Cholera dynamics on community networks (13rit168) BIRS Research in Teams Report

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1 Introduction

In recent years there has been a significant amount of work devoted to modeling cholera dynamics, in part reflecting recent severe outbreaks in several countries and regions, including Haiti, Zimbabwe, Somalia, the Chad Basin, Sierra Leone, West Africa, and elsewhere. These outbreaks present a serious public health burden in the affected regions, and have spurred computational modeling efforts to forecast the dynamics of ongoing outbreaks and assess intervention strategies [3, 4, 5, 20, 35]. On the other hand, mathematical studies have also recently been conducted on cholera dynamics [27, 28, 32, 33]. Several aspects of the disease make cholera of interest for mathematical models. For example, multiple time scales are involved: the persistence time of cholera bacteria in a free-living state in aquatic environments, which can be on the order of months or more [21]; the duration of infection-derived immunity, which may range from several weeks to years [15, 18]; and the age-dependent infectivity of excreted bacteria, with freshly shed bacteria (on the order of hours) being nearly 3 orders of magnitude more infectious than older bacteria [1, 12, 19]. These features suggest rich dynamics, and complex oscillations are in fact observed empirically [2, 22]. Furthermore, due to the aquatic nature of cholera bacteria, and the possibility of indirect transmission from contaminated water as well as direct human to human transmission, spatial spread of the disease can occur by water transport, as well as by human movement. This gives rise to a natural set of networks to consider for cholera dynamics, linking different communities in a landscape. Indeed, geographical studies have examined empirical patterns of spatial spread for past cholera outbreaks, in order to assess different connectivities between communities and mechanisms for spread of the disease [23, 30, 31]. Cholera models thus provide a rich setting for studying disease dynamics in community networks.

The study of population dynamics on community networks has a long history in ecology and epidemiology, for example in the context of metapopulations [10, 11, 14, 17, 25]. A central mathematical question is to understand how network structure and community ("patch") characteristics combine to affect disease dynamics. Recently, we have started to make progress in answering this question for two specific aspects of cholera dynamics: invasibility [34], and global stability [9]. In particular, we find that a generalization of the group inverse of the graph Laplacian matrix of the network plays a fundamental role in disease invasion and global stability. This generalized group inverse arises through a Laurent series expansion of a perturbation of the graph Laplacian L:

$$(L + \varepsilon D)^{-1} = \frac{1}{\varepsilon} X_{-1} + X_0 + \varepsilon X_1 + \dots \tag{1}$$

Here D is a diagonal matrix containing the pathogen decay rates in each community, and ε is the ratio of time scales for pathogen movement relative to decay. The singular term X_{-1} is related to the rooted spanning trees of the network, and the zeroth order term X_0 is a generalization of the group inverse of L [34]. This generalized group inverse was the primary focus of our research at BIRS.

2 New results

The results in this section concern star networks (Figure 1), consisting of a single hub surrounded by $n-1$ leaves.

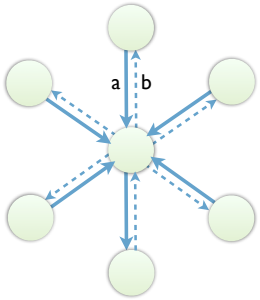

Figure 1: Star network schematic, with flow rate a from leaf to hub, and rate b from hub to leaf. For a balanced star network, $a = b$.

2.1 Generalized group inverse for star networks

A network is said to be *balanced* if the net inflow equals the net outflow for every vertex. For balanced star networks with equal pathogen decay rates in every community, we have the following explicit formula for X_0.

Proposition 1. *Consider a star network with n vertices, with vertex one corresponding to the hub and vertices two through n to the leaves. Let the network be balanced, with flow rate a between hub and leaf, and let the pathogen decay rates in each vertex be equal. Then X_0 is given by*

$$X_0 = \frac{1}{an^2}\begin{pmatrix} n-1 & -1 & -1 & \dots & -1 \\ -1 & n^2-n-1 & -n-1 & \dots & -n-1 \\ -1 & -n-1 & n^2-n-1 & \dots & \vdots \\ \vdots & \dots & \dots & \ddots & \vdots \\ -1 & -n-1 & \dots & -n-1 & n^2-n-1 \end{pmatrix}. \tag{2}$$

Expression (2) can be used to give insight into how differences in community characteristics between the hub and leaf patches affect $\mathcal{R}_0$. Let $\mathcal{R}_0^{(h)}$, $\mathcal{R}_0^{(\ell)}$ denote the basic reproduction numbers of the hub and leaf patches in isolation, respectively. Then the effect of X_0 on the domain basic reproduction number is approximately

$$\varepsilon \frac{n-1}{n^2} \frac{(\mathcal{R}_0^{(h)} - \mathcal{R}_0^{(\ell)})^2}{\mathcal{R}_0^{(h)} + (n-1)\mathcal{R}_0^{(\ell)}}. \tag{3}$$

This is reminiscent of the classic result that $\mathcal{R}_0$ is related to the variance in contact rates between groups [6, 7], and is consistent with the generalized group inverse X_0 being related to fluctuations from the stationary distribution generated by L [34].

