stability of the system. Hence, to know the significance of transfer rate or SNN, we simulate an SIS infectious disease on three kinds of metapopulation networks coupled with their respective SNNs. Metapopulation networks with 2000 subpopulations are generated following Molloy and Reed algorithm [27]. For sake of similarity, we assume that individuals in the same subpopulations travel along each link with the same probability. Hence, weights of links are $w_{ij}^{(1)} = 1/k_i^{(1)}$ for the metapopulation network, and $w_{ij}^{(2)} = 1/k_i^{(2)}$ for its SNN. With regard to each subpopulation i , the initial size of population depends on the degree of this subpopulation, i.e., $N_i = k_i^{(1)} / \langle k \rangle \bar{N}$. \bar{N} denotes the average population of whole network. Focusing on the effect of transfer rate, we keep other parameters unchanged, and they are $\bar{N} = 1000$, $\beta = 0.4$, $\gamma = 0.2$, $\delta = 0.1$.

First, we consider a simplest connected metapopulation network, whose nodes are arranged in a straight line (named as linear metapopulation network), and simulate the spread of disease on this network coupled with its SNN (shown in Fig. 5). This network can be regarded as a regular network with degree 2 when the number of nodes is large enough. In each panel, we make a comparison among three values of transfer rates: $q = 0$ for no transfer, $q = 0.5$ for half of travelers choosing to transfer, and $q = 1$ for all individuals traveling along the SNN. From Fig. 5, the fractions of infected subpopulations and infec-

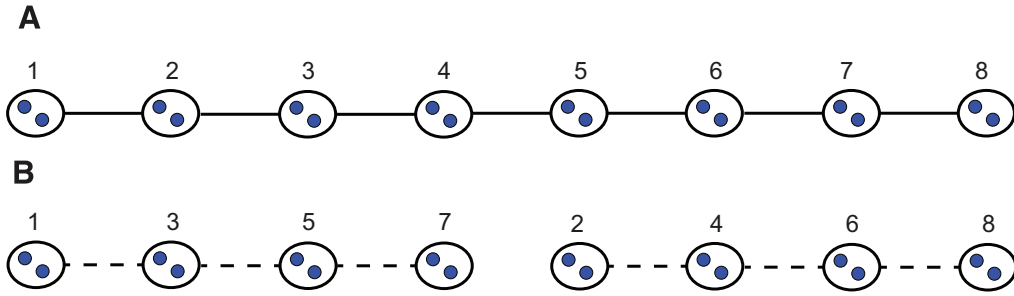


Fig. 6. A linear metapopulation network and its SNN. Panel A shows a linear metapopulation network, a network whose nodes are arranged in a straight line. The degree of all nodes equals to 2 except the first and the last nodes. Its SNN is composed of two linear networks with half of its nodes (see panel B) when the number of nodes is an even number.

