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2015 Mathematical Contest in Modeling (MCM) Summary Sheet
(Attach a copy of this page to each copy of your solution paper.)

Abstract

The first recorded Ebola outbreak occurred in Nzara, South Sudan in 1967 which infected 284 and killed 151. Since then, Ebola outbreak occurs frequently and there are nearly 20 cases of major or massive outbreaks till now, the most recent of which is the case in Liberia, Guinea and Sierra Leone in 2014. The case fatality rate ranges from 25%(Uganda, 2007) to 90%(Republic of Congo, 2002). Considering its high fatality rate and damage to human society, it is highly valuable to study the property of the spread of Ebola and to find out feasible strategy to fight against the virus.

In this paper, we attempted to untangle the convolution of parameters and variables concerning the spread of Ebola and to give a constructive suggestions regarding what strategy should be taken to deliver limited amount of drug and vaccine. Also, we planned to give an optimized plan to deliver vaccine and drug under a simplified case based on the real case of the recent outbreak in west Africa.

We constructed models based on the biological features of EVD, social features of human society and several reasonable assumptions. Our models consist of two parts: one is considering the the spread of disease within a single city with SIR model and serves as the base of the other; the other takes the people flow among the cities into account, the application of which gave us an optimized plan regarding how should we allocate the resources of medication such as vaccine. In fact, our model is a combination of classic SIR model and graph theory, which is a simple method to solve geography related disease spread problem.

Both of the models were applied to specific cases separately, and the results of computation which were carefully studied justified our model. Through our analysis of the model, we explored and explained the complex relationship among numerous variables and parameters. Then we find the existence of threshold values for those relationship, which indicates a limit condition for outbreak. According to the analysis and literature's instruction, we put forward our own criterion.

The effectiveness of medical treatment (including segregation, vaccination and pharmacotherapy) is verified by our model and the strategy to allocate vaccine and drug is revealed by our investigation. Specifically, the amount of vaccine or drug delivered to each city should be roughly proportional the scale of the city and the amount of vaccine or drug allocated per capita should be larger for the cities in the center of people flow network.

Contents

1 Introduction

Ebola virus disease (EVD), which is also called Ebola hemorrhagic fever or simply Ebola, is an infectious disease caused by one of the Ebola virus strains, alongside high lethality and rapid epidemicity. EVD was first discovered in 1976 near the Ebola river. Since then, outbreaks have appeared sporadically in Africa. In 2014, the largest outbreak of the disease occurred in West Africa and caused thousands of cases of death.[6] Due to the severity of its outbreak, a feasible method is required to outline its progression and to predict its trends, thus being able to form a strategy fighting against infectious diseases like EVD.

1.1 The problems we concern

As is known to all, the spread of EVD is influenced by various factors. Knowing these factors and the role they played can give us a depper understanding of EVD. Therefore, we are eager to figure out factors influencing the spread.

Another problem lies in the delivery system of drug and vaccine. Since *the World Medical Association* has announced a new medication (as is stated in the problem), the quantity and location of medication delivery became a problem of great concern. Considering that pharmaceutical industries may not capable of manufacturing enough drug and vaccine, we need to optimize the delivery plan to suppress the spread of EVD.

1.2 The models we are to construct

In this paper, our purpose is to construct mathematical models that can effectively solve these problems. To meet the goal, we attempt to divide the model into two main parts.

Firstly, we want to construct an initial model discussing the spread of disease in a single city. Some main factors that influence the spread of disease are considered in this model, but the influence and interaction with other cities are not included. This model can describe, at least roughly, the development of EVD in the city after some citizens are infected and measure the importance of different factors, but the spread among cities still cannot be seen. Accordingly, the optimized delivery plan cannot be made with the aim of this single model.

Secondly, we are going to construct a multiple-city model based on the first model. In this model, cities are connected by specific relation, thus allowing pathogen spreads from one city to another. This model can be used to describe the spread of disease in a rather vast geographic regions. With the aim of this model, we use genetic algorithm (GA) to optimize delivery plan.

2 Background

In this part, we would introduce some natural characters of EVD and historical records of EVD outbreaks. This will help us understand how it spreads and determine appropriate values for the parameters in our models, such as infection rate, recovery rate, etc.

2.1 Characters of Ebola and its spread

Many factors related to Ebola influence the spread of EVD or influence the construction of our models. These factors are divided into **Social factors** and **Biological factors** and they are

listed as follows.

2.1.1 Biological factors

- **Infectiousness**
  Infectiousness directly affects the disease's infection rate, which is defined as morbidity rate for uninfected people but exposed to virus carriers. And infectiousness is mainly affected by virulence of the virus and individual's immunity. In most cases, diseases' infection rate is regarded as constant.

- **Lethality**
  Lethality is how capable a disease is of causing death. It can be described by lethality rate, the ratio of the dead to the total patients. EVD has an average fatality rate of $55\% - 80\%$. Moreover, Individuals who was infected and cured won't be infected again in next ten years.

- **Incubation**
  Incubation means that there is a period during which the infected shows no sign or symptom of the disease and is not contagious[6]. Therefore, there may be difficulty to segregate people with infectious diseases. EVD's incubation period is 2 to 21 days.

- **Route of Transmission**
  EVD is mainly spread through direct contact with blood and body fluids of infected ones[6]. These routes of transmission are highly connected to public health situation and personal hygiene.

- **Environmental Condition**
  Ebola virus has moderate tolerance to heat, which indicates that EVD maintains a high infectiousness in most of human settlements. However, Ebola virus will be inactivated when exposed to a temperature over 60° for 60 minutes. Environment also affects the spread of EVD in aspect of natural reservoir. Though the reservoir remains unknown, it is reasonable to infer that contact with wide animals adds to the probability of getting infected.

2.1.2 Social factors

- **Population**
  In general, a large population means high potential of disease's spread. People in a populous area have a greater frequency of contacting the others than those in a sparsely populated area. According to the route of transmission, it is obvious that the probability of getting infected would be larger.

- **Traffic**
  Convinient traffic encourages population mobility, which contributes to the spread of EVD. However, It also encourages freightage, including medicine.

- **Medical Level**
  A society will be less affected by EVD if proper measures are taken efficiently and promptly. These measures include segregating patients and strengthening the sanitary control of public places. The manufacture of drugs and vaccines aiming at EVD is also an important part.

- **Regional Custom**
  Funeral is considered solemn in the African culture. The dead should be cleaned, kissed and touched before buried. This kind of culture facilitates EVD infections.

- **Other Social Factors**
  The spread of diseases is also influenced by factors like social development, health situation, individual's living condition, etc. These factors are not considered to simplify our models.

2.2 Information about the last break of Ebola in 2014

In 2014, the largest outbreak of the disease occurred in West Africa, affecting multiple countries mainly including Guinea, Liberia and Sierra Leone.[6]Up to February 4th, there have been 22,495 reported confirmed, probable, or suspected cases of EVD worldwide, with 8981 reported deaths. Among these reported cases, 99.84% of the cases (22,460) are reported in Guinea, Liberia or Sierra Leone, thus showing a strong regional characteristic and suggesting that we should focus our study mainly within these countries.

3 Previous work

Controlling the spread of infections is by no means a new problem, and many models have previously been used to describe the distribution and spread of epidemic diseases.

The models previous scientists used can mainly be divided into three categories. Brief overviews of the three by the sequence of their advent are as follows.

1. ***Standard SIR(susceptible-infected-removed) models and its deriveratives:*** The model is first put forward by **Kemraek** and **MeKendriek** in 1927[1]and is the most classic model. Many successive models are based on it. It regards the epidemic area as a whole and divides people into different groups, such as susceptible group, infected group and removed group. It depends on differential equations to describe the relationship between volumes of different groups, thus making scientific and quantitative description. Details of the model will be explained in the successive sections.

   Many other models are derived from this very basic SIR model, such as SIS model[2] which deals with situations where a infected and later recovered individual can turn back to be a susceptible individual, and SEIR model[4] which deals with the situations where incubation period of the epidemic disease is not negligible. Previous scientists gained great achievements by using SIR model - they simulated the trends of epidemic diseases, calculated the rough volume of each group in different periods of epidemics and, most importantly, successfully analyse the contribution of different parameters to stability of system.

   Despite the fundamental and important standing of SIR model, its drawbacks are easy to realize. It is difficult to study geographic characters of the spread of diseases, because the model doesn't contain any geographic information. Also, each person in the system is not individually recognized and the complex relationships among individuals are hardly considered, since it regards the epidemic area as a homogeneous system - in another word, each person in the system is just like a molecule in a cup of water and the relationships of any two pairs are identical. Additionally, it is a deterministic model witch hardly resemble the factual system in which many fortuitous factors matter.

2. ***Statistical model:*** This model is less intensely studied than the other two models. In this model, researchers mainly use possible functions whose forms are known but parameters unknown to fit the currently available data, aiming at predicting the trend of epidemics. Although the model is somewhat phenomenological and catch little intrinsic logic, it is quite useful in real practice and it allows us to have a quick view of the trend without getting convoluted into the depth of the problem. Anyhow, we will not go further into this kind of models.

3. ***Spatial simulation model:*** This category of models are the focus recently. They mainly contains models using cellular automaton (CA), models considering networks among people(eg. small world network), models using GIS[5], etc. Take models using CA as an example. We define different types of points, which are put in lattices of a plane, and regard the spread of diseases between people as the interaction between nearby points. The process of evolution and spatial distribution of virus can be simulated with the aid of computer program. Clearly, due to the consideration of individuals separately, the results are more accurate than previous two categories.

   This category of models taking the relationship among people and geographic information into account has advantages over others when figuring out the geographic characters of the spread. Moreover, it can give more accurate results since its high resemblance of real situation. Accurate as the models are, they are highly complicated and some of them are difficult to apply both for the complexity of programming and great amount of computation.

4 Models for a single city

In this section, we consider a single-city model, in which we use classic SIR [1] model to simulate the spread of disease.ignore the geographic factors between cities and complex relationships between individuals.

To construct our model, we should at first quantify the severity of the spread of disease. In our model, we mainly used fatality to represent the severity. Other parameters, such as the number of infected people, are representing the severity of the spread of epidemic disease, but what these parameters represent for are eventually reflected by the total death due to the disease. Hence, we chose fatality as the ultimate indicator of severity of spread.

We have outlined seven main factors to be discussed: **infectiveness** (whether the epidemic disease is easy to transmit from one person to another), **lethality** (how lethal is the disease), **incubation** (how long between infection and being infectious/symptomatic), **route of transmission**(air borne transmission, droplet transmission, contact transmission, etc.), **medication** (segregation, drug and vaccine), **population**, **flow of people**. The first four are the properties of epidemic disease and are determined by specific category of disease. The fifth is the concerned factor - we want to know how these factors influence the spread of epidemic diseases. The last one will be discussed in the next section of our article.

