

# Mathematical and computational approaches to epidemic modeling: a comprehensive review

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**Abstract** Mathematical and computational approaches are important tools for understanding epidemic spread patterns and evaluating policies of disease control. In recent years, epidemiology has become increasingly integrated with mathematics, sociology, management science, complexity science, and computer science. The cross of multiple disciplines has caused rapid development of mathematical and computational approaches to epidemic modeling. In this article, we carry out a comprehensive review of epidemic models to provide an insight into the literature of epidemic modeling and simulation. We introduce major epidemic models in three directions, including mathematical models, complex network models, and agent-based models. We discuss the principles, applications, advantages, and limitations of these models. Meanwhile, we also propose some future research directions in epidemic modeling.

**Keywords** mathematics, complex networks, agent-based models, epidemic modeling, human dynamics, infectious diseases

## 1 Introduction

Mathematical and computational approaches are dominant in epidemic modeling [1–3]. These approaches play an important role in understanding epidemic spread patterns and evaluating policies of disease control. In general, mathematical

models focus on the macroscopic regularities of epidemic spread [1]. Mathematical models make some reasonable assumptions, such as a homogeneous and well-mixed population, so as to represent the spread of epidemics at the macro level. Mathematical models also simplify the complex spreading process of epidemics. For example, only a few key factors are taken into account in mathematical models. These factors are embodied in some variables parameterized with average quantities or mean values in equations. These assumptions and simplifications endow mathematical models with the advantage of performing theoretical analysis of macroscopic regularities of epidemic diffusion, such as the epidemic threshold and final epidemic size. However, these assumptions and simplifications also limit the capability of mathematical models to represent the spread of epidemics in detail. Computational approaches make use of a wide array of simulation schemes to provide a more detailed representation of realities [4,5]. Computational approaches usually build epidemic models, such as complex network models and agent-based models, at an individual level [6]. However, the higher granularity of computational models requires large data availability and higher computational complexity, as well as greater computational power. Recently, with advances in data availability and affordable high performance computing, computational approaches are increasingly used to study the spread of epidemics.

The emergence of novel pathogens in human societies, such as severe acute respiratory syndrome (SARS) in 2003 and H1N1 influenza in 2009, have ignited worldwide epidemic outbreaks that attracted much research attention. Researchers in various fields have employed various mathemati-

cal methods and computational techniques to study epidemic diffusion in human societies, such as differential equations, stochastic processes, statistical analysis, graph theory, artificial life, artificial society, computer simulation, geographic information systems, and high performance computing. Epidemiology has become increasingly integrated with mathematics, sociology, management science, complexity science, and computer science. The cross of multiple disciplines causes the development of mathematical and computational approaches to epidemic modeling.

In this article, we carry out a comprehensive review of epi-

demical models so as to provide an insight into the literature of epidemic modeling and simulation. We aim at investigating current work and future research directions in epidemic modeling. Our contributions are twofold. On the one hand, we introduce major epidemic models in three directions: mathematical models, complex network models, and agent-based models. These models and their modeling methods discussed in the following sections are illustrated in Table 1. We will discuss the principles, applications, advantages, and limitations of these models. We also propose some future research directions for epidemic modeling.

**Table 1** Classification of epidemic models

Types	Names	Methods
Mathematical models	Compartmental models, Reed-Frost models	Differential equations, stochastic process, Monte Carlo, Markov chains
Complex network models	System dynamics models in complex networks, numerical simulations of epidemics in complex networks, meta-population models, weighted networks, adaptive networks	Differential equations, stochastic processes
Agent-based models	BioWar, EpiSims, FluTE, MASON, GeoGraphs, EpiSimdemics, EpiFast, Repast, Random walk, Levy flight, gravity model	Algorithms, computational techniques, mathematics, complex networks, cellular automaton, GIS, simulation

In Section 2, we introduce the mathematical model of epidemics in two directions: deterministic models and stochastic models. We also discuss the advantages and limitations of mathematical models of epidemics. In Section 3, we review three current research topics in complex network models of epidemics: the impact of network structures on epidemic dynamics, epidemic spread in weighted networks, and epidemic spread in adaptive networks. Next, we discuss the advantages and limitations of complex network models of epidemics. In Section 4, we introduce several large scale agent-based simulation systems of epidemics. We also discuss how to represent individual contact patterns and mobility patterns in agent-based models of epidemics. In Section 5, we propose some future research directions in epidemic modeling, including temporal-spatial modeling of epidemic spread, the heterogeneity of epidemic models, and the interplay between human dynamics and epidemic dynamics. In Section 6, we perform a comparison between mathematical models, complex network models, and agent-based models, and then conclude this article.

## 2 Mathematical models of epidemics

Mathematical modeling is the earliest method used to formulate epidemic spread [7,8]. In 1766 Daniel Bernoulli formulated a model to evaluate the effect of vaccination against the smallpox virus [7]. In 1906 Hamer proposed a discrete time

model to understand the recurrence of measles epidemics [7]. He recognized that the diminishing density of susceptible individuals bring epidemics to a halt. In 1911 Ross developed differential equations to investigate the effectiveness of various intervention strategies for malaria [7]. In the 1920s Lowell Reed and Wade Hampton Frost put forward a mathematical model to describe how diseases spread across a population, which is known as the Reed-Frost model [9–10]. Kermack and McKendrick extended Ross’s models to form a system dynamics model of infectious disease transmission, which is also called as the compartmental model [11]. They found that only if the basic reproduction number was larger than a threshold value, could an infectious disease spread in a susceptible population. These precursors created the foundations of mathematical models of epidemics. In the past few decades, research has extended the existing mathematical models of epidemics and developed new epidemic models.

Mathematical models of epidemics are usually classified into two categories: deterministic epidemic models and stochastic epidemic models.

### 2.1 Deterministic epidemic models

Compartmental models are the most widely used deterministic epidemic models [12–15]. The population is assumed to be homogeneous, well-mixed, and aggregated into a small set of compartments according to individual health states. Transitions of the population between different compartments are

formulated using differential equations, with variables modeling different factors such as the infection rate, onset rate of symptoms, and recovery rate.

Due to the variance in epidemic progress of different diseases, infected individuals may have a variety of health states. Different kinds of compartmental models have been proposed, such as SIR (susceptible, infectious, and recovered) model, SIS (susceptible, infectious, and susceptible) model, and SEIR (susceptible, exposed, infectious, and recovered) model, these are illustrated in Fig. 1.

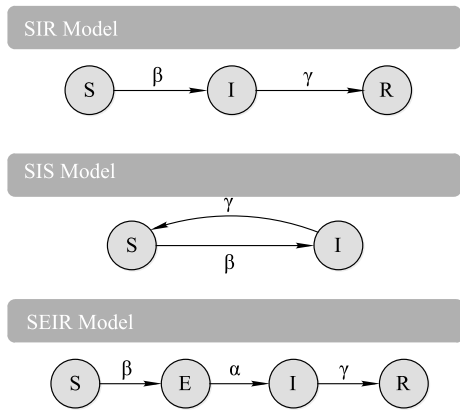


Fig. 1 Compartmental models

In the SIR model, individuals go through three health states: susceptible, infectious, and recovered. When susceptible individuals are infected by an epidemic with infection rate ( $\beta$ ), their states become infectious. Meanwhile, infectious individuals are able to transmit the epidemic. After the infectious period, infected individuals are then in a recovered state with recovery rate ( $\gamma$ ), and become immune to the epidemic. In the SIS model, infectious individuals will not enter the recovered state after infectious period, but return to the susceptible state. In the SEIR model, individuals go through one more state, the exposed state, before reaching the infectious state. The classic SIR model is represented as

$$\begin{cases} \frac{ds(t)}{dt} = -\beta s(t)i(t), \\ \frac{di(t)}{dt} = \beta s(t)i(t) - \gamma i(t), \\ \frac{dr(t)}{dt} = \gamma i(t), \end{cases} \quad (1)$$

where  $s(t)$ ,  $i(t)$ , and  $r(t)$  are the densities of susceptible individuals, infectious individuals, and recovered individuals, respectively.  $\beta$  ( $\beta > 0$ ) is infection rate;  $\gamma$  ( $\gamma > 0$ ) is recovery rate. The temporal evolution of  $s(t)$ ,  $i(t)$ , and  $r(t)$  is described in Fig. 2(a). It is shown that the density of infectious individuals increases exponentially, approximating to  $i(t) \sim \beta^t$ .

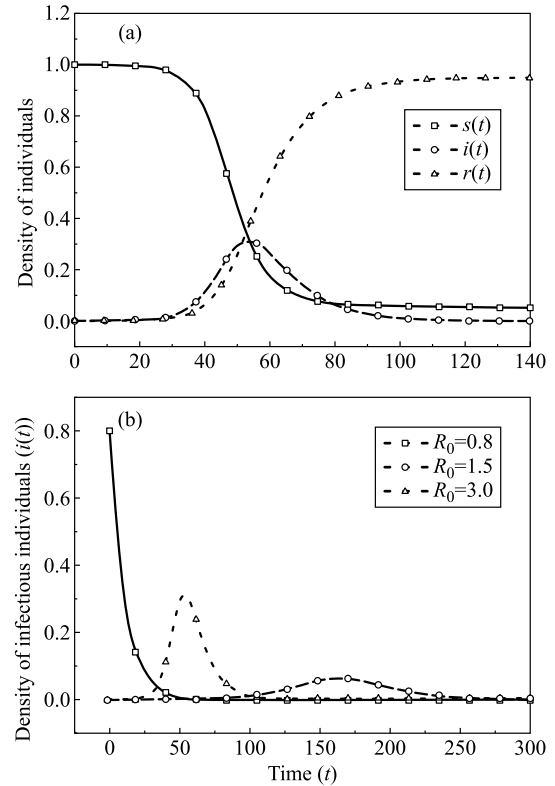


Fig. 2 Results of the SIR model (number of individuals  $N = 10^4$ ). (a) Temporal evolution of densities of susceptible, infectious, and recovered individuals ( $\beta = 0.3$ ,  $\lambda = 0.1$ ,  $i(0) = 10^{-4}$ ); (b) temporal evolution of densities of infectious individuals with different basic reproduction number ( $R_0 = 0.8$ :  $i(0) = 0.8$ ;  $R_0 = 1.5$  and  $R_0 = 3.0$ :  $i(0) = 10^{-4}$ ).

To obtain the basic reproduction number ( $R_0$ ), we rewrite the second equation in Eq. (2) as

$$\frac{di(t)}{dt} = \left( \frac{\beta}{\gamma} s(t) - 1 \right) \gamma i(t). \quad (2)$$

Due to  $s(t) \in [0, 1]$  and  $i(t) \in [0, 1]$ , the density of infectious individuals increases ( $di(t)/dt > 0$ ) in case of  $\beta/\gamma > 1$ ; the density of infectious individuals decreases ( $di(t)/dt < 0$ ) in case of  $\beta/\gamma < 1$ . The basic reproduction number is defined as  $R_0 = \beta/\gamma$ . When  $R_0 > 1$ , an infectious individual can spread the epidemic across a susceptible population. The temporal evolution of infectious individuals with different  $R_0$  is illustrated in Fig. 2 (b). Moreover, the final epidemic size is a function of  $R_0$ , described as

$$r(\infty) = 1 - s(0)e^{-R_0 r(\infty)}, \quad (3)$$

where  $s(0)$  is the density of susceptible individuals at time  $t = 0$ . The mathematical derivation of  $r(\infty)$  in the SIR model can be seen in [16,17].

## 2.2 Stochastic epidemic models

Stochastic epidemic models are usually built using a stochastic process, such as Markov Chains, and the Monte Carlo

method [16,18–23]. The Reed-Frost model is the most widely used stochastic epidemic model [24–27], it assumes that an infection event in contact between two individuals can be modeled as a binomial stochastic process. This model is defined as follows.

Consider a closed population consisting of  $N$  individuals. Each individual has the same chance to contact with each other. In a contact, a susceptible individual is infected with a certain probability by an infectious individual. Infected individuals become recovered and immune after going through the duration of infectious period. Initially, there is an infectious individual in the population just as  $I(0) = 1$ . The initial number of susceptible individuals is  $S(0) = N - 1$ .  $I(t)$  and  $S(t)$  denote the number of infectious individuals and susceptible individuals at time  $t$ , respectively. The infection probability in a contact between a susceptible individual and an infectious individual is  $p$ . The probability that a susceptible individual is not infected by an infectious individual in the contact is then  $q = 1 - p$ . The probability that a susceptible individual is not infected at time  $t$  is  $Q_{t+1} = q^{I(t)}$ . The reverse probability is then  $P_{t+1} = 1 - q^{I(t)}$ . Moreover, the expected number of new infected individuals at time  $t + 1$  is

$$E(I(t+1)|I(t), S(t)) = S(t)(1 - q^{I(t)}). \quad (4)$$

The original Reed-Frost model only formulates a simple binomial stochastic process of epidemic spread. Many researchers have extended the original Reed-Frost model to build stochastic epidemic models in their studies. It is reasonable to represent uncertainty or randomness in epidemic models. Thus, compared to deterministic epidemic models, stochastic epidemic models can offer a more realistic representation of epidemic diffusion. More comparisons between stochastic epidemic models and deterministic epidemic models can be found in [16,28–31].