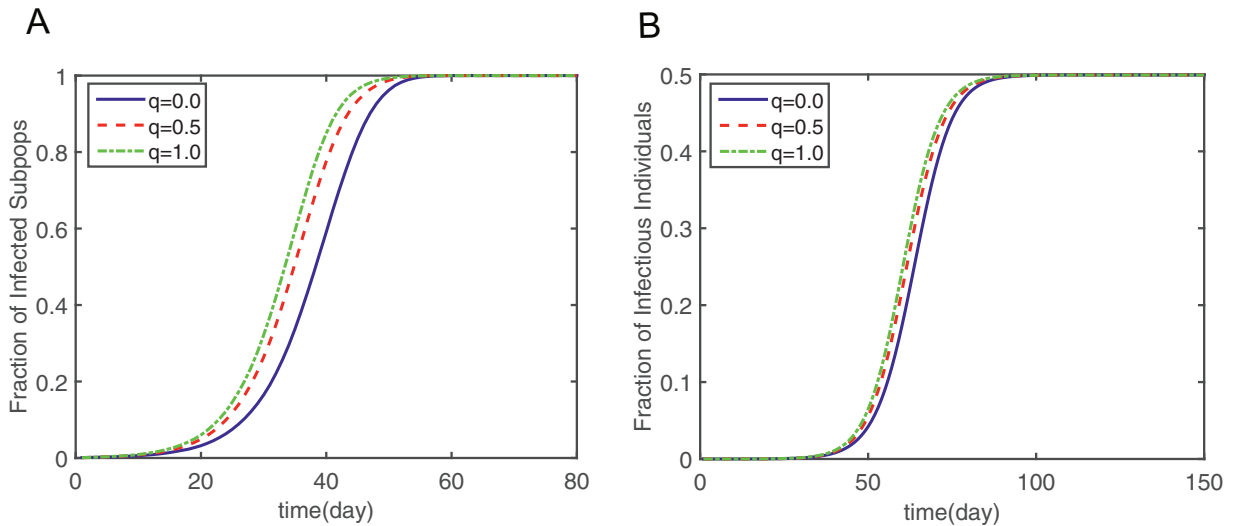


Fig. 7. The time evolution of infected subpopulations and infectious individuals on homogeneous metapopulation networks. The degree distribution is Poisson with $P_k^{(1)} = 7^k \exp(-7)/k!$. All values are obtained by averaging over 100 stochastic realizations. Others are similar to Fig. 5.

tious individuals both increase almost linearly. And the speed of disease transmission when $q = 0.5$ is nearly twice as fast as that of the other two cases. When transmission process reaches a steady state, the fractions of infected subpopulations and infectious individuals when all individuals travel along the SNN are nearly half of that of the other two cases. The reason is obvious. The SNN is not connected and it is composed of two linear subnets (shown in Fig. 6). The change in network connectivity hinders the spread of disease to some degree. However, moderate transfer rate does accelerate the transmission of disease. These two results hold for all cases where the metapopulation network is connected while its SNN not. Under these cases, controlling direct flights may limit the spread of disease to a relatively small area.

Second, we investigate two kinds of typical networks with the same average degree 7, and let the networks and their SNNs keep the same network connectivity. As illustrated in Figs. 7 and 8, comparing the left and right panels of these two figures, we find that at the early phase of transmission disease occurs and outbreaks in a small number of subpopulations and infectious individuals increase slowly. When there exist infectious individuals in majority of subpopulations, the fractions of infectious individuals rise sharply and then reach a steady state in a short time. It is easily seen that the behavior of individual transfer accelerates the transmission of disease. Increasing rates of transfer paves the way for infectious individuals transmitting disease to more susceptible subpopulations. However, transfer rate has little effect on the final fraction of infectious individuals, which is consistent with the theoretical results in Section 4.

Although transfer rate contributes to the global spread of infectious diseases, the effect of transfer rate differs in heterogeneity of next-nearest degrees. In Fig. 8, for power-law networks, moderate transfer rate is most conducive to the spread of infectious diseases. However, when $q = 1$, the speed of transmission is slightly slower than that of $q = 0.5$. Referring to Poisson networks (shown in Fig. 7), along the increase of transfer rate, the speed of spread displays an increase trend, at odds with power-law networks. This is owing to next-nearest degrees. For power-law networks (see Fig. 4(a)), with the number of second neighbors climbs from 4 to 537, weights of links of the SNN gradually decrease, which lower the probability of individuals traveling to second neighbors. In contrast, the distribution of next-nearest degrees for Poisson network is relatively concentrated.

