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Susceptible-infected-recovered epidemics in populations with heterogeneous contact rates

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Abstract. Heterogeneity of contact patterns is recognized as an important feature for realistic modeling of many epidemics. During an outbreak, the frequency of contacts can vary a great deal from person to person and period to period. Contact heterogeneity has been shown to have a large impact on epidemic thresholds and the final size of epidemics. We develop and apply a model which incorporates an arbitrary distribution of contact rates. The model consists of a low-dimensional system of ordinary differential equations which incorporates arbitrary heterogeneity by making use of generating functions of the contact rate distribution. We show further how this model can be applied to the study of simple intervention strategies, such as quarantine of public venues with probability proportional to size. The dynamic model allows us to investigate the effects of gradually implementing such strategies in response to an ongoing epidemic, and we investigate these strategies using data on the contact patterns within a large US city.

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Population heterogeneity can have a large impact on epidemic dynamics [3,4,9,10,12,17]. Such heterogeneity takes many forms, such as heterogeneity with respect to susceptibility, infectiousness, contact rates, or spatial and network structure. Inclusion of population heterogeneity in mathematical epidemic models is very difficult, and tends to lead to complicated equations in terms of PDEs or integro-differential equations as well as computationally intensive simulations.

Here we present an alternative method of modeling simple forms of population heterogeneity in terms of contact rates. It relies on a simple system of two ODEs and makes use of generating functions for the distribution of contact rates in the population [19]. The method could easily be adapted to heterogeneity of susceptibility or infectiousness. This model is not suitable for epidemics in static networks as contacts are presumed to be instantaneous and uncorrelated. The methods used here have, however, been successfully applied to both the static and dynamic network case [18,19]. Our approach offers an interesting alternative to that taken in [10,12,14] to study thresholds and final size in a static network SIR model. In that case, the authors presented a model very similar to ours, but only as a mean-field approximation to static networks. But this mean-field scenario, where contacts are uncorrelated and instantaneous, is worth studying in its own right, especially using a simplified framework such as we present here.

Our model can be easily applied to many epidemic scenarios using detailed information about contact rates which are frequently ignored in standard compartmental SIR models. We demonstrate our model by applying it to the hypothetical release of smallpox within a US city using a large data set of contact patterns within Portland, Oregon. Simulations have been used to model this scenario [6], however, our mathematical model offers greater interpratibility of results. And since it is based on a system of only two ODEs, it is extremely fast to explore epidemic dynamics over a large range of parameters and scenarios.

1 Model

Let each individual *ego* make contacts adequate for disease transmission at a specific contact rate r_{ego}. The probability of an individual having contact rate r will have a probability density $f(r)$. The following derivations makes use of the assumption that all contacts are instantaneous and uncorrelated, and therefore carry identical and independent probabilities of transmission. Variables and parameters of the model are summarized in Table 1.

In a standard SIR model, each individual makes contact at a constant rate, and the probability that contact occurs with an infectious node is I/N. With heterogeneity, the fraction of contacts with an infected must be calculated. Let M denote this quantity, that is, $M(t)$ will be the probability that a given contact at time t occurs with

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Table 1. Parameters and dynamic variables within the random mixing (RM) model.

r	Contact rate
μ	Recovery rate
τ	Transmission probability
$M(t)$	Fraction of contacts with infecteds
$S(t)$	Fraction of nodes susceptible
$I(t)$	Fraction of nodes infectious
$R(t)$	Fraction of nodes recovered
$\theta(t)$	Fraction of nodes with unit contact rate remaining susceptible

an infected.

$$M(t) = \int_r rf(r)\Pr[\text{Rate } r \text{ node infectious at } t]dr / \int_r rf(r)dr. \quad (1)$$

Then the hazard of a given susceptible individual of contact rate r becoming infected at some time t will be

$$\lambda_r(t) = \lim_{h\to 0}\frac{1}{h}\Pr[\text{Susceptible is infected in interval (t,t+h)}|r] = rM\tau \quad (2)$$

where τ is a parameter controlling the probability of a contact resulting in transmission. It follows that the fraction of individuals with contact rate r remaining susceptible at time t will be given by

$$\begin{aligned} u_r(t) &= e^{-\int_{s=0}^{t}\lambda_r(s)ds} \\ &= e^{-\int_{s=0}^{t} rM(s)\tau ds} \\ &= \left(e^{-\int_{s=0}^{t} M(s)\tau ds}\right)^r. \end{aligned} \quad (3)$$

This equation makes it clear that $u_r(t) = u_1(t)^r$ for all contact rates r. For convenience, let's define the dynamic variable $\theta = u_1(t)$ so that $u_r(t) = \theta^r$. Note that θ is always defined, whether or not there are any individuals with contact rate $r = 1$.

