MODELING THE SPREAD OF EBOLA

1. Summary

Ebola is a rare and deadly disease caused by infection with a strain of Ebola virus. The current 2014 Ebola epidemic outbreak in West Africa (first cases notified in March 2014) is the largest and most complex Ebola outbreak since the Ebola virus was first discovered in 1976, affecting multiple countries in West Africa. The Ebola virus causes an acute, serious illness, which is often fatal if untreated. Thus, it is important to give an epidemic model that considers not only the spread of the disease, but also possible feasible delivery system, speed of manufacturing of the vaccine or drug for Ebola so that we can optimize the eradication of Ebola.

We use existing data from Liberia and Sierra Leone and Guinea to parameterize a mathematical model of Ebola. We model the course of the outbreaks and the spread of the disease via an SEIR (susceptible-exposed-infectious-removed) epidemic model to predict the future scenario without any intervention. Using this method we find out that without any intervention, the Ebola will eventually be out of control, any individuals in S, E, I categories will eventually goes to R category.

After that we propose three approaches to optimize the eradication of Ebola: Vaccination intervention, Quarantine intervention, and Delivery system optimization. We simulate the vaccination intervention in assortative and proportionate mixing patterns. We simulate the vaccination intervention in assortative and proportionate mixing patterns, and compare the results for different vaccination rate. For quarantine intervention, we apply graph model to figure out the rate of contact between people. Based on that, we estimate the optimal number of people we need to remove to prevent the disease from spreading due to person-to-person interaction.

In conclusion, the spread of Ebola is disastrous but it can be well controlled. The three methods we developed tested across Liberia and Sierra Leone, and we got different reasonable simulation results.

2. Abstract

The current 2014 Ebola epidemic outbreak in West Africa (first cases notified in March 2014) is the largest and most complex Ebola outbreak since the Ebola virus was first discovered in 1976, affecting multiple countries in West Africa. Thus, it is important to give an epidemic model that considers not only the spread of the disease, but also possible feasible delivery system, speed of manufacturing of the vaccine or drug for Ebola so that we can optimize the eradication of Ebola.

We use existing data from Liberia and Sierra Leone and Guinea to parameterize a mathematical model of Ebola. We model the course of the outbreaks and the spread of the disease via an SEIR (susceptible-exposed-infectious-removed) epidemic model to predict the future scenario without any intervention. Using this method we find out that without any intervention, the Ebola will eventually be out of control, any individuals in S, E, I categories will eventually goes to R category.

After that we propose three approaches to optimize the eradication of Ebola: Vaccination intervention, Quarantine intervention, and Delivery system optimization. In conclusion, the spread of Ebola is disastrous but it can be controlled under several methods.

3. A Letter to the World Medical Association

World Medical Association: Greetings!

Since the World Health Organization (WHO) have reported a major Ebola outbreak in Guinea, in 2014, the disease then rapidly spread to the neighboring countries of Liberia and Sierra Leone, as well as multiple countries in West Africa, causing thousands of casualties. Mathematical models of disease outbreaks can be helpful by providing forecasts for the development of the epidemic that account for the complex and non-linear dynamics of infectious diseases and by projecting the likely impact of proposed interventions before they are implemented. Here, we use the SEIR model. By judging and weighting the relationship between the susceptible, exposed, infectious and removed individuals, we come up with intervention of vaccination, quarantine, and optimization of medical delivery system. By simulating and examining the potential impacts of those interventions, we can say with some confidence that although Ebola is disastrous, it is possible to control and reduce the infected individuals, and keep the balanced situation.

Cheers!

Contents

4. Introduction

4.1. **Background.** In March2014, the World Health Organization (WHO) reported a major Ebola outbreak in Guinea, the disease then rapidly spread to the neighboring countries of Liberia and Sierra Leone, as well as multiple countries in West Africa, causing thousands of casualties. According to WHO, 2014 Ebola first started in Guinea then spread across land borders to Sierra Leone and Liberia, by air (1 traveler only) to Nigeria, and by land (1 traveler) to Senegal.

