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T1	_____		F1	_____
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T3	_____		F3	_____
T4	_____		F4	_____
		Problem Chosen		
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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

Background The unprecedented Ebola virus disease (EVD) epidemic in west Africa has aroused great concern. Researchers seek to control it in many ways: new EVD treatment methods, mature EVD mathematic models along with effective delivery programs et al. We aimed to assess how these control interventions could be applied properly to avert future EVD cases and deaths.

Methods In order to track the evolution of an epidemic process over time, we use the data of Ebola virus disease in West Africa along with a developed discrete-time susceptible-exposed-infectious-recovered (SEIR) model, which has been imbedded in infectious diseases modeling for many years. For the purpose of capture the stochastic nature of the transitions between the compartmental populations in such a model we specify appropriate conditional binomial distributions. Considering the dynamic characteristic of the parameters, the realization of this model is designed based on the Markov chain Monte Carlo methods, which is able to explore the posterior distribution of the parameters in a short time. To make sure of feasible implement, we then divide the West Africa epidemic data into two parts: one to infer latent params of SEIR, the other to evaluate our model's quality. After that, We take a close look at the Liberias epidemic data which can expressly reflect the strengths and weaknesses of the emergency medical system. With respect to the medical control methods, a rapid response medical delivery system would be constructed on the basis of a logistics center location model with linear restrains. Finally we received a list of suitable logistics center locations owning the minimum objective function.

An Advanced Model Designed for Controlling Ebola

February 10, 2015

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Keywords: Ebola , SEIR , MCMC , SQP

1 Introduction

About Ebola *Ebola virus disease* (EVD; also *Ebola hemorrhagic fever*, or EHF), or simply Ebola, is transmitted via physical contact with body fluids, secretions, tissues, or semen from infected individuals (*Chowell et al., 2004*). Signs and symptoms typically start between two days and three weeks after contracting the virus with a fever, sore throat, muscle pain, and headaches. Then, vomiting, diarrhea and rash usually follow, along with decreased function of the liver and kidneys. At this time some people begin to bleed both internally and externally. The disease has a high risk of death, killing between 25 and 90 percent of those infected with an average of about 50 percent. This is often due to low blood pressure from fluid loss, and typically follows six to sixteen days after symptoms appear.

Epidemiology canonical models

1. SI (Susceptible-Infected)
2. SIR (Susceptible-Infected-Recovered)
3. SIS (Susceptible-Infected-Susceptible)

Absorbing states: I for the SI model, R for the SIR model. Transitions are irreversible in SI and SIR , but reversible in SIS .

SI SI model, a foundation.

- Initially some nodes are in state I (seeds), all others are in S .
- There is a probability p that a node in state I is operational, that is it infects its neighbours in state S .
- The process ends when no more susceptible nodes are tested.

If $p = 1$, I is an absorbing state. In a random network, all connected components that have a seed end up in I .

The operational probability may depend on the degree, so that $p = p_k$ for a node with degree k (*Chowell et al., 2000*).

If we assume that p is constant, we have a percolation model.

SIR SIR model, a new state: Recovered (or Removed)

- Initially some nodes are in state I (seeds), all others are in S .
- A node in state I has a probability p of infecting its neighbours in state S , which undergo the transition $S \rightarrow I$.

- There is a chance to recover , and each node entering state I remains infected for $t_I = 1/\delta$ steps.
- After t_I the node becomes recovered (that is removed) with the transition $I \rightarrow R$.
- Eventually all (connected) nodes are in R if $p = 1$, otherwise the absorbing state is one where S and R coexist, but not I .

SIS

- Initially some nodes are in state I (seeds), all others are in S .
- A node in state I has a probability p of infecting its neighbours in state S , which undergo the transition $S \rightarrow I$.
- A node remains in state I for a number t_I of time steps (or there is a chance to recover $= \frac{1}{t_I}$). t_I
- After t_I this node undergoes the transition $I \rightarrow S$.

