Team Control Number

or office use only

T1 _____

T2 _____

T3 _____

T4 _____

38835

Problem Chosen

A

For office use only

F1 _____

F2 _____

F3 _____

F4 _____

2015 Mathematical Contest in Modeling (MCM) Summary Sheet

(Attach a copy of this page to your solution paper.)

The on-going outbreak of Ebola has raised global concern. Owing to the fact that the amount of a new drug is usually limited, we want to set up a model to study the spread of the epidemic, the effect of drug on a group of people in a region, as well as the way of allocating the drugs.

In this paper, we apply digitization methods to build a dynamic model based on matrix in order to simulate the spread of Ebola and get statistical results. Besides, we use the method of linear programming to find the best way of drug delivery.

In the first part, we use an N-order matrix to simulate a city with a population proportional to N*N. Elements in this matrix vary from 0 to 5, representing different groups of people. Based on Ebola's characteristics we make spreading rules and let disease develop for certain iterations. Then we compare the patient numbers with data from WHO to confirm the effectiveness.

To simulate Ebola's propagation under with the antagonism of drugs, we suppose drug quantity is either sufficient or not in the second part, and make treatment rules based on materials. By observing the final distributions, we can judge if the rules can reduce mortality.

The third part is the optimization of drug delivery. We choose four major cities hit by Ebola in Sierra Leone. After considering factors including population, outbreak period and different drug delivery situations, we take different values for the parameters and gain statistical results. After linear programming we deduce optimal measures to control the outbreak.

In this model, we neglect the influence of profit and transportation. This is reasonable because drug allocation is not a commercial activity but an urgent public health issue, and since the areas of the regions like Sierra Leone are not large, we assume that with modern transportation drugs can be sent to any spot within one day. But still, we give preliminary methods when these two factors count, so this model can be applied to a broader context. Comparing with traditional differential models, this model takes fully advantage of computer's fast operation speed and applies statistical methods to gain relationships among different variables. It enjoys many strengths including high efficiency and convenience. However, we only finish the model framework, a lot of optimization can be further made.

Fighting Ebola

--Matrix and Linear Programming Model on Epidemic Evolution and Drug Effect

Contents

I. Introduction

Since the beginning of 2014, the Ebola outbreak in West Africa has committed thousands of people's lives, and is posing gigantic threat to public health throughout the world. Due to a lack of medical resource in less developed areas, efficient and economic methods to cure the patients and stop the spread are in urgent demand.

In this paper, we use matrix to set up a new kind of model to study the evolution of distribution of patients, the effect of medicine or treatment in epidemiology, as well as the role of drug allocation in the control of disease. Then we use recent data to demonstrate the model and determine the values of several parameters. Finally, we apply the model to real situation in Sierra Leone to design the transport of a new kind of medicine on condition that the provision is limited. By doing so, we derive several data and a general method that may be useful in the research of the spread of an epidemic, as well as the optimization of drug allocation. This method can apply to not only Ebola but also other kinds of epidemics.

II. Background

I) Ebola Virus Disease

Ebola is a fatal disease that is caused by Ebola virus, and is transmitted through direct contact between the patient and the healthy person. The death rate of Ebola outbreak varies from 25% to 90% in the past outbreaks, the average of which is around 50%.

According to statistics, the average incubation period is 4 to 10 days, during which the patient isn't infectious to others. After this period, symptoms like fever, diarrhea and vomiting start to appear, meanwhile he can transmit the virus to those who have direct contact with him. Then the patient may survive after 7 to 14 days, or, more commonly seen, will die in 6 to 16 days.

The chance of the recovered patient's transmitting virus to others is relatively small, though some body fluids still contain virus. Recovered patients develop antibody against Ebola virus, which is effective in the following 10 years. [Ebola Virus Disease Fact Sheets, WHO]

II) Ebola Epidemic in West Africa

The ongoing Ebola epidemic outbreak in West Africa started at the beginning of 2014, and is the most severe Ebola epidemic in history. Most cases and deaths are located in several countries in West Africa, such as Sierra Leone, Liberia and Guinea. More than 20,000 people have been infected and nearly half of them died. Besides, this is the first time that Ebola cases appear in more than one country, even outside Africa. Since the death rate is rather high, the continuous spread poses gigantic threat to world health and development. Owing to that, the fight against Ebola has become a worldwide issue.

III) Ebola Epidemic in Sierra Leone

Sierra Leone is one of the most severe countries in this Ebola Epidemic. Cases and deaths there take up nearly half of the total around the world. Four major areas or

cities across the country where the Ebola epidemic are the most severe are Freetown, Bombali, Port Loko and Kenema, in which Kenema owns smallest number of cases. Populations in the four areas range from 40,000 to 120,000, which serve as a reference for us to set the parameters.

There is only one international airport across Sierra Leone, namely the Lungi International Airport. So we assume that all the drugs received from abroad arrive at this airport at the very beginning, and are distributed nationwide afterwards.

III. Model Building

In order to simulate the spread of an epidemic in a region, we are supposed to classify people into different types, such as carrying virus without showing the symptoms, being infectious or having recovered. Then we can use different variables to represent the number of each kind of people and calculate their ratios in the region. Then we determine the reason for the change of the ratios, and derive a formula to express their evolution over time.

A commonly used model in epidemiology is SIR model. It uses differential equation to represent the reason for the change of the ratio of different parts. However, there are several limitations. For example, all the factors that can affect the spread of the disease is included in the equation set, which may make the equations complex and hard to read and correct. Besides, it is hard for us to apply the model to one certain kind of epidemic, because every disease has its own ways of transmission, and are difficult to be generalized by the same kind of equation.

Our model is inspired by Ising model in statistical physics. Ising model uses matrix to represent ferromagnetic materials. Each element of the matrix represents a magnetic moment, the value of which can be 0 or 1, which represents spin-up or spin-down respectively. Then the elements altogether show the distribution of magnetic moments in a material, which makes it easy to derive several physical properties.

In our first model, we use MATLAB to generate a matrix that represents a region, as is shown in Figure 1 below. Each element represents a single person. In this way we can simulate the outbreak, the spread and the treatment of the disease. If the whole process is shown in a plane, we can monitor the evolution of the epidemic and get the tendency of the change of several variables.