### 2.3 Advantages and limitations of mathematical models of epidemics

Mathematical models make some assumptions and simplifications of the complex spreading process of epidemics. These assumptions and simplifications endow mathematical models with the advantage of performing theoretical analysis of macroscopic regularities of epidemic diffusion, such as the epidemic threshold and final epidemic size. However, these assumptions and simplifications also limit the capability of mathematical models to represent the spread of epidemics in detail. The limitations of mathematical models of epidemics are summarized as follows.

- The assumption of homogeneous and well-mixed population results in difficulties in representing the variants of individual microscopic attributes and behaviors.
- A small set of variables in mathematical models are inadequate to capture the variety of factors associated with the epidemic spread process, especially the determining factor, human behavior.
- The Reed-Frost model and compartmental model both assume that individuals are fully connected and make a contact with each other in a time step. This assumption limits mathematical models to using heterogeneous links between individuals.
- Variables parameterized with average quantities and mean values, such as average infection rate and average recovery rate, cannot be used to describe the heterogeneous nature of epidemic spread, such as the heterogeneous contagiousness of infectious individuals and the heterogeneous time scale of epidemic progress.

To resolve these limitations, researchers have extended compartmental model and Reed-Frost model in their studies. First, to represent the variations of individual attributes and behaviors, the population is divided into more subgroups according to not only people's health states, but also their ages, occupations, and infectivity [32–36]. For example, Mkhathshwa et al. [33] divided infectious individuals into two subgroups: super spreaders and regular spreaders, when they studied super spreading events by using compartmental models. Second, researchers extended the variables in mathematical models so as to capture various factors associated with epidemic spread. For example, Fenichel et al. [37] integrated human behavior into the variable of average infection rate in order to study the impact that human behavioral change have on epidemic spread. Li et al. [38] used empirical distributions to realize the heterogeneous time scale of epidemic progress.

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## 3 Complex network models of epidemics

The last decade has witnessed a remarkable development in complex network models of epidemics [39–44]. Epidemic systems are described as complex networks where nodes represent individuals and links represent interactions among individuals. In general, complex network models of epidemics are classified into two categories: spreading dynamics in complex networks and numerical simulations of epidemics in complex networks. Models of spreading dynamics use mean-field theory to parse complex networks, and then build differ-

ential equations to represent the spread of epidemics [45,46]. As in compartmental models, individuals are divided into different groups according to their health states in complex networks models of spreading dynamics. The infectivity of infectious nodes is described as a function of average node degree in homogeneous networks. While, due to the heterogeneity of degrees, nodes are again divided into more subgroups according to degrees in heterogeneous networks. Numerical simulations of epidemics in complex networks use individual-based models to represent contact patterns between individuals and infection probability on links. Numerical simulations of epidemics in complex networks usually integrate with the Reed-Frost model to formulate the spreading process of epidemics [47,48].

Most complex network models of epidemics focus on the impact that network topologies have on epidemic spread, such as small-world networks and scale-free networks. In recent years, many researchers have paid attention to epidemic spread in weighted networks and adaptive networks.

### 3.1 The impact of network topologies on epidemic dynamics

Many researchers have investigated epidemic spread in random networks [49], small-world networks [50], and scale-free networks [51]. Their studies indicate that the topologies of social networks have a significant impact on epidemic dynamics [45,46,52–56]. For example, nodes with a higher degree are infected with a higher probability; epidemics spread faster in scale-free networks than in small-world networks at the early stage of epidemic outbreaks.

Pastor-Satorras et al. [46] used mean-field theory to formulate an SIS spreading dynamics model in complex networks. They assumed that a susceptible node is infected by an infectious neighbor with probability  $\nu$  for each time step, and enters the infectious state. Meanwhile, infectious nodes become susceptible again with a probability  $\delta$  for each time step. The average infection rate is then defined as  $\lambda = \nu/\delta$ . In homogeneous networks whose node degree approximates to average connectivity  $\langle k \rangle$ , such as small-world networks and random networks, the infectivity of infectious nodes is related to their degree. Pastor-Satorras et al. [46] defined the SIS spreading dynamics models in homogeneous networks as

$$\begin{cases} \frac{ds(t)}{dt} = -\lambda\langle k \rangle s(t) + \gamma i(t); \\ \frac{di(t)}{dt} = -\gamma i(t) + \lambda\langle k \rangle s(t), \end{cases} \quad (5)$$

where  $s(t)$  and  $i(t)$  are the densities of susceptible nodes and

infectious nodes at time  $t$ .  $\gamma$  is average recovery rate. Pastor-Satorras et al. set  $\delta = 1$  and derived the epidemic threshold as  $\lambda_c = 1/\langle k \rangle$ . Due to the heterogeneity of node degrees in scale-free networks, nodes are again divided into more subgroups. Spreading dynamics models of epidemics in scale-free networks are defined as [46]

$$\begin{cases} \frac{ds_k(t)}{dt} = -\lambda k s_k(t) \Theta(i_k(t)) + \gamma i_k(t); \\ \frac{di_k(t)}{dt} = -\gamma i_k(t) + \lambda k s_k(t) \Theta(i_k(t)), \end{cases} \quad (6)$$

where  $s_k(t)$  and  $i_k(t)$  are the respective densities of susceptible and infectious nodes with degree  $k$  at time  $t$ .  $\Theta(i_k(t))$  is the probability that any given link connects to an infected node. The epidemic threshold of the SIS model in scale-free networks is  $\lambda_c = \langle k \rangle / \langle k^2 \rangle$ . Moreover, a positive epidemic threshold does not exist in scale-free networks due to the uncorrelated node degrees.

In addition, researchers also studied vaccination strategies in complex networks [57,58], as well as the bifurcation and oscillation phenomena of epidemic dynamics in complex networks [59,60]. Recently, many researchers who focus on the impact that network topologies have on epidemic dynamics have transferred their attention to epidemic spread in hierarchy and modular networks with community structure [61–65].

### 3.2 Epidemic spreading in weighted networks

Many real world systems are described as weighted networks, in which the weights of edges represent the strength of interactions. Examples include airport networks in which edge weights represent the number of flights or available seats [66,67]; scientist collaboration networks in which edge weights represent the number of coauthored papers [66,68]; cell-phone communication networks in which edge weights are the number of calls or the total duration of calls [69]; gene co-expression networks in which edge weights represent a measure of co-expression [70]; protein-protein interaction networks [71–73]; criminal networks [74]; and economic networks or trade networks [75–77].

However, most previous complex network models of epidemics only focus on epidemic dynamics in unweighted networks, and lose sight of a detailed description of interaction patterns. Recently, epidemic spread in weighted networks has received much attention. Yan et al. [78] studied epidemic spread in weighted evolving scale-free networks also known as Barrat, Barthélemy, and Vespignani (BBV) networks [79]. BBV networks are constructed according to strength preferential attachment. At each time step, a new vertex  $n$  is added

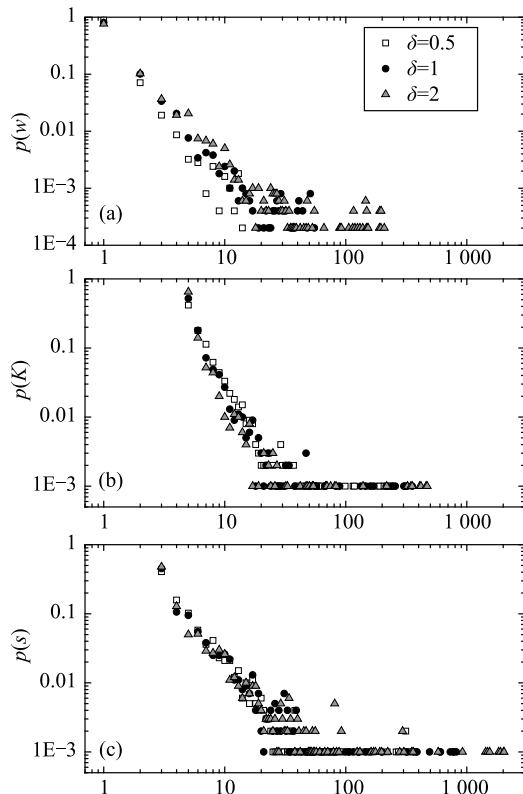
with  $m$  edges that are randomly attached to a previously existing vertex  $i$  according to the probability distribution

$$p_{n \rightarrow i} = \frac{s_i}{\sum_j s_j}, \quad (7)$$

where  $s_i$  is the strength of vertex  $i$ . The weight of each new edge is fixed to a value  $w_0$ . The weights between vertex  $i$  and its neighbors are rearranged according to the simple rule

$$w_{ij} \rightarrow w_{ij} + \delta \frac{w_{ij}}{s_i}. \quad (8)$$

This rule considers that the establishment of a new edge of weight  $w_0$  with the vertex  $i$  induces a total increase of traffic  $\delta$  that is proportionally distributed among the edges departing from the vertex according to their weights. Node degrees, node strength, and edge weights of BBV networks are subject to power law distributions with heavy tails, illustrated in Fig. 3.



**Fig. 3** The distributions of edge weights, node degrees, and node strengths in BBV networks ( $N = 10^3$ ,  $m = 5$ ,  $w_0 = 0.5$ ). (a) Weight distributions ( $p(w) \sim w^{-\alpha}$ ,  $\alpha = 2 + 1/\delta$ ); (b) degree distributions ( $p(k) \sim k^{-\gamma}$ ,  $\gamma = \frac{4\delta + 3}{2\delta + 1}$ ); (c) strength distributions ( $p(s) \sim s^{-\gamma}$ ,  $\gamma = \frac{4\delta + 3}{2\delta + 1}$ )

Yan et al. [78] assume a closed population consisted of  $N$  individuals. Each individual has two health states: susceptible and infected. They define the infection transmission on a

SI link by the spreading rate

$$\lambda_{ij} = \left( \frac{w_{ij}}{w_M} \right)^\alpha, \quad (9)$$

where  $w_{ij}$  is the weight of the edge between susceptible node  $i$  and its infected neighbor  $j$ .  $w_M$  is the largest value of  $w_{ij}$  in the network.  $\alpha$  ( $\alpha > 0$ ) is a positive constant. The probability that susceptible node  $i$  will be infected at the present time step  $t$  is then

$$\lambda_i(t) = 1 - \prod_{j \in N_i(t)} (1 - \lambda_{ij}), \quad (10)$$

where  $N_i(t)$  is the set of all infected neighbors of node  $i$  at time  $t$ . Moreover, Yan et al. [78] also define the spreading velocity  $V_{\text{inf}}(t)$  and the average strength  $\bar{S}_{\text{inf}}(t)$  of newly infected nodes as

$$\begin{cases} V_{\text{inf}}(t) = \frac{I(t) - I(t-1)}{N}; \\ \bar{S}_{\text{inf}}(t) = \frac{\sum (s(I_s(t) - I_s(t-1)))}{I(t) - I(t-1)}, \end{cases} \quad (11)$$

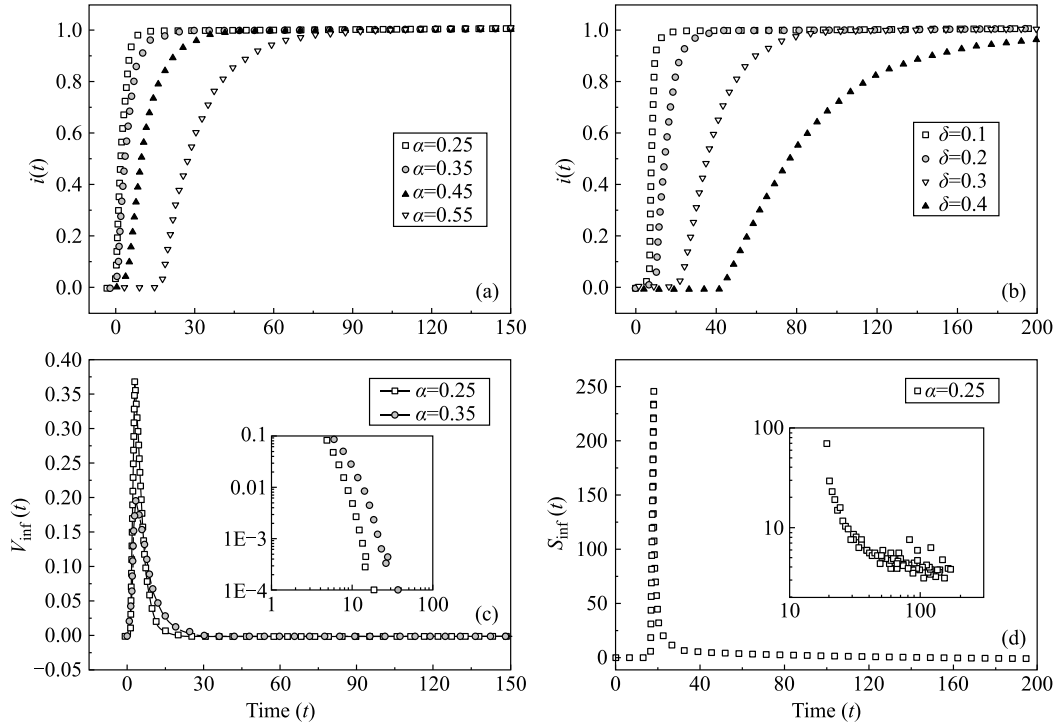
where  $I(t)$  is the number of infected nodes at time  $t$ .  $I_s(t)$  is the number of infected nodes with strength  $s$ .