Resuming, we have a transitions loop: $S \rightarrow I \rightarrow S \dots$

2 Data

Data of Ebola virus from March 22, 2014 to February 1, 2015 *wikipedia.org* [10]

Illustrated from Figure.1 and Figure.2, it is obvious that number of people infected and deaths have increased a lot. In order to process better later, Linear interpolation is adopted. After interpolation, the data of everyday could be got approximately. The result is shown in Figure 3. The red bar represents the increment of infected people everyday, and the blue bar represents the number of infected persons. It reflects that the situation does not seem optimistic. The scale of people infected everyday is becoming larger. As we know, the disease having a mortality rate of 50 ~ 90%, which is proved by the data above.

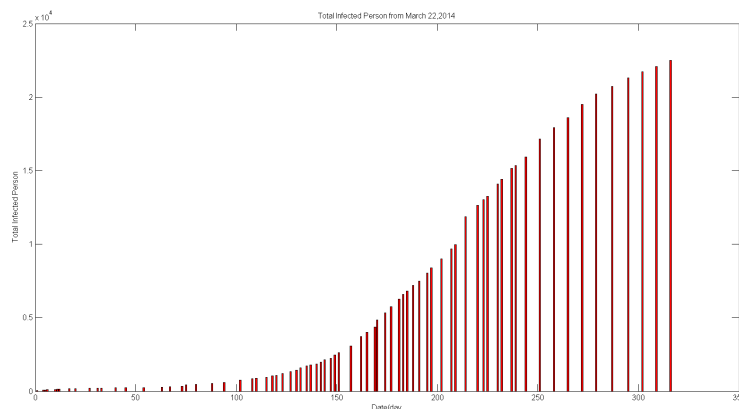


Figure 1: Total Dead Person from March 22, 2014

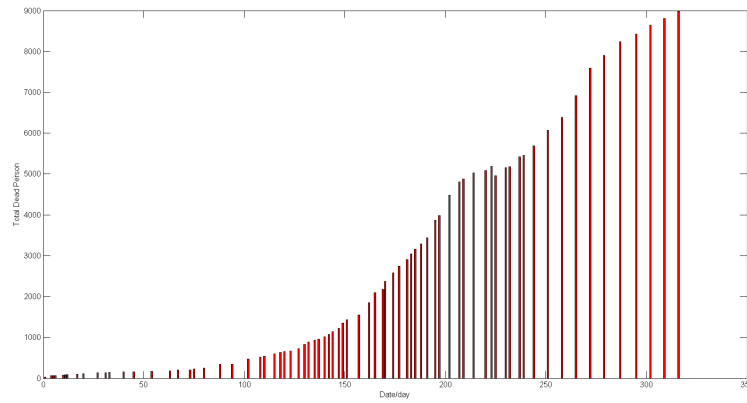


Figure 2: Total Infected Person from March 22,2014

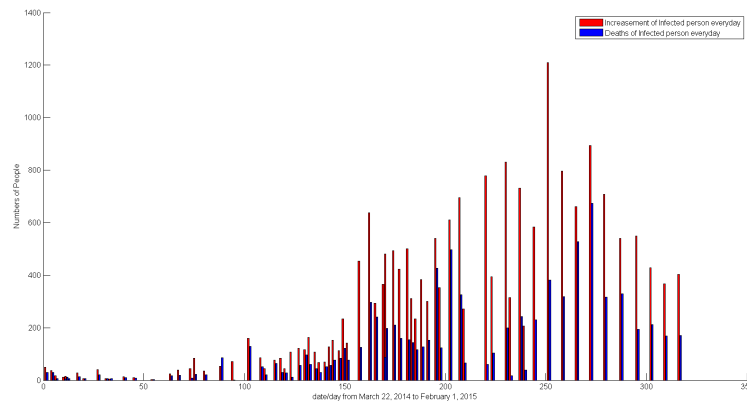


Figure 3: Changes in the number of Infected person and Deaths everyday

3 Methods

3.1 Optimized Model Based on SEIR

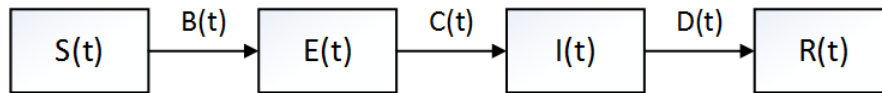


Figure 4: SEIR processing

The susceptible-exposed-infectious-recovered (SEIR) model is usually expressed as a system of differential equations. In this paper, we consider a time interval $(t, t+h]$, where h represents the length between the time points at which measurements are taken, here $h = 1$ day. Let $B(t)$ denote the number of susceptible individuals who become infected, $C(t)$ the number of cases by date of symptom onset, and $D(t)$ the number of cases who are removed (die or recover) from the infectious class during that time interval. Furthermore, let τ^* denote the time point when the epidemic goes extinct, that is, the first time point at which there are no exposed or infectious individuals in the population. Let

Table 1: Symbols

Symbol	Definition
$S(t)$	the number of susceptible individuals in the population at time t
$E(t)$	the number of exposed individuals in the population at time t
$I(t)$	the number of infectious individuals in the population at time t
$R(t)$	the number of removed individuals in the population at time t
