Influence of Topology and Intervention Methods in Epidemiological Contact Networks

Network models are powerful tools that can be used to describe social relations and other uses in fields such as computers, neuroscience and genomics to name just a few. A network is a mathematical structure where there are nodes that represent some attributes and are connected to other nodes by edges (Pellis et al., 2015; Bansal et al., 2010). The edge connection between nodes represents their relationship. Network analysis is the statistical modelling of networks that can model some social structures or is helpful in studying relationships and patterns within networks in many different fields.

In particular, networks are a useful tool for modeling the spread of epidemics. Contact network epidemiology is used to construct networks that are based on real-life contacts between individuals (Leitch et al., 2019). In network models of outbreaks, a v*ertex* is a person, an *edge* is a contact between people, and a *degree* is the number of contacts of a particular person. The *degree distribution* is the distribution of the number of contacts (Lauren et al., 2005). This social network represents the collection of social interactions, with edges between nodes who have interaction or are considered to be neighbors. Disease will spread along the edges of these social networks. An infected node with a higher degree is more likely to spread the disease to more people than a lower-degree node. Determining what factors will cause an epidemic to occur or to grow is essential for controlling the spread of an infection.

Many important factors that can affect epidemic dynamics include social structure, contact patterns, fluctuating population size, disease dynamics,disease mechanisms, social interaction changing in response to disease spread, and multiple modes of transmission (Leitch et al., 2019). Real life examples of this would include a city under quarantine; birth, death and migration rates changing due to outside factors; or disease mutation. Network models can be designed to reflect these factors that can affect the spread of disease. By using networks to simulate real life social interaction, it is also possible to study other factors that affect the spread of infections such as vaccine distribution methods and hesitancy towards vaccinations.

One factor that is highly influential is network topology. Examples of such topological differences could be certain nodes having many edges or a node being connected to another node that is farther away in terms of the edge connections. Examples of topologies would include:

- Core-periphery structure where there is a large concentration of nodes in the center and sparse number of loosely connected nodes around the outskirts of the network.
- Tree-like networks which have a hierarchical formation with a root node and many connected child nodes.
- Unique groupings taking a specific shape, such as smaller clusters or a circular shape.

Observing a network's topology is an important step in network analysis.The patterns of disease spread in a network will differ accordingly by changing the network topology. Understanding different network topologies that mimic human social networks and interactions can lead to

insights as to what network arrangements will reduce or accelerate the speed of disease spread in an epidemic.

Disease mechanisms are different ways that diseases work within the real world or within a network. For example, neighbors or friends are more likely to infect each other than a random person because of in-person interactions. This translates to infections spreading along the edges of a network and infecting connected nodes, instead of unconnected nodes. Other disease mechanisms could include different environments which could lead to outcomes such as superspreading events, different types of connections or special edges within a network (Leitch et al., 2019).

An epidemic threshold is a number that determines whether or not a pathogen will die out or lead to an epidemic. An important epidemic threshold is R0, the basic reproduction number, which measures the intensity of infectious diseases (Lloyd-Smith et al., 2005). When R0 is less than 1, the disease dies out, whereas when R0 is greater than 1, the disease will spread. Therefore, to prevent massive outbreaks, R0 must be kept below 1. R0 is different for every infectious disease and is dependent on both environmental and individual factors such as variation in infectiousness or quarantining. R0 can also vary depending on some of the topological or intervening factors mentioned above and in response to interventions. Specifically, interventions such as social distancing, vaccinations and wearing masks in public places would likely lower the R0 threshold. It is important to factor in the epidemic thresholds when creating the network and the effect of interventions strategies when creating a model.

Many commonly-used network models make assumptions that do not accurately reflect human behavior. For example, many of the models are static in nature and are unable to capture the changing dynamics of behavior or interventions that are made during an epidemic. Network models can help predict different outcomes of the pandemic and suggest effective intervention strategies by studying network topologies similar to human social networks. Finding ways to model these dynamics is key to better understanding what factors and behaviors mitigate and accelerate the spread of diseases (Eisenberg, 2020).

Question 1: How do different network topologies influence the spread of diseases through a network?

