Interventions in Networks
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Abstract

Interventions are made in networks to change the network or its values in a desired way. The intervention strategies evaluated in the study described here use network sampling designs to find units to which interventions are applied. An intervention applied to a network node or link can change a value associated with that unit. Over time the effect of the intervention can have an effect on the population that goes beyond the sample units to which it is directly applied. This paper describes the methods used for this study. These include a variety of link-tracing sampling designs in networks, a number of types of interventions, and a temporal spatial network model in which the intervention strategies are evaluated. An intervention strategy is associated with an agent and different intervention strategies interact and adapt to each other over time. Some preliminary results are summarized regarding potential intervention strategies to help alleviate the HIV epidemic.

Author Summary

Introduction

The purpose of the project described here is to create a sampling design and simulation system for evaluating the effectiveness of potential strategies for interventions in networks. The motivating problem for this work has been the effort to understand and reduce the spread of HIV. An effective intervention is one that helps in reducing the epidemic at least locally in an area of focus.

The approach taken uses a network or spatial sampling design to find units to which to make interventions. These designs in many cases involve tracing of links from sample units to add new units to the sample. The population network itself is the result of choices of individuals, and consensus of pairs of individuals, in forming and dissolving links between them. The tendencies of individuals in this process are viewed also as sampling designs.

A typical design in this study might use spatial sampling to find initial candidate nodes for selection. Subsequent selections can use link tracing to find additional candidate nodes. The sampling process includes a selection process for adding units to the sample and an attrition process by which nodes are removed from the sample.
An intervention strategy is the combination of a sampling design and the intervention made to its sample units. We think of a design or strategy as having an agent behind it. Sexually transmissible infections are often countered by public health agencies with seek and treat designs which follow sexual links from infected persons and test and treat their recent partners. A person choosing not to take on additional partners once he or she has a partner, on the other hand, is exercising individual agency. In a choice of a safer sex practice such as using a condom in a given situation, agency may be associated with the pair of individuals and their negotiations.

A natural agent such as a virus has its own sampling design. In the case of HIV it is a link-tracing design, reaching new individuals through sexual and blood-exposure links. The intervention is infection of the individual.

One intervention strategy interacts with another. An intervention design that follows links from individuals who test positive for HIV is influenced in where it goes by the pattern of virus spread. An intervention such as an antiretroviral prescription or, potentially, a vaccine or a cure, affects the virus by reducing its spread. Behavioral changes of individuals and pairs in cooperation affect the spread of the virus. The virus affects the population by increasing mortality rate of infected individuals and, as described later in this paper, affecting the link pattern or temporal network geometry of the population. Additionally, two types of virus such as HIV and herpes simplex virus 2 can catalyze the spread of each other.

The sampling designs are adaptive in that the probability of following a link or adding a unit to the sample can depend on the values of the originating or candidate nodes, on values associated with the links between, and on surrounding network conditions. In addition, a deeper adaptivity changes design parameters as virus strains evolve and people learn.

Because of the multiple agents, the interactions between designs, the adaptations to interventions, and effects of interventions unfolding over time, the births and deaths of nodes and the fornings and dissolvings of links, the problem is inherently complicated and it is helpful to find simplifications. A number of the designs, human and natural, have common features. Some variables in the overall process have stochastic stability properties given specific intervention strategies. In such cases we can view the summary effect of an intervention as the change in its equilibrium distribution once the intervention strategy is put into effect.

**Background**

Design-based inference methods using Markov Chain Monte Carlo sampling from a conditional distribution given a sufficient sample statistic are used in link-tracing designs in networks \[1,8\]. The current approach to likelihood-based inference with link-tracing designs most often assumes design ignorability in the sense of \[4\]. The likelihood approach to inference for link-tracing designs in networks is described \[5\], developed for
exact Bayes inference with a simple model/design combination in [6], and for computational Bayes inference with adaptive web sampling with a stochastic block network model in Kwanisai, M. (2005, Estimation in Link-Tracing Designs with Subsampling. Ph.D. thesis, The Pennsylvania State University, University Park, PA, USA). This approach was developed farther and for more complex network models in [7] and subsequent papers by those authors. In [8] the Bayes inference deals with both a network model and a network sampling design that is nonignorable. Issues of inference in network epidemic models are additionally discussed in [9].

[10] describe empirical likelihood based confidence intervals for adaptive cluster sampling. [11] analyze weighting systems for estimation in indirect sampling, a class of adaptive network designs.

Approaches combining design and model based methods include the random walk asymptotics-based estimators used with respondent driven sampling [12, 13], [14], [15], and [2]. A different approach is used in [16] and [17]. A different approach still combining design and model based methods is developed in [18]. Current methods in respondent driven sampling are assessed in [19], [20] and [21].