$B(t)$	the number of susceptible individuals who become infected
$C(t)$	the number of cases by date of symptom onset
$D(t)$	the number of cases who are removed (die or recover) from the infectious class during that time interval
h	the length between the time points at which measurements are taken
s_0	the initial conditions of $S(t)$
e_0	the initial conditions of $E(t)$
a	the initial conditions of $I(t)$
N	the population size
$\beta(t)$	the time-dependent transmission rate
$1/\delta$	the mean incubation period
$1/\gamma$	the mean infectious period
$\lambda(t)$	the compartment-specific rate
$P(t)$	the probability from $S(t)$ to $B(t)$
p_C	the probability from $E(t)$ to $C(t)$
p_R	the probability from $I(t)$ to $D(t)$
t_*	the time point at which control measures are introduced
β	the initial transmission rate
Θ	parameter vector
$R_0(t)$	effective reproductive number
m	a final size of infectious individuals
τ^*	the time point when the epidemic goes extinct
q	$q > 0$ is the rate at which $\beta(t)$ decays for $t > t_*$
$p(x)$	target distribution
$q(x * x(t_1))$	proposal distribution
α	The probability of accepting the proposal

$\mathbf{B} = \{B\}_{t=0}^{\tau^*}$ represent $t=0$ the time series of $B(t)$ from the beginning to the end of the epidemic and define \mathbf{C} and \mathbf{D} similarly. We use a discrete-time approximation to the stochastic continuous-time SEIR model (Gibson and Renshaw, 1998). Define $S(t)$, $E(t)$, $I(t)$, and $R(t)$ as the number of susceptible, exposed, infectious, and removed individuals in the population at time t , respectively. Given initial conditions $S(0) = s_0$, $E(0) = e_0$, $I(0) = a$, and the population size N , the discretized stochastic SEIR model is specified by

$$\begin{aligned} S(t+h) &= S(t) - B(t), \\ E(t+h) &= E(t) + b(t) - C(t), \\ I(t+h) &= I(t) + C(t) - D(t), \\ N &= S(t) + E(t) + I(t) + R(t), \end{aligned} \tag{1}$$

where

$$B(t) \sim \text{Bin}(S(t), P(t)), C(t) \sim \text{Bin}(E(t), p_C), D(t) \sim \text{Bin}(I(t), p_R),$$

are random variables with binomial $\text{Bin}(n, p)$ distributions with probabilities:

$$\begin{aligned} P(t) &= 1 - e^{-\frac{\beta(t)}{N} h I(t)}, \\ p_C &= 1 - e^{-\rho h}, \\ p_R &= 1 - e^{-\gamma h}, \end{aligned} \tag{2}$$