Our single-city model is based on the SIR model, and we adopted the classic model for the special case of EVD. Details of our model are shown as follows.

4.1 Symbols

Below are listed symbols we will use.

Symbol	Defination
$\mathcal{N}$	total volume of population in the city
$\mathcal{S}$	number of susceptible people
$\mathcal{I}$	number of infected but not segregated people
$\mathcal{G}$	number of segregated and also infected people
$\mathcal{D}$	number of death caused by EVD
$\mathcal{R}$	number of recovered people (also immunized)
$\mathcal{P}$	Total number of people in the city apart from the people who are dead and segregated
$\mathcal{C}$	the average number of people a single infected patient can have "close contact" with per day
β	infection rate
$days$	total number of days calculated
h	infection factor
T_{avg}	average period of time one remains infected
g	rate of infected people who become segregated per day
k_1	Probability of fatality per day when infected without medication
k_2	Probability of fatality per day when infected with segregation
r_s	Probability of natural recovery per day when infected
r_g	Probability of recovery with segregation per day when infected
$vacc$	number of susceptible people that can be vaccinated per day
$drug$	number of shares of drugs that can give to the segregated people

Table 1: The definition of the symbols.

4.2 Assumptions

- **Ebola spreads only by person-to-person transmission**
  Because the natural reservoir host of $Ebola$ viruses has not yet been identified, we ignore the possibilities that people becomes infected through contact with an infected animal.

- **Infection rate remains constant**
  In our model, medication or other measures make no difference to the infection rate. It is merely determined by diseases' intrinsic properties.

- **Difference among people can be neglected**
  Though most people contact with different people each day, we assume that they are in the same condition when the virus breaks out. This assumption also implys that the probability of any two people contact each other remains constant.

- **The Probability of death and recovery remain the same among the period of the disease**
  In reality, different periods of the disease show different characters, which is too complicated to be embodied in mathematical models. It is unwise to take this factor into our consideration.

- **The mutation of Ebola virus during the spread can be neglected**
  It takes a long period for Ebola virus to mutate. In the single-city model, we only focus on one certain outbreak. So the probability of mutation can be ignored.

- **The disease is the only factor of population change**
  Other factors, like birth or car crash, can also influence the city population. To fully embody the effect of EVD as well as simplify the model, these factors are not considered.

- **Recovered people are also immunized**
  According to what is mentioned previously, recovered people will be immunized in the next 10 years, which is a long time compared with epidemic period. Hence, it justifiable for us to suppose that recovered people are also immunized.

4.3 The construction of model

4.3.1 Group classification

In our model, we consider a single city or community. **N** refers to the total volume of population. According to the roles different people play in the spread of diseases, we mainly divide them into five groups.

- **Susceptible**
  People who have little immunity to EVD. They have a certain chance to become infected after being exposed to infected ones according to the infection rate.
- **Infected but not segregated**
  People who are infected with EVD. But for some reasons, they are not segregated so far. They cannot receive effective medical treatment.
- **Infected and segregated**
  People who are infected, recorded and sent to social medical institutions. These people are able to take medical treatment.
- **Dead**
  People who died because of the infection of EVD.
- **Recovered(immunized)**
  People who have been cured or naturally recovered from EVD. These people have immunity to EVD and will never be infected again in next 10 years. People who were vaccinated are also divided into this group.

4.3.2 Processes in the spread of disease

In the single-city model, different groups are analyzed separately. As figure 1 shows, the relationship between different groups is described as following seven processes. Labels in the figure are corresponding to the labels below.

1. **Infection process**
   The disease spreads from the infected to the uninfected through the means of contact infection. To quantify this progress, we defined the infection factor h, which represents for the probability of infection for a person who has "close contact" with one patient. Mathematically, h is given by
   $$h = \beta \frac{C}{\mathcal{N}} \tag{1}$$
   where β is the infection rate of the disease which is the intrinsic property of pathogen. C is the average number of people a single infected patient can have "close contact" with per day. $\mathcal{N}$ stands for the city population.

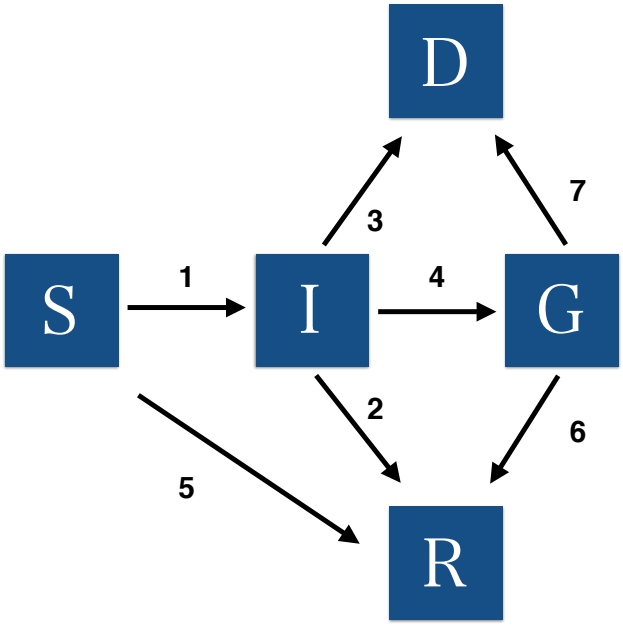


Figure 1: The processes in the spread of disease (also the relationship among the five groups of people)

2. **Natural Recovery process**
   EVD is not 100% fatal. Some patients may naturally recovered without medical treatment. This progress is quantified by r_s, the recovery rate without medication per day, in another word, what percentage of the infected can recover without any medication each day. It is defined as

$$r_s = \frac{\text{number of people become recovered in the day}}{\text{number of infected people till the day}} \quad \text{(without any medication)} \tag{2}$$

3. **Natural death progress**
   Those who are infected and do not receive any medical treatment stand a great chance of dying. This progress can be described by k_1, the fatality rate without medication per day. It is defined as

$$k_1 = \frac{\text{number of people die in the day}}{\text{number of infected people till the day}} \quad \text{(without any medication)} \tag{3}$$

4. **Segregation process**
   Some of the infected would be segregated by the health organization. In our model, this process is quantified as g, the probability of infected persons being segregated per day. g is raised because not all the patients can be recorded and there may be some omissions. Also, diagnosing Ebola in a person who has been infected for only a few days is difficult because the early symptoms, such as fever, are nonspecific to Ebola infection and are often seen in patients with more common diseases. In this case, some patients would not be segregated in time. the value of g is given by

$$g = \frac{\text{number of people get segregated in the day}}{\text{number of infected but not segregated people till the day}} \tag{4}$$

5. **Vaccination**
   Susceptible people would become immunized through vaccination and could be added

to the recovered group. This process is determined by the number of shares of vaccine, so we defined $vacc$ in our model, which stands for the number of shares of vaccine. In another word,

$$vacc = \text{number of shares of vaccine the city can allocate per day} \tag{5}$$

6. **Cure process**
Part of the segregated would be cured by drugs. This process is influenced by the amount of drug used and the drug's effectiveness. We use r_g, the recovery rate when segregated per day, to describe the process. r_g is defined as

$$r_g = \frac{\text{number of segregated people become recovered in the day}}{\text{number of segregated people till the day}} \tag{6}$$

and given by

$$r_g = c\frac{drug}{\mathcal{G}} + \left(1 - c\frac{drug}{\mathcal{G}}\right) r_s = r_s + (1 - r_s)c\frac{drug}{\mathcal{G}} \tag{7}$$

Where c is the effective rate of the drug; $drug$ is the number of shares of drugs the city can allocate per day; and $\mathcal{G}$ is the population of the segregated group. Given that $\mathcal{G}$ is a variable, r_g is not a constant. According to the problem statement, the drug aiming at EVD can cure those who are not infected for too long. We roughly assume that the percentage of people whose disease haven't advanced remains unchanged, and c is the corresponding parameter.

7. **Medication failure process**
Due to the amount of drug and the drug's effectiveness. Not all individuals can be cured after segregation. Some of the infected may die. This process is described by k_2, fatality rate with segregation per day. k_2 is defined as

$$k_2 = \frac{\text{number of segregated people die in the day}}{\text{number of segregated people till the day}} \tag{8}$$

and given by

$$k_2 = (1 - r_g)k_1 \tag{9}$$

k_2 is also not a constant.

4.3.3 Mathematical expression of the model

Finally, the model can be mathematically expressed as

$$\frac{d\mathcal{S}}{dt} = -h\mathcal{S}\mathcal{I} - vacc \tag{10a}$$

$$\frac{d\mathcal{I}}{dt} = h\mathcal{S}\mathcal{I} - (k_1 + r_s)\mathcal{I} - g(1 - k_1 - r_s)\mathcal{I} \tag{10b}$$

$$\frac{d\mathcal{G}}{dt} = gI - k_2\mathcal{G} - r_g\mathcal{G} \tag{10c}$$

$$\frac{d\mathcal{R}}{dt} = r_s I + r_d\mathcal{G} \tag{10d}$$

$$\frac{d\mathcal{D}}{dt} = k_1 I + k_2\mathcal{G} \tag{10e}$$

4.4 Analysis of the model

This single-city model turns out to be a multivariable model, in which C, g, $vacc$ and $drug$ are independent variables that determine the variables $\mathcal{N}, \mathcal{S}, \mathcal{I}, \mathcal{G}, \mathcal{D}, \mathcal{R}$. r_s, k_1 and c are fixed parameters that indicate the factual characters of EVD and the drug. These parameters should be correctly set and to make our model credible.

4.4.1 Parameter settings

According to the data, EVD has an infection rate of 32%, alongside an average fatality rate of 70%. So β can be directly set to 0.32.

As for r_s and k_1, they are both "every-day probability", which means we need to transfer the actual data of EVD into this form. on the basis of the forth assumption, k_1 can be given by

$$k_1 = \frac{0.7}{T_{avg}} \tag{11}$$

Where T_{avg} represents for the average period of time one remains infected. This identity is not mathematically strict, but enough for us to obtain a rather rational result. Considered that the infected end up either dead or recovered, The total recovery rate is simply 0.3.

$$r_s = \frac{0.3}{T_{avg}} \tag{12}$$

Essential as it is, we can't find the accurate data of T_{avg}. So we manually set it to 30 days according to literature. In accordance with it, r_s and k_1 are respectively set to 0.01 and 0.023.

No reliable data about the medication was found, including the drug's effectiveness. After referring to the data of other diseases and estimation, we believe it is plausible to assume the percentage of patients can't be cured by drugs is 20%. c is finally fixed to 0.8.

