Modeling Infectious Diseases through Contact Networks

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Introduction to Infectious Disease Modeling

Infectious diseases are the second leading cause of death worldwide[1]. From the Black Death of the Middle Ages, to the current Ebola crisis in Western Africa, infectious diseases have been and will continue to be a threat to the human race. Infectious diseases can also cause devastation to livestock or crops. For example, *Phytophthora infestans* decimated Ireland's potato crop in the early 19th century which led to the Irish potato famine.

Compartment-based modeling is a very common type of model for infectious diseases. It considers a set of different "compartments" to demonstrate how the population can move through the course of a disease. Common compartment-based models are SEIR, SIR, SIS and SI. Figure 1 shows an example of the SEIR model structure.

Although time can be modeled as discrete or continuous, here we focus only on continuous-time models. To understand how the hosts will move throughout the compartments we can use a system of differential equations. For example, a general SEIR model as shown in Figure 1 can be modeled by the system of equations in Figure 2.

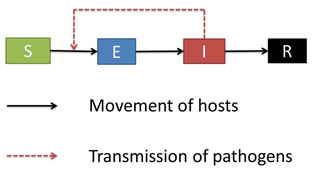

Figure 1. General SEIR model. Here S = Susceptible, E = Exposed, I = Infectious, R = Removed.

Movement to and from each of the compartments is based both on the amount of hosts in the compartments as well as probabilities that hosts will interact and that certain interactions will be "successful". For example, β is the rate at which hosts move from the Susceptible compartment to the Infectious compartment. However, β depends on both the probability of direct contact between hosts i and j ($c_{i,j}$), as well as the probability that a sufficient number of pathogens will be transmitted from host j to i ($v_{i,j}$). In short: $\beta \approx c_{i,j}v_{i,j}$

$$\frac{dS}{dt} = -\beta IS$$
$$\frac{dE}{dt} = \beta IS - \delta E$$
$$\frac{dI}{dt} = \delta E - \alpha I$$
$$\frac{dR}{dt} = \alpha I$$

Figure 2. Generalized system of equations used to model an SEIR model.

Contact Networks

Contact networks (a.k.a., graphs) are structures comprised of *nodes* and *edges* that represent hosts and their possible connections to other hosts. There are several important characteristics of a contact network, such as the *mean degree*, the *diameter,* the *network structure,* etc., that can give insight into the spread of a particular infectious disease[1,2].

Two key assumptions are often made to simplify the modeling process: 1) the assumption of homogeneity postulates that all hosts have the same individual characteristics; 2) the uniform mixing assumption, which can be modeled by a *complete graph* (shown in Figure 3), postulates that each host is equally likely to have contact with every other host in the system.

As network structure can drastically influence disease dynamics, we are interested in modeling the effects of various contact networks for different diseases. Below are two example contact networks.

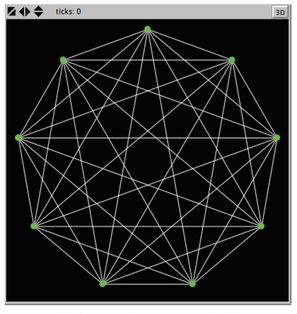

Figure 3. Complete graph with 9 nodes.

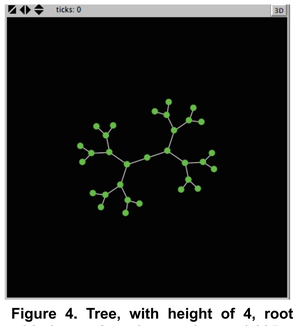

Figure 4. Tree, with height of 4, root with degree 2, and mean degree 1.935.

The Power of Simulation

To visualize the disease dynamics and to assist in model predictions, we are using a program developed by Just, Callender, and Lamar[3] written in the agent-based programmable modeling environment NetLogo[4]. Three central parameters in each of our models are: infection-prob, end-infection-prob, and end-latency-prob. Each probability corresponds to the movement of hosts between compartments. In a standard SIR model, the rate of growth in the infectious category—also called incidence—coincides with the probability for individual hosts to become infectious (i.e., an infection-prob of 0 means the individual will never become infectious; an infection-prob of 1 means it will be infectious by the next time step).