We randomly selected one initially infected node in Yan's models and conducted numerical simulations. This is shown in Figs. 4(c) and (d) that both the spreading velocity and the average strength of newly infected nodes exhibit a power-law time behavior. Meanwhile, the increase of parameter  $\alpha$  and  $\delta$  leads to a slower infection spreading in Figs. 4(a) and (b). Yan et al. [78] concluded that the larger dispersion of weights in networks results in slower spreading. They also infer that an epidemic spreads faster in unweighted scale-free networks than in weighted scale-free networks with the same conditions.

Chu et al. [80] studied epidemic spread in weighted scale-free networks with community structure. They used node degree to express edge weights just as

$$w_{ij} = w_0(k_i k_j)^\theta, \quad (12)$$

where  $w_{ij}$  is the weight of the edge between node  $i$  and node  $j$ .  $k_i$  and  $k_j$  are the degrees of these two nodes.  $w_0$  and  $\theta$  are two scaling parameters. Chu et al. introduced different values of parameter  $\theta$  to internal edges and external edges in weighted networks with community structure. Similarly, they also distinguishingly described the transmission rate on internal edges and external edges, which is a function of node



**Fig. 4** The time evolution of epidemic dynamics in BBV network ( $N = 10^4$ ,  $m = 3$ ,  $w_0 = 1$ ). (a) Density of infected nodes ( $\delta = 3$ ). (b) Density of infected nodes ( $\alpha = 2$ ). (c) Spreading velocity ( $\delta = 3$ ). (d) Average strength of newly infected nodes ( $\delta = 3$ ).

degrees, node strengths, and weights, described as

$$\begin{cases} \lambda_{ij}^{in} = \lambda k_i^{in} \frac{w_{ij}}{s_i^{in}}; \\ \lambda_{ij}^{out} = \lambda k_i^{out} \frac{w_{ij}}{s_i^{out}}, \end{cases} \quad (13)$$

where  $\lambda_{ij}^{in}$  and  $\lambda_{ij}^{out}$  are transmission rates on internal edges and external edges, respectively.  $k_i^{in}$  and  $k_i^{out}$  are internal degree and external degree of nodes.  $s_i^{in}$  and  $s_i^{out}$  are internal strength and external strength. Chu et al. investigated the time evolution of the density of infected nodes, spreading velocity, and the average degree of newly infected nodes. They find that the weights of external edges play a more important role in slackening the epidemic spread. Moreover, the strong community structure is no longer helpful for reducing the danger brought by the epidemic in weighted cases. In addition, Chu et al. [81] also studied epidemic spread with nonlinear infectivity in weighted scare-free networks.

Vaccination strategies in weighted networks are also studied. Eames et al. [82] used weighted networks to explore the influence of heterogeneous contact strengths on the effectiveness of control measures. They made use of data from a diary survey of social contact behaviors to parameterize a contact network. Then they studied targeting vaccination strategies in the contact network. Deijfen et al. [47,48] proposed a configuration model to construct weighted networks, where node

degree is dependent on edge weights. They demonstrated that an acquaintance vaccination strategy where vertices and their neighbors with large edge weights are vaccinated, outperforms a random vaccination strategy for a given vaccination coverage.

Other work related to epidemic spread in weighted networks is described as follows. Fournié et al. [83] described the live bird markets in northern Vietnam as a weighted and directed network to analyze the spread of H5N1 influenza. Duan et al. [84] studied super spreading events caused by severe acute respiratory syndrome (SARS) in weighted scale-free networks. To build differential equation models of epidemic spread in weighted networks, Yang et al. [85] proposed an edge-based mean-field solution for general weight distributions and investigated the non-equilibrium steady states of epidemic dynamics on weighted networks. Li et al. [86] studied epidemic spread in multi-relational networks. They used different values to weight various relationships among individuals. In many cases, researchers focused on epidemic threshold, epidemic final size, and epidemic prevalence in weighted networks [48,81,85,87–90]. Some others discussed the impact of weight distributions and different types of edge weights on epidemic spread, such as the correlation between edge weights and node degrees [91–94], and strong ties and weak ties in weighted networks [89,91].

### 3.3 Epidemic spreading in adaptive networks

Recently, human behavioral change in response to epidemic outbreaks raises many concerns. The self-protection behaviors of susceptible individuals may break their connections with infected partners. This might significantly alter the structure of contact networks and influence epidemic dynamics. However, most previous studies did not consider human behavioral change and relied on fixed and static networks. In contrast to static networks, some researchers investigated epidemic dynamics in adaptive networks that are characterized by the existence of a feedback loop between the dynamics on networks and the dynamics of networks [95–112].

Gross et al. [95] studied an SIS model in adaptive networks that can change structures by rewiring connections to reflect human behavioral change. They find that different proportion relations between an infection rate and a rewiring rate can cause various phenomena to emerge including an endemic state, a healthy state, bistability, and oscillatory states. They consider a network with a constant number of nodes  $N$  and links  $K$ . The nodes can be in two health states: susceptible and infected. A simple rewiring rule is adopted for connections. In each time step, for every SI link connecting an infected node with a susceptible node, the susceptible node breaks the link with a probability  $\omega$  and forms a new link to another randomly selected susceptible node. Then Gross et al represent differential equation models as

$$\begin{cases} \frac{di}{dt} = pl_{SI} - \gamma i; \\ \frac{dl_{II}}{dt} = pl_{SI} \left( \frac{l_{SI}}{s} + 1 \right) - 2\gamma l_{II}; \\ \frac{dl_{SS}}{dt} = (\gamma + \omega)l_{SI} - \frac{2pl_{SI}l_{SS}}{s}, \end{cases} \quad (14)$$

where  $p$  is the fixed infection rate of susceptible nodes for every SI link.  $\gamma$  is the fixed recovery rate of infected nodes.  $i$  is the density of infected nodes in the network.  $l_{SI}$ ,  $l_{II}$ , and  $l_{SS}$  are the densities of SI links, II links, and SS links that belong to every node, respectively.

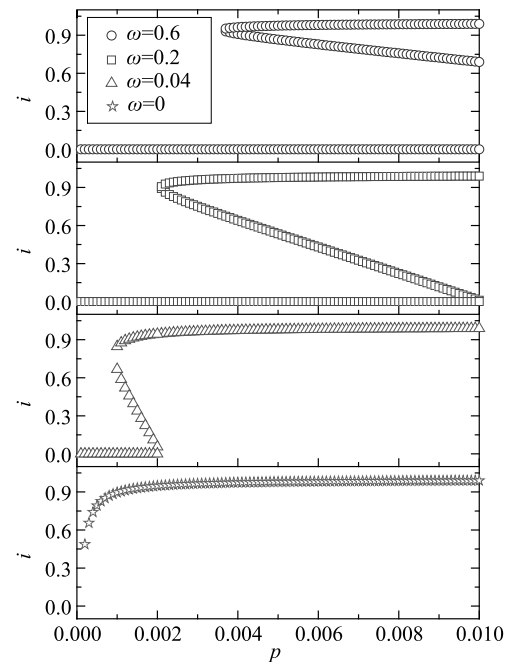
When  $\frac{di}{dt} = 0$ ,  $\frac{dl_{II}}{dt} = 0$ , and  $\frac{dl_{SS}}{dt} = 0$ , the state of epidemic systems reach equilibrium. Meanwhile, we get equations described as

$$\begin{cases} l_{SI} = \frac{\gamma i}{p}; \\ l_{II} = \frac{\gamma i^2 + pi(1-i)}{2p(1-i)}; \\ l_{SS} = \frac{(\gamma + \omega)(1-i)}{2p}. \end{cases} \quad (15)$$

In case of  $i = 0$  we get the disease-free equilibrium ( $i = l_{SI} = l_{II} = 0$ ); in the case where  $i \neq 0$  we get the equation

$$(\omega - p)i^2 + (p\langle K \rangle + p - 2\omega)i + r + \omega - p\langle K \rangle = 0, \quad (16)$$

where  $\langle K \rangle$  ( $\langle K \rangle = 2K/N$ ) is the average node degree in the network. To resolve the equation above, we discuss the conditions of existence of resolutions and depict the functional relationships between the infection rate  $p$  and the density of infected nodes under different rewiring rates  $\omega$  in Fig. 5. We observe bifurcation phenomena that are consistent with Gross's results.



**Fig. 5** Bifurcation diagram of the functional relationships between infection rate and the fraction of infected under different rewiring rates. ( $N = 10^5$ ,  $K = 10^6$ , and  $\gamma = 0.002$ )

Moreover, Gross et al. [95] also analyzed the functional relationships between the infection rate and the rewiring rate to get the regions of bistability, where either an endemic state or a disease-free steady state coexist.

Gross and Blasius provided a review of adaptive co-evolutionary networks [96]. Gross and Sayama represented the theory, models and applications of adaptive network models of epidemics [97]. The most recent work in epidemic spread in adaptive networks are discussed below.

Shaw and Schwartz considered an SIRS model in adaptive networks and obtain similar results to Gross's study [98]. They also investigated vaccination strategies in adaptive networks [99,100]. Lu et al. [101] elaborated on Gross's SIS model in adaptive networks and performed theoretical analy-



sis to find the phenomena of saddle-node bifurcation, trans-critical bifurcation, and Hopf bifurcation.

Most researchers focus on theoretical analysis to reveal the steady state of epidemic spread and dynamic features in adaptive networks. However, Marceau et al. [102] and Yang et al. [103] are concerned with the time evolution of diseases and underlying network topologies. Marceau et al. aggregated population into compartments according to not only people's health states, but also the health states of their neighbors.

Researchers usually studied epidemic spread in adaptive random networks. However, some others investigated epidemic spread in adaptive networks with different topologies [104–107]. Song et al. [104] studied epidemic spread in various adaptive networks, including adaptive random networks, adaptive nearest neighbor networks, adaptive small world networks, and adaptive scale free networks. They used cellular automata to study various rewiring strategies and the co-evolution of both epidemics and topologies. Yang et al. [103] investigated the dynamic evolution of community structure induced by the rewiring mechanism of adaptive networks, and studied control strategies of epidemic spread in adaptive networks with community structure. Jolad et al studied epidemic spread in preferred degree adaptive networks [105]. Wang et al investigated epidemic spread in multi-type networks consisting of a variety of nodes with adaptive rewiring [106].

Researchers introduced epidemic information as a feedback to control the adaptation of networks [107–110]. Segbroeck et al [108] deemed the state of neighbors as local information that caused the reshaping of contact networks. They studied SI, SIS, and SIR models in adaptive networks. Gross and Kevrekidis introduced the awareness of population to epidemics, and found the oscillations of both epidemics and topology of networks [109]. Zhang et al considered that individuals should reduce their contacts and activities with outside world in epidemic outbreaks, but not reconnect to others [110]. So in their adaptive network models, the topology of networks evolved not by rewiring links, but by breaking and recovering links. Zanette and Risau-Gusman also used a different rewiring rule in adaptive networks [111,112]. In their models, connections between susceptible individuals and infected individuals can be broken by either individuals, and then reconnected to a randomly chosen member of population.