Parameter Inference In statistics, Markov Chain Monte Carlo (MCMC) methods are a class of algorithms for sampling from a probability distribution based on constructing a Markov chain that has the desired distribution as its equilibrium distribution. The state of the chain after a number of steps is then used as a sample of the desired distribution. The quality of the sample improves as a function of the number of steps. We discuss one of the main ideas underlying MCMC, Monte Carlo sampling. Monte Carlo sampling allows one to estimate various characteristics of a distribution such as the mean, variance, kurtosis. Markov chains involve a stochastic sequential process where we can sample states from some stationary distribution. The target of MCMC is to design a Markov chain such that the stationary distribution of the chain is exactly the distribution that we are interested in sampling from. This is called the target distribution. That is, we would like the states sampled from some Markov chain to also be samples drawn from the target distribution. The idea is to use some feasible methods for setting up the transition function such that no matter how we initialize each chain, it will converge to the target distribution. There are a number of methods that achieve this goal using relatively simple procedures. We will discuss Metropolis which is the simplest of all MCMC methods.

Assume our goal is to sample from the target density $p(x)$, with $-\infty < x < \infty$. The Metropolis sampler creates a Markov chain that produces a sequence of values: $x(1) \rightarrow x(2) \rightarrow \dots \rightarrow x(t)$ where $x(t)$ represents the state of a Markov chain at iteration t . The samples from the chain, after burnin, reflect samples from the target distribution $p(x)$. In the Metropolis procedure, we initialize the first state, $x(1)$ to some initial value.

We then use a proposal distribution $q(x_*|x(t_1))$ to generate a candidate point x_* that is conditional on the previous state of the sampler. The next step is to either accept the proposal or reject it. The probability of accepting the proposal is:

To make a decision on whether to actually accept or reject the proposal, we generate a uniform deviate u . If $u \leq \alpha$, we accept the proposal and the next state is set equal to the proposal: $x(t) = x_*$. If $u > \alpha$, we reject the proposal, and the next state is set equal to the old state: $x(t) = x(t_1)$. We continue generating new proposals conditional on the current state of the sampler, and either accept or reject the proposals. This procedure continues until the sampler reaches convergence. At this point, the samples $x(t)$ reflect samples from the target distribution $p(x)$. Here is a summary of the steps of the Metropolis sampler:

1. Set $t = 1$
2. Generate a initial value u , and set $x(t) = u$
3. Repeat $t = t + 1$ Generate a proposal x_* from $q(x|x(t_1))$ Evaluate the acceptance probability

$$\alpha = \min(1, \frac{p(x_*)}{p(x(t-1))})$$

Generate a u from a Uniform(0,1) distribution If $u \leq \alpha$, accept the proposal and set $x(t) = x_*$, else set $x(t) = x(t_1)$.

4. Until $t = T$

Model Application Suppose we wish to generate random samples from the normal distribution, The probability density of the Normal is given by:

$$f(x) = \frac{1}{\sqrt{2\pi}} e^{-\frac{x^2}{2}}$$

Therefore, the Metropolis acceptance probability becomes

$$\alpha = \min(1, \frac{e^{-x_*^2/2}}{e^{-x(t)^2/2}})$$

We will use the binomial distribution as the proposal distribution. Our proposals are generated from a binomial $(S(x(t-1)), P(t))$ distribution.

3.2 SQP Algorithm

Sequential quadratic programming (SQP) methods have proved highly effective for solving constrained optimization problems with smooth nonlinear functions in the objective and constraints. Here we consider problems with general inequality constraints (linear and nonlinear). We assume that first derivatives are available and that the constraint gradients are sparse. Second derivatives are assumed to be unavailable or too expensive to calculate.