Since latency corresponds to an E compartment (exposed but not infectious), end-latency-prob in an SIR model is 0. A screenshot of the NetLogo program is shown in Figure 5, along a *regular lattice* contact network. *Prevalence*, the total number of infectious hosts at a given time, is graphed in the bottom right, showing the respective percentage of nodes which are susceptible (green), infectious (red), and removed (grey).

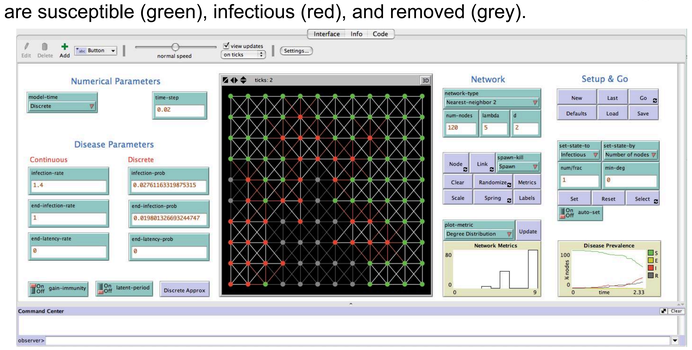

Figure 5. Regular Lattice graph with an ongoing infection

The Power of Theory

Mathematical theory can also provide key predictions for the disease. Of particular importance is the size of the basic reproductive ratio (R_0), the mean number of secondary infections caused by an average index case in an entirely susceptible population. R_0 can be determined using infection rates in continuous-time models, or infection probabilities in discrete-time models:

$$R_0 \approx bN \qquad R_0 = \frac{\beta N}{\alpha}$$

Theorems 1 and 2 and Figures 6 and 7 below reveal an important connection between the value of R_0 and the likelihood of a major outbreak.[2]

Theorem 1. *Assume homogeneity of hosts and uniform mixing in an SEIR-, SIR-, or SIS-model. If $R_0 \leq 1$ and if the population size is large, then with probability very close to 1, introduction of a single index case into an otherwise susceptible population will result only in a minor outbreak. There will be a constant B such that the expected number of hosts who will experience infection at some time during the outbreak will not exceed B, regardless of the population size N.*

Theorem 2. *Assume homogeneity of hosts and uniform mixing in an SIR- or SEIR-model. If $R_0 > 1$, then there are numbers $r(\infty)$, z_∞ that satisfy the inequalities $0 < r(\infty)$, $z_\infty < 1$ such that as long as the population size is large, then with probability very close to $1 - z_\infty$, introduction of a single index case into an otherwise susceptible population will result in a major outbreak with final size close to $r(\infty)$. The number $r(\infty)$ will be larger for larger values of R_0 and the number z_∞ will be smaller for larger values of R_0.*

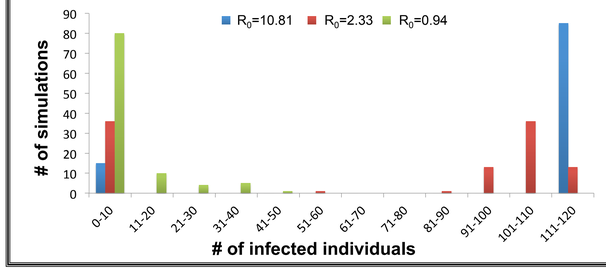

Figure 6. Frequencies of individuals experiencing infection for three different values of R_0 in a population of 120 on a complete network. 100 simulations were run for each R_0 value. Here we note that the majority of outbreaks (but not all) are minor when $R_0<1$, and the majority (but not all) are major when $R_0>1$.