### 3.4 Advantages and limitations of complex network models of epidemics

Complex network models of epidemics can integrate with

mean-field theory to build differential equation models that are known as spreading dynamics models in complex networks. We can use differential equation models to perform theoretical analysis of epidemic dynamics in complex networks. Compared to mathematical models of epidemics, complex network models have the advantage of representing heterogeneous population structure and interaction patterns among individuals, such as heterogeneous node degree and heterogeneous edge weight. Complex networks can be used to build individual-based models of epidemics. Then we can conduct numerical simulations to investigate the time evolution of epidemic spread. Compared to mathematical models of epidemics, complex network models can provide a more detailed representation of epidemic spread.

However, due to the complex spreading process of epidemics in human societies, complex network models are still inadequate to represent the heterogeneity of human behavior and interaction, and to capture more factors associated with the spread of epidemics, such as the daily activities, mobility, ages, and occupations of individuals. To amplify the ability of complex network models of epidemics, researchers have added more detailed features into networks. For example, human contact patterns are known to be highly dynamic and change at many time scales. In order to study epidemic spread in complex networks with more details of time, researchers extend the static network topology with temporal dimension. Recently, epidemic spread in temporal networks has become an increasingly hot research topic [113–115].

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## 4 Agent-based models of epidemics

In recent years, with the increasing understanding of macroscopic regularities of epidemic diffusion, desire to explore the complex evolutionary process of epidemic spread has grown. Epidemic models are required to represent detailed realities more accurately. Agent-based modeling is a promising computational approach that can provide a more detailed depiction of realities. This approach exhibits the advantage of realizing heterogeneity in individual attributes and behaviors, as well as incorporating the stochastic nature of epidemic spread. As a bottom-up approach, agent-based modeling emphasizes the representation of micro behavior and interaction of individuals, and resorts to the emergence of macro phenomena of epidemic spread. However, the higher granularity and resolution of agent-based models comes with the cost of data availability and computational complexity. Fortunately, increasing computational power, data availability, and devel-

opment of intelligent computational algorithms result in the increasing popularity of agent-based models in understanding the spread of epidemics [116–123].

#### 4.1 Large scale agent-based simulation systems of epidemics

Recently, many large scale agent-based simulation systems have been developed to investigate epidemic diffusion in communities or cities, such as MASON [116], GeoGraph [124], EpiSims [125], BioWar [126], and FluTE [127]. MASON is a set of Java-based agent-based simulation libraries. It supports the development of large scale agent-based simulation systems of epidemics. GeoGraph computational laboratory tools are designed to support controlled experiments for agent-based organizational and geographic simulations. Dibble et al. [124] developed a suite of tools in Geograph that can be used to explore the spatially explicit behavior of any SEIR epidemic model among heterogeneous spatially mobile agents. EpiSims is an epidemic simulation system that is developed based on an urban transportation simulation system (TranSims). In EpiSims, graph theory was applied to traffic networks that modeling human mobility patterns so as to analyze the pattern of infectious disease transmission. BioWar is an agent-based system of simulating epidemic outbreaks and biological attacks in cities. This system integrates a set of computational models of social networks, communication media, disease transmission, urban spatiality, population, weather, and district boundaries. FluTE is an individual-based model capable of simulating the spread of influenza across major metropolitan areas or the continental United States. FluTE builds population model and community structure according to census data. In each community, population is organized as a cluster of households in terms of family size distribution.

These large scale agent-based systems usually rely on the availability of demographic data and environment data. Meanwhile, GIS techniques are also used in these systems to visualize epidemic outbreaks in geographical landscapes. Large scale agents and high resolutions require a high computational power. Thus, intelligent algorithms and computing frameworks are developed to provide high computing performance for large-scale agent-based simulation systems of epidemics. For example, two parallel programming algorithms, EpiSimdemics [128] and EpiFast [129], were designed to advance the performance of EpiSims. Parker and Epstein developed a distributed platform for global-scale agent-based models of disease transmission [130].

We are also developing a large-scale agent-based simula-

tion system to study infectious disease transmission in Beijing city, this is illustrated in Fig. 6.



**Fig. 6** A large scale agent-based simulation of influenza epidemic transmission in Beijing city

We design the system on the basis of the ACP (Artificial societies, Computational experiments, and Parallel execution) approach [131–133]. We build an artificial society simulating Beijing city that integrates with census data (a population of 19 million individuals, 8 million households, 3 thousand schools, and 6 thousand hospitals) [134], traffic networks, and district boundaries. Using our systems, we conduct computational experiments to analyze the spread patterns of epidemics in Beijing city and evaluate the policies of disease control. To provide a high computing performance, we employ a mixed CPU and GPU computational architecture and use parallel algorithms to develop a computing engine [135,136]. In future work, we will connect the artificial society of Beijing city to a real data stream, which comes from disease detecting and warning systems, hospital records, and the Internet, etc. Unified simulation object models will be used as an interface to interchange data between real systems and artificial systems. Meanwhile, data mining and data driven approaches can be used to realize the co-evolution of both systems. The real data from real societies are applied to calibrate the parameters and models of artificial societies. The behaviors of artificial societies are used to support decision making on disease control.

#### 4.2 Agent contact patterns

Human contact patterns act as a force to drive the spread of epidemics. The precise representation of human contact patterns is crucial for agent-based models to cause reasonable macro phenomena of epidemic diffusion to emerge. To understand human contact patterns, researchers [137–152] col-

lected real data of human behaviors through social questionnaires, diaries, and wearable sensors, and then quantified human contact patterns. For example, Edmunds et al. [137] conducted a survey of a group of individuals to quantify contact patterns. The survey indicates that the number of contacts per individual per day can be approximated by a normal distribution whose mean and standard deviation are 16.8 and 8.5, respectively.

In agent-based models of epidemics, social networks are widely used to formulate agent contact patterns [84,120]. In many cases, researchers assume that the agent contact pattern is a full contact network, where each agent contact with all of its neighbors in each time step. However, others think human contact behaviors are heterogeneous, stochastic, and repetitive. They define contact probabilities between individuals to represent agent contact patterns. In EpiSims, transportation networks are employed to describe agent contact graphs [125]. In BioWar, social networks are applied to represent casual and chance contacts between a pair of agents who are randomly selected [126]. Moon et al. [153] used social networks to formulate interactions between terrorists. They defined interaction probabilities among terrorists according to different factors, including relative similarity (*RS*), relative expertise (*RE*), social distance (*SD*), and spatial proximity (*SP*) of terrorists, described as

$$P_{ij}^{Interaction} = \omega_1 RS_{ij} + \omega_2 RE_{ij} + \omega_3 SD_{ij} + \omega_4 SP_{ij}, \quad (17)$$

where  $\omega_1$ ,  $\omega_2$ ,  $\omega_3$ , and  $\omega_4$  are the weights of different factors. Moreover, weighted networks have been increasingly used to represent heterogeneous contact patterns between agents. Agent contact probabilities are usually defined as a function of edge weights [84,101,131]:

$$p_{ij} = \frac{w_{ij}}{\sum_{k \in N'_i(t)} w_{ik}}, \quad (18)$$

where  $p_{ij}$  is the probability that agent  $i$  contacts agent  $j$ ,  $w_{ij}$  is the weight of the edge between agent  $i$  and agent  $j$ , and  $N'_i(t)$  is the set of neighbors that agent  $i$  contact with at time  $t$ . Due to spatial constraints, temporal constraints, and non-pharmaceutical interventions,  $N'_i(t)$  is a dynamic and changing set over time.

To represent detailed contact patterns between agents, the spatial-temporal features of human contact behaviors are taken into account, such as temporal networks [113–115] and location-specific contact patterns [154]. In addition, this demonstrates that human activities are non-Poisson in nature [155]. The time heterogeneity of human activity dynamics is described by a power law waiting time distribution

( $p(\tau) = \tau^{-\alpha}$ ). This power law distribution is also employed to simulate the interactions of individuals in social systems [156,157]. In our previous work, we defined infection probability due to a single contact between a susceptible agent and an infected neighbor as a function of contact duration that is described as a power law distribution with the exponent  $\alpha = 1.5$ .

### 4.3 Agent mobility patterns

The pattern of human mobility is a determining factor of epidemic diffusion [158–162]. The random walk model [163] is often used to represent human mobility patterns. This model is a mathematical formulation of a path that consists of a succession of random steps. For example, an individual moves within a finite space, where the individual can move to each position with the same probability. Levy flight [164] is a random walk model that defines human movement distances as a set of independent identical distributed random variables:  $X_1, X_2, \dots, X_N$ . The probability density function of the sum of these random variables is in the same form as that of these random variables. Recently, many studies have indicated that human mobility distance is well approximated to a truncated power law distribution [165,166]. The Levy flight model with a power law distribution of mobility distances is a promising approach to exactly represent human mobility patterns. In large scale agent-based systems of simulating epidemic spread, agent mobility behaviors are usually abstracted as random walks. In BioWar, movement of agents between different locations are described as discrete flight events. Agents are randomly moved to appropriate locations at the beginning of each time tick.

Gravity models [167–169] are also used to describe and forecast human mobility patterns in agent-based models of epidemics

$$C_{ij} = \theta \frac{P_i^{\tau_1} P_j^{\tau_2}}{D_{ij}^\rho}, \quad (19)$$

where  $C_{ij}$  is the population interaction coefficient between location  $i$  and location  $j$ .  $P_i$  and  $P_j$  are the population size of location  $i$  and location  $j$ .  $D_{ij}$  is the distance between location  $i$  and location  $j$ .  $\rho$ ,  $\tau_1$ , and  $\tau_2$  are estimated parameters. Moreover, spatial networks are used to represent human mobility patterns, such as traffic networks [170] and airline networks [171].

We think that a weighted two mode network that integrates spatial networks and contact networks is a promising approach to represent the spatial-temporal contact patterns of agents. Nodes in weighted two mode networks are sepa-

rated into two types: agent nodes and location nodes. Edges in weighted two mode networks connect agent nodes with location nodes, and also connect agent nodes with agent nodes. The weights of edges between agent nodes and location nodes are used to define the probability of agent mobility in locations. The weights of edges between agent nodes are used to define contact probabilities between agents who are in the same location. We can design the activities of agents as discrete events in a schedule, and use activity-based models to drive agent mobility behaviors and contact behaviors.

#### 4.4 Advantages and limitations of agent-based models of epidemics

In agent-based models of epidemics, we can use complex networks to represent agent mobility patterns and contact patterns, and apply mathematical methods to formulate agent behaviors, such as stochastic process and probability models. Agent-based models of epidemics can not only employ the advantages of mathematical models and complex network models, but also exhibit the advantages of representing more detailed realities and more factors associated with epidemic spread, such as the affect and sociality of individuals [172,173].

However, agent-based models require high computational power and data availability. Though growing computing power and data availability result in the increasing popularity of agent-based models of epidemics, data related to human behavior and psychology is sometimes difficult to collect. Moreover, agent-based models and their algorithms may be too complex to be formalized.

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## 5 Future research directions in epidemic modeling

### 5.1 Spatial-temporal spreading patterns of epidemics

With the development of human societies, economics, and transportation, people are more closely related to each other. Individual movements and interactions also become more frequent and convenient. This advance makes pandemic or global outbreaks of epidemics more likely to take place. Spatial-temporal spreading patterns of epidemics and the assessment of corresponding intervention policies becomes an important research direction.

To discover the spatial-temporal spreading patterns of epidemics, researchers usually resort to empirical data analysis [165,166]. Epidemic modeling is also a helpful tool for understanding the spatial-temporal spreading patterns of epi-

demics and evaluating disease control policies. The meta-population model is a widely used measure used to investigate the spatial-temporal transmission of infectious diseases that combines compartmental models with spatial networks [174–177]. Like compartmental models, meta-population models assume mixed subpopulations that are defined in terms of geographical regions such as cities, districts, villages, and schools. Within each subpopulation, differential equations are used to describe epidemic dynamics. Furthermore, meta-population models also incorporate spatial networks to describe movements and interactions among subpopulations. Meta-population models are better than compartmental models to describe epidemic diffusion over spatially extended regions. However, the assumption of homogeneous and well-mixed subpopulations still limits the capability of meta-population models to represent the diffusion of epidemics in detail.

In addition, large scale agent-based simulation systems and large scale spatial networks are used to investigate the spatial-temporal spreading patterns of epidemics [39,124–127]. Service-based geographical information systems are also used for monitoring and management of spatial epidemic outbreaks [178,179].