Ebola is generally characterized by sporadic, primarily rural outbreaks, and has not been seen before in West Africa, or in an outbreak of this size. Ebola in humans is caused by four of five viruses of the genus Ebola virus. The four are Bundibugyo virus (BDBV), Sudan virus (SUDV), Ta Forest virus (TAFV) and one simply called Ebola virus (EBOV, formerly Zaire Ebola virus). EBOV, is the most dangerous of the known Ebola virus disease-causing viruses, and is responsible for the largest number of outbreaks. The fifth virus, Reston virus (RESTV), is not thought to cause disease in

humans, but has caused disease in other primates (Hoenen T, Groseth A, Feldmann H (July 2012). "Current Ebola vaccines"). Notably, Ebola is transmitted into the human population through physical contact with blood, secretions, organs or other bodily fluids of infected animals such as chimpanzees, gorillas, fruit bats, monkeys, forest antelope and porcupines found ill or dead or in the rain forest. It then spreads through human-to human transmission via direct contact (through broken skin or mucous membranes) with blood, secretions, organs or other bodily fluids of infected people, and with surfaces and materials contaminated with these fluids. Ebola is characterized by initial flu-like symptoms including sudden onset of fever, fatigue, muscle pain, headache and sore throat. This then rapidly progresses to vomiting, rash, symptoms of impaired kidney and liver function, and in some cases, both internal and external bleeding. Most infected persons die within 10 days after their initial infection (80%-90% mortality).

Using a simple SEIR(susceptible-exposed-infectious-removed) epidemic model and data from Ebola outbreaks in Sierra Leone and Liberia, 2014 , we calculate the tendency of the situation.

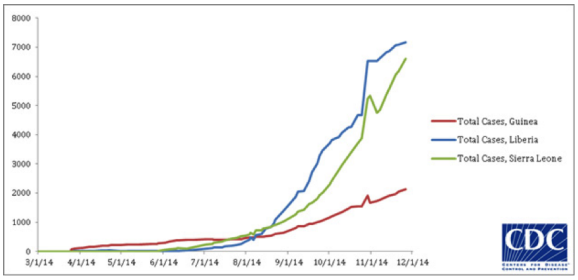
4.2. **Outbreak Data.** A time series of reported Ebola cases was collected from public data released by the WHO, based on the three most serious infected countries, Guinea, Liberia and Sierra Leone. From the comparison we can have the general idea of the impact that Ebola has on death rate in different regions in West Africa.

5. Modeling

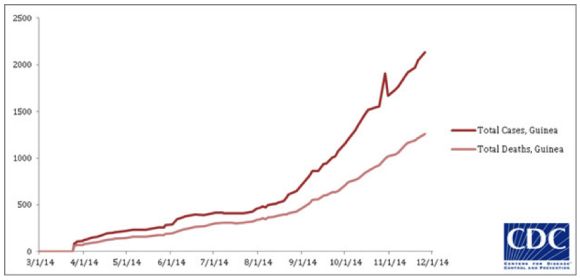
5.1. **A Rudimentary Model.**

5.1.1. *Epidemic model.* A compartmental model is introduced here, adapted from Legrand et al, which was previously used to describe the 2000 Uganda Ebola outbreaks. This is a stochastic compartmental model where individuals are classified as

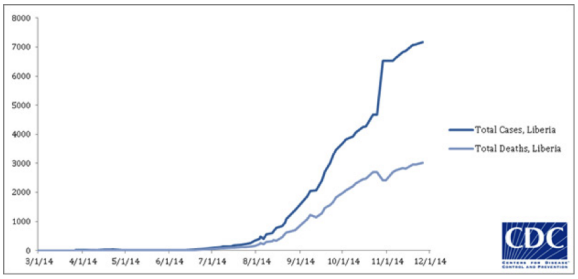
- S: Number of susceptible individuals, who can be infected
- E: Number of exposed individuals, who have been infected but not yet infectious
- I: Number of infectious cases in the community, who are capable of transmitting the disease



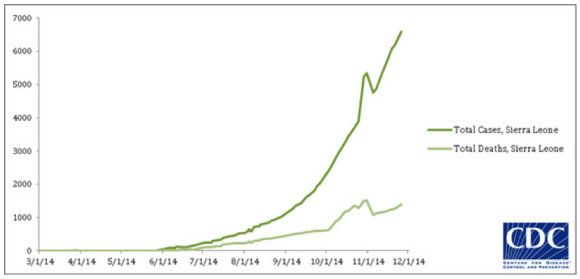
(A) Cumulative cases by data of reporting infection without control efforts in Guinea, Liberia, Sierra Leone, March 25, 2014 - November 26, 2014, by data of WHO Situation Report, $n = 15901$



(B) Cumulative cases by data of reporting infection without control efforts and deaths in Guinea, March 25, 2014 - November 26, 2014, by data of WHO Situation Report, $n = 2134$



(C) Cumulative cases by data of reporting infection without control efforts and deaths in Liberia, March 25, 2014 - November 26, 2014, by data of WHO Situation Report, $n = 7168$



(D) Cumulative Cases by Data of Reporting infection without control efforts and deaths in Sierra Leone, March 25, 2014 - November 28, 2014, by data of WHO Situation Report, $n = 659$