2.2 Disease control on star networks

Cholera control strategies such as vaccination and/or water sanitation in patch i can be guided using the type reproduction number T_i [13, 24, 26]:

$$T_i = e_i^T P_i K (I - K + P_i K)^{-1} e_i,$$

provided $\rho(K - P_i K) < 1$, where K is the "next generation" matrix [36], P_i a projection, and ρ the spectral radius. Biologically, if a proportion more than $1 - \frac{1}{T_i}$ of the host population in patch i can be vaccinated, then the disease can be eradicated from the whole network. Suppose that resources are limited, so that interventions can only be implemented in a single patch (e.g. only a single patch can be vaccinated). In this case, the patch with the lowest type reproduction number is the optimal patch to vaccinate [13, 24, 26].

For star networks, the question becomes whether to vaccinate the hub or a leaf. We answer this question in two special cases: (i) where the diagonal entries of the second generation matrix K corresponding to the leaves are zero, and (ii) where the diagonal entry of K corresponding to the hub is zero. The diagonal entries of K can be interpreted as disease transmission within the corresponding patch. Scenario (i) thus corresponds to the hub being a disease hot spot, and scenario (ii) corresponds to the leaves being hot spots. In case (i), $T_{hub} < T_{leaf}$: when the hub is a disease hot spot, the optimal control strategy is to target the hub. In case (ii), the sign of $T_{hub} - T_{leaf}$ depends upon the degree of flow between the hub and leaves, relative to patch transmission within the leaves. When the flow is small, the optimal strategy is to target a leaf (i.e. the disease hot spot). However, when the flow between hub and leaf is large, the optimal strategy is to target the hub, despite the lack of disease transmission within the hub. The optimal control strategy is thus influenced by both the network structure as well as the individual patch properties.

2.3 Radius of convergence of the Laurent series

The radius of convergence of the Laurent series (1) is determined by the spectral radius of $X_0 D$. This is due to the fact, proved by Langenhop [16], that the higher order terms in Laurent series involve power of X_0:

$$X_k = (-X_0 D)^k X_0, \; k > 0. \tag{4}$$

The Laurent series (1) thus involves a Neumann series, from which the radius of convergence can be deduced.

Proposition 2. *The Laurent series* (1) *converges for* $0 < \varepsilon < \frac{1}{\rho(X_0 D)}$*, where* ρ *denotes the spectral radius.*

3 Open problems

3.1 Generalized group inverse for star networks with unequal pathogen decay

Consider a balanced star graph with two different pathogen decay rates, δ_h in the hub, and δ_l in the leaves. We conjecture that in this case the generalized group inverse X_0 has the following form:

$$[(n-1)\delta_l + \delta_h]^2 [X_0]_{ij} = \begin{cases} (n-1)\delta_l^2, & i = j = hub, \\ -\delta_h \delta_l, & i = hub, j = leaf \\ -\delta_l(2\delta_h + (n-1)\delta_l), & i, j = leaf, i \neq j \\ \delta_h^2 + 2(n-2)\delta_h\delta_l + (n-1)(n-2)\delta_l^2, & i = j = leaf \end{cases} \tag{5}$$

Note that (5) reduces to (2) when $\delta_h = \delta_l = 1$.

3.2 Disease control on networks with bottlenecks to mixing

For star networks, the hub serves as a bottleneck to mixing, in the sense that flow between leaves occurs solely through the hub. Optimal control strategies hinge upon the degree of flow through the hub (see Section 2.2). Analogous results are likely to hold for non-star networks with bottlenecks to mixing. Bottlenecks to mixing and consequent clustering of patches together into meta-communities are related to the generalized group inverse X_0 [34], suggesting that X_0 may be used to help guide disease control efforts. Analytical and computational work are both needed for understanding the relationship between bottlenecks, X_0, and optimal disease control for general networks.

3.3 Applications and extensions

Applying the mathematical ideas described here to specific settings or cholera outbreaks is of interest. A key step is to estimate connectivity between the communities in question. Tracer studies and hydrological modeling may provide opportunities to estimate water connectivity. Knowledge of pathogen dynamics in environmental water sources is critical for understanding cholera dynamics [8], providing both a need and an opportunity for empirical studies. Recent years have seen an explosion of data on human movements (e.g. [29]). While the mathematical framework considered thus far has assumed that infected individuals are too sick to move, this assumption can be relaxed and the modeling framework extended to situations where pathogen movement is primarily through human movements. For diseases where the infectious period is long relative to transit times between communities, the same Laurent series approach taken here can be used to examine $\mathcal{R}_0$ and disease invasibility.

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