[22], [23], [24], and other authors have looked into the combined effect of experimental treatment-assignment designs and unit-selecting sampling designs on inference. A sample of units is selected from a population by some sampling design. This sample obtains the experimental units. An experimental design is then used to assign the experimental units to treatments. The experimental design enables inference regarding the effects of treatments to the experimental units, and the sampling design enables inferring how this potential effect extends to the population as a whole.

Recently a number of papers have come out with approaches to extending static network models to the dynamic situation. [25–28] and [29] developed an interesting class of network evolution models based on behavioral characteristics of actors/nodes such as tendencies toward reciprocity, transitivity, homophily, and assortative matching. At the same time he developed inference methods to estimate model parameters from incomplete longitudinal data. A summary of this work together with a review of other approaches to dynamic network modeling is contained in [30]. [31] present a dynamic network model based on exponential random graph models. A recent summary of statistical network models is provided by [32].

Latent space network models were introduced in [33] for static networks. A dynamic extension of that approach in which nodes move by small random increments was developed by [34].

In this paper I use the latent space approach with an underlying temporal spatial point processes having grouping and clustering tendencies and births and deaths of point-objects, which serve as the network nodes. The temporal network model on top of that has links forming and dissolving over time, allowing for link probabilities to depend on social distances between nodes, node characteristics including including sex of a potential partner, group identities, and various network properties such as degrees and component
memberships of each potential partner. This model is then used for the spread and adaptations of virus strains and evaluations of effectiveness of different sampling designs and intervention strategies.

**Methods**

In this project we are primarily interested in evaluating the effectiveness of sampling designs for bringing interventions to units in a population. The intervention is then applied to units in the sample, according to an intervention design. From this point of view, an experiment set in a population is an intervention with the purpose of inferring a cause and effect relationship between the intervention and its effect on sample units. For an experiment it is considered desirable that an intervention or treatment applied to one unit does not affect the response of any other unit. More broadly though, we are particularly interested in interventions that, when applied to a sample of units, have a desirable effect on the population as a whole, including units to which the intervention has not been applied.

The methods of the study consist largely of devising sampling designs and intervention strategies for implementation in spatial, temporal, and network settings. An intervention strategy consists of a sampling design for selecting the units to receive the intervention and a procedure for assigning interventions to units in the sample. Application of an intervention to a unit changes the value of some variable associated with the unit.

We think of the population as a network or graph structure $G$ consisting of nodes and edges and having values $y$ associated with nodes and $x$ associated with edges. The network and its values are stochastic and change over time, so that we have a stochastic process

$$\{G_t, t \in T\}$$

where $T$ is the time index set, which we will take to be discrete. In more detail the population at time $t$ is

$$G_t = \{U_t, E_t, y(U_t), x(E_t)\}$$

where $U_t$ is the set of units or nodes, $E_t$ is the set of edges or links between nodes, $y(U_t)$ represents the variables of interest associated with nodes, and $x(E_t)$ represents variables associated with the links. Note that $U_t$ and $E_t$ are random sets, containing different elements at different time point, with insertions and deletions of nodes and insertions and deletions of links taking place over time.

To make interventions in this population we need a sampling design to reach nodes or edges on which to make the interventions. At time $t$ the sample is a subset of the network and its values:

$$s_t \subset \{U_t, E_t\}$$
and we have a sampling process through time:

\[ \{s_t, t \in T\} \]

The sampling design is the probability of selecting the sample, which at time \( t \) typically depends on the sample, the network and values at times up to \( t \),

\[ P(s_t | s_{t'}, G_{t'}, \phi_{t'}, t' \leq t) \]

where \( \phi_t \) are design parameters, which also may change with time. Once the sample at time \( t \) is selected the intervention can change values \( y \) and \( x \) associated with nodes or links in the sample. Note that over time the sampling process can select units to add to the sample and units to drop from the sample.

An intervention to a sample unit is a procedure that changes a value \( y_u \) associated with a unit \( u \in s \), or a value \( x_{uv} \) associated with an edge \((u, v) \in s\) to a new value \( y'_u \) or \( x'_{uv} \). For example if the intervention is prescribing a medication to person \( u \), an indicator variable \( y_u \) might change from 0 to 1. The intervention is thus distinguished from the effects of an intervention program, which develop over time and might affect nodes and edges outside the sample as well as inside.

The set of nodes \( U_t \) is a stochastic point process. We model it as a spatial temporal point process with variable amounts of clustering in space and motion over time. Specifically, we construct a spatial temporal Poisson cluster process as follows. A set of \( k \) group center locations are initially selected independently and uniformly over a study region, which we take as the unit square. Let \( c_t \) be center location at time \( t \) for group a given group. At each time step \( t \) it is perturbed as follows. The most recent displacement was \( \delta_{t-1} = c_{t-1} - c_{t-2} \). The new displacement is \( \delta_t = \delta_{t-1} + \epsilon_t \). Assuming the spatial study region of interest is two dimensional, the random perturbation \( \epsilon_t \) is bivariate normal with means 0 a small standard deviation equal in each direction and zero correlation. For a process with directional motion one can add to the means or have unequal standard deviations and nonzero correlation. This produces clusters that drift around independently and have a momentum tendency in their ever changing direction and speed. Further, this drift is kept in its initial distribution by using a Markov Chain Monte Carlo (Metropolis-Hastings) selection step for each group at each time step.