### 5.2 Heterogeneity of epidemic spread

Mathematical models assume homogeneous and well-mixed population, and simplify epidemic spread process. Only a few variables parameterized with average quantities or mean values are used to formulate epidemic diffusion across a population. These assumptions and simplifications endow mathematical models with the advantage of performing theoretical analysis of macroscopic regularities of epidemic diffusion. However, with the increasing understanding of macroscopic regularities, people concentrate on the complex process of epidemic spread. They pay attention to micro modeling and simulation at individual level. Social heterogeneities, individual variants, and stochastic nature are crucial for micro epidemic models [180–182]. Heterogeneity of epidemic spread process becomes a key research direction, such as the heterogeneous time scales of epidemic progresses, the heterogeneous infectivity of infectious individuals, the heterogeneous immunity of susceptible individuals, heterogeneous social networks, and the heterogeneous contact patterns of individuals.

Super spreading events raised by the SARS epidemic in 2003 raise many concerns on the heterogeneous infectivity of infectious individuals [33,38,84,183–186]. To represent

the heterogeneous infectivity of SARS epidemic spreaders, Mkhathshwa et al. [33] divided infectious individuals into super spreaders and regular spreaders, and set a higher infection rate to super spreaders in compartmental models. To predict super spreading events, Li et al. [38] used probability models to describe heterogeneous time scales of SARS epidemic progress in compartmental models. We also proposed heterogeneous and stochastic agent-based models to explore super spreading events and analyze the characteristics of infectious diseases' super spreaders [84]. We used random variables subject to certain distributions coming from epidemiological statistics and human dynamics to represent the heterogeneity of the epidemic spread process.

Many researchers have studied epidemic spread in heterogeneous networks [187–189]. Network structures realize the heterogeneity in connectivity of individuals. Weighted networks go forward to describe the heterogeneity in interaction strength between individuals.

Though agent-based models have the advantage of representing the heterogeneity in individual attributes and behaviors, the heterogeneity of the epidemic spreading process is not well described due to data unavailability, especially data related to human behavior and psychology.

### 5.3 Interplay between human dynamics and epidemic dynamics

Interplay between human dynamics and epidemic dynamics is twofold. Firstly, pathogens invade human bodies as hosts and carriers. Human behaviors act as a force to drive the spread of epidemics. Secondly, epidemic outbreaks and infection risk may result in human behavioral change, such as wearing a facemask, avoiding crowds, improving personal hygiene, and taking antiviral drugs. Human protective behaviors react to the spread of epidemics so as to mitigate epidemic outbreaks. So, the feedback loop between human dynamics and epidemic dynamics makes them have an impact on each other.

However, most previous epidemic models only consider the impact of human dynamics on epidemic spread. For instance, there is no feedback loop between the onset of symptoms and agent behavioral change in EpiSims [125]. Recently, human behavioral change have been deemed an important factor in epidemic modeling [190,191]. Researchers have extended existing epidemic models to represent human behavioral change. They usually reduce infection probability or infection rate through mathematical models to reflect the impact of human behavioral change on epidemic dynamics.

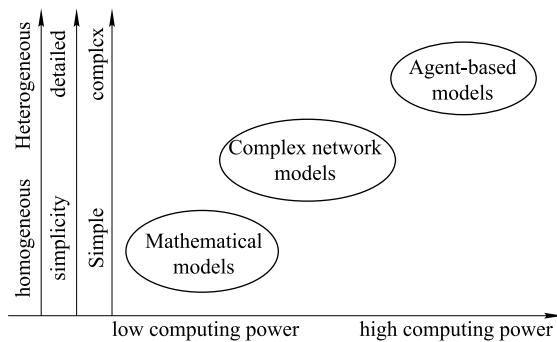
Researchers have also employed adaptive networks to study the interplay between human behavioral change and epidemic dynamics [95–112]. In agent-based models of epidemics, researchers study human behavioral change from three major perspectives discussed as follows.

- **Economic epidemiology:** researchers usually use utility functions to represent individual behavior decision in epidemic outbreaks [37]. The Bellman equation [37,192–194] is a widely used utility function of representing individual behavior decision. The Bellman equation considers the changes of individual health states due to the risky behavior, and defines the benefit of escaping from infection and the benefit of being infected. In addition, researchers also use game theory to study human behavioral change in epidemic outbreaks [195–198].
- **Psychological epidemiology:** researchers study human behavioral changes in epidemic outbreaks at the perspective of psychology. They proposed many psychological models, such as Health Belief Model [199], Theory of Reasoned Action [200], Social Cognitive Model [201], Protection Motivation Theory [202]. The Health Belief Model (HBM) is widely used to describe individual psychology and behavior decision in epidemic outbreaks [119,203]. HBM assumes that an agent health behavior is determined by agent beliefs and perceptions, including perceived severity, perceived susceptibility, perceived benefits, and perceived barriers. HBM only represents a framework of individual behavior decision due to individual psychology. To quantify agent beliefs and perceptions, logistic regression is integrated with HBM to build mathematical models of individual behavior and decisions [204–206]. Moreover, to estimate probability ratios in a logistic regression model, Durham et al. [205] conducted a behavior survey in Allegheny County, Pennsylvania, USA, to collect real data during the 2009-2010 H1N1 influenza pandemic.
- **Epidemiological information:** epidemic news is deemed as a feedback signal to control agent behavioral change. Epidemic information diffusion can change epidemic dynamics, such as oscillations and periodic outbreaks of epidemics [207–212]. Researchers have also studied a dual diffusion process of epidemic news and epidemics, human behavioral change and epidemics, or awareness and epidemics [2,213,214]. At the perspective of control mechanisms of multi-agent sys-

tems [215], we divide epidemic information into two categories: centralized epidemic information and local epidemic information. Centralized epidemic information is news published by the government, center of disease control and prevention (CDC) and social media [216] that reports epidemic prevalence, epidemic incidence, and infection risk, etc. Local epidemic information is messages that transmit across agents' personal networks, such as illness related words and advice among friends.

## 6 Conclusions

In this paper, we conduct a comprehensive review of epidemic models so as to provide an insight into the literature of epidemic modeling and simulation. We introduce major epidemic models in three directions, including mathematical models, complex network models, and agent-based models. We discuss the principles, applications, advantages, and limitations of these models. To address what type of models should be used in research, we perform comparison between mathematical models, complex network models, and agent-based models in Fig. 7.



**Fig. 7** Comparison of mathematical models, complex network models, and agent-based modes of epidemics

Mathematical models have the advantage of performing theoretical analysis of macroscopic regularities of epidemic diffusion. Moreover, mathematical models of epidemics are easier to understand and require low computing power. However, mathematical models of epidemics are limited in describing realities in detail. Agent-based models have the advantage of capturing heterogeneity in individual attributes and behaviors, as well as the process of epidemic spread. However, agent-based models of epidemics require data availability, complex algorithms, and high computing power. Complex network models of epidemics are located somewhere between mathematical models and agent-based mod-

els. Complex networks can not only be parsed using mean-field theory to build differential equations, but also be used to describe human contact patterns and build individual-based models. More comparison between mathematical models, complex network models, and agent-based models of epidemics can be found in [2,217,218].

Moreover, we propose some future research directions in epidemic modeling, including the spatial-temporal spreading patterns of epidemics, the heterogeneity of epidemic spread process, and the interplay between human dynamics and epidemic dynamics. Though researchers are already focused in these directions and have performed some studies, further work is needed in these directions in future. We expect these directions can guide future research in epidemic modeling. We hope the reader finds the key references provided in this paper helpful for future research and that our review has provided a better holistic comprehension of the topic.

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## References

1. Grassly N C, Fraser C. Mathematical models of infectious disease transmission. *Nature*, 2008, 6(6): 477–487
2. Epstein J M, Parker J, Cummings D, Hammond A. Coupled contagion dynamics of fear and disease: mathematical and computational explorations. *PLoS ONE*, 2008, 3(12): e3955
3. Ajelli M, Gonçalves B, Balcan D, Colizza V, Hu H, Ramasco J J, Merler S, Vespignani A. Comparing large-scale computational approaches to epidemic modeling: agent-based versus structure metapopulation models. *BMC Infectious Diseases*, 2010, 10(190): 1–13
4. Brown S T, Tai J H Y, Bailey R R, Cooley P C, Wheaton W D, Potter M A, Voorhees R E, LeJeune M, Grefenstette J J, Burke D S, McGlone S M, Lee B Y. Would school closure for the 2009 H1N1 influenza epidemic have been worth the cost: a computational simulation of Pennsylvania. *BMC Public Health*, 2011, 11(353): 1–11
5. Nsoesie E O, Beckman R J, Shashaani S, Nagaraj K S, Marathe M V. A simulation optimization approach to epidemic forecasting. *PLoS ONE*, 2013, 8(6): e67164
6. Burke D S, Epstein J M, Cummings D A, Parker J I, Cline K C, Singa R M, Chakravarty S. Individual-based computational modeling of smallpox epidemic control strategies. *Academic Emergency Medicine*, 2006, 13(11): 1142–1149
7. Kretzschmar M, Wallinga J. Mathematical models in infectious Disease. In: Krämer A, Kretzschmar M, Krickeberg K, eds. *Modern infectious disease epidemiology, Statistic for biology and health*. Springer Science+Business Media, LLC, 2010: 209–221
8. Fournié G, Walker P, Porphyre T, Métras R, Pfeiffer D. Health and animal agriculture in developing countries, natural resource manage-