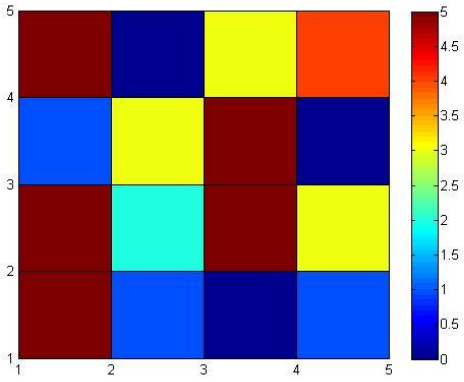
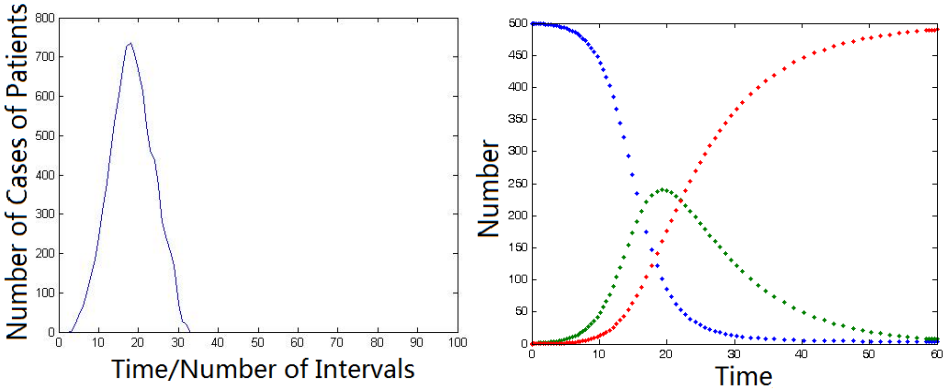


Figure 1|The distribution of different kinds of people. Different colors represent different kinds of people.

Moreover, we can use our model to derive the change of the number of patients with respect to prevalent time of the disease, and plot the curve as follows. Its tendency is the same with that in SIR model, which is shown in Figure 2 below.



(a) (b)

Figure 2|(a) The number of infected patients to the number of iteration. This curve is derived by our model.(b) relation curves between different groups and iteration derived by differential SIR model. The green curve corresponds to infected patient, the blue curve corresponds to susceptible patients, and the red curve corresponds to recovered patients[Wikipedia].

In our second model, we derive an objective function that measures the death toll, and use LINGO to do linear programming to make the death toll reaches its minimum. By doing so, we get the best way to allocate drugs among Sierra Leone's major regions in which Ebola epidemic is relatively severe.

I) The Propagation Model under Free Transmission

1. Assumptions

1.1 A mild patient can transmit the virus to all the eight people around him. This is rational because of the characteristics of Ebola virus as well as the frequent contact among adjacent people;

1.2 A severe patient can't transmit the virus to the neighborhood. People are aware of his symptoms and avoid direct contact with him, or he has been sent to the hospital and separated from the community.

1.3 Due to proper disposal, the remains of dead victims are unable to transmit the virus outside.

2. Initialization

2.1 Generate a *N*N* matrix to represent the area of Ebola outbreak, each element represents a person. *N*N* is proportional to the total population of this area.

2.2 Adopt periodic boundary condition, namely one side is adjacent to the opposite side, to approximate the real situation. It is reasonable because the practical area is usually much larger.

3. Digitization of status

Use different numbers to denote different groups of people. Here is the correspondence table:

Number	Group
0	Healthy people
1	Susceptible patient
2	Mild case
3	Severe case
4	Recovered patient
5	Dead

4. Digitization of time period

Set the time duration of each period to the average value of the actual range. After comparing the time duration of different periods, we set the unit time period for iteration to 4 days. In this condition, the length of incubation period equals 2 unit, the duration of mild period amounts 1 period, while the severe period can be regarded as 2 unit.

5. Transmission

5.1 All the elements in the matrix are zero at the beginning, which indicates all the people in this area are healthy before the outbreak.

5.2 Randomly switch one 0 into 1, and this becomes the first susceptible patient. In each iteration, randomly select a point in this matrix, if this element is 0, replace it by 1, through which we imitate the situation that distant people may get infected due to various factors that may lead to local population migration.

5.3 After two iterations, susceptible patient (denoted by 1) will develop into mild patient (denoted by 2), who is infectious to others through direct contact. During this process, element 2 will switch all 0 around it into 1.

5.4 After one iteration, a mild patient (denoted by 2) will become a severe one (denoted by 3). Considering that in real condition such patients appear visible symptoms and will be insulated, patients in status 3 are not infectious to others and will bring no effect to their neighbors.

5.5 After two iterations, 90% severe patient (denoted by 3) will die (denoted by 5) and

10% will recovered without medical care (denoted by 4). Since recovered patients gain life-long immunity, 4 and 5 will no more be influenced by other elements.

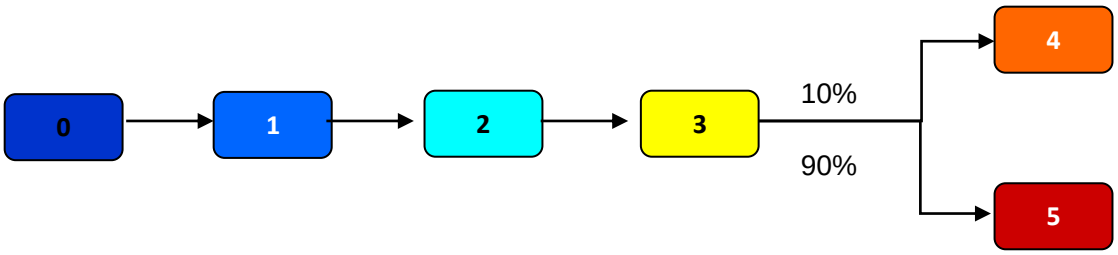
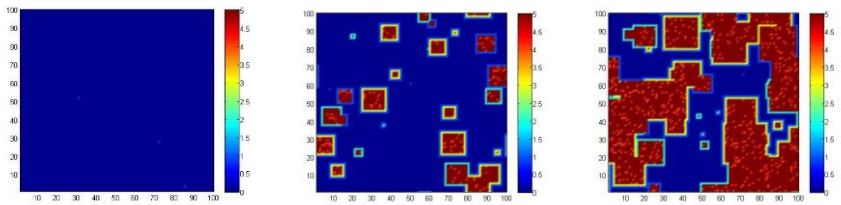


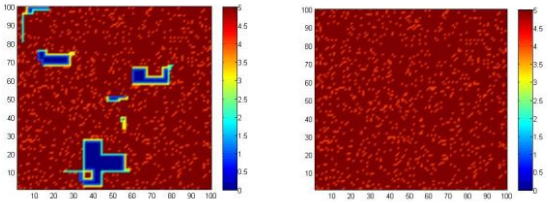
Figure 3| The flow chart of state transition between different groups of people in the order of time.

