Mathematical Modeling and Computational Issues of Dengue Epidemics

Lee,Yu-Hsun

Institute of Applied Mathematics
National Cheng Kung University

February 14, 2017

2017 Joint Seminar and Research Camp (JSRC) program on Mathematical Science in Niigata University, Japan

國立成功大學
National Cheng Kung University

Mathematical Modeling and Computational Issues of Dengue Epidemics

2017-04-20

Mathematical Modeling and Computational Issues of Dengue Epidemics

Lee,Yu-Hsun

Institute of Applied Mathematics
National Cheng Kung University

February 14, 2017

2017 Joint Seminar and Research Camp (JSRC) program on Mathematical
Science in Niigata University, Japan

Dear students and teachers, I'm Yu-Hsun Lee from National Cheng Kung University in Tainan, Taiwan. Thank Professor Tamaka to hold the wonderful camp for us. Today, I want to share my research work, Mathematical Modeling and Computational Issues of Dengue Epidemics. I would like to show you how to use the SEIR model to compute the total number of patients with respect to the effective contact rate. The efficiency of epidemic prevention can be also revealed from the simulations based on the open data of Dengue fever in 2015. In addition, I will show you the journey of applying computational mathematics to save the real world.

Outline

Mathematical Modeling and Computational Issues of
Dengue Epidemics

2017-04-20

$\quad$ └─Outline

- I will separate my talk into three parts. First, I'll give an introduction to dengue fever. And we use a mathematical model to determine an infectious disease will die out or not.

- Next, I'll talk about mathematical models in epidemiology which we used for epidemic simulation.

- Last, I'll demonstrate some simulation results based on the open data of Dengue fever in Tainan, Taiwan 2015.

Mathematical Modeling and Computational Issues of
Dengue Epidemics
└─Introduction

2017-04-20

└─What is dengue fever?

What is dengue fever? Dengue fever a mosquito-borne disease which is
prevalent in tropical and subtropical regions. To present in a better way, I
will show a short video downloaded from the website about the
introduction of the dengue fever.

An epidemic is the rapid spread of infectious disease to a large number of people in a given population within a short period of time.

$\Rightarrow$ How to determine an infectious disease will die out or be able to spread in a population ?

An epidemic is the rapid spread of infectious disease to a large number of people in a given population within a short period of time.

$\Rightarrow$ How to determine an infectious disease will die out or be able to spread in a population ?

Basic Reproduction Number R_0

Mathematical Modeling and Computational Issues of
Dengue Epidemics

└─Introduction

2017-04-20

└─Epidemic Model

Epidemic Model

An epidemic is the rapid spread of infectious disease to a large
number of people in a given population within a short period of
time.

⇒ How to determine an infectious disease will die out or be able
to spread in a population ?
Basic Reproduction Number R_0

- After watching the video, I think everyone have concept of dengue
  fever. Next one is an important question in an epidemic. How to
  determine an infectious disease will die out or be able to spread in a
  population ?

- The key is the Basic Reproduction Number. I will give an
  introduction in the following section. It is a bifurcation of epidemic
  model, and also an risk indicator of infectious disease.

$$
\begin{cases}
\frac{dS}{dt} = -\frac{\beta SI}{N} \\
\frac{dI}{dt} = \frac{\beta SI}{N} - \gamma I \\
\frac{dR}{dt} = \gamma I \\
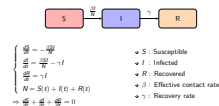N = S(t) + I(t) + R(t)
\end{cases}
$$
$$
\Rightarrow \frac{dS}{dt} + \frac{dI}{dt} + \frac{dR}{dt} = 0
$$

- S : Susceptible
- I : Infected
- R : Recovered
- β : Effective contact rate
- γ : Recovery rate

Mathematical Modeling and Computational Issues of
Dengue Epidemics

2017-04-20

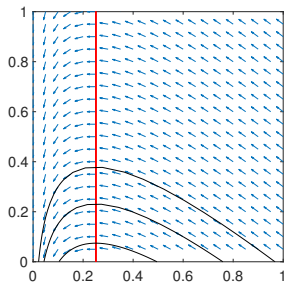└─Compartmental models in epidemiology

  └─SIR Model

- In this section, I'll take a short introduction on two model: SIR model and SEIR model. In these models, they describe the transfer of disease.

- First, this one is SIR model. As you can see, it stratify the population into three health states: Susceptible, Infected, and Recovered.

- We assume the total population is constant. It means there are no birth and death in the system.