- ment and policy. Food and Agriculture Organization of the United Nations, 2012: 183–205
9. Abbey H. An examination of the Reed-Frost theory of epidemics. *Human Biology*, 1952, 24(3): 201–233
  10. Maia J O C DE. Some mathematical developments on the epidemic theory formulated by Reed and Frost. *Human Biology*, 1952, 24(3): 167–200
  11. Kermack W O and McKendrick A G. A contribution to the mathematical theory of epidemics. *Proceedings of the Royal Society of London (Series A)*, 1927, 115(772): 700–721
  12. Siettos C I, Russo L. Mathematical modeling of infectious disease dynamics. *Virulence*, 2013, 4(4): 295–306
  13. Dimitrov N B, Meyers L A. Mathematical approaches to infectious disease prediction and control. J. J. Hasenbein, ed. *INFORMS Tutorials in Operations Research*. 2010, 1–25
  14. Keeling M J, Danon L. Mathematical modeling of infectious disease. *British Medical Bulletin*, 2009, 92(1): 33–42
  15. Garnett G P, Cousens S, Hallett T B, Steketee R, Walker N. Mathematical models in the evaluation of health programmes. *Lancet*, 2011, 378(9790): 515–525
  16. Britton T. Stochastic epidemic models: a survey. *Mathematical Biosciences*, 2010, 225(1): 24–35
  17. Keeling M J, Rohani P. *Modeling Infectious Diseases in Humans and Animals*. Princeton: Princeton University Press, 2007
  18. O'Neill P D. A tutorial introduction to Bayesian inference for stochastic epidemic models using Markov chain Monte Carlo methods. *Mathematical Bioscience*, 2002, 180(1–2): 103–114
  19. Korostil I A, Peters G W, Cornebise J, Regan D G. Adaptive Markov Chain Monte Carlo forward projection for statistical analysis in epidemic modelling of human papillomavirus. *Statistics in Medicine*, 2013, 32(11): 1917–1953
  20. Rorres C, Pelletier S T K, Smith G. Stochastic modeling of animal epidemics using data collected over three different spatial scales. *Epidemics*, 2011, 3(2): 61–70
  21. Forgoston E, Billings L, Schwartz I B. Accurate noise projection for reduced stochastic epidemic models. *Chaos*, 2009, 19(4): 043110
  22. Schwartz I B, Billings L, Bollt E M. Dynamical epidemic suppression using stochastic prediction and control. *Physical Review E*, 2005, 70(4): 046220
  23. Schwartz I B, Billings L, Dykman M, Landsman A. Predicting extinction rates in stochastic epidemic models. *Journal of Statistical Mechanics: Theory and Experiment*, 2009, 2009(1): 01005
  24. Esegbir A, Kissami A, Maroufy H E, Ziad T. A branching process approximation of the final size of multitype collective Reed-Frost model. *Journal of Statistics Application & Probability*, 2013, 2(1): 47–59
  25. Neal P. Multitype randomized Reed-Frost epidemics and epidemics upon random graphs. *The Annals of Applied Probability*, 2006, 16(3): 1166–1189
  26. O'Neill P D. Perfect simulation for Reed-Frost epidemic models. *Statistics and Computing*, 2003, 13(1): 37–44
  27. Jacquez J A. A note on chain-binomial models of epidemic spread: what is wrong with the Reed-Frost formulation? *Mathematical Bioscience*, 1987, 87(1): 73–82
  28. Kendall D G. Deterministic and stochastic epidemics in closed population. In: *Proceedings of the Berkeley Symposium on Mathematical Statistics and Probability*. 1956: 149–165
  29. Allen L J S, Burgin A M. Comparison of deterministic and stochastic SIS and SIR models in discrete time. *Mathematical Bioscience*, 2000, 163(1): 1–33
  30. Billings L, Spears W M, Schwartz I B. A unified prediction of computer virus spread in connected networks. *Physics Letters A*, 2002, 297(3): 261–266
  31. West R W, Thompson J R. Models for the simple epidemic. *Mathematical Bioscience*, 1997, 141(1): 29–39
  32. Kwok K O, Leung G M, Lam W Y, Riley S. Using models to identify routes of nosocomial infection: a large hospital outbreak of SARS in Hong Kong. *Proceedings of the Royal Society B*, 2007, 274(1610): 611–617
  33. Mkhathshwa T, Mummert A. Modeling super-spreading events for infectious disease: case study SARS. *IAENG International Journal of Applied Mathematics*, 2011, 41(2): 82
  34. Chowell G, Viboud C, Wang X, Bertozzi S M, Miler M A. Adaptive vaccination strategies to mitigate pandemic influenza: Mexico as a case study. *PLoS ONE*, 2009, 4(12): e8164.
  35. Zhang J, Lou J, Ma Z, Wu J. A compartmental model for the analysis of SARS transmission patterns and outbreak control measures in China. *Applied Mathematics and Computation*, 2005, 162(2): 909–924
  36. Ohkusa Y, Taniguchi K, Okubo I. Prediction of smallpox outbreak and evaluation of control-measure policy in Japan, using a mathematical model. *Journal of Infection and Chemotherapy*, 2005, 11(2): 71–80
  37. Fenichel E P, Castillo-Chavez C, Ceddia M G, Chowell G, Parra P A G, Hickling G J, Holloway G, Horan R, Morin B, Perrings C, Springborn M, Velazquez L, Villalobos C. Adaptive human behavior in epidemiological models. *Proceedings of National Academy of Sciences USA*, 2011, 108(15): 6306–6311
  38. Li Y, Yu I T, Xu P, Lee J H W, Wong T W, Ooi P L, Sleight A C. Predicting Super Spreading Events during the 2003 Severe Acute Respiratory Syndrome Epidemics in Hong Kong and Singapore. *American Journal of Epidemiology*, 2004, 160(8): 719–728
  39. Eubank S, Guclu H, Kumar A, Marathe M V, Srinivasan A, Toroczkai Z, Wang N. Modeling disease outbreaks in realistic urban social networks. *Nature*, 2004, 429(6988): 180–184
  40. Kuperman M N. Invited review: epidemics on social networks. *Paper in Physics*, 2013, 5: 050003.
  41. Leskovec J, Krause A, Guestrin C, Faloutsos C, VanBriesen J, Glance N. Cost-effective outbreak detection in networks. In: *Proceedings of the 13th ACM SIGKDD International conference on Knowledge discovery and data mining*. 2007: 420–429
  42. Brouqui P, Puro V, Fusco F M, Bannister B, Schilling S, Follin P, Gottschalk R, Hemmer R, Maltezuou H C, Ott K, Peleman R, Perronne C, Sheehan C, Siikamäki H, Skinhoj P, Ippolito G, EUNID Working Group. Infection control in the management of highly pathogenic infectious disease: consensus of the European network of infectious disease. *Lancet Infect Diseases*, 2009, 9(5): 301–311
  43. Cui P, Jin S, Yu L, Wang F, Zhu W, Yang S. Cascading outbreak prediction in networks: a data-driven approach. In: *Proceedings of the*

- 19th ACM SIGKDD International Conference on Knowledge Discovery and Data Mining. 2013: 901–909
44. Prakash B A, Vrekeen J, Faloutsos C. Spotting culprits in epidemics: how many and which ones? In: Proceedings of the 12th IEEE International Conference on Data Mining. 2012: 11–20
  45. Pasto-Satorras R, Vespignani A. Epidemic spreading in scale-free networks. *Physical Review Letters*, 2001, 86(4): 3200–3202
  46. Pasto-Satorras R, Vespignani A. Epidemic dynamics and endemic states in complex networks. *Physical Review E*, 2001, 63(6): 066117
  47. Deijfen M. Epidemics and vaccination on weighted graphs. *Mathematical Biosciences*, 2011, 232(1): 57–65
  48. Britton T, Deijfen M, and Liljeros F. A weighted configuration model and inhomogeneous epidemics. *Journal of Statistical Physics*, 2011, 145(5): 1368
  49. Bollobás B. *Random Graphs*. New York: Academic Press, 2001
  50. Watts D J, Strogatz S H. Collective dynamics of small-world networks. *Nature*, 1998, 393(6684): 440–442
  51. Barabási A L, Albert R. Emergence of scaling in random networks. *Science*, 1999, 286(543): 509–512
  52. Pasto-Satorras R, Vespignani A. Epidemic dynamics in finite size scale-free networks. *Physical Review E*, 2002, 65(3): 035108
  53. Zhou T, Liu J G, Bai W J, Chen G, Wang B H. Behaviors of susceptible-infected epidemics on scale-free networks with identical infectivity. *Physical Review E*, 2006, 74(5): 056109
  54. Liu J, Zhang T. Epidemic spreading of an SEIR model in scale-free networks. *Communications in Nonlinear Science and Numerical Simulation*, 2011, 16: 3375–3384
  55. Zhang H, Fu X. Spreading of epidemics on scale-free networks with nonlinear infectivity. *Nonlinear Analysis*, 2009, 70(9): 3273–3278
  56. Huang C Y, Sun C T, Hsieh J L, Lin H. Simulating SARS: small-world epidemiological modeling and public health policy assessments. *Journal of Artificial Societies and Social Simulation*, 2004, 7(7). <http://jasss.soc.surrey.ac.uk/7/4/2.html>
  57. Pastor-Satorras R, Vespignani A. Immunization of complex networks. *Physical Review E*, 2001, 65(3): 036134
  58. Madar N, Kalisky T, Cohen R, Ben-Avraham D, Havlin S. Immunization and epidemic dynamics in complex networks. *European Physical Journal B*, 2004, 38(2): 269–276
  59. Li X, Chen G, Li C G. Stability and bifurcation of disease spreading in complex networks. *International Journal of Systems Science*, 2004, 35(9): 527–536
  60. Hayashi Y, Minoura M, Matsukubo J. Oscillatory epidemic prevalence in growing scale-free networks. *Physical Review E*, 2004, 69(1): 016112
  61. Palla G, Derényi I, Farkas I, Vicsek T. Uncovering the overlapping community structure of complex networks in nature and society. *Nature*, 2005, 435: 814–818
  62. Chen J, Zhang H, Guan Z H, Li T. Epidemic spreading on networks with overlapping community structure. *Physica A*, 2012, 391(4): 1848–1854
  63. Griffin R H, Nunn C L. Community structure and the spread of infectious disease in primate social networks. *Evolutionary Ecology*, 2011, 26(7): 779–800
  64. Cauchemez S, Bhattarai A, Marchbanks T L, Fagan R P, Ostroff S, Ferguson N M, Swerdlow D. Role of social networks in shaping disease transmission during a community outbreak of 2009 H1N1 pandemic influenza. *Proceedings of National Academy of Sciences USA*, 2011, 108(7): 2825–2830
  65. Wang Y, Zeng D, Cao Z, Wang Y, Song H, Zheng X. The impact of community structure of social contact network on epidemic outbreak and effectiveness of non-pharmaceutical interventions. *Lecture Notes in Computer Science*, 2011, 6749: 108–120
  66. Barrat A, Barthélemy M, Pastor-Satorras R Vespignani A. The architecture of complex weighted networks. *Proceedings of National Academy of Sciences USA*, 2004, 101(11): 3747–3752
  67. Bagler G. Analysis of the airport network of India as a complex weighted network. *Physica A*, 2008, 387(12): 2972–2980
  68. Li M, Fan Y, Chen J, Gao L, Di Z, Wu J. Weighted networks of scientific communication: the measurement and topological role of weight. *Physica A*, 2005, 350(2–4): 643–656
  69. Onnela J P, Saramäki J, Hyvönen J, Szabo G, Menezes M A D, Kaski K, Barabasi A L, Kertesz J. Analysis of a large-scale weighted network of one-to-one human communication. *New Journal of Physics*, 2007, 9(6): 179
  70. Zhang B, Horvath S. A general framework for weighted gene co-expression network analysis. *Statistical Applications in Genetics and Molecular Biology*, 2005, 4: 17
  71. Li M, Wang J X, Wang H, Pan Y. Identification of essential proteins from weighted protein-protein interaction networks. *Journal of Bioinformatics and Computational Biology*, 2013, 11(3): 1341002
  72. Chua H N, Sung W K, Wong L. Exploiting indirect neighbors and topological weight to predict protein function from protein-protein interactions. *Bioinformatics*, 2006, 22(13): 1623–1630
  73. Dijk D V, Ertaylan G, Boucher C A B, Sloot P M A. Identifying potential survival strategies of HIV-1 through virus-host protein interaction networks. *BMC Systems Biology*, 2010, 4: 96
  74. Duijn P A C, Kashirin V, Sloot P M A. The relative ineffectiveness of criminal network disruption. *Nature Scientific Reports*, 2014, 4: 4238
  75. Latora V, Marchiori M. Economic small-world behavior in weighted networks. *The European Physical Journal B*, 2003, 32(2): 249–263
  76. Harrison F, Sciberras J, James R. Strength of social tie predicts cooperative investment in a human social network. *PLoS ONE*, 2011, 6(3): e18338
  77. Fagiolo G, Reyes J, Schiavo S. World-trade web: topological properties, dynamics, and evolution. *Physical Review E*, 2009, 79: 036115
  78. Yan G, Zhou T, Wang J, Fu Z Q, Wang B H. Epidemic spread in weighted scale-free networks. *Chinese Physics Letters*. 2005, 22(2), 510–513
  79. Barrat A, Barthélemy M, Vespignani A. Weighted evolving networks: coupling topology and weight dynamics. *Physical Review Letters*, 2004, 92(22): 228701
  80. Chu X, Guan J, Zhang Z, Zhou S. Epidemic spreading in weighted scale-free networks with community structure. *Journal of Statistical Mechanics: Theory and Experiment*, 2009, 2009(7): 07043
  81. Chu X, Zhang Z, Guan J, Zhou S. Epidemic spreading with nonlinear infectivity in weighted scale-free networks. *Physical A*, 2011, 390(3): 471–481
  82. Eames K T D, Read J M, Edmunds W J. Epidemic prediction and



