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Epidemic spreading dynamics with drug resistance and heterogeneous contacts

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ABSTRACT

Drug resistance and strong contacts actually play crucial roles in epidemic spread in complex systems. Nevertheless, neither theoretical model or methodology is proposed to address this. We thus consider an edge-based epidemic spread model considering the two key ingredients, in which the contacts are grouped into two classes: strong contacts and normal ones. Next, we present a unified edge-based compartmental approach to the spread dynamics on Erdös–Rényi (ER) networks and validate its results by extensive numerical simulations. In case that epidemic is totally drug-resistant, we both numerically and theoretically show a continuous growth of epidemics with infection probability when number of strong contacts is not enough for the emergence of null threshold. If the epidemic owns partial resistance, we would observe evident discontinuous growth with infection probability (discontinuous transitions) and larger final epidemic sizes for few strong contacts, instead of emergence of null threshold with increase of strong contacts. Inhibiting effect of infection threshold, positive roles of strong contacts and strength of strong contacts in promoting outbreaks are also approved. Throughout this paper, we could drive exact predictions through the analytical approach, showing good agreements with numerical simulations.

1. Introduction

In field of epidemic research, an actual non-negligible case that is recently gaining attention is drug resistance arisen from abuse of substance especially antibiotics, which contributes to the problem of drug resistance. Drug resistance refers to that individually applied therapies targeted at single pathogens in individual bodies would actually become environmental events to drive the evolution of pathogens and commensal bacteria alike far beyond bodies. Growing problems involving multi-resistant pathogens such as methicillin-resistant *Staphylococcus aureus* (MRSA) have been found in most European countries (Grundmann et al., 2006), more particularly infectious agents of tuberculosis (like multidrug-resistant tuberculosis (TB) or even extensively drug-resistant TB (Velayati et al., 2013) and gonorrhoea begin to capture much more attention than before, because these pathogens remaining high infection rates would make infected people difficult or impossible to be cured. For some extreme cases of multi-drug resistant epidemics like superbugs, even last-resort antibiotics fail (Chen, 2017; Udwadia et al., 2012). Therefore large amount of empirical studies have been conducted by epidemiologists, microbiologists, health economists and physicians to focus on the drug resistance especially antibiotic resistance, aiming to develop new medicines, therapies even coping strategies in the face of this crisis (Landecker, 2016).

In turning to studies related to epidemic spread in complex systems, lots of researchers have developed different models, estimation methods or efficient algorithms to explore the influence of spatial structure topology especially the edges on spread of epidemics, so as to design network-based prevention strategies (Pastor-Satorras et al., 2015). Furthermore, designing network-based prevention strategies requires knowledge on disease transmission through network edges and statistical methods for analyzing network data. Fortunately, data-driven method such as contact tracing is very effective, because this method could identify which contacts are key to the transmission, which facilitates so-called real time tracking of an epidemic (Wallinga and Teunis, 2004). One significant research progress of contact tracing is that there exist considerable differences among contact frequencies in real complex networks (Landovitz et al., 2013; Wallinga and Teunis, 2004), while the frequency of contact can be used as a proxy measure for the tendency of at-risk events for infection. This means that vari-

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ous contact frequencies would lead to multiple transmission rates (positively related to contact frequency) along different contacts. Hence, contact-based network models accessing nature of contact patterns could yielded more deep insights into infectious disease transmission, and to control their epidemiological significance.

Another important fact we could not ignore is that spread of epidemics with drug resistance is often accompanied by increasing number of some contacts with enough high strength (i.e. high contact frequency) which could be called strong contacts. And these strong contacts have been found to be widespread in reality, in forms of concurrent partnerships (spouse partnerships, cohabitation relationships and homosexual relations) (Brewer et al., 2006), compact communities (Auvert et al., 2005; Brody and Potterat, 2003), doctor–patient relationship (Barg, 1993; Bukhari et al., 1993) and so on. For example, gay relationship is always considered as a high risk contact for being infected with HIV compared with other forms of sexual contacts, through largely raised infection rate (Morris and Kretzschmar, 1997). Another well-known case is that of tuberculosis transmissions, which could occur more easily among family members; despite the possible infection through inhalation of aerosols or small droplets for example during a conversation between strangers (Lynn et al., 1997). Besides, doctor-patient relationship has been confirmed as a nearly 'straightway unblocked channel' to transfer streptococci and staphylococci (even MRSA), resulting in a serious cross-infection (Snyder et al., 2008). These studies indicate that the strength of contacts and drug resistances especially antimicrobial resistances can profoundly influence the spread of disease and should thus be incorporated into applicable epidemiological models. However, it still not clear how drug resistance regulates the epidemic diffusion in complex systems in presence of strong contacts. To our knowledge, no theoretical models have been proposed to center on this problem so far, to say nothing of a systemic methodology.