4.4.2 Connection between reality and independent variables

The porpose of generating model is to simulate the spread of EVD in reality, thus demanding us to figure out the relationship between variables and real world events. The main practical factor we considered in this model is medication, namely segregation, drug and vaccine. We now try to use independent variables to quantify these three separate parts:

- **Segregation**
  Segregation is consist of two methods. The first is that the infected would be sent to a centralized place to avoid any direct contact with others. This measure would decrease the possibility of the infected spread virus to others. g can be used to quantify the effectiveness or intensity of segregation. The more a society concentrate on segregation, the higher g will be. The second method is decreasing the frequency of individuals going outside and contact with other people to reduce the possibility of susceptible individuals getting in touch with the infected, accordingly decrease the value of C. So C is also a measure of segregation intensity.

- **Vaccination**
  Vaccination, in line with ordinary conception, can reduce the total number of susceptible individuals and constrain the spread of EVD. In our model, vaccine is assumed absolutely

effective, those who received vaccination will be transferred from susceptible group to recovered group once for all. As a result, the only variable linked to vaccination is $vacc$, which indicates the number of vaccine used every day.

- **Drug delivery**
  The drug would cure patients whose disease is not advanced. So the use of drug would decrease the number of the dead. People who were cured are divided into the recovered group. So it also affects the the share of susceptible group and would decrease the number of the infected. As the effectiveness of the drug is fixed in our model, the main factor that influence the effect of drug use is the amount of the drug, variable $durg$. $drug$ can also indicate the pharmaceutical factories' capability of manufacturing the drug.

4.5 Numerical computation of the model

4.5.1 Method of numerical computation

We are going to use numerical integration method to analyze a supposed case. As for practical case of numerical integration we should firstly convert the differential equations previously derived to difference equations that can be applied to numerical computation. Secondly, we should consider several boundary conditions that matter the process of numerical computation.

Previous derived differential equations can be transformed into difference equations as follows.

$$\frac{\mathcal{S}_{i+1}-\mathcal{S}_i}{\Delta t} = -\frac{h}{\sigma}\mathcal{S}_i\mathcal{I}_i - \frac{vacc}{\sigma} \tag{13a}$$

$$\frac{\mathcal{I}_{i+1}-\mathcal{I}_i}{\Delta t} = \frac{h}{\sigma}\mathcal{S}_i\mathcal{I}_i - \frac{(k_1+r_s)+g(1-k_1-r_s)}{\sigma}\mathcal{I}_i \tag{13b}$$

$$\frac{\mathcal{G}_{i+1}-\mathcal{G}_i}{\Delta t} = \frac{g}{\sigma}\mathcal{I}_i - \frac{k_2}{\sigma}\mathcal{G} - \frac{r_g}{\sigma}\mathcal{G} \tag{13c}$$

$$\frac{\mathcal{R}_{i+1}-\mathcal{R}_i}{\Delta t} = \frac{r_s}{\sigma}\mathcal{I}_i + \frac{r_d}{\sigma}\mathcal{G}_i \tag{13d}$$

$$\frac{\mathcal{D}_{i+1}-\mathcal{D}_i}{\Delta t} = \frac{k1}{\sigma}\mathcal{I}_i + \frac{k_2}{\sigma}\mathcal{G}_i \tag{13e}$$

σ is time-scale factor, since the converting rates from one group to another($h\mathcal{I}$,g,k_1,r_s,k_2 and r_g) are defined in the terms of one day. These converting rates are derived by σ to get a proper dimension of the equation. Obviously, σ and Δt should satisfy that

$$\Delta t \cdot \sigma = 1(day) \tag{14}$$

4.5.2 Other details of numerical computation

There are also some initial conditions, boundary conditions and the specific values of parameters that should be considered.

1. **Initial condition**
   At first, there are few infected people in the city - in our special case, we set the number to 10. All the other people in the city are supposed in "susceptible" group, and none is in "segregated", "recovered" or "dead" group.

2. **Boundary condition**
   The number of people in each group cannot be a negative number. If the volume of one group is zero, no one will be removed from the group.

   If the volume of drugs or vaccines is larger than the quantity they can be utilized (that is the number of shares of drugs or vaccines is greater than the volume of segregated or susceptible people correspondingly), the drugs or vaccines can be restored.

3. **Specific values of parameters adopted in the numerical computation**
   We use that the population of the city $\mathcal{N} = 1,000,000$ - which is the scale of a middle city in west Africa; $\beta = 0.32$ - which is based on previous discussion; the number of days that we set for time period limit, if not additionally stated, $days = 150$; also, $k_1 = 0.023$ and $r_s = 0.0103, \Delta t = 0.1(\text{days})$.

4.5.3 Result of numerical computation

In the numerical computation, we observed both outbreak situations (figure 2) and well-controlled situations (figure 3) with the variation of medication configurations (varying g, $drug$, $vacc$ or C).

On the other hand, according to the data on the official cite of WHO, we graphed the time history of the total amount of infected people in Freetown, the capital of Sierra Leone, in figure 4. As shown, the actual speed of the disease spread is somewhere between the speed in the two hypothetical situations with a similar tendency. The consistency between fact and speculation verified the rationality of our single-city model.

In outbreak situations as shown in figure 2, more than 7% of total population die and more people of a considerable proportion are influenced by the disease, whereas in a well-controlled situation only several dozens of people die and several hundreds of people influenced by the disease. It is clear that, in this outbreak situation, the relative small amount of vaccine (compared with the configuration in figure 3) accounts for the outbreak of the disease.

Apparently, $vacc$ is not the only variable influencing the system output. So we separately studied the influence of the four independent variables (g, $drug$, $vacc$ and C) on the ultimate fatality. The influence of them are shown in figure 5(a), 5(b), 5(c) and 5(d).According to figure

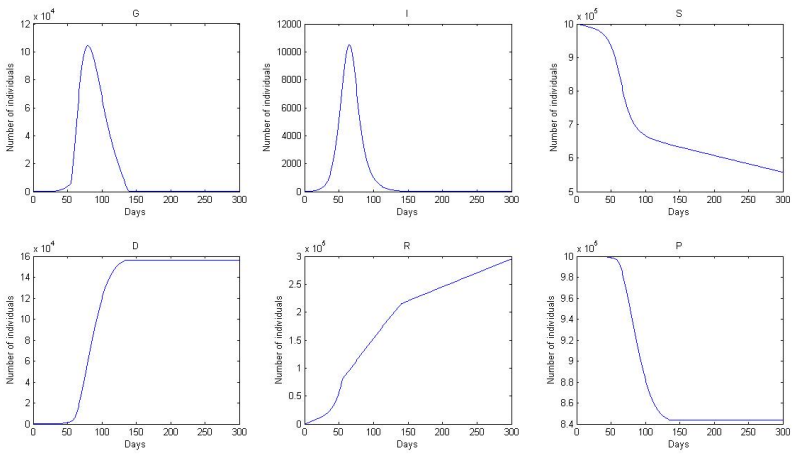


Figure 2: epidemic disease outbreaks with medication configuration: $g = 0.8$, $C = 3$,$drug = 1000$,$vacc = 500$

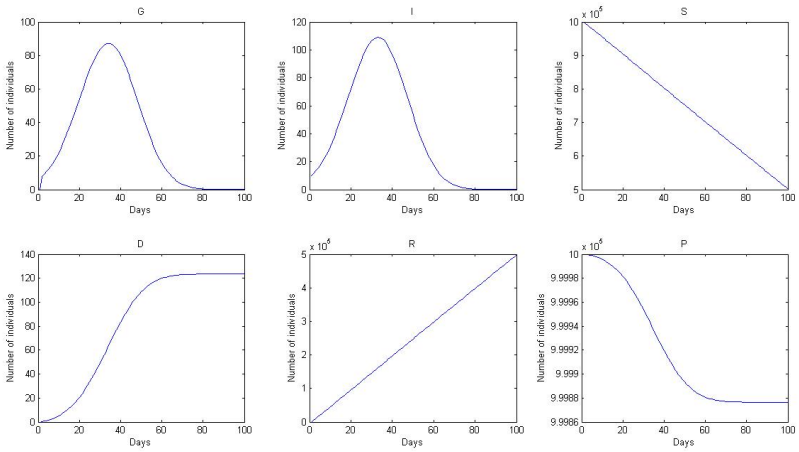


Figure 3: epidemic disease get controlled with medication configuration: $g = 0.8$, $C = 3$,$drug = 1000$,$vacc = 5000$

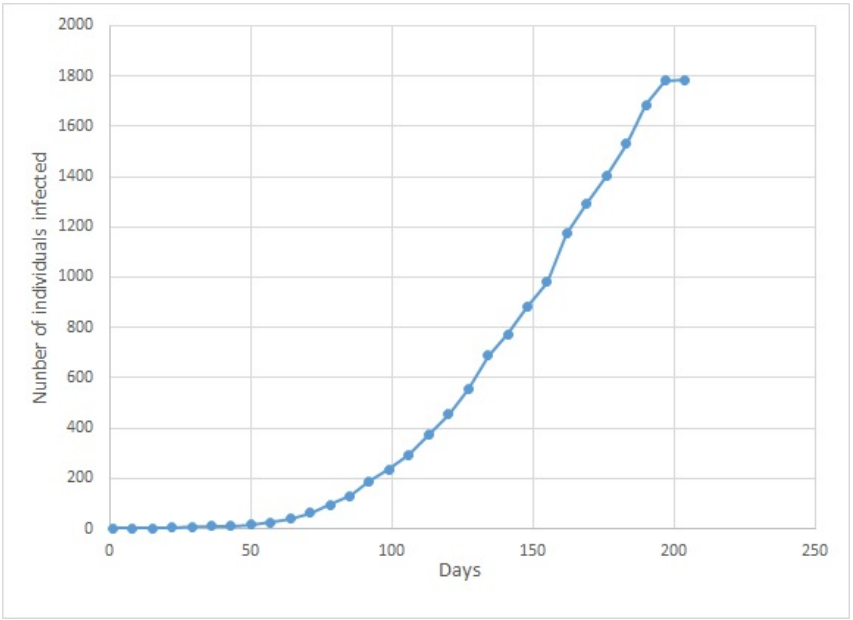


Figure 4: The spread of EVD in Freetown

5, we can affirm that all the four independent variables have significant impact on the fatality. Qualitatively, the ultimate fatality will be decreased with higher g, $vacc$ or $drug$, or increased with a higher C.

A turning point can be spotted in each graph of figure 5, where the gradient of graphs changes tremendously. It stands for a threshold value for each of the variables in our model. In figure 5(a), 5(b) and 5(c), the ultimate fatality remains small and nearly invariable after passing through the threshold. While in figure 5(d), the ultimate fatality rockets on the right side of the threshold. It is not predicted by us when constructing the model. With the model's credibility confirmed, a plausible explain of the threshold is required.

