

CasPPonNET: A predictive method to model the dynamics and control of Ebola

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Abstract

The world has been suffering from the Ebola virus disease (EVD) since March 2014. Recent days, a new round of outbreaks happened in West Africa. Imagine that we already have advanced medication for Ebola, but how can we develop a combination of optimal strategies to defeat Ebola in the most efficient and feasible ways?

We adopted a two-step framework to solve the problem. First, we built a predictive model to describe the spread of Ebola. Unlike traditional epidynamics model such as SIHR, we considered the effect of underlying network of the disease transmission based on geographical locations and population flow. We used a cascaded Poisson Process on the network, dubbed *CasPPonNet* to model the disease diffusion and progress. Hyper parameters 1 and 2 are used to control the ratio of transmission from the same location and other locations, and are learned from data.

Not only the number of new cases can be predicted precisely, but also outbreaks in new areas can be predicted. Secondly, we used the precious information our model yield to design theoretical optimal drug and vaccine delivery strategies.

Results from experiments on simulated data are proposed to demonstrate the performance of our model. Compared with baseline strategies, our strategy is better on both short term and long term goals. Based on our model and real-world data, we concluded Freetown(SL), Conakry(GN), Western rural(SL) and Port Loko(SL) are in urgent need of medicine and Dubreka(GN), Forecariah(GN) and Western rural(SL) are in need of vaccination now. We also determined the critical value for speed of manufacturing drug to bring the disease under control.

Keywords

Cascaded Poisson Process, Epidemic diffusion network, Epidemic control

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1 Introduction

1.1 Background

The Ebola virus causes an acute, serious illness which is often fatal if untreated.

The current outbreak in west Africa, (first cases notified in March 2014¹), is the largest and most complex Ebola outbreak since the Ebola virus was first discovered in 1976. There have been more cases and deaths in this outbreak than all others combined.

The most severely affected countries, Guinea, Sierra Leone and Liberia have very weak health systems, lacking human and infrastructural resources, having only recently emerged from long periods of conflict and instability. On August 8, the WHO Director-General declared this outbreak a Public Health Emergency of International Concern.

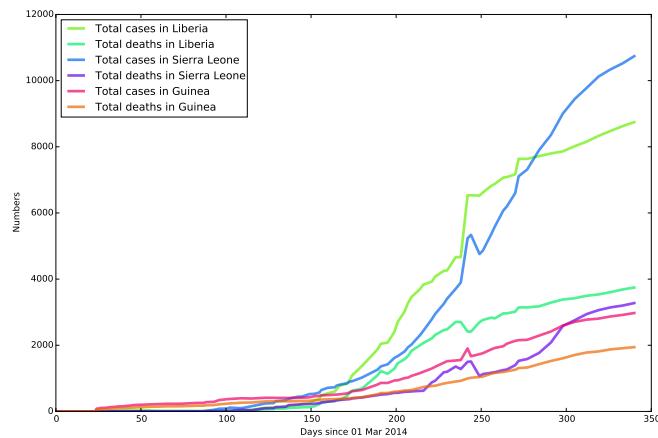


Figure 1: General statistics of Ebola outbreak in 2014

Fig. 1 shows the basic statistics of the Ebola outbreak in 2014. This is the cumulative cases and deaths in the three countries where the outbreak is the severe.²

1.2 Transmission

It is thought that fruit bats of the Pteropodidae family are natural Ebola virus hosts. Ebola is introduced into the human population through close contact with the blood, secretions, organs or other bodily fluids of infected animals such as chimpanzees, gorillas, fruit bats, monkeys, forest antelope and porcupines found ill or dead or in the rainforest.

Ebola then spreads through human-to-human transmission via direct contact (through broken skin or mucous membranes) with the blood, secretions, organs or other bodily fluids of

¹As the first case is observed in March 2014, we use the Δt from a certain time to March 2014 to mark the progress of Ebola spread in the rest of the paper

²The hump of the curve origin from the inconsistency of the data source, it changed on Nov 12 2014.

infected people, and with surfaces and materials (e.g. bedding, clothing) contaminated with these fluids.

It is reported that [1], 72% of infections occurred in households or in the general community , 17.5% in hospitals, and 10.4% at funerals. This observation is important for our modelling.

Human-to-human transmission gives rise to the wide spread such disease. It has spread between countries starting in Guinea then spreading across land borders to Sierra Leone and Liberia, by air (1 traveller only) to Nigeria, and by land (1 traveller) to Senegal.[2]

Figure. 2 shows the location of Ebola infected areas. We also got the geological location and other information such as population for the purpose of model calibration.

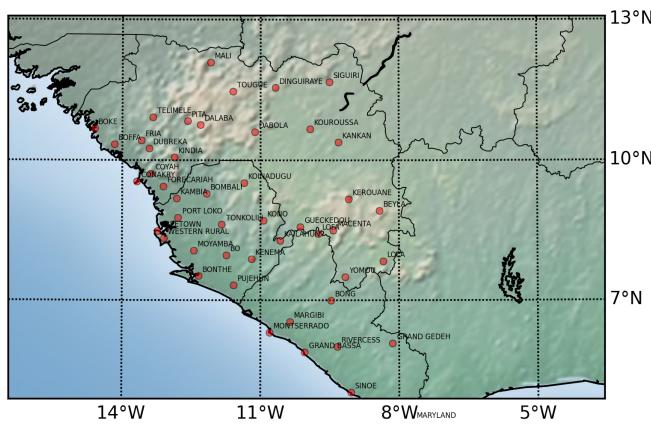


Figure 2: Location of Ebola infected cities

According to the observation of the outbreak data in Fig. 19 in the Appendix , we found there exists a strong correlation between infected areas in time. This observation validated that Ebola spread between countries on the land.

1.3 Medication

Supportive care-rehydration with oral or intravenous fluids and treatment of specific symptoms, improves survival. There is as yet no proven treatment available for EVD. However, a range of potential treatments including blood products, immune therapies and drug therapies are currently being evaluated. No licensed vaccines are available yet, but 2 potential vaccines are undergoing human safety testing.

However, in the modelling, we assume medicine and vaccines are found for treating Ebola. The mechanism of these two different types of medication methods plays different roles in controlling Ebola.

2 Problem Formulation

2.1 Problem Restatement

The world medical association has announced that their new medication could stop Ebola and cure patients whose disease is not advanced.

The goal is to bring Ebola under control and ultimately, eliminate this disease. To achieve this goal, a sensible model has to be built, taking not only the spread of the disease, the quantity of the medicine needed, possible feasible delivery systems, locations of delivery, speed of manufacturing of the vaccine or drug into consideration. Then use this model to optimize the eradication of Ebola.

It is natural to break this problem into two parts:

- The first part focuses on the Ebola itself. For this part, we need to build a model to describe how Ebola spreads and progresses.
- The second part is to build an optimization model to optimize the eradication of Ebola based on the intrinsic properties of Ebola.

2.2 Challenges

Previous research focuses on the statistical level of disease modelling[3][4][5][6][7] , thus detailed plan is not easily made from that. So it is challenging to build a fine grind model to assist detailed region-level healthcare plan-making.

The second challenge lies in the spread of disease. Many a time only one traveller from one area to another will cause infection and disease spread in that new area. Traditional statistical models views the population in as a whole, thus they are not able to track such phenomenon. The challenge is to view different areas as a network and consider the effect of population migration[8] .