6. Evolution

Let this model run certain times till all the elements become 4 or 5.



(a) (b) (c)



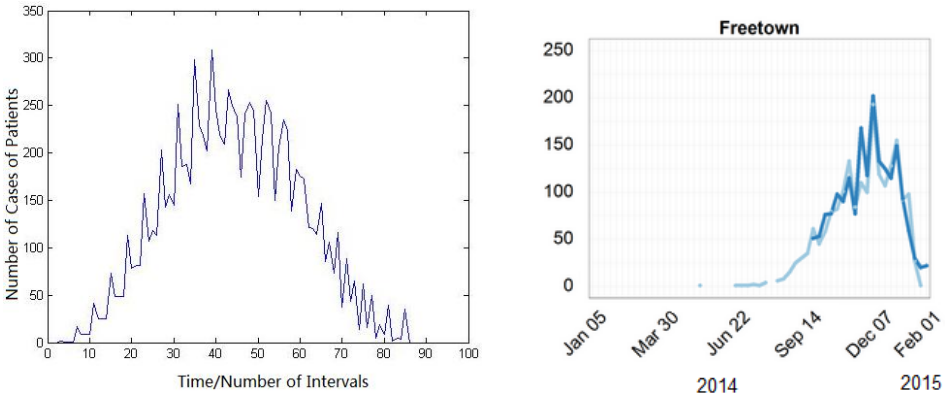
(d) (e)

Figure 4|The whole process of Ebola's free propagation in a region when *N*=100. (a) The initial status. The virus carrier is surrounded by large number of healthy people. (b) The accelerating period. Patients and deaths occur in several areas and the speed of the expansion is accelerating. (c) The fastigium. Rate of the increase of patients and deaths reach the maximum. (d) The decelerating period. The rate of the appearance of new cases slows down. (e)The end. A small number of people survived while most people died.

7. Statistical Analysis

By supervising the whole process, we can get several statistical results.

We calculate the number of the patients with each passing day, and plot the curve to show the tendency. Then we find that the tendency is rather similar to that of the new Ebola cases in Freetown, capital of Sierra Leone and a disaster area of the Ebola outbreak since the beginning of 2014.



(a) (b)

Figure 5|(a)The change of the number of new cases with respect to time. The length of the side of the region matrix is 100. (b) The number of Ebola cases in Freetown, Sierra Leone since the beginning of 2014.

The fluctuating line reflects the expansion mode of Ebola. Since the virus carrier isn't infectious to others unless he appears symptoms, the increased number of newly being infected by him is zero in this period. Consequently, the total number of cases is relatively low. Then, with his symptoms appearing and his transmitting the virus to others, people around him become asymptomatic virus carriers. Please note that in this period they aren't discovered by the public health system, during which the severe patients gradually die or recover and are removed from the survey, so the number of cases continues to decline and hit the bottom, namely the relative lowest point of the curve. However, after the incubation period, virus carriers develop into patients and the total number of cases rise sharply. The circle above lead to the fluctuation of the curve.

This proves that this model is able to explain the change of new cases in Ebola epidemic.

II) The Propagation Model under Drug Effect

1. Cases when drug is sufficient

1.1 Assumptions

1.1.1 Each patient can get drug and receive medical care, which means that the drugs are infinite.

1.1.2 If a mild patient(whose status is No.2) receives treatment, there is a 60% probability for him to change to status 4. Otherwise, his condition worsens and his status become 3.

1.1.3 For a severe patient, there is a 10% probability for him to survive naturally and another 10% probability for him to be cured by medicine. Or he will die.

1.2 Results

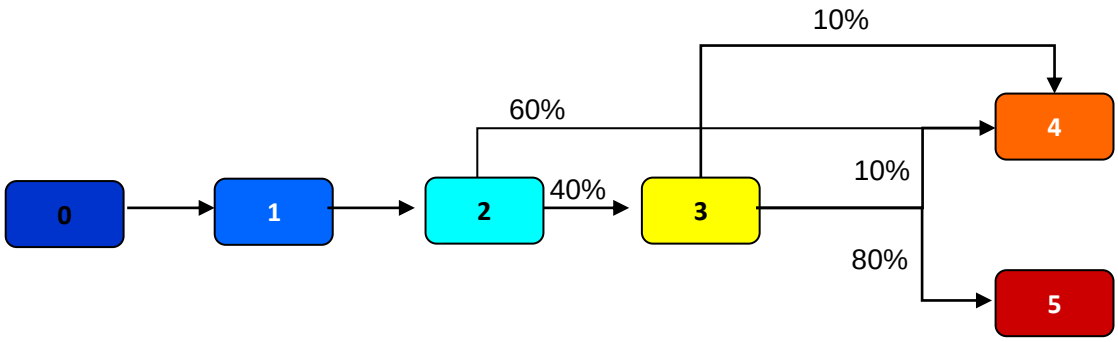
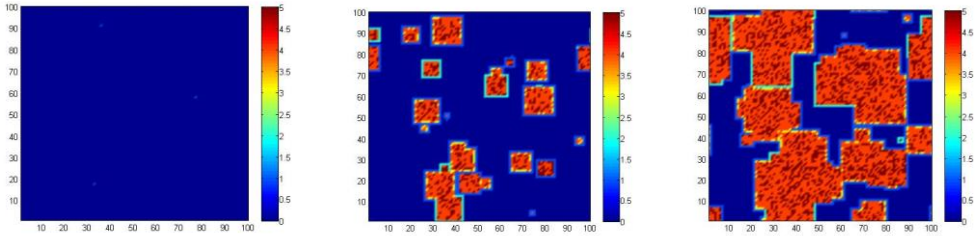
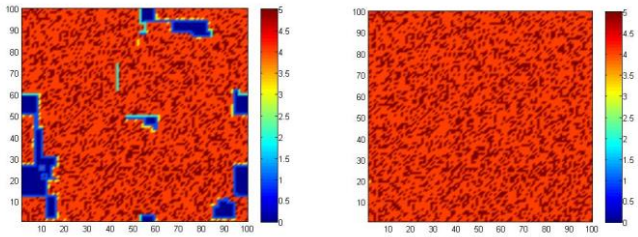


Figure 6|The flow chat of state transition among different groups of people when drug is applied. The percentage marked on each line represents the probability for the former status to develop into the next status which is pointed by the arrowhead.