Given θ, the number of susceptibles at time t can be calculated as

$$S = \int_{r=0}^{\infty} f(r)\theta^r dr = g(\theta) \quad (4)$$

where the function $g(\cdot)$ is the generating function

$$g(x) = \int_{r=0}^{\infty} f(r)x^r dr. \quad (5)$$

This generating function is closely related to the moment generating function for distribution $f(\cdot)$, as $\mathcal{M}_f(\ln(x)) = g(x)$.

Our goal is now to develop a system of equations in terms of θ and M to describe the dynamic epidemic prevalence in terms of equation (4). Using only equation (3) we have

$$\dot\theta = -\theta M\tau. \quad (6)$$

Deriving the dynamics of M requires more care. The rate of change in the number of infectious nodes is $-\dot S - \mu I$, where

$$\dot S = \dot\theta g'(\theta) = -\tau M\theta g'(\theta). \quad (7)$$

Each susceptible that becomes infected at time t will cause a transfer of cumulative contact rates between susceptibles and infecteds (e.g. an increase of M). Denote by δ_{SI} the average contact rate of a susceptible infected at time t. M should increase at a rate proportional to $-\dot S \times \delta_{SI}$. Also note that each infected that recovers at time t causes a decrease in M proportional to M.

The hazard of infection is proportional to contact rate, so the probability that susceptables changing state to infected at time t have contact rate r is proportional to r (i.e. probability $rf(r)/\int_r rf(r)\theta^r dr$). Then the the average contact rate of an individual changing from the susceptible to the infected state at time t is

$$\begin{aligned} \delta_{SI} &= \int_r r \times \Pr[r|\text{ Selected probability proportional to r}] \\ &\quad \times \Pr[\text{susceptible}|r]dr \\ &= \int_r r \times \left(\frac{rf(r)}{\int_r rf(r)\theta^r dr}\right) \times \theta^r dr \\ &= \frac{1}{\theta g'(\theta)}\int_r r^2 f(r)\theta^r dr \\ &= \frac{1}{\theta g'(\theta)}\left(\theta^2 g''(\theta) + \theta g'(\theta)\right). \end{aligned} \quad (8)$$

The last step in this derivation can be verified by expanding $g(\theta)$ in terms of the integral. M increases at a rate $(-\dot S) \times \delta_{SI} \times (1/g'(1))$, where the factor of $g'(1) = \langle r\rangle$ is a normalizer (normalization is required to keep M in the unit interval). M is decreased due to the recovery of infected nodes (rate μ). Then we have

$$\begin{aligned} \dot M &= -\mu I \times (M/I) + (-\dot S) \times \delta_{SI} \times \frac{1}{g'(1)} \\ &= -\mu I(M/I) + \frac{(-\dot S)}{\theta g'(\theta)}\left(\theta^2 g''(\theta) + \theta g'(\theta)\right)\frac{1}{g'(1)} \\ &= -\mu M + \tau M\left(\theta^2 g''(\theta) + \theta g'(\theta)\right)\frac{1}{g'(1)}. \end{aligned} \quad (9)$$

Equations (6) and (9) then form a closed system of two equations describing epidemic dynamics.

We will refer to this model as the *random mixing with heterogeneity* (RM) model, as we assume there is no spatial, assortative, or network structure in the population.