3 Disease Modelling

3.1 Assumptions

For the transmission of the disease, we made several assumptions:

- The transmission of Ebola has a certain mechanism. We mainly consider the man-to-man transmission and ignore the transmission from the environment.
- The flow of population is the mechanism of geographical spread of Ebola.
- The transmission of Ebola will not happen beyond the nodes we consider and no new node will join our network in the time we concern.

For the controlling of the disease, we assume:

- There exists medicine that could cure patients whose disease is not advanced.
- Those people who got vaccinated are immune to the disease in the future.
- Once cured, the patient has no chance to be infected again.

3.2 Notations

Notations	Descriptions
G	The network on which Ebola diffuses
N_i	The nodes on the network, i.e regions on the land
$\sigma_{i,j}$	The weights of edges on the network
Po_i	Population of node(region) i
Variables for SIHRonNET model	
S_i	number of people in state S(suspected) on node i
I_i	number of people in state I(infected) on node i
H_i	number of people in state H(in hospital) on node i
η	death rate of Ebola
R_i	number of people in state R(removed) on node i
Variables for CasPPonNET model	
μ_{i,t_k}	the intensity of Poisson Process on node i in time window t_k
P_{i,t_k}	the number of new cases on node i in time window t_k
Variables for disease controlling	
C_{i,t_k}	the number of people cured on node i in time window t_k
V_{i,t_k}	the number of people vaccinated on node i in time window t_k
μ'_{i,t_k}	the intensity of Poisson Process after disease controlling on node i in time window t_k
$w_{c,i}$	the weight of medicine on node i
$w_{v,i,k}$	the weight of vaccine on node i in time window t_k

Table 1: Notations

3.3 Network Building

When we consider the established models , we can see that some of them are based on statistics of either the total population[9] , which cannot describe the beginning of spatial spread perfectly.

Other researches[10], however, based their models on individual person. These models can work sometimes but cost a lot of time to simulate. These methods also leave a lot of parameters to calibrate.

So we came up with our model of the network.

The Ebola infected countries are divided into areas based on its political divisions. We denote the areas as nodes, N_i . And there exist links between every two nodes. We assign a

weight $\sigma_{i,j}$ on each edge to describe the ‘proximity’ of two areas.

Because we mainly consider the population flow, so we adopted the gravity model[11][12] in economics to estimate the population flow between two areas.

$$\sigma_{i,j} = \frac{Po_i^{\beta_1} Po_j^{\beta_2}}{d_{i,j}^{\beta_3}}, i \neq j$$

We denote the population of node i as Po_i and the geological distance between node i and node j . For simplification, we set:

$$\beta_1 = 1, \beta_2 = 1, \beta_3 = 2$$

This is commonly used in modelling population migration.

In order to calculate the distance between two nodes, we simply used the euclidean distance between two nodes.

We fetched the data of 55 infected areas. The link and the strength of links is visualized in Fig. 3, and the area of circles stands for the population.

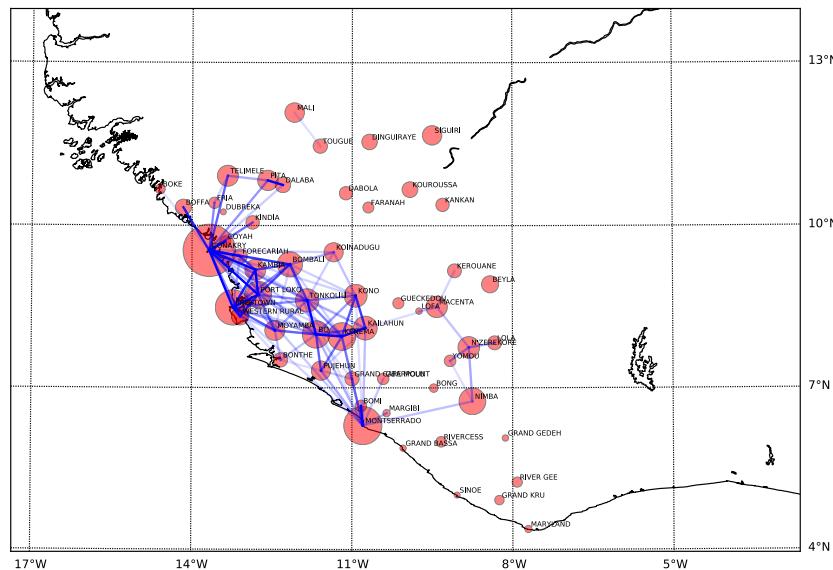


Figure 3: Underlying network of population flow

3.4 Differential equation model on the network : SIHRonNET

We proposed an assisted model based on the network structure and an assisted traditional SIR model.

Other assumptions have to be made. We classify the people into one of the following states:

- S: Suspected, not infected but possible for infections

- I: Infected, but not go to hospital
- H: Infected, and in hospital
- R: Removed, recovered or passed away

For simplification, we assume the ratio of death or recover is constant and can be observed from statistical data.

3.4.1 Differential Equation model without considering population flow

N denotes for the whole population. Because there are three main causes of infection, *household transmission, clinical transmission, and funeral transmission*.

So the rate is proportional to three terms, corresponding to the three causes.

$$\frac{dS}{dt} = -\frac{\beta_1 SI}{N} - \frac{\beta_3 SH}{N} - \frac{\beta_2 S}{N} \frac{dD}{dt}$$

$$\frac{dI}{dt} = \frac{\beta_1 SI}{N} + \frac{\beta_3 SH}{N} + \frac{\beta_2 S}{N} \frac{dD}{dt} - kI$$

$$\frac{dH}{dt} = kI - \gamma H$$

$$\frac{dR}{dt} = \gamma H$$

Because the ratio of death or recover is constant and can be observed from statistical data, so

$$D = \eta R.$$

3.4.2 Differential Equation model with considering population flow

The underlying network is the main dynamic of disease sprawling.

For every node $V_i \in V$

$$\frac{dS_i}{dt} = -\frac{\beta_1 S_i I_i}{N_i} - \frac{\beta_3 S_i H_i}{N_i} - \frac{\beta_2 S_i}{N_i} \frac{dD_i}{dt} + \sum_{j \in V, j \neq i} \theta(\sigma_{i,j} S_j - \sigma_{j,i} S_i)$$

$$\frac{dI_i}{dt} = \frac{\beta_1 S_i I_i}{N_i} + \frac{\beta_3 S_i H_i}{N_i} + \frac{\beta_2 S_i}{N_i} \frac{dD_i}{dt} - kI_i + \sum_{j \in V, j \neq i} \theta(\sigma_{i,j} I_j - \sigma_{j,i} I_i)$$

$$\frac{dH_i}{dt} = kI_i - \gamma H_i$$

$$\frac{dR_i}{dt} = \gamma H_i$$

Because the ratio of death or recover is constant and can be observed from statistical data, so

$$D_i = \eta R_i.$$

3.4.3 Two step model calibration

The first step of calibration is to determine the parameters for the overall data.

The parameters are $\beta_1, \beta_2, \beta_3, k, \gamma$.