In order to simulate the conditions of an epidemic, network models with different topologies will be generated. The disease mechanisms will be spread throughout the network and will be used to observe patterns of how the infection spread based on different model settings. This means that the disease will spread along the edges of the network. The spread of the infection will start with one randomly-selected node in the network being infected. For each iteration, which represents a day, the infected node(s) will have the ability to infect their neighboring nodes with some probability.

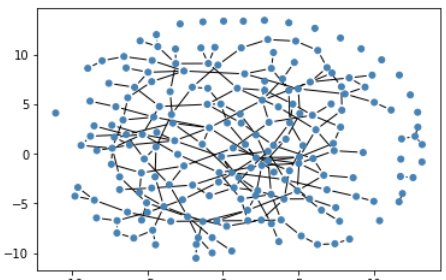


Figure 1a

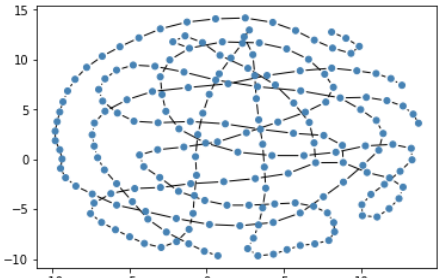


Figure 1b

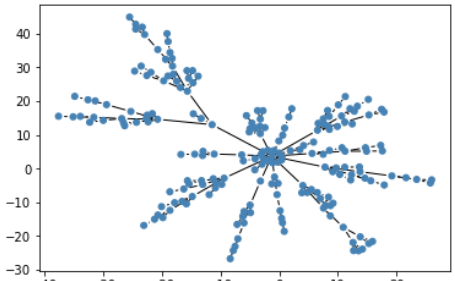


Figure 1c

The topology of the network can be changed using different network models. The following three network models are representative examples of varied topologies: Erdős-Rényi, Small World and Scale free networks. These models were chosen because they have very distinct topological properties that make them unique. An Erdős-Rényi random network is the simplest network model. In this model, there are a fixed number of vertices and there are edges placed between these vertices independently with a probability p (see Fig. 1a). This model does not reflect real world interactions very well because of its simplicity (Erdős-Rényi, 1959; Asma et al., 2020). In the real world, not everyone has the same number of friends or interactions, which is the same as having the same probability for an edge connection. Instead, real world networks exhibit degree heterogeneity, which is why preferential attachment models are used. Small world networks exhibit the small world property where any two vertices are reachable from one another by a short sequence of edges (Watts and Strogatz, 1998; Rüdiger et al., 2020). The Watts-Strogatz model generates a graph that maintains the small-world property (see Fig. 1b). Scale free models use preferential attachment where there are nodes that have many more connections and are likely to get more connections in comparison to other nodes in the network, known as “hub” nodes. Therefore the degree distribution of these networks follows a power law. Barabási–Albert is a network model that uses the properties of a Scale free model (see Fig 1c). Figure 1c displays a Barabási–Albert which has hub nodes at the center of the figure that have a high degree. Scale free models also do not have an epidemic threshold like other models and so the spread of disease is usually faster, being the model follows a power law (Asma et al., 2020). Thresholds such as R0 are not effective here because the rate of disease spread will vary over time and not stay constant, especially later on during an epidemic due to the hub nodes being able to infect the entire network very quickly. Scale free models are also a good representation of real world networks as the power law of the degree distribution is similar to that observed in real world networks.