- β and γ

Simplifying the system, consider the two-dimensional system

$$\begin{cases} \frac{dS}{dt} = -\frac{\beta SI}{N} \\ \frac{dI}{dt} = \frac{\beta SI}{N} - \gamma I \end{cases}$$

- S-nullclines : $I = 0, S = 0$

  I -nullclines : $I = 0, S = \frac{\gamma}{\beta} N$
- Phase portrait for the system.

  Suppose N=10000, $\frac{\gamma}{\beta} = 0.25$

Mathematical Modeling and Computational Issues of
Dengue Epidemics

└─Compartmental models in epidemiology

2017-04-20

└─SIR Model

SIR Model

Simplifying the system, consider the two-dimensional system
$$\begin{cases} \frac{dS}{dt} = -\frac{\beta SI}{N} \\ \frac{dI}{dt} = \frac{\beta SI}{N} - \gamma I \end{cases}$$

- S-nullclines : $I = 0, S = 0$
- I-nullclines : $I = 0, S = \frac{\gamma}{\beta} N$
- Phase portrait for the system.
  Suppose N=10000, $\frac{\gamma}{\beta} = 0.25$

- by $\frac{dS}{dt} + \frac{dI}{dt} + \frac{dR}{dt} = 0$, we can Simplifying the system to second order differential system.

- Use nullcline analysis, we can solve the disease-free equilibrium.

- suppose population is ten thousand, and ratio of γ and β to be a quoter, we can draw the phase portrait.

Basic Reproduction Number R_0

- It's a dimensionless number
- Defined by

$$R_0 \propto \left(\frac{\text{infection}}{\text{contact}}\right) \cdot \left(\frac{\text{contact}}{\text{time}}\right) \cdot \left(\frac{\text{time}}{\text{infection}}\right)$$
$$= \tau \cdot \bar{c} \cdot d$$

- $R_0 < 1$, the infection will die out.
  $R_0 > 1$, the infection will be able to spread.

Mathematical Modeling and Computational Issues of Dengue Epidemics

└─Compartmental models in epidemiology

2017-04-20

└─Basic Reproduction Number
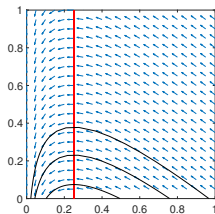
- Now, let's talk about basic reproduction number.

- We use it as a risk indicator of infectious disease.

- It is defined by three things:

  - τ: Probability of transmission per contact
  - $\bar{c}$: Number of contacts per unit time
  - d: Duration of infection

- $R_0 < 1$, the infection will die out.
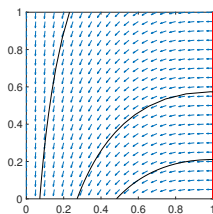 $R_0 > 1$, the infection will be able to spread.

Basic Reproduction Number of SIR model :

$\Rightarrow \beta = \tau \bar{c}, \ d = \gamma^{-1}$
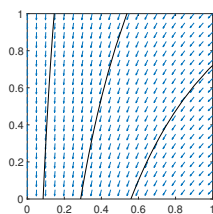
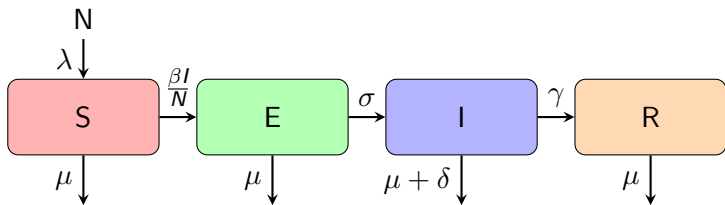$\Rightarrow R_0 = \tau \bar{c} d = \frac{\beta}{\gamma}$

(a) $R_0 = 4 > 1$ (b) $R_0 = 1$ (c) $R_0 = 0.5 < 1$

Mathematical Modeling and Computational Issues of
Dengue Epidemics

└─Compartmental models in epidemiology

  └─SIR Model

2017-04-20

- back to our model, we can derive the basic reproduction by definition.

- we can get $R_0 = \tau \bar{c} d = \frac{\beta}{\gamma}$

- It is same as the result we get in nullcline analysis.