The algorithm applies to constrained optimization problems of the form

$$\min_{x \in \mathbb{R}} f(x)$$

$$\text{subject to } l \leq \begin{pmatrix} x \\ c(x) \\ Ax \end{pmatrix} \leq u$$

where $f(x)$ is a linear or nonlinear objective function, $c(x)$ is a vector of nonlinear constraint functions $c_i(x)$ with sparse derivatives, A is a sparse matrix, and l and u are vectors of lower and upper bounds. We assume that the nonlinear functions are smooth and that their first derivatives are available (and possibly expensive to evaluate).

Considering program running efficiency, we introduced a *Matlab* function *fmincon* which uses SQP algorithm intrinsically(MathWorks [17]).

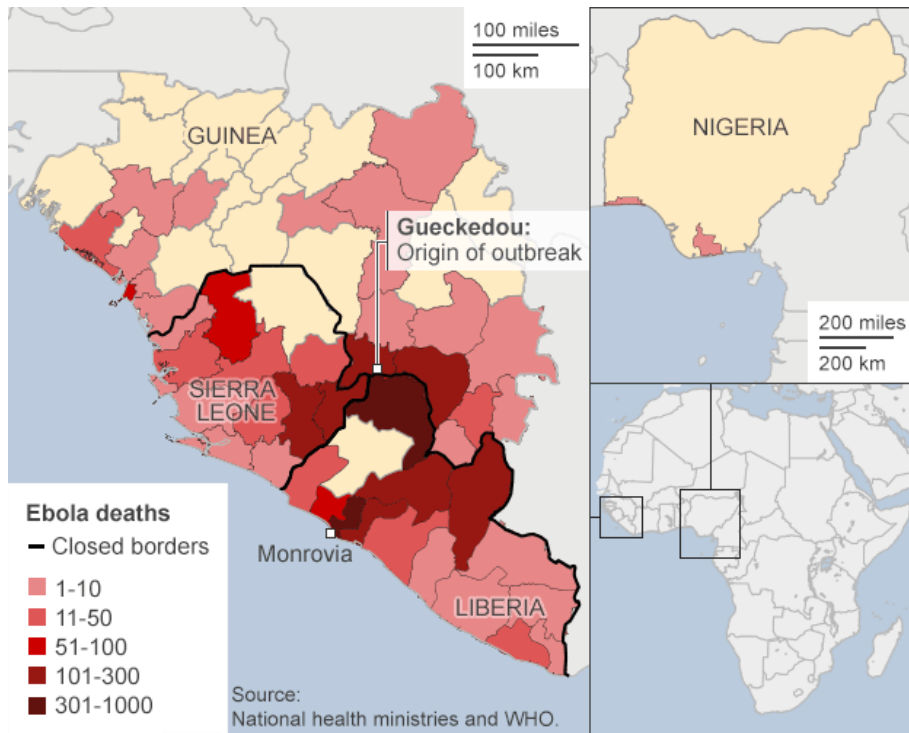


Figure 5: Ebola transmit situation in 10/ Aug/2014

Algorithm

1. Read image data shown in Figure.5.
2. Evaluate degree of infection by RGB data and Labels listed.
3. Extract sample dots every 5 pixels(both column and row) as shown in Figure.6
4. Using Euclidean distance as the objective function and minimize it with *fmincon*