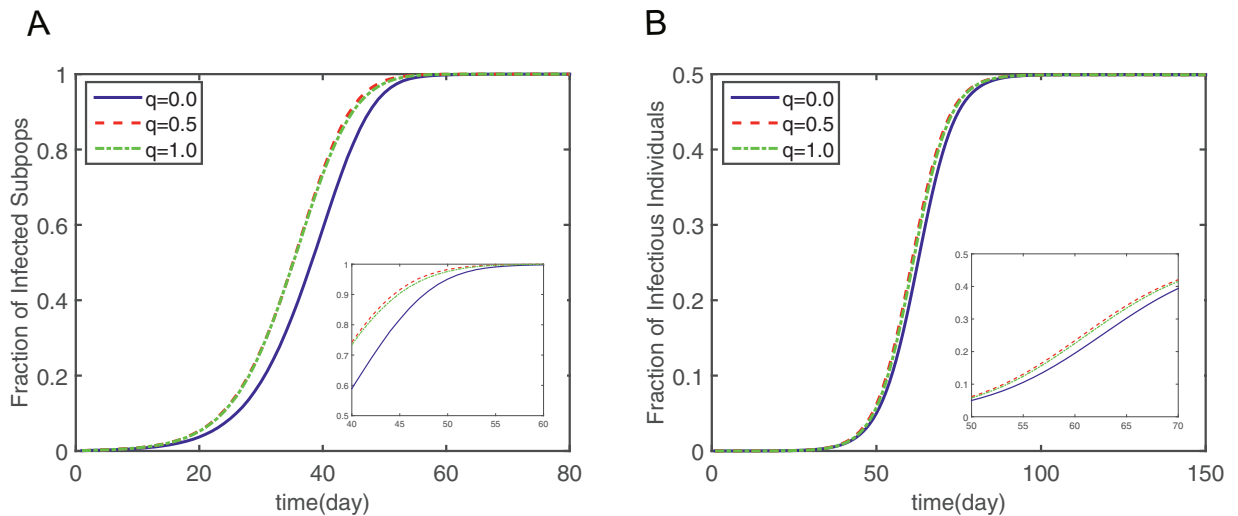


Fig. 8. The time evolution of infected subpopulations and infectious individuals on heterogeneous metapopulation networks. Degrees follow a truncated power-law distribution with $p_k^{(1)} = k^{-2.1674} / \sum_3^{44} k^{-2.1674}$. The inset in each panel illustrates disease transmission during a shorter time so that lines are more clearer. Others are similar to Fig. 7.

Under the circumstances, controlling direct flights may accelerate the global spread of disease. The role played by indirect flights can not be ignored. Maybe no traveling is the best measure.

6. Conclusions

In this paper, we took neglected indirect flights into account, and put forward a definition of SNN for a undirected network. Similar to general networks, we defined adjacency matrix, next-nearest degree and its distribution on this network. Upon these bases, we proposed an ordinary differential equation group to curve the effect of transfer rate on the global transmission of an infectious disease. Next, we obtained the limiting system of the model and gave the expression of the basic reproduction number, which depends only on disease parameters. Further, the global stability of DFE and EE has been proven.

Then, we presented some simulation results on three kinds of connected metapopulation networks with different average degrees and different degree distributions. One is a linear metapopulation network with average degree approximately equaling to 2, and the other two are with the same average degree 7. We find that if the SNN is not connected, controlling direct flights may hinder the spread of disease. On the contrary, if the SNN is also connected, controlling direct flights may accelerate the spread of disease. It is in common that moderate transfer rate contributes to the global spread of infectious diseases. In detail, for a linear network, the numbers of infected subpopulations and infectious individuals increase almost linearly. For a Poisson network, the dominant role is second neighbor because of its relatively homogeneous distribution. However, for the other two networks, moderate transfer rate is most conducive to the spread of infectious diseases, which means that although the existence of second neighbors may promote the global transmission of infectious diseases, the roles played by neighbors are still significant. Therefore, when an infectious disease occurs, the governments should adjust measures to local conditions. That is, if the network connectivity is reduced after controlling direct flights, this measure is effective; otherwise, if the network connectivity keep the same with the original network, this measure fails. It may be more effective to control all flights (direct or indirect) properly.

Our studies shed lights on disease control and prevention. But there may be some problems to be solved. When people travel, they may traverse more than one place before reaching their destinations. This case is rare for aviation network but common for high-speed train and rail networks. Under similar hypotheses, our model can be popularized to the third-neighbor network, the fourth-neighbor network, and so on, and then be applied to high-speed train and rail networks. It is worth noticing that more stops may lead to according change of time scale, such as a general train, whose speed is so slow that it is time-consuming traveling between two places with long distance.

