

Abstract

Infectious diseases pose a serious threat to humans, plants, and animals^[1]. Though vaccines can help control outbreaks of infectious diseases, there is typically not enough vaccine available for the entire population. In this case, certain *vaccination strategies* can be employed to maximize the benefits for the entire population. Using results from graph theory and the simulation tool IONTW (Infections On NeTWorks), we investigate various vaccination strategies on certain types of so-called *contact networks* that model the patterns of interactions within a population. In particular, we focus on a certain class of contact networks known as *small world models*, where individuals are randomly “connected”, i.e., can transmit and/or contract an infectious disease, along paths that are relatively *small* in relation to the overall population size^[2]. These types of networks tend to provide good estimations of the interactions of real populations when the exact contact network is unknown. However, the complexity and stochasticity of such networks create challenges in determining the best vaccination strategy. Here we discuss our preliminary results for vaccination strategies on small world models, including how many vaccines are needed (a notion related to a concept called the *herd immunity threshold*) and, for a given amount of vaccine, which individuals should be vaccinated in order to minimize the probability of major outbreaks.

Modeling Contact Networks

Contact networks are represented as mathematical *graphs*^[3]. A mathematical graph consists of nodes (also called vertices) and edges. In our graphs, nodes represent people and edges represent interactions people have in which the disease could be transmitted. Our research focuses on three types of contact networks: **Erdős-Rényi random graphs** (e.g., Fig. 1), **Nearest Neighbor 1-dimensional and 2-dimensional graphs** (e.g., Fig. 2), and **Small world models** (e.g., Fig. 3), which are constructed by taking the union of an Erdős-Rényi and a Nearest Neighbor graph. In Figures 1-3, nodes with green outlines are susceptible and nodes with red outlines are infectious.

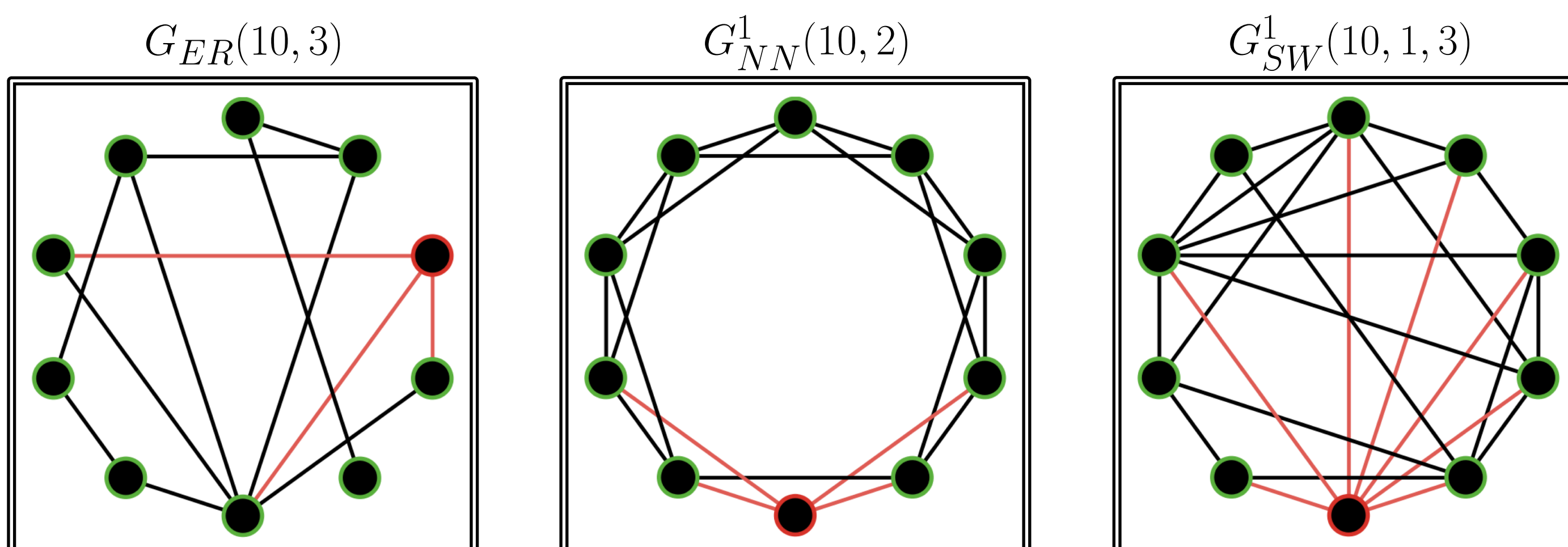


Figure 1. Erdős-Rényi graph with 10 nodes and expected mean degree (λ , the number of edges per node) equal to 3.
Figure 2. Nearest Neighbor 1 graph with 10 nodes and mean degree (d) equal to 2.
Figure 3. Small World 1 model with 10 nodes; union of Nearest Neighbor 1 with $d=1$ and Erdős-Rényi with $\lambda=3$.