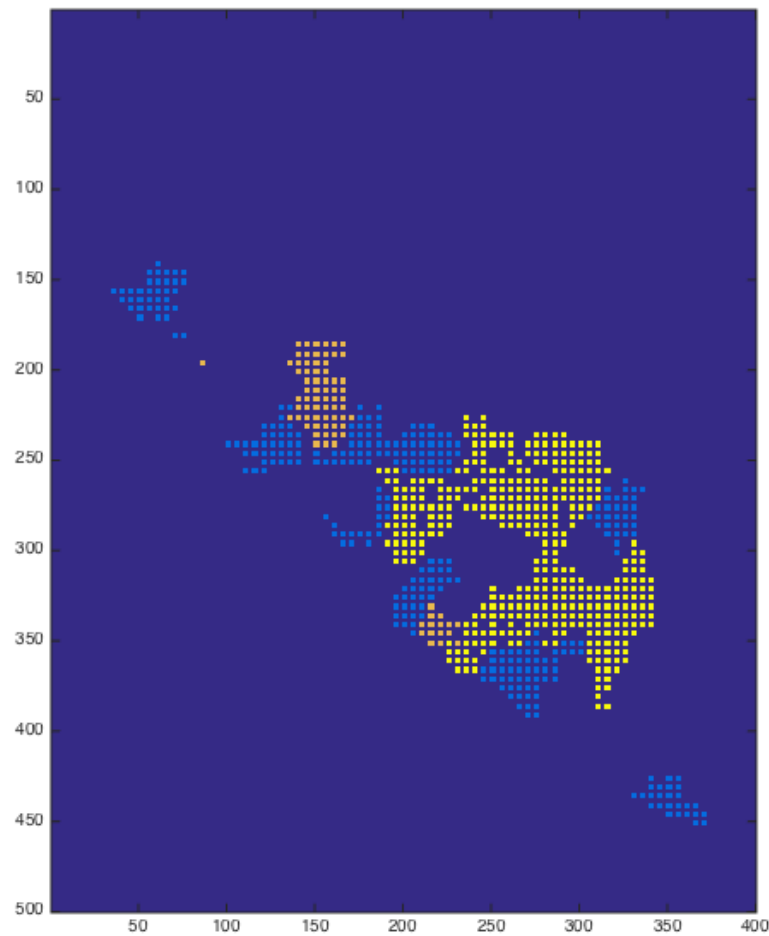


Figure 6: Dot

4 The Model Results

Using the parameter of *Phenyo and Barbel(2006)*, we can get the time series of $B(t)$ which can not be observed in real life(Figure.7.A). The results reflect that the number of susceptible individuals who become infected is more and more by date every day.

In Figure.7.B/C/D, The three picture reflect the trend of the population that are susceptible ,exposed, infectious during 345days. The effectiveness of interventions is often quantified in terms of the reproductive number R_0 after interventions are put in place.From t^* ,we introduce the control measures, putting in Vaccine from the 316 days.It is obvious that the basic reproductive number R_0 is below 1from the 319th days.The case $R_0 \leq 1$ is of special interest as it highlights the crossing of the threshold to eventual control of the outbreak.

So the disease is controled gradually by the interference measures. $R_0 < 0.01$ was used as Ebola fully controlled marker. In the result, R_0 begins to meet the request of $R_0 < 0.01$ from the 345 days.

