OPTIMIZING QUARANTINE REGIONS THROUGH GRAPH THEORY AND SIMULATION

by

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A THESIS

submitted in partial fulfillment of the requirements for the degree

MASTER OF SCIENCE

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KANSAS STATE UNIVERSITY
Manhattan, Kansas

2009

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Abstract

Epidemics have been modeled mathematically as a way to safely understand them. For many of these mathematical models, the underlying assumptions they make provide excellent mathematical results, but are unrealistic for practical use. This research branches out from previous work by providing a model of the spread of infectious diseases and a model of quarantining this disease without the limiting assumptions of previous research.

One of the main results of this thesis was the development of a core simulation that rapidly simulates the spread of an epidemic on a contact network. This simulation can be easily adapted to any disease through the adjustment of many parameters.

This research provides the first definition for a quarantine cut and an ellipsoidal geographic network. This thesis uses the ellipsoidal geographic network to determine what is, and what is not, a feasible quarantine region. The quarantine cut is a new approach to partitioning quarantined and saved individuals in an optimized way.

To achieve an optimal quarantine cut, an integer program was developed. Although this integer program runs in polynomial time, the preparation required to execute this algorithm is unrealistic in a disease outbreak scenario. To provide implementable results, a heuristic and some general theory are provided. In a study, the heuristic performed within 10% of the optimal quarantine cut, which shows that the theory developed in this thesis can be successfully used in a disease outbreak scenario.

Table of Contents

List of Figures iv
List of Tables v
Acknowledgements vi
Dedication vii
CHAPTER 1 - Introduction 1
  1.1 Ethics and Quarantines 2
  1.2 Motivation 3
  1.3 Contributions 4
  1.4 Overview 5
CHAPTER 2 - Background Information 7
  2.1 Graph Theory 7
    2.1.1 Cuts 10
  2.2 Epidemics 11
    2.2.1 Mathematical Models of Epidemics Spread 12
      2.2.1.1 Contact Networks 13
    2.2.2 Compartmental Disease State Models 14
      2.2.2.1 SIR Model 15
      2.2.2.2 SEIR Model 16
      2.2.2.3 MSIR Model 16
      2.2.2.4 Carrier State Model 17
      2.2.2.5 SIS Model 17
      2.2.2.6 SIQR Model 18
  2.3 Simulation 18
    2.3.1 Simulating Epidemics 19
CHAPTER 3 - Epidemic Simulation 21
  3.1 Simulation Core 21
    3.1.1 Contact Network, Disease States and Tracks 22
  3.2 Disease State Transition Example 24
  3.3 Simulation Examples 26
CHAPTER 4 - Optimizing Quarantine Regions 33
  4.1 Basic Ideas of a Quarantine 33
  4.2 Ellipsoidal Geographic Graphs 34
  4.3 Feasible Quarantine Cuts 38
  4.4 Optimizing Quarantine Regions 45
    4.4.1 Quarantine Integer Program Formulation 46
  4.5 Theory of Optimized Quarantine Cuts 51
    4.5.1 Heuristic 58
  4.6 Comparison of Heuristic to Optimal 61
CHAPTER 5 – Conclusion and Future Work 64
  5.1 Future Work 65
References 67

List of Figures

Figure 2.1 A Sample Graph and a Sample Directed Graph 8

Figure 2.2: SIR Model 15

Figure 2.3 SEIR Model 16

Figure 2.4: MSIR Model 17

Figure 2.5: SIC/R Model 17

Figure 2.6: SIS Model 18

Figure 2.7: SIQR Model 18

Figure 3.1: Iteration 0 24

Figure 3.2: Iteration 1 25

Figure 3.3: Iteration 2 25

Figure 3.4: Iteration 3 25

Figure 4.1: Logical Quarantines 34

Figure 4.2: Illogical Quarantines 34

Figure 4.3: The Nodes of a Geographic Graph 35

Figure 4.6: All of the Arcs of a Sample G_G 37

Figure 4.7: The Final G_G with Probabilities 37

Figure 4.8: Example of Alternate Structure and Edges Generated from Structure 38

Figure 4.9: Legal Quarantine Cut in G_G 39

Figure 4.10: Illegal Quarantine Cut in G_G 39

Figure 4.11: Graphical Representation of Theorem 4.1 40

Figure 4.12: Example Fully Quarantined $Z = 5.67$ 52

Figure 4.13: 1st Iteration $Z = 5.47$ 53

Figure 4.14: 2nd Iteration $Z = 5.27$ 55

Figure 4.15: 3rd Iteration $Z = 5.07$ 56

List of Tables

Table 3.1: WAJEC Disease Tracks 33
Table 3.2: Graphic Key 34
Table 4.1: Comparison of Heuristic to Optimal n = 100 69
Table 4.2: Comparison of Heuristic to Optimal n = 250 69
Table 4.3: Comparison of Heuristic to Optimal n = 500 69

Acknowledgements

This research was partially funded by the National Science Foundation grant number NSF SES-084112: “SGER: Exploratory research on complex network approach to epidemic spreading in rural regions”

Dedication

To my Mom and Dad for all of their support

CHAPTER 1 - Introduction

Nobel Prize winner Joshua Lederberg, Ph.D, stressed the importance of understanding epidemics when he wrote, “The single biggest threat to man’s continued dominance on the planet is the virus.” [Zimmerman (2002)]

Since the beginning of time, epidemics have plagued man’s existence. For many years, man has combated these same epidemics with quarantining the sick from the healthy with the goal of preventing the spread. As can be seen in Israel and recorded in The Holy Bible, Lepers were quarantined outside of town to prevent the spreading of this disease [Numbers 12:14]. In severe cases the value of quarantine is the loss of human lives. From 1347-1351 the Bubonic Plague killed approximately 75 million people wiping out one third of Europe’s population [Drexler (2002)]. In fact, the death toll was so vast that the Pope consecrated the Rhone River so bodies that were flung into the river could receive a Christian burial [Zimmerman (2002)]. Additionally, in 1918 the Spanish Flu spread to all corners of the world and eventually killed over 50 million people [Taubenberger and Morens (2006)]. Had an early quarantine been in place, these death tolls would have been drastically smaller.

Viruses and bacteria continue to evolve and grow stronger, providing new challenges for mankind. In 2007, a strain of evolved drug resistant staph infection spread to 94,000 people throughout the United States, and killed 19,000 [Manier (2007)]. Because of this, our knowledge of viruses and how to quarantine effectively should continue to grow in order to combat these epidemics and maintain mankind’s health.

After an outbreak occurs, it is vital to react quickly. With the proper knowledge of the disease and the proper counter measures in place, many lives can be saved. Once a serious outbreak occurs the government will most likely respond with a quarantine. The decision of where the quarantine line should be “drawn” is usually a best guess situation. However, there are many factors that aide this decision, such as the rate of spread and the symptoms of the disease. Obviously, a deadly disease with a rapid spread would cause the quarantine region to be much larger to reduce the margin of error that an infected subject was missed. However, a larger quarantine area condemns many healthy people to be isolated in an infected region.

Clearly, if the government had a tool that would analyze the region and the disease to determine a more optimal quarantine cut, many lives could be saved. This research provides mathematical theory that can teach decision makers how to create a logical quarantine area.

1.1 Ethics and Quarantines

Quarantines are both good and bad. Any quarantine has the possibility of not containing every subject that is infected. Additionally, any quarantine has the possibility of condemning healthy subjects to remain with the infected ones.

The issue of an optimal quarantine leads into some incredibly difficult ethical questions. What is the value of life? Is it acceptable to sacrifice few to save many? Whose job is it to determine who lives and who dies? We do not have the expertise, authority, or right to tackle these questions. Rather, this research provides a tool for such an individual that does have to make these incredibly difficult decisions (Government Agencies).

In society, the cost of quarantining a group of people is high. Once a quarantine has been set it is the quarantine enforcer’s job to ensure no infected subjects escape the quarantine. The act of confining subjects both healthy and infected together should cause wide spread panic. First, the infected subjects are terrified because they know what they have is bad enough to be quarantined. Second, the healthy subjects that are quarantined with the infected subjects will panic and might try to escape. The results of an attempted escape could be fatal for the escaping party as the quarantine enforcer must do anything to maintain the quarantine line. Furthermore, if the panicked subject manages to escape and happens to be carrying the disease, the quarantine line is broken and the epidemic continues to spread.

In addition to the effects of the individuals within the quarantine area, the surrounding society is also affected. Many individuals would refuse to leave their homes for fear of contacting the virus. While all of this makes for a great Hollywood movie, this can be detrimental to a society's economy, growth and survival.

1.2 Motivation

For years epidemics have been modeled mathematically as a way to safely understand them. The first and most basic mathematical model presented was the progression of three states: susceptible, infectious, and recovered. From this model, researchers have branched out by adding new and more complex states, such as exposed and quarantined states. For many of these mathematical models, the underlying assumptions they make provide an unrealistic model. Typical assumptions include that every individual is in direct contact with everyone else and no geographical distances are considered. This research branches out from previous work by providing a model of the spread of infectious diseases and a model of quarantining this disease without the limiting assumptions of previous research.

1.3 Contributions

This research utilizes a simulation that generates a contact network. Once the contact network is found, multiple replications of the simulation are used to find the probability of infection for each person. These probabilities are combined with a ellipsoidal geographic graph. With this structure, a heuristic is used to find an optimized way to quarantine the nodes. The following section provides more information on each of these stages.

This research begins by creating a contact network. In a contact network the people are represented by nodes and the probability of node i infecting node j is represented with an arc.

To estimate the probability of infection, a simulation model is created for the spread of infectious diseases. The model used in this research uses many parameters that can be adjusted to model a specific disease, such as the rate at which a subject progresses through each stage of the disease and the probability of an infected subject transmitting the disease to another person.

The simulation created for this research uses random number distributions to generate numbers for different factors such as, how rapidly a subject transitions through each stage of the disease and the links between each subject. With this randomized model, the simulation is run for multiple replications. To calculate the average probability the sum of all of the calculated probabilities for each arc are divided by the number of replications.

To consider the geographical distance of each node, the contact network then becomes the ellipsoidal geographic graph G_G. The arcs in G_G form an acyclic graph such that the arc (i,j) is in A_G if and only if node v_i is "closer" to the root node than v_j where "closer" is defined by an ellipse. For node v_i, an ellipse is created such that the beginning disease node and v_i are the antipodal points and the foci are calculated under the assumption that the width of the ellipse is some percentage of the distance between the two antipodal points. With this generated, there exists an arc from v_j to v_i (v_j,v_i) if, and only if, v_j is contained in this ellipse. In an outbreak scenario, the goal of a quarantine is to eliminate the disease by keeping the infected individuals away from the uninfected subjects. The Graph Theory definition of a partitioning a set of nodes into two groups is called a cut. This research defines a quarantine cut as a partition that has a logical geometric shape that would be easy to manage. For instance, a donut shape would be a bad quarantine, because the area in the middle would be hard to maintain.

A standard industrial engineering approach to difficult decisions is to assign penalties for bad outcomes. To determine an optimal quarantine cut, the penalties for not containing an infected subject, s, and condemning healthy a subject, q, are decided. These penalties are highly dependant on the severity of the disease. Once the penalties are decided, an integer programming formulation is made with the objective of minimizing these penalties.

In addition to the integer programming formulation, multiple heuristics and some theoretical results are presented. The results provide decision makers with ample knowledge of how to apply this research in a real life scenario.

1.4 Overview

The remainder of this thesis is organized as follows. Chapter 2 discusses the background that is the basis of this research. There is a graph theory section that specifically targets cuts as they are vitally important to this research. This chapter also discusses the importance of understanding epidemics and the current mathematical models for the spread of epidemics. Since simulation is used to model the spread of infectious disease, a section in this chapter also addresses simulation.

Chapter 3 discusses the computations that were preformed. The results of this simulation are analyzed here. Along with the simulation results, a study of the efficiency of the proposed heuristics will be discussed.

Chapter 4 provides the first mathematical definition of a quarantine cut and an ellipsoidal geographic graph. Additionally, this chapter describes how an ellipse is used to generate the arcs in a geographic graph. An integer program formulation along with multiple heuristics and general quarantine theory are also provided to optimize the quarantine. Graphical examples are provided to illustrate this theory.

Chapter 5 addresses final thoughts about this research. This section also provides detailed incite for the field of epidemic research. Additionally, future research and how this research should be applied are also discussed.

CHAPTER 2 - Background Information

Much research has been done on epidemics. This chapter provides a brief overview of these topics. Additional information can be found in Gordis (2000) or Rothman (2002).

This first section of this chapter discusses the graph theory principles that are the basis for this research. Specific attention is paid to cuts as this is a key concept for quarantining the spread of the epidemic. Since understanding the parameters of an epidemic is vital to this research, a section on epidemics is provided. The next two sections provide a summary of mathematical models of epidemics. The final section discusses simulation and how it can be used to study epidemics.

2.1 Graph Theory

A common method to model the spread of infectious diseases uses a contact network. A contact network is a special class of graphs. This section discusses some elementary graph theory topics. A more detailed discussion can be found in [Diestel (2000)].

The study of graphs has been applied to many aspects of our lives. From analyzing vehicle routes [Dietrich (1992), Klein, et al. (1994), Shirabe (2005)], to mapping a genetic code [Brown and Harrower (2004), Ferreira, et al. (2002)], graphical applications are everywhere. The following graph theory discussion helps to understand graphs and how they can be applied to the spread of infectious diseases.