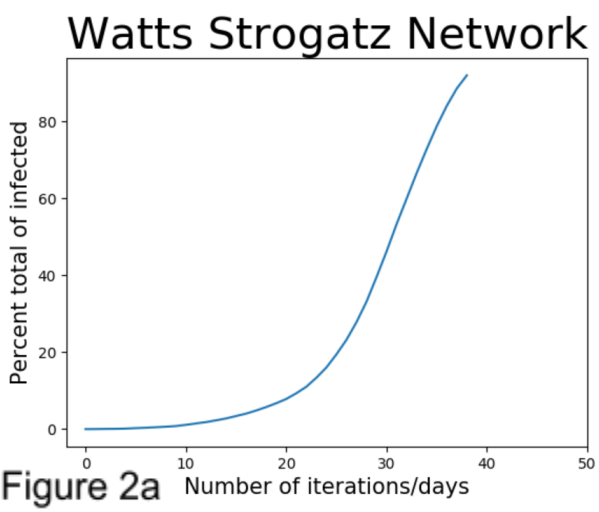


Figure 2a

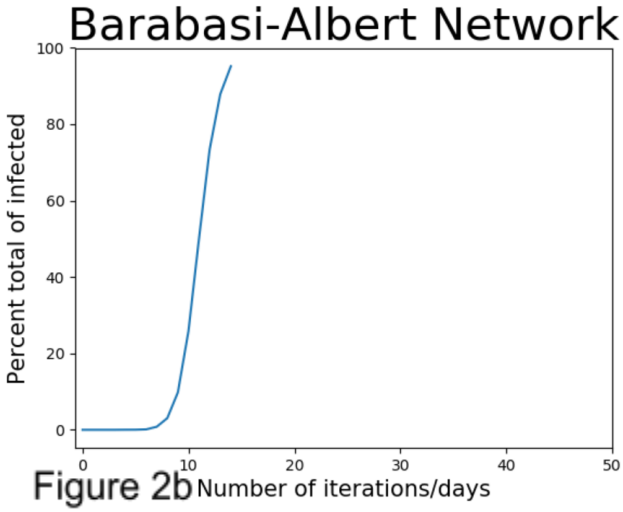


Figure 2b

There are certain attributes of the three models that affect the speed of the spread. Since Scale free models have no epidemic threshold, the spread of disease is much faster in comparison to Erdős-Rényi or Watts-Strogatz networks. Watts-Strogatz networks that have higher rewiring probabilities or more edges to distant nodes will also lead to faster spread of disease in comparison to a lower rewiring probability. Nodes in the Erdős-Rényi model will have approximately the same degree so there will be no "hub" nodes with more connections than other nodes. This is because the probability of connection for each node is the same, and the variance in the degree is less, which is not what is expected in a real social network. Comparing the two figures above, the Watts-Strogatz network (Fig. 2a) seems to take more time to reach the 90% threshold of infected nodes in comparison to the Scale free network (Fig. 2b). However, it is not a reasonable conclusion yet because the parameters of the two networks have not been tuned to match each other for one-to-one comparison.

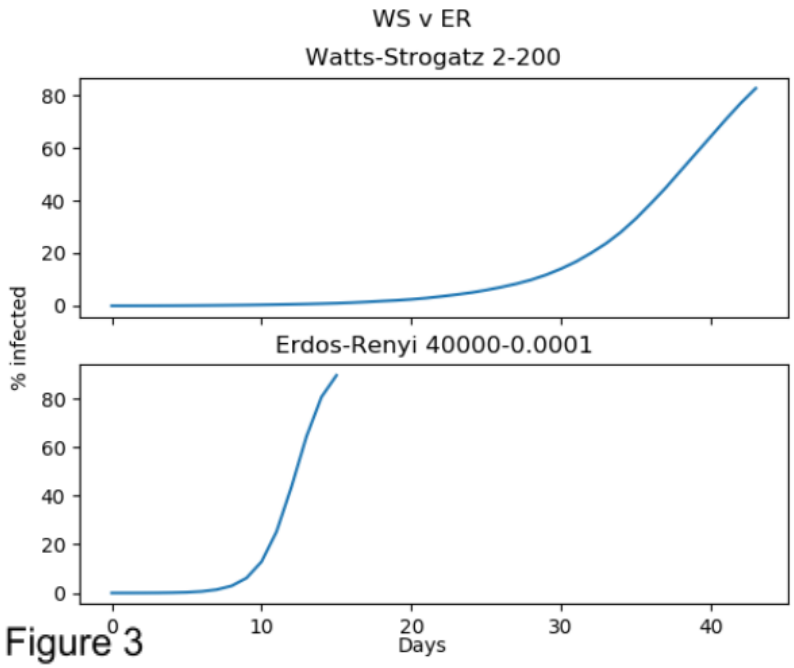


Figure 3

It is possible to create similar settings for comparison in terms of network size and network degree for the Erdős-Rényi and Watts-Strogatz models. However, since the Barabási–Albert network model does not have a degree distribution, it is hard to create an exact one-to-one comparison. Based on the figure 3, the Watts-Strogatz network takes a significantly longer time to reach the 90% infection threshold (around 40 days, given a small rewiring probability) in the network over the Erdős-Rényi network (around 15 days). Overall, the experiment's results mirror the expected output.