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References

- [1] L. Hufnagel, D. Brockmann, T. Geisel, Forecast and control of epidemics in a globalized world, *Proc. Natl. Acad. Sci. USA* 101 (42) (2004) 15124–15129.
- [2] F. Christophe, R. Cathy, Pandemic potential of a strain of influenza A (H1N1): early findings, *Science* 324 (5934) (2009) 1557–1561.
- [3] R.B. Gao, B. Cao, Y.W. Hu, Z.J. Feng, D.Y. Wang, W.F. Hu, J. Chen, Z.J. Jie, H.B. Qiu, K. Xu, Human infection with a novel avian-origin influenza A (H7N9) virus, *New. Engl. J. Med.* 368 (20) (2013) 1888–1897.
- [4] T.B. Chris, O. Tamer, Assessing the pandemic potential of MERS-CoV, *Lancet* 382 (9893) (2013) 662–664.
- [5] C. Poletto, M.F.C. Gomes, A.P. Piontti, L. Rossi, L. Bioglio, D.L. Chao, I.M. Longini, M.E. Halloran, C. V. V. A, Assessing the impact of travel restrictions on international spread of the 2014 West African Ebola epidemic, *Eur. Surveill.* 19 (42) (2014).
- [6] I.I. Bogoch, O.J. Brady, M.U. Kraemer, M. German, M.I. Creatore, S. Brent, A.G. Watts, S.I. Hay, M.A. Kulkarni, J.S. Brownstein, Potential for Zika virus introduction and transmission in resource-limited countries in Africa and the Asia-Pacific region: a modelling study, *Lancet Infect. Dis.* 16 (11) (2016) 1237–1245.
- [7] V. Colizza, A. Vespignani, Epidemic modeling in metapopulation systems with heterogeneous coupling pattern: theory and simulations, *J. Theor. Biol.* 251 (3) (2008) 450–467.
- [8] L. Cao, X. Li, B. Wang, K. Aihara, Rendezvous effects in the diffusion process on bipartite metapopulation networks, *Phys. Rev. E* 84 (1) (2011) 041936.
- [9] S.Y. Liu, A. Baronchelli, N. Perra, Contagion dynamics in time-varying metapopulation networks, *Phys. Rev. E* 87 (3) (2012) 411–427.
- [10] A.S. Mata, S.C. Ferreira, R. Pastor-Satorras, Effects of local population structure in a reaction-diffusion model of a contact process on metapopulation networks, *Phys. Rev. E* 88 (1) (2013) 042820.
- [11] B. Wang, T. Gouhei, S. Hideyuki, A. Kazuyuki, Epidemic spread on interconnected metapopulation networks, *Phys. Rev. E* 90 (3) (2014) 032806.
- [12] M. Tang, Z.H. Liu, B.W. Li, Epidemic spreading by objective traveling, *EPL* 87 (1) (2009) 18005.
- [13] S. Meloni, N. Perra, A. Arenas, S. Gómez, Y. Moreno, A. Vespignani, Modeling human mobility responses to the large-scale spreading of infectious diseases, *Sci. Rep.* 1 (62) (2011) 62–68.
- [14] B. Wang, N. Perra, A. Arenas, A. Kazuyuki, Safety-information-driven human mobility patterns with metapopulation epidemic dynamics, *Sci. Rep.* 2 (2) (2012) 887–894.
- [15] B. Wang, Y.X. Han, G. Tanaka, Interplay between epidemic spread and information propagation on metapopulation networks, *J. Theor. Biol.* 420 (2017) 18–25.
- [16] D. Balcan, A. Vespignani, Phase transitions in contagion processes mediated by recurrent mobility patterns, *Nat. Phys.* 7 (7) (2011) 581–586.
- [17] D. Balcan, A. Vespignani, Invasion threshold in structured populations with recurrent mobility patterns, *J. Theor. Biol.* 293 (1) (2012) 87–100.
- [18] C. Poletto, M. Tizzoni, V. Colizza, Heterogeneous length of stay of hosts' movements and spatial epidemic spread, *Sci. Rep.* 2 (2012) 476–486.
- [19] D. Brockmann, Human mobility and spatial disease dynamics, *Rev. Nonlinear Dyn. Complexity*, 2009.
- [20] A. Baronchelli, R. Pastor-Satorras, Mean-field diffusive dynamics on weighted networks, *Phys. Rev. E* 82 (1) (2010) 011111.
- [21] J. Arino, J.R. Davis, D. Hartley, R. Jordan, J.M. Miller, P. van den Driessche, A multi-species epidemic model with spatial dynamics, *Math. Med. Biol.* 22 (2) (2005) 129–142.
- [22] P. van den Driessche, J. Watmough, Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission, *Math. Biosci.* 180 (1–2) (2002) 29–48.
- [23] H. Minc, *Nonnegative Matrices*, Wiley Interscience, 1988.
- [24] S.S. Feng, Z. Jin, Moment closure of infectious diseases model on heterogeneous metapopulation network, *Adv. Differ. Equ.* 339 (2018).
- [25] X.Q. Zhao, Z.J. Jing, Global asymptotic behavior in some cooperative systems of functional differential equations, *Can. Appl. Math. Quart.* 4 (4) (1996) 421–444.
- [26] M.E.J. Newman, *Networks: An Introduction*, Oxford University Press, 2009.
- [27] M. Molloy, B. Reed, A critical point for random graphs with a given degree sequence, *Random Struct. Algorithm* 6 (2–3) (1995) 161–180.