A finite undirected graph, $G=(V,E)$, is a set of n vertices, $V = \{v_1,v_2,\ldots,v_n\}$, and a set of m edges, $E=\{e_1,e_2,\ldots,e_m\}$ where each edge is a set of two vertices $e_i=\{v_j,v_k\}$. Additionally, a finite directed graph, $G = (V,A)$ is defined as a finite set of n vertices, $V = \{v_1,v_2,\ldots,v_n\}$, and the set of arcs, $A=\{a_1, a_2,\ldots,a_m\}$ where an arc is an ordered set of two vertices, (v_j,v_k).

A graph can be considered weighted if a nonempty set of numbers is assigned to each edge or each node. These weights frequently represent cost, distances, probabilities, penalties or capacities of an edge or node and are denoted by w_{ij} for all edges $\{e_i, e_j\}$. A directed graph with weighted arcs and/or nodes is referred to as a network.

Figure 2.1 depicts a sample graph and a sample directed graph. The nodes, also called vertices, are $V=\{s,v,u,w,y,x,t\}$, and the edges are $E=\{\{s,v\}, \{v,u\}, \{v,y\}, \{u,y\}, \{u,w\}, \{y,w\}, \{w,t\}, \{y,t\}, \{y,x\}, \{t,x\}, \{x,s\}, \{s,y\}\}$. Furthermore, for the directed graph the nodes stay the same, but the arcs are $A = \{(s,v), (v,u), (v,s), (v,y), (y,u), (u,w), (u,v), (y,w), (t,w), (y,t), (x,y), (t,x), (x,s), (s,y)\}$.

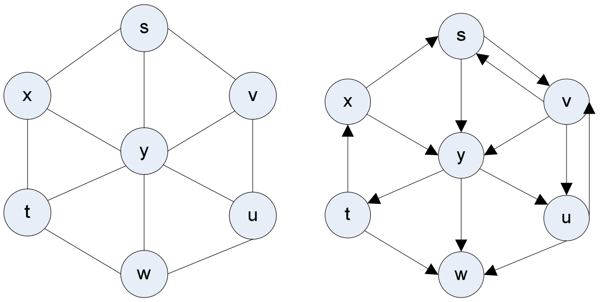


Figure 2.1 A Sample Graph and a Sample Directed Graph

A subgraph $G'=(V',E')$ of G is a graph where $V'\subseteq V$ and $E'\subseteq E$. For example, the node s, v, x, and y with the edge $\{s,x\}$, $\{s,v\}$, and $\{s,y\}$ form a subgraph of the sample graph above. An induced subgraph is given by a subset V' of nodes and the edges consist of all edges in E that only contain vertices in V'. For instance, the edges of the induced subgraph of *s*, *v*, *x* and *y* contains all edges that are incident to these nodes. These edges are {(s,v), (v,s), (s,y), (s,y), (s,x), (x,s), (x,y), (y,x), (y,v), (v,y)}.

A path is a set of sequential connected nodes in a graph. For example an *s*-*t* path in the directed graph above is the nodes $P = (s,y,t)$. Furthermore, two nodes *u* and *v* are connected if there exists a path from *u* to *v*. A graph is connected if every pair of its nodes is connected, if not, the graph is disconnected. A strongly connected digraph has a path from each node to every other node. Each group of connected nodes is called a component. A common algorithm for finding the number of nodes a single node is connected to is called Breadth First Search or BFS [Ahuja, et. al (1993)]. Another form of BFS is Reverse Breadth First Search, which is similar to BFS, but in reverse order.

A cycle is a set of sequentially connected nodes that returns to the initial node. An example of a cycle in the graph above is the nodes $C = (s,y,t,x)$. Alternately a graph is said to be acyclic if it contains no cycles.

Many substructures of graphs are well known because they have unique properties and their names help explain their distinct shape. For example a graph with a central hub that is connected to a ring of surrounding nodes is called a wheel. The graph in Figure 2.1 is an example of a wheel.

Another famous graph structure is a bipartite graph. A bipartite graph is a graph that has two partitions of V into V_1 and V_2 such that edge $\{u,v\}$ has $u \in V_1$ and $v \in V_2$. Famous problems associated with the bipartite graph are the assignment problem, where the users are in the partition V_1 and the jobs are in V_2.

A clique, or complete graph, is a graph in which every vertex is adjacent to each other. A clique, K_n is a graph with n vertices and $E = \{\{v_i , v_j\}: i,j \in \{1,\dots,n\},\ i \neq j\}$.

Clearly a clique has $\binom{n}{2} = n(n\text{-}1)/2$ edges. Notice that the above example graph contains a max clique of size three, also called a triangle.

The degree of a node in a graph is the number of edges coming into or out of a node. Additionally, the outdegree and indegree of a node in a digraph is the number of arcs coming out of and into it, respectively. A node with degree zero is considered to be isolated whereas a node with degree one is a pendant.

A few classical problems associated with weighted graphs are shortest path [Dijkstra (1959)], minimum cost spanning tree [Prim (1957), Kruskal (1956)] and maximum flow/minimum cut [Ford and Fulkerson (1956), Menger (1927)].

2.1.1 Cuts

In general, the definition of a cut is the separation of two entities. It is only natural to consider a cut when separating a body of individuals into quarantined and saved partitions. The following section defines a mathematical cut in a graph.

In mathematics, a cut in a graph, $G = (V,E)$, is defined as partition of vertices into two sets. That is, (V', V'') is a cut if and only if $V' \subseteq V$, $V'' \subseteq V$, $V' \cap V'' = \emptyset$, and $V' \cup V'' = V$. The cost of the cut is measured by summing the weights of all edges that cross the cut. Therefore, the cost of the (V', V'') cut is $\sum_{\{i,,j\} \in E : i \in V', j \in V''} w_{ij}$.

Some of the most famous cuts involve the minimum cut between two vertices, s and t. A minimum s-t cut is defined as the smallest value of a cut where $s \in V'$ and $t \in V''$ in a graph. The Ford Fulkerson Algorithm [Ford and Fulkerson (1956)] is used to find the minimum cut in pseudo polynomial time. The maximum cut on the other hand is $\mathcal{NP}$-Complete as shown by [Karp (1972)]. The max flow minimum cut theorem states that the maximum flow is equal to the minimum cut [Menger (1927)]. In other words, the amount of flow between any two vertices cannot exceed the capacity of the smallest set of edges between the two vertices. This is also known as being limited by your bottleneck.

Rather than looking at the traditional cut on edges this research looks at a nontraditional idea of a cut where the values are on the nodes with some restrictions as to what constitute a valid cut. These definitions are critical to this work and, due to their importance, are reserved for Chapter 4.

2.2 Epidemics

Dustin Hoffman's character in the 1995 movie Outbreak stressed the importance of understanding epidemics when he said, "The bug is one billionth our size and it's beating us."

Epidemics are fundamental to life on earth. The fossil of a bird over 90 million years old has shown symptoms of infectious disease [Zimmerman (2002)]. The fact that our history has always been plagued with epidemics only shows that there will continue to be epidemic problems. The benefits of advancing our understanding of epidemics can be reaped in many sectors of our lives. With our knowledge of epidemics come more advanced healthcare systems, longer life spans, and less fear of biological warfare.

Here, an epidemic is defined as an outbreak of a disease that spreads rapidly and widely. Various epidemics have hampered society for centuries including such famous cases as the bubonic plague, avian flu, and SARS. Of particular interest to this thesis is the Spanish Flu of 1918, because it began at Ft. Riley, Kansas. This virus spread to all corners of the earth from the Arctic to remote tropical islands. It is estimated that this epidemic killed 50 million people [Taubenberger and Morens (2006)], which is more than double of the death toll in World War I.

Understanding an epidemic requires the study of complex biological systems such as viruses, bacteria, parasites, and immune systems. It also requires understanding of how the epidemic affects the individual with respect to age, sex, and recovery rate. In addition, it also necessitates the understanding how epidemics spread, which includes, how the disease is transmitted, what the travel patterns of the subject are, and the geographical layout of the area.

Utilizing and controlling epidemics has been a vital part of world history. The Mongol attacks in the battle of Caffa consisted of catapulting plagued corpses over castle walls [Wheelis (2003)]. The defenders of Caffa contracted the plague and in their retreat helped spread the Black Death to the entire Mediterranean Region. Outbreaks of smallpox plagued the American Indians in an accidental biological attack and contributed to the settlement of the new world [Wheelis (2003)]. When an outbreak of this magnitude occurs the population's economy weakens as many fear to or cannot leave their residence. Society in general, slows down during an epidemic outbreak.

2.2.1 Mathematical Models of Epidemics Spread

Studying any complex systems is typically too difficult, costly or unethical, so researchers develop and study models of the system. Typically these models have underlying assumptions that enable the researcher to analyze the system and estimate or optimize the effects of changes to the system. The question always remains whether or not these assumptions enable a model that realistically describes the scenario.

Mathematical models of epidemics can be largely divided into two classes, host and spread. The host class focuses on the affect of the disease on the individual, while the spread class focuses on how the spread affects a group of individuals. The focus of this research is more on the spread of infectious disease and not the host. In order to further understand how a disease spreads, the host of the disease should also be understood.

Much research has been done on how a parasite affects a host. The host-parasite model simulates the spread of a parasite onto a host. This mathematical model provides an effective way to understand key factors in this area. Some versions of this include how a parasite selects its host and competition between parasites for hosts [Kumar (2002)]. Some models use optimization principles to further understand the parasite host relationship [Olsson (1996)]. These models are vital to further understand how an epidemic affects an individual and also when an individual can transmit an infection to another person.

A model of a spreading epidemic can be used to help understand how to group cities together to prevent the spread of diseases. It can also help understand why a certain group of people are more susceptible to a certain disease.

2.2.1.1 Contact Networks

When modeling an epidemic, a contact network is frequently used. A contact network models the chances that an individual infects another individual. Given a set of n people, $N=\{1,\ldots,n\}$ and an n x n probability matrix P where p_{ij} equals the probability of person i infecting person j with the disease being studied, then the contact network is constructed as follows. Let $G_C = (V_C, A_C)$ be the contact network where $v_i \in V_C$ for $i=1,\ldots,n$ and $(v_i,v_j) \in \mathrm{A_C}$ with a weight of p_{ij}. For simplicity, if $p_{ij}=0$, then the arc is not considered in A_C.

Accurate contact networks are difficult to generate, because estimating the probability of every person in a graph infecting each other is hard. In a crisis situation, it would be virtually impossible for a government agency to generate a contact network efficiently and accurately. For disease control purposes, a contact network should be developed before an outbreak occurs.

Once a contact network is generated, it can be used as input for a simulation and optimization software. The simulation and optimization software can use the contact network to decide where the best location for a quarantine line would be. Again, the biggest drawback to this approach is generating the necessary assumptions so that the contact network is accurate.

2.2.2 Compartmental Disease State Models

Once a contact network is established, researchers can then model the spread of epidemics. Modeling the spread of infectious disease has been a goal of researchers for many years. Because it is such a complex problem, a perfect model may never be created. Most current models for the spread of infectious disease have underlying assumptions that make the models unrealistic. Since the benefits are so high, an effort should always be made to model the spread of an epidemic more effectively.

2.2.2.1 SIR Model

One of the first, and most basic models for the spread of an epidemic is the Susceptible, Infectious, or Recovered (SIR) state model. At any moment of time each individual is classified into a state. Thus, at any given moment every individual is susceptible, infectious or recovered. The recovered state can either mean the subject no longer has the disease or the subject is dead.

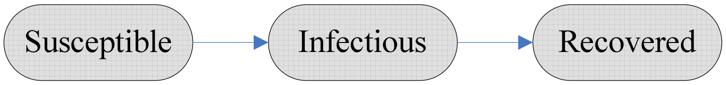


Figure 2.2: SIR Model

The current assumptions for a basic SIR model are that the contact network is a complete graph and no geographical distances are considered. Also each of these links between nodes transmits the disease with the same probability [Newman (2002)]. The SIR model uses differential equations to express the die out rate. This shows that the SIR model and the models that have branched from this are focused on natural selection and not how to mitigate the disease. While these assumptions provide nice mathematical results, in real life, none of these assumptions are true, as commented by Newman.

In the SIR model and most other mathematical models, individuals transition from each of these states. The rate of transition from susceptible to infectious is β and is used for the infection rate and γ is used for the recovery rate. Consequently, if β is much larger than γ, the infection will spread quickly. On the other hand, if the ratio of $\frac{\beta}{\gamma} < 1$, then the disease will die out. Ultimately, the smaller this ratio, the more rapidly the disease dies out.

Some specific examples of researchers using the SIR model include generating optimal vaccination strategies [Ogren (2000)], modeling the spread of influenza in a mixed population [Fuks, et al. (2006)] and modeling the spread of a computer virus in a network [Piqueira (2005)].

Due to the differences in diseases, researchers have expanded on the SIR model. By adding new states, these researchers can more accurately model different diseases. For instance, if a disease has a state where the subject is exposed but not infected, a new state can be added to model this. The following models are examples of how researchers have branched off of the basic SIR model.

2.2.2.2 SEIR Model

The SEIR model is similar to the previous SIR model except it adds an exposed state. This state is used to model a period where the subject is exposed to the disease. In this state the subject is said to be infected, but not infectious, meaning the disease cannot be transmitted from an exposed subject to a susceptible subject. Among many diseases, this model is also used to model the propagation of worms from computer to computer [Yu (2006)].