- R: Number of individuals removed from the chain of transmission.(cured or dead and buried)

The population will be constant during the outbreak, i.e., the total population at time t will be denoted by N where $N(t) = S(t) + E(t) + I(t) + R(t)$. Our model is:

$$\begin{aligned} \frac{\mathrm{d}S}{\mathrm{d}t} &= -\frac{\beta SI}{N} \\ \frac{\mathrm{d}E}{\mathrm{d}t} &= \frac{\beta SI}{N} - \delta E \\ \frac{\mathrm{d}I}{\mathrm{d}t} &= \delta E - \gamma I \\ \frac{\mathrm{d}R}{\mathrm{d}t} &= \gamma I \end{aligned} \tag{1}$$

The model we used above takes into consideration the number of people infected due to direct contact with an infected individual and the number of people infected due to direct contact with

latent individuals: $\beta SI/N$. Here, we have $\beta = pc$ where p denotes the probability of successfully getting infected when coming into contact with an infected individual, and c is the per-capita contact rate. The parameter $q(0 \leq q \leq 1)$ is a weight factor added to the model because a susceptible individual has a higher chance of getting infected from an infectious individual.

The individuals in the latent stage will eventually show the symptoms of the disease and enter into the infectious stage. This is denoted as δE, where δ is the per-capita infectious rate. In that case, $1/\delta$ becomes the average time for a latent individual to become infectious.

The death rate is denoted by γI, where γ is the per-capita death rate. Here, although recoveries do occur, we will not return these individuals to the susceptible class again (actually even if we do, the number of recovered individuals reported so far is extremely small, so it really doesn't matter here).

The method structure can be described in a flow chart (Table 1) as below, note that the arrows indicate the possible transitions, and the parameters that govern them.

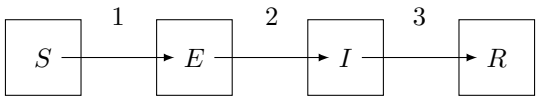


TABLE 1. The stochastic compartmental model

No.	**Transition**	**Transition Rate**
1	$(S, E) \to (S-1, E+1)$	$\beta SI/N$
2	$(S, E) \to (S-1, E+1)$	δE
3	$(I, R) \to (I-1, R+1)$	γI

5.1.2. *Model Fitting and Validation.* To solve the system of differential equations, we first make three assumptions:

(1) At the very first beginning of the epidemic, $N(t) = S(t)$.

(2) Initially, there is a constant number of individuals infected. (i.e., $\frac{\mathrm{d}I}{\mathrm{d}t} = 0$)

(3) In order for an individual to become infectious, he/she must pass through the latent stage. The data for the latent stage is thus the same as the data for the infectious stage.

TABLE 2. Model Parameters and Fitted Values for a model of an Ebola Epidemic in Liberia and Sierra Leone, 2014

Parameter	**Fitted values for Sierra Leone**	**Fitted values for Liberia**
Contact rate β	0.128	0.16
Incubation period $1/\delta$	10 days	12 days
Infectious Period $1/\gamma$	10.38 days	13.31 days

A deterministic version of the model was fit and validated against the current outbreak data using weighted least-squares optimization, with seed values from the Uganda outbreak described in Legrand et al. Notice that $1/\delta$ is the average time it takes for a latent individual to become infectious, and $1/\gamma$ is the average time it takes for an infectious individual to die. The model is given one-quarter of the weight, to capture improved case detection and the bulk of cases. There is no completed data on the Internet for Guinea; in that case, we eliminated it from the discussion. The fitted parameters for this model, as well as their descriptions, may be found in Table 2. Before the commencement of an analysis, we need to nondimensionalize the differential system. Below is the entirely analogous procedure:

$$[S], [I], [R], [E] : \text{individuals}$$

$$[S'], [I'], [R'], [E'] : \text{individuals / time}$$

$$[N] : \text{total number of individuals} : N = S + I + R + E$$

$$[\beta] : \frac{1}{\text{individuals} \cdot time}$$

$$[\gamma], [\delta] : \frac{1}{\text{time}}$$

$$[t] : \text{Time unit}$$

Next, we nondimensionalize the system using N for population size and $1/\gamma$ for time. We set the value of N to be unity and divide through with N. Since $N = 1$, all values remain unchanged.

