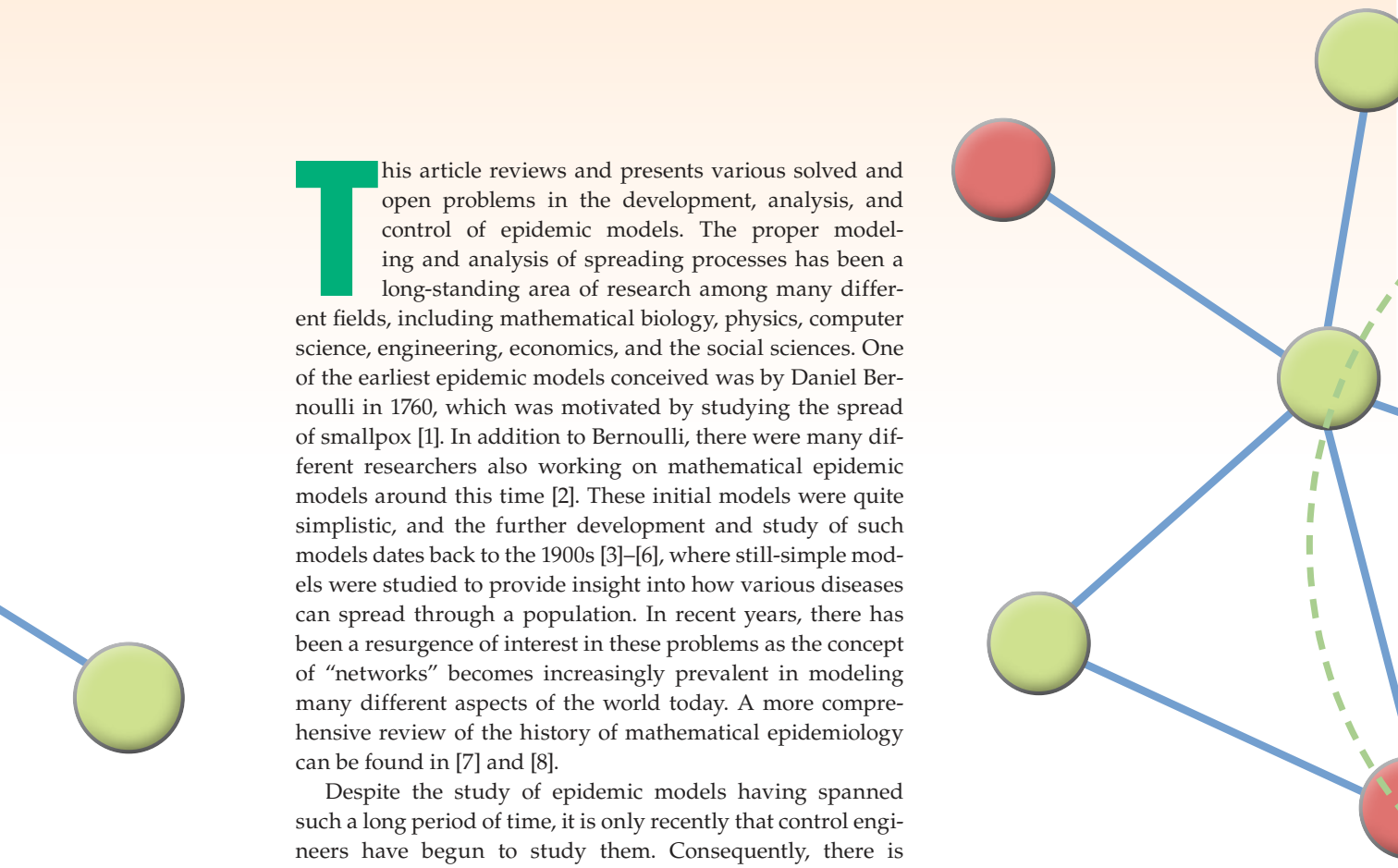
CAMERON NOWZARI, VICTOR M. PRECIADO,
and GEORGE J. PAPPAS

Analysis and Control of Epidemics

A SURVEY OF SPREADING PROCESSES ON COMPLEX NETWORKS



This article reviews and presents various solved and open problems in the development, analysis, and control of epidemic models. The proper modeling and analysis of spreading processes has been a long-standing area of research among many different fields, including mathematical biology, physics, computer science, engineering, economics, and the social sciences. One of the earliest epidemic models conceived was by Daniel Bernoulli in 1760, which was motivated by studying the spread of smallpox [1]. In addition to Bernoulli, there were many different researchers also working on mathematical epidemic models around this time [2]. These initial models were quite simplistic, and the further development and study of such models dates back to the 1900s [3]–[6], where still-simple models were studied to provide insight into how various diseases can spread through a population. In recent years, there has been a resurgence of interest in these problems as the concept of "networks" becomes increasingly prevalent in modeling many different aspects of the world today. A more comprehensive review of the history of mathematical epidemiology can be found in [7] and [8].

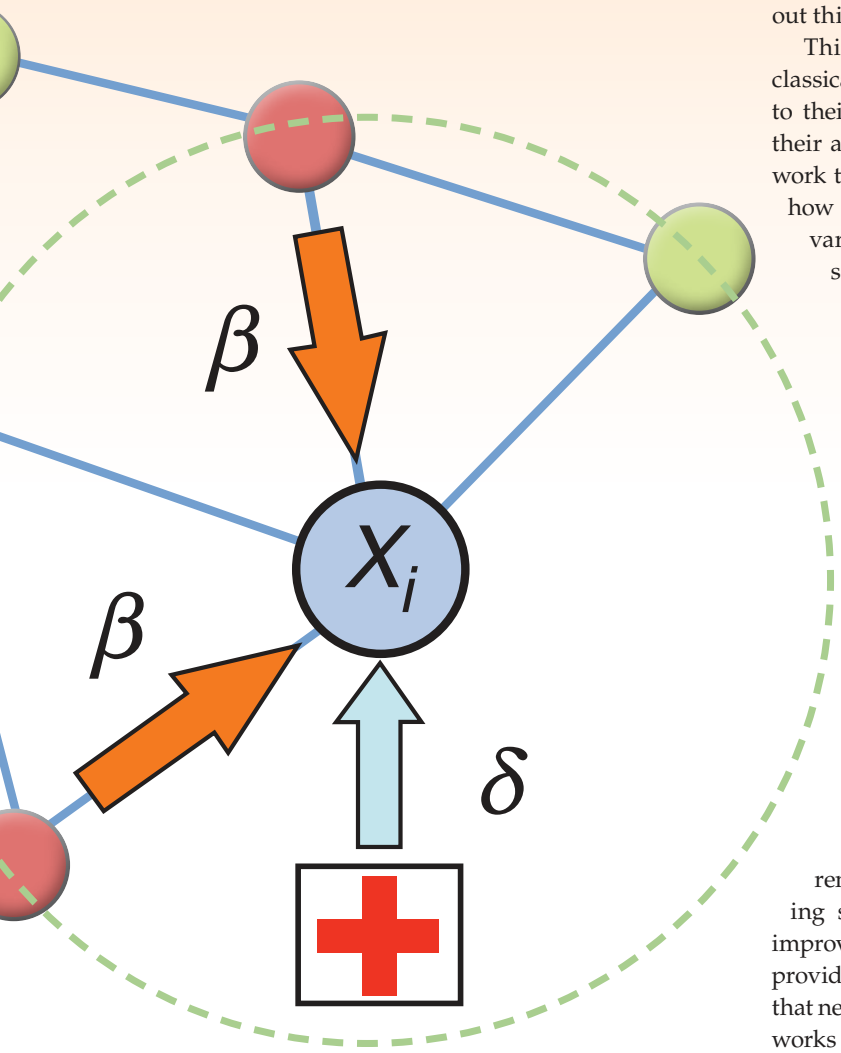
Despite the study of epidemic models having spanned such a long period of time, it is only recently that control engineers have begun to study them. Consequently, there is already a vast body of work dedicated to the development and

Digital Object Identifier 10.1109/MCS.2015.2495000
Date of publication: 19 January 2016

1066-033X/16©2016IEEE

Deterministic and stochastic models in the context of both population and networked dynamics have been presented and analyzed.

analysis of epidemic models, but far fewer works that provide proper insight and machinery on how to effectively control these processes. The focus of this article is to provide an introductory tutorial on the latter for new engineers looking to enter the field of spreading processes on complex networks. Furthermore, this article details some classical and recent results in the literature while also identifying numerous open problems that can benefit from the collective knowledge of optimization and control theorists.



Although this article focuses on the context of epidemics, the same models and tools presented are directly applicable to many different spreading processes on complex networks. Examples include the adoption of an idea or rumor through a social network like Twitter, the consumption of a new product in a marketplace, the risk of receiving a computer virus through the World Wide Web, and, of course, the spreading of a disease through a population [9]–[11]. For this reason, the terms individuals, people, nodes, and agents may be used interchangeably throughout this article.

This article begins by introducing and analyzing some classical stochastic epidemic models and their connections to their deterministic approximations. These models and their analysis are then extended to consider arbitrary network topologies. After providing a basic understanding of how spreading processes evolve, this article formulates various control problems for which some demonstrative solutions are presented.

In particular, three main categories of control problems are discussed. The first category is called *spectral control and optimization*, where a fixed number of resources must be optimally allocated among a population to best mitigate the effects of an undesired disease. The second category is *optimal control*, where optimal feedback control strategies are sought out, usually in the sense of balancing some control costs against performance. Unfortunately, there has not yet been much work done in this second category for arbitrary networks. Consequently, the third category is *heuristic feedback control*, where the model and feedback control strategies are codeveloped to yield a single closed-loop system of the model, whose stability properties can then be studied.

After describing the main shortcomings in the current literature for controlling epidemics and highlighting some recent preliminary works that are aimed at improving the current state of the art, this article closes by providing some insight into the current research challenges that need to be addressed to fully harness the power of these works and make a real societal impact.

MODELING AND ANALYSIS OF EPIDEMICS

Before jumping into the class of models studied here, note that there are many ways to model spreading processes. The underlying common factor that ties almost all epidemic models together is the existence of "compartments" into which individuals in a population are divided. The two most common compartments that exist in essentially every epidemic model are susceptible (S) and infected (I) [6], [7], [12]. In models that contain only these two compartments, a given population is initially divided into them. S represents individuals who are healthy but susceptible to becoming infected, and I represents individuals who are infected but are able to recover. From this basic compartmentalization, there are numerous ways that interactions within the population can be modeled.

The main focus of this article is on agent-based models, where individuals can randomly move from one compartment to another with some defined rates rather than deterministically, since stochastic models can better capture the dynamics of a spreading disease, such as influenza. For example, although an individual is more likely to become infected when surrounded by many infected individuals, it is not a guarantee.

Considering the simplest two-compartment model, healthy individuals can randomly transition from S to I with some infection rate that is a result of interactions with infected individuals. Similarly, infected individuals can randomly transition from I to S with some recovery rate that is a result of recovering from the infection. More details on how these rates are defined are provided later. Figure 1 shows the simple interaction described above.

In addition to models with only two compartments, there are also other epidemic models aimed at capturing more features of realistic diseases and spreading processes. Capturing more features of a particular disease or process is often done by adding more compartments, such as a removed (R) compartment representing individuals who are no longer susceptible to the infection. This compartment might refer to a deceased, vaccinated, or immune individual. For instance, this additional compartment may be helpful in modeling a disease like chicken pox, where an individual gains immunity after having recovered from the disease the first time. Other compartments have also been considered in the literature to study the effect of, for example, an incubation period, partial immunity, or quarantine in the spreading dynamics [13]–[19].

For brevity, this section focuses on two of the oldest epidemic models, known as the susceptible-infected-removed (SIR) and the susceptible-infected-susceptible (SIS) models [6]. Let N be the total number of individuals in a population. The state of node $i \in \{1,\ldots,N\}$ at time t is denoted by $X_i(t) \in \{S,I,R\}$. The state of the entire population is collected in a state vector $X(t) = (X_1(t),\ldots,X_N(t))^T$. The evolution of the states is then described by a Markov process as follows. A node i infected at time t recovers at a fixed rate $\delta_i > 0$. In other words, if node i is infected at time t, the probability that this node loses its infection in the time slot $(t, t+\Delta t]$ for small Δt is given by $\delta_i \Delta t + o(\Delta t)$. Depending on which model is used, this recovery rate describes the transition out of the infected state by

$$\Pr(X_i(t+\Delta t) = R \,|\, X_i(t) = I) = \delta_i \Delta t + o(\Delta t), \quad \text{(SIR)}$$
$$\Pr(X_i(t+\Delta t) = S \,|\, X_i(t) = I) = \delta_i \Delta t + o(\Delta t). \quad \text{(SIS)}$$

The above represents an *endogenous* transition, which occurs internally within each node, independent of the states of other nodes [20].

Similarly, an individual i that is susceptible at time t becomes infected at a rate β_i^{eff} that depends on the state of the entire population $X(t)$. This transition is known as *exogenous* because it is influenced by factors external to the node itself. These transitions are discussed at length in the sections to come. Figure 2 shows the simple interaction described above for the SIR model.

Remark 1: Other Spreading Models

This article excludes chain binomial models (such as the Reed–Frost model [8], [21]) and other similar types of models from percolation theory. Depending on the application at hand, the model for the spreading dynamics can vary. The main difference between the models considered here and ones like the Reed–Frost model is that this article focuses on models that allow infected individuals to continuously try to infect healthy ones. In the Reed–Frost model, an infected person only has one chance of

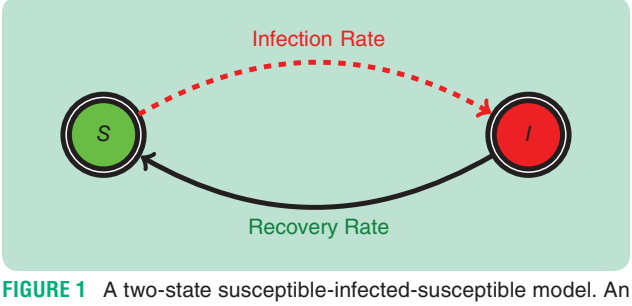


FIGURE 1 A two-state susceptible-infected-susceptible model. An individual in the infected state I transitions to the healthy or susceptible state S with some recovery rate and from the susceptible state to the infected state with some infection rate.

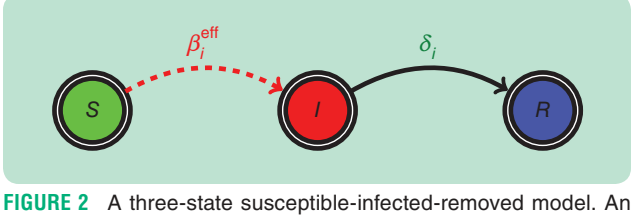


FIGURE 2 A three-state susceptible-infected-removed model. An individual i in the susceptible state S can transition to the infected state I with some infection rate β_i^{eff} and from the infected state I to the removed state R with some recovery rate δ_i.

infecting a healthy person. However, when thinking of a virus like the flu, a healthy person is continuously in danger of becoming sick when in contact with an infected individual, rather than a one-time chance. Conversely, the Reed–Frost model might be more suitable for modeling the spreading of an e-mail virus rather than an infectious biological disease, where a recipient might only decide one time whether or not to open the e-mail; see [8] and [21] for further details.

The study of chain binomial models and related problems is indeed an active area of research that draws more from results in computer science rather than the control-theoretic approaches taken in this article. Many works exist along this line on forecasting the cascading effects of a single infection or failure on a network [22], [23] and how they can be mitigated through vaccination [24]. On the other hand, it may be of interest to find the most influential nodes or to determine where to start an infection in a network to reach as many people as possible [25], [26]; this problem is often referred to as a seeding problem. Further extensions study attack and vaccination strategies on these models [27], and even cases in which there are multiple contagions on multiple networks [28].