Simulations in IONTW

All of our simulations are run using IONTW (Infections On NeTWorks)^[4], which was developed in the agent-based programming language of NetLogo^[5]. This software allows the user to develop a highly customized model, with a variety of options for contact networks, disease parameters, and initial state configurations. In particular, the user can easily test the efficacy of various vaccination strategies (e.g., Fig. 4), a primary focus of our research.

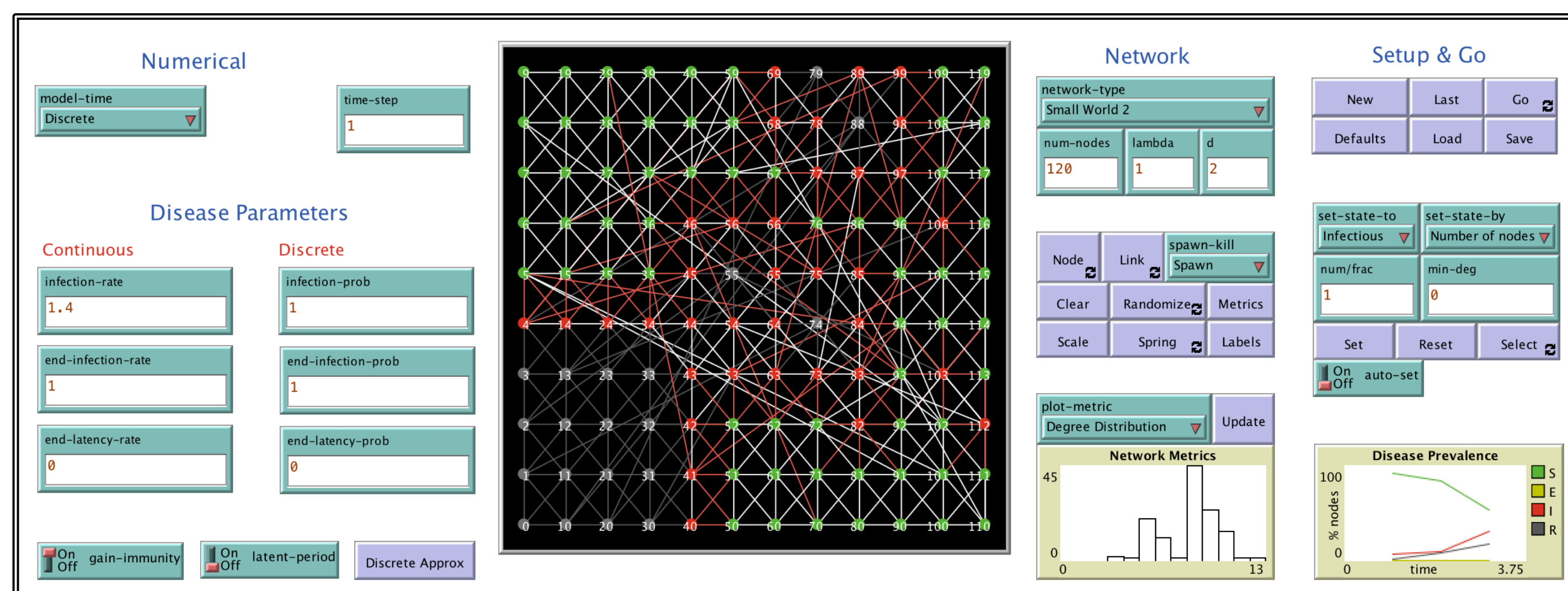


Figure 4. Snapshot of disease progression in a $G_{SW}^2(120, 1, 2)$ contact network, under a vaccination strategy where the lower left corner of nodes have been vaccinated (gray nodes).

Project 1: Herd Immunity Threshold

Here we investigate the Herd Immunity Threshold (HIT) for small world models $G_{SW}^{dim}(N, d, \lambda)$, where $dim = 1, 2$; N is the population size; d governs the degree of nodes from the Nearest Neighbor graph; and λ is the expected mean degree from the Erdős-Rényi graph.