The variables N, S, E, I, R become dimensionless, as they have the same unit as N. Let

$$\begin{aligned} \hat{S} &= \frac{S}{N} \\ \hat{I} &= \frac{I}{N} \\ \hat{R} &= \frac{R}{N} \\ \hat{t} &= \gamma t \end{aligned} \tag{2}$$

Therefore, the dimensionless series equations are then given by:

$$\begin{aligned} \frac{\mathrm{d}\hat{S}}{\mathrm{d}\hat{t}} &= -\frac{\beta}{\gamma}\hat{S}\hat{I} \\ \frac{\mathrm{d}\hat{E}}{\mathrm{d}\hat{t}} &= \frac{\beta}{\gamma}\hat{S}\hat{I} - \frac{\delta}{\gamma}\hat{E} \\ \frac{\mathrm{d}\hat{I}}{\mathrm{d}\hat{t}} &= \frac{\delta}{\gamma}\hat{E} - \hat{I} \\ \frac{\mathrm{d}\hat{R}}{\mathrm{d}\hat{t}} &= \hat{I} \end{aligned} \tag{3}$$

All the parameter values are known now, so we can solve the system of differential equations. The system of differential equations cannot be solved analytically, so we will solve it numerically. We will solve the system of linear equation using initial conditions with values corresponding to the two countries. Particularly we assume that for both countries the initial exposed populations are both 10% of the aggregate ones. In addition, the data 1 to 4 in the graph indicate S, E, R, and I respectively.

For Sierra Leone, we take the population taken in 2013, which is the latest one, to be the total population. Therefore the initial condition is (5.4828 (million), 0.6092 (million), 0, 0).

For Liberia, similarly we take population of 2013 to be the total amount. The initial condition is then (3.8646 (million), 0.4294 (million), 0, 0).

Both graphs state that the only equilibrium is $(0, 0, 0, R*)$ while R* equals the total population at the beginning. Due to the nondimentionalizing process the two graphs look similar despite the vertical axis. What is identical is that the system of each country reaches the equilibrium at the same moment in terms of the nondimentionalized time. In the real world, based on the model,

the populations in both countries are bound to drop to 0 if no control is executed. According to the collected data earlier, right now both countries are at the state when the slope of the removed population is still flat while the ones of the exposed and infectious population are growing steeper (somewhere around $t = 1$ in the graphs). Note that the output of the model does not fit the real data shown earlier, especially that the time period does not match. The reason is that our model assumes that populations are mixed together, which means each individual has an equal probability in meeting any other individual in the given area. However we all know that it's not true in the real world, people have higher probability meeting others who are in the nearby communities than meeting ones a few cities away, which limits the spread of virus. But our goal does not focus on predicting the time when the spread will grow out of control, but on how the result will be affected by the coefficients.

5.2. **A Model with Intervention.**

5.2.1. *Quarantine.* The model suggests that Ebola will eventually be out of control, yet we haven't found a way to cure Ebola, but we do have an effective way to prevent the spread, the quarantine. We introduce the variable Q to denote the infectious population being hospitalized by the governments and other medical organizations, and the variable α to denote the rate of infectious individuals being hospitalized. Here we assume that the hospitalized individuals share the same death probability with the normal infectious ones but do not infect any exposed individual or susceptible one. Hence the original system becomes as follows:

$$\begin{aligned}
\frac{\mathrm{d}S}{\mathrm{d}t} &= -\frac{\beta}{\gamma} \cdot S \cdot (1-\alpha) \cdot I \\
\frac{\mathrm{d}E}{\mathrm{d}t} &= \frac{\beta}{\gamma} \cdot S \cdot (1-\alpha) \cdot I - \frac{\delta}{\gamma} \cdot E \\
\frac{\mathrm{d}I}{\mathrm{d}t} &= \frac{\delta}{\gamma} \cdot E - I \\
\frac{\mathrm{d}R}{\mathrm{d}t} &= I \\
\frac{\mathrm{d}Q}{\mathrm{d}t} &= \alpha \cdot I
\end{aligned} \tag{4}$$

Note that it is impossible to hold as many quarantine spots as infectious population. However we need to hold a necessary amount, which is sufficient to control the spread. We will deem it sufficient if the dI/dt is not larger than dR/dt before $R = N$, that is, when the growth rate of infectious population is not greater than that of removed population. At that point, the spread of virus is under control, and we have the following relationship:

$$E \leq \frac{2\gamma}{\delta} \cdot I \tag{5}$$

At first the relation is false since the assumption based on the reality suggests that the initial I is zero while E is not. Therefore we modify it a bit. Instead of being true all the time, we need it to be true after the time when E reaches its peak value. Measures are taken to determine the approximate α in Sierra Leone and Liberia with the same initial conditions mentioned earlier. The graphs below illustrate the results. Note that, again, data 1 to 4 indicates S, E, I, and R respectively. In addition, data 5 represents $(2\gamma/\delta \cdot I - E)$.