The numbers of nodes per group are initially distribution Poisson(\( \lambda \)). The expected number \( \lambda \) can be constant or selected independently for each group from a lognormal distribution, producing more uneven sized clusters.

The locations of nodes are initially distributed with a bivariate normal distribution around group center locations. Relative to the group center, a node gets at each time step a random displacement according to an autoregressive process or order 2, with the parameters chosen to keep it in the initial bivariate normal distribution relative to its group center. Given the group centers, nodes move independently to each other.

Nodes are stochastically deleted over time depending on birth and immigration rates and deleted depending on mortality and emigration rates. Mortality rates depend on
things like ages and stages of nodes. Insertion rates are deliberately set to keep the population and the group sizes in fluctuating but stochastically stable distributions. There are many ways to do this, as is done in population dynamics models. Here we simply imagine that as nodes die or move out of the population, there is a tendency for new nodes to move in over time to maintain a relatively stable population, so that expected insertions is set accordingly. Actual insertions are Poisson with that mean value, and assignments of new nodes to groups is with probabilities proportional to target group sizes compared to current sizes.

Network links are inserted and deleted by the following process. An individual node has a selection function, centered on it and decreasing with distance, for making tentative selections of nearby nodes with whom to form a partnership. Probability of selection decreases with distance. A simple choice is a normal kernel function

\[ g(d) = a_i e^{-d^2/2\sigma_i^2} \]

where \( g \) is the probability of tentative selection by node \( i \) of a node \( j \) at distance \( d \) from it and \( \sigma \) is a spread parameter which can be node specific. Further we set \( g(d) = 0 \) for some \( d \) greater than some maximum reach distance such as \( 3\sigma_i \). Other selection function options include the logistic function, which has an additional shape parameter and the disk step function with is a constant out to the reach radius and 0 beyond it.

Meanwhile node \( j \) may be making a parallel selection decision on node \( i \) and a link tentatively forms with probability

\[ h(d) = a_i a_j e^{-d^2/2(1/\sigma_i^2+1/\sigma_j^2)} \]

In addition, the selection probability is further modified by dependence on values of the two nodes, including the current degree already of each, and by network values such as sizes of the components each node is in and whether they are already in the same component or not. Dependence on a value such as degree can be compensatory, as when a node will not take on a new partner if either it or the potential partner has already one or more partners already, or preferential attachment, when a node with high degree makes it more likely to take on another relationship.

In this way, the network formation process depends on \( N_t \) designs, where \( N_t \) is the number of nodes at time \( t \) and links are formed by consensus or negotiations between pairs of nodes. Deletion of a link is at the discretion of either node in a partnership, and the probability of deletion can similarly depend on current values.

In this way the design that creates, maintains, and changes the network is decentralized, with agency largely residing with individuals and pairs.

The sampling designs with which we reach into the network population can in some cases use a conventional frame such as a list of nodes and in other cases use spatial sampling techniques. A Bernoulli sample in a population of \( N_t \) units has \( N_t \) independent trials, selecting unit \( i \) with probability \( p_i \), for \( i = 1, ..., N_t \). The sample size is random,
with expected value $\sum_{i=1}^{N_t} p_i$. A conventional design for sampling with replacement from $N_t$ units has $n$ independent trials with unit $i$ having probability of selection $p_i$ on each of the trials. A random sample without replacement has equal probability of selection for each possible combination of $n$ distinct units, giving probability $n/N_t$ probability that unit $i$ is included in the sample.

Our focus of interest in this paper is on the link-tracing designs. These can be started with any of the simple designs above. In many cases of interest, the sampling process attains over time a stochastically stable distribution regardless of the initial design by which it started. Also nodes are being considered a sampling process that at time $t-1$ has a sample $S_{t-1}$. The sample $S_t$ is the result of following links out from $S_{t-1}$, supplemented by new nodes selected at random, spatially, or other design not relying on links. An edge going from node $i$ to node $j$ is a pair $(i, j)$ in the current edge set $E_t$, the pair being ordered if the link is directional.

A flexible type of link tracing design selects a Bernoulli sample of links out from the current sample to add new nodes to the sample. The probability $p_{(i,j)}$ of following link $(i, j)$ to add node $j$ to the sample, for $(i, j) \in E_{t-1}$, $i \in S_{t-1}$, and $j \notin S_{t-1}$ can depend on values associated with the origin node $i$, values associated with the destination node $j$, and values associated with the link $(i, j)$ between them. For a unit $i$ outside the sample, the probability it is added at time $t$ through link tracing is

$$p(i \in s_t \mid i \notin s_{t-1}) = 1 - \prod_{\{j : j \in s_{t-1}, e(j, i) \in E_{t-1}\}} (1 - p_{(i,j)})$$

In addition nodes may be added on occasion through direct Bernoulli sampling or random sampling without replacement.