Write the equations in matrix form.

$$\vec{x} = \begin{pmatrix} S \\ I \\ H \end{pmatrix}$$

$$A = \begin{pmatrix} 0 & -\beta_1 & -\beta_3 - \beta_2 \eta \gamma \\ 0 & \beta_1 - k & \beta_3 + \beta_2 \eta \gamma \\ 0 & k & -\gamma \end{pmatrix}$$

Considering the number infected is small comparing to the population. So

$$S_i \approx N_i,$$

$$\dot{\vec{x}} = A\vec{x}$$

The roots of equation $|pI - A| = 0$ are:

$$p_1 = 0$$

$$p_{2,3} = \frac{-k + \beta_1 - \gamma \pm \sqrt{(\beta_1 - \gamma - k)^2 - 4(\beta_1 - \gamma - mk + k\gamma)}}{2}$$

The general solution is

$$\psi = A \begin{pmatrix} 1 \\ 0 \\ 0 \end{pmatrix} + B \begin{pmatrix} -m \frac{p_2+k}{p_2} \\ m \\ p_2 - \beta_1 + k \end{pmatrix} + C \begin{pmatrix} -m \frac{p_3+k}{p_3} \\ m \\ p_3 - \beta_1 + k \end{pmatrix}$$

From statistical data we set $\beta_1 : \beta_2 : \beta_3 = 2 : 2 : 1$

$$\beta_1 = 2\beta, \beta_2 = 2\beta, \beta_3 = \beta$$

We fit the data to the first 2/3 data and get

$$\beta = 0.0612$$

in Fig. 4.

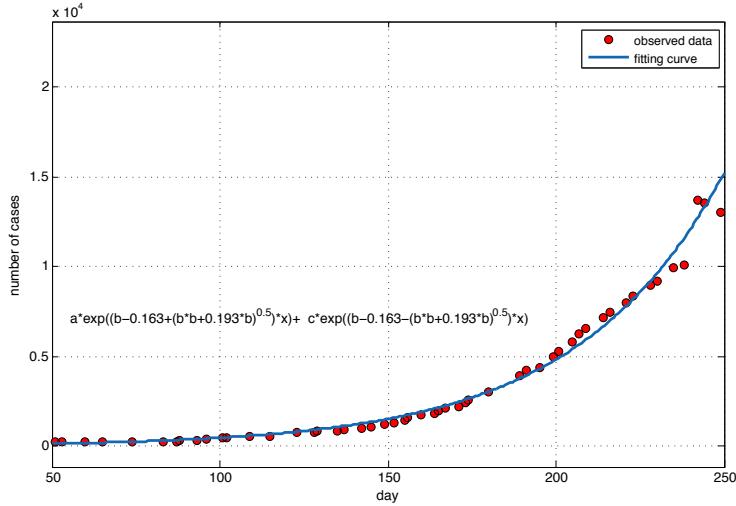


Figure 4: Estimate parameter β

The second step of calibration considered the population flow. During the calibration, data of different times at different nodes is used as our initial conditions and after our simulation, we can obtain the prediction for new cases after a fixed time period. And the norm of prediction error can thus be gotten. Thus the best fitted theta can be considered as the one that make the prediction error smallest. The relationship between error and theta can be show as:

We can see that the best theta is about

$$\theta = 0.3 \times 10^{-3}$$

Since θ is such a key parameter which we can conduct the influence ratio between node itself and its neighbourhood, we now give a short discussion. From the right side of second differential equation, we express the influence ratio as

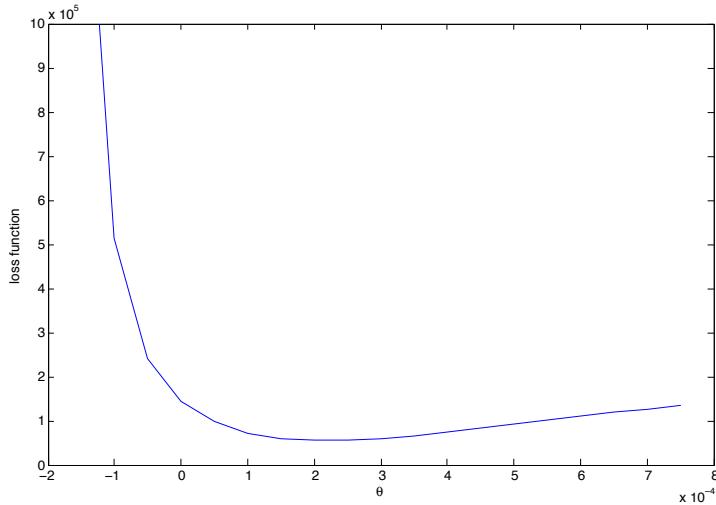
$$\frac{\sigma_{i,j} I_i}{\beta_1 \frac{S_i I_i}{N_i}} = \frac{\theta \sigma_{i,j} N_i}{\beta_1 S_i}$$

We can estimate the ratio because we konw:

$$\sigma_{i,j} \sim 10^0, N_i \sim S_i, \beta \sim 10^{-2}, \theta \sim 10^{-3}$$

Thus the ratio is about 10^{-1} , meaning that the influence given by a node itself is about 10^1 times stronger than that obtained from its neighbours.

This ratio is critical to us since it models the geological spread of Ebola.

Figure 5: Estimated θ

3.4.4 Model Analysis

During our modeling process using SIHRonNet model, some weakness of these differential model has been exposed clearly, which can be summarized in three aspects:

- Bad Timescale: SIHR model does make sense to describe the entire process of a disease outbreak, but its description to the beginning of an outbreak is trivial an exponential-like increase can't give us the detailed information we want.
- No Randomness: In these models, all the interactions between different states of people is modelled using a proportional relationship, meaning that the model is based on statics. This erases the randomness, which is an unique characteristic at the beginning of an outbreak.
- Rely heavily on parameters: A lot of parameters are involved in SIHRonNET model, making it hard to calibrate each of them precisely and even impossible to consider the change of parameters over time.

Above all, though we can still use SIHRonNET model to estimate some trend of the evolution of the illness, a much more timescale-matched, random and parameter-free model is needed to tell us exactly how to eradicate Ebola.

3.5 Cascaded Poisson Process Model: CasPPonNET

3.5.1 Proposed model

Multi-dimensional Hawkes process[13][14] are used to model repeated events and influence between people. It provided inspiration for us to model the infections of disease as a inhomogeneous

Poisson Process to track the temporal and spatial behaviour of disease transmissions.

One person being infected is a point process, so viewing it from a higher level, the infection is a Poisson Process.

We call it a *cascaded* Poisson Process because the intensity of such poisson process comes from many aspects. Those influence cascade and contributed to the intensity.

From Fig. 19 in Appendix we can see the new infections, we model the new infections as a diffusion process. We consider the diffusion process using discrete time steps.

The intensity in one city/area depends on two parts, one part comes from itself, and the second part comes from all other cities. All historical infections has effect on the intensity to a certain extent.

$$\mu_{i,t_k} = \lambda_1 \sum_{m=1}^{k-1} P_{i,t_m} e^{-\beta(k-m)\Delta t} + \lambda_2 \sum_{j:j \neq i} \sum_{m=1}^{k-1} P_{j,t_m} \sigma_{j,i} e^{-\beta(k-m)\Delta t}$$

3.5.2 Model Calibration

We do a MLE to fit the data to the model and get λ_1 and λ_2 .

