Methods of Preventing and Eradicating Ebola

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1 Introduction

With an ever growing population, the world becomes more susceptible to mass spread of disease. This is why it is important to find and treat infected individuals to prevent any mass spread. Ebola is a disease that recently had a large out break in West Africa. During this epidemic, there were over 28,000 cases with over 11,000 deaths in West Africa. Without proper treatment and heath care practices, the devastation of the disease could have been even more wide spread. Determining the best method of treatment could lead to the elimination of the virus or other diseases[1].

By outlining the issues that need to be observed and researched, we will model the spread of Ebola with a given cure. We must consider the spread of the disease, as well as anything related to the production or delivery of our new cure. We do not need to create a cure as that is not the aim of the study. Instead we must assume a cure has been created, and come up with a method or plan to ensure that Ebola does not create mass devastation on a population.

$$\Delta u \tag{1}$$

$$\Delta v \tag{2}$$

$$\Delta \frac{u}{2} \tag{3}$$

$$\Delta \frac{v}{2} \tag{4}$$

The goal of this research is to determine a model that will effectively eliminate Ebola, or its current strain. In order to do so, important parameters must be considered, and applied to models that will depict an outbreak and its outcome. We will look into two models that will aid in determining an effective method to eliminate Ebola. However, to determine a solution, we need to understand more about Ebola and how it affects and infects people. Our models suggest that a Cellular Automata approach works best for modeling an outbreak of Ebola with an effective cure. Using this agent-based model with

a cure, we can see that the number of recovered people exceeds the number of dead people.

2 Background

Ebola is a virus, meaning that it can only survive and multiply by invading a host. The Ebola virus has the ability to infect humans and non-human primates.[1] The Ebola virus enters its human host and directly attacks the immune system. Unlike most viruses, it invades dendritic cells, which effectively stops the production of any antigens that could combat the virus. Simultaneously, it attacks the liver, which causes several organ failures. Ebola leads to mass fluid loss that can end up as the cause of death if not properly treated. On average, fifty percent of all infected patients die from the infection. Ebola was first discovered in 1976 in Sudan. Prior to the mass outbreak in 2014, there have been several smaller outbreaks throughout Africa. This is where the Ebola virus originates and is believed to come from infected bats. Ebola has the potential to progress quickly and infect a large population, which makes it particularly deadly. And while it was previously said that fifty percent of all infected people die from the disease, the actual amounts for previous outbreaks has ranged from twenty five to ninety percent death rates [4].

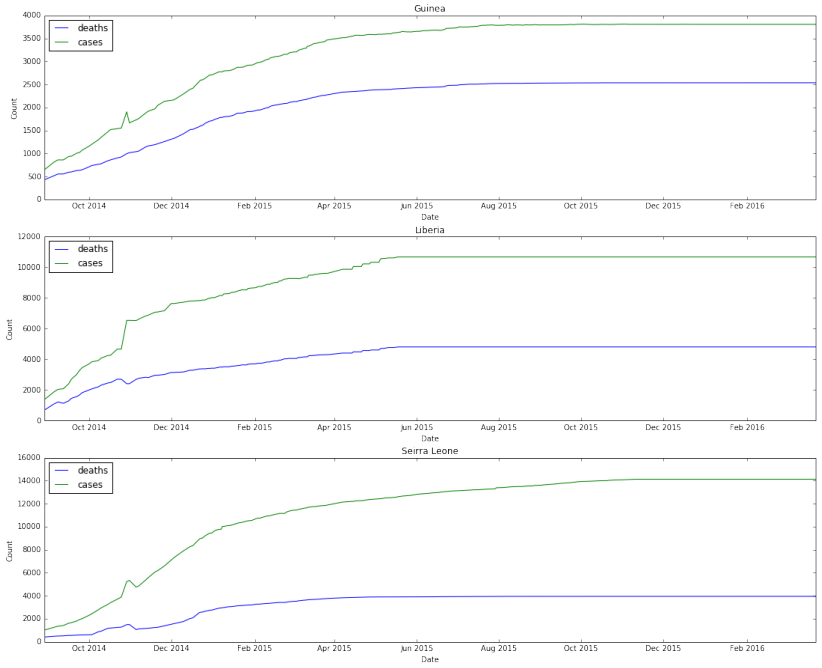

Figure 1: Data collected by WHO which presents the death and number of recorded cases for Guinea, Libera, and Sierra Leone.