Primary goal: Since our small world models are random networks, we seek to find a proportion, HIT, of hosts to vaccinate (at random) such that as $N \rightarrow \infty$, the probability that an outbreak is a major one approaches 0. Restated: We seek to find an HIT such that all outbreaks are limited to minor ones *asymptotically almost surely* (a.a.s.)^[1].

Figures 5 and 6 suggest the existence of an HIT, but further research is needed to determine the precise dependence of the HIT on a , b , d , and λ . In each of these figures, the histogram reveals the number of simulations (out of 200 total runs) in which certain percentages of the susceptible population experienced infection.

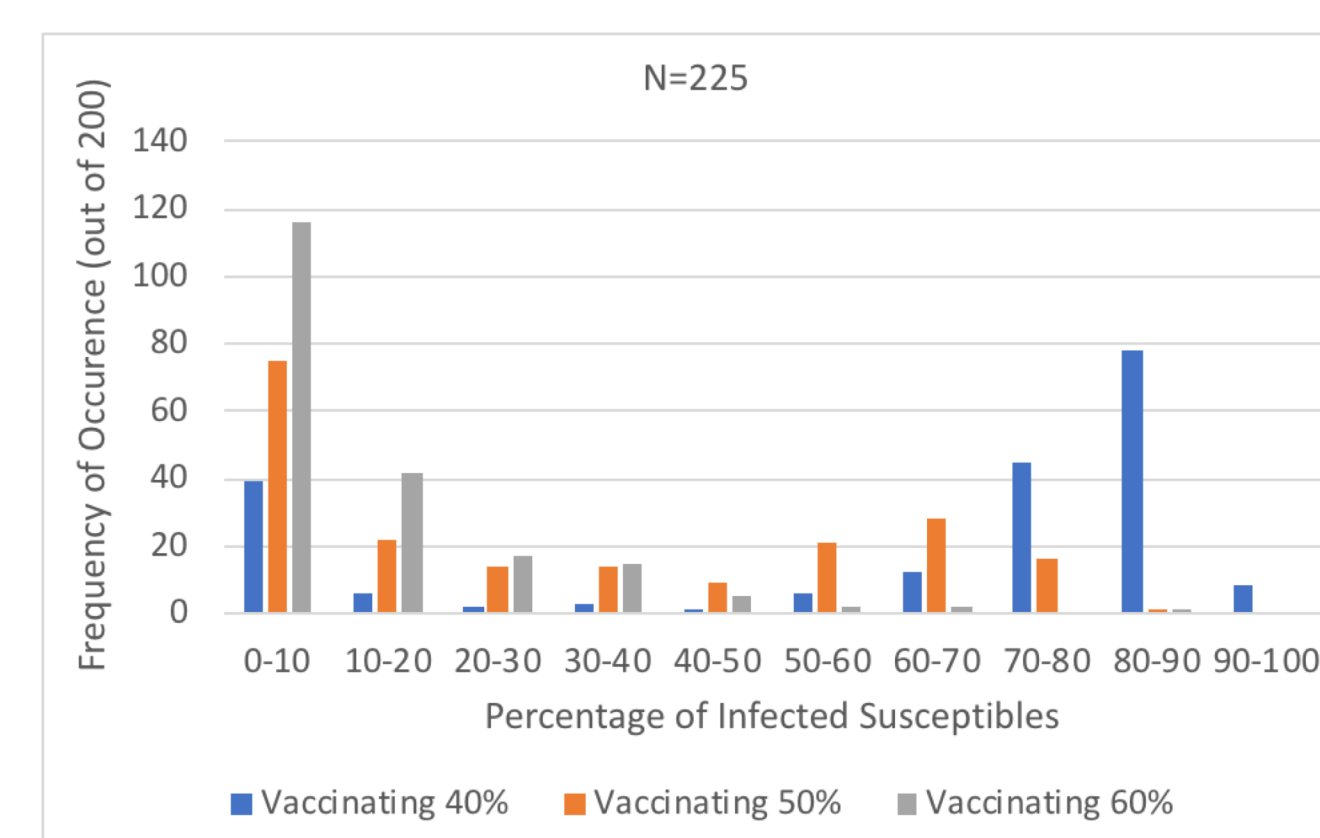


Figure 5. Histogram for % of infected susceptibles on a $G_{SW}^1(225, 2, 0.5)$ network with $a=1$, $b=0.5$, when vaccinating various percentages of the population.