The likelihood function is:

$$L(\lambda_1, \lambda_2) = \prod_{i \in V} \prod_k \frac{(\mu_{i,t_k} \Delta t)^{P_{i,t_k}} e^{-\mu_{i,t_k} \Delta t}}{P_{i,t_k}!}$$

$$\log L(\lambda_1, \lambda_2) = \sum_{i \in V} \sum_k [P_{i,t_k} \log (\mu_{i,t_k} \Delta t) - \mu_{i,t_k} \Delta t - \log P_{i,t_k}!]$$

$$\frac{\partial \log L(\lambda_1, \lambda_2)}{\partial \lambda_1} = \sum_{i \in V} \sum_k \left[P_{i,t_k} \frac{\frac{\partial \mu_{i,t_k}}{\partial \lambda_1}}{\mu_{i,t_k}} - \frac{\partial \mu_{i,t_k}}{\partial \lambda_1} \Delta t \right]$$

$$\frac{\partial \log L(\lambda_1, \lambda_2)}{\partial \lambda_2} = \sum_{i \in V} \sum_k \left[P_{i,t_k} \frac{\frac{\partial \mu_{i,t_k}}{\partial \lambda_2}}{\mu_{i,t_k}} - \frac{\partial \mu_{i,t_k}}{\partial \lambda_2} \Delta t \right]$$

Solve for equation 1:

$$\frac{\partial \log L(\lambda_1, \lambda_2)}{\partial \lambda_1} = \sum_{i \in V} \sum_k \left[\frac{P_{i,t_k} \sum_{m=1}^{k-1} P_{i,t_m} e^{-\beta(k-m)\Delta t}}{\lambda_1 \sum_{m=1}^{k-1} P_{i,t_m} e^{-\beta(k-m)\Delta t} + \lambda_2 \sum_{j:j \neq i} \sum_{m=1}^{k-1} P_{j,t_m} \sigma_{j,i} e^{-\beta(k-m)\Delta t}} \right. \\ \left. - \left(\sum_{m=1}^{k-1} P_{i,t_m} e^{-\beta(k-m)\Delta t} \right) \Delta t \right]$$

solve for equation 2:

$$\frac{\partial \log L(\lambda_1, \lambda_2)}{\partial \lambda_2} = \sum_{i \in V} \sum_k \left[\frac{P_{i,t_k} \sum_{j:j \neq i} \sum_{m=1}^{k-1} P_{j,t_m} \sigma_{j,i} e^{-\beta(k-m)\Delta t}}{\lambda_1 \sum_{m=1}^{k-1} P_{i,t_m} e^{-\beta(k-m)\Delta t} + \lambda_2 \sum_{j:j \neq i} \sum_{m=1}^{k-1} P_{j,t_m} \sigma_{j,i} e^{-\beta(k-m)\Delta t}} \right. \\ \left. - \left(\sum_{j:j \neq i} \sum_{m=1}^{k-1} P_{j,t_m} \sigma_{j,i} e^{-\beta(k-m)\Delta t} \right) \Delta t \right]$$

All the terms are positive. So use gradient descent to find the solution.

$$\lambda_1^* = \lambda_1 - \gamma \frac{\partial \log L(\lambda_1, \lambda_2)}{\partial \lambda_1}$$

$$\lambda_2^* = \lambda_2 - \gamma \frac{\partial \log L(\lambda_1, \lambda_2)}{\partial \lambda_2}$$

γ is the step size.

We get β from statistical data.

It was reported that EVD has a high risk of death, this is often due to low blood pressure from fluid loss, and typically follows six to sixteen days after symptoms appear. We considered that when patients appears symptoms of EVD, he will be sent to the hospital, then, considering the characteristics of EBV described earlier, we make median lethal time $t_{1/2} = 7$ days. Thus, $\beta = \frac{\ln 2}{t_{1/2}}$. We'll prove that our model is not sensitive to this assumption later.

$$\beta \approx 0.1$$

We set the step size $\gamma = 1 \times 10^{-7}$ and started experiments from initial value $\lambda_1 = 0.6$ and $\lambda_2 = 0.01$.

After 400 iterations, λ_1 and λ_2 converge to 0.2136 and 0.01134.

$$\sigma_{i,j} \sim 10^0$$

So $\lambda_1 : \lambda_2 \sigma_{i,j} \sim 10^1$, this is consistent with the result in Section 3.4.3. From this result, we can conclude our idea of modelling the spread of Ebola on the network is sensible.

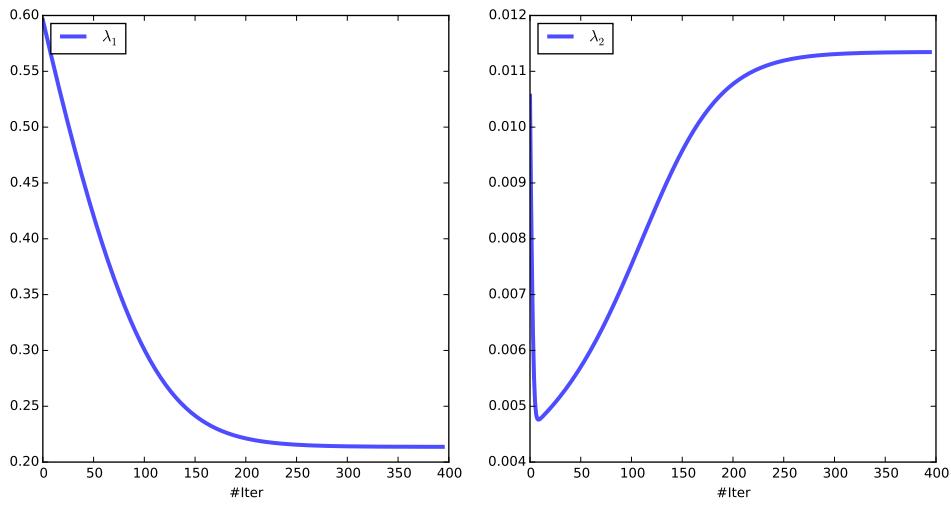
3.6 Model Validation

3.6.1 Validate the model with observed data

We use the estimated λ_1 and λ_2 to do the estimation of Ebola outbreak for every time step(2 weeks) based on historical data. Fig. 10 shows the result of the estimation. The estimated values match well with the ground truth, thus, our model is valid.

3.6.2 Validate the model with case study

In the previous section, we showed our model fits very well with the data. Thus, our model is good at tracking the progress of the disease in one area.

Figure 6: Estimated λ_1 and λ_2

Apart from that, our model has strong predictive abilities because it is built on the network. We obtained the real data to estimate which areas are prone to be transmitted.

We did a case study on the prediction of our model.

For example, from observing the data till week 7 since the outbreak, our model produced prediction that there will be outbreak in Freetown and Port Loko. Then in week 8, those two areas are infected indeed. Moreover, the news[2] confirmed that the outbreak of Ebola in Freetown and Port Loko is due to transmission from adjacent areas.

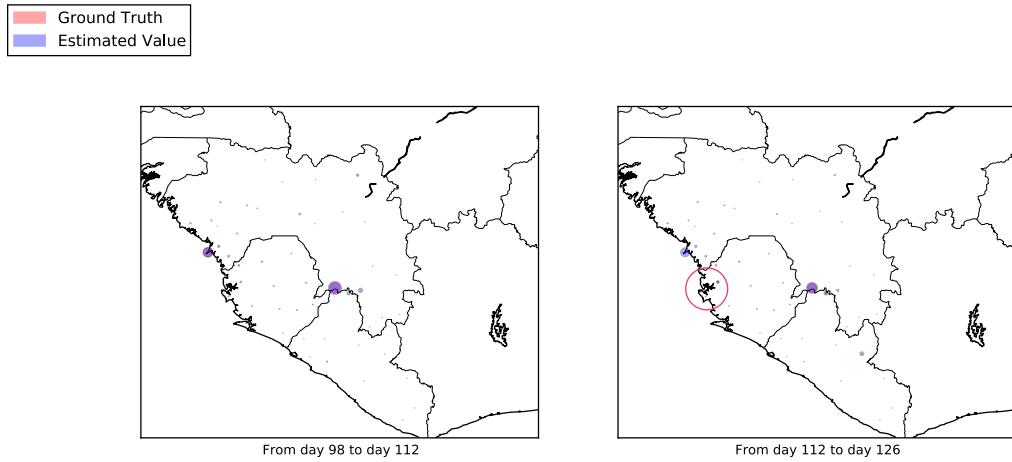


Figure 7: Estimated outbreak in Freetown and Port Loko

3.7 Model Analysis

3.7.1 Sensitivity analysis

To evaluate the sensitivity of our model, we tested the effect β on parameter learning.