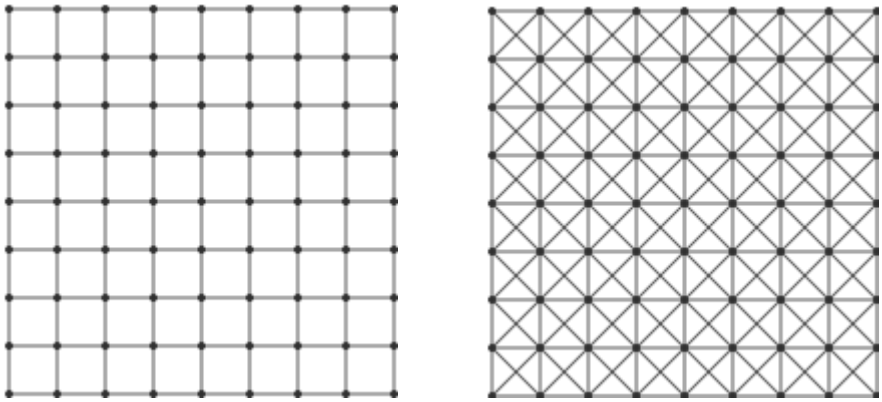
For Sierra Leone, the measured α is about 0.7, the initial condition is (5.4828 (million), 0.6092 (million), 0, 0).

For Liberia, the measured α is about 0.5, the initial condition is (3.8646 (million), 0.4294 (million), 0, 0).

Based on the graphs above, we find that to hold the epidemic spread under control, the hospitalized rate, which is defined to be the rate of hospitalized infectious population versus the total infectious population, needs to be around 0.7 or 0.8. Therefore we claim that if the residents in Sierra Leone or Liberia are mixed so each individual has an equal probability meeting any other in the country (which is the worst case), when Ebola breaks out about 80% of the infectious population must be held in quarantine. But neither of the countries are able to reach this level.

Instead, graph theory can be applied to cope with quarantine problem. Let N be the total population size, that is, the combined population of Liberia, and Sierra Leone. The estimated population is $\hat{N} = 10,386,000$. k will be the number of connections. The first model that can be applied here is the basic square grid graph, assuming that each people in the infected region has $k = 4$ connections. The grid graph is not infinite, that is, bounded in that the borders of the

three countries is under control, and there is Atlantic Ocean that constrains people from escpaing the boundary. The estimated population size $= \hat{N} = 10,386,000 \approx 1019^2$. Thus, the grid graph with odd number of nodes on the horizon and vertical will be considered. Further assumption will be that the graph is 2-dimensional. People in the infected region will generally move on ground, and the infection can only take place by person-to-person direct contact, hence the validity of the supposition. The graph will look like the following(9×9 : case):



The left graph is the one of our interest, while the right one is a more complex case with $k = 6$. The dots represent individuals. We want to isolate all the individuals by removing a number of dots. Removing them in a way that minimizes the number of removal will produce the following sequence. The sequence is particularly for the cases of (odd number $\times$ odd number):

N	**Size** $= (2n-1) \times (2n-1)$	**Removal**
1	1×1	0
9	3×3	4
25	5×5	12
49	7×7	24
91	9×9	40
121	11×1	60
$\vdots$	$\vdots$	$\vdots$

Therefore number of removal $= \sum_{k=1}^{n-1} 4k = 2n(n-1)$. Since N $\approx 1019^2$, $n = 1019$, hence $2 \cdot 1019 \cdot 1018 = 2,074,684$.

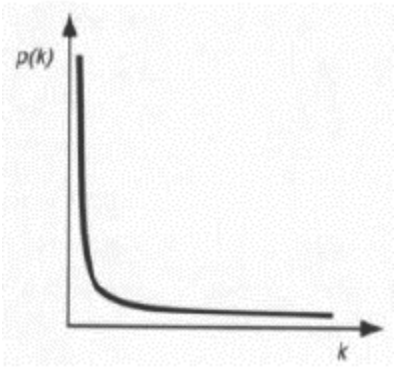
This gives us a more realistic estimate of $\alpha = 0.2$. It is still a large number. Nonetheless, this is the number of people that should be removed in order to isolate every individual.

In the more complex case, where $k = 6$, the following sequence takes place:

N	**Size** $= (2n-1) \times (2n-1)$	**Removal**
1	1×1	0
9	3×3	5
25	5×5	16
49	7×7	33
91	9×9	56
121	11×1	85
$\vdots$	$\vdots$	$\vdots$

The number of removal in this case is $(n-1)(4n-1)$. Plugging $n = 1019$ results in 4,148,350 removals. This is also the case with any $k > 6$. This infers $\alpha = 0.4$, which is still an improvement, though, too large to apply in the real world situation.