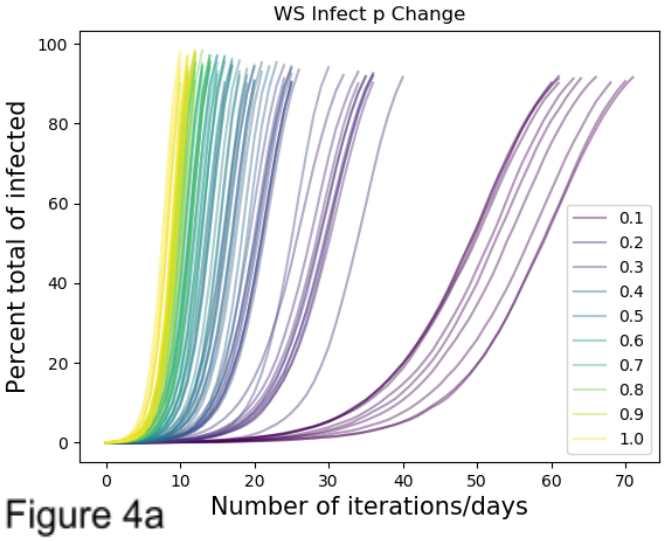


Figure 4a

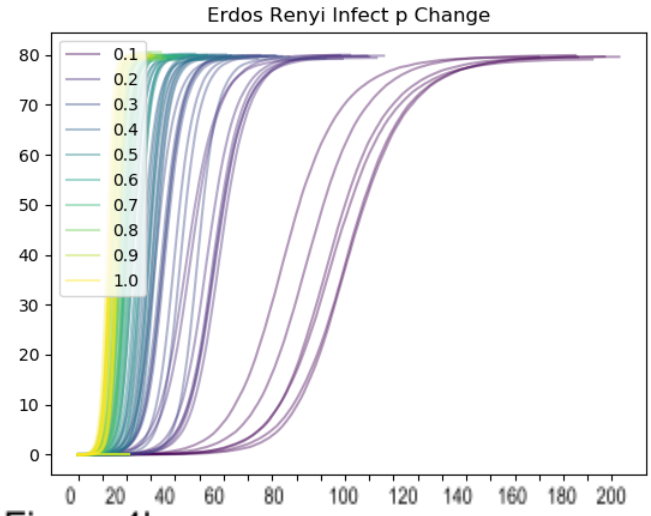


Figure 4b

The infection probability was kept constant during the experiments examining disease spread through different network topologies. However, changing some of these parameters that are important to the network structure and speed of spread changed behavior in various ways. One of the parameters that was further investigated was the infection probability, *p*. This probability determines the likelihood that an infected node in the network will spread the disease to its neighbors. The goal of this experiment is to try to find trends or significant differences between the different choices of *p*. Figures 4a and 4b show results of the repetitions at every 0.1 interval of *p* for both the Watts-Strogatz and Erdős-Rényi networks (keeping the same settings as above). As seen by both networks, there seems to be some breaks between the different values of *p*, especially between the 0.1 to 0.4 range and specifically after 0.4. The *p* values from 0.5 to 1.0 seemed to have very similar results, since the disease spreads very quickly at these values.

After examining the differences in network topology, the next step of the experiment was to include a form of intervention. Vaccinations are intervention methods that are extremely effective at stopping the spread of infections, which seemed like a very interesting simulation to run since it is a relevant topic during the current pandemic . The method of distributing the

vaccinations can have varied effects on how quickly the infection stagnates and how many people are infected by the disease.

Question 2: What are the differences between the different vaccination strategies? Which vaccination strategies are the most effective overall?

In the paper by Ma, Junling, et al., (2013), four vaccine strategies were cited as potential strategies which were used as reference to implement the following simulations. Some of the same settings were kept in line with the paper's experiments. For instance, with each of these strategies, there was a certain number of vaccines available each day set ahead of time and the start date of vaccinations within the network could be varied. In the following experiments, the possible starting dates in the experiment were day 0 and day 40.