- control in weighted networks. *Epidemics*, 2009, 1(1): 70–76
83. Fournié G, Guitian J, Desvaux S, Cuong V C, Dung D H, Pfeiffer D U, Mangtani P, Ghani A C. Interventions for avian influenza A (H5N1) risk management in live bird market networks. *Proceedings of National Academy of Sciences USA*, 2013, 110(22): 8751–8752
  84. Duan W, Cao Z, Cui K, Zheng X, Qiu X. Heterogeneous and stochastic agent based models for analyzing infectious diseases' super spreaders. *IEEE Intelligent Systems*, 2013, 28(4): 18–25
  85. Yang Z, Zhou T. Epidemic spreading in weighted networks: an edge-based mean-field solution. *Physical Review E*, 2012, 85(5): 056106
  86. Li R Q, Tang M, Hui P M. Epidemic spreading on multi-relational networks. *Acta Physica Sinica*, 2013, 62(16): 168903
  87. Kamp C, Moslonka-Lefebvre M, Alizon S. Epidemic spread on weighted networks. *PLoS Computational Biology*, 2013, 9(12): e1003352
  88. Sun Y, Liu C, Zhang C X, Zhang Z K. Epidemic spreading on weighted complex networks. *Physics Letters A*, 2014, 378(7–8): 635–640
  89. Cui A X, Yang Z, Zhou T. Strong ties promote the epidemic prevalence in susceptible-infected-susceptible spreading dynamics. 2013, arXiv:1311.5932v1
  90. Zhu G, Chen G, Xu X J, Fu X. Epidemic spreading on contact networks with adaptive weights. *Journal of Theoretical Biology*, 2013, 317: 133–139
  91. Cui A X, Yang Z, Zhou T. Roles of ties in spreading. Cornell University Library, 2012, arXiv: 1204.0100v1
  92. Karsai M, Juhász R, Iglói F. Nonequilibrium phase transitions and finite-size scaling in weighted scale-free networks. *Physical Review E*, 2006, 73: 036116
  93. Yang R, Zhou T, Xie Y B, Lai Y C, Wang B H. Optimal contact process on complex networks. *Physical Review E*, 2008, 78: 066109
  94. Wu Z X, Peng G, Wang W X, Chan S, Wong E W M. Cascading failure spreading on weighted heterogeneous networks. *Journal of Statistical Mechanics: Theory and Experiment*, 2008, 2008: P05013
  95. Gross T, D'Lima C J D, Blasius B. Epidemic dynamics on adaptive network. *Physical Review Letters*, 2006, 96(20): 208701
  96. Gross T, Blasius B. Adaptive coevolutionary networks: a review. *Journal of The Royal Society Interface*, 2008, 5(20): 259–271
  97. Gross T, Sayama H. *Adaptive Networks: Theory, Models and Applications*. Berlin: Springer-Verlag, 2009
  98. Shaw L B, Schwartz I B. Fluctuating epidemics on adaptive networks. *Physical Review E*, 2008, 77(6): 066101
  99. Shaw L B, Schwartz I B. Enhanced vaccine control of epidemics in adaptive networks. *Physical Review E*, 2010, 81(4): 046120
  100. Schwartz I B, Shaw L B. Rewiring for adaptation. *Physics*, 2010, 3(17): 1–6
  101. Lu Y L, Jiang G P, Song Y R. Stability and bifurcation of epidemic spreading on adaptive network. *Acta Physica Sinica*, 2013, 62(13): 130202
  102. Marceau V, Noël P A, Hébert-Dufresne L, Allard A, Dubé L J. Adaptive networks: coevolution of disease and topology. *Physical Review E*, 2010, 82(3): 036116
  103. Yang H, Tang M, Zhang H F. Efficient community-based control strategies in adaptive networks. *New Journal of Physics*, 2012, 14(12): 123017
  104. Song Y R, Jiang G P, Xu J G. An epidemic spreading model in adaptive networks based on cellular automata. *Acta Physica Sinica*, 2011, 60(12): 120509
  105. Jolad S, Liu W, Schmittmann B, Zia R K P. Epidemic spreading on preferred degree adaptive networks. *PLoS ONE*, 2012, 7(11): e48686
  106. Wang B, Cao L, Suzuki H, Aihara K. Epidemic spread in adaptive networks with multitype agents. *Journal of Physics A: Mathematical and Theoretical*, 2011, 44(3): 035101
  107. Demirel G, Gross T. Absence of epidemic thresholds in a growing adaptive network. 2012, arXiv: 1209.2541
  108. Segbroek S V, Santos F C, Pacheco J M. Adaptive contact networks change effective disease infectiousness and dynamics. *PLoS Computational Biology*, 2010, 6(8): e1000895
  109. Gross T, Kevrekidis I G. Robust oscillations in SIS epidemics on adaptive networks: coarse graining by automated moment closure. *Europhysics Letters*, 2008, 82(3): 38004
  110. Zhang H, Small M, Fu X, Sun G, Wang B. Modeling the influence of information on the coevolution of contact networks and the dynamics of infectious diseases. *Physics D*, 2012, 241(18): 1512–1517
  111. Risau-Gusman S, Zanette D H. Contact switching as a control strategy for epidemic outbreaks. *Journal of Theoretical Biology*, 2009, 257(1): 52–60
  112. Zanette D H, Risau-Gusman S. Infection spreading in a population with evolving contacts. *Journal of Biological Physics*, 2008, 34(1–2): 135–148
  113. Masuda N, Klemm K, Eguíluz V M. Temporal networks: slowing down diffusion by long lasting interactions. *Physical Review Letters*, 2013, 111: 188701
  114. Lee S, Rocha L E C, Liljeros F, Holme P. Exploiting temporal network structures of human interaction to effectively immunize populations. *PLoS ONE*, 2012, 7(5): e36439
  115. Holme P. Epidemiologically optimal static networks from temporal network data. *PLoS Computational Biology*, 2013, 9(7): e1003142
  116. Dunham J B. An agent-based spatially explicit epidemiological model in MASON. *Journal of Artificial Societies and Social Simulation*, 2005, 9(1). <http://jasss.sos.surrey.ac.uk/9/1/3.html>
  117. Jacintho L F O, Batista A F M, Ruas T L, Marietto M G B, Silva F A. An agent-based model for the spread of the Dengue Fever: a swarm platform simulation approach. In: *Proceedings of Spring Simulation Multiconference*. 2010: 1–8
  118. Roche B, Drake J M, Rohani P. An agent-based model to study the epidemiological and evolutionary dynamics of influenza viruses. *BMC Bioinformatics*, 2011, 12(87): 1–10
  119. Dion E, Vanschalkwyk L, Lambin E F. The landscape epidemiology of foot-and-mouth disease in South Africa: a spatially explicit multi-agent simulation. *Ecological Modelling*, 2011, 222(13): 2059–2027
  120. Mei S, Sloot P M A, Quax R, Zhu Y, Wang W. Complex agent networks explaining the HIV epidemic among homosexual men in Amsterdam. *Mathematics and Computers in Simulation*, 2010, 80(5): 1018–1030
  121. Yang Y, Atkinson P M, Ettema D. Analysis of CDC social control measures using an agent-based simulation of an influenza epidemic in a city. *BMC Infectious Disease*, 2011, 11(199): 1–10

122. Duan W, Cao Z, Ge Y, Qiu X. Modeling and simulation for the spread of H1N1 influenza in school using artificial societies. In: Proceedings of the Pacific Asia Workshop on Intelligence and Security Informatics. 2011, 121–129
123. Liu T, Li X, Liu X P. Integration of small world networks with multi-agents systems for simulating epidemic spatiotemporal transmission. *Chinese Science Bulletin*, 2009, 54(13): 3834–3843
124. Dibble C, Feidman P G. The GeoGraph 3D computational laboratory network and terrain landscapes for RePast. *Journal of Artificial Societies and Social Simulation*, 2004, 7(1). <http://jasss.soc.surrey.ac.uk/7/1/7.html>.
125. Mniszewski S M, Valle S Y D, Stroud P D, Riese J M, Sydoriak S J. EpiSims simulation of a multicomponent strategy for pandemic influenza. In: Proceedings of Spring Simulation Multiconference. 2008: 556–563
126. Carley K M, Fridsma D B, Casman E, Yahja A, Altman N, Chen L C, Kaminsky B, Nave D. BioWar: scalable agent-based model of bioattacks. *IEEE Transactions on Systems, Man, and Cybernetics-Part A: Systems and Humans*, 2006, 36(2): 252–265
127. Chao D L, Halloran M E, Obenchain V J, Longini I M Jr. Flu T E, a publicly available stochastic influenza epidemic simulation model. *PLoS Computational Biology*, 2010, 6(1): e1000656
128. Barrett C, Bisset K, Eubank S G, Feng X, Marathe M V. EpiSimdemics: an efficient and scalable framework for simulating the spread of infectious disease on large social networks. In: Proceedings of the 2008 ACM/IEEE conference on Supercomputing. 2008, 37
129. Bisset K R, Chen J, Feng X. EpiFast: a fast algorithm for large scale realistic epidemic simulations on distributed memory systems. In: Proceedings of the 23rd ACM International Conference on Supercomputing. 2009, 430–439
130. Parker J, Epstein J M. A distributed platform for global-scale agent-based models of disease transmission. *ACM Transactions on Modeling and Computer Simulation*, 2011, 22(1): 2
131. Duan W, Cao Z, Wang Y, Zhu B, Daniel Z, Wang F Y, Qiu X, Song H, Wang Y. An ACP approach to public health emergency management: using a campus outbreak of H1N1 influenza as a case study. *IEEE Transactions on Systems Man and Cybernetics: Systems*, 2013, 43(5): 1028–1041
132. Wang F Y. Toward a paradigm shift in social computing: the ACP approach. *IEEE Intelligent Systems*, 2007, 22(5): 65–67
133. Wang F Y. Parallel control and management for intelligent transportation systems: concepts, architectures, and applications. *IEEE Transactions on Intelligent Transportation Systems*, 2010, 11(3): 630–638
134. Report of the 6th Chinese population census data in 2010. Beijing Statistical Information Net. [http://www.bjstats.gov.cn/xwgb/tjgb/pcgb/201105/t20110504\\_201363.htm](http://www.bjstats.gov.cn/xwgb/tjgb/pcgb/201105/t20110504_201363.htm)
135. Guo G, Chen B, Qiu X G, LI Z. Parallel simulation of large-scale artificial society on CPU/GPU mixed architecture. In: Proceeding of the 26th ACM/IEEE/SCS Workshop on Principles of Advanced and Distributed Simulation. 2012: 174–177
136. Chen B, Guo G. A two-tier parallel architecture for artificial society simulation. In: Proceeding of the 26th ACM/IEEE/SCS Workshop on Principles of Advanced and Distributed Simulation. 2012: 184–186
137. Edmunds W J, O'Callaghan C J, Nokes D J. Who mixes with whom? A method to determine the contact patterns of adults that may lead to the spread of airborne infections. *Proceedings of the Royal Society B*, 1997, 264(1384): 949–957
138. Mossong J, Hens N, Jit M, Beutels P, Auranen K, Mikolajczyk R, Massari M, Salmaso S, Tomba G S, Wallinga J, Heijne J, Malgorzata S T, Rosinska M, Edmunds W J. Social contacts and mixing patterns relevant to the spread of infectious diseases. *PLoS Medicine*, 2008, 5(3): 381–390
139. Kretzschmar M, Mikolajczyk R T. Contact profiles in eight European countries and implications for modelling the spread of airborne infectious diseases. *PLoS ONE*, 2009, 4(6): e5931
140. Eames K T D, Tilston N L, Ellen B P, Edmunds W J. Measured dynamic social contact patterns explain the spread of H1N1v influenza. *PLoS Computational Biology*, 2012, 8(3): e1002425
141. Melegaro A, Jit M, Gay N, Zagheni E, Edmunds W J. What types of contacts are important for the spread of infections? Using contact survey data to explore European mixing patterns. *Epidemics*. 2011, 3(3–4): 143–151
142. Ogunjimi B, Hens N, Goeyvaerts N, Aerts M, Damme P V, Beutels P. Using empirical social contact data to model person to person infectious disease transmission: an illustration for varicella. *Mathematical Biosciences*, 2009, 218(2): 80–87
143. Mikolajczyk R T, Kretzschmar M. Collecting social contact data in the context of disease transmission: Prospective and retrospective study designs. *Social Networks*, 2008, 30(2): 127–135
144. Edmunds W J, Kafatos G, Wallinga J, Mossong J R. Mixing patterns and the spread of close-contact infectious diseases. *Emerging Themes in Epidemiology*, 2006, 3(10): 1–8
145. Wallinga J, Edmunds W J, Kretzschmar M. Perspective: human contact patterns and the spread of airborne infectious diseases. *Trends in MicroBiology*, 1999, 7(9): 372–377
146. Beutels P, Shkedy Z, Aerts M, Damme P V. Social mixing patterns for transmission models of close contact infections: exploring self-evaluation and diary-based data collection through a web-based interface. *Epidemiology and Infection*, 2006, 134(6): 1158–1166
147. Stehlé J, Voirin N, Barrat A, Cattuto C, Isella L, Pinton J F, Quaghiotto M, Broeck W V D, Régis C, Lina B, Vanhems P. High-resolution measurements of face-to-face contact patterns in a primary school. *PLoS ONE*, 2011, 6(8): e23176
148. Wallinga J, Teunis P, Kretzschmar M. Using data on social contacts to estimate age-specific transmission parameters for respiratory-spread infectious agents. *American Journal of Epidemiology*, 2006, 164(10): 936–944
149. Salathé M, Kazandjieva M, Lee J W, Levis P, Feldman M W, Jones J H. A high-resolution human contact network for infectious disease transmission. *Proceedings of National Academy of Sciences USA*, 2010, 107(51): 22020–22025
150. Isella L, Romano M, Barrat A, Cattuto C, Colizza V, Broeck W V D, Gesualdo F, Pandolfi E, Rava L, Rizzo C, Tozzi A E. Close encounters in a pediatric ward: measuring face-to-face proximity and mixing patterns with wearable sensors. *PLoS ONE*, 2011, 6(2): e17144
151. Isella L, Stehlé J, Barrat A, Cattuto C, Pinton J F, Broeck W V D. What's in a crowd? Analysis of face-to-face behavioral networks. *Journal of Theoretical Biology*, 2011, 271(1): 166–180