In common with standard SIR dynamics, there is an analytic expression for final size that does not require integrating the equations. For the standard SIR dynamics it is well known [2] that the final size must satisfy $S(\infty) = e^{-R_0(1-S(\infty))}$. For the RM equations

$$\theta(\infty) = e^{-\frac{\tau}{\mu}\frac{g'(1)-\theta(\infty)g'(\theta(\infty))}{g'(1)}}, \quad (10)$$

which can be seen by noting that the cumulative hazard of an individual with unit contact rate becoming infected

is proportional to the number of contacts ever made by an infectious individual. Since an individual is infected on average for a duration $1/\mu$, the cumulative hazard is

$$\frac{\tau}{\mu}(1 - M_S(\infty)) = \frac{\tau}{\mu}\left(1 - \theta(\infty)g'(\theta(\infty))/g'(1)\right).$$

The solution to equation (10) can be found by standard root-finding methods. The final epidemic size (cumulative incidence) is then $1 - g(\theta(\infty))$.

A few caveats are required before applying this model. Contacts are instantaneous and uncorrelated. By analogy to networks, there is no clustering or transitivity of partnerships, and the local topology of contacts is always tree-like. For low-levels of clustering, this should be an adequate approximation.

1.1 RM model in bipartite populations

In many networks, individuals have contact only through intermediaries. For example, in a heterosexual population, males may be connected through common female partners [13]. This analogy carries over to airborne infectious diseases such as influenza and smallpox, where two individuals have contact if they are in a common location at the same time [11]. In this case, a bipartite network would consist of individuals and time/location points (TL). Frequently we have only information about affiliation structure rather than about explicit contacts. In Section 2 we will show how to induce a bipartite network from transportation data for the study of smallpox.

To apply the theory to bipartite populations, several adjustments must be made to equations (6) and (9). In our terminology, we will specifically refer to the case where one mode of the population consists of individual persons, and the other mode consists of TL points where individuals make contact. Let $g(x)$ generate the distribution of contact rates r as above, but now let this specifically refer to the rate at which an individual visits a unique TL. For example, a high rate corresponds to an individual that visits many public locations over the course of a day. We will also have the function $h(x)$ which generates the discrete probability distribution of the number of individuals contacted at uniform random TL. If two individuals are at a common TL, we say that an epidemiologically significant contact has occurred between them. Note that $h(x)$ does not generate the *number* of people co-located at a TL but rather the number of people *contacted*. We have

$$h(x) = \sum_k p_k x^k \tag{11}$$

where p_k is the probability of k individuals being contacted at a TL chosen uniformly at random.

For example, an individual *ego* may have a low contact rate such that only two TLs would be visited over the course of the day. Perhaps by chance the first TL would be a classroom, which has on average 30 people co-located there. The other TL may be a post-office, which has only two people co-located at any time. Then the individual would have a total of 32 epidemiologically significant contacts over the course of their day. The TL framework can have counter-intuitive implications. For example, the classroom may have three classes over the course of the day, for a total of 90 students. Nevertheless only 30 of these happen at the same time, so the functional degree is thirty. The post-office may have 300 visitors over the course of the day, but on average only two people are co-located there at any time, so that the functional degree is very small (only two).

The quantity M will as before be defined as the fraction of contacts with infecteds (Eq. (1)).

Given a susceptible of rate r, the total rate at which contacts are made will be

$$\sum_k rkp_k = rh'(1). \tag{12}$$

At time t, a fraction $M(t)$ of these contacts will be with infecteds. Therefore the hazard of infection for a rate r individual is

$$\lambda_r(t) = \lim_{h\to 0}\frac{1}{h}\Pr[\text{Susceptible is infected in interval (t,t+h)}|r] = rMh'(1)\tau. \tag{13}$$

This is similar to what we had before, but with an extra factor of $h'(1)$. The epidemic dynamics are then derived as in the last section.

$$\begin{aligned}\dot{\theta} &= -\theta\tau Mh'(1)\\ \dot{M} &= -\mu M + \tau Mh'(1)\left(\theta^2 g''(\theta) + \theta g'(\theta)\right)\frac{1}{g'(1)}.\end{aligned} \tag{14}$$