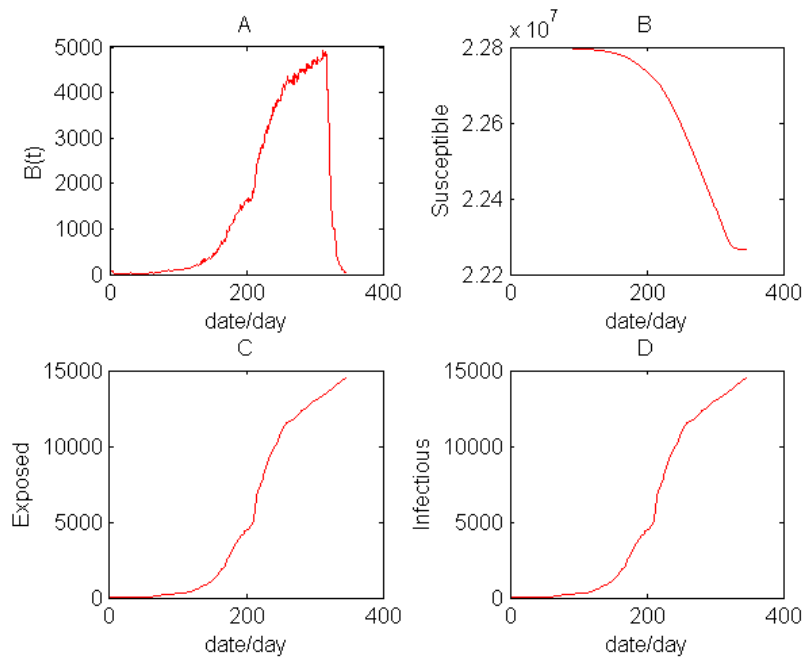


Figure 7: Results

5 Conclusions

In this paper, we investigated the variation of the population that are susceptible ,exposed, infectious in west Africa which is suffering the unprecedented Ebola virus disease (EVD) epidemic.

Through SEIR model, we received the number of susceptible individuals who become infected during whole process. The use of Markov Chain Monte Carlo methods (MCMC) have optimized the model. After implementing control measures, we also considered the possible feasible delivery systems by using SQP Algorithm. Simulation results show that MCMC methods can get more suitable results, also SQP Algorithm gives a suitable logistic center location which makes the vaccine delivered more optimized.

6 Model Evaluation

Strengths

- Using MCMC model makes it more realistic
- SQP model provides a more reasonable Program to delivery Vaccine
- Getting more data by Interpolation,it is useful to construct a model

Weaknesses

- Using conventional parameters may introduce some unnecessary errors

Nontechnical explanation

Background Ebola which outbroken in West Africa recently has constituted "unusual event" and pose a public health risk to other countries; Due to the virulence of the virus in the community and the intensive mode of transmission in health facilities, as well as currently affected and high-risk countries only have weak health systems, the consequences of the disease in the world could lead to the further spread more serious. Need for a coordinated international response to prevent and reverse the international spread of the Ebola virus.

Our Model We propose a SEIR model which is based on MCMC methods, the model can predict the trend of infectious diseases after intervention of the vaccine, in addition to the use of SQP algorithm, the optimal solution of vaccine delivery can be constructed, and thus the spread of Ebola can be restrained in the greatest degree.

Advices

- A head of state should declar a national emergency , notice National People personally, indicating the status quo, the steps taken in response to the epidemic and key role of community in ensuring rapid disease control; providing immediate emergency funding to initiate and sustain operations; at the same time take all necessary measures to ensure that compensation of health care workers.
- the state should ensure care workers to get adequate security measures,the timely payment of salaries and on infection prevention and control, including appropriate education and training on the proper use of personal protective equipment, methods.
- If it is confirmed Ebola virus propagation,the country should be based on epidemiological and risk at the national or sub-national level to implement all the recommendations for countries with the spread of the Ebola virus.

Outlook Now many countries and organizations are actively committed to the development of Ebola virus in the vaccine, I believe that we will succeed in developing a vaccine in the future, in order to better benefit the people of the world, improve people's lives better. That would be a common good for all over the world.

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Appendices

Appendix A First appendix

Here are simulation programmes we used in our model as follow.

Implementation of the methods described in this article was done with a modern standard computer using the *Matlab 2014b* software and the code is available to interested readers on request to the authors. Computation time was less than 45 minutes for each of the Markov chain runs.