(a) (b) (c)



(d) (e)

Figure 7|The whole process of Ebola's propagation in a region when drug is provided.
(a) The initial status. The virus carrier is surrounded by a large number of healthy people. (b) The accelerating period. Patients and deaths occur in several areas and the speed of the expansion is accelerating, but apparently the death rate is lower compared with the free propagating case. (c) The fastigium. Rate of the increase of patients and deaths reach the maximum. (d) The decelerating period. The rate of the appearance of new cases slows down. (e)The end. A small number of people survived while most people died.

2. Cases when drug is insufficient and starts to be provided from the very beginning

2.1 Assumptions

2.1.1 There is a hospital at the center of the area.

2.1.2 The amount of drug provided per day is fixed, which is reasonable because of the limitation of productivity. The former who get sick should receive the drug in higher priority. This principle should be followed to ensure the equality of all

the lives.

2.1.3 The patient who is nearer to the hospital have an easier access to medical care. Considering the medical resources are limited, this assumption helps to ensure the number of people receiving medical care reaches the maximum.

2.1.4 The amount of drug needed by a patient depends on his condition. Assume that for a mild patient, he needs 1 unit of drug every iteration. For a severe patient, he needs 3 unit of drug every iteration.

2.2 Interpretation of the assumptions 2.1.2 and 2.1.3

Considering the assumptions 2.1.2 and 2.1.3, we make the following supposition: the possibility of each patient's receiving medical care is dependent on both the total drug stock and the distance from the patient to the hospital.

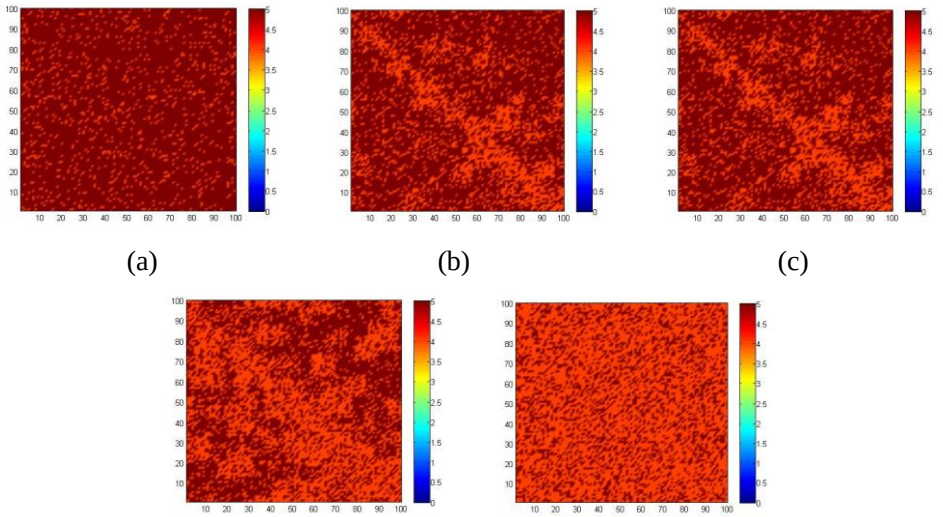
There is a positive correlation between the possibility and the stock, and a negative correlation between the stock and the distance. Then we assume that the distance between two points is the sum of the difference of x coordinate and y coordinate respectively. This is rational because the streets are usually horizontal and vertical lines, and the only way to get to the hospital is to follow the streets.

2.3 Results

2.3.1 At first all the patients can receive medical care, and the redundant drugs can be stored to prepare for the outbreak.

2.3.2 As time goes by, due to the increase of the number of patients and the lack of the drug's productivity, the daily provision gradually becomes unable to meet the demand.

2.3.3 Eventually when all the people arrive at status 4 or 5, the total death rate is larger than the case when drug is sufficient, but is smaller than the case when there is no treatment.



(a) (b) (c)

(d) (e)

Figure 8|The final distribution of people in a region with different amount of drug supply

per day. *S* is a parameter to represent the daily drug supply, it is proportional to the amount of drug provided to this region per iteration. Through monitoring the development of the system, we observe that earlier discovered patients have larger probability to be cured. (a) *S*=3. The mortality is 89%. (b) *S*=30. The mortality is 81%. (c) *S*=60. The mortality is 73%. (d) *S*=120. The mortality is 55%. (e) *S*=300. The mortality is 32%.

III) Sensitivity and Robustness Analysis: Several Statistical Relationships Hidden

After considering several factors in reality and examining the four Ebola-hit regions in Sierra Leone, we come up with a general method to make several adjustments about the unit we use.

First, from now on, we change the unit of time from iteration to day for convenience.

Additionally, thanks to geographical separation and several disease control and prevention methods, such as inspection and quarantine, only those who live in a small 'dangerous part' of the region are highly likely to get infected. As a result, we time an index to the side length of the matrix in the previous model. The index is related to the geographical and environmental conditions of the region as well as its sanitation system. For Freetown, Port Loko and Bombali, the index is 0.28; for Kenema, the index is 0.17. Denote the converted side length of the matrix as N' instead of N.

Besides, we need to understand that even in those 'dangerous parts' of the regions, the number of people who are actually exposed to the virus is still far less than the actual population. To take this into consideration, we divide the previous number of patients (now the side length is already modified) by 7.3.

After making these adjustments, we can derive the similar curve of cases of Ebola epidemic in these areas, whose maximum values on the curve are similar to statistics.

1. Equilibrium time of the system with respect to side length of matrix

Equilibrium time means the number of iteration, during which the system evolves and finally arrive at a status in which all the elements are in status 4 or 5 after the last iteration. This means that all the people in the system either recover or die after the evolution. Considering the magnitude of population of cities we study is tens of thousands, we change the length of matrix from 300 to 800, and plot the number of iteration respectively on a graph.