Classical Models

Based on the above discussion, the dynamics of the SIR model is described by a 3^N-dimensional Markov process. The exponential size of the state space makes this model hard to analyze. One standard method to simplify the analysis is to consider the evolution of the total number of healthy and infected individuals rather than the state of each individual separately. These dynamics are commonly referred to as *population dynamics* [29], [30]. Furthermore, the recovery and infection rates are often assumed to be the same for all individuals; that is, $\delta_i = \delta$ and $\beta_i^{\text{eff}} = \beta^{\text{eff}}$, for all i. Standard population dynamics assume a *well-mixed population*, which means all individuals affect and are affected by all other individuals equally. Figure 3 shows the described interactions of this well-mixed population.

Stochastic Population Models

The SIR population model is described as follows. Letting $N^I(t), N^R(t) \in \{0,1,\ldots,N\}$ be the number of infected and removed individuals at some time t, respectively, the number of susceptible individuals is necessarily given by $N^S(t) = N - N^I(t) - N^R(t)$. A common choice for the infection rate is given by $\beta^{\text{eff}} = \beta N^I N^S$ [7], [31], [32] for some $\beta > 0$, known as the mass-action law. In other words, the rate at which the total number of susceptible individuals becomes infected is proportional to the product of the number of susceptible and infected individuals in the population. The state at some time $t + \Delta t$ is then given by

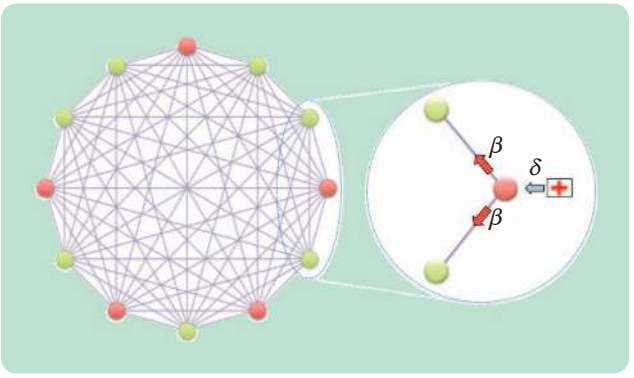


FIGURE 3 Population dynamics of the two-state susceptible-infected-susceptible model. These models assume a well-mixed population, meaning that each individual in the population is equally likely to contract a disease from anyone else in the population. An infected individual (red) naturally recovers at a rate $\delta > 0$, depicted by the red cross. A healthy individual (green) is affected by each infected individual in the population with rate β, depicted by the red arrows.

$$(N^I, N^R) \to \begin{cases} (N^I + 1, N^R) & \text{with probability } \beta N^I N^S \Delta t + o(\Delta t), \\ (N^I - 1, N^R + 1) & \text{with probability } \delta N^I \Delta t + o(\Delta t), \\ (N^S, N^R) & \text{with probability } 1 - (\beta N^I N^S + \delta N^I)\Delta t + o(\Delta t). \end{cases} \tag{1}$$

For the SIS model, there are no individuals in the removed state, forcing $N^R = 0$ at all times, which simplifies the dynamics to

$$N^I \to \begin{cases} N^I + 1 & \text{with probability } \beta N^I N^S \Delta t + o(\Delta t), \\ N^I - 1 & \text{with probability } \delta N^I \Delta t + o(\Delta t), \\ N^I & \text{with probability } 1 - (\beta N^I N^S + \delta N^I)\Delta t + o(\Delta t). \end{cases} \tag{2}$$

Removing the explicit definition of time, the SIS process can then be seen as a random walk on a line for $N^1 > 0$ [32]–[35] (a similar Markov chain can be described for the SIR model)

$$\begin{aligned} N^I &\to N^I + 1 \text{ with probability } \frac{\beta(N - N^I)}{\beta(N - N^I) + \delta}, \\ N^I &\to N^I - 1 \text{ with probability } \frac{\delta}{\beta(N - N^I) + \delta}. \end{aligned} \tag{3}$$

An important observation about (3) is that it is a Markov chain with a single absorbing state $N^I = 0$ in which all agents are healthy. In other words, once the entire population is healthy, the infection cannot suddenly reemerge. It is known from the theory of Markov chains that, given enough time, the infection will eventually die out with probability one (see [36] for a review of Markov chains and relevant properties). Thus, the study of these systems is often interested in answering the question of *when* or *how*

quickly the infection will die out. This question is revisited in Remark 3.

To further simplify the problem, various works often consider a deterministic approximation of these stochastic dynamics. In fact, the simpler deterministic dynamics introduced next predate the introduction of the stochastic model above [6].

Deterministic Population Models

The models presented next are perhaps the two most studied epidemic models in the literature and are covered in a large number of books [6], [8], [10]–[12], [37]–[44]. These books also discuss a variety of extensions, including more complicated disease models that have more than two states, consider birth and mortality rates, allow for different types of infection rates, and different categories for each disease state, for example, based on age or gender. Only the most basic models are presented here to help simplify the discussion.

Assuming a large population size N, define $p^I = N^I/N$ and $p^S = (N - N^I - N^R)/N$ as the fractions of infected and susceptible individuals, respectively. Then, the deterministic SIR version of (1) can be written as

$$\begin{aligned} \dot{p}^S &= -\beta p^I p^S, \\ \dot{p}^I &= \beta p^I p^S - \delta p^I, \end{aligned} \tag{4}$$

and the deterministic SIS version of (2) as

$$\begin{aligned} \dot{p}^S &= -\beta p^I p^S + \delta p^I, \\ \dot{p}^I &= \beta p^I p^S - \delta p^I. \end{aligned} \tag{5}$$

These are derived by leveraging Kurtz's theorem while assuming N to be very large [43]. Kurtz's theorem is essentially a law of large numbers for a Markov process that says as N approaches its thermodynamic limit, the deterministic and stochastic systems behave similarly.

Consider the deterministic SIS model (5). Because $N^R = 0$ and the population size N is fixed, $p^S = 1 - p^I$ and (5) are redundant and can be simplified to

$$\dot{p}^I = \beta p^I (1 - p^I) - \delta p^I. \tag{6}$$

Given an initial condition $p^I(0)$, the solutions of (6) can be analytically solved [8], [45], [46] (note that the SIR model can also be solved analytically). The solution of the SIS model is

$$p^I(t) = \begin{cases} \dfrac{e^{(\beta-\delta)t}}{\dfrac{\beta(e^{(\beta-\delta)t}-1)}{\beta-\delta} + \dfrac{1}{p^I(0)}}, & \beta \neq \delta, \\ \dfrac{1}{\beta t + \dfrac{1}{p^I(0)}}, & \beta = \delta. \end{cases}$$

Given the exact solution of $p^I(t)$, the following result characterizes its equilibrium points.

Theorem 2: Solutions to Deterministic Population Model

The solution of $p^I(t)$ approaches $1 - \delta/\beta$ as $t \to \infty$ for $\beta > \delta$, and 0 as $t \to \infty$ for $\beta \leq \delta$.

Remark 3: Deterministic Versus Stochastic Population Models

Note that the deterministic models are only approximations of the stochastic models. A natural question is then to see what the threshold result of Theorem 2 can tell us about the original stochastic model (3). The first thing to note is that in the stochastic model, given enough time, the system will reach the disease-free state with probability one. However, Theorem 2 shows that for $\beta > \delta$, the deterministic model will converge to an endemic equilibrium, meaning the disease never dies out. Thus, rather than studying the equilibrium values of the two models, the authors in [35], [45], and [47] look at the expected time $E[T]$ for the stochastic model to reach the disease-free equilibrium. Interestingly, they are able to show that for $\beta < \delta$, the expected

Graph Theory

A *graph,* a mathematical description of a given network, consists of distinct nodes, or vertices, and links between the nodes, or edges, that describe the interactions between the nodes. In the context of epidemics, the meaning of a single node depends on the granularity of the considered model. For example, a *node* at the lowest level can represent a single person and *links* to other nodes can represent the interactions this person has with others. On a much higher level, a single node can represent an entire city of people, and links to other nodes can represent the interactions this city has with others, for example, traffic flow between cities. See "Metapopulation Models" for further details.

Formally, a *directed graph* $\mathcal{G} = (V, E)$ is a pair consisting of a set of N vertices V and an ordered set of edges $E \subset V \times V$. The adjacency matrix $A \in \mathbb{R}_{\geq 0}^{N \times N}$ of $\mathcal{G}$ satisfies $a_{ij} = 1$ if and only if $(v_i, v_j) \in E$. Edges are directed, meaning that they are traversable in one direction only. The sets of *in-neighbors* and *out-neighbors* of $v \in V$ are, respectively

$$\begin{aligned} \mathcal{N}^{\text{in}}(v) &= \{v' \in V \,|\, (v', v) \in E\}, \\ \mathcal{N}^{\text{out}}(v) &= \{v' \in V \,|\, (v, v') \in E\}. \end{aligned}$$

A graph is *undirected* if for all $a_{ij} = 1$, it is also true that $a_{ji} = 1$. In this case, the set of in-neighbors and out-neighbors for each node are identical.

A *directed path* P, or in short path, is an ordered sequence of vertices such that any two consecutive vertices in P form an edge in E. A graph $\mathcal{G}$ is *strongly connected* if, for all vertices $v \in V$, there exists a path to all other vertices $v' \in V$.

time $E[T]$ is upper-bounded by $N\beta/\delta$. In this case, the disease is said to die out "quickly." On the other hand, when $\beta > \delta$, the expected time $E[T]$ grows exponentially with N.

The analysis of the deterministic model results in a precise threshold result that translates directly to the stochastic model as discussed in Remark 3. Threshold conditions are often given in terms of a *reproduction number* R_0, which is the expected number of individuals a single infected individual will infect [7], [48] over the course of its infection period. In other words, given a fully healthy population, if a person i is randomly infected, R_0 is the expected number of other individuals who will become infected over the course of person i's infection. The reproduction number is a useful metric with a critical value of $R_0 = 1$. When $R_0 < 1$ the disease does not spread quickly enough, resulting in a decay in the number of infected individuals (in expectation). On the other hand, when $R_0 > 1$ the infected population grows over time (in expectation) [10]. In the simple model considered above, the reproduction number is given by β/δ. Furthermore, the exact solutions and asymptotic behavior of the system can be found analytically.

The reproduction number is an important parameter that epidemiologists are interested in identifying for various diseases and environments [49] because it is a single number that can predict whether a certain outbreak of a disease will become an epidemic or die out on its own. Of course, the problem is that computing R_0 for a particular disease is not trivial because there is no database for things like infection rates and recovery rates for various diseases.

The main drawback of these population models is that they are crude models derived by making many simplifying assumptions including i) a homogeneous incidence rate β^{eff} and recovery rate δ for all individuals, ii) a low number of states, iii) a constant population size, and iv) a well-mixed population (or a contact network that is a complete graph). Particularly in the context of diseases spreading in a population, these simplifying assumptions might be a limiting factor in properly modeling the dynamics. For instance, homogeneous incidence rates and a well-mixed population assume everyone in the population equally affects and is equally affected by everybody else. However, it is more reasonable to think that a person is much more likely to contract a disease from an infected family member rather than an infected stranger. These drawbacks were evident when scientists attempted to estimate the reproduction number of SARS in China in 2002–2003 but grossly overestimated it. This incorrect estimation of R_0 then led to SARS scares making global headlines, which eventually fizzled out because the actual reproduction number was far lower than estimated due to the crude population models. More details on how this error occurred can be found in [50], but the upshot is that more refined models are needed.

Network Models

To create more refined epidemic models, it is clear that the entire population cannot just be lumped into two compartments defined by a single number. Ideally, the model would be able to account for the states of all N individuals independently and allow for arbitrary interactions among them. Not surprisingly, analyzing these models is not a trivial task.

This section focuses on spreading processes on a given, arbitrary topology. Before jumping into the models of interest, it should be noted that there is a body of work dedicated to extending the population models to network models with simple topologies. More specifically, before jumping to completely arbitrary networks, there are many works that study various, specific structures. For instance, some works study how a disease spreads on a two-dimensional lattice or star graph [51]–[53]. Others consider more complex interconnection patterns, such as power-law and small-world networks, which still have some exploitable structure [54], [55]. In this context, a common method to analyze these networks is to assume that nodes are infected at a rate proportional to the number of neighbors they have [56]–[61]. These methods are justified depending on the assumptions enforced on the network topology. A review of these types of models can be found in [62]. The following instead focuses on epidemiological models on arbitrary network topologies.

Stochastic Network Models

This section studies an SIS epidemic model described as a continuous-time networked Markov process. Consider a network of N nodes represented by a connected, undirected graph $\mathcal{G} = (V, E)$ where V is the set of nodes and $E \subset V \times V$ is the set of edges. The adjacency matrix $A \in \mathbb{R}_{\geq 0}^{N \times N}$ of the graph is defined component-wise as $a_{ij} = 1$ if node i can be directly affected by node j, and $a_{ij} = 0$ otherwise. See "Graph Theory" for further details.

Let $X_i(t)$ denote the state of node i at time t, where $X_i(t) = 1$ indicates that i is infected and $X_i(t) = 0$ indicates that i is healthy at time t. Infected nodes can transmit the disease to their neighbors in the graph $\mathcal{G}$ with rate $\beta > 0$. Simultaneously, infected nodes recover from the disease with rate $\delta > 0$. Figure 4 shows the described interactions on an arbitrary network. The SIS spreading process can then be modeled using the Markov process

$$\begin{aligned} &X_i : 0 \to 1 \quad \text{with rate } \beta \textstyle\sum_{j \in N_i} X_j, \\ &X_i : 1 \to 0 \quad \text{with rate } \delta. \end{aligned} \tag{7}$$

Notice that there exists one absorbing state in this Markov process (corresponding to the disease-free equilibrium) that can be reached from any state $X(t) = [X_1(t), \ldots, X_N(t)]^T$. This absorbing state implies that, regardless of the initial condition $X(0)$, the epidemic eventually dies out in finite time with probability one. A useful measure of the virality of a spreading process is then the expected time $E[T]$ it takes for the epidemic to die out. In [55] and [63], the following

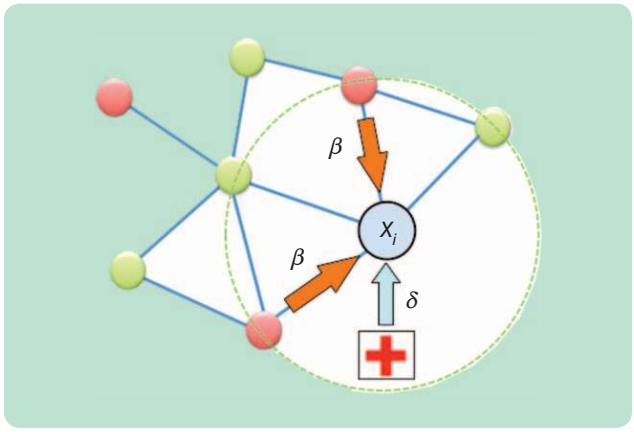


FIGURE 4 The network dynamics of the two-state susceptible-infected-susceptible model. A node i has a natural recovery rate δ, depicted by the red cross, at which it transitions from the infected state I to the susceptible state S and is affected by each infected neighbor j with rate β, depicted by the orange arrows.

threshold conditions are provided in terms of the infection strength $\tau = \beta/\delta$.