β	λ_1	λ_2	λ_1/λ_2
0.04	0.156878175309	0.0103198999254	15.201520988
0.05	0.168281029925	0.0110653981448	15.20786037
0.1	0.239070310929	0.0156758779473	15.250840287

Table 2: Results of proposed model

It is natural for λ_1 and λ_2 to decrease when β increase, because the influence from previous time step decreases when β increase. However λ_1/λ_2 remains constant, so our model is robust.

Then We test our model against another parameter wd , this parameter is used to trim the exponential decaying kernel. For $wd = \infty$, we consider all historical data, for $wd = k$, we only consider previous k time steps.

wd	λ_1	λ_2	λ_1/λ_2
1	0.168281029925	0.0110653981448	15.20786037
3	0.170180726118	0.0108785370316	15.643714373
∞	0.21365953932028273	0.01134447988647677	18.833788896

Table 3: Sensitivity of proposed model

So our model is relatively stable against parameter wd .

3.7.2 Prediction abilities analysis

We experimented on the prediction ability of our model. For each time step, we will predict a value for each region that is not yet infected.

We used a threshold to determine whether there will be an outbreak. We calculated the false positive, false negative, true positive and true negative for our predictions.

Fig. 8 and Fig. 9 shows the receive operating curve of the prediction task. The prediction result is good and is already validated by case study.

4 Disease Controlling

4.1 Objective

We break the control of the disease into two steps with considering different factors.

The first step is to temporarily bring the Ebola under control. We formalize this problem as following:

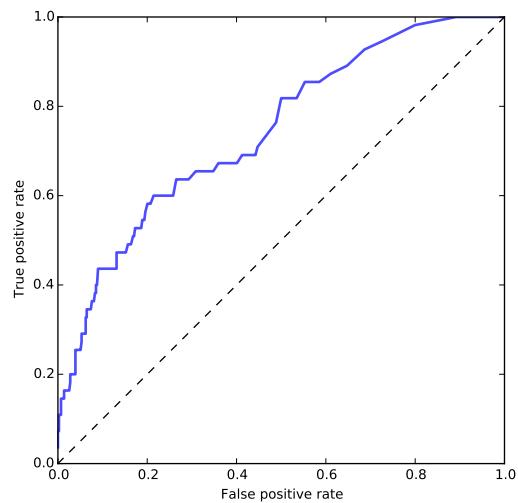


Figure 8: ROC of prediction

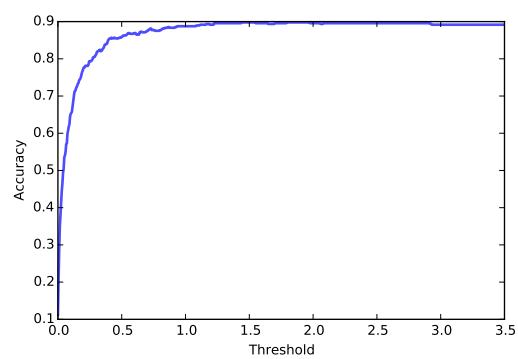


Figure 9: Accuracy of prediction

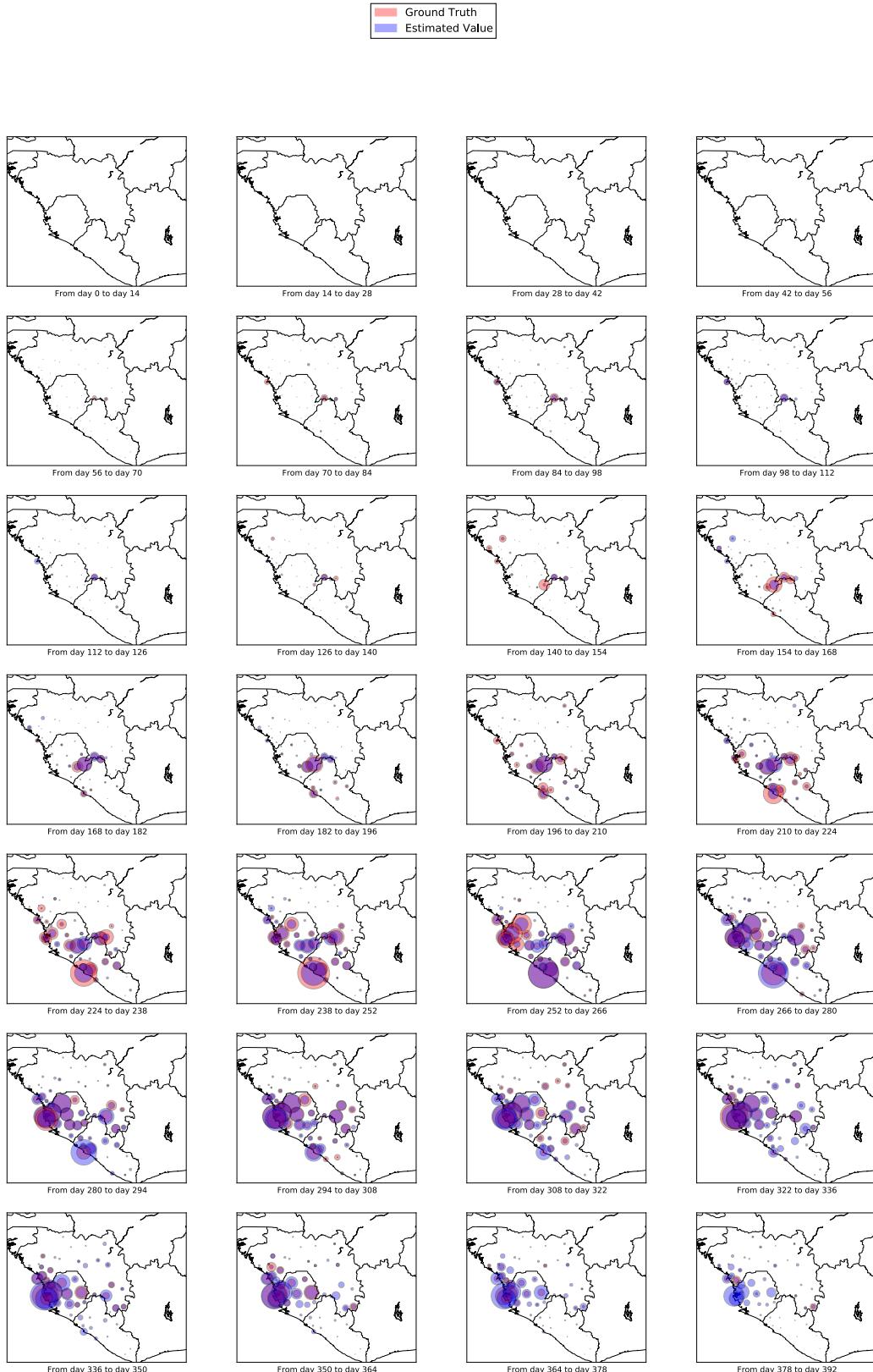


Figure 10: Estimated spatiotemporal spread of Ebola. The red marker means the ground truth and the blue marker means the estimated value. And the area of the circle means the scale of the outbreak. For the well estimated outbreaks, the two colors mix to make purple.