2.1 Contracting Ebola

Ebola is contracted through physical contact with an infected person or animal. There are several possibilities of infection through direct contact as listed by the CDC:

- Blood or bodily fluids of an infected person or someone who has died from Ebola
- Objects that have been contaminated by an infected person's bodily fluids
- Infected fruit bats or primates
- Semen from a male who has recently recovered from Ebola

2.2 Stages of Infection

The Ebola virus progresses quickly through the immune system once it has been infected. According to the World Health Organization, the amount of time from being infected to becoming infectious is anywhere between 2-21 days. Humans are only infectious when showing symptoms. When an infected person begins to show symptoms, they can look similar to other common diseases in West

Africa such as malaria or cholera. Early symptoms resemble a common cold, with a fever, headache, fatigue and muscle pain. These progress into diarrhea, vomiting, some organ failure and sometimes can develop internal or external bleeding. The ultimate death of infected people is typically through a massive loss in bodily fluids.

2.3 Treatment

Treatment of Ebola and even identifying a person as being infected is dangerous because any sample taken is an extreme biohazard. Without sampling of a patient there would be no exact way to determine if it was Ebola or some other disease. Because of the extremely infectious nature any healthcare professional that comes in contact with an infected person has the potential of getting infected with such close contact.

3 Models

We are investigating a model in which a cure for the current strain of Ebola (EBOV) has been developed. One of the most recent outbreak of Ebola has been the most severe making this model relevant in today's world. The ways of becoming infected, listed above, show that in highly populated areas there will be an increased risk of infection. Prior to the most recent outbreak, most, if not all, outbreaks have been in rural areas. This difference in locals of the infected zones is a major factor when considering the impact of the virus on a population. The goal of this investigation is to find an optimal solution to the eradication of the Ebola virus for its current strain. To do so we need to determine the parameters from the above information. Each of the models will take on different parameters and will both be discussed in greater detail below. After implementing and testing both models, we will assess the practicality of each model.

3.1 SEIR Model

We are going to model this system using an SEIR model. This means we will have at least 4 differential equations that tell us the rate of susceptible, exposed, infected, and recovered individuals for those who have contracted Ebola. Additionaly, we will have to introduce the rate of cure production and the rate at which individuals recover using this cure. To this end, we will have to research incubation and exposed time. We will have to add these as differential equations to our system. The differential equations can incorporate different rates of cure production and model how these affect the populations. We can interpret which cure rate helps eradicate or at least contain Ebola.

3.2 Cellular Automata Model

Our second model will be much more complex that our first. We will implement a cellular automata strategy. In cellular automata models, a grid with agents in certain cells are in a given state. Changes to an agent's state can occur based on a set of probabilistic rules. Cellular automata can be thought of as a much more realistic model when compared to the ideal model created by differential equations. This is because the agents that inhabit the grid 'wander' about, making the clearly defined rules created by our SEIR model less obvious. Instead the agents states depend on the states of their neighbors. Our environment or cells will be an area with agents being a parametrized number of individuals who live in this area. We will utilize the compartmental approach from the SEIR model and have individuals represented by states. The states will be the same: susceptible, exposed, infected, and recovered. However, to visualize the data that we are presented better, we will add in death as a fifth state. This will allow us to compare the cellular automata to the real world examples. Additionally, we will have a parametrized number of WHO agents (also implemented as agents to the environment) who are responsible for administering the cure to individuals who have the Ebola virus. We are assuming that the WHO agents are immune, as if they are wearing the anti contamination suits that prevent the transmission of Ebola. We will be able to see the effects of this model overtime.

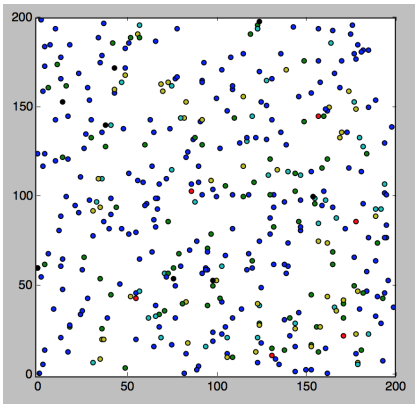

Figure 2: Example of a single frame from a cellular automata model. The different colors represent the different agents within a model.

4 Sensitivity Testing of SEIR Model

In the SEIR model, there are susceptible, exposed, infected, and recovered individuals. Here, we are clustering dead and recovered people together. This will not change the general trends of our differential equations. We are going to assume that our cure only works on individuals in the exposed stage. For

simplification, we are also going to assume that the cure works instantly once administered to a patient. We can represent this compartmental model as shown (Figure 3).