Nodes are removed from the sample through Bernoulli removals. Thus

$$p(i \notin s_t \mid i \in s_{t-1}) = q_i$$

The probability $q_i$ for removing node $i$ from the sample may depend on values associated with the node such as how long it has been in the sample. In many cases the Bernoulli removals may be independent from one sample node to another. In other cases, however, dependence results from limited resources or designs which increase or decrease probabilities of removal depending on current sample size. In addition a node $i$ is removed from the sample when it is deleted from the population.

Different variations of this type of design can select a random sample of without replacement of $n_t$ links out from the sample, where $n_t$ may have a fixed target value but be constrained to be no greater than the number of links out. If the number of links out is less than $n_t$, the additional desired units can be selected by simple random sampling from those not in the sample. In another variation links out are selected with replacement using $n_t$ independent trials with link $(i, j)$ having probability of selection $p_{(i,j)}$ for $(i, j) \in E_{t-1}$, $i \in S_{t-1}$, and $j \notin S_{t-1}$. Further variations include designs of a type used in respondent
driven sampling of members of a hidden population in which each person in the sample is
given a set number $k$ of recruitment coupons with which she can recruit up to $k$ individuals
with whom she is linked.

In the temporal setting, sampling without replacement has more than one potential
meaning. It can mean that we do not select a unit that is already in the current sample,
and keeping track of the number of times a unit is selected or else only keeping track of
the set of distinct units selected. Alternatively, without-replacement sampling can mean,
after a unit has been removed from the sample, we will not later select it back into the
sample. Further we can generalize the concept of replacement to a continuous variable
ranging from 0 to 1. In that case we multiple the usual selection probability $p_i$ for unit $i$
times $r$, so that $r = 1$ corresponds to complete replacement and $r = 0$ is strictly without-
replacement. An intermediate value of $r$ means that selection probability is damped for
a unit previously in the sample. In addition $r$ can depend on how long it has been since
the unit was last in the sample.

A random walk in a graph is a simple design that has received much study in the static
network setting but little in the temporally stochastic graph setting. A simple random walk
design has one unit in the sample at a time. One link is followed at random to find the
new sample unit, and the current one is dropped. Letting $d_{ti}$ be the degree, or number of
links out from node $i$ at time $t$,

$$p(s_t = \{i\} \mid s_{t-1} = \{j\}) = 1/d_{ti}$$

This is often supplemented with a probability $p$ of taking a random jump to a different
unit in the population, giving

$$p(s_t = \{i\} \mid s_{t-1} = \{j\}) = p(1/d_{ti}) + (1-p)(1/(N_t - 1))$$

so that the walk does not get stuck in a single component of the network. The classical
random walk is with replacement, so that in the static graph setting it forms a Markov
chain with the current state of the process being the node in the current sample. This
viewpoint runs into some complications in the temporal stochastic graph setting of interest
here. The nodes themselves are transient entities, because of the birth and death process,
so that they can not form recurrent states of a stochastic process. Further, we can follow
a link to a node, only to have the link be deleted at that time step, so we may have the
sample stuck for a long time on a single isolated node until a new link might connect to it.
Thus the design might be modified to take a random jump with some higher probability
if that happens. Still further, the current node may itself be deleted while it is the sample
node, and the sampling process will have ended unless we again modify the design to start
a new random walk from a randomly selected node. Also, as network links change the
connected components of the graph change, and a simple random walk that is stuck in
one component can move to a different component when they transiently merge.

The population process together with the sampling process gives us a complex stochas-
tic process. Even though what would appear to be basic entities of the process, like nodes,
links, and sample members are transient, we find that under a wide range of conditions stochastic stability properties of some variables are apparent. By stochastic stability we refer to variables that have stationary distributions or ergodic properties over time. A variable in such a distribution is forever varying, or fluctuating, but its distribution stays the same, once equilibrium is reach.

Although it is not necessary to have stationary of limiting distribution of variables in order to study the effectiveness of intervention strategies, it is convenient in a number of ways. With stochastic stability, population values will stay in a predictable distribution in the absence of any interventions. If we make an intervention, a simple measure of its effect is the equilibrium distribution that results over time, in comparison with the equilibrium distribution without the intervention.

In many cases an agent we make an intervention against, adapts over time to counter our intervention. More generally, one intervention design interacts with another. The effect of the intervention is most simply measured as the equilibrium that results after all adaptations and interactions attain their new equilibrium distributions.