In literature [3], parameter R_0 is used to judge whether an outbreak would occur. R_0 is defined as the amount of people a patient can infect during the infection on average. If R_0 is less than 1, which means the population of the infected keeps dropping over time, the disease will not spread. Otherwise an outbreak is destined. In our model, the number of people who are infected and segregated every day is given by

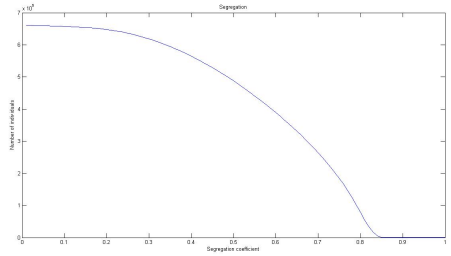
$$\text{number of the people infected per day} = \frac{\beta C \mathcal{S} \mathcal{I}}{\mathcal{N} - \mathcal{D}} \tag{15}$$

$$\text{number of the people segregated per day} = g\mathcal{I} \tag{16}$$

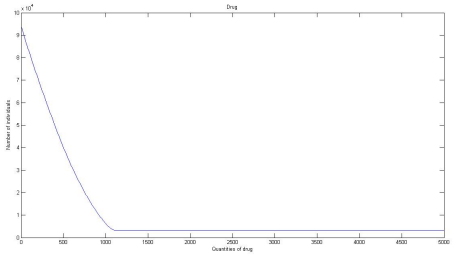
Follow the same idea in literature, we can quantitatively define an outbreak as bellow

$$\begin{cases} \dfrac{\beta C \mathcal{S}}{\mathcal{N} - \mathcal{D}} < g \text{ outbreak} \\ \dfrac{\beta C \mathcal{S}}{\mathcal{N} - \mathcal{D}} > g \text{ controlled} \end{cases} \tag{17}$$

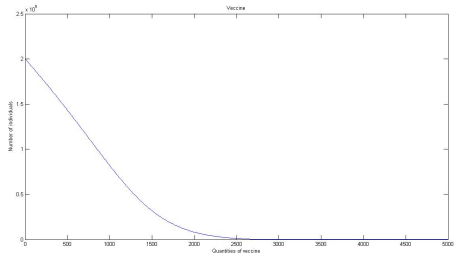
It is easy to find out the independent variables' impact on the so-defined outbreak, and accordingly solve the problem of threshold. Take C for example. In initial status, $\mathcal{S}/(\mathcal{N} - \mathcal{D})$is considered as 1. When $\beta = 0.32$ and $g = 0.9$, which is the exact setting of figure 5(d), The threshold value of C should be about 3. This deduction perfectly in line with the actual output.



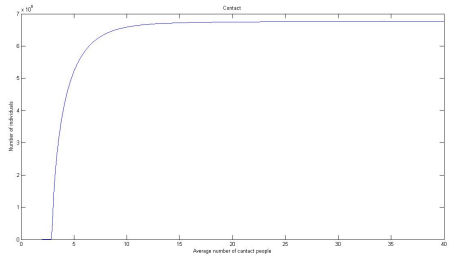
(a) fatality (y axis) influenced by g (x axis)



(b) fatality (y axis) influenced by $drug$ (x axis)



(c) fatality (y axis) influenced by $vaccine$ (x axis)



(d) fatality (y axis) influenced by C (x axis)

Figure 5: the influence of independent variables on the ultimate fatality

Though $drug$ and$vacc$ are not appeared in the definition, they also have an impact on the outbreak as they influence $\mathcal{S}$ and $\mathcal{D}$. However, the threshold of these two variables may disappear as their impact is indirect and deeply affected by the value of β, C and g. This can be a proof of our explain. Figure 6 shows the relationship between the ultimate fatality and $vacc$ with different C. The graphs indicate that there would be no threshold of $vacc$ if g and βC are far from equivalent.

To make the process of outbreak more clear, we choose five points closed to the threshold value for each independent variable and plot the evolution of the number of dead people in these five conditions. Their results are shown separately in figure 7(a), 7(b), 7(c) and 7(d). It is obvious that the progression have a great difference on different side of the threshold.

4.6 Stability analysis

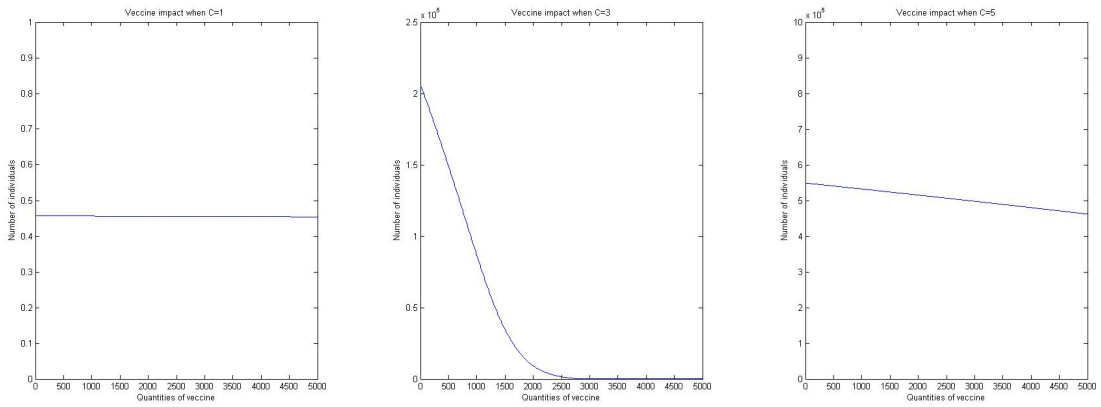
In our model, we choose certain values for some parameters according to the fact. In general it is reasonable. But taking random occasions into consideration, there would be perturbation to these values. This part is to analyze how the perturbation in these constant parameters would affect the spread system.

4.6.1 Analysis to the three parameters

- T_{avg}
  In our model, we set T_{avg} as 30 days according to the fact. Now we change its value and observe its influence. There is a peak in Figure 8 at a value about 50 and 30 days.

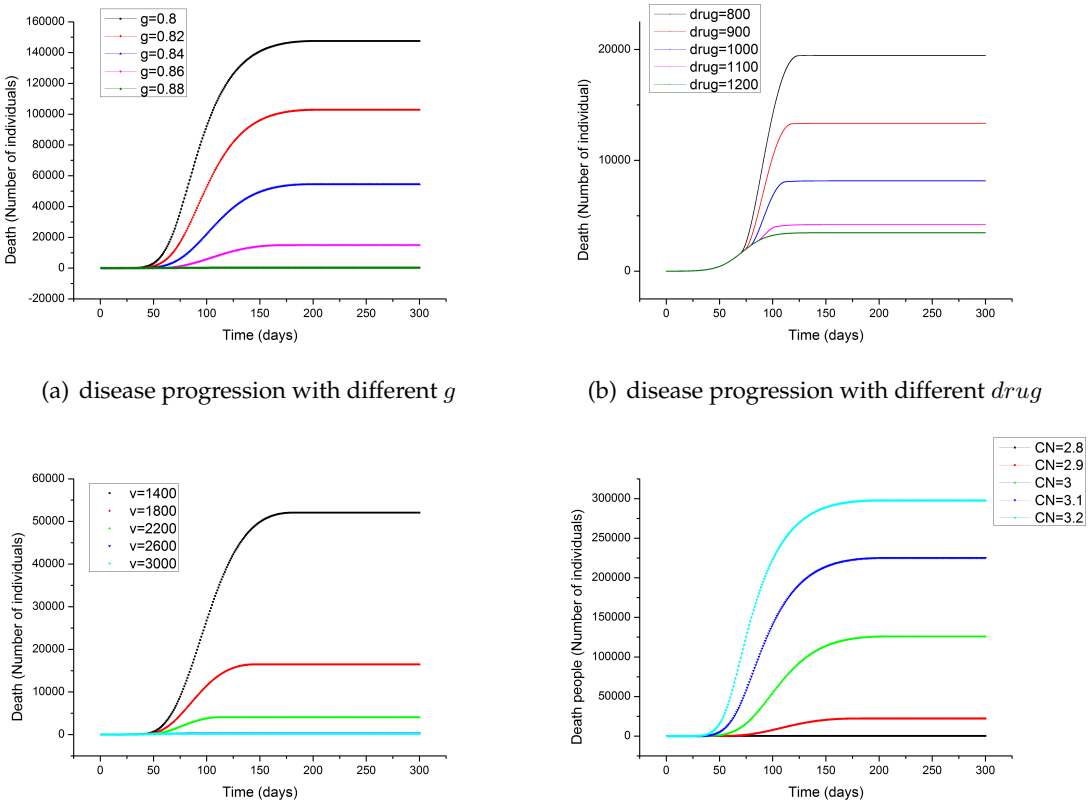
  The result is easy to understand. When the value increases at the beginning, it make the infected live longer and the infection chance would become larger and more people would get infected. Then the dead people would increase. When its value goes over the threshold value, the infected live longer and would increase the chance to receive the drug. Then the dead people would decrease.

- **fatality rate**



(a) $C = 1$ (b) $C = 3$ (c) $C = 5$

Figure 6: fatality influenced by $vacc$ with different C



(a) disease progression with different g

(b) disease progression with different $drug$

(c) disease progression with different $vaccine$

(d) disease progression with different C

Figure 7: disease progression with different value of independent variables

In our model, we set the natural fatality rate as 0.7. We then observed the influence of perturbation in its value. The results are shown in figure 9.

From these curves, We can conclude that the relationship between fatality rate and the number of the dead is almost linear. There is no threshold or peak in this situation.

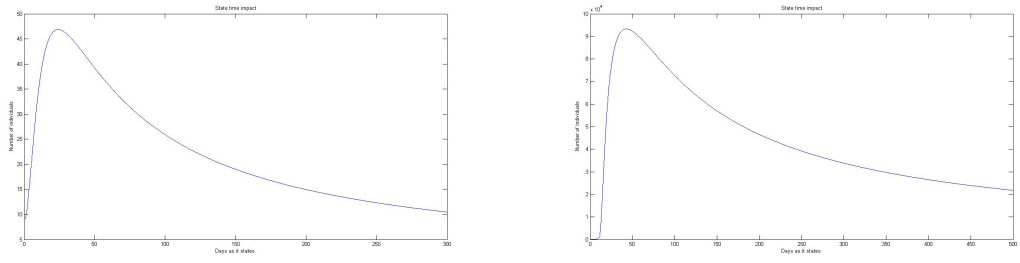
- **Infection rate**
  Figure 10 shows how the amount of the dead changes with β in stable and outbreak conditions. The tendency shows the same character with the C we have mentioned before. This result strongly support our models that it is the product of β and C but not themselves affect the result.

4.6.2 The influence of perturbation

In natural conditions, the perturbation is always under 10%. Then we adjust the value around the standard point and observe the accurate impact. The results are shown in figure 13.