- N: Total Population
- S: Susceptible Population who can become exposed
- E: Exposed Population who can become infected over time
- I: Infected Population who may recover
- R: Recovered Population who are no longer susceptible to Ebola

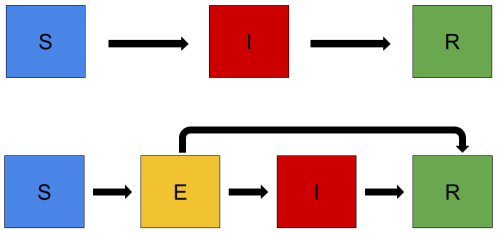

Figure 3: On the top is a simple SIR model, which does not have an exposed compartment. In the SEIR model, exposed individuals who have been administered the cure can go directly into the recovered stage.

4.1 Differential Equations

The following differential equations model the behavior of each compartment over time. First, we will list some important rates:

- β: Transmission rate from susceptible to exposed individuals
- α: Infection rate from exposed to infected individuals
- μ: Recovery rate from infected to recovered individuals
- λ: Cure rate from exposed to recovered individuals

$$\frac{dS}{dt} = -\beta SE\frac{1}{N} \tag{5}$$

$$\frac{dE}{dt} = \beta SE\frac{1}{N} - \alpha E - \lambda E \tag{6}$$

$$\frac{dI}{dt} = \alpha E - \mu I \tag{7}$$

$$\frac{dR}{dt} = \mu I + \lambda E \tag{8}$$

4.2 Varying Cure Rate

Let's now test the SEIR model with different cure rates. We will use set values for all other rates. These values were collected over existing compartmental models of Ebola and averaged in order to incorporate a cure rate [3]. We will also use population data for Liberia as a base for this test. As seen in the differential equations α, λ, and μ have units of $\frac{1}{time}$, while β has units of $\frac{1}{populuation*time}$:

α	0.090
β	0.163
μ	0.089

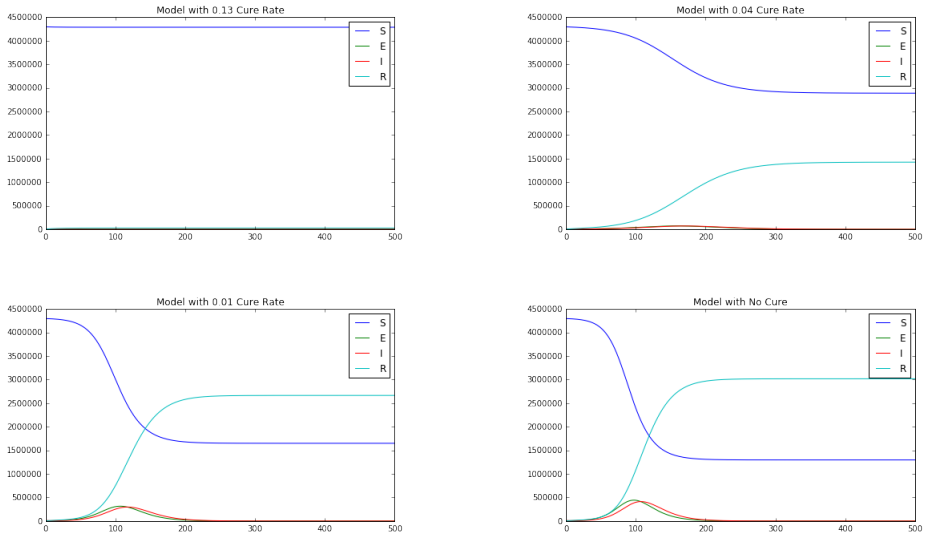

Figure 4: Several SEIR models with different cure rates.

4.3 Drawbacks of Model

Currently, our model does not take into consideration a cure production or a cure amount; it assumes that any population has a set cure rate. Therefore, the cure is not varying over time, as a more realistic model would.

5 Sensitivity Testing of Cellular Automata

For the cellular automata model we can no longer use the rates from the SEIR model. This is because the rates were used against the entirety of the population, but in this new model each individual agent is dependent on its own state, and sometimes the states of immediate neighbors. How the population moves between states in the cellular automata and the exact interactions between the different agents present in the model will be described in more detail.

5.1 Population

The population of this model can be thought of as a small town or a section of a city. Each of the agents, or citizens, contain their own independent state. Each agent also has an internal clock, which is how we will move them between the different states. The states for this model are exactly the same with the addition of death as a new state [2].

- S: Susceptible Population
- E: Exposed Population
- I: Infected Population
- R: Recovered Population
- D: Dead Population

An individual agents ability to move around is dependent on their state. We assumed that susceptible and recovered people moved about normally. This means that they are always making some move. When an agent is exposed, their chance of movement is decreased slightly. This is to account for when you feel sick, you tend to want to move less. This chance is even further decreased when an agent is at the infected state. When an agent is Infected they are in the severe stage of the virus, meaning they are extremely sick, incurable and are likely to not move much.