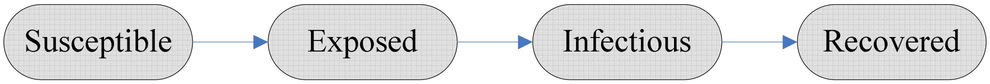


Figure 2.3 SEIR Model

2.2.2.3 MSIR Model

For many epidemics, most notably measles, babies are born with a temporary immunity to the disease. For this reason, researchers have added another state to the standard SIR model. This state allows for a period of immunity in babies. The chart below shows the progression of the MSIR model [Cristea (1992)].

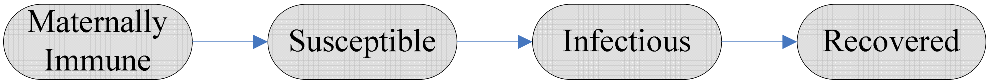


Figure 2.4: MSIR Model

2.2.2.4 Carrier State Model

For some epidemics such as tuberculosis, the infected individual can never actually recover. When an individual is in this state they are know as a carrier and thus the carrier state model was created to represent this [Kolesin (2007)]. The most famous case of a carrier state model is Mary Mallon, best known as Typhoid Mary. Mary, a carrier of typhoid fever, spread the disease to 22 people over a span of 7 years [Rosenberg (1997)].

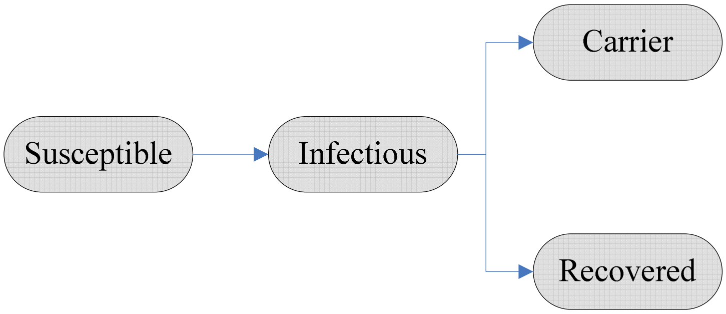


Figure 2.5: SIC/R Model

2.2.2.5 SIS Model

Some infections such as the common cold do not have a period of immunity and thus have no recovered state. This model then continues to bounce between susceptible and infectious [Neal (2008)]. The chart of this model can be seen below.

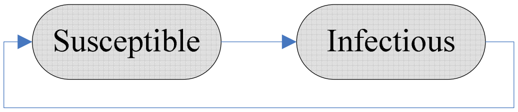


Figure 2.6: SIS Model

2.2.2.6 SIQR Model

To model the effects of a quarantine in a disease spread scenario, the SIQR model was developed. The SIQR model shown below, adds a quarantined state to the normal SIR model. This model has been proven to work effectively on single strain epidemics [Nuno (2008)]. In a perfect world, where as soon as someone is infected they can be quarantined, this model would be accurate. However, many times in a quarantine scenario, susceptible subjects are quarantined with infectious. Therefore, in real life people transition from susceptible into quarantined.

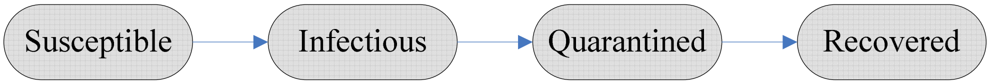


Figure 2.7: SIQR Model

Much research has been done on the aforementioned state models. The assumptions made with each of these models provide good mathematical results, but frequently cause the model to be unrealistic. To approach this problem differently, researchers use simulation to model how disease spread through a society.

2.3 Simulation

Simulation is used to model processes that are either too costly or unethical to perform experimentation. More specifically a computer simulation models a hypothetical situation to study how the actual system works. The fundamentals of simulation focus on using random numbers to mimic the randomness of the system. Once the model is created, multiple replications provide significant data. With this data, statistical analysis is done to support a decision or recommendation.

Some impressive simulations include flight simulators, video games, and weather simulations. To model most systems, some assumptions must be made to explain parts of the process that cannot be modeled. The assumptions made for a simulation define the accuracy of the model.

The goal of any simulation is to use statistics of multiple replications of data to show that the simulation is representative of the actual system. Through statistics, confidence intervals can be used to support the results of a simulation. The justification of results is vital for a credible model. Without statistically justified data, a simulation model is less valuable.

2.3.1 Simulating Epidemics

Simulation is beneficial to advancing epidemic research, because it allows us to test a scenario before implementing a policy. For instance if a government agency wants to see the effects of vaccinating a whole city as a way to prevent a disease, they can do this without real life consequences. One of the drawbacks of simulation is that it takes time to run a model. If a decision is needed in a short time span, simulation may not be the best option.

Much research has been done in the area of host simulation. This type of simulation models the effects of a disease on an individual. Specifically the work done on simulating cancer has given medical doctors information on how to cure this disease [Roberts, et al. (2007)]. An example of how simulation can improve medical care is the use of simulation to optimize the checkup intervals for breast cancer [Michaelson, et al. (1999)].

Since an epidemic spread does not happen frequently and would not be safe to do real tests with, simulation is an excellent tool to help understand how epidemics spread. Specifically, simulation has been used to see how a small-pox outbreak would affect the city of Portland [Barrett (2005)]. This simulation gave authorities in this city the knowledge of how to vaccinate in a way to minimize the spread. Simulation can also be used to see how a disease would affect a network of cities. For instance, a simulation was conducted to model the spread of influenza in 128 cities in Russia [Rvachev (1968)]. The result of this gave authorities incite on where to focus their aid if an outbreak did occur.

There are many factors to consider when modeling a disease spread such as how rapidly a subject transitions through each stage of the disease and how to generate probability between each subject. Most models use random number generators to simulation these factors.

Much research has been done on simulating the spread of infectious diseases. Many of these simulations are disease specific, and don’t allow the user to tailor the simulation to their needs. The following chapter presents the design considerations for the simulation that was created for this research, which fixes many of these problems.

CHAPTER 3 - Epidemic Simulation

This research began by creating a core simulation model for the spread of an infectious disease in rural Kansas. Although I made significant contributions to this simulation, it has been a combined effort of four students under the direction of my advisor Dr. Easton. The three other students are Joe Anderson, Mathew James and David Willis.

The simulation core simulates the spread of an epidemic on a contact network. The goal of this simulation was to create a simulation that can be easily adapted to any disease. The best property of this simulation is its versatility. Given a contact network of individuals, this core simulation can be modified to model any disease in less than an hour. This simulation can also model the spread of a disease on large networks rapidly. Joe Anderson and I focused our research efforts on building this simulation core.

A fundamental assumption that led to this research is that a disease would spread much differently in a rural region than in a large city. To test the simulation core, this simulation is applied to a small rural town in Kansas. The team selected Clay Center because Mathew James is from there and has first hand knowledge of the area. Mathew James and David Willis focused their research on modeling the geographical locations and contacts of individuals in Clay Center, KS.

3.1 Simulation Core

The motivation for creating a disease simulation that is extremely versatile is so it can be applied to any disease. The following section discusses the requirements for such a simulation. A detailed description of how the simulation core operates is also discussed here.

3.1.1 Contact Network, Disease States and Tracks

Ideally, the input to the simulation core is a contact network and a set of infected nodes. The contact network needs an x and y location to represent the geographical location of an individual. Also, each individuals arcs (i,j) are required with the probability p_{ij} of infecting each person.

If a contact network is not provided, a random contact network can be generated. As seen in Section 3.3, the Clay Center contact network was generated by examining the population and layout of the town. In this simulation an infected individual is selected at random. Several other random contact networks were generated to test the quarantine theory discussed in Chapter 4.

A main assumption for this simulation is that it uses discrete time intervals. For example, in the simulation below, a person will remain exposed for a certain number of days and then transition into another state.   This time period can be adjusted to represent any time unit such as a minute, hour or day. For this study, one day was selected as the time period. Thus an individual must be in a state for an entire day; therefore, an individual cannot be susceptible for one half of a day and infectious for the other half.   If a disease allows this, the time period should be set to hours or half days.

In a given day of a disease outbreak scenario, an infectious subject has the possibility to spread the disease to individuals in contact with the subject. To simulate this, every node in the graph that is in the infectious state generates a random number for every susceptible node that has an arc from the infectious node. This number is then compared to the number from the contact network associated with the arc between each node. If the random number is less than the number on the arc, then the disease spreads to that node, else the node may contract the disease from another node in this time or some time in the future.

This simulation can easily be adapted to any disease due to a disease track model. A disease track is comprised of multiple states of a disease. These states are vital to a disease, because each state of a disease is different. For instance, in a given disease an older person may follow a SID path, where D stands for dead, while a baby could follow a SIR path.

This simulation allows a specific disease to follow multiple disease tracks with different probabilities. For instance with typhoid fever, a subject could become a carrier (Typhoid Mary) while others could recover from this disease. If a subject becomes a carrier 10% of the time, then a uniform random number is generated before once a node contracts the disease and this random number determines what track a particular subject will follow.

The time spent in each state is also random. As in real life, one person can be infected with a cold for 3 days while another will be infected for 1 day. This randomness is captured in this model. Currently, a uniform random number is generated to determine the length of time in each state, but this can be adjusted to any probability distribution that models a specific disease.

3.2 Disease State Transition Example

Figure 3.1 is an example of a small contact network that is used to describe the simulation core. For this example, assume there are two disease tracks that have an equal probability of occurrence and have the following states: Susceptible, Infectious, Susceptible, and Susceptible, Infectious, Dead. In Figure 3.1 susceptible is represented by green, infectious is represented by purple, and dead is represented by black. Also, subjects can spend anywhere from 1-3 time periods in each state. At time period 0, subject *A* starts out in the SID track and in the infectious state. A random number for the time in this state is generated between 1 and 3 and happens to be 2. Therefore, subject *A* will be infectious for 2 time periods.

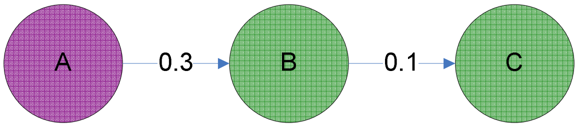


Figure 3.1: Iteration 0

Also during iteration time 0, a uniform random number between 0 and 1 is generated for all contacts of the infectious node. This number is then checked with the weight on the arc. If the random number is less than the arc weight, the node contracts the disease.

For example, if the number generated for the arc between node *A* and *B* is 0.5, then node *B* would remain susceptible until the next time period. The next time period is similar to the first. Since node *A* has one more time period in the infectious state, it can still infect any susceptible adjacent nodes. To simulate this, another random number is generated, say 0.01. Since this value is less than the arc weight of 0.3, node *B* has contracted the disease. To determine what disease track *B* is in, a random number is generated, say 0.6. Since this number is above 0.5 node *B* is in the SIS track. Thus, node *B* is classified as infectious and a uniform random number between 1 and 3 is generated to determine the state duration. For this example, assume the number generated is 1. Figure 3.2 represents this transition.

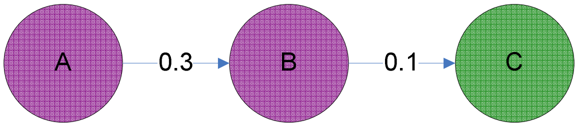


Figure 3.2: Iteration 1

The next time period has a new transition. Since node *A* has been in the infectious state for its allotted time, it now transitions into the terminal dead state. Also in this time period, node *B* has a chance of infecting node *C*. To simulate this, a uniform random number is generated between 0 and 1 and is 0.7. Since this number is larger than the arc weight between node *B* and *C*, node *B* does not infect node *C*.

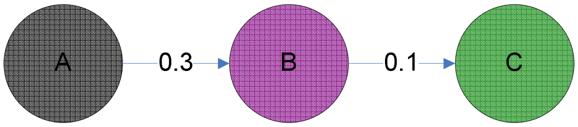


Figure 3.3: Iteration 2

Since the duration of node *B*'s infection is only 1 time period, the next time period yields the susceptible state for node *B*. Finally since all nodes are either dead or susceptible, there is no way for the disease to spread. This means all nodes are in their terminal state.

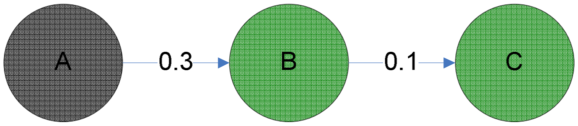


Figure 3.4: Iteration 3

The state transitions example presented above is a vital concept of the collaborative disease simulation created. The following section is a more detailed example of how these concepts can be applied to a network of people in Clay Center, Kansas.

3.3 Simulation Examples

This section discusses how the simulation core is applied to a contact graph that resembles the population and density of Clay Center, Kansas. Because Clay Center has a population of approximately 4,600 people and is not as densely populated as a city such as Portland, Oregon [Barrett (2005)], an epidemic outbreak should spread differently than in Portland.

For this research, an example disease was created to show how a disease can be simulated. This disease is named the WAJEC disease for its creators. As with most diseases, WAJEC can have multiple disease tracks. A person can be in any of the disease tracks in Table 3.1. The number at the top shows the probability of each track that a subject that contracts the disease can follow.

Track 1 Prob. = 0.4	**Track 2 Prob. = 0.4**	**Track 3 Prob. = 0.2**
Susceptible	Susceptible	Susceptible
Exposed	Contagious Symptoms	Carrier
Carrier	Dead	Recovered
Contagious Symptoms		
Symptoms Not Contagious		
Immune		

Table 3.1: WAJEC Disease Tracks

To display how WAJEC spreads, a graphic user interface was created. This interface visually shows the user how the disease spreads. The graphics in the figures below represent the town of Clay Center. As you can see, there are colored nodes that represent each person and their disease state. The disease states and corresponding color for WAJEC are listed in Table 3.2.