The reproductive ratio R_0 can be calculated in this situation, and is similar to the result obtained in mass-action SIR models. The result is the following[1]:

$$R_0 = \frac{\tau}{\mu}\frac{h'(1)g''(1)}{g'(1)}. \tag{15}$$

1.2 Quarantine

Quarantine of public spaces can easily be incorporated in the model (Eq. (14)) by appropriate modification of $h(x)$ which generates the random number of individuals at a given TL. A common practice is to close schools, theaters, and other venues in response to an epidemic. We hope to develop a more principled strategy to determine which public spaces to close and when. Theoreticians have previously proposed closing all public spaces exceeding a given size. Here we propose a mathematically convenient alternative motivated by our use of PGFs. We will close a venue with a probability given by an exponential function of size. Equivalently we will refer to this as quarantine

[1] A manuscript containing a derivation of this formula is currently in preparation by the authors.

with log-probability proportional to size (LPPS). Let α be the quarantine parameter between zero and one. Then we propose to close a space of size k with probability $1-\alpha^k$. It follows that given α, the fraction of spaces *not* quarantined is

$$\sum_k p_k \alpha^k = h(\alpha). \tag{16}$$

And, the fraction of contacts eliminated per unit time will be

$$1 - \sum_k k p_k \alpha^k / \sum_k k p_k = 1 - \alpha h'(\alpha)/h'(1). \tag{17}$$

This strategy is motivated by mathematical convenience, however quarantine spaces could be selected by basic survey methodology. For example, choosing an individual at random and following them to a location would be equivalent to selecting a location with probability proportional to size. One could develop a profile of spaces to close that would be distributed across many sectors, rather than simply closing schools or theaters.

The dynamics during the quarantine period will be similar to the previous section, but with a modified generating function for TL sizes.

$$\begin{aligned} \dot{\theta} &= -\theta\tau M \alpha h'(\alpha) \\ \dot{M} &= -\mu M + \tau M \alpha h'(\alpha) \left(\theta^2 g''(\theta) + \theta g'(\theta)\right) \frac{1}{g'(1)}. \end{aligned} \tag{18}$$

2 Applications

Detailed simulations based on transportation surveys have recently been developed to model the dynamic contact patterns within a large urban setting [1]. These simulations, based on Portland, Oregon, have so far been applied to the study of smallpox dynamics, such as intential bioterrorist introduction [6]. Because of the large heterogeneity within the population revealed by these data, epidemic modeling of smallpox has mostly been conducted with large-scale simulations [7,16] (but see [8]). We here show how our model can be applied to the Portland data. For convenience, we will consider the case of introduction of smallpox via a single infected individual.

The data consist of the movements over a 24 hour period of approximately 1.5 million residents belonging to 632,626 unique households. Over 40 000 unique public locations (not counting homes) are visited over this sample window. Because smallpox rapidly spreads within households [5], we have chosen to use households rather than individuals as the units of analysis for this study. For example, far more time is spent in a household TL (more than 90% spend more than 8 hours at home), and virtually every member of a household will be exposed if any individual is infected.Our results will be reported as the fraction of households in a susceptible, infected, or recovered state, where a household is considered to be infected if any member of the household is infected.

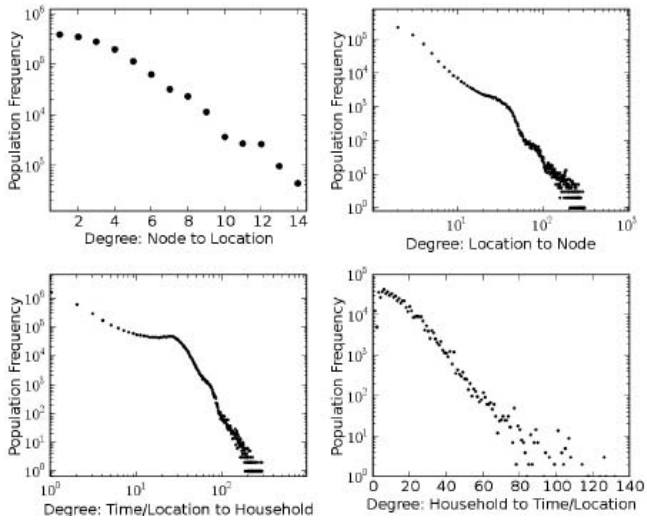

Fig. 1. Degree distributions giving the number of contacts made from one category to another over the sample period. Top left: Individual persons ("nodes") to locations. Top right: Locations to individual persons. Bottom left: Time/location points to households. Bottom right: Households to time/locations.