Theorem 4: Threshold for Sublinear Expected Time to Extinction

If $\tau < 1/(\lambda_{\max}(A))$, where $\lambda_{max}(A)$ is the maximum real eigenvalue of A, then

$$E[T] \leq \frac{\log N + 1}{\delta - \beta\lambda_{\max}(A)},$$

for any initial condition $X(0)$.

Note that Theorem 4 only provides a sufficient condition for "fast" extinction of a disease. Despite many efforts to determine whether this condition is also necessary, it remains an open question on general graphs at the time of writing. The works [43], [64], and [65] show that there exists some critical value τ_c of the infection strength for which the expected time to extinction grows exponentially with N when $\tau \geq \tau_c$. The following result formalizes this statement and provides a lower bound on the critical values [66], [67]; however, it is noted that stronger statements exist when considering graphs with a fixed structure (such as a lattice or star) [43].

Theorem 5: Threshold for Exponential Expected Time to Extinction

There exists

$$\tau_c \geq \frac{1}{\lambda_{\max}(A)}$$

such that, for $\tau > \tau_c$, the expected time to extinction $E[T] = O(e^{kN})$, where k depends on τ and the structure of the graph $\mathcal{G}$.

The maximum eigenvalue $\lambda_{\max}(A)$ of an adjacency matrix is a parameter that captures how "tightly connected" the graph is. More connections usually mean a larger $\lambda_{\max}(A)$. Intuitively, the results of Theorems 4 and 5 are saying that the more tightly connected the graph is, the easier it is for a disease to spread.

Note that although the result of Theorem 4 provides an upper bound on the *expectation* of the extinction time, the possibility of a persisting epidemic is not ruled out. For example, it has been shown for star graphs that, regardless of the infection strength τ, there is a positive probability that the time to extinction is superpolynomial in the number of nodes [54], [55], [68]. Furthermore, for high-degree or scale-free networks (such as preferential attachment [54] or power-law configuration model graphs [55]), it has been shown that this threshold goes to zero as the number of nodes increases [69] because the maximum eigenvalue grows unbounded with N.

Deterministic Network Models

This section presents the deterministic version of the SIS dynamics over arbitrary networks [20], [70]–[74]. For now, assume homogeneous recovery and infection rates; this assumption will be relaxed in the following section. The natural recovery rate of each node is given by $\delta > 0$, and the infection rate at which a node is affected by infected neighboring nodes is $\beta > 0$. The dynamics of the spread are described by the set of ordinary differential equations

$$\dot{p}_i = -\delta p_i + \sum_{j=1}^{N} a_{ij}\beta p_j(1 - p_i), \tag{8}$$

where $p_i(t) \in [0,1]$ describes the (approximated) probability that an individual i is infected at time t. See "Networked Mean-Field Approximations" for further details. This variable has another interesting interpretation in the context of metapopulation models. In a metapopulation model, each node does not represent an individual, but a large subpopulation (such as an entire district or city). In this context, p_i can be interpreted as the fraction of the ith subpopulation that is infected. See "Metapopulation Models" for further details.

As with all other epidemic models, the disease-free equilibrium $p_i = 0$ for all $i \in \{1,\ldots,N\}$ is a trivial equilibrium of the dynamics. The stability properties of this equilibrium are discussed next. Letting $p = (p_1,\ldots,p_N)^T$ and recalling the infection strength $\tau = \beta/\delta$, the following result from [74]–[77] characterizes the convergence properties of these dynamics.

Theorem 6: Threshold Condition for Networks

Given the dynamics (8) for any $p(0) \neq 0$, the equilibrium $p^* = 0$ is globally asymptotically stable if and only if $\tau \leq 1/\lambda_{\max}(A)$. Furthermore, for $\tau > 1/\lambda_{\max}(A)$, there exists $p^{**} \in \mathbb{R}^N_{(0,1)}$ such that p^{**} is globally asymptotically stable.

Remark 7: Deterministic Versus Stochastic Network Models

Similar to the discussion in Remark 3, there is a connection between the deterministic result in Theorem 6 and the

Metapopulation Models

This article often refers to "individuals" and the state of "all individuals" in a network. However, especially in the context of diseases spreading through populations, the number of individuals N in a given network can be quite large. Instead of considering the entire population of interest together, metapopulation models allow groups of individuals to be lumped together into subpopulations under some assumptions.

Consider the heterogeneous network SIS dynamics (9). This model is originally introduced in this article with p_i referring to the probability that an individual i is infected (see "Networked Mean-Field Approximations" for further details). However, this model means an N-dimensional system must be analyzed to properly study how this model evolves, which can be difficult for large N.

Instead of studying the state of each individual in the population separately, $M \ll N$ subpopulations can be created to approximate the dynamics of the entire N-dimensional system. This reduction was originally done and analyzed for $M = 2$ and turned out to be easily extendable [S1].

Let $i \in \{1,\ldots,M\}$ denote the ith subpopulation with n_i individuals, where each individual from the original population with N people is assigned to exactly one subpopulation. In other words, the total population is still fixed at $\sum_{j=1}^{M} n_j = N$. Note that the number of individuals in each subpopulation do not need to be the same.

The dynamics of the metapopulation model is then defined assuming that each subpopulation i is well mixed and has a homogeneous recovery rate δ_i'. In other words, within each subpopulation i, each individual is assumed to have equal contact with everyone else. This method is the same way the deterministic SIS population dynamics (6) are derived; however, subpopulation models require the extra consideration that subpopulations can affect each other as well. In other words, the population dynamics (6) can be seen as a metapopulation model with $M = 1$ subpopulation. The infection rate β_{ji}' captures the effect that subpopulation j has on subpopulation i. Note that it is not required that $\beta_{ji}' = \beta_{ij}'$ nor does it make sense to. Since subpopulations can have different numbers of people, it is reasonable to think that one subpopulation i can affect another subpopulation j more than j can affect i. Letting x_i denote the fraction of individuals in subpopulation i that are infected, the dynamics of the metapopulation model can be described by

$$\dot{x}_i = -\delta_i' x_i + \sum_{j=1}^{M} \beta_{ji}' x_j (1 - x_i). \tag{S1}$$

The original N-dimensional system has now been reduced to M-dimensional. In addition to the size reduction, it might make more sense to begin by considering a metapopulation model instead of the original network model. Properly defining the full network SIS dynamics (9) requires parameters that describe the natural recovery rates and interconnections of all individuals within the population. Instead, it is more reasonable to believe that these parameters can be estimated for groups of people at a time, and a reasonable metapopulation model can be described with the same level of granularity. State information in the metapopulation model can be determined by looking at numbers of infected individuals in a given subpopulation compared to the total numbers of individuals n_i in this subpopulation. For example, a node $i \in \{1,\ldots,M\}$ at the lowest level of granularity recovers the full network SIS dynamics with $M = N$, where each node represents a single person and links to other nodes represent the interactions this person has with others. On a much higher level with $M \ll N$, a single node can represent an entire city of people, and links to other nodes can represent the interactions this city has with others, for example, traffic flow between cities.

REFERENCE

[S1] N. T. J. Bailey, "Macro-modelling and prediction of epidemic spread at community level," *Math. Model.*, vol. 7, no. 5–8, pp. 689–717, 1986.

stochastic result in Theorem 4. Since $X = 0$ is an absorbing state, the stochastic dynamics will eventually reach the disease-free state with probability one. However, Theorem 6 claims that for $\beta\lambda_{\max}(A) > \delta$ the deterministic model will converge to an endemic equilibrium, meaning the disease never dies out. To resolve this apparent contradiction, recall the expected time $E[T]$ for the stochastic model to reach the disease-free equilibrium. Remarkably, Theorem 4 provides a sufficient condition for a disease to quickly die out that is in agreement with the threshold result of Theorem 6. However, as suggested by Theorem 5, it has not yet been shown whether the same threshold condition holds for persistence of the disease in the stochastic network model.

A major drawback of (8) is that it assumes a constant infection rate β and recovery rate δ for all individuals. More refined models allow different recovery rates for each person and different infection rates for each type of contact, which allows for a more general model that can capture more realistic scenarios. For instance, it is not realistic to assume that everyone an individual comes in contact with has an equal chance to infect him or her. A family member or a spouse is much more likely to infect him or her than a stranger or even a casual acquaintance. To capture these heterogeneous effects in real populations, heterogeneous network models are developed next.

Heterogeneous Network Models

This section considers the dynamics of the SIS model with heterogeneous recovery and infection rates over arbitrary strongly connected directed graphs $\mathcal{G} = (V, E)$. The recovery rate of node i is given by $\delta_i > 0$. The infection rates are instead considered to be edge dependent. In other words,

Networked Mean-Field Approximations

The method of going from a stochastic model to a deterministic mean-field approximation is certainly not one that should be overlooked. The derivations of these approximations, their accuracy, and they say about the original stochastic models is an area of research all by itself.

The following exposition briefly reviews how to go from the stochastic model (7) to the deterministic one (8). Recall the stochastic model

$$X_i : 0 \to 1 \quad \text{with rate } \beta \sum_{j \in \mathcal{N}_i} X_j,$$
$$X_i : 1 \to 0 \quad \text{with rate } \delta.$$

Given the entire state $X(t)$ at some time t, the probability of state i at a future time $t' = t + \Delta t$ for small Δt is given by

$$\begin{aligned}
&P(X_i(t') = 0 \mid X_i(t) = 1, X(t)) = \delta \Delta t + o(\Delta t),\\
&P(X_i(t') = 1 \mid X_i(t) = 1, X(t)) = 1 - \delta \Delta t + o(\Delta t),\\
&P(X_i(t') = 1 \mid X_i(t) = 0, X(t)) = \beta \sum_{j \in \mathcal{N}_i} X_j(t) \Delta t + o(\Delta t),\\
&P(X_i(t') = 0 \mid X_i(t) = 0, X(t)) = 1 - \beta \sum_{j \in \mathcal{N}_i} X_j(t) \Delta t + o(\Delta t).
\end{aligned}$$

As Δt goes to zero in these forward Kolmogorov equations, the exact dynamics of the expectation can be written as

$$\begin{aligned}
\frac{dE[X_i]}{dt} &= -E\left[\delta + (1 - X_i)\beta \sum_{j \in \mathcal{N}_i} X_j(t)\right]\\
&= -E[X_i]\delta + E\left[(1 - X_i)\beta \sum_{j \in \mathcal{N}_i} X_j(t)\right].
\end{aligned}$$

The complication now comes from the term $E[X_iX_j]$ relating the covariance of the random variables X_i and X_j with their independent probabilities. The mean-field approximation (8) (and similar ones for different variations of the stochastic model) is then obtained by assuming that $E[X_iX_j] = E[X_i]E[X_j]$ for all $i \neq j$. In other words, it is assumed that all the random variables have zero covariance.

Unfortunately, it is not necessarily true that $E[X_iX_j] = E[X_i]E[X_j]$, which means that for any fixed population with a stochastic model, the deterministic approximations studied are just that—approximations. Naturally, this begs the questions of how accurately the approximations describe their stochastic counterparts.

Although the deterministic models only approximate the expected values p_i, it has actually been shown that these are upper bounds on the actual probabilities [72], [73], [78] (this bound is essentially found by showing that $E[X_iX_j] \geq 0$ for all $i \neq j$). Fortunately, this bound has positive implications on attempting to control the underlying stochastic process by using the deterministic mean-field model. By stabilizing the deterministic approximations, claims like the ones presented in Remark 7 can be made. More specifically, if it can be guaranteed that the disease-free equilibrium of the deterministic model is globally asymptotically stable, then the stochastic system will reach the disease-free absorbing state in sublinear time (with respect to the size of the network) in expectation.

In [S2], the authors begin looking at how accurate the deterministic mean-field approximations are in describing the stochastic models, rather than just guaranteeing the upper bound. However, this issue is still an open problem for arbitrary networks.

Furthermore, all works above only consider the SIS dynamics. Although the recent work [S3] provides this type of analysis for a three-state SIRS model, rigorous analysis for more complicated models in general are still unsolved problems.

REFERENCES

[S2] P. V. Mieghem and R. van de Bovenkamp, "Accuracy criterion for the mean-field approximation in Susceptible-infected-susceptible epidemics on networks," *Phys. Rev. E*, vol. 91, p. 032812, Mar. 2015.

[S3] N. A. Ruhi and B. Hassibi, "SIRS epidemics on complex networks: Concurrence of exact Markov Chain and approximated models," arXiv:1503.07576, 2015.

the infection rate at which a node i is affected by an infected node j is given by $\beta_{ij} > 0$ if $(i,j) \in E$. For simplicity, let $\beta_{ij} = 0$ if $(i,j) \notin E$. The dynamics of the SIS model in an arbitrary network are then described by [75]

$$\dot{p}_i = -\delta_i p_i + \sum_{j=1}^{N} \beta_{ij} p_j (1 - p_i), \tag{9}$$

where $p_i \in [0,1]$ can be seen as either the fraction of the ith subpopulation that is infected (in the metapopulation case), or the probability that an individual i is infected [73], [75]–[79].

In this model, the disease-free state $p_i = 0$ for all $i \in \{1,\ldots,N\}$ is again a trivial equilibrium. In what follows, conditions for when this equilibrium is globally asymptotically stable are presented. Let $p = (p_1,\ldots,p_N)^T$ denote the state vector of the system, $D = \operatorname{diag}(\delta_1,\ldots,\delta_N)$ the diagonal matrix of recovery rates, and $B = [\beta_{ij}]$ the matrix of infection rates. The dynamics (9) can then be written as

$$\dot{p} = (B - D)p + h,$$

where $h_i = -\sum_{j=1}^{N} \beta_{ij} p_i p_j$. The following result from [75], [76], and [80] characterizes the convergence properties of these dynamics.

Theorem 8: Threshold Condition for Heterogeneous Networks

Given the dynamics in (9), for any $p(0) \neq 0$, the equilibrium $p^* = 0$ is globally asymptotically stable if and only if $\lambda_{\max}(B - D) \leq 0$. Furthermore, for $\lambda_{\max}(B - D) > 0$, there exists $p^{**} \in \mathbb{R}^N_{(0,1)}$ such that p^{**} is globally asymptotically stable.

These stability results have recently been extended to other, more complicated models, such as the three-state susceptible-alert-infected-susceptible (SAIS) model [81], the four-state generalized susceptible-exposed-infected-vigilant

(G-SEIV) model [82], and even the SI^*V^* model, which allows for an arbitrary number of compartments or states [83].

Equipped with a basic understanding of how the SIS process evolves and the connections between the stochastic processes and their deterministic approximations as discussed in Remark 7, the remainder of this article formulates and studies some relevant control problems.

CONTROL OF EPIDEMICS

The previous section presented several approaches for modeling the dynamics of spreading processes taking place on arbitrary contact networks. These models were then analyzed, and several stability results for both the deterministic and stochastic cases were introduced. This section describes several results aimed at controlling the dynamics of the spreading processes.

The ultimate goal in these problems is controlling the stochastic network models to stop the spreading of a disease as quickly as possible. However, before getting to the details, a discussion on the available control levers in treating an epidemic is required. Consider the heterogeneous SIS dynamics (9)

$$\dot{p}_i = -\delta_i p_i + \sum_{j=1}^{M} \beta_{ij} p_j (1 - p_i),$$

as a metapopulation model with M subpopulations. That is, each node i is some subpopulation (such as a town) of n_i individuals in a larger population (such as a country) of N individuals (see "Metapopulation Models" for further details). The parameters affecting the dynamics are then the recovery rates δ_i for each subpopulation and the infection rates β_{ij} that describe the interactions between various subpopulations.