As you can see the square blocks of the residential areas of Clay Center are separated by primary streets of the town and are represented by white space in the graph. The large white area in the graph is the town center that is not a residential area. Also notice that there are some nodes that live far away from the town center. Their geographical distance is represented accordingly.

Node Color	State
Green	Susceptible
Yellow	Exposed
Red	Carrier
Purple	Contagious
Blue	Symptoms/Not Contagious
Teal	Immune
Black	Dead
Olive	Recovered

Table 3.2: Graphic Key

Before WAJEC is simulated, a contact network is built. To build the contact network for Clay Center, approximately 4,600 nodes were given locations. These locations were random, but were confined to certain areas, such as the square blocks. Also, a random family size was generated between 1 and 5. The geographic locations of families outside of town were also randomly generated.

The contact between one node and another is represented by an arc. For this simulation there are three levels of arc existence based on the distance from each node. Additionally, there is a probability that each of these arcs exists. For the base case below, the probability that a short arc exists is 0.2. This means that the residence of Clay Center have contact with 20% of the people that reside within two blocks.

Along with the probability that an arc exists, there is a maximum level of contact. This level means that if the arc exists, there is a certain probability the disease can spread between these two people. For the base case below, this means that of the 20% of close contacts, the maximum probability of infecting a node is 50%. Thus, if such an arc exists, then a uniform (0.5) number is generated and this becomes the probability that an infectious node transmits the disease to its contact. These parameters are further explained in the following examples.

Similarly to the short contact, there are also medium and long contacts. A medium contact is defined as someone within a 5 square block radius. On the other hand, a long contact is a contact that is either across town or outside of the town. Once such an arc exists, a probability of infection is generated.

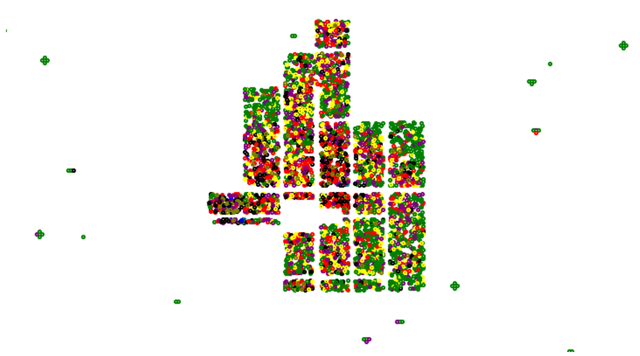
The following example is the base case for this simulation. The parameters for the contact network are presented below along with the graphical representation of how these parameters affect the spread of WAJEC for 10, 15 and 20 days. For this study, the time spent in each state is fixed at 3 days, and a single individual starts the disease.

Base Case

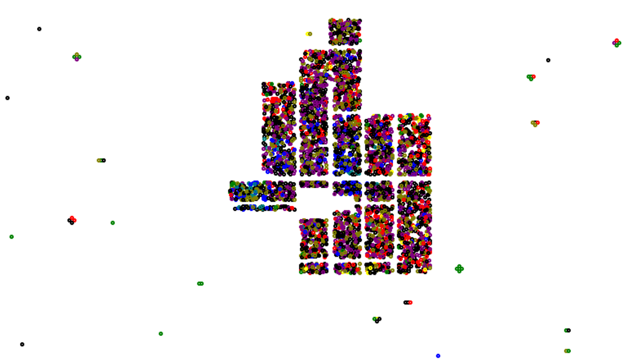
Probability of Short Arc Existence: 0.2; Maximum Probability: 0.5
Probability of Medium Arc Existence: 0.05; Maximum Probability: 0.5
Probability of Long Arc Existence: 0.01; Maximum Probability: 0.5

Day: 10

Day: 15



Day: 20



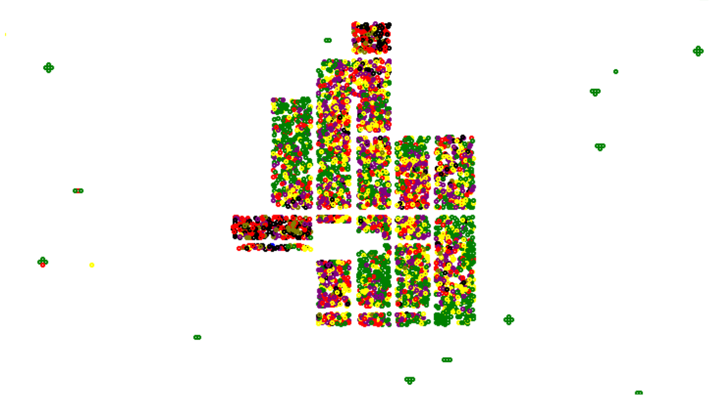
As you can see, the number of days greatly affects how an individual transitions through a disease. By day 20, most individuals where the disease started are either recovered or dead. Notice that some individuals on the outside of town have yet to be exposed to the disease.

To see how the arc existence and the maximum probability affect the spread of the disease, the following study was conducted. In this study, the probability of the arc existence is doubled while the maximum probability of infection is set to the base case (remains the same). These graphical results are compared to doubling the maximum probability of assigning a disease track and leaving the edges the same.

Double the Probabilities of Arc Existence

Probability of Short Arc Existence: 0.4; Maximum Probability: 0.5
Probability of Medium Arc Existence: 0.1; Maximum Probability: 0.5
Probability of Long Arc Existence: 0.02; Maximum Probability: 0.5

Day: 10



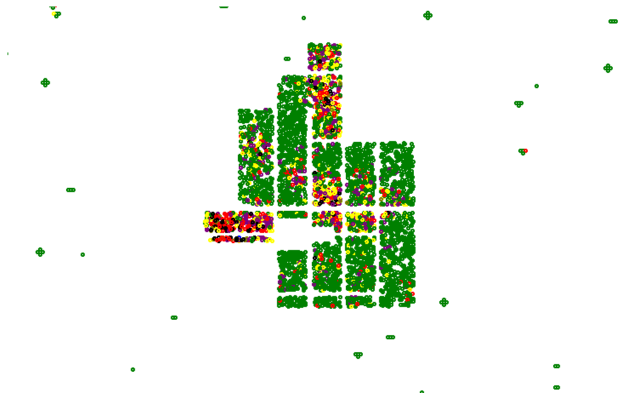
Day: 15

Day: 20

Double the Maximum Probabilities of Contracting the Disease

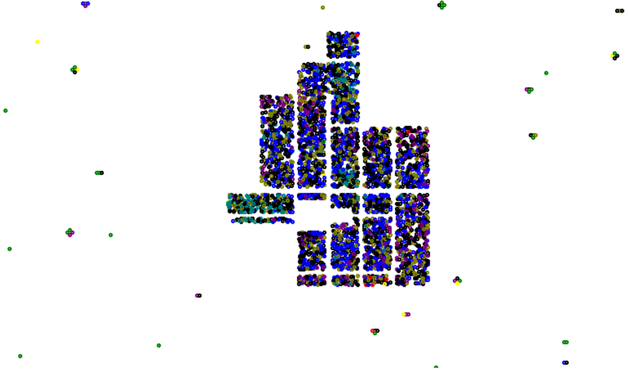
Probability of Short Arc Existence: 0.2; Maximum Probability: 1.0
Probability of Medium Arc Existence: 0.05; Maximum Probability: 1.0
Probability of Long Arc Existence: 0.01; Maximum Probability: 1.0

Day: 10



Day: 15

Day: 20



By examining day 10, it is evident that doubling the arc existence spreads the disease much more rapidly than doubling the probability of an arc existence. With this said, by the 20th day, both studies have similar results. As you can see the 20th day yields most subjects in either the, immune, dead, recovered or symptoms but not contagious state. Once this steady state is reached, the probability of arc existence and the probability of assigning a disease track are equally important. This means that when generating the contact network, each of these parameters is important.

The study provides important incite on how to quarantine diseases. If a government agency is given the choice to have a disease that spreads half as quickly or a network of people with half as many contacts, the agency would want the network with fewer contacts.

After examining this study and the base case graphs, it is evident that after 10 days, of this disease spread the whole town should be quarantined. As far as the families on the outskirts of Clay Center, it seems that the spread does not start to reach them until day 15. This means that if a government agency had identified this disease after 10 day of it starting, the whole town except for the families in the outskirts of town should be quarantined.

A fundamental question of this research is after a certain amount of days, where should the quarantine region be? The following chapter discusses theory on how to optimize a quarantine region. The theory presented in this chapter can help decision makers decide where the best quarantine should be in a disease outbreak scenario.

CHAPTER 4 - Optimizing Quarantine Regions

The goal of this research is to provide an optimized method for quarantining a group of infected subjects. Quarantines can come in various sizes depending on the severity of the outbreak. Although the idea of a quarantine is relatively simple, the consequences of applying a quarantine are immense. A common industrial engineering technique for optimizing a scenario with negative consequences is to assign penalties to negative results. These areas are addressed in this chapter.

4.1 Basic Ideas of a Quarantine

In an outbreak scenario, the goal of a quarantine is to eliminate the disease by keeping the infected individuals away from the uninfected subjects. Therefore, no subject is allowed to leave a quarantine area. To accomplish this, all sides of a quarantine area must be enforced by military, police or natural barriers. In order to enforce a quarantine area, the area should be a continuous region with a reasonable shape, because it is impractical and unmanageable for the government to maintain several large quarantine areas.

A logical quarantine is defined as a region that can be easily enforced. Clearly in a disease outbreak scenario the entity that begins the disease, defined as the root node, as well as any person that has contracted the disease, should be quarantined. Assuming the root node is colored in black, the quarantine cuts, denoted in red, shown in Figure 4.6 are logical quarantine regions, and Figure 4.7 shows illogical ways to quarantine an infection given the geographic position of the nodes.

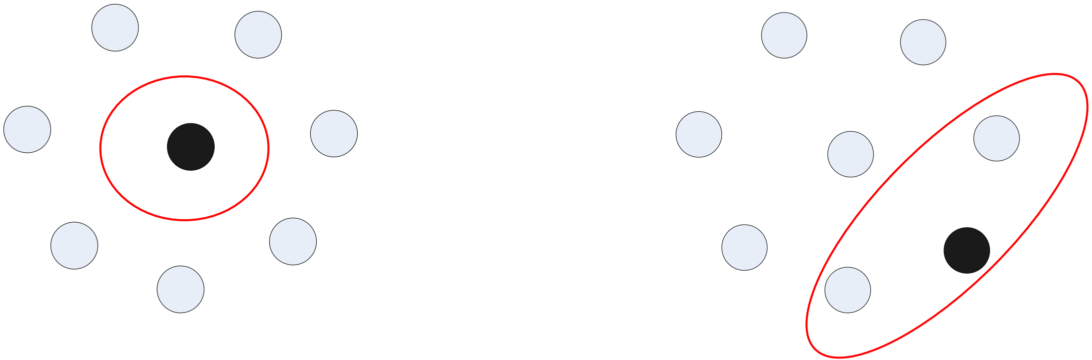


Figure 4.1: Logical Quarantines

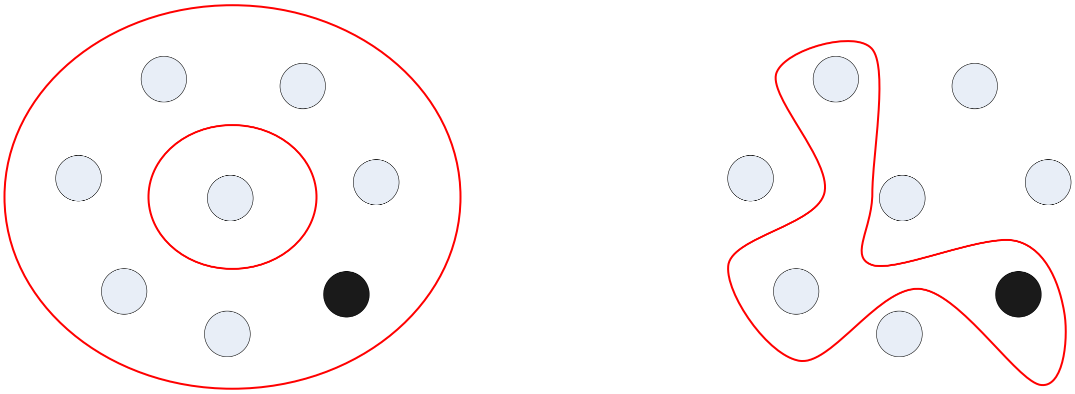


Figure 4.2: Illogical Quarantines

4.2 Ellipsoidal Geographic Graphs

This thesis uses a geographic network to determine what is, and what is not a feasible quarantine (a quarantine of a reasonable shape). Formally, a geographic network G_G is a network with a root node v_r, where each node has two parameters (x_i,y_i) that correspond to the geographic position of node $v_i \ \forall \ i \in \{1,\ldots,n\}$. The arcs in G_G form a graph such that the arc (i,j) is in A_G if, and only if, v_i is "closer" to the root node than v_j where "closer" is some well-defined measure. Figure 4.3 shows some nodes with their respective locations of a G_G with the root node denoted as a black circle.