In more detail, the effect of an intervention is the distribution of sample paths over time, compared to the distribution of sample paths without the intervention, regardless of whether the processes are in equilibrium. In terms of a simulation study, an advantage of processes that attain equilibrium distributions of effects over time is that the distributions can be determined from a single realization over a long time span, or a few such realizations, rather than in every case needing to be run for a large number of realizations.

Because the overall stochastic process is complex and changes in values of input parameters can change a process from stable to non-stable, we examining stability properties empirically. Helpful tools for doing this include time series plots of variables of interest, cumulative mean functions of such functions, cumulative histograms, and cumulative empirical characteristic functions (ECF) of key variables. The empirical characteristic function of a stochastic process variable $X_t$ is defined as

$$c_x(a) = \frac{1}{t} \sum_{t' = 0}^{t} e^{iaX_{t'}} = \frac{1}{t} \sum_{t' = 0}^{t} [\cos(aX_{t'}) + i \sin(aX_{t'})]$$

We are interested not only in when the process is stochastically stable, but when it is changing. In particular, once we initiate an intervention strategy, we would like to see early signs that it is changing. The tail of the ECF is sometimes described as reflecting the roughness of a distribution. In many cases when a process starts to change, as the distribution starts to change in the direction of the new equilibrium, the tail of the ECF appears to go wild, writhing like a snake that has become restless, calling attention to the change.

Many parameters of the network model and designs are individual, by node. They can be changed for one individual in the course of a simulation run. In this case we can ask, what is the benefit to that a single individual of making this change. Individual
parameters include tendencies in forming links, compensatory changes for high degrees of self or other, or preferential attachment tendencies.

In designing interventions against a virus spreading in a human network, we would like to be able to anticipate or infer where the virus might spread next, and which units to distribute our intervention to in order to have the most beneficial effect. To do this we devise a simple type of design based inference in the network. This is done as follows.

Consider the link tracing design that was described above that samples with replacement regarding units that were previously in the sample and without replacement regarding units currently in the sample. Bernoulli tracing of links, independently with probability $p$ for each link leading out of the sample, is supplemented by some small chance for selecting random units, which is done with independent Bernoulli selections from the units outside the sample with small probability $p_r$. Given the current sample size $n_t$ after link tracing additions and a target sample size $n_{\text{target}}$, units are removed from the sample by independent Bernoulli removals, each having probability $q$, where $q = (n_t - n_{\text{target}})/n_t$ if $n_t - n_{\text{target}} > 0$ and $q = 0$ if $n_t - n_{\text{target}} \leq 0$. If we give the design a high rate $p$ of tracing links out, the sample moves very fast through the population. Its sample size varies but stays in a stable distribution around the target size.

Hazard function based on Bernoulli ($p$) per time step has expected time to event $E(x) = 1/p$. Hazard function based on a Weibull distribution discrete approximation,

$$f(x) = \lambda \beta \lambda^{(\beta-1)} e^{(-x\lambda)^\beta}$$

$$E(x) = \Gamma(1 + 1/\beta)/\lambda$$

set $E(x) = 1/p$ and solve for $\lambda$, giving

$$\lambda = p \Gamma(1.0 + 1.0/\beta)$$

$$h(x) = (\lambda \beta)(\lambda x)^{(\beta-1)}$$

A daily probability $p$ of an event such as mortality based on a longer term rate $p_a$ such as probability per year is calculated from $p_a = 1 - (1 - p)^k$ or its inverse

$$p = 1 - (1 - p_a)^{1/k}$$

where $k$ is the number of time steps in the longer time rate, such as 365 days in a year.

**HIV Epidemic**

The HIV epidemic serves as a motivating example for the methods of this project. We focus in particular on the heterosexual epidemic. The virus uses a link-tracing design to select a sample of people. It makes an intervention by infecting each person in its sample. The links followed are sexual partnership links, and transmissions provide the link tracings. The probability of tracing is very low per contact event, often but not
always less than one one-thousandth. We model the design as without replacement, though that is a simplification since in some cases there may be multiple infection of an individual with different strains of virus. Since there is currently no practical cure available for HIV, the design is without replacement. Removal of a node from the sample occurs only with deletion of the node from the population, at death or emigration out of the study population. The probability of tracing depends on values of the origin node, the destination node, and the link between them. For example, the probability of transmission of HIV per sexual contact event depends on the stage of infection in the infected individual, the susceptibility to infection of the exposed individual, and on the details of the type of contact in that event.

For the virus’ design parameters, there is a tradeoff in which a high tracing rate is associated with a decrease in survival time of its host. Letting $\alpha$ represent virulence or host mortality rate and $\beta$ represent transmission rate, a simple form of function characterizing the tradeoff is (Boyker, Fraser) $\beta = c \alpha^{1/\gamma}$ where $\gamma > 1$. Thinking of virus modifying its transmission rate by small increments over time, with the per-time-step mortality rate of the host human being affected as a result, the relationship can be written

$$\alpha_t = a \beta_t^\gamma$$

where $a$ is a constant related to $c$ and $\gamma$ is a curvature parameter.