The two ways to help mitigate the effects of an epidemic are to increase the recovery rates δ_i and decrease the infection rates β_{ij}. Increasing the recovery rate of a given subpopulation can be done by providing better treatment to sick individuals. For instance, allocating more resources to a particular subpopulation can allow that subpopulation to afford more doctors or better methods of treatment for fighting a particular disease. Decreasing infection rates can be done in numerous ways. Limiting traffic/travel between subpopulations can help decrease the infection rate. Completely quarantining a subpopulation i is equivalent to setting $\beta_{ji} = 0$ for all j since i can no longer affect other subpopulations. Other ways of decreasing infection rates include milder methods of prevention, such as distributing masks to a population to minimize chance of infection, or even just raising awareness about a disease to make people less likely to contract the disease.

If resources are not an issue, it is intuitive that by quarantining everyone and treating every infected individual with the best possible treatment, the disease is likely to die out quickly. However, this solution is undesirable because quarantining everybody in a given population is not pragmatic. Thus, given a fixed budget of some sort, it is imperative to identify exactly which parameters are most critical in mitigating the effects of the disease as much as possible. These problems are formulated, and the current state of the art is discussed next.

Spectral Control and Optimization

This section presents various optimal resource allocation problems. More specifically, given a fixed budget, the idea is to optimally invest resources to best hinder the spreading of a disease. Leveraging the results of Theorems 4–6 and 8, a natural option to mitigate the effects of a possible epidemic is to make $\lambda_{\max}(B - D)$ as small as possible.

For simplicity, consider the homogeneous SIS dynamics (8) where δ and β are fixed parameters for all nodes; this simplification will be relaxed later. Hence, Theorems 4 and 6 suggest that the goal is to make $\lambda_{\max}(A)$ as small as possible, which can be achieved by modifying the network structure.

The effect of the network structure on the maximum eigenvalue has been studied [84] and two strategies have been proposed for decreasing $\lambda_{\max}(A)$. The first is to remove nodes from A, which might physically be done by either quarantining or immunizing certain individuals, making them unable to contract the disease and, perhaps more importantly, unable to spread it. Another way to reduce $\lambda_{\max}(A)$ is to remove links rather than completely removing nodes, which might physically be done by restricting traffic between certain cities or restricting interactions between certain individuals. The caveat is that removing nodes or edges is likely to be costly in the real world. For this reason, optimal allocation solutions are desired in which the minimum number of nodes or links can be removed while still guaranteeing some level of performance. The node and link removal problems of interest are then described as follows.

Problem 9: Optimal Node Removal

Given an original graph A and a fixed budget $C > 0$, minimize $\lambda_{\max}(A)$ by removing at most C nodes from A.

Problem 10: Optimal Link Removal

Given an original graph A and a fixed budget $C > 0$, minimize $\lambda_{\max}(A)$ by removing at most C links from A.

Unfortunately, the node and link removal problems described above are NP-complete and NP-hard, respectively [85]. As a result, several papers instead solve convex relaxations or propose heuristics to approximately solve these problems. An intuitive example is one in which the nodes with the highest degrees (largest numbers of neighbors) are removed one by one until the budget is exhausted. Other heuristics are based on various network metrics, such as betweenness centrality [86], PageRank [87], or susceptible size [88], to decide which nodes should be removed first. Similarly, there are works that are concerned with

Geometric Programming

Let $\mathbf{x} \in \mathbb{R}^N_{>0}$, where $x_1, \ldots, x_N > 0$ denote N decision variables. In the context of geometric programs, a *monomial* function $h(\mathbf{x})$ is a real-valued function of the form $h(\mathbf{x}) = c_0 x_1^{a_1} x_2^{a_2} \cdots x_N^{a_N}$ with $c_0 > 0$ and $a_i \in \mathbb{R}$ for all $i \in \{1, \ldots, N\}$. A *posynomial* function $q(\mathbf{x})$ is a real-valued function that is the sum of monomials, $q(\mathbf{x}) = \sum_{k=1}^{K} c_k x_1^{a_{1,k}} x_2^{a_{2,k}} \cdots x_N^{a_{N,k}}$, where $c_k > 0$ and $a_{i,k} \in \mathbb{R}$ for all $i \in \{1, \ldots, N\}$ and $k \in \{1, \ldots, K\}$.

Before stating the definition of a geometric program, the following class of functions will be useful.

DEFINITION S1

A function $f : \mathbb{R}^N \to \mathbb{R}$ is *convex in log-scale* if the function

$$F(\mathbf{x}) = \log f(\exp \mathbf{x}) \tag{S2}$$

is convex in $\mathbf{x}$ (where exp $\mathbf{x}$ indicates component-wise exponentiation).

REMARK S2

Note that posynomials (hence, also monomials) are convex in log-scale [S4].

A geometric program (GP) is an optimization problem of the form

$$\begin{aligned} \underset{\mathbf{x}}{\text{minimize}} \quad & f(\mathbf{x}) \\ \text{such that} \quad & q_i(\mathbf{x}) \leq 1, i = 1, \ldots, m, \\ & h_i(\mathbf{x}) = 1, i = 1, \ldots, p, \end{aligned} \tag{S3}$$

where f is a function that is convex in log-scale, q_i are posynomial functions, and h_i are monomial functions for all i. A comprehensive treatment of GPs is provided in [S5]. A GP is a quasiconvex optimization problem [S4] that can be transformed to a convex problem using a logarithmic change of variables $y_i = \log x_i$, and a logarithmic transformation of the objective and constraint functions. The GP in (S3) can then be written in the transformed coordinates by

$$\begin{aligned} \underset{\mathbf{y}}{\text{minimize}} \quad & F(\mathbf{y}) \\ \text{such that} \quad & Q_i(\mathbf{y}) \leq 0, \quad i = 1, \ldots, m, \\ & b_i^T \mathbf{y} + \log d_i = 0, \quad i = 1, \ldots, p, \end{aligned} \tag{S4}$$

where $Q_i(\mathbf{y}) = \log q_i(\exp \mathbf{y})$ and $F(\mathbf{y}) = \log f(\exp \mathbf{y})$. Also, given that $h_i(\mathbf{x}) = d_i x_1^{b_{1,i}} x_2^{b_{2,i}} \cdots x_N^{b_{N,i}}$, the equality constraint above is obtained, where $b_i = (b_{1,i}, \ldots, b_{N,i})$.

Since $f(\mathbf{x})$ is convex in log-scale, $F(\mathbf{y})$ is a convex function. Furthermore, since q_i is a posynomial (and therefore convex in log-scale), Q_i is also a convex function, which shows that (S4) is a convex optimization problem in standard form and can be efficiently solved in polynomial time [S4].

REFERENCES

[S4] S. Boyd and L. Vandenberghe, *Convex Optimization*. Cambridge, U.K.: Cambridge Univ. Press, 2004.

[S5] S. Boyd, S. J. Kim, L. Vandenberghe, and A. Hassibi, "A tutorial on geometric programming," *Optim. Eng.*, vol. 8, no. 1, pp. 67–127, 2007.

link removal rather than node removal [85], [89], [90]. In [91], the authors solve a convex relaxation of the problem and effectively project its optimal solution onto the original problem.

The drawbacks of the above strategies are highlighted in [92], where the authors study the worst-case scenarios of these suboptimal strategies to show that network-based heuristics can perform arbitrarily poorly. Thus, it is difficult to evaluate a priori how well suboptimal solutions to Problems 9 and 10 will perform. Furthermore, completely removing nodes or even links might not be practical solutions, since it would require fully quarantining certain subpopulations or completely shutting down certain roads or methods of travel between various subpopulations.

Instead, consider tuning the values of the parameters δ_i and β_{ij} in the heterogeneous network model (9) rather than completely changing the network structure. The authors in [93] formulate this problem as an optimization problem to minimize the steady-state infection values over heterogeneous recovery rates. A gradient-descent algorithm is then designed to find feasible local minima. Another alternative is to use the result of Theorem 8. In this direction, several works consider the minimization of $\lambda_{\max}(B - D)$ under various constraints. The effect of minimizing this eigenvalue is to maximize the exponential decay rate of the system toward the disease-free equilibrium.

When tuning the spreading and recovery rates, the problem can be formulated as a discrete optimization problem in which these rates can only be set to a fixed number of feasible values. This problem has been shown to be NP-complete in [94]. Alternatively, this problem can be relaxed by allowing these rates to take values in a feasible continuous interval. In this case, the authors in [95] and [96] developed efficient methods for allocating resources to minimize the dominant eigenvalue of relevant matrices. In [97] and [98], the problem of minimizing $\lambda_{\max}(B - D)$ is cast into a semidefinite program framework for undirected networks. In [99] and [100], this problem is solved for directed graphs using geometric programming, where the solution can be obtained using standard off-the-shelf convex optimization software. Furthermore, geometric programs allow for the simultaneous optimization over both the infection rates and recovery rates; see "Geometric Programming" for further details.

In what follows, a simplified version of the optimization problem considered in [100] is presented, and it is shown how it can be reformulated as a geometric program. Consider the deterministic heterogeneous SIS model (9) with natural recovery rates $\delta_i = \underline{\delta}_i > 0$ and infection rates $\beta_i = \overline{\beta}_i > 0$ for all $i \in \{1, \ldots, N\}$, where $\beta_{ij} = \beta_i$ for $j \in \mathcal{N}_i^{\text{in}}$ and $\beta_{ij} = 0$ otherwise. In other words, the rate at which a node i is infected is a node-dependent parameter rather

than an edge-dependent one; this is relaxed in [101]. The recovery rate δ_i can be increased up to some maximum $\overline{\delta}_i > \underline{\delta}_i$ for a cost. Alternatively, the infection rate β_i can be decreased down to some minimum $\underline{\beta}_i < \overline{\beta}_i$ for another cost. The control parameters are then given by δ_i and β_i, where $\underline{\delta}_i \le \delta_i \le \overline{\delta}_i$ and $\underline{\beta}_i \le \beta_i \le \overline{\beta}_i$.

The cost functions describing the associated cost to increase δ_i and decrease β_i are given by $g_i(\delta_i)$ and $f_i(\beta_i)$, respectively. In this context, given a fixed budget $C > 0$, the goal is to minimize $\lambda_{\max}(B - D)$ while satisfying the constraint that the total cost does not exceed the given budget. This problem is formally stated below.

Problem 11: Budget-Constrained Allocation

Given a fixed budget $C > 0$,

$$\begin{aligned} \underset{\{\beta_i,\delta_i\}_{i=1}^N}{\text{minimize}} \quad & \lambda_{\max}(B - D), \\ \text{such that} \quad & \sum_{i=1}^N f_i(\beta_i) + g_i(\delta_i) \le C, \\ & \underline{\beta}_i \le \beta_i \le \overline{\beta}_i, \\ & \underline{\delta}_i \le \delta_i \le \overline{\delta}_i. \end{aligned}$$

Note that solving Problem 11 is not trivial since the objective function (maximum eigenvalue) is not necessarily convex. However, the following result guarantees that, under mild assumptions on the cost functions, this problem can be solved exactly by rewriting it as a geometric program, which can be efficiently solved (in polynomial time) using standard off-the-shelf convex optimization software. See [100] for further details on this equivalence.

Theorem 12: Solution to Budget-Constrained Allocation Problem

Problem 11 can be solved by solving the following auxiliary geometric program

$$\begin{aligned} \underset{\lambda,\{\beta_i,\tilde{\delta}_i,u_i\}_{i=1}^N}{\text{minimize}} \quad & \lambda \\ \text{such that} \quad & \sum_{j=1}^N a_{ij}\beta_i u_j + \overline{\delta}_i u_i \le \lambda u_i, \\ & \sum_{j=1}^N f_j(\beta_j) + \tilde{g}_j(\tilde{\delta}_j) \le C, \\ & \phi - \overline{\delta}_i \le \tilde{\delta}_i \le \phi - \underline{\delta}_i, \\ & \underline{\beta}_i \le \beta_i \le \overline{\beta}_i, \end{aligned} \tag{10}$$

for all $i \in \{1,\ldots,N\}$, with $\phi > \max_j \overline{\delta}_j$ and $\tilde{g}_j(\tilde{\delta}_j) = g_j(\phi - \tilde{\delta}_j)$, where β_i^* and $\delta_i^* = \phi - \tilde{\delta}_i^*$ solve Problem 11 with rate $\lambda_{\max}(B - D) \le \lambda^* - \phi$, where the superscript $*$ corresponds to the optimal solution of (10).

Aside from the discussed SIS model, other works have also applied these ideas to more general models. The authors in [102] formulated the semidefinite program for a three-state SAIS model developed in [81], where the concept of alertness against a possible epidemic is also modeled. A more general four-state SEIV model is considered in [103], for which the authors develop equivalent geometric programs to optimize the dominant eigenvalue over various parameters of the model simultaneously.

These types of optimal allocation strategies have been recently compared to fair strategies in [104], where resources must be allocated evenly across all nodes, to show their effectiveness in targeting resources rather than evenly spreading them.

However, there are still some drawbacks of these spectral control approaches that need to be addressed before their solutions can be fully taken advantage of in weakening the impact of diseases in the future. The first main drawback is that they do not take into account the current state of the system. This shortcoming means that even nodes that are not at immediate risk of being infected might be allocated resources to raise their recovery rates or decrease their infection rates. Second, solving these problems exactly requires a great deal of knowledge. In addition to knowing the natural recovery rates and infection rates, exact knowledge of the entire graph is also assumed, which is unlikely. Third, these are centralized solutions that may take a long time to compute. Although some variants of this problem, as discussed above, can be solved efficiently (in polynomial time with respect to the size of the network), computing solutions for large networks can still be a computational burden. Lastly, it is also assumed that once the optimal solution is found, the recovery rates and infection rates can be instantaneously set to the desired values.

The current efforts to address these issues and what still needs to be done are discussed in the following sections. The next section begins relaxing the first drawback stated above by looking at optimal control problems with feedback control solutions, rather than the one-time optimal resource allocation solutions presented in this section.

Optimal Control

This section discusses various optimal control problems formulated for mitigating epidemics under the SIS and SIR dynamics. Because there has been only a little work done for the network models thus far, the classical models are studied first.

Classical Models

To formulate a control problem, the SIS population model (6) needs a slight modification to allow for a control action. Following [105], the original SIS population model can be rewritten with $\delta = \delta_1$ as

$$\dot{p}^I = \beta p^I(1 - p^I) - \delta_1 p^I, \tag{11}$$

where $\delta_1 > 0$ is the natural recovery rate of an individual. Assume that this system can now be controlled by increasing the recovery rate of individuals in the population from δ_1 to $\delta_2 > \delta_1$. Increasing the recovery rate can be achieved, for instance, by allocating antidotes or providing other

forms of treatment to a fraction of the population. The control signal $u \in [0,1]$ is then the fraction of the population that treatment is provided to. For simplicity, assume that the recovery rates of any number of individuals in the population can be changed instantaneously; this assumption will be relaxed later. The dynamics of the controlled SIS population model is then given by

$$\dot{p}^I = \beta p^I(1-p^I) - ((1-u)\delta_1 + u\delta_2)p^I. \tag{12}$$

Applying the result of Theorem 2, the following corollary is obtained for a fixed $u(t) = \bar{u}$.

Corollary 13: Population Dynamics Threshold Condition

The solution of $p^I(t)$ approaches zero as $t \to \infty$ for

$$\bar{u} \geq \frac{\beta - \delta_1}{\delta_2 - \delta_1}.$$

Since $\bar{u} \in [0,1]$, Corollary 13 implies that if $(\beta - \delta_1)/(\delta_2 - \delta_1) > 1$, the disease is too strong and will never die out regardless of the chosen control. On the other hand, when $\delta_1 \geq \beta$ the natural recovery rate is high enough to ensure extinction of the disease without any control action ($\bar{u} = 0$). Otherwise, to ensure eventual extinction of the disease with the smallest possible fixed control signal, the control signal should be chosen as $\bar{u} = (\beta - \delta_1)/(\delta_2 - \delta_1)$. However, it may be desirable in certain cases to use more control effort, such that the infection dies out faster than it would naturally. For instance, having a population with many sick individuals could incur a drastic social cost that instead could have been offset by a smaller initial cost of treatment. This tradeoff is formulated as an optimal control problem next.