The first vaccination strategy is prioritized vaccination, in which the people most likely to be in contact with the most people are given vaccines first. When implementing this strategy within the networks, these correspond to the nodes with the highest degree. This is known to be the most effective vaccination strategy in most cases, as it targets the people with the most opportunity for exposure and to spread the disease if infected. This is similar to how hospital and other front-line workers are prioritized for vaccination first, since they have the most interaction with people who can be infected.

The second strategy is the "follow-links" vaccination strategy. This strategy is useful for vaccinating isolated groups of people who interact with each other in succession, reducing the risk of infection in those subpopulations. This is implemented in the network by randomly vaccinating a single node and its susceptible neighbors, then repeating the process by randomly selecting one of the previous susceptible neighbors and vaccinating its susceptible neighbors. When all susceptible neighbors are found, then a new random node is vaccinated and the process begins again until there are no vaccines remaining for that day.

The third strategy is based on contact tracing. This strategy tries to keep track of all infected people and vaccinate those who might have been in contact with an infected person but are not infected themselves. In an ideal situation, this vaccination strategy would most likely prevent the spread of the disease. This can be achieved in the network, however, by tracking all of the infected nodes, then vaccinating their closest neighbors to curb the spread. However, in reality, it is a complicated process to trace all people who are exposed and their recent contacts and makes it somewhat unrealistic to implement in the real world.

The fourth strategy is the random vaccination strategy, where people are given vaccines randomly. This strategy is a useful baseline as it is comparatively easy to implement in the real world. It can be hard to determine priority or find neighbors of others in the real world, such as in the contact tracing strategy. In the network, this would mean that people are randomly selected to be vaccinated, subject to vaccine availability.

Along with implementing these four strategies, it was also necessary to add features such as recovery and vaccine effectiveness to the network which were not previously present in the

network topology experiments. As a starting point, this experiment was only done using the small-world network due to previous experience with using this network model.