As explained above we are no longer using the rates found in the SEIR model, so we will use days as the unit for transition between the states. There is clear information in many articles on the approximation of the time periods of each stage. Some stages are up for interpretation, and we will use what we believe to be the best time frames for the model. Below are the time frames that we are currently using for movement between the states.

- Susceptible to Exposed: Instantaneous if next to Infected person
- Exposed to Infected: 15 days [4]
- Infected to Dead: 7 days after infection [2]
- Infected to Recovered: 4 days after, there is a 50% chance of recovering

WHO agents also have a single state, for now, called *curing*. We assume that WHO agents are not able to be infected. Instead, they are able to wander the world and interact with the population. These states of the population and WHO agents tell us how an individual agent will interact with its surrounding neighbors.

5.2 Agent Interactions

In order for some agent to become infected they must have a neighbor that has an infected state. A neighbor, in this case, is defined as the four cells that share a side with the current cell, and the four that share a corner with the current cell. This is known as a Moore Neighborhood. In the current model all agents wander around, taking a random direction each time. As explained above, some states have limiting factors for the movement of an agent with that state. Infected agents and WHO agents are the only ones that currently can modify the states of their neighbors.

WHO agents are affected by the infected, and exposed agents. When an agent is exposed they have a chance of giving off a signal. When a person is infected, they always give off a signal. In both cases, WHO agents monitor the world they exist in, looking for the signals. When they detect one, they move upwards in a gradient towards the source of the signal. This is how the WHO agents are able to cure infected people. Without this attraction WHO agents would just randomly walk around the world. So this attraction is a more realistic method for the WHO agents knowing where an infected person is in the world.

5.3 Sensitivity of Model

Changing the amount of time that an individual agent was at any of the stages changed the model drastically. Originally we were defining exposed as individuals that had been infected up to when they show symptoms. However, that time period of just 10 days proved to be far too short, and people nearly immediately moved to being infected. This meant that our WHO agents had to be very close to the exposed individual to cure them. And if a WHO agent got hung up somewhere, some other group of exposed individuals may be spreading into infected.

If agents have some chance, that after a certain period of time of being infected, to recover from Ebola. We know from studies that the death rate of previous outbreaks can be any where between 25-90%, however 50% was the

percentage that was an average for the outbreaks. [4] So we know that with out a cure the number of recovered and dead agents should be about equal to each other. So because there is a three day difference between the time when you can possibly recover and when the last day is. Each day the agents take 5 steps, so there is a difference of 15 in the clocks. This means that our probability of still being infected during this time needs to ensure that the end result of the recovered and dead agents are equal. So we can do the following equation to compute this probability:

$$x^{15} = 0.5 \tag{9}$$

This gives us an x value: the probability of not recovering of 0.9548. So for our model we will use a rounded version and use 0.05 for the probability of recovering each time step. When using this probability with no cure the two end at nearly the same number. In order to have no cure, the WHO agents can not interact with the environment. Ten trials of four hundred time steps were run and compiled to create an average over ten trials.

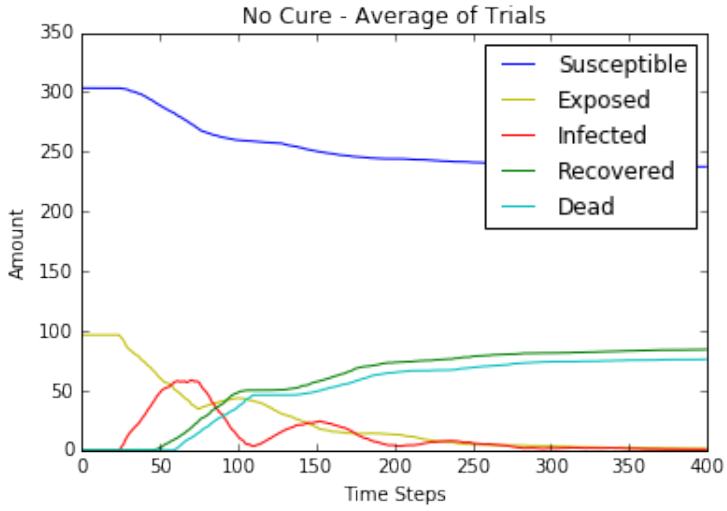

Figure 5: End results of ten trials of cellular automata. You can see that the green and cyan lines end at nearly the same place. This is exactly what we we are looking for with no cure.