Let the cost of treatment be linear with the number of individuals treated, and similarly let the cost of infection be linear with the number of infected individuals. The objective function to be minimized is then given by

$$J_T = \int_0^T (cp^I(t) + d \times u(t))\,dt, \tag{13}$$

where $c > 0$ is associated with the cost of infection, $d > 0$ is associated with the cost of treatment, and $T > 0$ is the time horizon. Using Pontryagin's maximum principle, it can be shown [105]–[107] that the optimal solution is

$$u^*(t) \in \begin{cases} \{0\} & \text{for } f(t) > 0, \\ [0,1] & \text{for } f(t) = 0, \\ \{1\} & \text{otherwise,} \end{cases}$$

with

$$f(t) = \psi p^I(\delta_2 - \delta_1) + d,$$

where ψ is the costate variable with dynamics

$$\dot{\psi} = c - \psi(\beta(1-2p^I) - ((1-u)\delta_1 + u\delta_2)).$$

It can now be shown [105] that for $\beta/(\delta_2 - \delta_1) < c/d$, the optimal solution is to initially treat the entire population until some time t' at which point nobody should be treated. For $\beta/(\delta_2 - \delta_1) > c/d$, the optimal solution is $u(t) = 0$ for all $t \in [0,T]$. This bang-bang solution, with at most one switch, is common in similar problems. Other works with this same kind of solution have been studied in many variations of this problem, including considering efficiency of control [108] or control over both δ and β simultaneously [109]. Other models have also been considered, such as the SIR model [110] with different incidence rates [111], [112] or a four-state SIRD model [113].

Although the bang-bang solution is common, it is possible to obtain different types of solutions for various formulations of the optimal control problem. For example, it is shown in [114] and [115] that for alternative problem formulations, the optimal solution may not be a bang-bang controller for certain classes of cost functions. In [116], an SIR model with quadratic control costs over both δ and β is considered. In this case, the optimal solution is again not a bang-bang controller. A four-state SIRC model, for which the optimal solution is again not a bang-bang controller, is considered in [117].

Thus far it has been assumed that the control signals can be instantaneously set to their desired values. Other works consider the case in which the rate of the control signal (its time derivative) can be controlled instead [33], [34], [118], [119]. The technical details of these works have been omitted because the methods are similar to the example presented above. It turns out that the results from these works often admit bang-bang controllers with at most one switch as optimal solutions as well. As a final note, it is acknowledged that in certain contexts it may be desirable to maximize the impact of a spreading process (for instance a viral marketing campaign) [112], [120] rather than minimizing it.

Network Models

As mentioned before, the population models are quite crude because they often lump an entire population's state into just a few numbers. Instead, network models allow each individual in a network to have its own state, which provides a more accurate description of the global state of the system. However, little work has been done thus far on optimally controlling these processes on arbitrary networks. Three relevant papers that consider this problem in the context of networks are [107], [121], and [122]. Before discussing these works, this section starts by proposing an optimal control problem for the SIS dynamics on networks that has yet to be solved.

Recall the SIS network dynamics with heterogeneous recovery and infection rates (9). Theorem 8 shows that the necessary and sufficient condition for extinction is $\lambda_{\max}(B - D) \leq 0$. In the previous section, this result was used as a constraint to solve one-time optimal allocation problems. Instead, the following problem is an optimal control problem, where the curing rates δ_i are allowed to vary over time, depending on the evolving state of the system.

Problem 14: Optimal Control of an SIS Network

Given a linear cost of infection c_i and control d_i for all $i \in \{1,\ldots,N\}$, minimize

$$J_T = \int_0^T \left(\sum_{i=1}^N c_i p_i(t) + d_i \delta_i(t) \right) dt, \tag{14}$$

subject to the dynamics (9) and $\delta_i(t) \in [\underline{\delta}, \overline{\delta}]$ for some $0 < \underline{\delta} < \overline{\delta}$ for all $t \in [0,T]$.

Problem 14, along with most of its variations, is currently an open problem. Variations include problems similar to the optimal control problems for deterministic population models discussed earlier, such as control over infection rates, noninstantaneous control, or different objective functions. The only work known to have tackled this problem is [122], where the authors study the linearization of (9) around the disease-free equilibrium and showed, for the linear dynamics, that the optimal solution is a bang-bang controller with at most one switch, similar to many results obtained for the population models. However, the connection with this optimal solution to the one of the original problem is unclear.

Although Problem 14 is still an open problem for the SIS dynamics, a closely related problem has been solved in the context of containing computer viruses [107], [121]. A simpler version of the problem originally posed in [107] is presented here. Consider the dynamics

$$\begin{aligned} \dot{p}_i^S &= -p_i^S \sum_{j=1}^N \beta_{ij} p_j^I - p_i^S p_i^R u_i, \\ \dot{p}_i^I &= p_i^S \sum_{j=1}^N \beta_{ij} p_j^I - p_i^I R_i u_i, \\ \dot{p}_i^R &= p_i^S p_i^R u_i + p_i^I R_i u_i, \end{aligned} \tag{15}$$

where, as before, p_i^S and p_i^I are the fraction of a subpopulation that are susceptible and infected, respectively. Then, $p_i^R = 1 - p_i^S - p_i^I$ is the fraction of individuals who are removed. This fraction refers to individuals who are immune from the infection, either from being vaccinated or recovered from the disease and no longer susceptible to it. Additionally, u_i is the control that dictates the rate at which susceptible and infected individuals become removed.

Problem 15: Optimal Control of an SIR Network for Malware Epidemics

Given a linear cost of infection c_i, control h_i^1 and h_i^2, and benefit of recovery ℓ_i for all $i \in \{1,\ldots,N\}$, minimize

$$J_T = \int_0^T \left(\sum_{i=1}^N -\ell_i p_i^R + c_i p_i^I + p_i^R h_i^1 u_i + p_i^R (p_i^S + p_i^I) h_i^2 u_i \right) dt, \tag{16}$$

subject to the dynamics (15) and $u_i(t) \in [0, \overline{u}_i]$ for some $\overline{u}_i > 0$ for all $t \in [0,T]$.

The following result follows from Pontryagin's maximum principle [107].

Theorem 16: Optimal Control of an SIR Network for Malware Epidemic

There exists $\tau_i \in [0,T]$ for all i such that the optimal control is given by

$$u_i^*(t) = \begin{cases} \bar{u}_i & \text{for} \quad t < \tau_i, \\ 0 & \text{for} \quad \tau_i \le t \le T. \end{cases}$$

Again, Theorem 16 is consistent with many other optimal control solutions for epidemics in that the optimal solution is a bang-bang controller with at most one switch. Given the freshness of these results, there are still many variations of this work that need to be studied. Although the dynamics (15) considered here are certainly similar to the epidemic models discussed throughout the article, they are not immediately applicable due to the term $R_i u_i$. In the context of patching, R is a state of nodes that have a patch and are thus immune, and so they can spread this patch to healthy and infected nodes. However, this concept does not seem to translate directly to epidemics; a sick person cannot get better by interacting with healthy people.

In many of the problems discussed above, it was assumed that direct control of the infection rates β_{ij} and recovery rates δ_i were possible. However, this simplistic scenario assumes that these parameters can be controlled for the entire population instantaneously, which is unfeasible in the context of disease spreading. In an effort to address this oversimplification, there is a rising body of current work in which more realistic control actions are explored, which is discussed next.

Heuristic Feedback Policies

This section presents various models that are used to capture possible human behaviors or other countermeasures employed to deter the spreading of a disease. Rather than explicitly attempting to control the SIS dynamics as described above, the works discussed here are essentially extensions to the SIS model for which stability conditions are derived. The models are created by assuming various actions people might take, and then the closed-loop system stability is analyzed. More specifically, rather than separately considering a model and control strategies, the model and control strategies are codeveloped to yield a sense of closed-loop control model. For lack of better terminology, these are referred to as heuristic feedback policies.

Many works consider various feedback strategies that determine when nodes or links should temporarily be removed [89], [123]–[129]. Closed-loop models are then constructed for the various strategies whose stability properties can then be analyzed. These strategies are often based on some sort of perceived risk that individuals have of becoming infected, causing them to either remove links to infected neighbors or completely remove themselves from the network (for example, by staying home from work or becoming vaccinated). This section begins by presenting some of these control strategies for the simpler classical models, which will later be extended to network models.

Classical Models

As mentioned above, these heuristic feedback policies are all essentially different epidemic models for which stability results are obtained. As an illustrative example, consider [128], where, in addition to the susceptible state S and infected state I, an additional protected state P is introduced. The protected state refers to individuals who have decided to immunize themselves in one way or another and are thus not immediately susceptible to contracting the disease. The model is described as follows. Letting Y_i be the number of infected neighbors a susceptible node i has in a given graph, node i transitions from the susceptible state S to the infected state I with rate βY_i. However, a node in the protected state P transitions to the infected state with rate $\beta_0 Y_i$, where $\beta_0 < \beta$ captures the decreased risk of infection due to being protective or alert. A type of control is then to decide how susceptible individuals transition to the protected state. Finally, as in the normal SIS model, individuals who are infected naturally recover to the susceptible state with a natural recovery rate δ. Figure 5 shows the interactions of this three-state SPIS model. The authors then consider the extension of the SIS population dynamics (5) (by assuming a complete network topology, meaning all individuals are equally likely to affect one another) to include the protected state

$$\begin{aligned}\dot{p}^S &= -\beta p^I p^S + \delta p^I - p^S f(p^S,p^I,p^P) + p^P g(p^S,p^I,p^P),\\ \dot{p}^I &= \beta p^I p^S - \delta p^I,\\ \dot{p}^P &= p^S f(p^S,p^I,p^P) - p^P g(p^S,p^I,p^P),\end{aligned} \tag{17}$$

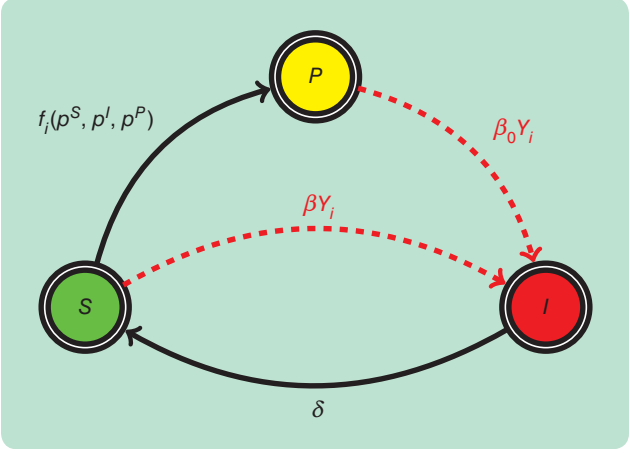


FIGURE 5 A three-state compartmental susceptible-protected-infected-susceptible model. An individual i in the infected state I transitions to the healthy or susceptible state S with a natural recovery rate δ. An individual in the susceptible state transitions to the protected state P at a rate $f_i(p^S,p^I,p^P)$ that depends on the entire network state and to the infected state at a rate βY_i proportional to the number of infected neighbors Y_i possessed by node i. An individual in the protected state transitions to the infected state at a rate $\beta_0 Y_i$, where $\beta_0 < \beta$ captures the fact that this individual is in a less susceptible state than normal, for instance, due to behavioral changes or vaccination.

where $f(\cdot)$ and $g(\cdot)$ are functions that determine how susceptible individuals are protecting themselves. Recall that p^S corresponds to the fraction of individuals in a population who are in the susceptible state with p^I and p^P defined similarly for the infected and protected states, respectively. As in the case of the deterministic SIS population dynamics (5), one of these equations is redundant and can be removed by using $p^S + p^I + p^P = 1$ because the population size is constant. This model is referred to as the three-state susceptible-protected-infected-susceptible (SPIS) model.

The authors then explore various strategies for designing f and g and analyze the stability of the system for these choices. As mentioned above, this type of control strategy is called a heuristic feedback policy because a specific control structure is already defined and built into the model, rather than the objective of the work to be designing the controller itself. More specifically, if the functions $f(\cdot)$ and $g(\cdot)$ can be chosen arbitrarily in the example above, the best thing to do is set $g(\cdot) = 0$ and have $f(\cdot)$ be as large as possible, which means everybody immediately protects themselves. In this case, it is intuitive to think that the disease will die out quickly as well. Instead, it is useful to explicitly model a cost for infection and/or control as done in the previous section. These population models are extended to network models next.

Network Models

Similar to the classical models, various network models have been built to capture possible human behaviors or other countermeasures employed to deter the spreading of a disease on networks [130], [131]. As before, many works consider various feedback strategies that determine when nodes or links should temporarily be removed [20], [132]–[135]. Closed-loop models are then constructed for the various strategies whose stability properties can then be analyzed. These strategies are developed in the same way as in the classical models case.

The model considered next can be seen as a network extension of the three-state SPIS population model (17) presented in [128] and is similar to the three-state SAIS model presented in [81] where the authors introduce an alert state A, which is similar to the protected state P considered here. This state captures the possibility of human behaviors and actions lowering the chance of contracting a disease. For simplicity, consider homogeneous parameters, meaning the recovery and infection rates are set the same at all nodes. The deterministic version of this model is then

$$\begin{aligned}\dot{p}_i^S &= -\beta p_i^S \sum_{j=1}^N a_{ij} p_j^I + \delta p_i^I - p_i^S f_i(p^S,p^I,p^P),\\ \dot{p}_i^I &= \beta p_i^S \sum_{j=1}^N a_{ij} p_j^I + \beta_0 p_i^P \sum_{j=1}^N a_{ij} p_j^I - \delta p_i^I,\\ \dot{p}_i^P &= p_i^S f_i(p^S,p^I,p^P) - \beta_0 p_i^P \sum_{j=1}^N a_{ij} p_j^I,\end{aligned}$$

where $f_i(p^S, p^I, p^P)$ is a function that determines how susceptible individuals are protecting themselves. Conditions can then be derived for the parameters and the function f such that the disease-free equilibrium is globally asymptotically stable [81]. The authors in [136] then treat the design of this function f as an optimal information dissemination problem. However, as in the population dynamics case, these are structured methods of control that are ultimately built into the models.

A critical shortcoming of these types of solutions is that they are too specific. Often times a specific model with a specific control structure is developed and studied. Unfortunately, it is often unclear what type of spreading process each model is good for describing, if any. In [137], the author does a great job highlighting the fact that there are far too many slight variations of existing models. This section closes with a small anecdote from the epilogue of [137], in which the author effectively created 10^5 different models:

> In the book [sic], *A Thousand and One Nights*, Scheherezade had to entertain King Shahriyar with a new story each evening in order to avoid being killed. If they were mathematical biologists and she had only to present one new epidemiological model each night to entertain him, then she could have survived each night for at least 270 years. Of course, the King would probably have become disenchanted by the "new" models if they were only very slight variations on previous models and would have killed Scheherezade. Similarly, referees (the Kings) might become disenchanted if the papers which they receive contain models which are only slight variations on previous models. Thus I suggest that we as modelers and mathematicians should be cautious and not assume that every mathematical analysis of a slightly different model is interesting.

This anecdote helps instill the idea that not all epidemic models are useful. This issue and other technical challenges are discussed in the following section.

FUTURE OUTLOOK

The previous section provided a high-level overview of the current state of the art involving the control of epidemics. However, there are still many shortcomings of the results presented that need to be taken into account to take full advantage of their proposed solutions. This section highlights several of the main research challenges, how they are currently being addressed, and what still needs to be done.

