Epidemics 10 (2015) 58–62

Contents lists available at ScienceDirect

Epidemics

journal homepage: www.elsevier.com/locate/epidemics

Eight challenges for network epidemic models

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ARTICLE INFO

Article history:
Received 15 February 2014
Received in revised form 25 July 2014
Accepted 28 July 2014
Available online 4 August 2014

Keywords:
Infectious disease models
Transmission dynamics
Contact networks
Random graphs
Dynamic networks
Control measures

ABSTRACT

Networks offer a fertile framework for studying the spread of infection in human and animal populations. However, owing to the inherent high-dimensionality of networks themselves, modelling transmission through networks is mathematically and computationally challenging. Even the simplest network epidemic models present unanswered questions. Attempts to improve the practical usefulness of network models by including realistic features of contact networks and of host–pathogen biology (e.g. waning immunity) have made some progress, but robust analytical results remain scarce. A more general theory is needed to understand the impact of network structure on the dynamics and control of infection. Here we identify a set of challenges that provide scope for active research in the field of network epidemic models.

Introduction

Networks (or *graphs*) are extremely flexible tools for representing complex systems of interacting components (Boccaletti et al., 2006; Durrett, 2007; Newman, 2010). Each component is represented by a *node* (or *vertex*) and each *link* (or *edge*) between nodes describes some sort of interaction between them. Here, we focus on the specific application of networks in the field of infectious disease modelling (Andersson, 1999; Danon et al., 2011).

Because of their flexibility, networks have been used to model infection spread in different forms. Nodes can describe single individuals, groups of individuals (e.g. households, farms, cities) or locations to which individuals are connected (e.g. see Riley et al., in this issue). Links can represent infectious attempts or transmission events (in which case the network is directed) or simply acquaintances between them (social or sexual relationships through which the infection can spread, usually in both directions), movements of animals between farms (direct or via intermediate markets), flight routes, etc.

This apparent simple and intuitive representation of a population of interacting components has the drawback that it might be difficult to work with. Even in the case of a simple undirected network with n nodes, we still need $n(n-1)/2$ binary digits to fully describe the presence or absence of each possible edge. Thus, particularly for large networks, the general approach is to summarise most of the network information in a small set of statistics and then study their impact on infection spread. Among the myriad network properties (Boccaletti et al., 2006; Newman, 2010), in this paper we consider some of those that appear both epidemiologically relevant and amenable to analysis, such as: *degree distribution*, the distribution of the number of links from each node; *assortativity*, the propensity of epidemiologically similar nodes to be connected to each other, an important example of which is the *degree correlation* between neighbouring nodes; *clustering*, the propensity of two nodes with a common neighbour to be neighbours of each other (i.e. the fraction of triplets that form triangles); *modularity*, the partitioning of the network into internally well-connected groups; and *betweenness centrality* of a node, i.e. the number of shortest paths between all pairs of nodes that pass through that node.

Here, we have in mind nodes as individuals and links as acquaintances between them, and therefore primarily consider infection spread on *undirected* networks. Furthermore, we mostly have

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http://dx.doi.org/10.1016/j.epidem.2014.07.003

in mind permanently immunising infections (i.e. SIR epidemic models). Although most challenges apply also in the absence of permanent immunity (i.e. SIS and SIRS models), this analytically much harder case is the focus of Section 'Incorporating waning immunity in network epidemic models'. In Section 'Understanding the effect of heterogeneity on parameter estimation and epidemic outcome', we consider the so-called configuration model (Danon et al., 2011; Durrett, 2007, Chapter 3): beside the Erdös-Rényi random graph (Durrett, 2007, Chapter 2), this is the most analytically tractable network because of its locally tree-like structure, but it lacks many features of real-world networks that can dramatically impact transmission dynamics. We then discuss complex networks (i.e. not locally tree-like), first unweighted and static (Section 'Developing analytical methods to generate and study epidemics on static unweighted complex networks') and then weighted and dynamic (Section 'Developing analytical methods to model weighted and dynamic networks and epidemics thereon'). Approximate methods are discussed in Section 'Developing and validating approximation schemes for epidemics on networks'. Finally, in Sections 'Clarifying the impact of network properties on epidemic outcome', 'Strengthening the link between network modelling and epidemiologically relevant data' and 'Designing network-based interventions' we discuss the impact of network structure on infection spread, the relationship between network models and data, and interventions, respectively.