- Here are results of three kinds of R_O

  – In first picture, we can see the disease explode in exponential ,then decay.
  – second one, there is a transcritical bifurcation at $R_O = 1$
  – last one, disease-free equilibrium point is locally asymptotically stable.

$$
\begin{cases}
\frac{dS}{dt} = \lambda N - (\frac{\beta I}{N} + \mu)S \\[2mm]
\frac{dE}{dt} = \frac{\beta SI}{N} - (\sigma + \mu)E \\[2mm]
\frac{dI}{dt} = \sigma E - (\gamma + \mu + \delta)I \\[2mm]
\frac{dR}{dt} = \gamma I - \mu R \\[2mm]
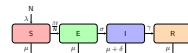N(t) = S(t) + E(t) + I(t) + R(t)
\end{cases}
$$

- S:Susceptible, E:Exposed, I:Infected, R:Recovered
- β:Effective contact rate, σ:Latency period, γ:Recovery rate
- μ:Host mortality, λ:Birth rate, δ:Disease-induced death rate

Mathematical Modeling and Computational Issues of Dengue Epidemics

└─Compartmental models in epidemiology

└─SEIR Model

- Now, we move on SEIR Model.

- In this model, it has four compartments. It has another part called Exposed. And the time elapsed between exposure and infection We called it "Latency period".

- For example, people who have Dengue Epidemics take about 7 days from exposure to infection stage.

- In this model, we can see the total population may change.

- Derive R_0 for compartmental model in epidemiology
- Mathematical Model

$$\frac{\mathrm{d}\mathbf{x}}{\mathrm{d}t} = \mathbf{F}(\mathbf{x}) - \mathbf{V}(\mathbf{x})$$

$$\mathcal{F} = \left[\frac{\partial F_i}{\partial x_j}(x_0)\right], \mathcal{V} = \left[\frac{\partial V_i}{\partial x_j}(x_0)\right]$$

$$\mathcal{G} = \mathcal{F}\mathcal{V}^{-1}$$

- In SEIR Model

$$\mathbf{F}(\mathbf{x}) = (\beta SI, 0)^T$$

$$\mathbf{V}(\mathbf{x}) = ((\sigma + \mu)E, -\sigma E + (\gamma + \mu + \delta)I)^T$$

Mathematical Modeling and Computational Issues of
Dengue Epidemics

└─Compartmental models in epidemiology

2017-04-20

└─Next-Generation Method

Next-Generation Method

- Derive R_0 for compartmental model in epidemiology
- Mathematical Model

$$\frac{dx}{dt} = \mathbf{F}(x) - \mathbf{V}(x)$$

$$\mathcal{F} = \left[\frac{\partial F_i}{\partial x_j}(x_0) \right], \mathcal{V} = \left[\frac{\partial V_i}{\partial x_j}(x_0) \right]$$

$$\mathcal{G} = \mathcal{F} \mathcal{V}^{-1}$$

- In SEIR Model

$$\mathbf{F}(x) = (\beta SI, 0)^T$$
$$\mathbf{V}(x) = ((\sigma + \mu)E, -\sigma E + (\gamma + \mu + \delta)I)^T$$

- We can't derive R_0 in the same way. We use another one called Next-Generation Method.

- $F_i(x)$ represents the rate of appearance of new infections in compartment i

- $V_i(x)$ represents the rate of transfer of individuals into/out compartment i

- disease-free equilibrium :

$$x_0 = \{S^* = \lambda/\mu, E^* = 0, I^* = 0, R^* = 0\}$$

- The largest eigenvalue of $\mathcal{G}$ is R_0

$$\mathcal{G} = \mathcal{F}\mathcal{V}^{-1} = \begin{bmatrix} 0 & 0 \\ \beta\lambda/\mu & 0 \end{bmatrix} \begin{bmatrix} (\sigma + \mu) & -\sigma \\ 0 & (\gamma + \mu + \delta) \end{bmatrix}^{-1}$$

- Basic Reproduction Number of SEIR model :

$$R_0 = \frac{\sigma\beta\lambda}{\mu(\sigma + \mu)(\gamma + \mu + \delta)}$$

Mathematical Modeling and Computational Issues of
Dengue Epidemics

└─Compartmental models in epidemiology

    └─Next-Generation Method

2017-04-20

Next-Generation Method

- disease-free equilibrium :
$$x_0 = \{S^* = \lambda/\mu, E^* = 0, I^* = 0, R^* = 0\}$$
- The largest eigenvalue of $\mathcal{G}$ is R_0
$$\mathcal{G} = \mathcal{F}\mathcal{V}^{-1} = \begin{bmatrix} 0 & 0 \\ \beta\lambda/\mu & 0 \end{bmatrix} \begin{bmatrix} (\sigma+\mu) & -\sigma \\ 0 & (\gamma+\mu+\delta) \end{bmatrix}^{-1}$$
- Basic Reproduction Number of SEIR model :
$$R_0 = \frac{\sigma\beta\lambda}{\mu(\sigma+\mu)(\gamma+\mu+\delta)}$$

then calculate the largest eigenvalue of $\mathcal{F}\mathcal{V}^{-1}$, we can get the Basic
Reproduction Number of SEIR Model.