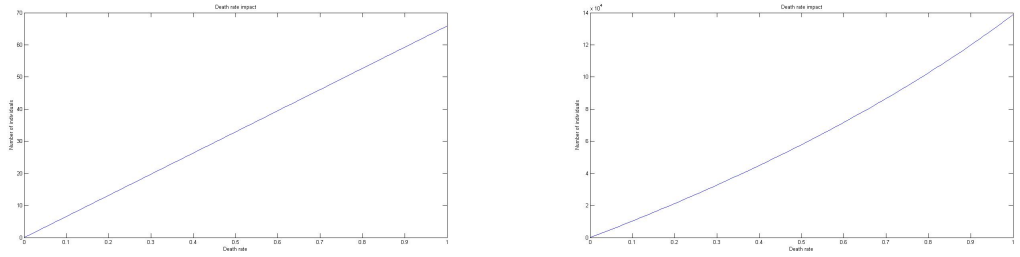
To make the figure more credible and valid, we choose relative variable ratio percentage to describe the perturbation of parameters and the difference of results.

The red points in each of the curve stands for the range of the perturbation. After calculation, we find most of the results' change are less than 10% except for β's impact in controlled situation. That's because its value is around the threshold and are much more sensitive to perturbation than other parameters.



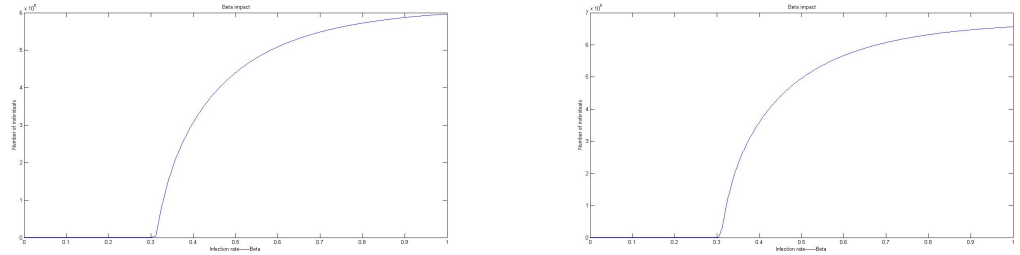
(a) fatality influenced by T_{avg} in controlled situation (b) fatality influenced by T_{avg} in outbreak situation

Figure 8: The influence of perturbation in T_{avg} in two situations.



(a) fatality influenced by $fatalityrate$ in controlled situation (b) fatality influenced by $fatalityrate$ in outbreak situation

Figure 9: The influence of perturbation in fatality rate in two situations.



(a) fatality influenced by β in controlled situation (b) fatality influenced by β in outbreak situation

Figure 10: The influence of paramenters in β in two situations.

On the other hand, we can get a conclusion that the change in controlled situation is usually less than that in outbreak situation. That means the results in controlled situation are more stable in our model.

Based on these two phenomenons, a conclusion can be made: to build a stable model, we should construct the controlled situation, which is exactly our purpose, and keep the value of parameters away from perturbation.

4.7 Error in computation step length

In our initial program of single-city model, the step length, namely Δt, was set to 1 day. Though the output graph showed the correct trend of the death toll, things got a little tricky when we came to the variable C's influence on the dead. We spotted an irregular oscillation on the second half of the curve, which can neither be explained by common sense nor our mathematical model. To verify the source of this phenomenon, we changed the step length and reran the program. The result is displayed in figure 14.

As shown, the oscillation is eliminated when choosing a smaller step length. So it should be an error of computation rather than the deduction of our model. With a closer look at figure 14, we can figure out the exact influence the step-length error made on the graph: The error dramatically changes the graph's appearance by adding an uncontrollable oscillation. The gradient of the curve is also decreased along with the step length increased. However, amazingly, the thresholds in four graphs remain the same.

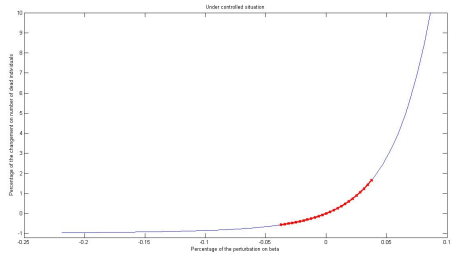
To be acquainted with the influence the error makes on the whole model, we need to know how it affect dependent variables' connection with other variables, which is embodied in figure 15, 16 and 17.

The graph of g, $drug$ and $vacc$ are not impacted as much as C's. The tendency of the curves are not affected, with only exact figures of points on the curve changed. However, the influence is still visible. So the output of the model will be deviated.

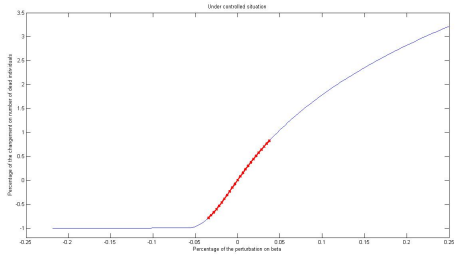
To minimize the error brought by computation step length, we should decrease the step length in our program. However, an improper small step length will add to the operation time, reduce the efficiency of the program. By referring to our output data, we spotted that a step length of 0.1 days can keep a balance between the accuracy and efficiency.

5 Model for multiple cities

In previous section we have constructed a model based on classic SIR model. This model, however, cannot give us more information about geographic spread of epidemic disease, thus contributing little to settle the problem how drugs and vaccines should be allocate. Hence, we propose a model considering geographic and demographic data in different cities. This model is on the base of previous single-city model, in another word, we suppose that in each individual city, the spread of the epidemic disease follows the single-city model previously constructed in the previous section. In addition, people flows among cities are added in to previous model.

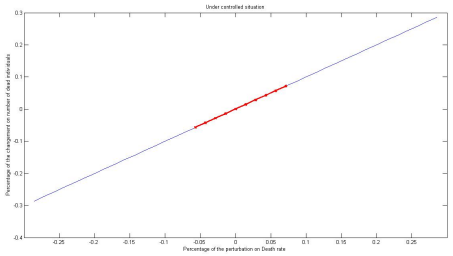


(a) relative variable ratio of fatality (y axis) influenced by relative variable ratio of β (x axis) in controlled situation

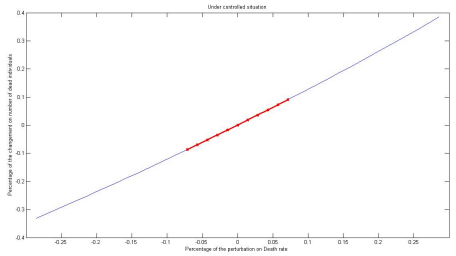


(b) relative variable ratio of fatality (y axis) influenced by relative variable ratio of β (x axis) in outbreak situation

Figure 11: The influence of perturbation in β in two situations.

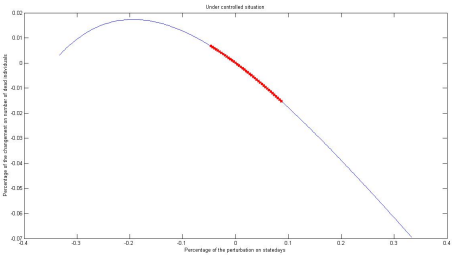


(a) relative variable ratio of fatality (y axis) influenced by relative variable ratio of fatality rate (x axis) in breakout situation

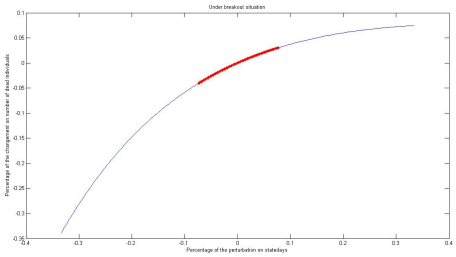


(b) relative variable ratio of fatality (y axis) influenced by relative variable ratio of fatality rate (x axis) in outbreak situation

Figure 12: The influence of perturbation in fatality rate in two situations.

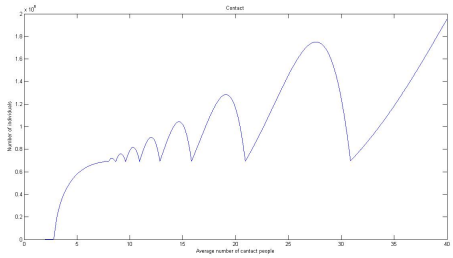


(a) relative variable ratio of fatality (y axis) influenced by relative variable ratio of T_{avg} (x axis) in outbreak situation

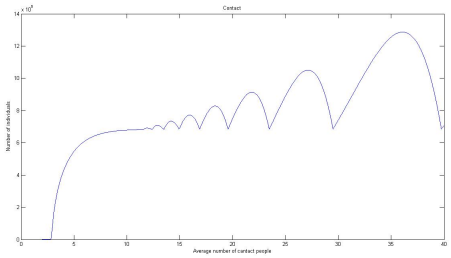


(b) relative variable ratio of fatality (y axis) influenced by relative variable ratio of T_{avg} (x axis) in breakout situation

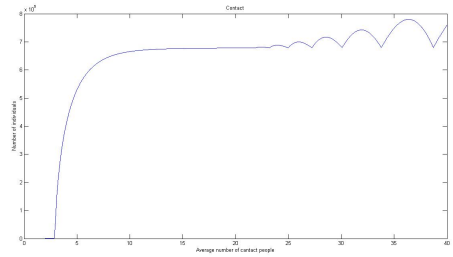
Figure 13: The influence of perturbation in T_{avg} in two situations.



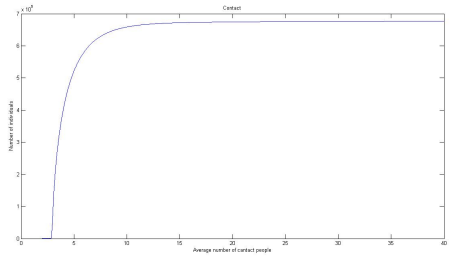
(a) fatality influenced by C, step length = 1 day