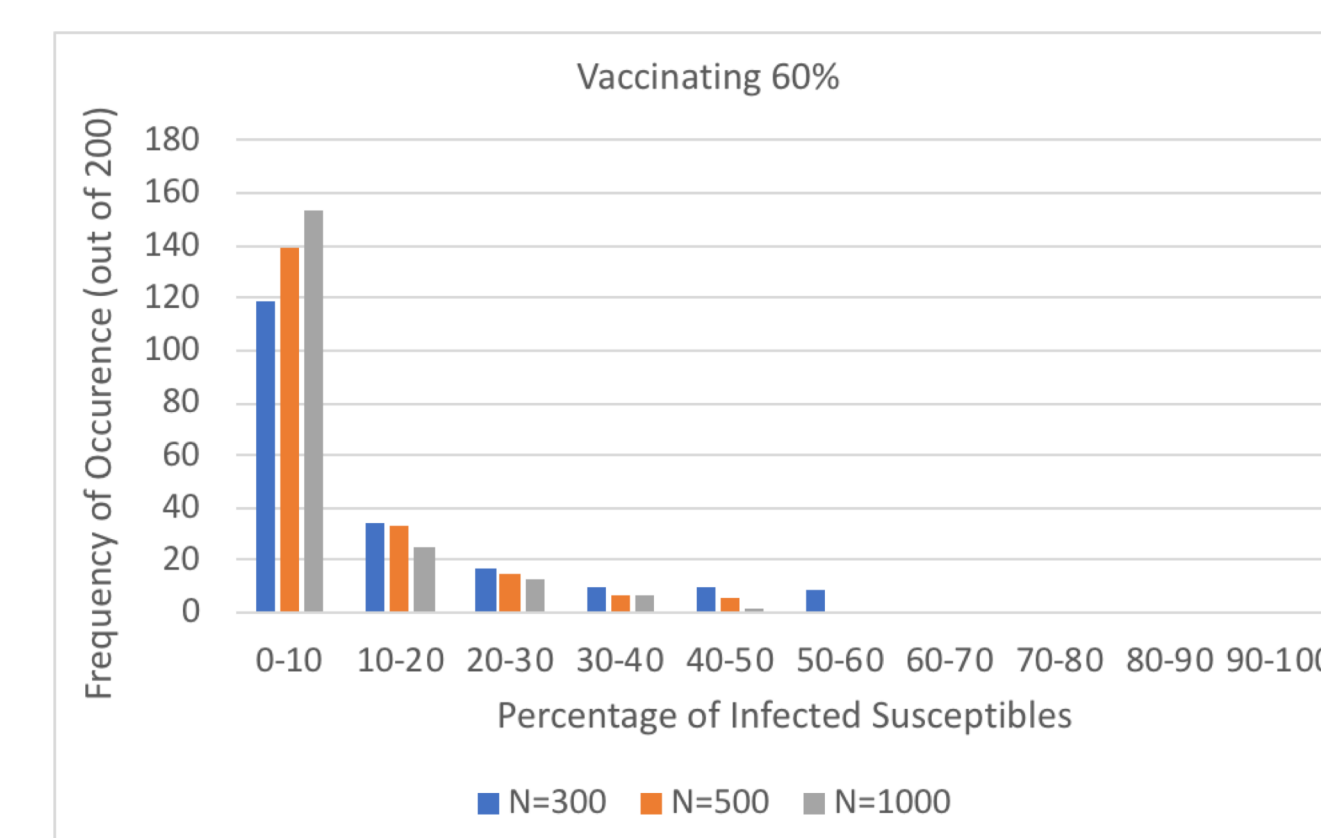


Figure 6. Histogram for % of infected susceptibles on a $G_{SW}^1(N, 2, 0.5)$ network with $a=1$, $b=0.5$, when vaccinating 60% of the population, for varying N .

Project 2: Vaccination Strategies

Here we consider the same small world models, but assume that we only have a fixed number of vaccines (v), whose proportion to the population was presumably less than the HIT. Our goal is to rigorously define two vaccination strategies: $B(x)$ and $H(x)$, where $B(x)$ would create evenly spaced “barriers” within the population, and $H(x)$ would vaccinate only those individuals with the highest degrees. Then we strive to determine whether $B(x)$, $H(x)$, or some combination of the two will be the best vaccination strategy.

$$G_{SW}^1(N, d, \lambda = 0)$$

Best strategy: $B(x)$ (see, e.g., Fig. 7)

Define the following:

- $v = \#$ of vaccines available
- $d = (\text{degree of each node})/2$
- $c = v/d = \#$ of vaccinated clusters of size d
- $s = (N-v) / (v/d) = \text{size of susceptible clusters}$
- $B(x)$, which returns 1 if node x should be vaccinated and 0 if node x should remain susceptible and is defined by:

$$f(x) = \begin{cases} 1, & x \equiv m \pmod{d+s} : 0 < m \leq d \\ 0, & x \equiv m \pmod{d+s} : d < m < d+s \\ 0, & x \equiv 0 \pmod{d+s} : m = 0 \end{cases}$$

$$G_{SW}^1(N, d, \lambda \neq 0)$$

Best strategy: $H(x)$ (see, e.g., Fig. 8) combined with $B(x)$, as described in the flowchart below.

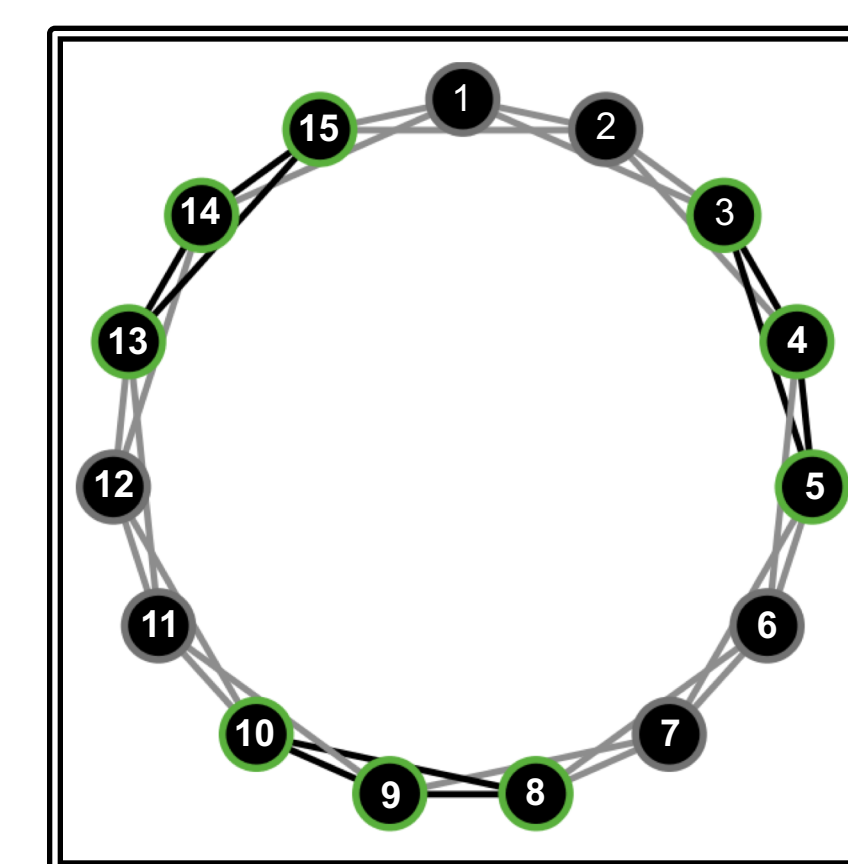
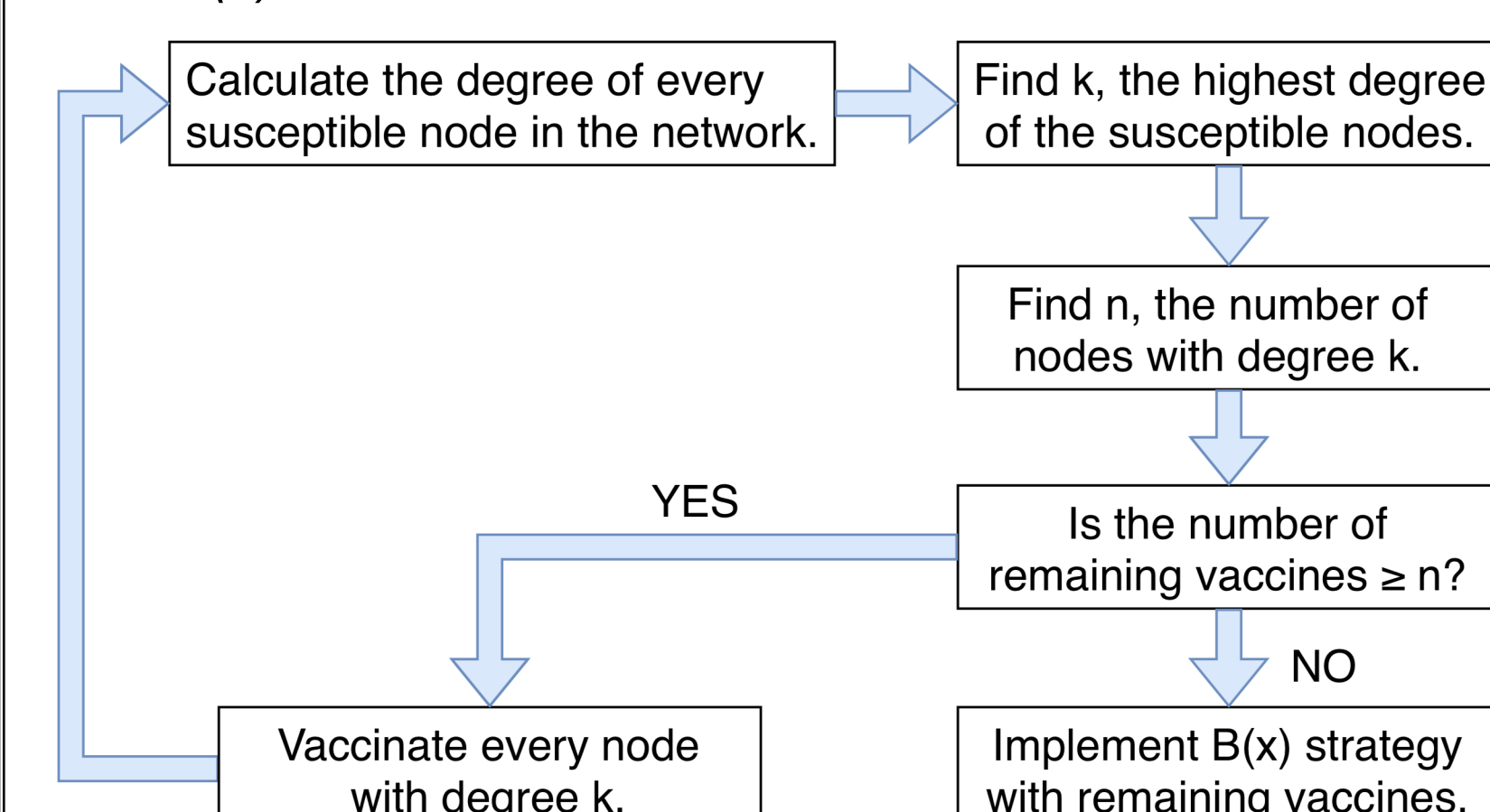