The function for simple linear regression is

$$T = 1.6914N' + 236.38$$

with Pearson's r satisfies $r^2 = 0.9666$. So we can postulate that the number of days for the epidemic to last increases by approximately 1.7 if the length of the side of the region increase by 1.

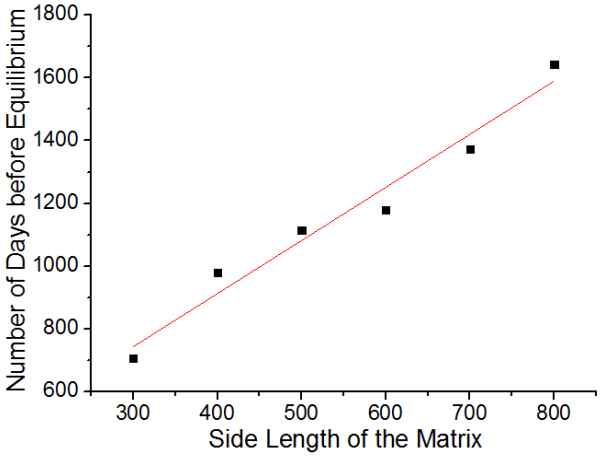


Figure 9|The relationship between number of days before equilibrium and the side length of the matrix.

2. The change of death rate with respect to the change of daily drug supply

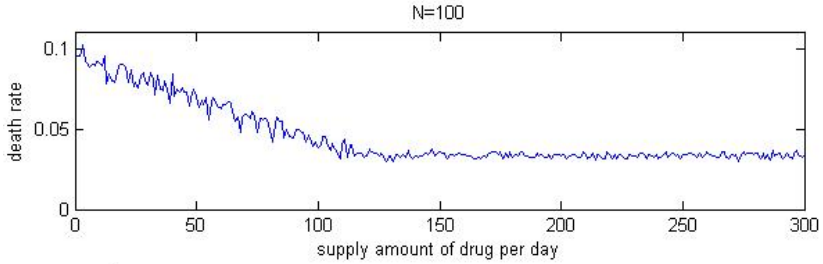


Figure 10|The relationship between total death rate and daily drug supply. The side length of the matrix is 100.

2.1 Assumption

There are 10,000 people in this region.

2.2 The appearance of the curve

2.2.1 With the increase of daily drug supply, we can see that at first the total death rate declines, but when the daily drug supply reaches a certain value, after which the death rate remains stable with only slight fluctuation. That value is the drug demand.

2.2.2 When the drug is inadequate, the relationship between death rate and daily drug supply is almost linear.

2.3 Conclusion

2.3.1 The supply of drug changes from inadequate to adequate within the whole process.

3. The declination of death toll with respect to the number of people in a region

We alter the side length of the matrix, and calculate the declination of death toll in each situation.

The horizontal axis represents the side-length of the matrix, and the vertical axis

represents how many added survivals one more unit of medicine every day can cause when the medicine is delivered on time. From the figure, we can conclude that as the side length grows longer, one more unit of medicine every day can cure more patients and the relationship is linear.

Denote the declination of death toll as α, so α is a function of N'. From the above linear regression we derive

$$\alpha = 0.0213N' + 2.1737$$

with Pearson's r satisfies $r^2 = 0.9962$. So the death toll reduces about 0.0213 with the unit increase of matrix's side length.

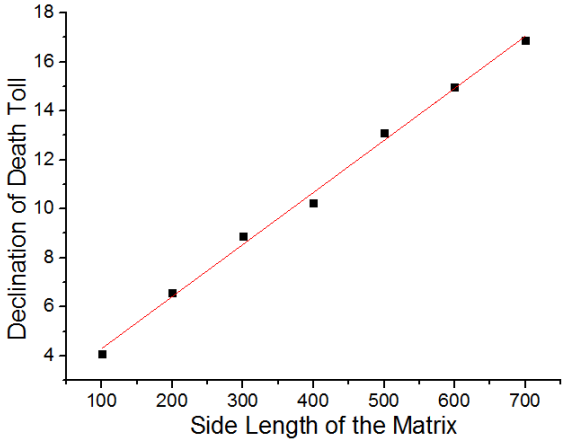


Figure 11|The relationship between declination of death toll and side length of the matrix.

4. Region's Demand of Medicine with respect to the Side length of the Matrix

This line shows the relationship between the side length of the matrix(labeled by N')and the region's demand (labeled by s) of drugs.

The function of linear regression is

$$s = 3.5326N' - 204.81$$

with Pearson's r satisfies $r^2 = 0.9973$.

Consequently, the demand of drugs per day increases by about 3.53 when the side length of the matrix increases by 1.

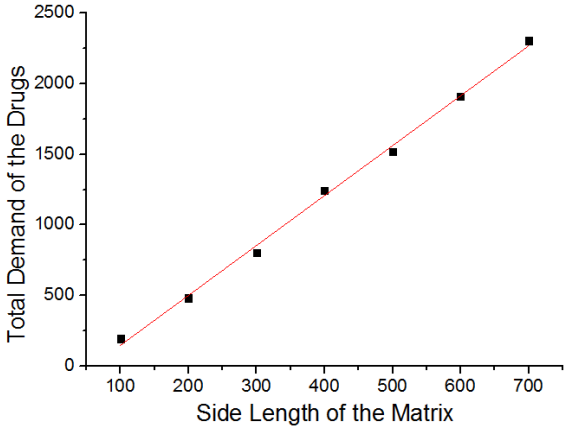


Figure 12|The relationship between the total demand of the drugs and side length of the matrix.

5. Efficiency of the Drug with respect to the Length of Delay

5.1 Assumption: There is a delay for the first time the region receives drug supply.

5.2 The meaning of the name of vertical axis

The efficiency of the drug means the number of people one unit of drug can save at a specific length of delay and population. In this case, we calculate the total death rate, and derive the death toll by multiplying the population. Besides, we derive the efficiency of the drug at a specific side length by linear regression between death rate and the amount of drug supply per day. Finally we compare the current death toll with the original death toll and get the efficiency of the drug.

5.3 Tendency shown in the graph

When $N'=300$, from the graph we can see that there is approximately a linear interaction between the efficiency of the drug and the length of delay. The result of linear regression is

$$y=-0.0115x+8.7263$$

with Pearson's r satisfies $r^2=0.9627$.