(b) fatality influenced by C, step length = 0.5 days

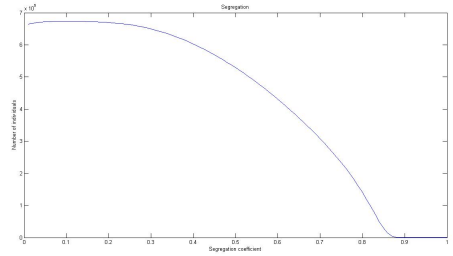


(c) fatality influenced by C, step length = 0.2 days

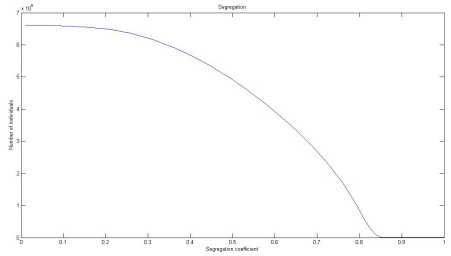


(d) fatality influenced by C, step length = 0.05 days

Figure 14: error of computation step length on fatality-C graph

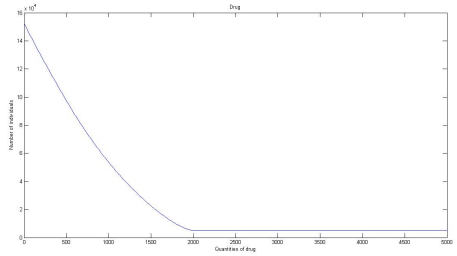


(a) fatality influenced by g, step length = 1 day

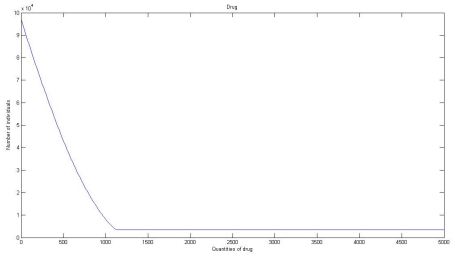


(b) fatality influenced by g, step length = 0.1 days

Figure 15: error of computation step length on fatality-g graph

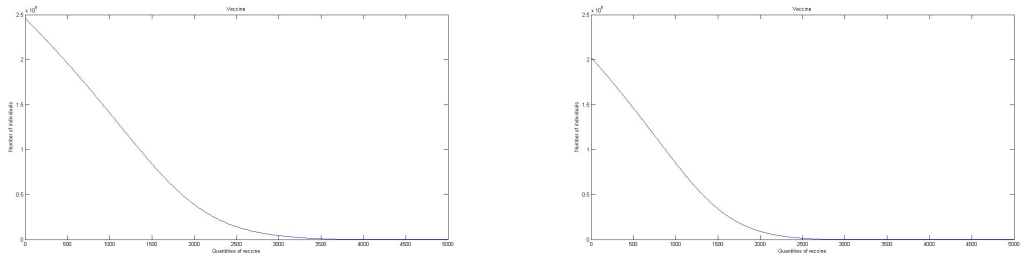


(a) fatality influenced by $drug$, step length = 1 day



(b) fatality influenced by $drug$, step length = 0.1 days

Figure 16: error of computation step length on fatality-$drug$ graph



(a) fatality influenced by $vacc$, step length = 1 day (b) fatality influenced by $vacc$, step length = 0.1 days

Figure 17: error of computation step length on C

5.1 Symbols

Symbols that newly appear in this section are listed in table 2. Some of the symbols in table 1 are also used in this section and are not listed here.

Symbol	Defination
$\mathcal{N}_i$	total volume of population in city i
$\mathcal{S}_i$	number of susceptible people in city i
$\mathcal{I}_i$	number of infected but not segregated people in city i
$\mathcal{G}_i$	number of segregated and also infected people in city i
$\mathcal{D}_i$	number of death caused by EVD in city i
$\mathcal{R}_i$	number of recovered people (also immunized) in city i
P_i	Total number of people in city i apart from the people who are dead and segregated
$t_{i,j}$	number of people transmit from city i to city j indeed
α	transmission coefficient
$d_{i,j}$	distance from city i to city j
$vacc_{tot}$	the number of shares of vaccine that can be provided to all the cities every day
$vacc_i$	the number of shares of vaccine that can be provided to city i every day

Table 2: The definition of the symbols.

5.2 Assumptions

- **People flow exists between any two cities**
  Because no city would be quarantined totally in reality, there is connection between any two cities more or less, which means that there are flows of people between any two cities, although few people are flowing from one far-away small town to another.

- **Cities are different**
  To analyze the influence of delivery plan of medicines, it is better to consider that the population, location and initial status of each cities are different. To make our model realistic, we analyzed the last breakout of Ebola in west Africa in 2014 and chose some cities in the epidemic area. We consider information including geographic location, population of cities and distance between cities.

- **Deterministic factors of people flow**
  We assume that quantities of people leaving one city remains constant. Considering that

the cities are laying on a 2-D plane, the intensity of people flow from one city to another is obviously inversely proportional to the distance between the two cities.

We also assume that, for any individual, the probability of the one go out and link with (go to another city to visit friends, handle business affairs, etc.) any other individual are equal. Hence, it comes out that the people flow from one city to another is proportional to the product of populations of the two cities.

- **Several properties of the system are time independent**
  To simplify our model, we assume that the quantities of drugs and vaccines delivered to each city per day are determined at the beginning and would not change with time. It means that the daily received quantity of drugs and vaccines for each city are constant.

  We assume that the birth rate and natural mortality rate are generally equilibrium and fatality due to the disease is negligible compared with total population. It comes out that the total population (including fatality) is unchanging with time and the people flow among cities is also time independent.

- **The segregated and dead would not transmit from one city to another**
  The S(Segregated) and D(dead due to the epidemic disease) are certainly not able to go from one city to another. Hence, when we calculated how many people from specific group are transmitted from one city to another, only the other three groups (the susceptible, the infected but not segregated, and the recovered and immunized) are taken into account.

5.3 Construction of general model considering multiple cities

This model considering multiple cities are based on the previous single-city model. The difference between them is that in this multi-city model we consider the people flow among cities.

Under assumptions previously mentioned, it is easy to conclude that the number of people transmitted from one city to another can be determined by

$$t_{j,i} = t_{i,j} = \alpha \cdot \frac{1}{d_{i,j}} \cdot P_i \cdot P_j \tag{18}$$

where

$$P_i = \mathcal{S}_i + \mathcal{I}_i + \mathcal{R}_i \tag{19}$$

α is transmission coefficient which is a constant among all the cities, and $t_{i,j}$ is the number of people transmitted from city i to city j.

Different groups of people that are transmitted among cities are proportional to their proportion in departure city. Explicitly, for each day,

$$\mathcal{S}_j = \mathcal{S}_j + \sum_i \frac{\mathcal{S}_i}{P_i} \cdot t_{i,j} \tag{20}$$

$$\mathcal{I}j = \mathcal{I}_j + \sum_i \frac{\mathcal{I}_i}{P_i} \cdot t_{i,j} \tag{21}$$

$$\mathcal{R}_j = \mathcal{R}_j + \sum_i \frac{\mathcal{R}_i}{P_i} \cdot t_{i,j} \tag{22}$$

Hence, previous derived difference equations can be written as

$$\frac{\mathcal{S}_{i+1}-\mathcal{S}_i}{\Delta t} = -\frac{h}{\sigma}\mathcal{S}_i\mathcal{I}_i - \frac{vacc}{\sigma} + \sum_i \frac{\mathcal{S}_i}{P_i}\cdot t_{i,j} \tag{23a}$$

$$\frac{\mathcal{I}_{i+1}-\mathcal{I}_i}{\Delta t} = \frac{h}{\sigma}\mathcal{S}_i\mathcal{I}_i - \frac{(k_1+g+r_s)}{\sigma}\mathcal{I}_i + \sum_i \frac{\mathcal{I}_i}{P_i}\cdot t_{i,j} \tag{23b}$$

$$\frac{\mathcal{G}_{i+1}-\mathcal{G}_i}{\Delta t} = \frac{g}{\sigma}\mathcal{I}_i - \frac{k_2}{\sigma}\mathcal{G} - \frac{r_g}{\sigma}\mathcal{G} \tag{23c}$$

$$\frac{\mathcal{R}_{i+1}-\mathcal{R}_i}{\Delta t} = \frac{r_s}{\sigma}\mathcal{I}_i + \frac{r_d}{\sigma}\mathcal{G}_i + \sum_i \frac{\mathcal{R}_i}{P_i}\cdot t_{i,j} \tag{23d}$$

$$\frac{\mathcal{D}_{i+1}-\mathcal{D}_i}{\Delta t} = \frac{k1}{\sigma}\mathcal{I}_i + \frac{k_2}{\sigma}\mathcal{G}_i \tag{23e}$$

5.4 Numerical Computation of general model considering multiple cities

At first, we exam the multi-city model with a simplified situation in which the quantities of drugs and vaccines delivered to each city are the same. We will show that it properly figures out the general trend of the spread of disease among cities and show us some significant character of the process.

5.4.1 Process of numerical computation

The steps of calculation are listed below:

1. **Initial conditions**
2. **Calculation based on single-city model for each city**
3. **Simulate people flows among cities**
4. **Repeat Step 2 and Step 3 for the next moment**
5. **Until the preset** $days$

In fact, from single-city model to multiple-city model, we simply added step 3.

Other parameters that we are used in the computation, if not stated specifically, are the same as single-city model. For clarity, we also list them here.

$\beta = 0.32$, $k_1 = 0.023$, $r_s = 0.0103$, $days = 150$, $\Delta t = 0.1$(days).

5.4.2 Selection of geographic data

Since the outbreak of EVD are usually constrained in regional areas (mentioned in background), the geographic data that we selected to simulate the last break of EVD is all from the three countries in west Africa (Guinea, Liberia and Sierra Leone). There are 145 cities in these three countries (geographic locations are plotted in figure 19). If all taken into account, it is not only beyond the computational ability of our computers, but also, even if results are given, is difficult for us to study the details of the results. Hence, we select 18 representative cities, among which there are big cities and also small towns; there are cities that are close to each other and there are cities far away. The data of the selected 18 cities are listed in table 3. For the convince of later analysis, a visualized version of data of the cities are ploted in figure 18.

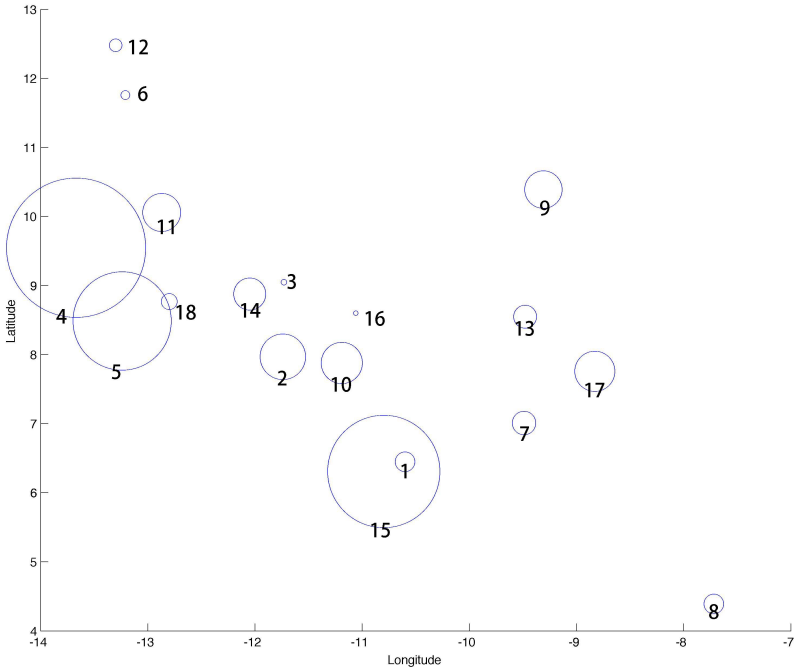


Figure 18: Information of 18 selected cities. Each circle stands for a city - the center of circle stands for location and the area of circle stands for population. The labels on or nearby the circles are corresponding to the labels in table 3