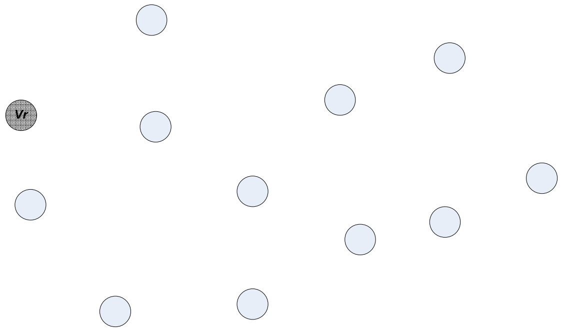


Figure 4.3: The Nodes of a Geographic Graph

The primary idea of closer is to not allow a quarantine to be an unreasonable shape. If a quarantine region has an unreasonable shape, then the citizens along the poor borders are likely to revolt. Just consider either of the two illogical quarantines depicted in Figure 4.2. Clearly, the northeast individual can complain that they are further from the epicenter of the disease than someone who is not quarantined. Thus, this northeast individual should try to move closer to the disease, because there is a node that is closer that is in the "saved" area.

In this paper, an ellipse is used to generate the idea of "closer." In such a case, the geographic graph is called an ellipsoidal geographic graph. This graph draws an ellipse from the root node to node v_i. This means that if the node v_i is in the quarantine region, any node that is contained within the ellipse between the root node and v_i, must also be in the quarantine, since these other nodes are "closer."

To find the ellipse generated from the antipodal points v_i and v_r begin by finding two foci f_1 and f_2 such the distance from f_1 to v_i plus the distance f_2 to v_i equals the distance from f_1 to v_r plus the distance f_2 to v_r, which also equals the distance from v_i to v_r. The ellipse consists of all points $p \epsilon R^2$ such that the distance from f_1 to p plus the distance from f_2 to p is equal to the distance from v_i to v_r .

Clearly, there are an infinite number of choices for f_1 and f_2 the distance between f_1 and f_2 determines the width of the ellipse. If f_1 and f_2 are equal, then the ellipse is a circle and if f_1 and f_2 are the antipodal points, then the ellipse is a line segment.

For this work we chose f_1 and f_2 such that the distance between the antipodal points on the major axis was twice the distance between the antipodal points on the minor axis. This ratio of the major axis and the minor axis is denoted by α, where $\alpha \leq 1$. This implies that the location of focal points are given by $((x_{v_r} + \lambda(x_{v_i} - x_{v_r})),(y_{v_r} + \lambda(y_{v_i} - y_{v_r}))$, where for this research f_1 and f_2 have $\lambda = \left(\frac{2-\sqrt{3}}{4}\right),\left(\frac{2+\sqrt{3}}{4}\right)$, respectively. Observe that $\alpha \neq \lambda$ and given α, λ can be generated by applying Pythagorean Theorem.

To generate a ellipsoidal geographic graph with parameter α, which is equal to the minor axis divided by the major axis, there exists an arc from v_j to v_i (v_j,v_i) if, and only if, v_j is contained in the ellipse generated by the antipodal nodes v_r and v_i. The development of this graph is shown in Figures 4.4 – 4.7. As you can see, the nodes that are interior to the ellipse are the nodes that must be quarantined if v_r is the root node and v_1 is in the quarantine area. This is because these nodes are closer to v_r than v_1 is closer to v_r. Using the ellipse structure, the geographic network from the root node v_r to v_1 is established in Figure 4.5.

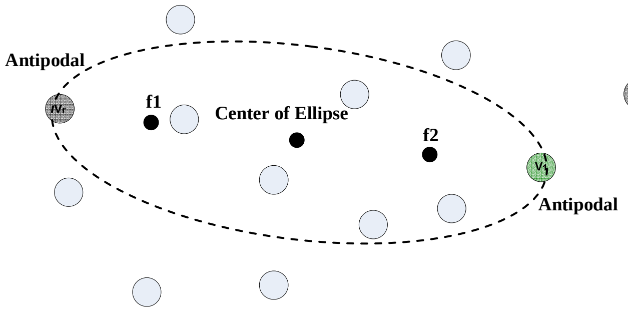


Figure 4.4: Generating an Ellipse

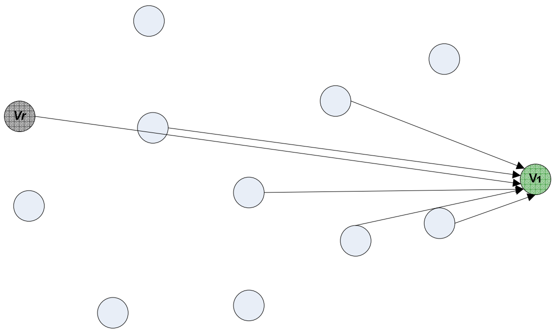


Figure 4.5: G_G with Contacts from v_r to v_1

Continuing this process for all nodes in G_G generates all of the arcs in G_G. As you can see by the geographic graph generated in Figure 4.6, by using an ellipse as a way to generate the arcs, there are no cycles in the graph because v_i is "closer" to the root node than v_j.

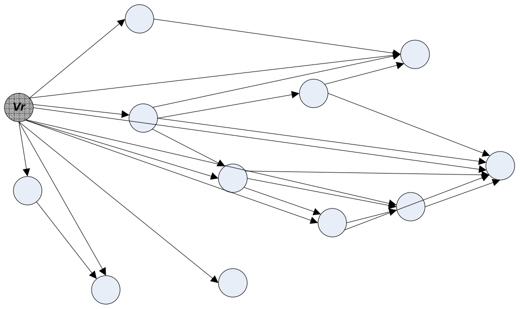


Figure 4.6: All of the Arcs of a Sample G_G

The final step is to include the probability that each node has the disease. In this research, p_i is used to define the probability of infection for node i. The full ellipsoidal geographic graph is shown in Figure 4.7. The number on the interior of the nodes indicates the individuals corresponding probability of infection.

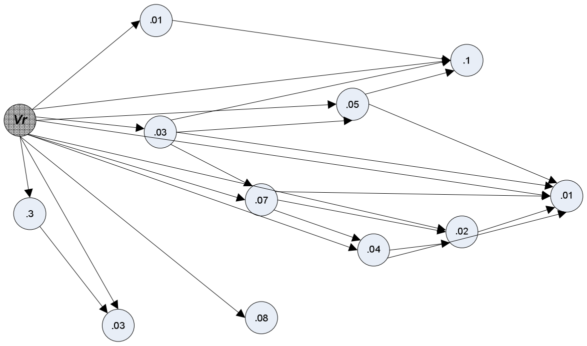


Figure 4.7: The Final G_G with Probabilities

Various other structures could be used to define "close," such as circles, diamonds, norms, etc. Figure 4.8 demonstrates a diamond structure that could be used to find which nodes should be contained if v_1 is contained. Some care must be taken in defining “closer”, which is described in the next section.

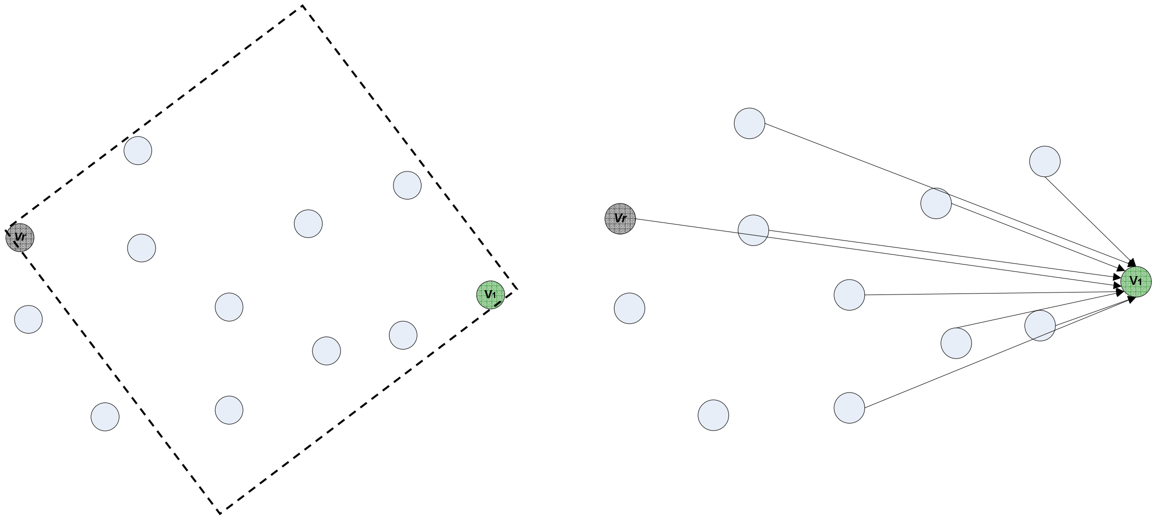


Figure 4.8: Example of Alternate Structure and Edges Generated from Structure

4.3 Feasible Quarantine Cuts

The focus of this research is to find the optimal quarantine cut. Consider an outbreak of a deadly disease. The government’s obvious response is to seal off the area and eliminate any travel into or out of the area. Some medical individuals may be called in to help out with the situation, but these individuals will be “cleansed” before they can leave the area. The area that the government seals off is called a quarantine.

A fundamental advancement of this research is the mathematical model and corresponding optimization of a quarantine region. Here this quarantine region is modeled as a cut in a geographic graph. The cut partitions the nodes into two sets, a quarantine set, V_Q, and a saved set, V_S. Clearly, the quarantine set must have the starting infected individual.

Finding a feasible quarantine cut requires a geographic graph $G_G = (V_G, A_G)$ and a beginning disease node, v_r as input. A cut (V_Q, V_S) is a quarantine cut if, and only if, V_Q

$\cup V_S = V_G$, $V_Q \cap V_S = \emptyset$, $v_r \in V_Q$ and $v_i \in V_S$ and $v_j \in V_Q$ implies $(v_i,v_j) \notin A_G$. For ease of notation, a quarantine cut (V_Q, V_S) can also be referred to as V_Q or V_S since $V_Q = V \setminus V_S$.

With an ellipsoidal geographic graph, a legal quarantine cut can now be described. Figure 4.9 shows a legal quarantine cut. In this sense, a quarantine cut is legal if all predecessors of the nodes contained in the quarantine side are also in this side.

In contrast, Figure 4.10 shows an infeasible quarantine cut. If node v_j is contained in the quarantine, then its predecessor, node v_i must also be in the quarantine. Thus, this quarantine region is not feasible.

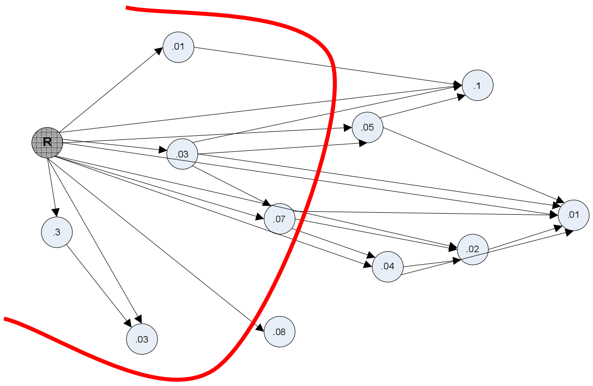


Figure 4.9: Legal Quarantine Cut in G_G

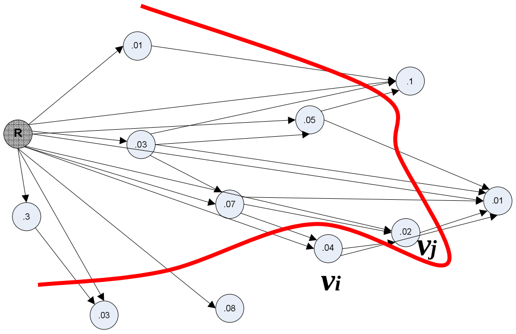


Figure 4.10: Illegal Quarantine Cut in G_G

Now, imagine a quarantine line has been breached. A government agency must increase the size of the quarantine region. A naïve person might think that just adding all "closer" individuals to this node is sufficient for the quarantine. This is not the case as the following example illustrates.

If the preexisting quarantine is represented by the circle in Figure 4.9, and the breached quarantine is predicted to have reached the shaded node, then this figure represents what the new quarantine would look like. Notice that an ellipse is drawn from the shaded node to quarantine. This ellipse shows all of the nodes that should be included in the new quarantine with the shaded node. However, any node in this first ellipse also creates its own ellipse, which may include nodes that the first ellipse missed. This process continues as needed, and performing reverse breadth first search is sufficient to determine the smallest quarantine region for this breach as described in Theorem 4.1.