In the real world, network between people follow power-law distribution:



This shows that, the more connection there is, the less probability of contact. In addition, regarding the fact that population in Liberia and Sierra Leone is sparsely located(The population density is

$31/km^2$ and $79/km^2$ respectively. The avergage density of 248 countries is $364.387/km^2$). Therefore, we may assume a small number of k, in order to estimate the extent of quarantine.

Lastly we may assume a case where $k = 3$. In this case, the square grid graph is not applicable. This results in the following sequence:

N(n)	**Removal(n)**
1	0
4	1
10	3
22	7
46	15
94	31
⋮	⋮

In this case $N(n) = 1 + \sum_{k=1}^{n-1} 3 \cdot 2^{k-1}$ and removal $= 2^{n-1} - 1$. In this case we can let $n = 23$, so that $N = 12582910$ and the removal $= 4194302$, which is much larger than 2,074,684, which is the case with $k = 4$. When regarding that the estimate of the total number of exposed individuals$(E) =$ 1038600, our first graph model$(k = 4)$ fits the data the best. After all, we do not have to remove 70 80% of population for a quarantine measure. Removal of approximate 20% of the population will assure that there will be no infection by physical contact.

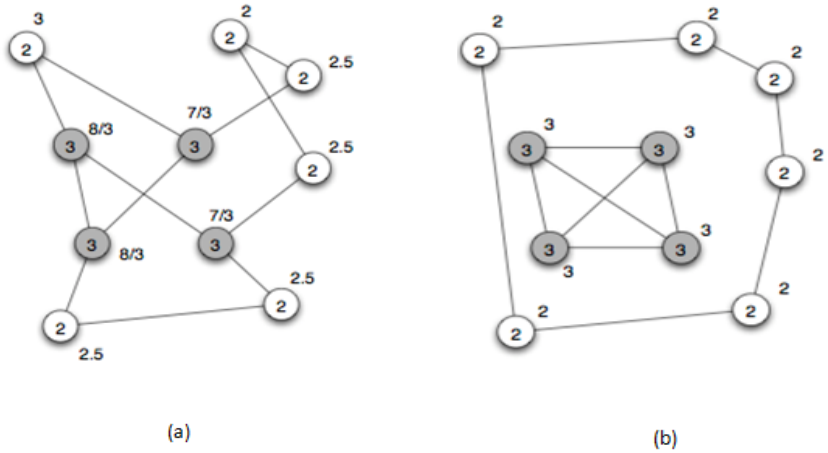
5.2.2. *Vaccination.* We introduce a fifth class of individuals by letting V(t) be the number of individuals who have been vaccinated. We let the vaccination rate be given as a function of time by (t). Thus (t) is the number of individuals being vaccinated per unit time at time t. The differential equations model then becomes:

$$\begin{aligned} \frac{\mathrm{d}S}{\mathrm{d}t} &= -\frac{\beta SI}{N} - \eta \\ \frac{\mathrm{d}E}{\mathrm{d}t} &= \frac{\beta SI}{N} - \delta E \\ \frac{\mathrm{d}I}{\mathrm{d}t} &= \delta E - \gamma I \\ \frac{\mathrm{d}R}{\mathrm{d}t} &= \gamma I \\ \frac{\mathrm{d}V}{\mathrm{d}t} &= \eta \end{aligned} \tag{6}$$

Here, we will have N = S(t) + E(t) + I(t) +R(t) + V(t). Letting (t) = 0 predicts the spread of the infection through the population. From the previous model we know that the resulting spread is unacceptable. Introducing a vaccination program, which is used to prevent the epidemic, could alter the courses of infection. After normalize the dependent variables and treat the proportion of susceptible, exposed, infective, removed, and vaccinated individuals, we will have:

$$\begin{aligned}
\frac{\mathrm{d}\hat{S}}{\mathrm{d}\hat{t}} &= -\frac{\beta}{\gamma}\hat{S}\hat{I} - \hat{\eta} \\
\frac{\mathrm{d}\hat{E}}{\mathrm{d}\hat{t}} &= \frac{\beta}{\gamma}\hat{S}\hat{I} - \frac{\delta}{\gamma}\hat{E} \\
\frac{\mathrm{d}\hat{I}}{\mathrm{d}\hat{t}} &= \frac{\delta}{\gamma}\hat{E} - \hat{I} \\
\frac{\mathrm{d}\hat{R}}{\mathrm{d}\hat{t}} &= \hat{I} \\
\frac{\mathrm{d}\hat{V}}{\mathrm{d}\hat{t}} &= \hat{\eta}
\end{aligned} \tag{7}$$