Problem 1:

Given the Ebola spread models in Section 3, and a certain medication model M , with the current situation $P_{j,t_m}, j \in V, t_m \leq T$. Propose the best allocation of medicine, to minimize the loss $L(T')$ at time T' , $T' > T$, and determine the impact of important factors to the disease controlling process.

Problem 2:

The second step is to ultimately eliminate the Ebola disease from the earth. This goal is formalized as following:

Given the Ebola spread models in Section 3, and a certain medication model M , with the current situation $P_{j,t_m}, j \in V, t_m \leq T$. Propose the best allocation of medicine, to minimize the cumulative loss $\int_T^\infty L(t)dt$, and determine the critical factors having effect on whether the disease can be eliminated, i.e, $\lim_{t \rightarrow \infty} L(t) = 0$

For different perspectives in Problem 1 and 2, either proposed disease spreading model has advantages, so we will use the most suitable model for analysing different tasks in those problems.

4.2 Disease Controlling based on CasPPonNET

4.2.1 Drug allocation based on CasPPonNET

The mechanism of medicine on a patient P : If the disease is not advanced (less than T_0), P is recovered and removed from the system. And P will not have any effects on the next time step.

We set T_0 to two weeks.

If the observation window is long, for example if $\Delta t = T_0$, then only patients in last time step can be cured.

Assume we have m amount of medicines for m patients. And we want to maximize the effect of these medicines.

$$\mu_{i,t_k} = \lambda_1 \sum_{m=1}^{k-1} P_{i,t_m} e^{-\beta(k-m)\Delta t} + \lambda_2 \sum_{j:j \neq i} \sum_{m=1}^{k-1} P_{j,t_m} \sigma_{j,i} e^{-\beta(k-m)\Delta t}$$

Denote C_{i,t_m} is the number of patients cured in area i and time step m , $C_{i,t_m} \leq P_{i,t_m}$.

$$\sum_i C_{i,t_m} = C_{t_m}$$

$$\mu'_{i,t_k} = \lambda_1 \sum_{m=1}^{k-1} (P_{i,t_m} - C_{i,t_m}) e^{-\beta(k-m)\Delta t} + \lambda_2 \sum_{j:j \neq i} \sum_{m=1}^{k-1} (P_{j,t_m} - C_{i,t_m}) \sigma_{j,i} e^{-\beta(k-m)\Delta t}$$

$$E[\sum_n P'_{n,t_k}] = \sum_i \mu'_{i,t_k} = \lambda_1 \sum_n \sum_{m=1}^{k-1} P'_{i,t_m} e^{-\beta(k-m)\Delta t} + \lambda_2 \sum_n \sum_{j:j \neq i} \sum_{m=1}^{k-1} P'_{j,t_m} \sigma_{j,i} e^{-\beta(k-m)\Delta t}$$

$$\lambda_1 \sum_n \sum_{m=1}^{k-1} (P_{i,t_m} - C_{i,t_m}) e^{-\beta(k-m)\Delta t} + \lambda_2 \sum_n \sum_{j:j \neq i} \sum_{m=1}^{k-1} (P_{j,t_m} - C_{i,t_m}) \sigma_{j,i} e^{-\beta(k-m)\Delta t}$$

The coefficient of C_{i,t_m} is $-\lambda_1 e^{-\beta(k-m)\Delta t} - \lambda_2 \sum_{j:j \neq i} e^{-\beta(k-m)\Delta t}$

Then we find the node with the max weight:

$$w_{c,i} = \lambda_1 + \lambda_2 \sum_{j:j \neq i} \sigma_{j,i}$$

In this case, the weight of areas is only related to $\sum_{j:j \neq i} \sigma_{j,i}$.

If the observation window is smaller, for example $\Delta t = \frac{1}{u} T_0$, then patients in last u time steps can be cured.

$$w_{c,i,m} = \lambda_1 e^{-\beta(k-m)\Delta t} + \lambda_2 \sum_{j:j \neq i} e^{-\beta(k-m)\Delta t}, k-u \leq m < k$$

Allocation Strategy:

First satisfy the needs of areas with highest w .

If the patients are all cured in an area, deliver the drugs to the area with the next highest w .

4.2.2 Vaccine allocation based on CasPPonNET

Vaccination:

The vaccination is applied to a number of citizens in a certain area i at a certain time t_m , then they are immune to Ebola in the future $t, t > t_m$.

$$Va_{i,t_m} = \delta Po_i$$

$$\sum_i Va_{i,t_m} = Va_{t_m}$$

Then

$$\mu'_{i,t_k} = (1 - \delta) \mu_{i,t_k}, k > m$$

$$\begin{aligned} E\left[\sum_{i \in n} P'_{n,t_k}\right] &= \sum_{i \in n} \mu'_{i,t_k} = \lambda_1 \sum_{i \in n} \left(1 - \frac{Va_{i,t_{<k}}}{Po_i}\right) \sum_{m=1}^{k-1} P_{i,t_m} e^{-\beta(k-m)\Delta t} \\ &\quad + \lambda_2 \sum_{i \in n} \left(1 - \frac{Va_{i,t_{<k}}}{Po_i}\right) \sum_{j:j \neq i} \sum_{m=1}^{k-1} P_{j,t_m} \sigma_{j,i} e^{-\beta(k-m)\Delta t} \end{aligned}$$

The benefit from $Va_{i,t_{<k}}$ is:

$$w_{v,i} = \lambda_1 \sum_{m=1}^{k-1} \frac{P_{i,t_m}}{Po_i} e^{-\beta(k-m)\Delta t} + \lambda_2 \sum_{j:j \neq i} \sum_{m=1}^{k-1} \frac{P_{j,t_m}}{Po_i} \sigma_{j,i} e^{-\beta(k-m)\Delta t} = \frac{E[P_{i,t_k}]}{Po_i}$$

Allocation Strategy:

First satisfy the needs of areas with highest w .

If the population are all vaccinated in an area, deliver the drugs to the area with the next highest w .

4.2.3 Drug/Vaccine delivery system

When we consider the cost of transport in practical cases, all we need to do is to add resistance on each edge of the network. We can then describe it mathematically by adding a constraint to the optimization problem we describe in 4.2.1 and 4.2.2. What's more, if the resistance is proportional to the transport quantity, the weight of each node in transportation can be estimated.

4.2.4 Experimental validation

We adopted the strategy in Section 4.2 to test their effects on disease controlling.

We tested the proposed method against other trivial methods such as assign medicine proportional to number of new cases and showed our method is optimal.

If the number of medicine is fixed, it can be inferred from Figure.11 that no matter how much the amount of the drug is, our strategy is always the best.

In Figure. 12, we tested the proposed vaccination method against other general methods such as assign vaccine proportional to number of new cases and showed our method is optimal.

We can draw a conclusion from Figure. 13 that when the amount of vaccine is a constant number. On the scale of the amount, our proposed vaccination method is better than other methods.