152. Zhao K, Stehlé J, Bianconi G, Barrat A. Social network dynamics of face-to-face interactions. *Physical Review E*, 2011, 83(5): 056109
153. Moon I C, Carley K M. Modeling and simulating terrorist networks in social and geospatial dimensions. *IEEE Intelligent Systems*, 2007, 22(5): 40–49
154. Wang L, Wang Z, Zhang Y, Li X. How human location-specific contact patterns impact spatial transmission between populations? *Nature Scientific Reports*, 2013, 3: 1468
155. Barabási A L. The origin of bursts and heavy tails in human dynamics. *Nature*, 2005, 435(7039): 207–211
156. Oliveira J G, Vazquez A. Impact of interactions on human dynamics. *Physica A*, 2009, 388(2-3): 187–192
157. Min B, Goh K I, Vazquez A. Spreading dynamics following bursty human activity patterns. *Physical Review E*, 2011, 83(3): 036102
158. Meloni S, Perra N, Arenas A, Gómez S, Moreno Y, Vespignani A. Modeling human mobility responses to the large-scale spreading of infectious diseases. *Scientific Reports*, 2011, 1(62): 1–7
159. Merler S, Ajelli M. The role of population heterogeneity and human mobility in the spread of pandemic influenza. *Proceedings of the Royal Society B*, 2009, 277(1681): 557–567
160. Zeng D, Chen H, Cao Z, Zhen X. Disease surveillance based on spatial contact networks: a case study of Beijing 2003 SARS epidemic. *IEEE Intelligent Systems*, 2009, 24(6): 77–82
161. Keeling M J, Danon L, Vernon M C, House T A. Individual identity and movement networks for disease metapopulations. *Proceedings of National Academy of Sciences USA*, 2010, 107(19): 8866–8870
162. Balcan D, Colizza V, Gonçalves B, Hu H, Ramasco J J, Vespignani A. Multiscale mobility networks and the spatial spreading of infectious diseases. *Proceedings of National Academy of Sciences USA*, 2009, 106(51): 21484–21489
163. Codling E A, Plank M J, and Benhamou S. Random walk models in biology. *Journal of the Royal Society Interface*, 2008, 5(25): 813–834
164. James A, Plank M J, Edwards A M. Assessing levy walks as models of animal foraging. *Journal of the Royal Society Interface*, 2011, 8(62): 1233–1247
165. González M C, Hidalgo C A, Barabási A L. Understanding individual human mobility patterns. *Nature*, 2008, 453(7196): 779–238
166. Brockmann D, Hufnagel L, Geisel T. The scaling laws of human travel. *Nature*, 2006, 439(7075): 462–465
167. Truscott J, Ferguson N M. Evaluating the adequacy of gravity models as a description of human mobility for epidemic modelling. *PLoS Computational Biology*, 2012, 8(10): e1002699
168. Jandarvo R, Haran M, Bjørnstad O, Grenfell B. Emulating a gravity model to infer the spatiotemporal dynamics of an infectious disease. <http://arxiv.org/pdf/1110.6451v3.pdf>
169. Li X, Tian H, Lai D, Zhang Z. Validation of the gravity model in predicting the global spread of influenza. *International Journal of Environmental Research and Public Health*, 2011, 8(8): 3134–3143
170. Meloni S, Arenas A, and Moreno Y. Traffic-driven epidemic spreading in finite-size scale-free network. *Proceedings of National Academy of Sciences USA*, 2009, 106(40): 16897–16902
171. Epstein J M, Goedecke D M, Yu F, Morris R J, Wagener D K, Bobashev G V. Controlling pandemic flu: the value of international air travel restrictions. *PLoS ONE*, 2007, 2(5): e401
172. Duan W, Qiu X. Fostering artificial societies using social learning and social control in parallel emergency management systems. *Frontiers of Computer Science*, 2012, 6(5), 604–610
173. Zheng X, Zhong Y, Zeng D, Wang F Y. Social influence and spread dynamics in social networks. *Frontiers of Computer Science*, 2012, 6(5), 611–620
174. Hufnagel L, Brockmann D, Geisel T. Forecast and control epidemics in a globalized world. *Proceedings of National Academy of Sciences USA*, 2004, 101(42): 15124–15129
175. Watts D J, Muhamad R, Medina D C, Dodds P S. Multiscale, resurgent epidemics in a hierarchical metapopulation model. *Proceedings of National Academy of Sciences USA*, 2005, 102(32): 11157–11162
176. Colizza V, Barrat A, Barthélemy M, Vespignani A. Epidemic predictability in meta-population models with heterogeneous couplings: the impact of disease parameter values. *International Journal of Bifurcation and Chaos*, 2007, 17(7): 2491–2500
177. Colizza V, Barrat A, Barthélemy M, Valleron A J, Vespignani A. Modeling the worldwide spread of pandemic influenza: baseline case and containment interventions. *PLoS Medicine*, 2007, 4(1): e13
178. Savini L, Weiss C, Colangeli P, Conte A, Ippoliti C, Lelli R, Santucci U. A web-based geographic information system for the management of animal disease epidemics. *Veterinaria Italiana*, 2007, 43(3): 761–772
179. Laosuwan T. Online web GIS-based services for spatial data and sharing of leptospirosis epidemiology information; development of pilot project in Mahasarakham province Thailand. *International Journal of Geomatics and Geosciences*, 2012, 3(1): 121–133
180. Woolhouse M E J, Dye C, Etard J F, Smith T, Charlwood J D, Garnett G P, Hagan P, Hii J L K, Ndhlovu P D, Quinnell R J, Watts C H, Chandiwana S K, Anderson R M. Heterogeneities in the transmission of infectious agents: implications for the design of control programs. *Proceedings of National Academy of Sciences USA*, 1997, 94(1): 338–342
181. Xuan H, Xu L, Li L. A CA-based epidemic model for HIV/AIDS transmission with heterogeneity. *Annals Operations Research*, 2009, 168(1): 81–99
182. Lafuerza L F, Toral R. On the effect of heterogeneity in stochastic interacting-particle systems. *Scientific Reports*, 2013, 3: 1189
183. Galvani A P, May R M. Dimensions of super spreading. *Nature*, 2005, 438(7066): 293–295
184. Lloyd-Smith J O, Schreiber S J, Kopp P E, Getz W M. Super spreading and the effect of individual variation on disease emergency. *Nature*, 2005, 438(7066): 355–359
185. Stein R A. Super-spreaders in infectious diseases. *International Journal of Infectious Diseases*, 2011, 15(8): e510–e513
186. Small M, Tse C K, Walker D M. Super-spreader and the rate of transmission of the SARS virus. *Physica D*, 2006, 215(2): 146–158
187. Yang R, Wang B H, Ren J, Bai W J, Shi Z W, Wang W X, Zhou T. Epidemic spreading on heterogeneous networks with identical infectivity. *Physics Letters A*, 2007, 364(3–4): 189–193
188. Wang J Z, Liu Z R, Xu J. Epidemic spreading on uncorrelated heterogeneous networks with non-uniform transmission. *Physica A*, 2007, 382(2): 715–721
189. Barthélemy M, Barrat A, Pastor-Satorras R, Vespignani A. Dynamical

- patterns of epidemic outbreaks in complex heterogeneous networks. *Journal of Theoretical Biology*, 2005, 235(2): 275–288
190. Ferguson N. Capturing human behaviour. *Nature*. 2007, 446: 733
  191. Funk S, Salathé M, Jansen V A. Modeling the influence of human behaviour on the spread of infectious disease: a review. *Journal of the Royal Society Interface*, 2010, 7(50): 1247–1256
  192. Auld M C. Choices, beliefs, and infectious disease dynamics. *Journal of Health Economics*. 2003, 22(3): 361–377
  193. Zhang H, Zhang J, Li P, Small M, Wang B. Risk estimation of infectious diseases determines the effectiveness of the control strategy. *Physica D*, 2011, 240(11): 943–948
  194. Chen F H. Modeling the effect of information quality on risk behavior change and the transmission of infectious disease. *Mathematical Biosciences*, 2009, 217(2): 125–133
  195. Shim E, Chapman G B, Galvani A P. Decision making with regard to antiviral intervention during an influenza pandemic. *Medicine Decision Making*, 2010, 30(4): e64–e81
  196. Fu F, Rosenbloom D I, Wang L, Nowak M A. Imitation dynamics of vaccination behaviour on social network. *Proceedings of the Royal Society B*, 2011, 278(1702): 42–49
  197. Reluga T C. Game theory of social distancing in response to an epidemic. *PLoS Computational Biology*, 2010, 6(5): e1000793
  198. Bauch C T, Galvani A P, Earn D J D. Group interest versus self-interest in smallpox vaccination policy. *Proceedings of National Academy of Sciences USA*, 2003, 100(18): 10564–10567
  199. Rosenstock I M. The health belief model and preventive health behavior. *Health Education & Behavior*, 1974, 2(4): 354–386
  200. Ajzen I, Fishbein M. *Understanding Attitudes and Predicting Social Behavior*. Englewood Cliffs: Prentice-Hall, 1980: 1–278
  201. Bandura A. *Self-efficacy: the Exercise of Control*. New York: Freeman, 1997: 1–600.
  202. Rogers R W. *A Cognitive and Physiological Process in Fear Appeals and Attitude Change: a Revised Theory of Protection Motivation*. New York: Guilford, 1983: 153–176
  203. Hayden J A. *Introduction to Health Behavior Theory*. Jones and Bartlett, 2009: 1–148
  204. Durham D P, Casman E A. Incorporating individual health-protective decisions into disease transmission models: a mathematical framework. *Journal of the Royal Society Interface*, 2012, 9(68): 562–570
  205. Durham D P, Casman E A, Albert S M. Deriving behavior model parameters from survey data: self-protective behavior adoption during the 2009-2010 influenza A (H1N1) pandemic. *Risk Analysis*, 2012, 32(12): 2020–2031
  206. Tang C S, Wong C. Factors influencing the wearing of facemasks to prevent the severe acute respiratory syndrome among adult Chinese in Hong Kong. *Preventive Medicine*, 2004, 39(6): 1187–1193
  207. D’Onofrio A, Manfredi P. Information-related changes in contact patterns may trigger oscillations in the endemic prevalence of infectious diseases. *Journal of Theoretical Biology*, 2008, 256(3): 473–478
  208. Zhang H F, Zhang W Y, Sun G Q, Zhou T, Wang B H. Time-delayed information can induce the periodic outbreaks of infectious diseases (in Chinese). *Scientia Sinica Physica, Mechanica & Astronomica*, 2012, 42(6): 631–638
  209. Kiss I Z, Cassell J, Recker M, Simon P L. The impact of information transmission on epidemic outbreaks. *Mathematical Biosciences*, 2010, 225(1): 1–10
  210. Gong X, Xiao R. Research on multi-agent simulation of epidemic news spread characteristics. *Journal of Artificial Societies and Social Simulation*, 2007, 10(31). <http://jasss.soc.surrey.ac.uk/10/3/1.html>
  211. Myers S, Zhu C, Leskovec J. Information diffusion and external influence in networks. In: *Proceedings of the 18th ACM SIGKDD international conference on Knowledge discovery and data mining*. 2012, 33–41
  212. Cui P, Wang F, Liu S, Ou M, Yang S, Sun L. Who should share what? Item-level social influence prediction for users and posts ranking. In: *Proceedings of the 34th international ACM SIGIR conference on Research and development in Information Retrieval*. 2011, 185–194
  213. Mao L, Bian L. Agent-based simulation for a dual diffusion process of influenza and human preventive behavior. *International Journal of Geographical Information Science*, 2011, 25(9): 1371–1388
  214. Funk S, Gilad E, Watkins C, Jansen V A. The spread of awareness and its impact on epidemic outbreaks. *Proceedings of National Academy of Sciences USA*, 2009, 106(16): 6872–6877
  215. Tommasi M, Weinschelbaum F. Centralization vs. decentralization: a principal-agent analysis. *Journal of Public Economic Theory*, 2007, 9(2): 369–389
  216. Dredze M. How social media will change public health. *IEEE Intelligent Systems*, 2012, 27(4): 81–84
  217. Rahmandad D, Sterman J. Heterogeneous and network structure in the dynamics of diffusion: comparing agent-based and differential equation models. *Management Science*, 2008, 54(5): 998–1014
  218. Bagni R, Berchi R, Cariello P. A comparison of simulation models applied to epidemics. *Journal of Artificial Societies and Social Simulation*, 2002, 5(3). <http://jasss.soc.surrey.ac.uk/5/3/5.html>



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