All Control Methods Discussed So Far Have Been for Deterministic Models

Ultimately, the desired goal is controlling the original stochastic epidemic models from which the deterministic models are derived. Results like Theorems 4 and 5 help draw connections between the two, but these connections have only been made for simple cases so far. Furthermore, while these results help justify how using spectral control and optimization methods for deterministic models translate to the original stochastic models, it is unclear how the optimal feedback control solutions found for deterministic models relate to their stochastic counterparts.

Only a few works are available on controlling epidemic processes on networks for the original stochastic models. In [68], the authors consider the SIS model with a simple heuristic control law where the curing rates δ_i for each node are proportional to the number of neighbors. The authors are then able to show that, on any graph with bounded degree, this policy can achieve sublinear expected time to extinction with a budget proportional to the number of nodes in the network. A drawback of the above method is that it does not take into account the current state of the system. This means that nodes with no infected neighbors may be assigned high curing rates. Instead, [138] uses a heuristic PageRank algorithm to allocate curing resources given a fixed budget, based on the initial condition of infected nodes. The authors are then able to provide probabilistic upper bounds on the expected extinction time. More recently, [139] proposes an algorithm for which the expected time to extinction is sublinear using only a sublinear budget (in the number of nodes) for graphs satisfying certain technical conditions. A similar problem is considered in [140], for which various algorithms are developed using a Markov decision process framework.

All Control Methods Discussed So Far Have Admitted Centralized Solutions

Having only centralized solutions is problematic since human contact networks can be massive in practice, and it may not be computationally possible to solve these problems in a centralized setting. In this direction, distributed allocation and control strategies are a useful alternative. Again, there are only a few recent works that have looked at this problem [107], [141], [142]. As more work in optimization and control of epidemic processes is done, distributed versions of these algorithms are desirable.

All Control Methods Discussed So Far Have Assumed There Are No Uncertainties

Acknowledging uncertainties is an important issue in the context of epidemics. Throughout all the modeling, analysis, and control solutions presented thus far, perfect knowledge of everything, including recovery rates, state information, and network structures, has been assumed. These are clear oversimplifications because, in practice, these parameters are not readily available and must be estimated in one way or another. A review of analysis and approximation techniques considering uncertainties in the spreading parameters is provided in [143].

In the context of control, far less work has been done for the case where the topology is unknown. Observed

infection data of a discrete-time SIS process is used in [144] to estimate the network topology. Optimization and control methods can then be applied to the estimated topology; unfortunately, it is unclear how well these solutions will perform on the actual topology. Instead, a data-driven approach to optimally allocate resources has recently been studied in [145], where only empirical data about the spreading of a disease is available. In this work, the authors assume that the spreading rates are unknown. Alternatively, the authors assume that the responsible health agency has access to historical data describing the evolution of the disease in a network during a relatively short period of time. In this context, the authors in [145] construct a set of possible parameters that are consistent with the observed data and propose a robust optimization framework to allocate resources based on this set.

Another issue related to assuming perfect knowledge is assuming that the recovery and infection rates can be set to any desired values. To deal with this additional issue, studies are needed into how various control solutions perform when these rates cannot be set exactly.

The assumption of being able to observe exact state data is an issue that has received little to no attention in the context of control. This assumption does not apply to the spectral optimization or heuristic feedback control methods but certainly affects the optimal control methods.

More General Epidemic Models Are Needed

Although there are many works on modeling beyond the SIS and SIR dynamics on which this article has focused, there is still a lack of generalized models. More specifically, a majority of works that studies spreading processes begin with a single model with a fixed number of states and possible interactions. Many of these models are created by first looking at empirical data of a spreading process like AIDS [146] or a computer virus [69] and then determining what type of model and how many states should be used to capture its behavior. Instead, few works propose more general models with arbitrarily many states or layers on which the disease can spread [40], [83], [147]. The further development, analysis, and control of these generalized models can allow rapid prototyping of models for spreading processes that might not even exist today, in addition to completely generalizing the myriad specific models available today.

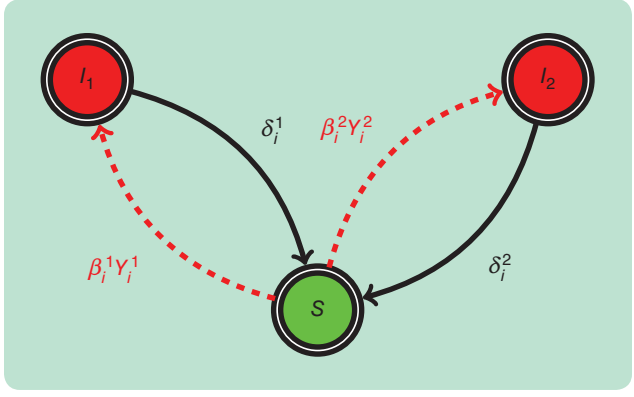


FIGURE 6 A three-state compartmental SI_1SI_2S model for two diseases. An individual i can be in the healthy or susceptible state S or infected by one of two possible infections, but not both simultaneously. An individual in the first infectious state I_1 recovers to the susceptible state at a natural recovery rate δ_i^1. Similarly, an individual i in the second infectious state I_2 recovers at a natural recovery rate δ_i^2. An individual in the susceptible state transitions to the infectious state I_k at rate $\beta_i^k Y_i^k$ for $k \in \{1,2\}$, where Y_i^k is the number of neighbors of i that are in infectious state I_k. The parameter β_i^k captures the effect that neighbors of node i has on it for infection I_k.

All models discussed in this article so far have only considered the spreading of a single disease or process. Extending existing models to capture multiple diseases that coevolve in a network has recently been gaining attention [148]–[154]. These diseases are often assumed to be mutually exclusive, meaning an individual can only be infected with one type of infection at a time. While it is discussed here in the context of disease and epidemics, these models are more aptly used in studying belief propagation or product adoption. For instance, the mutual exclusion of infections is useful in modeling competition in politics (such as Democrats versus Republicans) or competition in a marketplace (such as iPhone versus Droid versus Galaxy). A competitive model on arbitrary networks that was studied in [155] and further analyzed in [156] is presented next.

The competitive three-state, two-infection SI_1SI_2S model is described as follows. Let Y_i^1 be the number of neighbors of node i infected by the first disease I_1. A node i in the susceptible state S transitions to the infected state I_1 with rate $\beta_i^1 Y_i^1$. Similarly, a node i in the susceptible state transitions to the infected state I_2 with rate $\beta_i^2 Y_i^2$. Each node has its own recovery rate for each disease given by δ_i^1 and δ_i^2. For example, a node i in the infectious state I_1 recovers to the susceptible state at rate δ_i^1. Figure 6 shows the interactions of this three-state SI_1SI_2S model.

The deterministic version of this model is

$$\dot{p}_i^S = -p_i^S \sum_{j=1}^{N} a_{ij}(\beta_i^1 p_j^{I_1} + \beta_i^2 p_j^{I_2}) + \delta_i^1 p_i^{I_1} + \delta_i^2 p_i^{I_2},$$

$$\dot{p}_i^{I_1} = p_i^S \sum_{j=1}^{N} a_{ij}\beta_i^1 p_j^{I_1} - \delta_i^1 p_i^{I_1},$$

$$\dot{p}_i^{I_2} = p_i^S \sum_{j=1}^{N} a_{ij}\beta_i^2 p_j^{I_2} - \delta_i^2 p_i^{I_2}.$$

For simplicity, this model has been presented assuming that both infections evolve over the same graph structure A. Instead, [155] and [156] provide analysis for these dynamics over possibly different topologies. A few recent works have studied the problem of controlling multiple diseases in different scenarios [156]–[158]; however, these works are still in their infancy and there are still many open problems left to be solved.

All the works about epidemics on networks discussed in the article so far have assumed a fixed graph structure.

However, this assumption may not be fair depending on the time scale of a spreading process. For instance, in the context of diseases, the network of contacts in a human population is constantly changing. Hence, a time-varying network model might be more appropriate, albeit more challenging, to analyze. At the time of this writing, there is still only a little bit of work analyzing these types of time-varying models, which seems to be a promising new branch of epidemics research [159]–[161]. As with optimal control, similar problems have been studied in different contexts such as information dissemination in mobile networks [162], but far fewer has been considered in the context of epidemics thus far.

In addition to the models presented in this article, it is worth mentioning that many works present the same types of models from a game-theoretic perspective [130], [131], [163]–[165]. Game-theoretic formulations of epidemic models is another space in which there is not yet a significant amount of study, but some seminal works have shown its usefulness in modeling spreading processes, especially in the context of control and optimization [166]–[169].

CONCLUSIONS

This article has reviewed and analyzed some of the most popular models studied in epidemiology. In particular, deterministic and stochastic models in the context of both population and networked dynamics have been presented and analyzed. Many results concerning the optimization and control of epidemics have been discussed, and a number of new avenues for further exploration in this field has also been identified. Although the focus of this article was on disease and epidemics, it is worth reiterating that the same mathematical tools and results apply almost directly to many different spreading processes including information propagating through a social network, malware spreading in the World Wide Web, or viral marketing.

Despite the vast literature studying the problems discussed in this article, there are many interesting control problems left to be solved, particularly those in the context of networked dynamics. Plenty of work is still left to be done to really harness the power of these results and make a real societal impact, especially in understanding how to effectively control these processes on complex networks. In this respect, control engineers truly have much to offer in this reemerging field of research.

AUTHOR INFORMATION

Cameron Nowzari (cnowzari@seas.upenn.edu) received the M.S. and Ph.D. degrees in engineering sciences from the University of California, San Diego, in December 2010 and September 2013, respectively. He is currently working as a postdoctoral research associate at the University of Pennsylvania. He was a finalist for the Best Student Paper Award at the 2011 American Control Conference and received the 2012 O. Hugo Schuck Best Paper Award in the theory category. His current research interests include dynamical systems and control, sensor networks, distributed coordination algorithms, robotics, applied computational geometry, event- and self-triggered control, Markov processes, network science, and spreading processes on networks. He can be contacted at Electrical and Systems Engineering, Moore Room 203-C, University of Pennsylvania, 200 South 33rd St., Philadelphia, PA 19104 USA.

Victor M. Preciado received the Ph.D. degree in electrical engineering and computer science from the Massachusetts Institute of Technology, Cambridge, in 2008. He is currently the Raj and Neera Singh Assistant Professor of Electrical and Systems Engineering at the University of Pennsylvania. He is a member of the Networked and Social Systems Engineering program and the Warren Center for Network and Data Sciences. His current research interests include network science, dynamic systems, control theory, complexity, and convex optimization with applications in social networks, technological infrastructure, and biological systems.

George J. Pappas received the Ph.D. degree in electrical engineering and computer sciences from the University of California, Berkeley, in December 1998. He is currently the Joseph Moore Professor and chair of the Electrical and Systems Engineering Department at the University of Pennsylvania. He also holds secondary appointments in the Computer and Information Sciences, and Mechanical Engineering and Applied Mechanics Departments. He is a member of the GRASP Lab and the PRECISE Center. He currently serves as the deputy dean for research in the School of Engineering and Applied Science. His current research interests include hybrid systems and control, embedded control systems, cyberphysical systems, hierarchical and distributed control systems, networked control systems, with applications to robotics, unmanned aerial vehicles, biomolecular networks, and green buildings.

REFERENCES

[1] D. Bernoulli, "Essai d'une nouvelle analyse de la mortalité causée par la petite vérole et des advantages de línoculation pour la prévenir," *Mem. Math. Phys. Acad. Roy. Sci.*, Paris, pp. 1–45, 1760.

[2] K. Dietz and J. A. P. Heesterbeek, "Daniel Bernoulli's epidemiological model revisited," *Math. Biosci.*, vol. 180, nos. 1–2, pp. 1–21, 2002.

[3] R. Ross and H. P. Hudson, "An application to the theory of probabilities to the study of a prior pathometry," *Proc. Roy. Soc. A*, vol. 92, no. 638, pp. 204–230, 1916.

[4] R. Ross and H. P. Hudson, "An application to the theory of probabilities to the study of a prior pathometry. Part II," *Proc. Roy. Soc. A*, vol. 93, no. 650, pp. 212–225, 1917.

[5] R. Ross and H. P. Hudson, "An application to the theory of probabilities to the study of a prior pathometry. Part III," *Proc. Roy. Soc. A*, vol. 93, no. 650, pp. 225–240, 1917.

[6] W. O. Kermack and A. G. McKendrick, "A contribution to the mathematical theory of epidemics," *Proc. Roy. Soc. A*, vol. 115, no. 772, pp. 700–721, 1927.

[7] H. W. Hethcote, "The mathematics of infectious diseases," *SIAM Rev.*, vol. 42, no. 4, pp. 599–653, 2000.

[8] N. T. Bailey, *The Mathematical Theory of Infectious Diseases and Its Applications*. London, U.K.: Griffin, 1975.