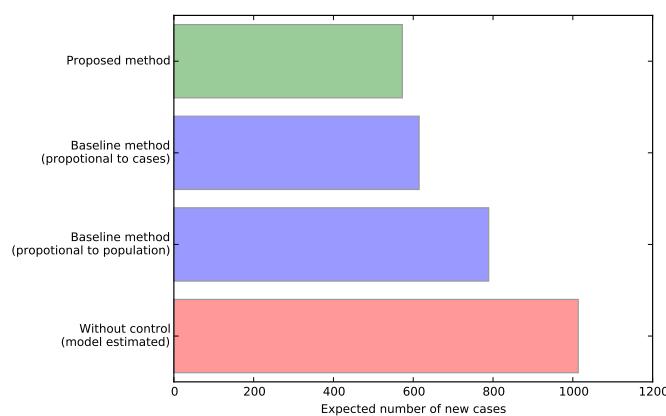


Figure 11: Effect of different medication strategies

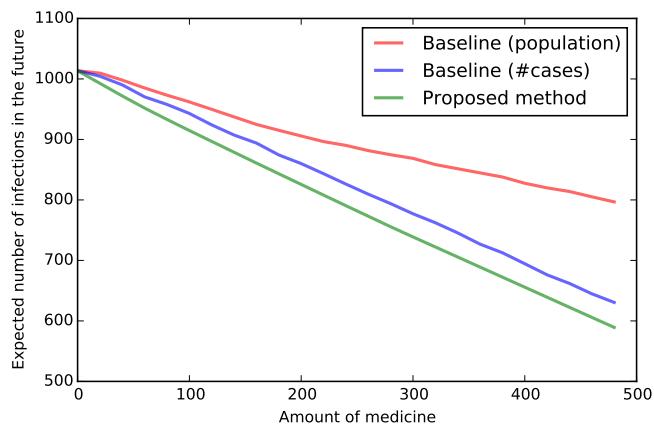


Figure 12: Effect of different medication strategies over time

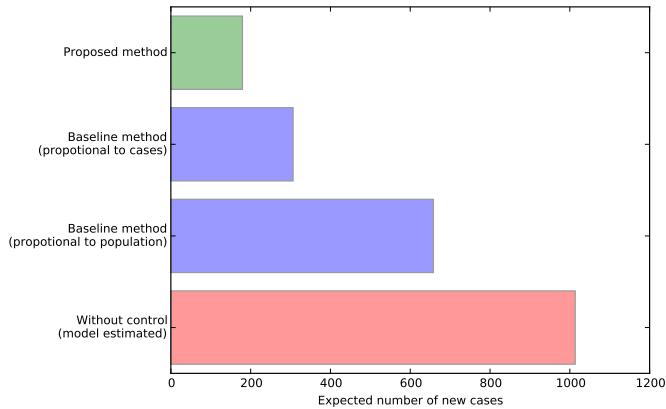


Figure 13: Effect of different vaccination strategies

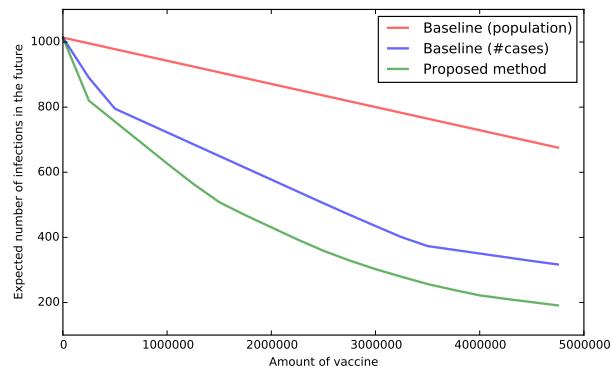


Figure 14: Effect of different vaccination strategies over time

4.2.5 Realistic Results

In order to produce realistic results to assist controlling the disease. We fed the real world data into our model and calculated w_c and w_v and the ranking of areas. This indicate how needed an area is for medicine or vaccine.

As for w_v , it is irrelevant to the disease progress and remains constant during the whole timespan.

However, for w_m , it depends on the current situation. So we calculated them for a typical time week 34 when disease began to spread in large scales and *now* (Feb 9 2014).

The results are shown in Table 4.

Rank	Need medicine	Need vaccination(week 34)	Need vaccination(now)
1	Freetown(SL)	Lofa(LR)	Dubreka(GN)
2	Conakry(GN)	Margibi(LR)	Forecariah(GN)
3	Western rural(SL)	Dubreka(GN)	Western rural(SL)
4	Port loko(SL)	Bong(LR)	Lola(GN)
5	Kenema(SL)	Grand bassa(LR)	Coyah(GN)
6	Bo(SL)	Bomi(LR)	Freetown(SL)
7	Kambia(SL)	Montserrado(LR)	Port loko(SL)
8	Montserrado(LR)	Macenta(GN)	Kambia(SL)

Table 4: Results of proposed model

4.3 Determination of Manufacturing rate

The manufacturing rate plays an important role in the disease controlling process. In order for the disease to be controlled, the $E[\sum_{i \in n} P'_{n,t_k}]$ has to decay to zero.

For this objective, due to the complexity of the distribution of disease, a theoretical solution is hard to obtained. So we did experiments to determine the critical value.

In our simulation, m represents the medicine which is put into the system per two weeks under the best disease controlling strategy. All the initial condition of simulation is set to be the same as that of the 34th week.

Our simulation shows that different manufacturing rates do affect the evolution of the number of cases. When no or not enough medicine is manufactured, the EVD will be developed monotonically. In contrast, when sufficient supply of medicine is guaranteed, the disease will finally be defeated.

In order to find the singular point leading to the bifurcation, a more detailed simulation is given and we find the least number of medicine manufacturing is about 52 per two weeks.

It is easy to see that the earlier the medicine is putted into the West Africa, the more important role it will take. To simulate the time effect of the medicine delivery, we use a constant manufacturing rate but started at different time, we can see that even 100 per two weeks can not control the EVD when 38 weeks past.

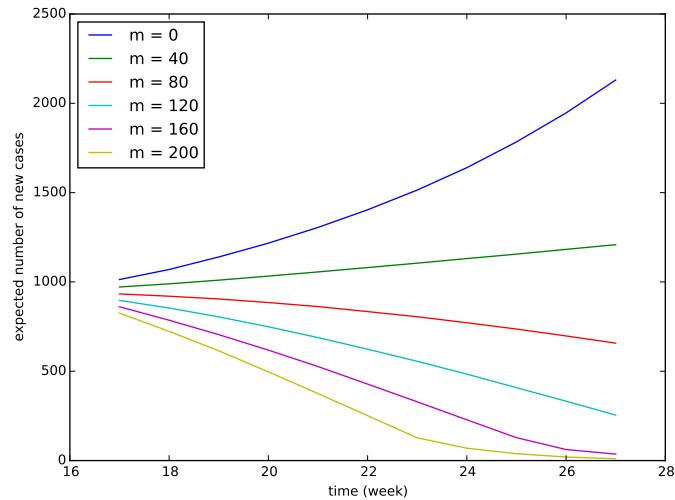


Figure 15: Comparison to random prediction

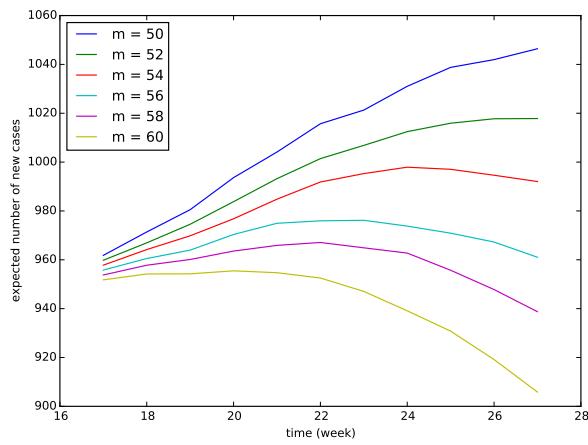


Figure 16: Effect of different start time of medication

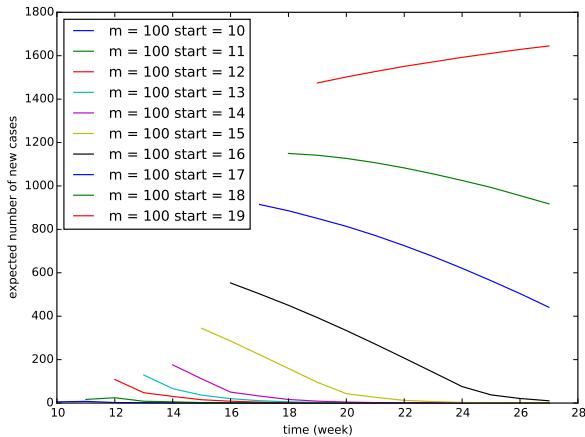


Figure 17: Effect of different start time of medication

4.4 Disease Precautioning System

Apart from drug and vaccine, other general precautions can be made to those regions which have risk of potential outbreak in the future.