Figure 7. Example of $B(x)$ strategy for a $G_{SW}^1(15, 2, 0)$ network.

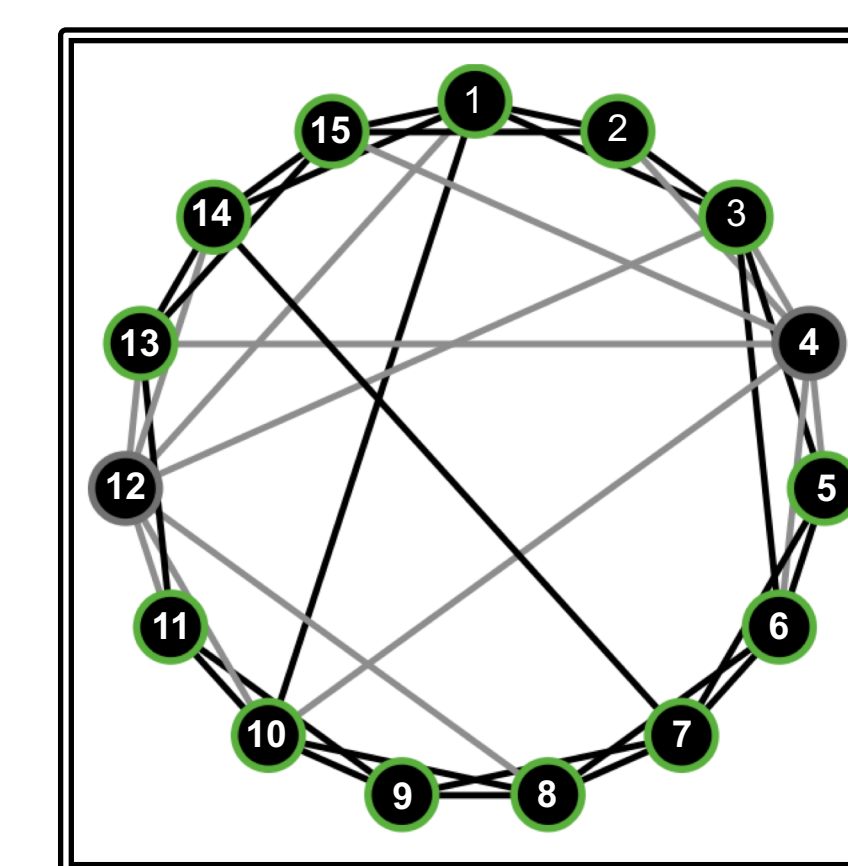


Figure 8. Example of $H(x)$ strategy for a $G_{SW}^1(15, 2, 2)$ network.

Project 2: Vaccination Strategies cont.

The task of developing vaccination strategies for 2-dimensional small world models, $G_{SW}^2(N, d, \lambda)$, is significantly more challenging than for 1-dimensional models. The simplest case is when $\lambda=0$ and $d=1$ (each node is only connected to the nodes within a radius of 1) and there is enough vaccine for 50% of the population. Here, the best strategy is to vaccinate nodes along every other diagonal (see Fig. 9). In this case, no matter where the initially infected node is located, the infection cannot spread to any other node.

To make this process more rigorous, we first map each node to the Cartesian plane using the following, for networks in which N is a perfect square:

$$X(x) = (x - 1) \pmod{\sqrt{N}}$$

$$Y(x) = \frac{(x - 1) - X(x)}{\sqrt{N}}$$

where $(X(x), Y(x))$ is the ordered pair corresponding to node x .

To vaccinate every other diagonal, vaccinate all nodes on the line

$$Y(x) = X(x) + 2c \quad \text{if } \sqrt{N} \text{ is even}$$

$$Y(x) = X(x) + (2c - 1) \quad \text{if } \sqrt{N} \text{ is odd}$$

for $c \in \mathbb{Z}$ such that

$$|c| \leq \frac{(\sqrt{N}-2)}{2} \quad \text{if } \sqrt{N} \text{ is even}$$

$$|c - \frac{1}{2}| \leq \frac{(\sqrt{N}-1)}{2} \quad \text{if } \sqrt{N} \text{ is odd}$$

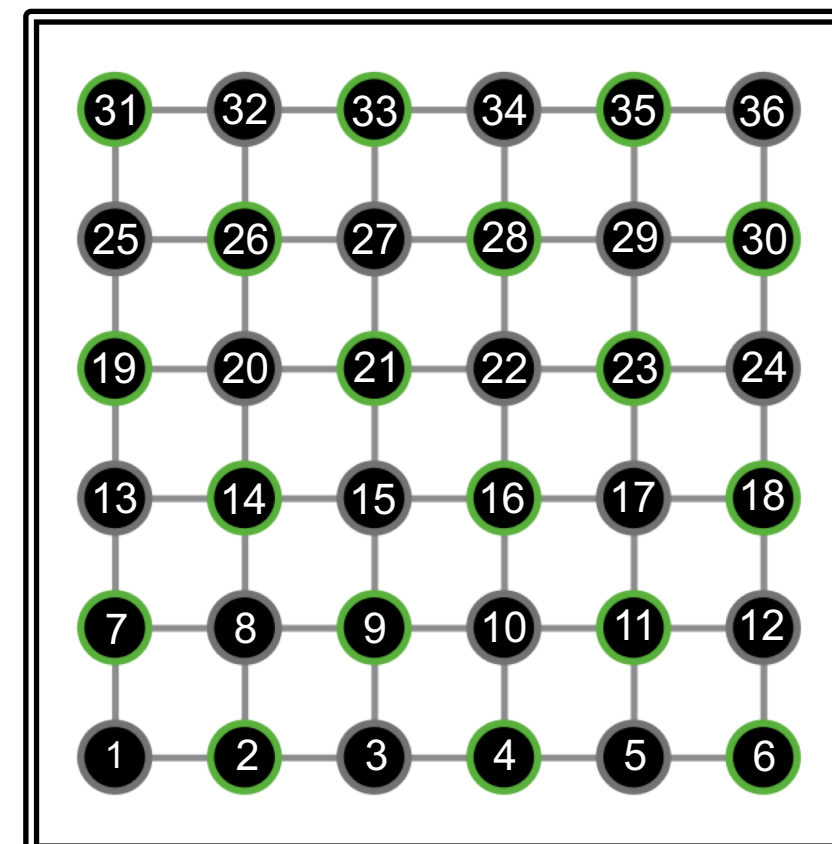


Figure 9. $B(x)$ vaccination strategy when amount of available vaccine is 50% of the population.