[9] S. Boccaletti, V. Latora, Y. Moreno, M. Chavez, and D. U. Hwang, "Complex networks: Structure and dynamics," *Phys. Rep.*, vol. 424, no. 4, pp. 175–308, 2006.
[10] D. Easley and J. Kleinberg, *Networks, Crowds, and Markets: Reasoning About a Highly Connected World*. Cambridge, U.K.: Cambridge Univ. Press, 2010.
[11] M. E. J. Newman, *Networks: An Introduction*. Cambridge, U.K.: Cambridge Univ. Press, 2010.
[12] R. M. Anderson, R. M. May, and B. Anderson, *Infectious Diseases of Humans: Dynamics and Control*. New York: Wiley, 1992, vol. 28.
[13] P. van den Driessche and J. Watmourgh, "Reproduction numbers and subthreshold endemic equilibria for compartmental models of disease transmission," *Math. Biosci.*, vol. 180, nos. 1–2, pp. 29–48, 2002.
[14] S. Funk, E. Gilad, and V. A. A. Jansen, "Endemic disease, awareness, and local behavioural response," *J. Theor. Biol.*, vol. 264, no. 2, pp. 501–509, 2010.
[15] I. Z. Kiss, J. Cassell, M. Recker, and P. L. Simon, "The impact of information transmission on epidemic outbreaks," *Math. Biosci.*, vol. 225, no. 1, pp. 1–10, 2010.
[16] N. Perra, D. Balcan, B. Gonasalves, and A. Vespignani, "Towards a characterization of behavior-disease models," *PLoS ONE*, vol. 6, no. 8, p. e23084, Aug. 2011.
[17] P. Poletti, B. Caprile, M. Ajelli, A. Pugliese, and S. Merler, "Spontaneous behavioural changes in response to epidemics," *J. Theor. Biol.*, vol. 260, no. 1, pp. 31–40, 2009.
[18] D. Breda, O. Diekmann, W. F. de Graaf, A. Pugliese, and R. Vermiglio, "On the formulation of epidemic models (an appraisal of Kermack and McKendrick)," *J. Biol. Dyn.*, vol. 6, no. 2, pp. 103–117, 2012.
[19] M. M. Hikal, "Dynamic properties for a general SEIV epidemic model," *SIAM Rev.*, vol. 2, no. 1, pp. 26–36, 2014.
[20] B. A. Prakash, D. Chakrabarti, N. C. Valler, M. Faloutsos, and C. Faloutsos, "Threshold conditions for arbitrary cascade models on arbitrary networks," *Know. Inform. Syst.*, vol. 33, no. 3, pp. 549–575, 2012.
[21] T. Britton, "Stochastic epidemic models: A survey," *Math. Biosci.*, vol. 225, no. 1, pp. 24–35, 2010.
[22] M. Garetto, W. Gong, and D. Towsley, "Modeling malware spreading dynamics," in *Proc. INFOCOM Joint Conf. IEEE Computer Communications Societies*, San Francisco, CA, 2003, pp. 1869–1879.
[23] L. M. Sander, C. P. Warren, I. M. Sokolov, and J. Koopman, "Percolation on heterogeneous networks as a model for epidemics," *Math. Biosci.*, vol. 180, no. 1, pp. 293–305, 2002.
[24] E. Kenah and J. C. Miller, "Epidemic percolation networks, epidemic outcomes, and interventions," in *Interdisciplinary Perspectives on Infectious Diseases*, vol. 2011. New York: Hindawi, 2011, p. 543520.
[25] D. Kempe, J. Kleinberg, and E. Tardos, "Maximizing the spread of influence through a social network," in *Proc. ACM SIGKDD*, 2003, pp. 137–146.
[26] J. Kleinberg, "Cascading behavior in networks: Algorithmic and economic issues," in *Algorithmic Game Theory*. Cambridge, U.K.: Cambridge Univ. Press, 2007, pp. 613–632.
[27] M. Lelarge, "Efficient control of epidemics over random networks," in *Proc. 11th Int. Joint Conf. Measurement Modeling Computer Systems*, Seattle, WA, 2009, pp. 1–9.
[28] O. Yagan and V. Gligor, "Analysis of complex contagions in random multiplex networks," *Phys. Rev. E*, vol. 86, no. 3, p. 036103, 2012.
[29] R. M. Anderson, *Population Dynamics of Infectious Diseases*. London, U.K.: Chapman and Hall, 1982.
[30] F. Brauer and C. Castillo-Chavez, *Mathematical Models in Population Biology and Epidemiology*. Berlin, Germany: Springer-Verlag, 2012.
[31] N. T. Bailey, *The Mathematical Theory of Epidemics*. London, U.K.: Griffin, 1957.
[32] K. Dietz, "Epidemics and rumours: A survey," *J. Roy. Stat. Soc.*, vol. 130, no. 4, pp. 505–528, 1967.
[33] A. Abakuks, "An optimal isolation policy for an epidemic," *J. Appl. Probab.*, vol. 10, no. 2, pp. 247–262, 1973.
[34] A. Abakuks, "Optimal immunisation policies for epidemics," *Adv. Appl. Probab.*, vol. 6, no. 3, pp. 494–511, 1974.
[35] R. J. Kryscio and C. Lefévre, "On the extinction of the SIS stochastic logistic epidemic," *J. Appl. Probab.*, vol. 26, no. 4, pp. 685–694, 1989.
[36] P. Bremaud, *Markov Chains: Gibbs Fields, Monte Carlo Simulation, and Queues*. Berlin, Germany: Springer-Verlag, 1999.
[37] D. J. Daley and J. M. Gani, *Epidemic Modelling: An Introduction*. Cambridge, U.K.: Cambridge Univ. Press, 1999.
[38] O. Diekmann and J. A. P. Heesterbeek, *Mathematical Epidemiology of Infectious Diseases: Model Building, Analysis and Interpretation*. Hoboken, NJ: Wiley, 2000.
[39] H. Andersson and T. Britton, *Stochastic Epidemic Models and Their Statistical Analysis*. Berlin, Germany: Springer-Verlag, 2000.
[40] M. J. Keeling and P. Rohani, *Modeling Infectious Diseases in Humans and Animals*. Princeton, NJ: Princeton Univ. Press, 2007.
[41] P. Magal and S. Ruan, *Structured Population Models in Biology and Epidemiology*. Berlin, Germany: Springer-Verlag, 2008.
[42] P. V. Mieghem, *Performance Analysis of Communications Networks and Systems*. Cambridge, U.K.: Cambridge Univ. Press, 2009.
[43] M. Draief and L. Massoulié, *Epidemics and Rumours in Complex Networks*. Cambridge, U.K.: Cambridge Univ. Press, 2010.
[44] O. Diekmann, H. Heesterbeek, and T. Britton, *Mathematical Tools for Understanding Infectious Disease Dynamics*. Princeton, NJ: Princeton Univ. Press, 2012.
[45] G. H. Weiss and M. Dishon, "On the asymptotic behavior of the stochastic and deterministic models of an epidemic," *Math. Biosci.*, vol. 11, no. 3, pp. 261–265, 1971.
[46] H. W. Hethcote, "Qualitative analyses of communicable disease models," *Math. Biosci.*, vol. 28, no. 3–4, pp. 335–356, 1976.
[47] R. H. Norden, "On the distribution of the time to extinction in the stochastic logistic population model," *Adv. Appl. Probab.*, vol. 14, no. 4, pp. 687–708, 1982.
[48] O. Diekmann, J. A. P. Heesterbeek, and J. A. J. Metz, "On the definition and the computation of the basic reproduction ratio R_0 in models for infectious diseases in heterogeneous populations," *J. Math. Biol.*, vol. 28, no. 4, pp. 365–382, 1990.
[49] K. Dietz, "The estimation of the basic reproduction number for infectious diseases," *Stat. Methods Med. Res.*, vol. 2, no. 1, pp. 23–41, 1993.
[50] L. A. Meyers, "Contact network epidemiology: Bond percolation applied to infectious disease prediction and control," *Bull. Amer. Math. Soc.*, vol. 44, no. 1, pp. 63–86, 2007.
[51] M. E. J. Newman, "Spread of epidemic disease on networks," *Phys. Rev. E*, vol. 66, no. 1, p. 016128, 2002.
[52] K. Oles, E. Gudowska-Nowak, and A. Kleczkowski, "Efficient control of epidemics spreading on networks: Balance between treatment and recovery," *PLoS ONE*, vol. 8, no. 6, p. e63813, June 2013.
[53] A. M. Masucci and A. Silva, "Information spreading on almost torus networks," in *Proc. IEEE Conf. Decision Control*, Florence, Italy, 2013, pp. 3273–3280.
[54] N. Berger, C. Borgs, J. T. Chayes, and A. Saberi, "On the spread of viruses on the Internet," in *Proc. ACM-SIAM Symp. Discrete Algorithms*, Vancouver, Canada, 2005, pp. 301–310.
[55] A. Ganesh, L. Massoulié, and D. Towsley, "The effect of network topology on the spread of epidemics," in *Proc. INFOCOM Joint Conf. IEEE Computer Communications Societies*, Miami, FL, 2005, vol. 2, pp. 1455–1466.
[56] M. Barthelemy, A. Barrat, R. Pastor-Satorras, and A. Vespignani, "Dynamical patterns of epidemic outbreaks in complex heterogeneous networks," *J. Theor. Biol.*, vol. 235, no. 2, pp. 275–288, 2005.
[57] R. Pastor-Satorras and A. Vespignani, "Epidemic dynamics and endemic states in complex networks," *Phys. Rev. E*, vol. 63, p. 066117, Feb. 2001.
[58] R. E. Kooij, P. Schumm, C. Scoglio, and M. Yousef, "A new metric for robustness with respect to virus spread," in *Networking* (Series Lecture Notes in Computer Science, no. 5550), L. Fratta, H. Schulzrinne, Y. Takahashi, and O. Spaniol, Eds. Berlin, Germany: Springer-Verlag, 2009, pp. 562–572.
[59] Y. Moreno, R. Pastor-Satorras, and A. Vespignani, "Epidemic outbreaks in complex heterogeneous networks," *Eur. Phys. J. B*, vol. 26, no. 4, pp. 521–529, 2002.
[60] M. Youssef, R. Kooij, and C. Scoglio, "Viral conductance: Quantifying the robustness of networks with respect to spread of epidemics," *J. Comput. Sci.*, vol. 2, no. 3, pp. 286–298, 2011.
[61] M. Youssef and C. Scoglio, "An individual-based approach to SIR epidemics in contact networks," *J. Theor. Biol.*, vol. 283, no. 1, pp. 136–144, 2011.
[62] R. Pastor-Satorras, C. Castellano, P. V. Mieghem, and A. Vespignani, "Epidemic processes in complex networks," arXiv:1408.2701, 2014.
[63] Y. Hu, H. Chen, J. Lou, and J. Li, "Epidemic spreading in real networks: An eigenvalue viewpoint," in *Proc. Symp. Reliable Distributed Systems*, 2003, pp. 25–34.
[64] T. Mountford, J. Mourrat, D. Valesin, and Q. Yao, "Exponential extinction time of the contact process on finite graphs," arXiv:1203.2972, 2012.

[65] P. V. Mieghem, "Decay towards the overall-healthy state in SIS epidemics on networks," arXiv:1310.3980, 2013.
[66] P. V. Mieghem, "Exact Markovian SIR and SIS epidemics on networks and an upper bound for the epidemic threshold," arXiv:1402.1731, 2014.
[67] P. V. Mieghem, F. D. Sahneh, and C. Scoglio, "An upper bound for the epidemic threshold in exact Markovian SIR and SIS epidemics on networks," in *Proc. IEEE Conf. Decision Control*, Los Angeles, CA, 2014, pp. 6228–6233.
[68] C. Borgs, J. Chayes, A. Ganesh, and A. Saberi, "How to distribute antidote to control epidemics," *Random Struct. Alg.*, vol. 37, no. 2, pp. 204–222, 2010.
[69] R. Pastor-Satorras and A. Vespignani, "Epidemic spreading in scale-free networks," *Phys. Rev. Lett.*, vol. 86, no. 14, pp. 3200–3203, 2001.
[70] D. Chakrabarti, Y. Wang, C. Wang, J. Leskovec, and C. Faloutsos, "Epidemic thresholds in real networks," *ACM Trans. Inform. Syst. Secur.*, vol. 10, no. 4, pp. 1–26, 2008.
[71] P. V. Miegham, J. Omic, and R. Kooij, "Virus spread in networks," *IEEE/ACM Trans. Netw.*, vol. 17, no. 1, pp. 1–14, 2009.
[72] P. V. Mieghem, "The n-intertwined SIS epidemic network model," *Computing*, vol. 93, nos. 2–4, pp. 147–169, 2011.
[73] C. Li, R. van de Bovenkamp, and P. V. Mieghem, "Susceptible-infected-susceptible model: A comparison of N-intertwined and heterogeneous mean-field approximations," *Phys. Rev. E*, vol. 86, p. 026116, Aug. 2012.
[74] H. J. Ahn and B. Hassibi, "Global dynamics of epidemic spread over complex networks," in *Proc. IEEE Conf. Decision Control*, Florence, Italy, 2013, pp. 4579–4585.
[75] A. Lajmanovich and J. A. Yorke, "A deterministic model for gonorrhea in a nonhomogeneous population," *Math. Biosci.*, vol. 28, no. 3, pp. 221–236, 1976.
[76] A. Khanafer, T. Basar, and B. Gharesifard, "Stability properties of infected networks with low curing rates," in *Proc. American Control Conf.*, Portland, OR, 2014, pp. 3579–3584.
[77] A. Khanafer, T. Basar, and B. Gharesifard, "Stability properties of infection diffusion dynamics over directed networks," in *Proc. IEEE Conf. Decision Control*, Los Angeles, CA, 2014, pp. 6215–6220.
[78] E. Cator and P. V. Mieghem, "Second-order mean-field susceptible-infected-susceptible epidemic threshold," *Phys. Rev. E*, vol. 85, p. 056111, May 2012.
[79] P. V. Mieghem and J. Omic, "In-homogeneous virus spread in networks," arXiv:1306.2588, 2014.
[80] A. Fall, A. Iggidr, G. Sallet, and J.-J. Tewa, "Epidemiological models and Lyapunov functions," *Math. Model. Natural Phenomena*, vol. 2, no. 1, pp. 62–68, 2007.
[81] F. D. Sahneh and C. Scoglio, "Epidemic spread in human networks," in *Proc. IEEE Conf. Decision Control*, Orlando, FL, 2011, pp. 3008–3013.
[82] C. Nowzari, V. M. Preciado, and G. J. Pappas, "Stability analysis of generalized epidemic models over directed networks," in *Proc. IEEE Conf. Decision Control*, Los Angeles, CA, Dec. 2014, pp. 6197–6202.
[83] C. Nowzari, M. Ogura, V. M. Preciado, and G. J. Pappas, "A general class of spreading processes with non-Markovian dynamics," in *Proc. IEEE Conf. Decision Control*, Osaka, Japan, Dec. 2015, to be published.
[84] V. M. Preciado and A. Jadbabaie, "Spectral analysis of virus spreading in random geometric networks," in *Proc. IEEE Conf. Decision Control*, Shanghai, China, 2009, pp. 4802–4807.
[85] P. V. Mieghem, D. Stevanovic, F. Kuipers, C. Li, R. van de Bovenkamp, D. Liu, and H. Wang, "Decreasing the spectral radius of a graph by link removals," *Phys. Rev. E*, vol. 84, p. 016101, July 2011.
[86] P. Holme and B. J. Kim, "Attack vulnerability of complex networks," *Phys. Rev. E*, vol. 65, p. 056109, May 2002.
[87] J. C. Miller and J. M. Hyman, "Effective vaccination strategies for realistic social networks," *Phys. A: Stat. Mech. Appl.*, vol. 386, no. 2, pp. 780–785, 2007.
[88] C. M. Schneider, T. Mihaljev, S. Havlin, and H. J. Herrmann, "Suppressing epidemics with a limited amount of immunization units," *Phys. Rev. E*, vol. 84, p. 061911, Dec. 2011.
[89] D. H. Zanette and S. Risau-Gusman, "Infection spreading in a population with evolving contacts," *J. Biol. Phys.*, vol. 34, no. 1–2, pp. 135–148, 2008.
[90] S. Saha, A. Adiga, B. A. Prakash, and A. K. S. Vullikanti, "Approximation algorithms for reducing the spectral radius to control epidemic spread," arXiv:1501.06614, 2015.
[91] A. N. Bishop and I. Shames, "Link operations for slowing the spread of disease in complex networks," *Europhys. Lett.*, vol. 95, no. 1, p. 18005, 2011.
[92] M. Zargham and V. M. Preciado, "Worst-case scenarios for greedy, centrality-based network protection strategies," in *Proc. Conf. Information Sciences Systems*, Princeton, NJ, 2014, pp. 1–6.
[93] E. Gourdin, J. Omic, and P. V. Mieghem, "Optimization of network protection against virus spread," in *Proc. 8th Int. Workshop Design Reliable Communication Networks*, 2011, pp. 86–93.
[94] B. A. Prakash, L. Adamic, T. Iwashnya, H. Tong, and C. Faloutsos, "Fractional immunization in networks," in *Proc. SIAM Int. Conf. Data Mining*, Austin, TX, 2013, pp. 659–667.
[95] Y. Wan, S. Roy, and A. Saberi, "Network design problems for controlling virus spread," in *Proc. IEEE Conf. Decision Control*, New Orleans, LA, 2007, pp. 3925–3932.
[96] Y. Wan, S. Roy, and A. Saberi, "Designing spatially heterogeneous strategies for control of virus spread," *Syst. Biol. IET*, vol. 2, no. 4, pp. 184–201, 2008.
[97] V. M. Preciado, M. Zargham, C. Enyioha, A. Jadbabaie, and G. J. Pappas, "Optimal vaccine allocation to control epidemic outbreaks in arbitrary networks," in *Proc. IEEE Conf. Decision Control*, Florence, Italy, 2013, pp. 7486–7491.
[98] V. M. Preciado and M. Zargham, "Traffic optimization to control epidemic outbreaks in metapopulation models," in *Proc. IEEE Global Conf. Signal Information Processing*, Austin, TX, 2013, pp. 847–850.
[99] X. Zhai, L. Zheng, J. Wang, and C. W. Tan, "Optimization algorithms for epidemic evolution in broadcast networks," in *Proc. IEEE Wireless Communications Networking Conf.*, Shanghai, China, 2013, pp. 1540–1545.
[100] V. M. Preciado, M. Zargham, C. Enyioha, A. Jadbabaie, and G. J. Pappas, "Optimal resource allocation for network protection: A geometric programming approach," *IEEE Trans. Control Netw. Syst.*, vol. 1, no. 1, pp. 99–108, 2014.
[101] V. M. Preciado, M. Zargham, and D. Sun, "Traffic control for network protection against spreading processes," in *Proc. Conf. Information Sciences Systems*, Princeton, NJ, 2014, pp. 1–9.
[102] V. M. Preciado, F. D. Sahneh, and C. Scoglio, "A convex framework for optimal investment on disease awareness in social networks," in *Proc. IEEE Global Conf. Signal Information Processing*, Austin, TX, 2013. pp. 851–854.
[103] C. Nowzari, V. M. Preciado, and G. J. Pappas, "Optimal resource allocation in generalized epidemic models," *IEEE Trans. Control Netw. Syst.*, 2015, doi: 10.1109/TCNS.2015.2482221.
[104] A. Vijayshankar and S. Roy, "Cost of fairness in disease spread control," in *Proc. IEEE Conf. Decision Control*, Maui, HI, 2012, pp. 4930–4935.
[105] G. A. Forster and C. A. Gilligan, "Optimizing the control of disease infestations at the landscape level," *Proc. Natl. Acad. Sci. U.S.A.*, vol. 104, no. 12, pp. 4984–4989, 2007.
[106] R. Morton and K. H. Wickwire, "On the optimal control of a deterministic epidemic," *Adv. Appl. Probab.*, vol. 6, no. 4, pp. 622–635, 1974.
[107] S. Eshghi, M. H. R. Khouzani, S. Sarkar, and S. S. Venkatesh, "Optimal patching in clustered epidemics of malware," *IEEE Trans. Network.*, 2015, doi: 10.1109/TNET.2014.2364034
[108] K. H. Wickwire, "Optimal isolation policies for deterministic and stochastic epidemics," *Math. Biosci.*, vol. 26, nos. 3–4, pp. 325–346, 1975.
[109] E. Hansen and T. Day, "Optimal control of epidemics with limited resources," *J. Math. Biol.*, vol. 62, no. 3, pp. 423–451, 2011.
[110] G. Zaman, Y. H. Kang, and I. H. Jung, "Stability analysis and optimal vaccination of an SIR epidemic model," *Biosystems*, vol. 93, no. 3, pp. 240–249, 2008.
[111] H. Behncke, "Optimal control of deterministic epidemics," *Optim. Contr. Applicat. Methods*, vol. 21, no. 6, pp. 269–285, 2001.
[112] T. K. Kar and A. Batabyal, "Stability analysis and optimal control of an SIR epidemic model with vaccination," *Biosystems*, vol. 104, nos. 2–3, pp. 127–135, 2011.
[113] M. H. R. Khouzani, S. S. Venkatesh, and S. Sarkar, "Market-based control of epidemics," in *Proc. Allerton Conf. Communications, Control Computing*, Monticello, IL, 2011, pp. 314–320.
[114] M. H. R. Khouzani, S. Sarkar, and E. Altman, "Dispatch then stop: Optimal dissemination of security patches in mobile wireless networks," in *Proc. IEEE Conf. Decision Control*, Atlanta, GA, 2010, pp. 2354–2359.
[115] M. H. R. Khouzani, S. Sarkar, and E. Altman, "Optimal control of epidemic evolution," in *Proc. IEEE INFOCOM*, Shanghai, China, 2011, pp. 1683–1691.
[116] D. Iacoviello and G. Liuzzi, "Optimal control for SIR epidemic model: A two treatments strategy," in *Proc. 16th Mediterranean Conf. Control Automation*, Ajaccio, France, June 2008, pp. 842–847.
[117] D. Iacoviello and N. Stasio, "Optimal control for SIRC epidemic outbreak," *Comput. Methods Program. Biomed.*, vol. 110, no. 3, pp. 333–342, 2013.
[118] E. Verriest, F. Delmotte, and M. Egerstedt, "Control of epidemics by vaccination," in Proc. *American Control Conf.*, Portland, OR, 2005, pp. 985–990.
[119] P. Chen, S. Cheng, and K. Chen, "Optimal control of epidemic information dissemination over networks," *IEEE Trans. Cybern.*, vol. 44, no. 12, pp. 2316–2328, 2014.