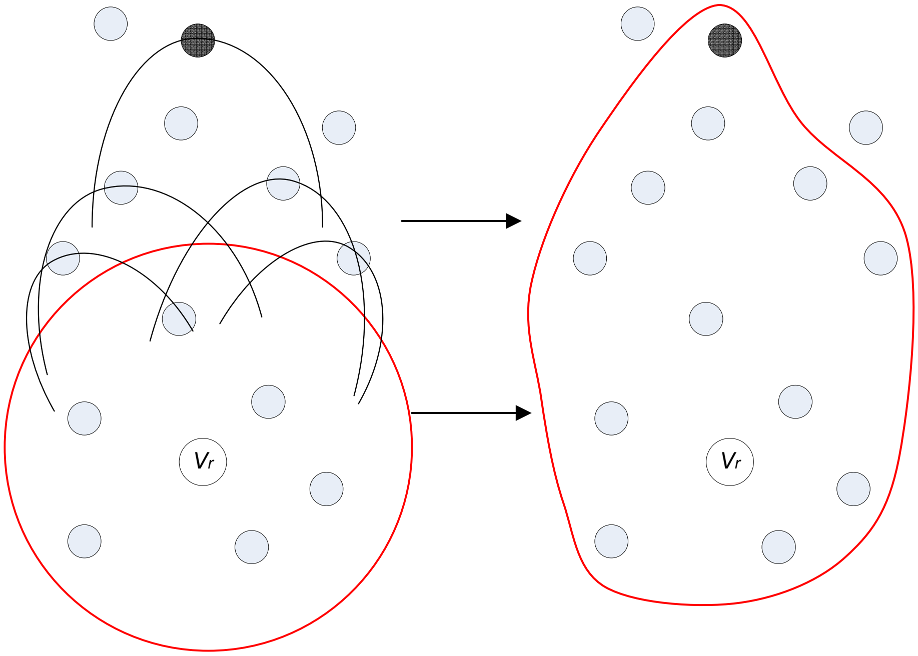


Figure 4.11: Graphical Representation of Theorem 4.1

Theorem 4.1: Given any directed graph G and a set of nodes $Q \subseteq V$. The smallest cardinality quarantined partition V_Q that contains Q is unique and is the set of all nodes encountered by performing reverse breadth first search starting from all of the vertices in Q.

Proof: It suffices to show that V_Q is a quarantine cut and that any quarantine cut $V_{Q'}$ that contains Q has at least as many vertices as V_Q.

For contradiction, assume V_Q is not a quarantine cut. Thus, there exists an arc (v_i,v_j) such that v_i is in V_S and v_j is in V_Q. However, this contradicts reverse breadth first search, because vertex v_i would have been added to the visited vertices since it is on a path that terminates in some vertex in Q.

For contradiction, assume $V_Q \neq V_{Q'}$ is a quarantine cut that contains Q and $|V_{Q'}| \leq |V_Q|$. Therefore, there exists a vertex $q_p \in V_Q$ such that $q_p \in V_{S'}$. Due to reverse breadth first search, there exists a path from some vertex $q_1 \in Q$ to q_p, $P = q_1, \ldots, q_p$. Thus, there exists some $j \in \{1,\ldots,p\}$, such that $q_{j-1} \in V_{S'}$ and $q_j \in V_{Q'}$. Therefore, $(V_{Q'},V_{S'})$ is not a quarantine cut, a contradiction, and the result follows.

□

The result of Theorem 4.1 provides useful incite for valid quarantine cuts of directed graphs, regardless of weights. Thus, if an individual is known to be ill and is to be quarantined, then a simple reverse breadth first search on G_G would result in the smallest possible quarantine region.

The following theorem is similar to Theorem 4.1 and should be used if a government agency wants to save a particular person in a quarantine region. Imagine the President is near a quarantine region, and the agency must save the President. It would be illogical for the government to say the President can be safe, but the people that are further away from the disease should still be quarantined. The question then is who must be saved to save the President? The following theorem formally describes everything that is necessary to move a set of nodes from the quarantine region into the saved region.

Theorem 4.2: Given any directed graph G and a set of nodes $S \subseteq V$. The smallest cardinality saved partition V_S that contains S is unique and is the set of all nodes encountered by performing breadth first search starting with all of the vertices in S.

Proof: It suffices to show that V_S is a quarantine cut and that any quarantine cut $V_{S'}$ that contains S has at least as many vertices as V_S.

For contradiction, assume V_S is not a quarantine cut. Thus, there exists an arc (v_i,v_j) such that v_i is in V_S and v_j is in V_Q. However, this contradicts breadth first search, because vertex v_i would have been added to the visited vertices since it is in V_S. Furthermore, when v_i is evaluated, v_j is one of its neighbors and it would have been added to V_S also.

For contradiction, assume $V_S \neq V_{S'}$ is a quarantine cut that contains S and $|V_S'| \leq |V_S|$. Therefore, there exists a vertex $q_p \in V_Q \backslash V_Q'$ such that $q_p \notin V_Q$. Due to breadth first search, there exists a path from some vertex $q_1 \in S$ to q_p, $P = q_1, \ldots, q_p$. Now there exists some $j \in \{1,\ldots,p\}$, such that $q_{j-1} \in V_S'$ and $q_j \in Q$. Therefore, V_S' is not a quarantine cut and the result follows.

□

Besides generating this smallest saved region, Theorem 4.1 and 4.2 also have strong implications for what types of directed graphs should be considered when trying to find optimal quarantine cuts. These theorems imply that if the directed graph is strongly connected (there is a path from every node to every other node), then the only quarantine cut is the entire graph. Formally, the result is as follows.

Corollary 4.3: Every strongly connected digraph has one quarantine cut, namely the entire vertex set.

Proof: Every strongly connected graph has a directed path from every node to every other node. Applying breadth first search or reverse breadth first search to any node results in every node being encountered. Since the root node must always be in the quarantine region, the entire graph must be quarantined.

□

Applying Corollary 4.3 on any cycle of a directed graph, implies that either none of the nodes in the cycle are in a quarantine or all of the nodes are in the quarantine. Thus, any digraph with a cycle can be reduced by contracting the cycle into a super node. This means households should be considered a single node. Thus, any work on quarantine cuts must be performed on acyclic directed graphs. One of the best properties of ellipsoidal geographic graphs is that they are acyclic as the following two results show.

Theorem 4.4: If G_G is an ellipsoidal geographic graph and v_i and v_j do not have the same coordinates and the distance from node v_i to the root node is at least as big as the distance from the root node to node v_j, then (v_i, v_j) is not in A_G.

Proof: Assume G_G is an ellipsoidal geographic ellipsoid graph. Furthermore, assume v_i and v_j are not at the same location and the distance from node v_i to the root node is at least as big as the distance from the root node to node v_j. For contradiction assume $(v_i,v_j) \in A_G$.

To find the ellipse generated from the antipodal points v_j and v_r begin by finding two foci f_1 and f_2 such the distance from f_1 to v_j plus the distance f_2 to v_j equals the distance from f_1 to v_r plus the distance f_2 to v_r equals to the distance from v_j to v_r. The ellipse consists of all points $p \in R^2$ such that the distance from f_1 to p plus the distance from f_2 to p is equal to the distance from v_j to v_r .

Since $(v_i,v_j) \in A_G$, the distance from v_i to f_1 plus the distance from v_i to f_2 is less than or equal to the distance from v_r to v_j. If v_i is on the line passing through both v_j and vr, then v_i is closer to the root node than $v_{j,}$ a contradiction or v_i is further from the root node than $v_{j,}$ and is not in the ellipse also a contradiction.

Next examine the three points v_r, f_1 and v_i. The triangle inequalities implies that the distance from v_r to v_i is less than or equal to the distance from f_1 to v_r plus f_1 to v_i. Since v_i is in the ellipse, the distance from f_1 to v_i is strictly less than the distance from f_1 to v_j. Consequently, the distance from v_r to v_i is strictly less than the distance from v_r to v_j, a contradiction.

□

The previous theorem describes the nature of the ellipsoidal geographic graph, an acyclic graph. This structure is vital to this research, because if the graph is not acyclic then the entire area should be quarantined as previously mentioned. The formal result is as follows.

Corrollary 4.5: An ellipsoidal geographic graph G_G with no two nodes at the same location is acyclic.

Proof: For contradiction assume there exists a cycle with edge set equal to $\{(v_1,v_2), (v_2,v_3)\ldots,(v_{c-1},v_c), (v_c,v_1)\}$ in an ellipsoidal geographic graph. Define $d(v_r,v_i)$ to be the distance from the root node to v_i. From Proposition 4.3 and the existence of the arc (v_i,v_{i+1}), one obtains $d(v_r,v_i) < d(v_r, v_{i+1})\ \forall\ i=1,\ldots,c-1$. Thus, $d(v_r,v_1) < d(v_r, v_2) <\ldots< d(v_r,v_c)$. However, (v_c,v_1) is an edge and so $d(v_r,v_c) < d(v_r,v_1)$, which contradicts the previous expression and the result follows.

□

Now that the feasibility of quarantine cuts has been discussed, this thesis now turns to optimizing quarantine cuts. Section 4.4 is focused on this topic.

4.4 Optimizing Quarantine Regions

Quarantine cuts are both good and bad. Any quarantine has the possibility of not containing every subject that is infected. Additionally, any quarantine has the possibility of condemning healthy subjects to remain with the infected ones.

A standard industrial engineering approach to difficult decisions is to assign penalties for bad outcomes. Before an optimal quarantine cut can be determined, the penalties for not containing every infected subject and condemning healthy subjects should be decided.

For instance, a contagious disease has been discovered in a town and the military may think it is 10 times as bad to have an infected subject outside the quarantine as it is to have a healthy subject in the quarantine. Therefore, the penalty for an infected person outside the quarantine line is 10 and the penalty for condemning a healthy person would be 1. This means the military would be willing to sacrifice 10 healthy subjects before they would allow an infected individual outside of the quarantine zone.

These penalties are highly dependant on the severity of the disease. If for instance, the disease was deadly and spread almost instantaneously, the penalty for having an infected subject outside the quarantine could approach infinity. Therefore, the quarantined area would be much larger as the quarantine enforcers would not risk the spread. With a more severe disease, it would be more likely for the military to quarantine entire states or even countries. SARS was an excellent example of this type of disease. On the other hand, if a disease is very unlikely to spread (HIV) or has minor symptoms (Influenza), the penalty for having an infected person outside of the quarantine could approach zero. In this case, the quarantine could be as small household or one person or even no quarantine.

Once the penalties for not quarantining an infected subject and condemning a healthy subject have been established for some ellipsoidal geographic graph G_G, an optimal quarantine cut can be established. Prior to some theoretical results on G_G, an integer program is first introduced that finds the optimum quarantine cut.

4.4.1 Quarantine Integer Program Formulation

Integer programming is a widely used optimization tool. If a problem has variables that are integer and the objective function and the constraints are linear, then the problem can be represented as an integer program. Integer programs have been used to solve problems in routing goods and equipment [Arunapuram and Solow (2003), Kaufmanand and Smith (1998), Toth (1997)], generating airline schedules [Hoffman and Padberg (1993), Klabjan, et al. (2001), Alefragis, et al. (2000)], managing portfolios [Pinto and Rustem (1998), Bertsimas, et al. (1999)], researching genetics [Brown and Harrower (2004), Ferreira, et al. (2002)], and developing sports schedules[Urban (2003), Easton, et al. (2003)].

It has been shown that solving an integer program is $\mathcal{NP}$-Hard [Karp (1972)], and thus there exists integer programs that cannot be solved in polynomial time, unless $\mathcal{P} = \mathcal{NP}$. The most common algorithm for solving integer programs is called branch and bound. The major problem is that branch and bound has an exponential run time and there are still numerous integer programs that cannot be solved.

When optimizing a quarantine region, the best possible outcome is to have all of the infected individuals in the quarantine region and all the healthy individuals in the saved region. To achieve this, the objective function could be focused on maximizing the benefit of having an infected individual for example. For this research, the objective function is focused on the opposite, which is minimizing the penalty of having infected individuals in the saved region and having saved individuals in the quarantined region. Clearly, both objective functions would work similarly.

Due to the additive nature of any IP's objective function, an exact probability of an epidemic moving past a quarantine region would require an exponential number of variables, due to the inclusion exclusion principle. For instance, assume a_1, a_2, and a_3 are the only individuals in a saved region. This means the probability that the epidemic is not contained is

$$P(a_1 \cup a_2 \cup a_3) = P(a_1)+P(a_2)+ P(a_3)- P(a_1 \cap a_2) - P(a_1 \cap a_3) - P(a_2 \cap a_3) + P(a_1 \cap a_2 \cap a_3).$$

More people require more terms in this expression and the terms grow on the order of 2^n. Thus, an exact IP would require each region of a Venn diagram with n regions to have its own variable and the IP would have 2^n variables. Writing such a large IP is not feasible, let alone solving such a problem. Thus, this research assumes to be conservative in its quarantine region by overestimating the probability that an infection leaves the quarantine area. That is, none of the second or higher order terms from the inclusion-exclusion principle are used in the objective function. Thus, optimal quarantine generated by this IP is slightly conservative.

This research developed the first integer programming formulation to find the optimal quarantine cut. This integer program is as follows.

Optimal Quarantine Integer Program (OQIP)

Sets:

$N=\{1,\ldots,n\}$: the set of the nodes of a graph

Decision Variables:

x_i = 1 if node i is in the saved partition

0 if node i is in the quarantine partition.

Parameters:

p_i - Probability of infection for node i.

s - Penalty for allowing an infected subject in the saved partition.

q - Penalty for having a healthy subject in the quarantine partition.

Objective Function:

Minimize: $s \sum_{i \epsilon V} x_i\, p_i + q \sum_{i \epsilon V} (1\text{-}x_i)(1\text{-}\ p_i)$

Subject to:

$x_i \leq x_j\ \forall\ (j,i) \in A_G$

$x_i \in \{0,1\}\ \forall\ i \in V_G$

The decision variable x_i is a binary variable that is used to decide which nodes are in the saved region. Obviously any nodes that are not included in this region are included in the quarantine region.

The goal of a quarantine is to partition the unhealthy subjects in the quarantine, while saving the healthy subjects. If for instance, an infected subject is not quarantined, there is a penalty s. On the other hand, if a healthy subject is quarantined, there is a penalty q.