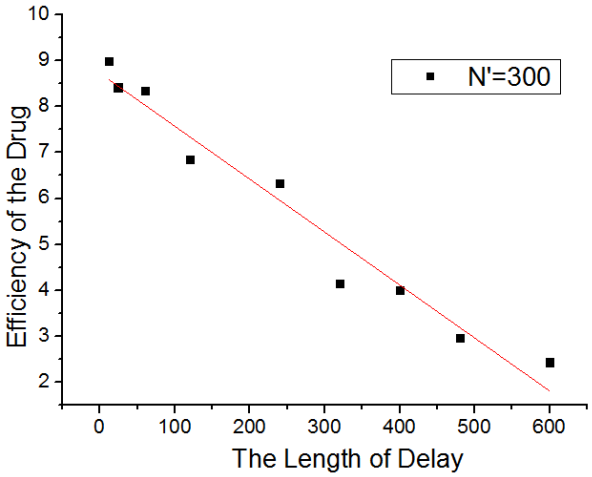


Figure 13|The relationship between the efficiency of the drug and the length of delay.

5.4 The change of Drug's Efficiency on Controlling the Epidemic

When N' varies, there is only a slight difference between the slopes above. On average we get 0.0119, which can be denoted as k, which means the unit declination of drug's efficiency when the length of delay increases.

From the above discussion, we can use $\alpha-kt$ (in which t is the length of delay) to represent the number of people a single unit of drug can cure in a certain region within one day, and that which is the drug's efficiency index.

IV) The Best Way of Drug Allocation among major areas of Sierra Leone

Since there is only one international airport in Sierra Leone, the Lungi international airport, we assume that all the drugs from abroad are transported to that airport, and then be allocated nationwide.

1. The 2-region System: a Simple Case

Denote the converted side length of matrix which represents the people in a region as N', epidemic duration as T, and the total supply of medicine per day as s.

1.1 Assumptions

1.1.1 There are two regions labeled 1 and 2. Region 1 has a larger population, which leads to a bigger N', a longer epidemic duration ($T_1 > T_2$) as well as larger demand of medicine ($s_1 > s_2$).

1.1.2 When the medicine is insufficient but enough to meet the need of one region (namely $s_1, s_2 < s$ and $s_1 + s_2 > s$), s' units of medicine are delivered to region 2, while the rest are delivered to region 1.

1.1.3 When the epidemic situation in region 2 comes to an end, the remained medicine would be delivered to region 1.

1.2 Total number of extra survivals due to the effect of medicine

Assume that $s - s_1 < s' < s_2$, the expression can be written as

$$\alpha_2 s' + \alpha_1 (s - s') + (s_1 + s' - s)(a_1 - kT_2)$$

in which $(s_1 + s' - s)(a_1 - kT_2)$ means that after the epidemic situation ends in region 2, $(s_1 + s' - s)$ units of medicine are sent to region 1. Because these units of medicine are not sent to the region on time, the medicine is not that effective and the effective index becomes $(a_1 - kT_2)$.

The largest amount of extra survivals are as follows:

When $kT_2 > \alpha_2$, $s - s_1 = s'$, we need to satisfy the need of region 1 first.

When $kT_2 < \alpha_2$, $s' = s_2$, we need to satisfy the need of region 2 first.

Whether $kT_2 > \alpha_2$ or not depends on the population of region 2. If N' is larger than 545, kT_2 would be larger than α_2, otherwise it wouldn't.

2. The Multi-region System: a Linear Programming Problem

2.1 Assumption

There are *n* regions labeled *1,2,…,N*， which satisfy the inequality $N_1'<N_2'<...<N_n'$.

2.2 Objective Function

The meaning of objective function is the number of cases who survive with the help of medicine. We make linear programming to make the function reaches its maximum.

$$(\alpha_1 s_{11} + \alpha_2 s_{21} + ... + \alpha_n s_{n1})$$

$$+[(\alpha_2 - kT_1)(s_{22} - s_{21}) + (\alpha_3 - kT_1)(s_{32} - s_{31}) + ... + (\alpha_n - kT_1)(s_{n2} - s_{n1})]$$

$$+[(\alpha_3 - kT_2)(s_{33} - s_{32}) + (\alpha_4 - kT_2)(s_{43} - s_{42}) + ... + (\alpha_n - kT_2)(s_{n3} - s_{n2})]$$

$$+... + (\alpha_n - kT_{n-1})(s_{nn} - s_{nn-1})$$

In which s_m means the daily demand of the region No.m, s_{ij} means the amount of medicine that the region No.i receives in the period No.j. The meanings of α and k are the same as the above. The specific values are determined by the population of the cities.

2.3 Problem Constraints

2.3.1 For any m,

$$\sum_{i=m}^{n} s_{im} \le s$$

which means that the total amount of medicine provided every day is limited.

2.3.2 For any $i \le j$ and m,

$$s_{mi} \le s_{mj}$$

which means that the amount of medicine delivered from the regions where epidemic has ended are non-negative.

2.3.3 For any m,

$$s_{mi} \le s_m$$

which means when the demand is meet, it's meaningless to continue to make the amount of medicine delivered every day larger.

2.4 Values of Parameters

Labels and Cities	4	3	2	1
	Freetown	Port Loko	Bombali	Kenema
α	8.70428	6.390248	6.103976	4.845998
s	878.2852	494.5035	447.0254	238.39
T	754.534	570.9324	548.2188	448.4074

2.5 The linear programming problem in this case

Objective function:

$$(4.846 * s_{11} + 6.104 * s_{21} + 6.390 * s_{31} + 8.704 s_{41})$$

$$+[0.767(s_{22} - s_{21}) + 1.053(s_{32} - s_{31}) + 3.368(s_{42} - s_{41})]$$

$$+[-0.1312(s_{33} - s_{32}) + 2.183(s_{43} - s_{42})] + 1.909(s_{44} - s_{43})$$

Problem constraints:

$$s_{11} + s_{21} + s_{31} + s_{41} \le s;$$

$$s_{22} + s_{32} + s_{42} \le s;$$

$$s_{33} + s_{43} \le s;$$

$$s_{44} \le s;$$

$$s_{22} - s_{21} > 0; \quad s_{32} - s_{31} \ge 0; \quad s_{42} - s_{41} \ge 0;$$

$$s_{33} - s_{32} \ge 0; \quad s_{43} - s_{42} \ge 0; \quad s_{44} - s_{43} \ge 0;$$

$$s_{11} \le 238; \quad s_{21} \le 447; \quad s_{22} \le 447; \quad s_{31} \le 495; \quad s_{32} \le 495; \quad s_{33} \le 495;$$

$$s_{41} \le 878; \quad s_{42} \le 878; \quad s_{43} \le 878; \quad s_{44} \le 878;$$

2.6 Results and Analysis of the Four Sierra Leone Regions

The results derived from LINGO are as follows.