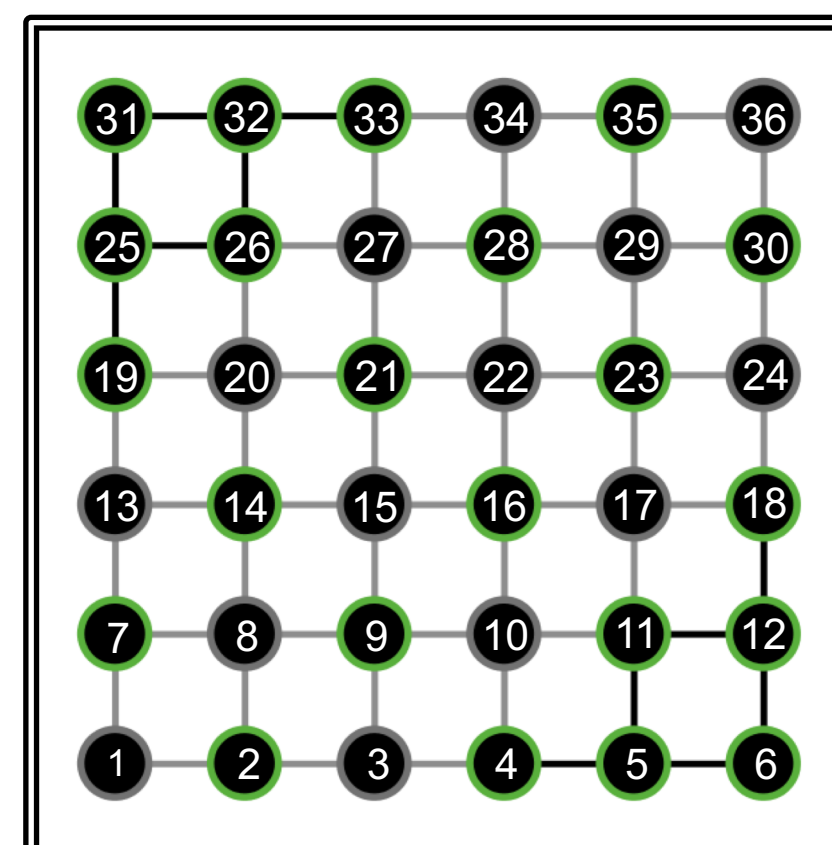


Figure 10. $B(x)$ vaccination strategy when amount of available vaccine is ~39% of the population.

Conclusions and Future Work

Our first task was to determine whether or not the HIT existed for small world models $G_{SW}^{dim}(N, d, \lambda)$. We have obtained promising results that suggest this threshold does in fact exist, but more research is needed to verify this proposition and to determine the relationship between the HIT, the network parameters d and λ , and the disease parameters a and b . This remains an area of focus for our research team.

Next we set out to determine the best vaccination strategies for various small world models. We found a formula for the best strategy for 1-D networks where $\lambda=0$, and we have a proposed best strategy for $\lambda \neq 0$. Our future work will include attempts to rigorously prove these are in fact the best strategies. We also have preliminary results for the best strategy for 2-D networks (see Figs. 9 and 10), but this remains a work in progress.

Once rigorous proofs have been obtained for our proposed best vaccination strategies, we plan to investigate additional scenarios, including those in which only certain individuals are actually able to receive vaccination, whether it be to logistical issues or health reasons. We would also like to look into how our strategies should be modified in the case where we allow for rewiring of the original contact network during the course of the outbreak.

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, 193-215.
- [2] Winfried Just and Hannah Callender Highlander (2018); *Vaccination Strategies for Small Worlds*. In: Wootton, A., Peterson, V., and Lee, C., editors. *A Primer for Undergraduate Research: From Groups and Tiles to Frames and Vaccines*. New York, NY: Springer, 223-264.
- [3] 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, 217-235.
- [4] Winfried Just, Hannah Callender, and Drew Lamar. Exploring Transmission of Infectious Diseases on Networks with NetLogo. <http://www.ohio.edu/people/just/IONTW/>. Accessed 9/28/18
- [5] Uri Wilensky. NetLogo Home Page <http://ccl.northwestern.edu/netlogo/>. Accessed: 9/28/18