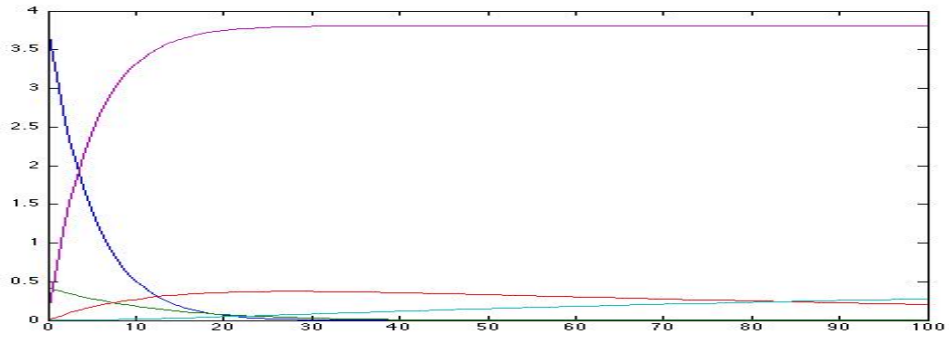
Next, we consider the spread of epidemic in different connection network. Connections between individuals are often described in terms of the mixing pattern of the network. We will consider two types of mixing patters here: **Assortative mixing** and **Proportionate mixing**. Assortative mixing describes situations in which individuals are more likely to interact with other individuals who are similar to them in some respects; Proportionate mixing (or random mixing) occurs when interactions have no particular preference.



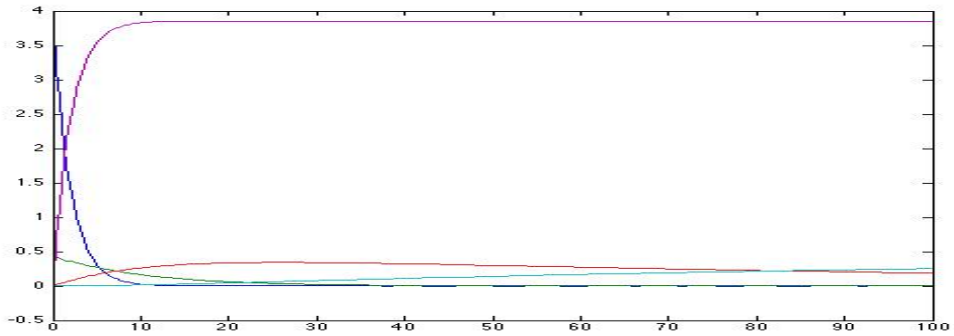
The networks exhibit (a) proportionate, and (b) assortative mixing patterns. In each case, the network has six individuals who have two neighbors and four individuals who have three neighbors. In each case, the average connectivity of individuals is 2.4. The connection pool contains in total 62+43 =24 elements with equally weighted proportion from both six individuals and four individuals.

From the graph above we know that for proportionate mixing, the average connectivity of the neighbors of individuals (2.5) exceeds that in assortative mixing pattern (2.4). Based on this fact, we will raise the vaccination rate relatively in proportionate mixing pattern compared to assortative mixing pattern. Setting $\eta(t) = 0.5$ for proportionate mixing patterns in both Sierra Leone and Liberia and $\eta(t) = 0.2$ in assortative mixing patterns in both Sierra and Liberia, together with the initial condition, we will have:

