Epidemic control analysis: Designing targeted intervention strategies against epidemics propagated on contact networks

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HIGHLIGHTS

- A deterministic SIS model of dynamics on networks is presented.
- A control analysis is implemented to understand and control epidemics on networks.
- This is a practical tool which outperforms other methods of intervention.
- The sites to target emerge from interplay between dynamics and network structure.

ABSTRACT

In cases where there are limited resources for the eradication of an epidemic, or where we seek to minimise possible adverse impacts of interventions, it is essential to optimise the efficacy of control measures. We introduce a new approach, Epidemic Control Analysis (ECA), to design effective targeted intervention strategies to mitigate and control the propagation of infections across heterogeneous contact networks. We exemplify this methodology in the context of a newly developed individual-level deterministic Susceptible-Infectious-Susceptible (SIS) epidemiological model (we also briefly consider applications to Susceptible-Infectious-Removed (SIR) dynamics). This provides a flexible way to systematically determine the impact of interventions on endemic infections in the population. Individuals are ranked based on their influence on the level of infectivity. The highest-ranked individuals are prioritised for targeted intervention. Many previous intervention strategies have determined prioritisation based mainly on the position of individuals in the network, described by various local and global network centrality measures, and their chance of being infectious. Comparisons of the predictions of the proposed strategy with those of widely used targeted intervention programmes on various model and real-world networks reveal its efficiency and accuracy. It is demonstrated that targeting central individuals or individuals that have high infection probability is not always the best strategy. The importance of individuals is not determined by network structure alone, but can be highly dependent on the infection dynamics. This interplay between network structure and infection dynamics is effectively captured by ECA.

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1. Introduction

Traditionally, epidemic models and control strategies have been considered in homogeneous populations where each individual is the same, so the transmission of infection between any two individuals is equally likely and all individuals have the same probability of recovery (Anderson and May, 1992; Murray, 1993).

However, real populations typically consist of individuals that have biological, physiological, social, behavioural, spatial, or other differences (Amaral et al., 2000; Anderson and May, 1992; Diekmann and Heesterbeek, 2000). The underlying connectivity between individuals, as well as other heterogeneities, can be represented by a network (or graph) (Behzad et al., 1979; Dorogovtsev and Mendes, 2003), which is a collection of units (the nodes) interacting via links. Each node represents an individual and every link between two nodes represents an interactive relationship. Networks have also been used to represent connections between nodes comprising of collections of individuals such as cities, communities and organisations. The impact that the

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contact structure can have on epidemic propagation has prompted extensive studies of epidemics on networks (Bansal et al., 2007; Danon et al., 2011; Keeling and Eames, 2005). Such studies have increased understanding of the factors that affect the spread of epidemics on networks, which is fundamental to the formulation of strategies for their control. Classic control strategies apply interventions (for example vaccinate or increase biosecurity) to individuals chosen uniformly at random (Anderson and May, 1992), but for heterogeneous contact structures such control strategies can be impractical. For example, on scale-free networks it has been shown that when applying uniformly random interventions, almost all individuals have to be removed from the transmission process in order to eradicate an epidemic (Albert et al., 2000; Callaway et al., 2000; Cohen et al., 2000). More generally, constraints on the number of available resources due to, for example, limitations in the budget, time and medical personnel, or the possible severe side effects of interventions, necessitate the design of targeted strategies.

Many of the existing targeted intervention strategies rank and target nodes according to centrality measures (Borgatti, 2005) which give an indication of how 'central' a node is in the contact structure, ignoring the dynamics of the infection. Here we develop a targeted intervention strategy that takes into account both the impact of the contact network and the infection dynamics. We show that by using a class of epidemic model (Sharkey, 2008, 2011) which transforms stochastic systems into approximate deterministic ones, a systematic sensitivity analysis, or Epidemic Control Analysis (ECA), can be performed. A practical tool for the systematic sensitivity analysis of these random epidemic processes on networks has not been developed in previous studies. To a large extent this is due to the stochastic nature of these systems, making the direct impact of specific targeted interventions difficult to determine.

We focus on infections that can remain endemic in the population leading to a quasi-stationary distribution in the number of infectious individuals. To delineate the present study, we mainly limit ourselves to epidemic models of the Susceptible-Infectious-Susceptible (SIS) type (Anderson and May, 1992; Weiss and Dishon, 1971). In these models, susceptible individuals can become infectious through a contact with infectious individuals and then, after a period of time, recover and return to the susceptible state. We assume that transmission and recovery are governed by Poisson processes. Despite their simplicity, SIS-type models are widely applicable and have received considerable attention, especially in the context of diseases caused by bacteria, such as the sexually transmitted disease gonorrhea (see for example Hethcote and Yorke, 1984). Apart from their application to modelling the spread of diseases in human and animal populations, these models also have a range of other applications such as modelling of the spread of viruses in computer networks (see for example Kephart and White, 1991). We also briefly consider the generalisation of ECA to Susceptible-Infectious-Removed (SIR) epidemic dynamics in which infectious individuals recover from the infection permanently (Anderson and May, 1992; Hethcote, 2000; Kermack and McKendrick, 1927).