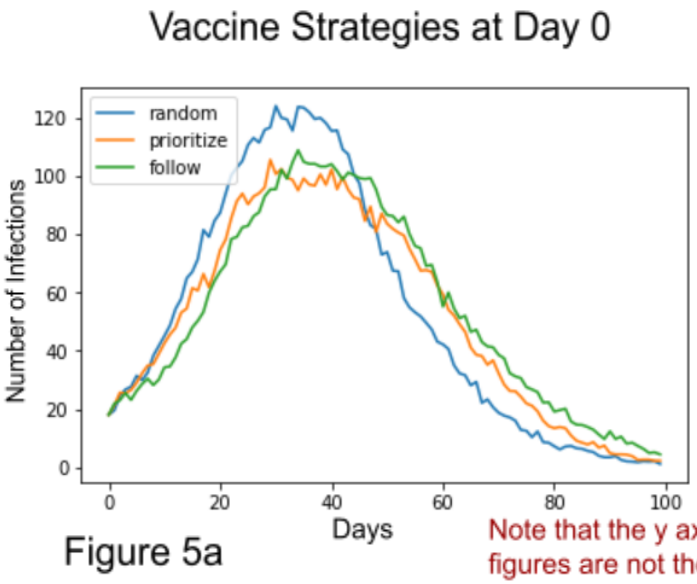


Figure 5a

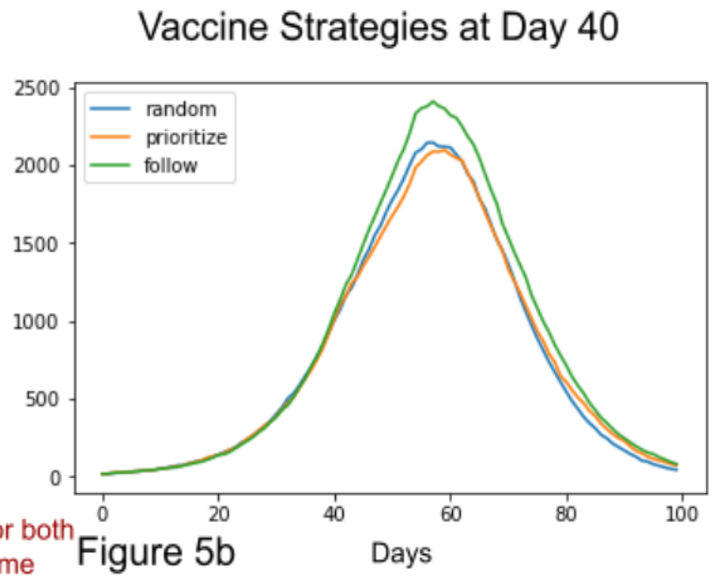


Figure 5b

Note that the y axis for both figures are not the same

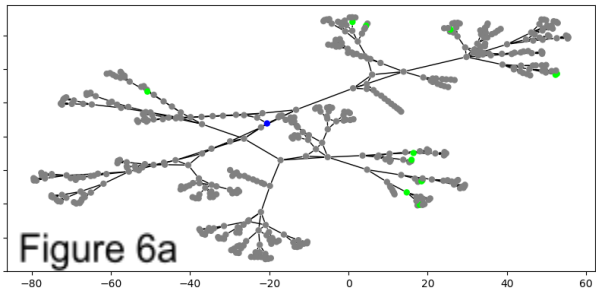
The contact tracing vaccination implementation was overperforming significantly since the implementation was able to unrealistically track all possible connections in the network model. Therefore, the decision was made to not include it in the visualization for the vaccination strategies. The figures 5a and 5b show the result of each of the different vaccination strategies averaged over 25 repetitions. The first image depicts the vaccination start date at day 0 and the second start date at day 40. The results of the experiment were very similar to what was expected: vaccinations slowed down the spread of diseases significantly and the vaccine distributions strategies performed as summarized in the paper. Overall, the prioritized vaccination strategy performs the best. In both figures, the prioritized vaccination strategy has a lower peak in the number of total infections. However, the random vaccination strategy performs similarly when the vaccinations begin later on during the simulation. This seems to be a worse strategy to use when vaccines are available from day 0. The follow-links vaccination strategy performs similarly to the prioritized vaccinations when vaccines are distributed from the start. However, they perform significantly worse than the other strategies when vaccines are not available until day 40. Starting vaccinations early does have an effect on stopping the overall spread of infection.

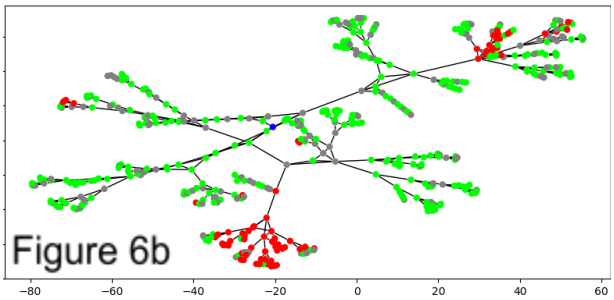
In light of the experiments above, there are still many questions about the effects of vaccine hesitancy on the overall spread of infections during an epidemic. As seen by the previous simulations, a community receiving and accepting vaccinations early on will likely preemptively stop a lot of possible infections. Therefore, understanding the rationale behind the decision to get vaccination, especially during the COVID-19 pandemic, is relevant and important. Vaccine hesitancy is defined by WHO (SAGE) as “ a delay in acceptance or refusal of vaccination despite availability of vaccination services. Vaccine hesitancy is complex and context specific, varying

across time, place, and vaccines. It is influenced by factors such as complacency, convenience and confidence ("Vaccine Hesitancy")." A common trait of vaccine hesitancy is that it usually only occurs in certain sections of the population. Therefore, it is important to determine and understand *who* is hesitant, *what* are their concerns and *where* they are located (geographically, socially, politically, etc) to minimize vaccine hesitancy. The rationale behind accepting, delaying or refusing a vaccine can fall into three categories: contextual, individual or group or vaccine specific (Larson, Heidi J., et al., 2015). Research also concludes that vaccine hesitancy and perceived risk is clearly associated with vaccine refusal, with refusal fluctuating depending on variable risk factors (Shih, Shu-Fang, et al., 2021). Vaccine acceptance is motivated by personal protection against the virus and the largest cause of hesitancy is by side effects of the vaccine (Machingaidze, Shingai, and Charles Shey Wiysonge., 2021).There is a psychological model assessing vaccine hesitancy in higher income countries known as the "5C psychological antecedents of vaccination". The five individual based metrics include complacency, constraints/convenience, risk calculation, confidence and collective responsibility (Betsch, Cornelia, et al., 2018). Since there are so many compounding influences that can play a role in this hesitancy, modelling this idea of hesitancy can be done in a number of ways.