Existing and potential interventions to reduce the epidemic include behavior changes affecting patterns of relationships between individuals, safer sexual practices used strategically, antiretroviral drug combination treatments, vaccines, cures, pre-exposure prophylactic treatments for partners of infected individuals, and control of catalyzing infections such as Herpes simplex virus 2 (HSV2). In counter-response, HIV adapts to interventions against it with mutations, recombinations, and their selections.

**Network epidemic dynamics and rates background**

Rates of heterosexual transmission of HIV per coital act and frequency of coital acts are estimated in [35] in a study of 171 monogamous couples in which one member was HIV positive, in Rakai, Uganda. Probability of transmission to the other partner in the longitudinal study was estimated as a function of viral load. Rates were about 4 times higher is the presence of genital ulceration disease (GUD). [36] have estimates for stage specific rates of HIV transmission based on serodiscordant heterosexual couples in Rakai, Uganda. They estimate a 26 times for early stage and 7 times for late stage compared to chronic stage. The estimate early stage infection lasts about three months. For this study I’ve used initial estimates of HIV transmission rates with and without catalyzing genital ulceration disease (GUD) such as herpes simplex virus type 2 (HSV-2) from the metastudy [37].

Effectiveness of condom use in reducing heterosexual HIV transmission is reviewed in [38].
Infectious agents typically run into a tradeoff in the evolution of transmission rates. Higher transmission rate is associated with increased virulence, increasing the mortality rate of the host which in turn slows down the spread of the pathogen strain in the population. Tradeoff functions have the general form that transmission rate is a decelerating function of virulence. In this study I use a simple tradeoff function from [39], who uses rate data from [40] for HIV. Other functions with similar tradeoff properties have been used by other authors such as [41].

[42] presents opposing views of different researchers on the relative importance of early stage in the transmission of HIV. [42] presents opposing views of different researchers on the relative importance of early stage in the transmission of HIV.

Dynamic epidemic models showing selective advantage of virulent strains in early stage of an epidemic and advantage shifting to less virulent strains, which allow their host to survive longer, as the epidemic matures were compared to laboratory studies with colonies two competing strains of bacteria [43], finding agreement with the model predictions. [42] presents opposing views of different researchers on the relative importance of early stage in the transmission of HIV.

[44] describes some of the challenges in developing an HIV cure based on antiretrovirals together with an agent for releasing the virus from latency.

Properties of networks in which relationships shift preferentially that are missed by static network epidemic models are examined in [45]. The stability of casual contact and close contact patterns over time was studied [46] using diary based methods with 49 volunteers, finding that the close contacts tended to be more stable than casual contacts.

Network structure and change patterns in relation to individual behaviors were investigated in [47] for syphilis among young people and HIV among drug users, finding in both studies that spread of disease was associated with network cohesion, in the form of separation of components or local density of connections.

The importance of concurrent relationships in the spread of the HIV epidemic is investigated in [48] and [49]. Interaction of early transmission rate and concurrency in sexual links is discussed in [50]. A modeling approach combining network models and compartment models is used in [51] to evaluate the importance of concurrency.

[52] describes a modeling approach based on a set of partial differential equations with the addition of some temporal network aspects such as degree distributions in which contacts change, describing mean behavior for infinite network size and approximate behavior for moderate size. [53] and [54] describe a network of 50,185 sexual contacts between 6,642 escorts and 10,106 sex buyers as reported on a Web discussion forum.

[55] (and especially its Supplement 1) modeled the individual variability of adherence over time for an individual as well as the variability between individuals. Their model, used for the purpose of estimating parameters, is individual based but not network based except to the extent of having assumed degree distributions. This study uses an inference method that appears to essential be approximate Bayesian computation.

An approach bringing network effects to epidemic compartment models by having dif-
ferent groups with different network degrees is described in [56]. Epidemic threshold properties of simple dynamic network models in which degree says constant but neighbors exchange, that is, identity of partners change instantaneously at random times are described in [57]. Compartmental models are modified to add some network effects in [58]. [59] examine network effects in compartmental models by including a contact or mixing matrix into the model, comparing assortative mixing patterns, in which individual’s contacts tend to be within their own group and dissortative patterns, in which contacts tend to be between groups. Early work in modeling the dynamics of the HIV epidemic includes [60,61] and [62].

The models for dynamic spatial network populations and interacting designs developed in work also have some relationship to the literature on evolutionary dynamics. [63] provides a summary of models of species interactions, epidemics, and selection based on systems of partial differential equations. [64] describe recent work on stochastic point process models built on top of that approach. Among the many cases of ecological systems exhibiting the sort of spatial, temporal, and network patchiness addressed by the models and designs of this paper, a good example is described by [65].