Discussion on Control Measures

Mathematical modeling can provide insight into the effectiveness of control measures in delaying or reducing the probability of a major outbreak. All measures have advantages and disadvantages that must be balanced to find the most practical result. For example, border control is effective in delaying an outbreak, yet costly and difficult to impose. Such a delay is useful in order to develop a way of reducing the outbreak size. Other control measures may *only* reduce the outbreak size; e.g. behavior modification, quarantine, culling (for some plant or animal diseases), and vaccinations. Rarely do methods both delay and reduce the final outbreak.

Epidemiologists use *final size,* the proportion of individuals in the population who experienced infection at some point during the outbreak, to measure the severity of an outbreak. Vaccinations tend to be the most efficient at reducing the final size, and a surprising phenomenon called *herd immunity* plays a large role in this result. The *herd immunity threshold,* denoted by K, defines the minimum proportion of the population that needs to be vaccinated in order to make the probability of contracting the disease sufficiently small. K can be calculated using the reproductive ratio, R_0, and the total population size, N:

$$K = -\frac{N}{R_0} + N$$

Figure 7 shows an example of an infection that began at node 0 in an *Erdös-Rényi random graph* and has infected one additional node. If a sufficient proportion of nodes were initially vaccinated, the probability of an individual actually contracting the disease is vanishingly small. Figures 8 and 9 show the effects of vaccinating a fraction of the population when the underlying contact network is an Erdos Renyi graph.

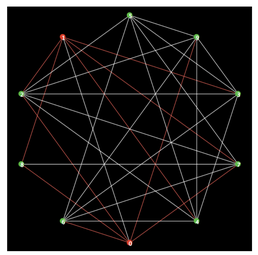

Figure 7. *Erdös-Rényi* random graph

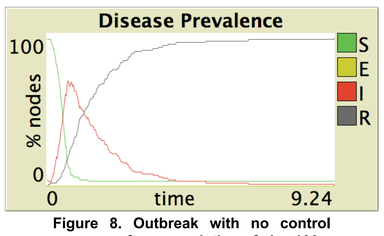

Figure 8. Outbreak with no control measures for a population of size 100.

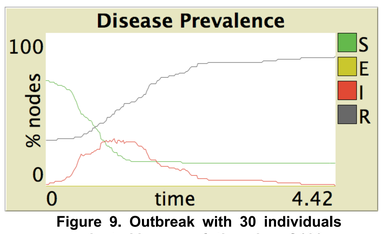

Figure 9. Outbreak with 30 individuals vaccinated in a population size of 100.

Future Work

An area of interest is how the concept of *assortative mating* affects the dynamics of disease spread. Currently all of our models assume a homogeneous population, where the likelihood of disease transmission is the same for each pair of individuals connected by an edge on the graph. Under the assumption of assortative mating, some individuals interact more with certain groups than with others. To accurately model this scenario, we need to reassess the transmission probabilities according to these preferences. This would give a more reliable prediction for how non-random interactions work in a population and how these various groupings affect the transmission of a disease.

We are also interested in investigating how the disease dynamics are affected by network parameters, such as the *diameter* of a given network (defined as the largest distance between any two nodes in the graph) and the *mean* or *median distance* between nodes in the network.

References

[1] Winfried Just, Hannah Callender, M. Drew LaMar, and Natalia Toporikova (2015); *Transmission of infectious diseases: Data, models, and simulations.* In Raina Robeva (ed.), *Algebraic and Discrete Mathematical Methods for Modern Biology*, Academic Press.

[2] Winfried Just, Hannah Callender, and M. Drew LaMar (2015); *Disease transmission dynamics on networks: Network structure vs. disease dynamics.* In Raina Robeva (ed.), *Algebraic and Discrete Mathematical Methods for Modern Biology*, Academic Press.

[3] Winfried Just, Hannah Callender, and Drew Lamar. Exploring Transmission of Infectious Diseases on Networks with NetLogo. http://www.ohio.edu/people/just/IONTW/. Accessed 10/30/14

[4] Uri Wilensky. NetLogo Home Page http://ccl.northwestern.edu/netlogo/. Accessed: 10/30/14