The point of this research was to present an optimal cure that would help eradicate Ebola. So we now make the WHO agents active, and allow them to cure the exposed individuals. The effect that this should have on the ratio of recovered to dead agents, should make the number of recovered agents significantly higher than that of the dead ones. Again ten trials with four hundred

time steps was used to take an average of the ten trials. This will ensure that the data is more accurate, and further proves the trend.

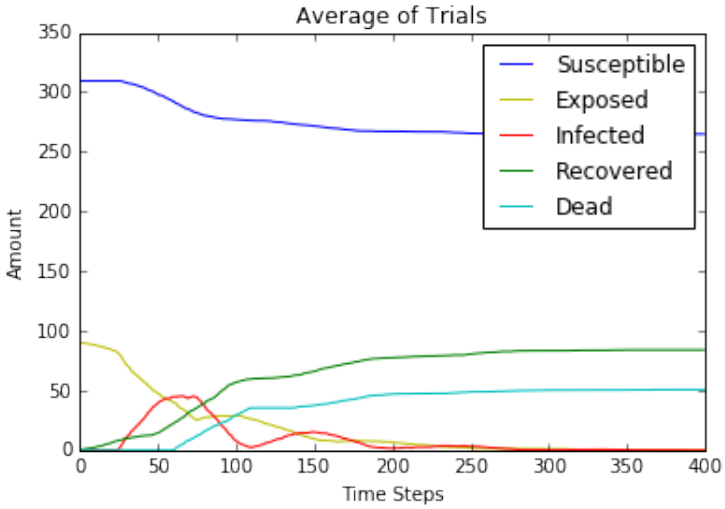

Figure 6: Final data from ten trials of the CA simulation. This graph shows that there is a clear difference in the amount of recovered and dead individuals.

The biggest difference is, when using the cure, there appears to be a much greater decrease in the number of exposed people. Meaning that the WHO agents are properly curing people. This in turn made the number of infected people phase out much quicker. The peak of infected people is also much lower than when no cure is used. These graphs show that this model is on the correct path towards depicting an optimal solution to an Ebola outbreak.

5.4 Drawbacks of Model

A noticeable drawbacks are that the WHO agents often get stuck in the gradients of signals given off by exposed and infected individuals. This means that their efficiency of curing people is diminished. Another drawback is that this population is just a generalized location, there are no gathering places or road ways. This model is very simplistic, but it does a good job at modeling the interactions between individual agents.

6 Evaluation

6.1 SEIR Model

In this highly simplified SEIR model, it appears that a cure rate between 0.01 and 0.04 $\frac{1}{time}$ would influence the SEIR model in a positive manner. However,

this model was only tested on the population of Liberia and must be expanded as mentioned later on in Future Work to produce meaningful results.

6.2 Cellular Automata Model

The cellular automata approach for a single city shows promising results when comparing a simulation without cure to a simulation with cure. The simulation without the cure holds true to the nature of WHO data as shown in Figure 1. The method of implementing the cure through WHO agents is realistic when compared to the SEIR model.

7 Conclusions

We conclude that the cellular automata model is a more realistic model for preventing the spread of Ebola. This model seems to give us the most realistic conclusions, as the interactions between different agents are completely random, which differs from the SEIR model. It is also able to depict the individual interactions between people in a world, where as the SEIR model took rates for the population. The SEIR is good for a general prediction, but if we want to know exactly how a cure will affect a population, using cellular automata is the best way to do so.

8 Future Work

This section is for ideas of future work that can be completed on either model. Both models have room for improvement and these improvements will be discussed below.

8.1 SEIR Future Work

For this model, we will need to implement a cure production rate and an initial cure amount for a given population. This will make the model more realistic and inform us if our cure rate is accurate. It would be interesting to see a cure rate that works over a different time range than the infection rate.

8.2 Cellular Automata Future Work

For future work on the CA model, we may want to add in more separation of the population. Instead of having the agents randomly spread throughout, have them concentrated into 'cities' or 'towns' and randomly travel a path between them. This would create an even more realistic model, and better show how Ebola could spread, not just within a city, but between cities. Additional future work may include putting some sort of limit on the amount of cure that a WHO agent has on them at a time. This would add in another factor in how we well we can produce and get the cure to its intended destinations.

References

[1] http://www.cdc.gov/vhf/ebola/about.html

[2] Simpson DIH (1977). "Marburg and Ebola virus infections: a guide for their diagnosis, management, and control" (PDF). WHO Offset Publication No. 36. p. 10f

[3] Rachah, A., Torres, D.F.M.: Predicting and controlling the Ebola infection. Math. Methods Appl. Sci. doi:10.1002/mma.3841 (in press)

[4] http://www.who.int/mediacentre/factsheets/fs103/en/