Results

In this section we look at some results of using the network sampling approach to evaluate the effectiveness of intervention designs, using the HIV epidemic as our test example. The first type of result we look at are what are the characteristics of the virus design and how does it respond to human network activity over time. The second result we look at is what can one individual or two in cooperation accomplish to reduce the risk to themselves or others. And the third result we look at involves network effects of two types of ideal interventions we hope are available at a future date, namely treatments that cure or clear an infected individual’s body of HIV.

Virus adaptation to temporal network geometry

Most link-tracing designs through networks select nodes having more links in to them with higher probability than nodes with fewer links. This is true of simple random walk designs, snowball designs of various types, and adaptive web sample designs among others. It is true of a natural link-tracing design such as HIV uses in selecting people following sexual links, and which we model here as independent Bernoulli selections, without-replacement, with unequal probabilities of transmission tracing depending on node and like characteristics. The only designs I am aware of for which this is not true are targeted random walk designs in which a random walk in a graph is modified using Markov chain Monte Carlo techniques in order to achieve desired long term selection probabilities including having them equal for all nodes.
Combined with network clustering tendencies in which certain sets of nodes are at least temporarily more highly connected than average, the link-tracing design of the virus leads to a pattern of spread in the population over time characterized by local explosions, even if the explosions occur in relative slow motion, followed by longer periods of little spread. We can document this trend by tabulating the average degree of nodes recently selected into the virus' sample, compared to the average degree of nodes not in the sample and to nodes that have been in the sample for longer. We find the degree of nodes recently selected is higher. The same is true for their out-degree, the number of links a node in the sample has to nodes not in the sample.

In a node that has recently been infected, a strain of virus with a high transmission rate will have an advantage, on average, relative to a strain with a low rate. The high rate strain can take advantage of the high number of links out to spread farther. There is a tradeoff, however, since the higher virulence associated with the high transmission rate brings a higher mortality rate to the host person. Later in the same person, there tends to be fewer if any links out to nodes not already infected. At that stage a strain of virus with low transmission rate is favored. With the longer expected survival time of the host, the virus has a chance over time of new links being formed.

The advantage to the virus of having a high transmission rate early for a short time and a low transmission rate later for a long time is amplified by clustering of network links in time and space. As infection spreads through a cluster a strain with higher transmission rate, particularly higher early rate, will spread explosively through the cluster, faster than other strains, and become locally more predominant. Over time their are fewer links to uninfected nodes in the cluster, as more of the nodes locally are infected. Over a longer period of time the cluster breaks up through social drift. Survival time of a host person is higher for a low virulence, which gives that strain a better chance of being the lead strain in igniting the next cluster, should it be encountered in the drift over time as old links dissolve and new ones are formed.

The pattern of simulation results comparing strains adds further light on this issue. Comparing strains with fixed early and chronic rates, an optimal strain having a transmission probability per sexual contact of about 0.008 during chronic stage and about 15 times that during early stage emerges. Compared to a strain with the same chronic rate and an early rate the same as that, that is, an early rate factor of 1, the strain with low early rate reaches over time reaches an equilibrium presence about ten percent lower. More noticeably, the low early rate strain tends to take much longer to get off the ground, starting from just one or a few cases. A strain with a very high early rate of 50 times or more tends to rise very fast and then crash to a lower equilibrium because of the higher host mortality induced. Strains with an early factor between about 5 and 35 perform about as well as the optimal strain, in terms of equilibrium level. In each run a single strain exists in a single population.

When we put two strains with fixed rates together in competition, the optimal strain almost always nearly completely dominate over time over either the one with low early
rate or very high early rate.

Next we put in a random selection of strains and let them evolve together. When a strain transmits to a new node, the new early transmission rate is the value of the one in the transmitting node plus a small random increment (uniform or normal), constrained to not go below zero or above 1.0. The result, over time, is independent of the initial distribution and tends to produce a variable distribution of early rates in the population, with mean early rate factor between 15 and 20 and the bulk of the distribution between 5 and 40. Contributing factors to the persistence of variability of early rate in the population are the variability at transmission, producing genetic drift, and the fact that at any given moment different nodes are under different selective pressures, depending on the number of open links around them.

The two-pronged strategy of HIV with a high early transmission rate for a short period followed by a low transmission, low mortality rate for a longer period, presents challenges for interventions to lower the incidence and prevalence of HIV in a human population. The highest transmission rate comes before the virus can be detected with standard tests. Explosions into concentrated clustered tend to be well established before responses can be readied. And in the survival period that that averages around ten years without treatment only a few of those cases need to make an ignition of a new explosive area for the epidemic to persist.

Pair consensus intervention strategy of safer sex early in relationship followed by HIV home testing

Individuals and pairs of individuals have the most direct agency in forming and dissolving links, which creates and maintains the network over time and potentially can change it. As described earlier we think of this as $N_t$ designs, as many as there are individuals. The seemingly insignificant day to day choices and actions of individuals create the uneven temporal network topology in which the HIV epidemic expands or shrinks locally and throughout the world.