2.6.1 When s=600, medicine is insufficient

Objective value=5222, with the values of variables

Time	$0 \sim T_1$				$T_1 \sim T_2$			$T_2 \sim T_3$		$T_3 \sim T_4$
Drug Provision/unit	S_{11}	S_{21}	S_{31}	S_{41}	S_{22}	S_{32}	S_{42}	S_{33}	S_{43}	S_{44}
	0	0	0	600	0	0	600	0	600	600

2.6.2 When s=1200, medicine is insufficient

Objective value=9700, with the values of variables

Time	$0 \sim T_1$				$T_1 \sim T_2$			$T_2 \sim T_3$		$T_3 \sim T_4$
Drug Provision/unit	S_{11}	S_{21}	S_{31}	S_{41}	S_{22}	S_{32}	S_{42}	S_{33}	S_{43}	S_{44}
	0	0	322	878	0	322	878	322	878	878

2.6.3 When s=1800, medicine relatively sufficient

Objective value=13412, with the values of variables

Time	$0 \sim T_1$				$T_1 \sim T_2$			$T_2 \sim T_3$		$T_3 \sim T_4$
Drug Provision/unit	S_{11}	S_{21}	S_{31}	S_{41}	S_{22}	S_{32}	S_{42}	S_{33}	S_{43}	S_{44}
	0	427	495	878	427	495	878	495	878	878

2.6.4 When s=2100, medicine is sufficient

Objective value=14687, with the values of variables

Time	$0 \sim T_1$				$T_1 \sim T_2$			$T_2 \sim T_3$		$T_3 \sim T_4$
Drug Provision/unit	S_{11}	S_{21}	S_{31}	S_{41}	S_{22}	S_{32}	S_{42}	S_{33}	S_{43}	S_{44}
	238	447	495	878	447	495	878	495	878	878

With the calculation above, in Sierra Leone's case, we can simply derive the sequence of priority by comparing a_i. For those who have higher a_i, we should satisfy their demand first. In this case, we should first satisfy the need of Freetown, then Port Loko, then Bombali, and finally Kenema.

2.7 Results and Analysis of Larger Regions

But it isn't always the case. As is shown in the 2-region problem, if the side length of the smaller region is larger than 545 (which means the population of the smaller region is higher than 3.8 million), the smaller city deserves the higher priority.

So we consider 4 regions with large populations. The results are as follows,

Label of the Region	4	3	2	1
Population	9,000,000	7,000,000	6,000,000	3,000,000
N'(Side length)	840	741	686	485
α	20.0657	17.952961	16.782457	12.503651
s	2762.574	2412.1767	2218.0489	1508.41
T	1657.156	1489.3867	1396.4387	1056.6654

2.7.1 When s=1500, medicine is extremely insufficient

Objective value=30690, with the values of variables

Time	$T_1 \sim T_2$				$T_1 \sim T_2$			$T_1 \sim T_2$		$T_1 \sim T_2$
Drug Provision/unit	S_{11}	S_{21}	S_{31}	S_{41}	S_{22}	S_{32}	S_{42}	S_{33}	S_{43}	S_{44}
	0	1500	0	0	1500	0	0	1500	0	1500

In this case, we should first send medicine to region 2, then region 3, then finally region 4.

2.7.2 When s=3000, medicine becomes a little bit more sufficient
Objective value=60560, with the values of variables

Time	$0 \sim T_1$				$T_1 \sim T_2$			$T_2 \sim T_3$		$T_3 \sim T_4$
Drug Provision/unit	S_{11}	S_{21}	S_{31}	S_{41}	S_{22}	S_{32}	S_{42}	S_{33}	S_{43}	S_{44}
	0	2218	781	0	2218	781	0	2412	587	2762

Consequently, to maximize the survival rate, we'd better satisfy the demand from region 2 first, and when the epidemic of region 2 ends, we could satisfy the need of region 3 and send the rest of the medicine to region 4.

2.7.3 When s=6000, medicine becomes more sufficient
Objective value=112818, with the values of variables

Time	$0 \sim T_1$				$T_1 \sim T_2$			$T_2 \sim T_3$		$T_3 \sim T_4$
Drug Provision /unit	S_{11}	S_{21}	S_{31}	S_{41}	S_{22}	S_{32}	S_{42}	S_{33}	S_{43}	S_{44}
	0	2218	2412	1370	2218	2412	1370	2412	2762	2762

So the need of regions 2,3,4 are prior to that of 1.

Consequently, the sequence of priority becomes 2>3>4>1, which means that the larger city doesn't necessarily own the higher priority in all the cases, and we should make calculations to get the appropriate sequence.

V) A General Method for Drug Allocation among Several Countries in West Africa

In this part, we come up with a general method that can be adopted in the arrangement of allocation and transportation. This can be applied to variable cases, not only the on-going Ebola epidemic in West Africa, but also other diseases in other parts of the world.

1. Target

Rearrange the limited drugs in the most efficient way to minimize the death toll.

2. Assumptions

2.1 Drugs are transported from other parts of the world to major countries in Ebola epidemic area, such as Sierra Leone, Liberia and Guinea.

2.2 The disease is on-going in each country, hence they all demand drug assistance.

2.3 There are several international airports among these countries, drug and other medical resources arrive at these places every day.

2.4 The speed of transporting drugs within a country is much faster than that of transporting across several countries.

2.5 The amount of provision in each country isn't strictly equal to the demand, because the stage of the epidemic evolution in each country is different.

3. Modeling

3.1 Set up a graph, the abstract data type, to represent the area. Each node represents a country(or a district, if the transportation among them are rather inconvenient). Then due to the diversity of the time cost on each edge, we set different edge values, which are all non-negative.