In section 3.7.2 we discussed that our model has strong abilities to predict future outbreak.

We would like to use this prediction result to do precautions such as improving healthcare infrastructures. Without building a detailed model, we assume a certain *cost* to false positive predictions and false negative predictions.

False negative predictions will have heavy costs because it will lead to huge outbreaks.

False positive predictions will have small costs.

$$Cost = gFN + FP$$

g is the ratio of two different costs, $g \gg 1$ and is determined empirically to optimize the threshold for alerting and precautioning system.

For example, in Fig .18 we set $g = 8$ and the optimal value for threshold is 0.2. The least cost is about 2/3 the cost based on random guess.

5 Discussions and Future works

5.1 Superiority

- Our model is based on geographical network, so it's a good method to model the Ebola's geographical spread due to people migration. We use the data to estimate our parameters. Then we can evaluate how important each term is.
- A lot of our conclusions are based on the theoretical derivation, some assumptions also

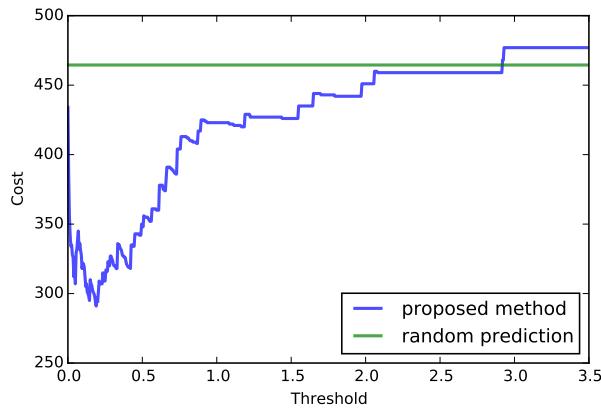


Figure 18: Comparison to random prediction

established in Ebola's characteristics.

- By comparing with other models especially SIHR, we can fully exploit its strengths in prediction and optimization.

5.2 Weakness

- A data-driving model has a naturally problem: cold start. It is suitable for the infectious disease outbreak soon but not fully developed.
- Due to the restriction of computer simulation, some of our assumptions are highly ideal, such as the ‘Gravity Model’ of population flow.

5.3 Future Research

- If the medicines and drugs really exist. We can get a lot of data to test our model, to formulate the optimized strategies in many other independent variables.
- Some medical treatment such as isolation can have an unambiguous influence in our model. For example, exponential decay is faster than before. We will consider it in our model in an explicit way.
- Population migration determines the geographical spread of EVD, but the migration model based on the simple gravity model. If we have enough time to meditate, the output of the model will be more realistic.

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Appendix

1. The data is mainly from the WHO website. We also wrote a script to fetch the geographical data.
2. Some large figures are plotted in this section to save space for the main paper.

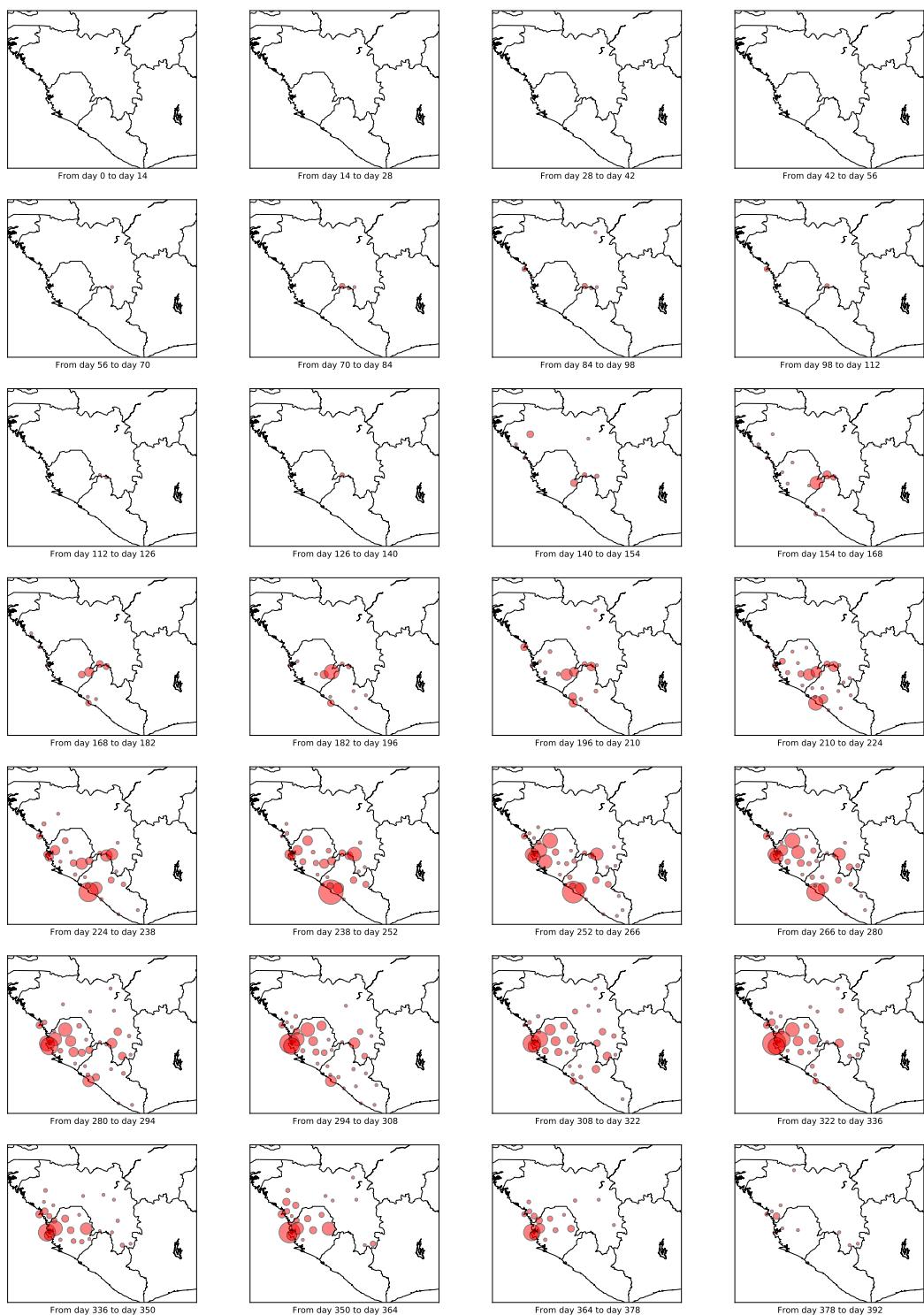


Figure 19: Spread of Ebola disease