Question 3: What is the best method to model vaccine hesitancy in an epidemiological contact network? Is this model consistent or comparable to infection spread patterns in the real world?

A model idea was that vaccine hesitancy is spread on a separate, more sparse network, similar to spread of a disease. Once "infected" by a neighbor with hesitancy, the node would refuse to receive the vaccine if offered. This would mimic a social media network since hesitancy is not only spread from person to person, but with more long distance connections geographically. However, the choice to encode vaccine hesitancy as a binary value led to results with either far too many or far too few people rejecting the vaccine than what should be the case in reality. Therefore the model was modified, making vaccine hesitancy a decimal value between zero and one for every node in the network. These values of hesitancy would have to be calculated every time a new "day" occurs and ranges of hesitancy (the decimal values) would allow measurement of different likelihood of vaccinations. Using this as a starting point, the initial values of the hesitancy towards the vaccine was determined by a beta distribution. Instead of updating hesitancy of one node who was "infected", vaccine hesitancy values would be updated by the weighted average of a node's current vaccine hesitancy and the average of its neighbors' hesitancies, with the weighting determined by a "stubbornness" parameter. This references the notion that most communities have a large effect on each other and their hesitancy towards vaccination will be influenced by that. Further emphasizing this idea, pockets of more hesitant communities were also introduced to the model as well.





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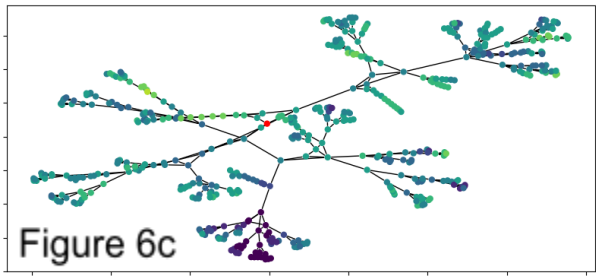

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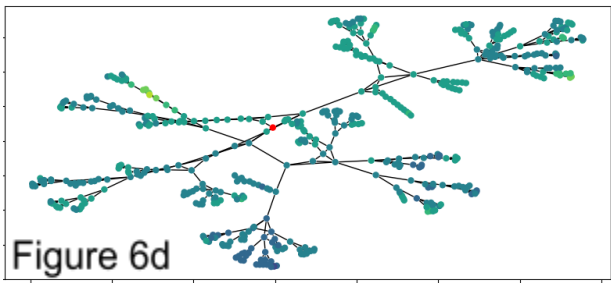

Random induced subnetworks were chosen to be analysed further, with Fig 6a and 6b depicting the subnetwork of the status of the nodes (infected as red, vaccinated as green, or susceptible as grey) and Fig 6c and 6d as the network depicting the hesitancy values with darker colors indicating more hesitant and lighter colors as less vaccine hesitant. Note that the green as vaccinated status does not relate to the green in the hesitancy subnetwork. Hesitancy is only applicable for nodes that have not been vaccinated or not been infected. Hesitancy and status are also separated into two different networks, having the same structure. Fig 6a and 6c depict the network at day 5 and Fig 6b and Fig 6d are at day 90, where typically the peak of the simulated epidemic is reached at day 50. The areas that were more hesitant (as seen by Fig 6c and 6d) seemed to also get infected in this induced graph over the 90 days. Over time, the more and less hesitant values also seemed to get closer to the average value of hesitancy since the hesitancy values have been influenced slowly by the neighboring nodes.

The next step in this experiment is to compare this model to real world data. The goal is to apply the vaccine hesitancy model that was created to county-level data using from the Wisconsin Health Department to confirm accuracy of the model.

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