Based on the above arguments, we herein put forward an edge-based epidemic spread model to capture the two realistic mechanisms: drug resistance and strengths of contacts. In the present model, contacts are directly classified into two types: normal contacts and strong ones, which allows us to develop a unified edge-based compartmental theory so as to deeply understand the effects of drug resistance and strong contacts on the spread dynamics. We elucidate the issue in two different situations at length: (1) Epidemic is totally drug-resistant; (2) Epidemic own partial resistance. In the first case, we both numerically and theoretically show a continuous growth (continuous transition) of epidemics when number of strong edges (i.e., strong contacts) is not sufficiently enough for the emergence of null threshold i.e., the system exhibits the lack of an epidemic threshold and always show a finite fraction of infected population (Moreno et al., 2002). We then extend the analytical approach to the latter case to derive a number of predictions, including the final infection sizes, the positions of the thresholds and the nature of the transitions. Both the theoretical approach and agent-based simulations indicate the occurrences of discontinuous growth (discontinuous transition) and larger final epidemic sizes with few strong contacts in networks, instead of emergence of null threshold with increasing fraction of strong contacts. In both cases, numerical simulations perfectly fit the analytical predictions.

The paper is organized as follows. In Section 2, we present a detailed description of our model. Then we give a detailed theoretical analysis of the spread dynamics by means of the unified edge-based compartmental theory in Section 3. Section 4 is devoted to show a deep numerical investigation of the epidemic spread dynamics on different networks. In addition, theoretical predictions are given to enable a comparison with numerical simulations. Finally, we list conclusions of this study in Section 5.

2. Model

One propose a model to give a framework to curve spread of highly mutated epidemics which could avoid inhibitory effect of antibiotics, such as influenza virus, TB bacteria, staphylococci and so on. As we know, in the classical SIR model, each individual can be in one of three different states: susceptible (S, individuals that are healthy, and could be infected), infected (I, individuals who get infected and can transmit the pathogen), or removed (R, dead or recovered and immunized individuals). At each time step, each infected individual shifts into removed state with probability γ, while she transmits the pathogen to each of her susceptible neighbors with infection probability p.

In the present model, the epidemic spread is formulated in the terms of a modification of the susceptible-infected-recovered (SIR) model, where one class the edges of networks into two groups: strong edges and normal ones, corresponding to the strong contacts and normal contacts which have been observed in reality. The reason that only two classes of edges are assumed in the model is to enable us to develop a unified edge-based compartmental approach to analysis the spread dynamics, without loss of one important feature of human contacts – heterogeneous contributions to epidemic diffusion caused by different contact frequencies. At the same time, we introduce infection threshold T to depict drug resistance of epidemics. Like what happens in the SAR model for social contagions (Wang et al., 2015), one susceptible individual successfully becomes infected only if it has received the pathogen from its connected infected neighbors for at least T times (i.e., infection threshold). This infection rule with infection threshold is actually a nice mirror to reflect how epidemics with drug-resistant ability diffuse in real complex systems (Landecker, 2016). The case $T = 1$ represents the situation that the epidemic is multi-resistant or even totally-resistant, so that it could attacked people most severely, which means that individuals would easily get infected if they receive pathogen of the epidemic from the infected guys for just one time. For the case $T > 1$, we know that people have more choices in the antibiotic lists because the epidemic owns partial resistance or even no. In this case, the epidemic could be timely suppressed or repelled by acting antibiotics so that the hosts could not infect others, until the pathogen begins to evolve certain drug-resistance under the stress of antibiotics (receive times is beyond infection threshold T).

Specifically, for two individuals i (susceptible) and j (infected) located on two ends of one edge e_{ij} in the complex network, i will receive the epidemic pathogen passed from j at a probability p if the edge e_{ij} is a normal edge. Instead, if e_{ij} is a strong edge, i will be more likely to get infected by the epidemic transmitted from j at a raised infection probability q. That is why our model is edge-based. It must be stressed in our model that the individuals who are suffering the epidemic are not considered to be in infected state before they gaining the ability to infect others.

Our model is simulated on Erdös–Rényi (ER) network of size $N = 10^4$ with mean degree $\langle k \rangle = 10$. We adopt discrete-time updating rule (synchronous updating (SU) rule) (Schönfisch and de Roos, 1999), which means that an individual who get infected at time t will try to transmit the infection to all its susceptible neighbors at time $t + 1$ (for exactly one time step), and after that it would become recovered or die and never transmit the infection again, i.e., the recover probability is $\gamma = 1.0$. In the simulations, N_r (ranging from 500 to 2000) independent realizations are needed. Moreover, ρ_0 of the population are randomly chosen to be in the infected (I) state as epidemic seeds, while the remaining nodes are susceptible. A proportion μ of randomly chosen edges in the networks are regarded as strong edges while the remaining edges are normal ones.