The objective function displays the goal for the integer program. In this case, the objective is to minimize the total penalties. This function multiplies the penalty for an infected subject to be in the saved region, s, by the sum of all of the nodes in saved region times their probability of being infected, p_i. Similarly, this summation is added to the penalty for a healthy subject to be quarantined, q, with infected subjects multiplied by the sum of the subjects in the quarantine region ($1\text{-}x_i$) multiplied by the probability that they are not infected or healthy ($1\text{-}\ p_i$).

The single set of constraints is the restriction of a feasible cut. These constraints are generated from the ellipse principle. In general, the constraint $x_i \leq x_j$ states that if any node v_i contained in the quarantine region, then each of its predecessors, determined by the ellipse, must also be in the quarantine region.

Fortunately, OPIQ is Totally Unimodular. A totally unimodular matrix is a matrix where all square submatrices have a determinant of 0, 1 or -1. TUM is important because any integer program that has a totally unimodular constraint matrix can be solved with linear programming as long as the right hand side is integer. This result is especially important because it reduces the running time of a traditional integer program from $\mathcal{NP}$-Hard to polynomial time. Theorem 4.5 formally describes why OQIP is TUM.

Theorem 4.6 The constraint matrix of OQIP is TUM.

Proof: Let *A* be the constraint matrix of any OQIP. Strong induction on the number of rows is used to prove that *A* is TUM. For a base case, consider a single row. This matrix is clearly TUM as every submatrix is a 1x1 square and the determinant is either 0, 1 or -1.

By strong induction assume that every *A* matrix of OQIP with fewer than *k* rows is TUM. To show that *A* is TUM for *k* rows, let *B* be any square submatrix of *A*. Clearly, *B* could be represented as an acyclic graph with the addition of two dummy nodes, and *B* must be a *k*x*k* matrix or the result follows from the induction assumption.

Clearly, *B* has at least one row with at most one nonzero element or at least one column with at most one nonzero element. To find the determinant of *B*, expand upon this row or column. Clearly, such an expansion only changes the sign of the determinant or moves the determinant to 0. So by the induction assumption, *B* has a determinant that is either 0, l or -1 and the result follows.

□

In a real life outbreak scenario, it would be illogical and almost impossible for a decision maker to run an integer program to find the optimal quarantine region. The next section provides decision makers with general theory and heuristics for how to optimize a quarantine region in a disease outbreak scenario.

4.5 Theory of Optimized Quarantine Cuts

When deciding where to implement a quarantine, the probability of infection should be analyzed. As mentioned earlier, p_i is used to define the probability of infection for node i. The threshold, τ, of a quarantine cut is defined as the quarantine penalty, q, divided by the sum of the quarantine penalty and the saved penalty, s; thus, $\tau = \frac{q}{s+q}$. These penalties are user defined and the threshold is analyzed with the probability of infection to determine where the quarantine should be.

Given a defined threshold, an optimal quarantine contains only the connected nodes whose average probability of infection exceeds the defined threshold. If a set of connected nodes or any node with an outdegree of 0 does not meet this condition it is assigned to the saved set in the optimal quarantine cut.

Figure 4.12 provides a small graphical example of how the theory of this research should be applied to find an optimized quarantine cut. Imagine that an official from a government agency is assigned to this portion of the graph and each node represents a city. He/she knows that this group of cities is on the edge of a large quarantine and wants to know if any of these cities should be saved given the previously mentioned threshold. The following shows how the theory of the previous sections can help make optimized decisions.

The government agency should begin by considering the entire population in the quarantine region. Starting this way allows the agency to decide which nodes should be removed from the quarantine region. As seen in Figure 4.12 below, all nodes start in the quarantine region as denoted by the red line.

In this example, the penalty for a healthy subject to be condemned in a quarantine region or the q is 1 and the penalty for an infected subject to be in a healthy region or the s is 19. Therefore, the overall threshold is $\tau = \frac{1}{1+19} = 0.05$. This threshold means that it is an improvement in the objective value for any group of nodes whose average probability is less than 0.05, to move from the quarantine region to the saved region.

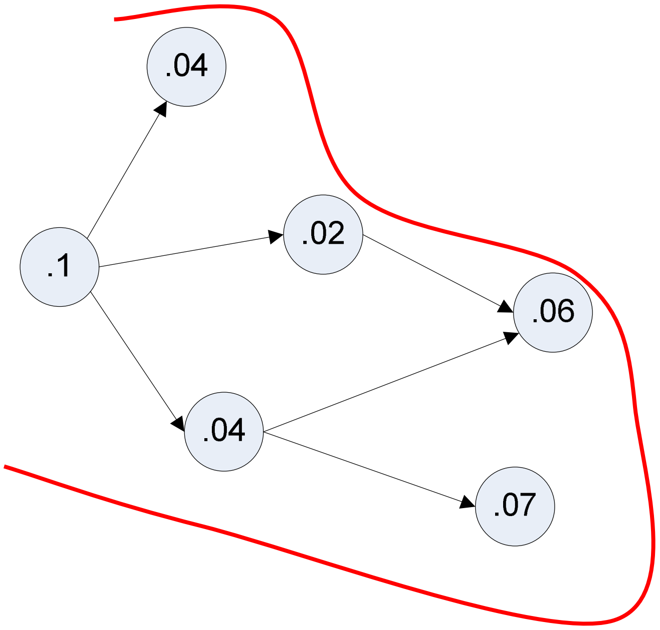


Figure 4.12: Example Fully Quarantined *Z* = 5.67

Recall the objective function for an optimal quarantine is: Minimize: $s \sum_{i\epsilon V} p_i x_i + q \sum_{i\epsilon V} (1- p_i)(1-x_i)$. As you can see from Figure 4.9 since every node is quarantined, the right half of the objective function is only used or $q \sum_{i\epsilon V} (1- p_i)(1-x_i)$. Numerically, this objective value is 1((0.93)+(0.96)+(0.94)+(0.98)+(0.96)+(0.90)) = 5.67.

Clearly the pendant node with probability of 0.04 can be moved to the saved region and still maintain a feasible quarantine cut. If there was an arc from the 0.04 node to the 0.02 node, this would not be a feasible cut. Figure 4.13 shows this scenario.

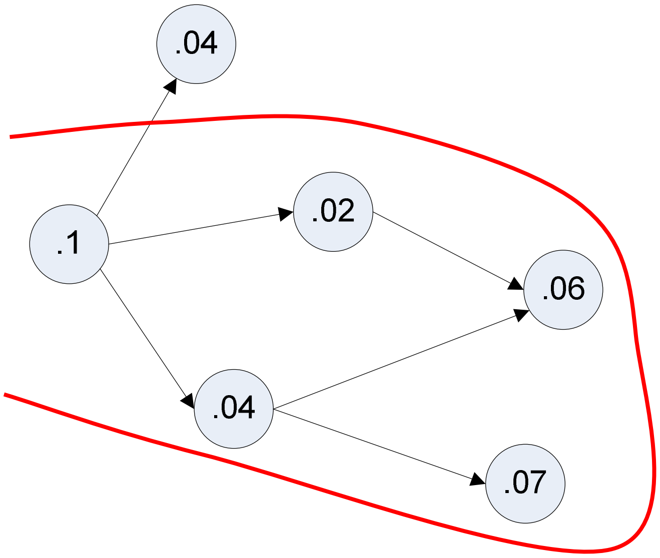


Figure 4.13: 1st Iteration *Z* = 5.47

Using OQIP's objective function, the objective value would calculated as follows: 19((0.04))+1((0.96)+(0.90)+(0.93)+(0.94)+(0.98)) = 5.47. As you can see, since the pendant node is added to the saved region, there is a 0.04 chance that the node is infected in the saved region. Thus, the objective function is increased by 19* 0.04, but decreases by 1*0.96 and the overall objective value decreases by 0.2. Thus, any pendant node in a quarantine that has a probability of infection below the threshold of 0.05, reduces the objective value if it is added to the saved region. This result is formally described by Theorem 4.6.

Theorem 4.6: If $p_i < \frac{q}{q+s}$ and the outdegree of node v_i is 0 in G_G, then node v_i is in the saved partition of the optimal quarantine cut.

Proof: For contradiction, assume node v_i has $p_i < \frac{q}{q+s}$, the outdegree of node v_i is 0 in G_G and the optimal cut (V_Q^*,V_S^*) has node $v_i \in V_Q^*$ with an objective value of Z^*. Let's examine the cut given by $(V_Q^*\backslash\{v_i\},V_S^*\cup\{v_i\})$. Since the out degree of v_i is 0 and (V_Q^*,V_S^*) is a quarantine cut, $(V_Q^*\backslash\{v_i\},V_S^*\cup\{v_i\})$ also has no edges from a node in $V_S^*\cup\{v_i\}$ to a node in $V_Q^*\backslash\{v_i\}$. Thus $(V_Q^*\backslash\{v_i\},V_S^*\cup\{v_i\})$ is a quarantine cut.

The value of the $(V_Q^*\backslash\{v_i\},V_S^*\cup\{v_i\})$ quarantine cut is the value of (V_Q^*,V_S^*) minus the probability that node i is healthy times the penalty to quarantine a healthy person plus the probability that the person is infected times the penalty of not quarantining an infected person or $Z^* - \mathrm{s}(p_i)+q(1-p_i) = Z^* +q - qp_i - sp_i = Z^* +q - p_i(q+s) < Z^*$, which contradicts (V_Q^*,V_S^*) being the optimal quarantine cut and the result follows.

□

Continuing the OQIP process, if the four nodes in the bottom right are removed from the quarantine region as Figure 4.14, then there is still a feasible quarantine. The objective function becomes

$$19((0.02)+(0.06)+(0.07)+(0.04)+(0.04))+1((0.90)) = 5.27.$$

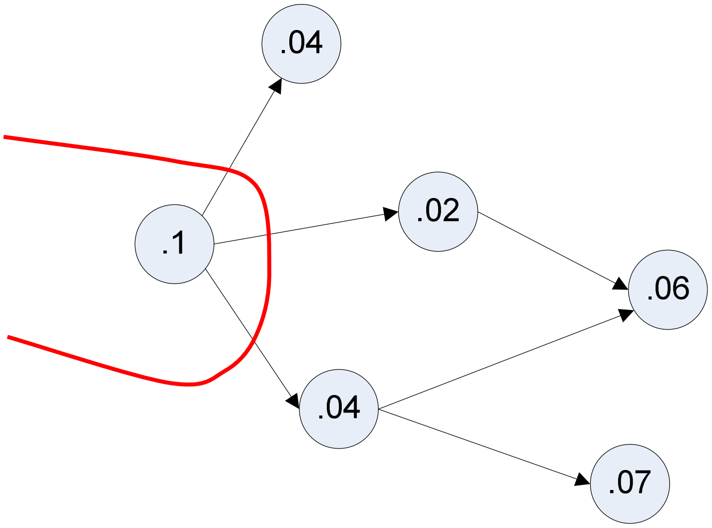


Figure 4.14: 2nd Iteration Z = 5.27

Notice that the objective value has improved from 5.47 to 5.27. This is because the average probability of these four nodes is 0.0475 which is less than the threshold of 0.05. Theorem 4.7 formally describes why removing the previous four nodes improves the objective value.

Theorem 4.7: Let $V_{Q'}$ be any quarantine partition with $V_{S'}$ as the corresponding saved partition. If $S \subseteq V_{Q'}$ such that $(V_{Q'} \backslash S, V_{S'} \cup S)$ is a quarantine cut and $\sum_{j\in S} p_j < |S| \left(\frac{q}{q+s} \right)$, then the value of the quarantine cut $(V_{Q'} \backslash S, V_{S'} \cup S)$ is strictly better than the value of $(V_{Q'}, V_{S'})$.

Proof: Let $(V_{Q'}, V_{S'})$ be a quarantine cut with value Z'. Let $S \subseteq V_{Q'}$ such that $(V_{Q'} \backslash S, V_{S'} \cup S)$ is a quarantine cut and $\sum_{j\in S} p_j < |S| \left(\frac{q}{q+s} \right)$. The value Z'' of the $(V_{Q'} \backslash S, V_{S'} \cup S)$ quarantine cut is the value of the (*VQ'*, VS') cut minus the penalty of having S in the quarantine partition plus the penalty of having S in the saved partition. Formally, $Z''=Z' + \sum_{j \epsilon S} s(p_j) - \sum_{j \epsilon S} q(1-p_j)) = Z' + s\sum_{j \epsilon S} (p_j) - q|S| + q\sum_{j \epsilon S} p_j = Z' + (q+s) \sum_{j \epsilon S} (p_j) - q|S| < Z'$

+ $q|S|$ - $q|S|$ = Z'. The inequality follows from $\sum_{j\in S} p_j < |S| \left(\frac{q}{q+s}\right)$, which implies $(q+s)\sum_{j\in S}(p_j) < q\,|S|$. Thus, $Z'' < Z'$ and the results follows.

□

Since the last node in the quarantine has a probability of 0.1 which is larger than the threshold, it should be kept in the quarantine region. A naïve person may think that this is the optimal solution to this example because the most possible nodes are in the saved region. However, when evaluating the objective function which is based on penalties, this is not true. This example shows that it is not always optimal to remove a group of nodes with an average probability that is less than the threshold.