Input matlab source:

```
x0 = [200,100,300,250];
lb=[50,50,50,50];
ub=[500,400,500,400];
global imz;
[im1,im2,im3,im4,im5]=ploo();
imz=gen(im1,im2,im3,im4,im5);
[x,fval]=fmincon(@trans,x0,[],[],[],[],lb,ub,@con);
```

```
function [c,ceq] = con(x)
c=( (x(1)-x(3))^2+(x(2)-x(4)))+50;
ceq=[];
end
```

```
function imz=gen(im1,im2,im3,im4,im5)
imz = zeros(500,400);
for i=1:10:500
    for j=1:10:400
        if(isnan(im1(i,j,1)))
            imz(i,j)=1;
        else if(isnan(im2(i,j,1)))
            imz(i,j)=11;
        else if(isnan(im3(i,j,1)))
            imz(i,j)=51;
        else if(isnan(im4(i,j,1)))
            imz(i,j)=101;
        else if(isnan(im5(i,j,1)))
            imz(i,j)=301;
        end
    end
end
end
end
end
imz(400:500,1:50)=0;
```

```
function [im1,im2,im3,im4,im5]=ploo()
im = imread('2.png');

imt = im(:,1:400,:);
im1 = single(imt);

for i=1:500
    for j=1:400
```

```
        if(im1(i,j,1)==231 && im1(i,j,2)==135 && im1(i,j,3)==135)
            im1(i,j,:)=NaN;
        end
    end
end

imshow(im1)

imt = im(:,1:400,:);
im2 = single(imt);
for i=1:500
    for j=1:400
        if(im2(i,j,1)==223 && im2(i,j,2)==86 && im2(i,j,3)==86)
            im2(i,j,:)=NaN;
        end
    end
end

imshow(im2)

imt = im(:,1:400,:);
im3 = single(imt);
for i=1:500
    for j=1:400
        if(im3(i,j,1)==205 && im3(i,j,2)==0 && im3(i,j,3)==0)
            im3(i,j,:)=NaN;
        end
    end
end

imshow(im3)

imt = im(:,1:400,:);
im4 = single(imt);
for i=1:500
    for j=1:400
        if(im4(i,j,1)==151 && im4(i,j,2)==24 && im4(i,j,3)==18)
            im4(i,j,:)=NaN;
        end
    end
end

imshow(im4)

imt = im(:,1:400,:);
im5 = single(imt);
for i=1:500
    for j=1:400
        if(im5(i,j,1)==98 && im5(i,j,2)==18 && im5(i,j,3)==14)
            im5(i,j,:)=NaN;
        end
    end
end

imshow(im5)



---


function f=trans(x)
```

```

global imz;
f=0;
for i=1:500
    for j=1:400
        f=f+imz(i,j)*sqrt((x(1)-i)^2+(x(2)-j)^2+(x(3)-i)^2+(x(4)-j)^2);
    end
end

end

function y = cauchy( thetai )
    y = 1 ./ (1 + thetai.^2);
end

%we have known the parameter beta,xita,gam and q ,after using that and the
%date C,D of West African countries in the mixed model,
%we receive B,t*
S=[];E=[];I=[];
load('C.mat');load('D.mat');
beta=0.194;xita=0.201;gam=0.144;q=0.17;
pc=1-exp(-xita);pr=1-exp(-gam);
N=22800000;
S(1)=N;E(1)=1;I(1)=0;
T=1000;t0=316;
sigma=1;
Bmin=0;Bmax=max(C);
B=[];
seed=1;
rand('state', seed); randn('state',seed);
B(1)=round(median(C));
%% Start sampling
t=1;
R0=0.01;
while (fbeta(t)/gam)>=R0
    t=t+1;
    I(t)=I(t-1)+C(t-1)-D(t-1);
    S(t)=S(t-1)-B(t-1);
    E(t)=E(t-1)+C(t-1)-D(t-1);
    B0=binornd(S(t-1),fp(t-1,I));
    %Propose a new value for B using a binomial proposal density
    alpha = min( [ 1 norm(B0)/norm(B(t-1))] );%using a normal proposal density
    u = rand;
    if u < alpha
        B(t)=B0;
    else
        B(t)=B(t-1);
    end
    if t>t0
        C(t)=round(normrnd(C(t-1),1));
        D(t)=round(normrnd(D(t-1),1));
    end
end
end

function y = fbeta(t)
beta=0.194;t0=316;q=0.17;
if t<=t0
    y=beta;
else
    y=beta*exp(-q*(t-t0));
end

```

```
end
end
```

```
function y = fp(t,I)
N=12000000;
y=1-exp((-fbeta(t)/N)*I(t));
end
```

```
function y=norm(x)
y=exp(-x^2/2);
end
```