1. Understanding the effect of heterogeneity on parameter estimation and epidemic outcome

In homogeneously mixing populations, the relationships between key epidemiological quantities are generally well understood. For example, it is well known that for SIR epidemics in the large population limit (starting with a negligible fraction of the population infected), R_0 and the final size of a large outbreak, z say, are strongly linked by the simple relationship $1-z=\mathrm{e}^{-R_0 z}$ (Diekmann et al., 2013).

However, even for an SIR epidemic on a configuration-type network, this simple relationship is lost: R_0 and final size of a large outbreak both depend on the degree distribution, but the former is affected by the degree variance, which is much more sensitive to changes in probabilities of high-degree than low-degree vertices, while the latter is highly dependent on the exact probabilities of low-degree vertices, but hardly depends on high-degree ones. Similar considerations apply when individuals vary in susceptibility and/or infectivity, with the additional problem that attainable data are unlikely to provide much information of this type.

It therefore remains an important problem to understand how, not only R_0, probability of a large outbreak and its final size, but also duration of the epidemic and peak incidence, relate to each other and how the dependencies are affected by potentially unobserved heterogeneity in susceptibility/infectivity and degree.

Furthermore, during an outbreak, early predictions for public health purposes are typically needed. Therefore, it is important to quantify how such heterogeneities affect early parameter estimates (e.g. of R_0) and the repercussions of potential estimation biases on epidemic predictions.

2. Developing analytical methods to generate and study epidemics on static unweighted complex networks

Although convenient for its analytical tractability, the configuration model fails to capture some important properties of realistic contact networks. The POLYMOD study (Mossong et al., 2008) revealed strong assortativity by age (people make more contacts of similar age to their own than of others) with the additional trans-generational contact between children and adults, while Read et al. (2008) highlighted significant clustering in an empirically measured social network. Metapopulation and multitype epidemic models (see Ball et al., in this issue) are epidemiologically important examples of modular networks. Spatial (see Riley et al., in this issue) and highly heterogeneous networks of size n, unlike the configuration model, exhibit path lengths of order other than $\log(n)$. Finally, higher-order correlations such as four-motif structure or correlations at the triple level are likely to occur in any network generated by complex social processes (Miller, 2009).

A number of models for constructing random networks have been developed to incorporate realistic graph properties. Generally, as the random graph model under consideration becomes more complex, rigorous results about the properties of the resulting network, and of epidemics running on it, become less general. For example, the preferential attachment network model allows for rigorous analysis of most network properties and also asymptotic epidemic threshold behaviour (Durrett, 2007, Chapter 4). For random geometric graphs network properties are known but analysis of epidemic dynamics has so far required Monte Carlo simulation (Isham et al., 2011). For exponential random graphs (Danon et al., 2011) and related models that seek to generate networks with specified properties in the most random way possible, there are essentially no exact results.

Rigorous analysis is, however, possible for SIR epidemics defined on some random network models with clustering. These include models incorporating small cliques of individuals, e.g. random intersection graphs, triangle- or household-based models (see Ball et al., 2013, and references therein). However, analytical tractability stems from the fact that all such models have a tree-like structure at some level (e.g. a tree of fully connected cliques).

Although these models enable analysis of the effect of clustering and sometimes also degree correlation on epidemic properties, it must be recognised that the networks they produce are rather special and not easily generalisable. Also, epidemics on distinct network models having common degree distribution, clustering coefficient and degree correlation may have different properties (Ball et al., 2013). Therefore, major challenges involve identifying which, if any, of the current models reflects reality well enough for the question at hand and developing other network models that are both sufficiently realistic and amenable to rigorous mathematical analysis.

3. Developing analytical methods to model weighted and dynamic networks and epidemics thereon

Links within real-world social networks are not all identical: some interactions carry a greater risk of disease transmission than others. To account for this additional heterogeneity, we can consider weighted networks, in which a link's weight (which may vary over time) can be thought of as its relative transmission potential. Some models have attempted to include information about link weights (Kamp et al., 2013), but their inherent high-dimensionality is a significant challenge if the intention is to avoid detailed micro-simulations. Furthermore, it is not always clear how the transmission potential relates to observable quantities, as available data in social networks are limited, and are always restricted to information that is easily measured or estimated (see Eames et al., in this issue): for example, contact diary studies often ask about whether an encounter included physical (skin-to-skin) contact, how long it lasted, and how often a specific individual is encountered (Mossong et al., 2008); networks measured using electronic proximity sensors offer more precise estimates of the duration of an encounter (Stehlé et al., 2011), but only of an encounter