3.2 In order to find the shortest path between two nodes, we can use Dijkstra's algorithm if the system is rather complex.

IV. Application Prospect

The application of this model is not only the spread and control of Ebola, but also various infectious diseases. Due to the fact that Ebola is extremely infectious, the patient distribution in the above graph appears to be in square shape, which in realistic corresponds to the situation where diseases spread to all neighbors, centering on mild patients. If the mock object is another less infectious disease, the distribution of patient will be like the following graph, which is a more general case.

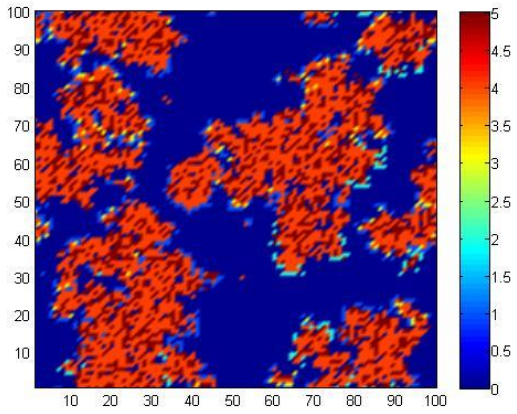


Figure 14|The patient distribution of another disease with lower infection rate compared with Ebola.

Taking distinctive features of specific epidemic into consideration and following all the statistical processes we have gone through, this model will be able to assist researchers to predict the tendency of the spread of disease and take optimal anti-epidemic measures to prevent the outbreak.

V. Conclusion

1. From the above three steps of model establishment and analysis, which are free propagation model, cure model with sufficient drug supply and drug delivery model, we get a panoramic view of the Ebola spread and control system.

1.1 When drugs are not involved in this issue, the tendency of the patient number will first increase and then decrease back to zero, but there is constant oscillation in

the system development, which is caused by the specific feature of Ebola that susceptible patients are not infectious. This tendency matches well with the real data we get from WHO.

1.2 If sufficient drug is provided, mortality will be lower. The stronger the drug efficacy is, the more patients will be cured.

1.3 If the drug amount is limited, drug delivery issue should be considered According to the statistical results, many factors in this issue has linear relation with the square root of population, so in some situation in order to minimum the global mortality, we have to give up cities with the less population.

2. Applying this model to the real case in four cities of Sierra Leone, we give the optimal delivery plans in several situation when the available drug supply amount is different.
3. Through the construction and analysis of this model, we enhance our ability to solve problems, but that is not all. This issue raises our care to the suffering patients of Ebola. We express our continuous concern to all the affected countries and hope to carry out further study about this model to help them. Hope they can get over this misery in the near future.

VI. References

1. Magill, Alan. Hunter's Tropical Medicine and Emerging Infectious Diseases(9th ed.) [M]. New York: Saunders, 332(2013).
2. Sunit K. Singh, Daniel Ruzek. Viral Hemorrhagic Fevers[M]. CRC Press. 444(2013).
3. Ebola Situation Report - 4 February 2015. World Health Organization. 4 February 2015. http://apps.who.int/ebola/en/ebola-situation-report/situation-reports/ebola-situation-report-4-february-2015
4. Ebola Virus Disease Fact Sheet No. 103. World Health Organization. September 2014.
5. Wolfram, Stephen. Statistical Mechanics of Cellular Automata[J]. Reviews of Modern Physics 55 (3): 601–644(1 July 1983).
6. Xia Jiang, Gregory F Cooper. A Bayesian spatio-temporal method for disease outbreak detection[J]. Journal of the American Medical Informatics Association 17 (4): 462–71 (1 July 2010).

WMA Announcement on Ebola Viral Disease

1. BACKGROUND

The 2014 Ebola outbreak is the most severe in history since 1976 with regard of both the number of human cases and fatality. Numerous countries and continents have been involved into the battle towards Ebola virus, examples are Sierra Leone, Guinea, and Liberia in Africa, Spain in Europe and the United States in North America. Statistics show that at least 22,495 people have been infected and 8,981 are killed since March 2014, and so far the epidemic propagation doesn't appear to be slowing down. With approximately 50-95% mortality, Ebola virus has become one of the most harmful diseases to human beings.

Ebola virus belongs to the Filoviridae family which can cause epidemics of haemoeehagic fever. After being infected, patients remain asymptomatic for a period of 2 to 21 days. During this time, test result of the virus is negative and patients are not infectious. However, once the patients become symptomatic, virus will spread through contact with body fluids including blood. The infectious rate is extremely high.

Traditional management is primarily through infection control, the use of personal protective equipment and supportive care for sick patients. But those treatments are somewhat ineffective and will put health care workers under risk.

2. VACCINE DEVELOPMENT

Effective vaccines have already been preliminary developed. By now it should be the optimal treating method.

However, at present the production capacity as well as the drug efficacy are quite limited. Sufficient vaccine supply is not guaranteed. Besides, the drug hasn't passed all the compulsory preliminary tests by drug administrations, which may take years to finish. This usually serves as a barricade in clinical application.

3. CURRENT SITUATION

Due to the limited production capacity and the fact that the more severe condition corresponds to higher drug demand and lower recovery possibility, although reluctantly, vaccine allocation should be seriously considered. According to research, with insufficient drug, we are supposed to put regions with less patients in lower priority and invest larger amount of drugs per capita to regions with larger population in order to minimum the death rate.

4. RECOMMENDATIONS

To get over the current dilemma and ensure every patient has equal right to receive treatment, the world medical association (WMA) calls on the following actions.

4.1 The WMA calls on all those developing vaccines to speed up the research process, all

those supporting the vaccines developing research to enhance the investment. Drug with strong efficacy is the most robust guarantee for disease control.

4.2 The WMA calls on governments of those countries that are struck by Ebola to accelerate the construction of their treatment facilities, attach more emphasis to the discovery, inspection and quarantine of infectious patients. Disease control will be easier when the infection sources are early isolated.

4.3 The WMA calls on drug administrations worldwide to accelerate the pace of drug and vaccine approval. In extreme cases, some exceptions are also acceptable to save lives and protect public health.

4.4 The WMA calls on all countries and international organizations to support affected countries materially and financially. With joint effort huge quantity of drugs can be produced under current condition, which will bring hope to the suffering people as well as lower the potential risk to all the human beings.