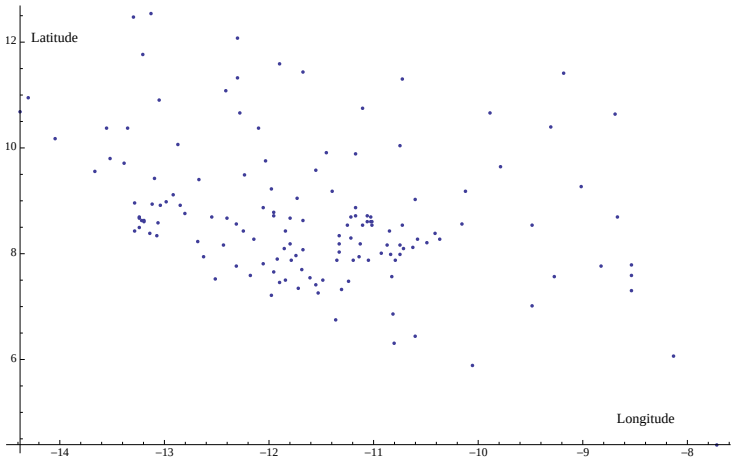


Figure 19: Locations of cities in the three countries

Label	City	Province/Region	Country	Latitude	Longitude	Population
1	Bensonville	Montserrado	Liberia	6.45	-10.6	33188
2	Bo	Southern	SierraLeone	7.97	-11.74	167144
3	Bumbuna	Northern	SierraLeone	9.05	-11.73	3222
4	Conakry	Conakry	Guinea	9.55	-13.67	1548470
5	Freetown	Western	SierraLeone	8.49	-13.24	772873
6	Gaoual	Gaoual	Guinea	11.76	-13.21	7461
7	Gbarnga	Bong	Liberia	7.01	-9.49	45835
8	Harper	Maryland	Liberia	4.39	-7.72	32661
9	Kankan	Kankan	Guinea	10.39	-9.31	114009
10	Kenema	Eastern	SierraLeone	7.88	-11.19	137696
11	Kindia	Kindia	Guinea	10.06	-12.87	117062
12	Koundara	Koundara	Guinea	12.48	-13.3	13990
13	Macenta	Macenta	Guinea	8.55	-9.48	43102
14	Makeni	Northern	SierraLeone	8.88	-12.05	85017
15	Monrovia	Montserrado	Liberia	6.31	-10.8	1010970
16	Ndoyogbo	Eastern	SierraLeone	8.6	-11.06	1870
17	Nzerekore	Nzerekore	Guinea	7.76	-8.83	132728
18	PortLoko	Northern	SierraLeone	8.77	-12.8	21961

Table 3: Information of the 18 selected cities

5.4.3 Results of numerical computation

Similarly, we observed both outbreak situations and well-controlled conditions when we change any one of the four independent variables(g, $drug$, $vacc$ and C).

Figure 20 shows clearly how the outbreak of disease spread from one city to another. We have observed that: 1) the order of severity (measured by fatality) is larger in the city which is the onset of disease (in our special case it is city 1) ; 2) epidemic outbreak occurs earlier in the city which is the onset of disease, in another word, the general trend of others has somewhat 'lag effect'; 3) the general trend of the city close to the onset of disease resembles more to the onset of disease in terms of severity and time sequence (in our special case it is city 15).

Figure 21 shows that when giving vaccines to the cities, the severity greatly decreases, which indicates the great influence medication has on the spread of disease. Additionally, we have observed a new phenomenon that big cities are more easy to get influenced by epidemic diseases if all the cities are given identical amount of drug or vaccine. In our special case, the trend of city 4 is showing the phenomenon. Similar features are observed when varying the value of $drug$, C, or g.

The observed phenomenon also indicates that some of the cities need more medications than the others. Hence, a carefully organized plan to delivery drugs and vaccines is needed, which will be discussed next.

5.5 Model for optimizing the medication plan

We have seen that different medication plans (the plans to allocate drugs and vaccines) can influence the severity of the spread of disease (measured by the total death due to the disease). Hence, here comes the question: how can we develop a plan that can reduce the number of death as much as possible.

Let us first consider a practical problem where the amount of vaccine that can be provided

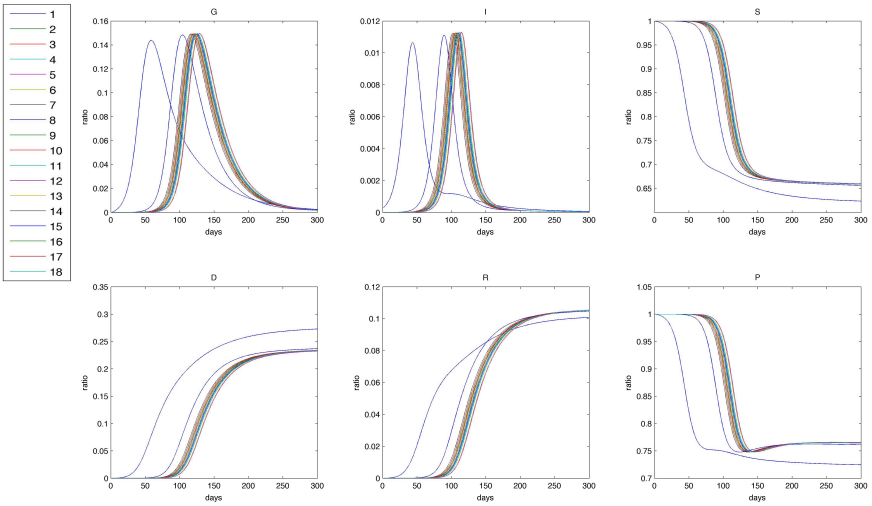


Figure 20: epidemic disease breakout in different cities. $days = 300$, $\alpha = 10^{-4}$, $drug = 0, vacc = 0, C = 3, g = 0.8$ and the y axis is the number of people in the group divided by the total number of people in corresponding city. Initially, 10 people are infected in city 1, and all the other people in all the cities are susceptible. The dark blue line far away from others represents city 1. The next dark blue line which is easy to distinguish from others represents city 15 which is geographically close to city 1.

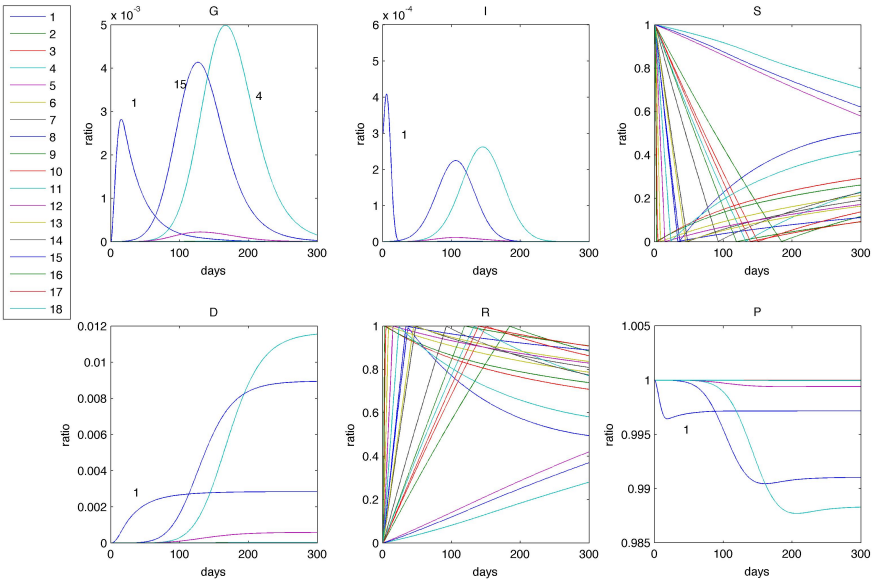


Figure 21: epidemic disease breakout in different cities. $days = 300$, $\alpha = 10^{-4}$, $drug = 0, vacc = 1000, C = 3, g = 0.8$ and the y axis is the number of people in the group divided by the total number of people in corresponding city. Initially, 10 people are infected in city 1, and all the other people in all the cities are susceptible. The dark blue with label '1' represent city 1. The other dark blue line represents city 15 which is geographically close to city 1. The light green line with label '4' represent city 4 which is the biggest city in the all 18 cities.

every day is a constant $vacc_{tot}$ (in the later computation we set the value to $vacc_{tot} = 1800$), and we are required to find out a plan to allocate the vaccines in order that the total death is as small as possible.

5.5.1 Genetic algorithm

Since there are many degrees of freedom of the possible plans, it is justifiable for us to use optimization algorithm to solve the problem. In order to use genetic algorithm, which is one of the most effective optimization algorithm, it is required that the degree of freedom of the plan which is to be optimized should be encoded into the form of binary 'chromosome'. We encoded them into a 180-bit chromosome which is illustrated in figure 22. The 180-bit chromosome is divided into 18 segments, each of which is representing the amount of vaccines that can be allocated to a city. The length of each segment representing a single city is $chromoUnitLength = 10$, which is capable of donating value from 0 to $2^{10} - 1$. We may as well donate the value of city i as w_i, Hence, we can decide the amount of vaccines each city can get. The number of shares of vaccines that city i can get per day is

$$vacc_i = \frac{w_i}{\sum_{j=1}^{18} w_j} vacc_{tot} \tag{24}$$

The process of genetic algorithm we adopted are shown in figure 23.

On the stage of initialization (step 1 labeled in the figure), we set the number of generations to be calculated to $generationNum = 1000$, the number of individuals in each generation to $popSize = 200$, the rate of mutation to $mutationRate = 0.01$ and the rate of crossover to $crossoverRate = 0.6$.

On the stage of calculating fitness (step 2), we set the fatality rate as the target function and take it as the value of fitness.

The stage of selecting, crossover and mutation (step 3,4 and 5) are conform the very classic process of genetic algorithm.

5.5.2 Results of computation

With parameters shown in table 4. A optimized result is given by our program, which is shown in table 5.

The number of death declined from 2768 with randomly generated plan to 380 with the optimized plan shown in table 5. The declining trend can be easily seen in figure 24.