In the next section we discuss the structure of the underlying SIS model and the ECA methodology. In addition to synthetic networks, we also apply this to two real-world networks, the Guppy network (Croft et al., 2004) and the Co-authorship network (Newman, 2006), to investigate real-world heterogeneous structures which are not found in more idealised networks. Although not directly derived from epidemic observations, these networks represent social interactions which typically underpin epidemic dynamics. We then show that ECA gives superior results to other methods and uncover some novel and possibly emergent properties of control. Matlab codes for the solution of the SIS model and

for the implementation of ECA on arbitrary networks are provided as Supplementary material.

2. Methods

We first describe the individual-level moment-closure SIS model and the implementation of ECA. We also discuss how we could apply ECA to SIR-type dynamics. This is followed by a description of four methods for identifying influential nodes on contact networks which we use to benchmark the ECA methodology.

2.1. The SIS moment-closure model

We develop an approximate deterministic SIS model at the individual level for the study of complex epidemic dynamics on arbitrary static networks. The model is based directly on the construction of the deterministic SIR epidemic models of Sharkey (2008, 2011) (see also Nagy and Simon, 2013 where the same SIS model has been developed in the special case of epidemics propagated on the cycle graph).

A network of N nodes can be described by the adjacency matrix G, where $G_{ij} = 1$ if node j is connected to node i and $G_{ij} = 0$ otherwise, and where $i, j \in \{1, 2, ..., N\}$. We assume that there are no self-contacts; $G_{ii} = 0 \ \forall i \in \{1, 2, ..., N\}$.

For SIS dynamics, we suppose that a node $i \in \{1, 2, ..., N\}$ is either in the susceptible state with probability $\langle S_i \rangle$, or the infectious state with probability $\langle I_i \rangle = 1 - \langle S_i \rangle$. We assume that the transition between the two states is described by a Poisson process. The transmission of the infection between the nodes can be represented by the transmission matrix T where element T_{ij} is the rate at which an infectious node $j \in \{1, 2, ..., N\}$ transmits the infection to a susceptible node $i \in \{1, 2, ..., N\}$ through a direct contact and $T_{ii} = 0 \ \forall i \in \{1, 2, ..., N\}$. T_{ij} is thus a weighted adjacency matrix. An infectious node i recovers and enters the susceptible state with recovery rate γ_i. The stochastic dynamics are consistent with the following equations:

$$\langle \dot{S_i} \rangle = -\sum_j T_{ij} \langle S_i I_j \rangle + \gamma_i \langle I_i \rangle, \quad \langle \dot{I_i} \rangle = \sum_j T_{ij} \langle S_i I_j \rangle - \gamma_i \langle I_i \rangle, \quad (1)$$

$$\langle \dot{S_i S_j} \rangle = -\sum_{k, k \neq j} T_{ik} \langle I_k S_i S_j \rangle - \sum_{k, k \neq i} T_{jk} \langle S_i S_j I_k \rangle + \gamma_j \langle S_i I_j \rangle + \gamma_i \langle I_i S_j \rangle, \quad (2)$$

$$\langle \dot{S_i I_j} \rangle = \sum_{k, k \neq i} T_{jk} \langle S_i S_j I_k \rangle - \sum_{k, k \neq j} T_{ik} \langle I_k S_i I_j \rangle - T_{ij} \langle S_i I_j \rangle - \gamma_j \langle S_i I_j \rangle + \gamma_i \langle I_i I_j \rangle, \quad (3)$$

$$\langle \dot{I_i I_j} \rangle = \sum_{k, k \neq j} T_{ik} \langle I_k S_i I_j \rangle + \sum_{k, k \neq i} T_{jk} \langle I_i S_j I_k \rangle + T_{ij} \langle S_i I_j \rangle + T_{ji} \langle I_i S_j \rangle - \gamma_i \langle I_i I_j \rangle - \gamma_j \langle I_i I_j \rangle, \quad (4)$$

where $\langle A_i B_j \rangle$ is the probability that node i is in state A and node j is in state B. Similarly, $\langle A_i B_j C_k \rangle$ denotes the probability that nodes i, j and k are in states A, B and C, respectively.

Here, we close the system at the level of pairs by approximating the probabilities $\langle A_i B_j C_k \rangle$ in terms of pair-level and individual-level probabilities. In particular, the probability of a closed triple $\langle A_i B_j C_k \rangle$ in which there is a link between nodes k and i (in addition to some link between i and j and between j and k) is approximated as

$$\langle A_i B_j C_k \rangle \approx \frac{\langle A_i B_j \rangle \langle B_j C_k \rangle \langle C_k A_i \rangle}{\langle A_i \rangle \langle B_j \rangle \langle C_k \rangle}. \quad (5)$$

The probability of the open triple $\langle A_i B_j C_k \rangle$ in which nodes i and k are not connected in any direction is approximated by the following expression:

$$\langle A_i B_j C_k \rangle \approx \frac{\langle A_i B_j \rangle \langle B_j C_k \rangle}{\langle B_j \rangle}. \quad (6)$$