Figure 4.15 shows that in fact the nodes at the bottom of the graph should not have been included in the saved region. If they are added back into the quarantine as the figure suggests, the objective function becomes

$$19((0.02)+(0.06)+(0.04))+1((0.90)+(0.96)+(0.93)) = 5.07.$$

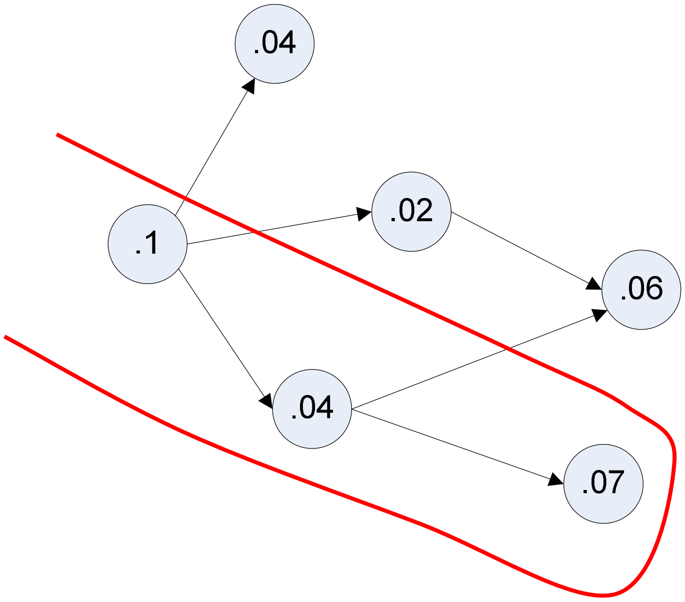


Figure 4.15: 3rd Iteration *Z* = 5.07

As you can see, the optimal solution does not always include the most nodes in the saved region. In fact, this shows it is not always optimal to remove a group of nodes whose average probability is less than the threshold. The following theorem discusses this scenario.

Theorem 4.8: Let $V_{Q'}$ be any quarantine partition with $V_{S'}$ being the corresponding saved partition. If $Q \subseteq V_{S'}$ such that $(V_{Q'} \cup Q, V_{S'} \backslash Q)$ is a quarantine cut and $\sum_{j \in Q} p_j > |Q| \left(\frac{q}{q+s} \right)$, then the value of the quarantine cut $(V_{Q'} \cup Q, V_{S'} \backslash Q)$ is strictly better than the value of $(V_{Q'}, V_{S'})$.

Proof: Let $(V_{Q'}, V_{S'})$ be a quarantine cut with value Z'. Let $Q \subseteq V_{S'}$ such that $(V_{Q'} \cup Q, V_{S'} \backslash Q)$ is a quarantine cut and $\sum_{j \in Q} p_j > |Q| \left(\frac{q}{q+s} \right)$. The value Z'' of the $(V_{Q'} \cup Q, V_{S'} \backslash Q)$ quarantine cut is the value of the $(V_{Q'}, V_{S'})$ cut minus the penalty of having Q in the saved partition plus the penalty of having Q in the quarantine partition. Formally, $Z''=Z' - \sum_{j \epsilon Q} s(p_j) + \sum_{j \epsilon Q} q(1-p_j) = Z' - s\sum_{j \epsilon Q} (p_j) + q|Q| - q\sum_{j \epsilon Q} p_j = Z' - (q+s) \sum_{j \epsilon Q} (p_j) + q|Q| < Z' + q|Q| - q|Q| = Z'$. The last inequality follows from $\sum_{j \in Q} p_j > |Q| \left(\frac{q}{q+s} \right)$, which implies $(q+s)\sum_{j \epsilon Q} (p_j) > q\,|Q|$. Thus, $Z''<Z'$ and the results follows.

□

Figure 4.15 shows the optimal solution to the example graph. This example shows that there is a trade off when removing a node from a quarantine region. In terms of penalties, when removing a node from the quarantine, you subtract off the probability of a healthy node being in a quarantine region multiplied by this penalty, but you gain the probability of an infected node being in a saved region multiplied by this penalty. Therefore, to determine the change in the objective value for moving a set nodes from the quarantine region to the saved, the value $q(p_i)$-$s(1-p_i)$ for all nodes moving should be subtracted from the previous objective value. In the example above, notice that this marginal value is equal to 0.20 for all iterations.

Clearly if the sum of probabilities is equal to the threshold, then it is the digression of the decision maker to either keep the group quarantined or move them to the save zone. If the decision maker wants to be conservative, he/she should keep the group in the quarantine.

4.5.1 Heuristic

In a real life scenario, it would be infeasible for a government agency to run an integer program to find the optimal quarantine region even though the integer program is TUM and runs quickly. The goal of this section is to provide real-time guidelines for finding near optimal quarantine regions through a heuristic, called Greedy Quarantine (GQ). Although GQ may not find the optimal quarantine region, it provides a rapid method for a decision maker to adapt a quarantine area in a dynamic scenario.

Greedy Quarantine

Initialization:

```
    Given a geographic ellipsoidal graph with weighted nodes and a defined threshold $\tau = q/(q+s)$.
    Set $o_j$ := the outdegree $v_j \in V_Q \forall v_j \in V$. Let $V_S := \emptyset$ and $V_Q := V$.
    Set Flag:=True
```

```
Main Step:
    While Flag = True
        Flag:=False
        if there exists a node $v_i$ with $o_i = 0$ and $p_i < q/(q+s)$
            $V_S := V_S \cup \{v_i\}$, $V_Q := V_Q \setminus \{v_i\}$
            For all $(v_j,v_i) \in A$ set $o_j := o_j - 1$ (update the outdegrees of $V_Q$)
            Flag:=True
        else
            Run a subroutine or several subroutines to add multiple nodes to $V_S$.
            If the size of $V_S$ has changed, update the outdegrees of $V_Q$ and Flag:=True
        End else
    End While loop
    Go to termination
Termination
    Report $(V_Q,V_S)$ as the optimized quarantine cut.
```

Subroutines to add multiple nodes to V_S

The first heuristic, Interior Greedy, starts with the nodes with the smallest probability of infection. With this, a breadth first search is run to a degree zero node. If the average probability of the nodes encountered by this breath first search is less than the threshold, then the nodes are added to the saved region. This heuristic utilizes this low probability node so as to have a greater chance of finding a group of nodes that have a lower average probability than the threshold.

Interior Greedy

```
Let $v_i \in V_Q$ such that $p_i$ is minimum and $p_i<q/(q+s)$.
Let $C$ be the set of all nodes can be reached from $v_i$ (run breadth first search from $v_i$)
If $\sum_{i \in C} p_i < (q/(q+s))|C|$, then
    $V_S:=V_S \cup C$, $V_Q:=V_Q \setminus \{C\}$
```

The next heuristic, Greedy Exterior Greedy, starts with the node that has the smallest probability and is a degree zero node. From this node reverse breadth first search is run to the root node. Within the nodes encountered, take the node with the smallest probability and run breadth first search. This breadth first must include the starting node with the out-degree zero. If the average probability is below the threshold add it to the quarantine. This heuristic is greedy by choosing the smallest probability node with out-degree zero and the smallest node encountered by a reverse breadth first search.

Greedy Exterior Greedy

```
Let $v_i \in V_Q$ such that $v_i$ has outdegree zero in $V_Q$ and has the minimum $p_i$ value of all such nodes.
Let $D$ equal the set of all nodes that must be quarantined if $v_i$ is quarantined (run reverse breadth first search from $v_i$).
Let $v_j$ be the node in $D$ with the smallest $p_j$ value. Let $C$ be all the nodes encountered by running breadth first search starting with $v_j$.
If $\sum_{\mathrm{i} \in \mathrm{C}} p_i < (q/(q+s))|C|$, then
    $V_S:=V_S \cup C$, $V_Q:=V_Q \setminus \{C\}$
```

The goal of a heuristic is to be close to optimal and run fast. Since we have established that a government agency would not realistically use an integer program to find the optimal quarantine, the next section discusses how accurate the agency could be if they used the theory mentioned in the previous section.

4.6 Comparison of Heuristic to Optimal

The motivation for this section is to compare the performance of the heuristic, GQ, to the optimal solution found by OQIP. Since a government agency implementing a quarantine region would most likely not use an integer program to find the quarantine, the following study shows how accurate this agency can be if it uses the logic provided by the heuristic and theorems discussed in Chapter 4.

To compare these two objective values, a basic SIR model on a random geographic graph was chosen. In this study, 30 random graphs were used. To see how the size of the graph affected the optimal value versus the heuristic value, three different sizes of graphs were used. Also, three different variations of the penalties were used to see their effect.

To find the probabilities that a node is infected, a thousand replications of each random graph were run. The probability of infection for each node is cumulated for these replications and divided by 1,000 to find the average. Thus, if v_i contracts the disease in 100 of the 1000 replications, then $p_i = 100/1000 = 0.1$. These probabilities are used in the ellipsoidal geographic graph, which is then used to determine the quarantine cut.

As you can see for a graph size of 100 nodes, the average percent error is the highest. This is because as the graph size increases to around 500 nodes, the probability of infection is higher. This means it is easy for the heuristic to decide that everyone should be quarantined. Tables 4.1 – 4.3 show the average results for the 30 random graphs.

n	100		
	Avg. Z_h	**Avg. Z***	**Avg. % Error**
q=1,s=19	46.48	45.42	2.34%
q=1,s=9	36.23	34.06	6.35%
q=1,s=4	22.09	21.67	1.91%

Table 4.1: Comparison of Heuristic to Optimal n = 100

n	250		
	Avg. Z_h	**Avg. Z***	**Avg. % Error**
q=1,s=19	157.49	157.34	0.10%
q=1,s=9	148.44	147.17	0.87%
q=1,s=4	127.91	125.21	2.16%

Table 4.2: Comparison of Heuristic to Optimal n = 250

n	500		
	Avg. Z_h	**Avg. Z***	**Avg. % Error**
q=1,s=19	219.33	219.33	0.00%
q=1,s=9	218.68	218.64	0.02%
q=1,s=4	211.56	211.29	0.13%

Table 4.3: Comparison of Heuristic to Optimal n = 500

It is important to note that if the probabilities of infection were closer to the threshold, the heuristic value was further from optimal. This is because it is harder for the heuristic to make the optimal decision.

This study confirms that with large graphs, GQ performs with less than 1% error of the optimal value. These results also show that the number of nodes in the graph and the penalties has an effect on how well GQ performs. In general, the further the probabilities of infection are from the threshold, the better GQ performs. In cases where the probabilities are close to the threshold like in Table 4.16, GQ performs with less than 10% error of optimal.

These results show that government agencies should utilize the theory in this research. Although they may not run an integer program to find the optimal decision, they can achieve close to optimal quarantine regions by utilizing the decision making tools provided in this research.

CHAPTER 5 – Conclusion and Future Work

One of the main results of this thesis was the development of a core simulation that rapidly simulates the spread of an epidemic on a contact network. Although the simulation core was developed by a team, I have made significant contributions to it.

The goal of this simulation was to create a simulation that can be easily adapted to any disease. Given a contact network of individuals, this simulation core can be modified to model any disease in less than an hour. If a contact network is not given, the simulation core has the capability of generating a random contact network with various parameters.

The simulation created for this research uses random number distributions to generate numbers for different factors such as, how rapidly a subject transitions through each stage of the disease and the links between each subject. With this randomized model, the simulation is run for multiple replications. With these replications, the average probability of infection can be found and an ellipsoidal geographic graph is created.

This research provides the first definition for a quarantine cut and an ellipsoidal geographic network. This thesis uses the ellipsoidal geographic network to determine what is, and what is not a feasible quarantine region. The quarantine cut is a new approach to partitioning quarantined and saved individuals in an optimized way.

To execute the quarantine cut, an optimum quarantine integer program, OQIP, was developed. The objective function of OQIP is focused on minimizing the penalty of having infected individuals in the saved region and having saved individuals in the quarantined region. This integer program is proven to be totally unimodular and thus, runs in polynomial time.

Since OQIP is not practical for a real-life scenario, a heuristic, Greedy Quarantine (GQ), and some theoretical results were created. The results provide decision makers with ample knowledge of how to apply this research in a real life scenario. After performing a study on the how well GQ's value is to the optimal value, I can conclude that GQ performs with less than 10% error of optimal when the threshold is close to the probabilities of infection. If the threshold is not close to these probabilities, GQ performs even closer to optimal.

5.1 Future Work

The development of OQIP and the various accompanying theorems and heuristics provide implementable principles and exhaust majority of the theoretical approaches to this research. Any future work on this research should be performed on real-life applications.

It is vital for our society to continue to model the spread of disease as a way to safely understand them. Given a specific disease, a complex simulation study could be conducted. This would include adjusting various parameters to see how each effect the spread of the disease. The results of this in-depth study could then be compared to actual disease spread data.

In the future, this research can be used to model the spread of any disease in animals such as skunks. The simulation core of this research could also be used to model the spread of information in a contact network. Another real world application that could be simulated would be the spread of viruses on a computer network.

Additional future work could be conducted on the effect of pre-clustered graphs. This would show how a quarantine line could change if contact clusters are established. To demonstrate how a media broadcast of a quarantine region affects people's actions, a simulation could also be conducted. This might entail reducing each person's number of edges because they would be unwilling to leave their home.

To model the spread of disease to rural towns, each town could be considered a single node. This model would operate under the assumption that if a town is infected, the entire town should be quarantined. This would provide a high level quarantine for multiple rural towns.

As Nobel Prize winner Joshua Lederberg, Ph.D, stressed "The single biggest threat to man's continued dominance on the planet is the virus." [Zimmerman (2002)] The future work conducted in this field will save lives, and it is imperative for humanity's survival.

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