Figure 22: Encoding

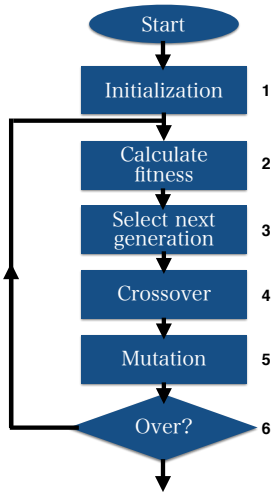


Figure 23: The process of genetic algorithm

β	k_1	r_s	$days$	Δt	g	C	$drug$	number of initial infected people
0.32	0.023	0.0103	150	0.1	0.8	3	0	10(in city 1)

$vacc_{tot}$	$chromoUnitLegth$	$generationNum$	$popSize$	$mutationRate$	$crossoverRate$
1800	10	1000	200	0.01	0.6

Table 4: Parameters in computation

label of city	$vacc_i$	population of city	vaccine per capita ($\times 10^{-3}$)
1	32	33190	0.96983
2	367	167100	2.1956
3	3	3222	0.9082
4	315	1548000	0.20345
5	185	772900	0.23947
6	55	7461	7.4029
7	40	45840	0.86178
8	14	32660	0.41439
9	31	114000	0.26952
10	98	137700	0.71456
11	41	117100	0.34673
12	94	13990	6.7195
13	24	43100	0.55164
14	48	85020	0.5679
15	329	1011000	0.32562
16	51	1870	27.1889
17	27	132700	0.20398
18	47	21960	2.132

Table 5: A optimized plan for allocating vaccine with $vacc_{tot} = 1800$

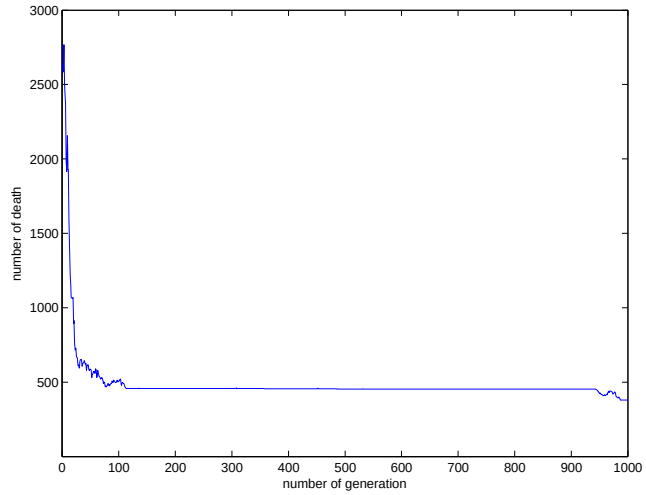


Figure 24: The number of death declines with the optimization of the plan. The x axis is for the number of generations of genetic algorithm and the y axis is for the number of death in all the 18 cities.

5.5.3 Analysis of the result

The result is analyzed from following aspects.

1. The two biggest cities - city 4 and city 15 - are allocated for more than 300 shares of vaccines, which is remarkably more than others. This outcome is easy to understand. The more people in the city, the more shares of vaccine are needed.

2. Some of cities are allocated more shares of vaccine compared with their population, where city 16 is a significant example. City 16 is a small town, but it has the largest amount of vaccine per capita. It is easy to understand considering the geographic location of city 16. City 16 lies in the center of the cities we selected, which plays a significant role in the transmission of pathogen from one city to another. Once huge amount of vaccine is delivered to this city, the route of transmission of pathogen is greatly cut off.

   That the city near the center of network needs more vaccine per capita is clearly shown in figure 25.

3. The largest amount of vaccine is allocated to city 2, which is a relatively big city and locates relatively in the center of all the cities, confirming the previous inference.

4. Since people flow is supposed to be determined by the distances between cities, the amount of vaccine per capita is related to geographic location of cities. In real practice, the people flow is determined by more factors, such as convenience of traffic, so it is not difficult to imagine that **the cities that lie in the center of people flow network need larger amount of vaccine and drug per capita**.

5. The computation above is varying the delivery plan for vaccine when the plan for drug is invariant. When the delivery plan for vaccine is invariant, the optimized delivery plan for drug has similar characteristics. Hence, we just list the mere optimized plan for drug in table 6 and are not repeating the similar interpretation.

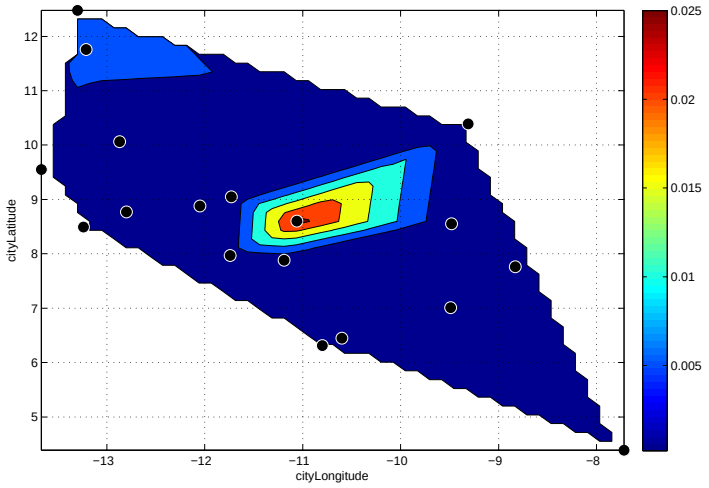


Figure 25: The contour plot of vaccine per capita. The black spots represent locations of the 18 cities.

label of city	$drug_i$	population of city	drug per capita ($\times 10^{-3}$)
1	32	33190	0.9497
2	111	167100	0.6643
3	113	3222	34.9531
4	93	1548000	0.060143
5	112	772900	0.14476
6	76	7461	10.1765
7	59	45840	1.2819
8	37	32660	1.1336
9	14	114000	0.12545
10	107	137700	0.78005
11	31	117100	0.26779
12	1	13990	0.077239
13	6	43100	0.1433
14	57	85020	0.67318
15	108	1011000	0.10657
16	22	1870	11.6608
17	9	132700	0.067749
18	12	21960	0.54899

Table 6: A optimized plan for allocating drug with $drug_{tot} = 1800$

6 Discussion

6.1 Strengths

1. **Our model is simple and easy to understand**
   Our model is the simplest model we can conceive to reflect the impact of concerned independent variables (factors regarding medication) and to solve the problem lifted by the question.

   Our single-city model is based on the most elegant model in the field of epidemiology - the SIR model, and we reconstruct the model (mainly add two clusters of people) in order to introduce concerned independent variable into our system.

   Our multi-city model is based on our single-city model and introduce only one 'people flow' to obtain the geographic characteristic of the spread of disease.

2. **Our model is effective and in good agreement with the reality**
   Simple as they are, they are effective in reflecting the complex relationships between numerous variables and parameters, and they not only reveal the intrinsic characteristics of the spread of disease itself but also successfully link factors of medication to the spread of disease.

   Comparing with the data we have find from several resources, the results of our model not only correspond the general trend of the records but also resemble the reality in some critical features.

3. **Good extensibility**
   Flow of people is a critical factor determining the spread of disease. Although our multi-city model only set the volume of people flow as a function of mere geographic distribution and population of cities, the determinants of people flow can be adjusted when other possible factors are considered. Then, the adjusted model can be applied to study the impact of other possible factors relating to epidemiology.

6.2 Weaknesses

1. **Our model is just a rough model**
   For simplicity, we have neglected many potential parameters, variables or processes, and have made numerous assumptions. Eg. we did not consider the relationship between separate individuals and we did not dig deeper into the properties of social network which is a quite essential part determining the spread of disease. Some important general or specific factors are also neglected by us, a interesting example of which is a folk custom prevalent in the studied region that relatives kiss the death, which plays a significant role in the spread of disease and is categorized into *Super Spread Event*(SSE) academically.

2. **Our model is only a continuous model**
   Numbers of people, number of shares of drug/vaccine, etc. are important quantities in all the process of modeling and computation. For simplicity, we regard the numbers as directly real numbers instead of integers. It is justifiable when the numbers are large, since the decimal part of the number is negligible; when the system scales down, however, the statistics dose not work and the outcome deviates a lot from reality.

7 Conclusion

In this paper, we have constructed our models based on the biological features of EVD, social features of human society and several reasonable assumptions. Our models consist of two parts: one is considering the the spread of disease within a single city and serves as the base of the other; the other takes the people flow among the cities into account, the application of which gives an optimized plan regarding how should we allocate the resources of medication such as vaccine.

Both of the models are applied to specific cases separately, and the results of computation which are carefully studied justified our model. Through our analysis of the model, we explored and explained the complex relationship among numerous variables and parameters.

The effectiveness of medical treatment (including segregation, vaccination and pharmacotherapy) is verified by our model and the strategy to allocate vaccine and drug is revealed by our investigation.

8 Letter

Dear readers,

In March 2014, the Ministry of Health of Guinea reported an outbreak of Ebola virus disease (EVD) in four southeastern districts: Guekedou, Macenta, Nzerekore and Kissidougou. A total of 86 suspected cases, including 59 deaths was reported as of March 24. Since then, the spread of EVD in West Africa has explosively grew. According to the latest statistics, EVD has caused 13855 cases and 9004 deaths. Faced with the havoc, the world have expressed their deep concern. In the last year, a mess of aid and donations converged on West Africa, medical orgnizations all over the world also dedicated to the researh of medication for EVD. With respect to people's determination of eradicating EVD, we now present our new progress on medication research.

The drug we developed aiming at EVD has been proved to have an amazing curative effect for the patients whose main organ hasn't been damaged. According to the data on clinical trial, 18 of 23 volunteers were cured, with an average recovery time of 8.4 days. It is gratifying that, with goverment's ratification, the drug has been put into mass production now. So patients will be able to receive effective medical treatment before long. The corresponding vaccine has also been developed, which is still in test stage. Vaccination against EVD can be expected soon.

However, as much as we might wish it, we can't provide the drug to all the patients without enough production capacity. To minimize the damage West Africa suffered, our only choice is to set cities' priority in drug delivery according to its population and location. Outbreak in populous cities is more destructive and uncontrollable, while cities near the epidemic focus stand a great chance of breaking out EVD. These cities will be firstly considered in our delivery system. Transportation hubs also have a high priority in our system as EVD may spread through transportation networks. Glacial as it sounds, this method has the highest efficiency in current situation. The latest arrangement details of medication delivery can be checked on our official website.

Though we are still in lack of effective medication, it is worth emphasizing that the confrontation against EVD needs not only medical researches, but also efforts of every single individual. A lot can be done to protect yourselves as well as others from infection. Some useful tips are given as follow

- **Scale back on going out** the transmission of EVD requires direct contact with the infected or their body fluids and blood. Reducing the contact with others is a proper way of avoiding infection.
- **Maintain personal hygiene** This tip goes without saying. Personal hygiene is always of great significance even no epidemic disease is spreading. Maintain personal hygiene also means do not go to public places with appalling sanitary conditions.
- **Check data updates** Keep focused on the data updates of EVD. This can help you get better acquainted with the situation and be prepared.
- **Be cautious** If you feel uncomfortable, go to the medical institution nearby as soon as possible. You can suggest your friends to do the same. This act may prevent lives from fading away.

If you are unfortunately infected with EVD, don't panic. EVD is not absolute lethal. You can still stand a good chance of recovery as long as doctor's advices are followed.

The status of fighting against EVD remains severe now, and we will continue our efforts in medication development and medical assistance. To our belief, EVD will be thoroughly eradicated in the near future.

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