[120] A. Karnik and P. Dayama, "Optimal control of information epidemics," in *Proc. 4th Int. Conf. Communication Systems Networks*, Bangalore, India, Jan. 2012, pp. 1–7.
[121] M. Bloem, T. Alpcan, and T. Basar, "Optimal and robust epidemic response for multiple networks," *Contr. Eng. Pract.*, vol. 17, no. 5, pp. 525–533, 2009.
[122] A. Khanafer and T. Basar, "An optimal control problem over infected networks," in *Proc. Int. Conf. Control, Dynamic Systems, Robotics*, Ottawa, ON, Canada, 2014, paper 125, pp. 1–6.
[123] F. H. Chen, "A susceptible-infected epidemic model with voluntary vaccinations," *J. Math. Biol.*, vol. 53, no. 2, pp. 253–272, 2006.
[124] B. Buonomo, A. d'Onofrio, and D. Lacitignola, "Global stability of an SIR epidemic model with information dependent vaccination," *Math. Biosci.*, vol. 216, no. 1, pp. 9–16, 2008.
[125] J. O. Kephart and S. R. White, "Measuring and modeling computer virus prevalence," in *Proc. IEEE Symp. Research Security Privacy*, Oakland, CA, 1993, pp. 2–15.
[126] I. B. Schwartz and L. B. Shaw, "Rewiring for adaption," *Physics*, vol. 3, no. 17, 2010, doi: 10.1103/Physics.3.17.
[127] H. Zhang, J. Zhang, P. Li, M. Small, and B. Wang, "Risk estimation of infectious diseases determines the effectiveness of the control strategy," *Phys. D: Nonlinear Phenom.*, vol. 240, no. 11, pp. 943–948, 2011.
[128] G. Theodorakopoulos, J. Y. Le Boudec, and J. S. Baras, "Selfish response to epidemic propagation," *IEEE Trans. Autom. Contr.*, vol. 58, no. 2, pp. 363–376, 2013.
[129] I. Tomovski and L. Kocarev, "Simple algorithm for virus spreading control on complex networks," *IEEE Trans. Circuits Syst.*, vol. 59, no. 4, pp. 763–771, 2012.
[130] S. Funk, E. Gilad, C. Watkins, and V. A. A. Jansen, "The spread of awareness and its impact on epidemic outbreaks," *Proc. Natl. Acad. Sci.*, vol. 16, no. 106, pp. 6872–6877, 2009.
[131] S. Funk, M. Salathe, and V. A. A. Jansen, "Modelling the influence of human behaviour on the spread of infectious diseases: A review," *J. Roy. Soc. Interface*, vol. 7, no. 50, pp. 1247–1256, 2010.
[132] Z. Ruan, M. Tang, and Z. Liu, "Epidemic spreading with information-driven vaccination," *Phys. Rev. E*, vol. 86, p. 036117, Sept. 2012.
[133] Q. Wu, X. Fu, Z. Jin, and M. Small, "Influence of dynamic immunization on epidemic spreading in networks," *Phys. A: Stat. Mech. Applicat.*, vol. 419, no. 1, pp. 566–574, 2015.
[134] X. Peng, X. Xu, X. Fu, and T. Zhou, "Vaccination intervention on epidemic dynamics in networks," *Phys. Rev. E*, vol. 87, p. 022813, Feb. 2013.
[135] C. Enyioha, V. M. Preciado, and G. J. Pappas, "Bio-inspired strategy for control of viral spreading in networks," in *Proc. 2nd ACM Int. Conf. High Confidence Networked Systems*, New York, 2013, pp. 33–40.
[136] F. D. Sahneh and C. M. Scoglio, "Optimal information dissemination in epidemic networks," in *Proc. IEEE Conf. Decision Control*, Maui, HI, 2012, pp. 1657–1662.
[137] H. W. Hethcote, "A thousand and one epidemic models," in *Frontiers in Mathematical Biology* (Series Lecture Notes in Biomathematics, no. 100), S. A. Levin, Ed. New York: Springer-Verlag, 1994, pp. 504–515.
[138] F. Chung, P. Horn, and A. Tsiatas, "Distributing antidote using PageRank vectors," *Internet Math.*, vol. 6, no. 2, pp. 237–254, 2009.
[139] K. Drakopoulos, A. Ozdaglar, and J. N. Tsitsiklis, "An efficient curing policy for epidemics on graphs," in *Proc. IEEE Conf. Decision Control*, Los Angeles, CA, 2014, pp. 4447–4454.
[140] R. Sabbadin, N. Peyrard, and N. Forsell, "A framework and a mean-field algorithm for the local control of spatial processes," *Int. J. Approx. Reason.*, vol. 53, no. 1, pp. 66–86, 2012.
[141] E. Ramirez-Llanos and S. Martinez, "A distributed algorithm for virus spread minimization," in *Proc. American Control Conf.*, Portland, OR, 2014, pp. 184–189.
[142] C. Enyioha, A. Jadbabaie, V. M. Preciado, and G. J. Pappas, "Distributed resource allocation for epidemic control," arXiv:1501.01701, 2015.
[143] L. Zager and G. Verghese, "Epidemic thresholds for infections in uncertain networks," *Complexity*, vol. 14, no. 4, pp. 12–25, 2009.
[144] I. Tomovski and L. Kocarev, "Network topology inference from infection statistics," *Phys. A: Stat. Mech. Applicat.*, vol. 436, no. 1, pp. 272–285, 2015.
[145] S. Han, V. M. Preciado, C. Nowzari, and G. J. Pappas, "Data-driven allocation of vaccines for controlling epidemic outbreaks," *IEEE Trans. Netw. Sci. Eng.*, 2015. doi: 10.1109/TNSE.2015.2500158.
[146] A. Vazquez, "Epidemic outbreaks on structured populations," *J. Theor. Biol.*, vol. 245, pp. 125–129, Sept. 2007.
[147] F. D. Sahneh, C. Scoglio, and P. V. Mieghem, "Generalized epidemic mean-field model for spreading processes over multilayer complex networks," *IEEE/ACM Trans. Network.*, vol. 21, no. 5, pp. 1609–1620, Oct. 2013.
[148] M. E. J. Newman, "Threshold effects for two pathogens spreading on a network," *Phys. Rev. Lett.*, vol. 95, no. 10, p. 108701, 2005.
[149] W. Mei and F. Bullo, "Modeling and analysis of competitive propagation with social conversion," in *Proc. IEEE Conf. Decision Control*, Los Angeles, CA, 2014, pp. 6203–6208.
[150] X. Wei, N. C. Valler, A. Prakash, I. Neamtiu, M. Faloutsos, and C. Faloutsos, "Competing memes propagation on networks: A network science perspective," *IEEE J. Select. Areas Commun.*, vol. 31, no. 6, pp. 1049–1060, June 2013.
[151] A. Stanoev, D. Trpevski, and L. Kocarev, "Modeling the spread of multiple concurrent contagions on networks," *PLoS ONE*, vol. 9, no. 6, p. e95669, 2014.
[152] X. Wei, N. Valler, B. A. Prakash, I. Neamtiu, M. Faloutsos, and C. Faloutsos, "Competing memes propagation on networks: A case study of composite networks," *ACM SIGCOMM Comput. Commun. Rev.*, vol. 42, no. 5, pp. 5–12, 2012.
[153] A. Beutel, B. A. Prakash, R. Rosenfeld, and C. Faloutsos, "Interacting viruses in networks: Can both survive?" in *Proc. 18th ACM SIGKDD Int. Conf. Knowledge Discovery Data Mining*, Beijing, China, 2012, pp. 426–434.
[154] B. A. Prakash, A. Beutel, R. Rosenfeld, and C. Faloutsos, "Winner takes all: Competing viruses or ideas on fair-play networks," in *Proc. 21st Int. Conf. World Wide Web*, Lyon, France, 2012, pp. 1037–1046.
[155] F. D. Sahneh and C. Scoglio, "Competitive epidemic spreading over arbitrary multilayer networks," *Phys. Rev. E*, vol. 89, p. 062817, June 2014.
[156] N. J. Watkins, C. Nowzari, V. M. Preciado, and G. J. Pappas, "Optimal resource allocation for competing epidemics over arbitrary networks," in *Proc. American Control Conf.*, Chicago, IL, July 2015, pp. 1381–1386.
[157] G. Elena and Q. Zhu, "Optimal control of influenza epidemic model with virus mutations," in *Proc. European Control Conf.*, Zürich, Switzerland, 2013, pp. 3125–3130.
[158] X. Chen and V. M. Preciado, "Optimal coinfection control of competitive epidemics in multi-layer networks," in *Proc. IEEE Conf. Decision Control*, Los Angeles, CA, 2014, pp. 6209–6214.
[159] E. Hernandez-Vargas, P. Colaneri, R. Middleton, and F. Blanchini, "Discrete-time control for switched positive systems with application to mitigating viral escape," *Int. J. Robust Nonlinear Contr.*, vol. 21, no. 10, pp. 1093–1111, 2011.
[160] S. Xu, W. Lu, L. Xu, and Z. Zhan, "Adaptive epidemic dynamics in networks: Thresholds and control," *ACM Trans. Auton. Adapt. Syst.*, vol. 8, no. 4, Article #19, pp. 1–19, 2014.
[161] M. Ogura and V. M. Preciado, "Disease spread over randomly switched large-scale networks," in *Proc. American Control Conf.*, Chicago, IL, 2015, pp. 1782–1787.
[162] M. Sathiamoorthy, K. R. Moghadam, B. Krishnamachari, and F. Bai, "Helper node allocation strategies for content dissemination in intermittently connected mobile networks," in *Proc. IEEE Int. Conf. Sensing, Communication, Networking*, Singapore, 2014, pp. 55–63.
[163] C. T. Bauch and D. J. D. Earn, "Vaccination and the theory of games," *Proc. Natl. Acad. Sci. U.S.A.*, vol. 101, no. 36, pp. 13391–13394, 2004.
[164] A. Khanafer and T. Basar, "Information spread in networks: Control, games, and equilibria," in *Proc. Information Theory Applications Workshop*, San Diego, CA, 2014, pp. 1–10.
[165] J. Omic, A. Orda, and P. V. Mieghem, "Protecting against network infections: A game theoretic perspective," in *Proc. IEEE INFOCOM*, Rio de Janeiro, Brazil, 2009, pp. 1485–1493.
[166] Y. Hayel, S. Trajanovski, E. Altman, H. Wang, and P. V. Mieghem, "Complete game-theoretic characterization of SIS epidemics protection strategies," in *Proc. IEEE Conf. Decision Control*, Los Angeles, CA, 2014, pp. 1179–1184.
[167] S. Trajanovski, Y. Hayel, E. Altman, H. Wang, and P. V. Mieghem, "Decentralized protection strategies against SIS epidemics in networks," arXiv:1409.1730, 2014.
[168] A. Fazeli and A. Jadbabaie, "Game theoretic analysis of a strategic model of competitive contagion and product adoption in social networks," in *Proc. IEEE Conf. Decision Control*, Maui, HI, 2012, pp. 74–79.
[169] A. Fazeli, A. Ajorlou, and A. Jadbabaie, "Optimal budget allocation in social networks: Quality or seeding?" in *Proc. IEEE Conf. Decision Control*, Los Angeles, CA, 2014, pp. 4455–4460.