Our goal is to extract contact rate distributions from the Portland data. This will be used for the construction of $g(x)$ and $h(x)$ and applied to our model. Figure 1 shows the degree distributions from individual persons (or "nodes") to and from locations (top), and households to and from time/location points (bottom). A household is considered to be in contact at a TL when any member of that household is at the TL. Degree distributions based on individual movement to specific locations have previously been used in static network models [6,15]. Instead, we will work with the distributions based on households and TL points. There are two reasons: Our distributions must correspond to the unit of analysis (in this case households); and, we are interested in the number of household units which are co-located at a given TL, rather than the number of household units which have contacted a location over the course of the sample period.

The node to location and household to TL distributions both have exponential tails. The location to node and TL to node distributions, in contrast, have power law tails. It may be possible to fit analytical distributions to these data and to use the corresponding moment and probability generating functions for our model. But in the model that follows, we will use the empirical distributions to construct the generating functions term by term. This is of course, a discrete distribution of daily contact rates, whereas our model was defined in terms of the continuous distribution $f(r)$ (Sect. 1), however there are no theoretical problems with substituting a discrete valued distribution and a corresponding probability generating function for $g(x)$. Alternatively one might fit a continuous distribution to this data.

It is difficult to determine accurate parameter choices for smallpox. A conservative choice for the duration of the infectious period is 4 days, which includes the prodromal

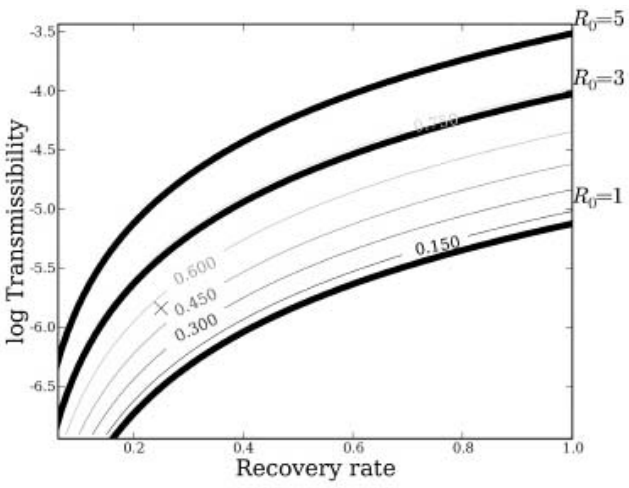

Fig. 2. The final size is shown in color versus the log transmissibility $\log(\tau)$ and recovery rate μ. Also shown are the contours for $R_0 = 1, 3, 5$ as calculated from equation (15). The x symbol marks the point representing our best guess of parameter values for τ and μ, and corresponds to a final epidemic size of 53% of households.

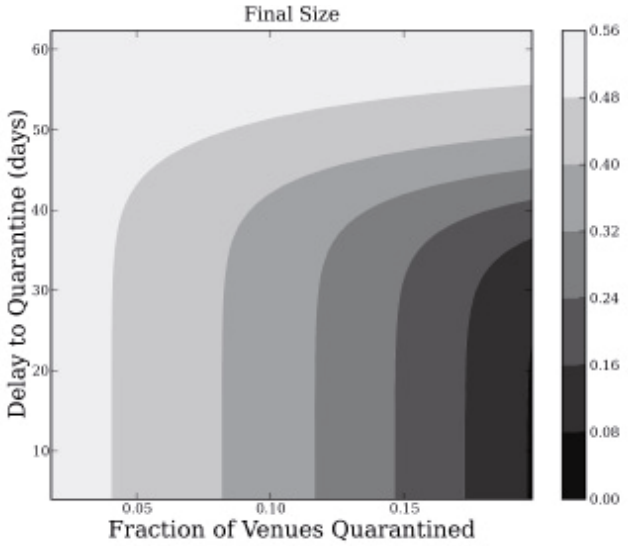

Fig. 3. The final epidemic size is shown in color versus the time delay before quarantine (T) and the quarantine parameter (α). $\tau = 0.29\%$ and $\mu = 0.25$.