In this section we look at a strategy that relies on the agency of individuals and cooperating pairs. The idea is to counteract the virus strategy with it’s high rate of transmission in the early stage of an infection. The problem is, the standard tests of for the presence of HIV are not sensitive in the early part of an infection, and the person having an infection in early stage is likely not to know they are infected. Instead, we consider the strategy in which a pair uses safer sex practices early in a relationship, followed by each person testing the other. We consider the use of one of the new, cheek swab home tests.

The strategy is as follows. The couple use safer sex practices during the first $k$ weeks of a relationship, followed by HIV tests. If both tests are negative, then the restriction to safer sex practices is lifted. If both tests are positive, then also the pair can abandon the safer sex practices with each other. If one test is positive and the other negative, the
pair continues to use the safer sex practices.

A safer sex practice is one that reduces probability of transmission in a contact to a specified proportion $p_s$ of penetrative intercourse. In the simulations on the heterosexual epidemic I use the value $p_s = 0.10$. The literature is sparse but appears that not just the use of a condom but alternatively a range of sexual techniques collectively referred to as “outercourse” reduce transmission probability to something like 10 percent of what it would be. These include various methods of oral sex and hand-genital contacts. We omit from the list fellatio involving ejaculation into a partner’s mouth, as one study estimated is transmission rate as 50 percent that of penetrative sex.

For the duration of the safer sex period from the start of a relationship the simulations use 12 weeks, or 84 days. The expected duration of early stage infection from the start of HIV infection in the simulations is 75 days, or between 10 and 11 weeks. In this way the infection has a high probability of being detectable when the tests are given and the chance of being exposed to the high transmission rate from a new partner is greatly reduced.

In simulations when everyone in a population is using this strategy it is surprisingly effective in bringing down the epidemic even in dense preferential attachment situations. Suppose only 50 percent, or 10 percent of the population uses this strategy. What is the effect on them, what is the effect for others. The answer depends on the pattern of adoption of the strategy. If individuals with the strategy tend to assort to relationships with others using the same strategy the benefit for them is great and others are relatively unaffected. If the two types of behaviors mix randomly to benefit to the people using it is dampened and others accrue benefit. We can this type of exploration to the extreme and ask, what is the effect on one person if she uses this strategy while others do what they will do anyway, including dense, high risk social settings. To use this strategy takes the cooperation of both partners in a relationship. If her partner has other relationships also, her risk is affected if the partner uses the strategy with just her or with their other partners as well, at least while they are in a relationship with her.

The concept of a strategy of this type is that individuals and cooperating pairs bring down the potential rates of transmission in relationships, with particular focus on early rates and untestable periods.

**Two types of cures, one conferring immunity**

At the time of writing there is no practical cure for HIV infection, that is, no treatment that will clear the virus completely from the body and leave the person in good health. There is, however, plausible theory on approaches for developing cures for HIV. One person has apparently been cleared of the virus through stem cell transfusion giving him immune cells having a protective mutation but for various reasons it is not considered practical to spread this approach widely. A cure would be the the best thing that could happen to an individual who is infected with HIV and in our simulations a cure emerges
as having the best network dynamics for bringing the epidemic down through prevention of further spread, even in very difficult network situations.

In the simulation two types of cures, both equally effective in curing an individual, emerge as having markedly different network dynamics. One type of cure clears the virus from the person but leaves him or her susceptible to reinfection. The other type of cure, in addition to clearing the virus, confers subsequent immunity to infection. In between are cures that would confer some degree of immunity, which is incorporated as a resistance factor between 0 and 1.

One research approach uses antiretroviral drugs to deeply suppress reproduction of HIV particles in the blood or other body fluids and seeks another class of drugs to induce the virus in refuge as protovirus segments of human DNA to express themselves and emerge to be in turn prevented from further reproduction. A second research approach in seeking a cure involves gene therapies to insert strengthening proteins or other HIV resistant features in immune cells. There is no apparent reason to anticipate that the first type of cure would confer immunity whereas the second type could reasonably expected to confer at least some degree of immunity following cure.

Each of the interventions studied in the simulation can be effective in bringing down the epidemic in many network settings and can be overwhelmed by others. The most difficult of the temporal networks in the simulation are dense and highly clustered in terms of links, and are represented in the simulations by preferential attachment tendencies in the formations of links, giving a high degree of clustering in space and in time. What happens with the cure that does not confer immunity is that the high-degree, highly connected, or high-change individual who is most likely to be infected and serve as a conduit of transmission to others, once cured is likely to be reinfected and again serve as a conduit as least over near time. The cure of an individual by the second type of cure not only reduces prevalence in the population by one but also makes the links of that person unavailable or unconducive for further spread.

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