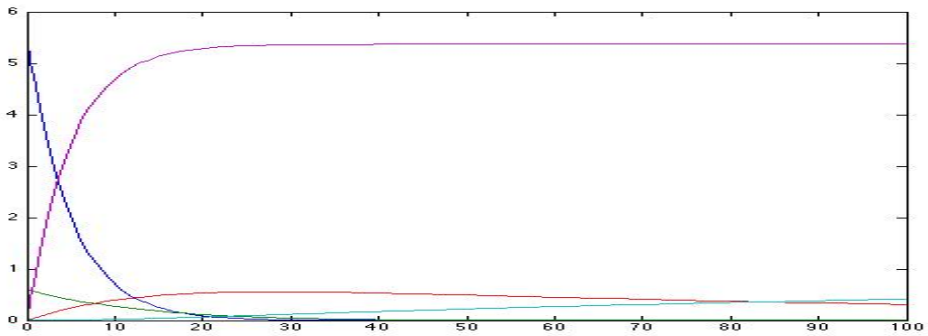
(A)Liberia with $\eta(t) = 0.2$



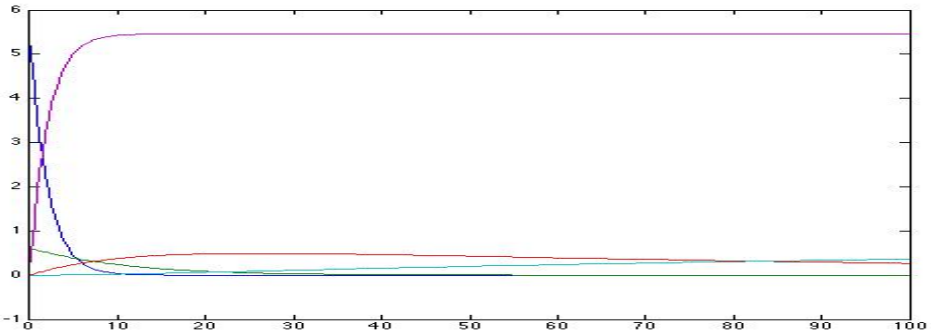
(B)Liberia with $\eta(t) = 0.5$



(C)Sierra Leone with $\eta(t) = 0.2$



(D)Sierra Leone with $\eta(t) = 0.5$



5.2.3. *Delivery.* At the outbreak of an epidemic such as Ebola, a prompt delivery of medical supplies is crucial in thwarting the growth of the plague. This section considers the problem of delivering medical supplies to cities that have reported infectious individuals. The complexity of this problem is self-evident: numerous factors can influence the best way of delivery: the distance from the cities to the national medical center where a delivery car is dispatched, the reported number of infectious individuals (I), the rate of increment in the number of infectious patients ($\mathrm{d}I/\mathrm{d}t$), etc. To discuss this problem in a concrete manner, first we need to formally define our problem.

Suppose n cities $C_1, \ldots, C_n$ have found and reported instances of infectious individuals. Denote by I_i the current (reported) number of infectious individuals found in city C_i. The numbers I_i's are not constants, obviously, as they may increase or decrease over time. In order to distribute medical supplies to the infected cities, the national medical center C_0 wants to visit every infected city C_i in such an order that minimizes the total number of infectious people.

Define a *Hamiltonian path* P to be a path that traverses the medical center as well as each city exactly once in some order $P : C_{\pi(0)} \to \cdots \to C_{\pi(n)}$ where $\pi(\cdot)$ is the permutation function. We use $\pi_{\mathcal{P}}(i)$ to indicate the index of C_i in the path $\mathcal{P}$. For ease of notation in the rest of the paper, we drop the subscript and simply write $\pi(i)$ when the path $\mathcal{P}$ is clear from the context. Then our goal is to find a Hamiltonian path $\mathcal{P}$ starting at C_0: $C_{\pi(0)} \to \cdots \to C_{\pi(n)}$ that minimizes the following sum:

$$\sum_{pq \in \mathcal{P}} t_{pq} \sum_{\pi(k) > \pi(p)} (I_k + \frac{\mathrm{d}I_k}{\mathrm{d}t}) \tag{8}$$

Note that $\pi(0) = 0$ as all paths in the context of this problem start at the medical center. In (8), $I_k + \frac{\mathrm{d}I_k}{\mathrm{d}t}$ is summing over all cities C_k that will be visited later than C_p in the path $\mathcal{P}$.

This problem can be thought of as a generalization of the famous Traveling Salesman Problem(TSP), which is NP-hard. The goal of the classical TSP is to find the *shortest possible route* that visits each city exactly once. The "weights" of the edges in TSP are distances between cities, hence are constants. Our delivery problem is harder than TSP since the weights of the edges in our problem are in nature much more complex to compute and it is thus impossible to find an efficient algorithm that solves our delivery problem specified in (8). Despite this, since the number

of infected cities tend to be reasonably small, one can simply try all $n!$ permutation of the cities to find an optimal ordering.

6. Conclusion

The world is currently having a difficult time fighting ebola virus. Nonetheless, the deadly virus must be dealt with. This is not merely fighting against a disease. This is an event where different nations and companies cooperate for the common cause. Mankind may face similar situation, or worse. Coming up with an efficient solution for this problem will definitely contribute to the challenges that we might face in the future. In this paper, we came up with a mathematical model that can be applied to the fight against ebola. First, we applied a rudimentary SEIR model, then added three intervention variables that will offset the limits of the original model.

According to the original model, the number of people we need to remove as a part of the quarantine measure is too large to apply. Therefore, a graph model is used to cope with this problem. By doing so, we can reduce the removal rate by 50 60%.

In case of vaccination, we used the linear model. In the real setting, the case may be more complex. On the other hand, by simulating the difference according to the vaccination rate, we were able to figure out the optimal vaccination rate. Then we constructed a mathematical model for optimal delivery of vaccine. This model may have its limits, though, it was built upon strong data. It has a more realistic approach to solving the problem, which will work much more efficiently under the premise that the current cooperation remains.

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