period and early rash period [5,6]. This leads to a recover rate of $\mu = 0.25$. The rash period may last up to 20 days, but it is most likely that an infected would self-isolate before this time. The transmissibility τ (i.e. the probability that a contact will result in transmission) is most difficult to estimate. Influenza is more infectious than smallpox [7], therefore we have chosen to tune τ so that it leads to similar final size of major influenza epidemics. This is a conservative choice which likely over-estimates the true extent of a smallpox epidemic. A typical final size for pandemic flu is 40% [7]. Considering that roughly 75% of individuals in an infected home will themselves be infected, this implies that 53% of homes would be in the infected state. This leads to $\tau = 0.29\%$. This choice is somewhat arbitrary, but our qualitative results should hold for other values. Also note that smallpox features a latency period lasting on average 12 days. For convenience, we have left this out of the model, though it could easily be included.

Figure 2 shows the final size as predicted by our model 18 over a range of transmissibilities and recovery rates. The x symbol marks the point of our best estimate for these parameter values. Also shown are contours corresponding to $R_0 = 1, 3$, and 5 as predicted by equation 15. The figure shows that epidemics only become possible when $R_0 > 1$. Using the estimates of $\tau = 0.29\%$ and $\mu = 0.25$, we calculate $R_0 = 1.96$. This figure also demonstrates that the final size is very sensitive to the transmissibility parameter, which follows from the heterogeneous contact rate distribution and is typically not the case for a homogeneous standard SIR model [13]. For example, at $\mu = 0.25$, an increase in transmissibility from $\tau = 0.15\%$ to $\tau = 0.67\%$ is sufficient to go from no epidemic with $R_0 < 1$ to $R_0 = 5$ and a final size of 80%.

The effects of quarantine using the LPPS strategy are shown in Figure 3. Two factors impact the effectiveness of LPPS quarantine:

- The parameter α which controls the probability that a size k TL will be closed.
- The time delay T from the initial infection in the population to the implementation of quarantine.

The final size in this case is calculated by piecewise integration of our model (Eq. (18)), with $\alpha = 1$ prior to time T and $\alpha = \alpha'$ after time T, where α' is our parameter choice. If α is small, many TLs will be closed and an epidemic is prevented, provided that the intervention is implemented early enough. But as Figure 3 shows, if not enough TLs are closed, or if the quarantine is implemented too late, a large epidemic is possible. For the example in Figure 3, $\alpha = .97$ corresponds to a quarantine of 19.8% of TLs which results in a decrease by 49% in contacts per unit time. At the other extreme, $\alpha = 0.998$ corresponds to a quarantine of 1.8% of TLs which results in a decrease by 5.1% in contacts per unit time.

For early quarantine (small T), the final size increases almost linearly in the quarantine parameter α. In contrast there is rapid transition from outbreak to large epidemic in terms of T, showing that there is a characteristic time before which quarantine must be implemented for it to be effective.

These conclusions must come with the caveat that the latency period would affect the temporal behavior of the epidemic. This would have a noticeable impact on our results reported in Figure 3, as it would essentially slow down the rate of epidemic spread. A latency period would not, however, affect our qualitative conclusions.

3 Discussion

We have introduced a simple mathematical model of infectious disease in populations which feature arbitrary heterogeneity of contact rates. The model comprises only two ODEs, just as the standard mass-action SIR model, and is easily adapted to data on the dynamic contact patterns. We have demonstrated this by applying our model to data based on transportation surveys in Portland, Oregon. These methods offer most of the advantages of low-dimensional compartmental SIR models, such as simplicity, interpretability of results, and computational efficiency, but does not require unrealistic assumptions about homogeneity of contact rates.

Future work should focus on extensions to heterogeneity in terms of biological parameters, such as susceptibility or infectiousness. It would also be desirable to include additional structure to our population, such as assortativity by age or type, and possibly spatial structure.

A more realistic applicaton of our model to quarantine strategies would take into account the latency period of smallpox infections, as well as variable transmissibilities of different contact types, and variable outbreak sizes within households. Our proposed quarantine strategy (LPPS) awaits a rigorous comparison to other strategies, such as convenience-quarantine (closing down low-priority venues like schools), and threshold-quarantine (closing venues exceeding a given size).

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