(2015 Dengue Epidemics in Tainan)

Assume most of parameters in R_0 is constant, for example :

- $\lambda = \mu = \frac{1}{3494}$
- $\sigma = \tau = 1$
- $\delta = 0.0035$

$\Rightarrow R_0 = \frac{\sigma\beta\lambda}{\mu(\sigma+\mu)(\gamma+\mu+\delta)} = 0.996\beta$

Mathematical Modeling and Computational Issues of
Dengue Epidemics

└─Real Case

2017-04-20

  └─Real Case

Real Case

(2015 Dengue Epidemics in Tainan)
Assume most of parameters in R_0 is constant, for example :
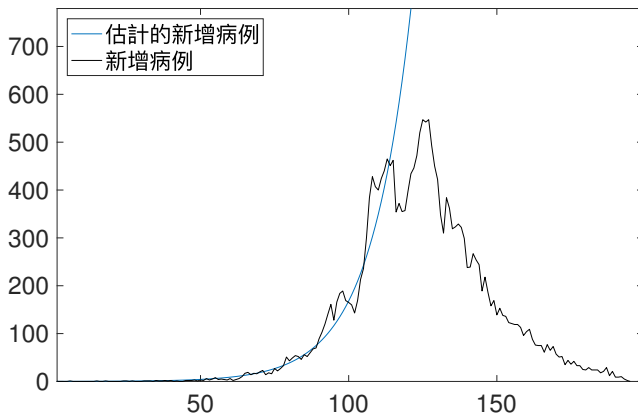- $\lambda = \mu = \frac{1}{3384}$
- $\sigma = \tau = 1$
- $\delta = 0.0035$
$\Rightarrow R_0 = \frac{\sigma \beta \lambda}{\mu(\sigma+\mu)(\tau+\mu+\delta)} = 0.996\beta$

- Final, let's talk about real case.

- Assume natural birth rate, death rate, latency and recover rate and Host disease-induced death rate are constant.

- After reduced, we can get the R_0 directly proportional to β
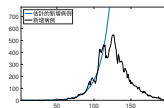
⇒ If β also a constant ?

Mathematical Modeling and Computational Issues of
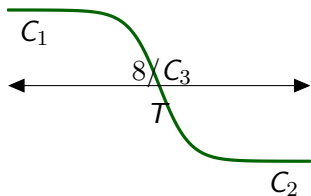Dengue Epidemics
└─Real Case

2017-04-20

└─Real Case

- What if β also a constant ?

- Blue line is estimated new cases. Black line is our historical data of new cases at day t.

- As you can see, in the beginning of the epidemics, it fit well. But the disease will spread widely.

- So we guess β is a function of t, and it will decay when epidemic prevention have been done.

- Model of β

$$\beta(t) = (c_1 - c_2)\frac{1 - \tanh(c_3(t - T))}{2} + c_2$$

2017-04-20

Mathematical Modeling and Computational Issues of
Dengue Epidemics

└─Real Case

└─Real Case

Real Case

- Model of β

$$\beta(t) = (c_1 - c_2)\frac{1 - \tanh(c_3(t - T))}{2} + c_2$$

- we use hyperbolic tangent to estimate the beta.

- At last, I'll show our fitting results.

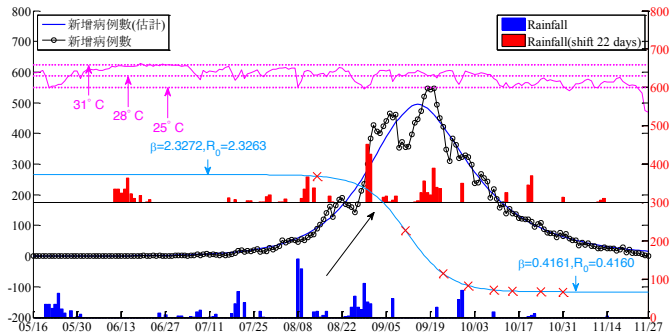Figure: 2015 Dengue Epidemics fitting results

Mathematical Modeling and Computational Issues of
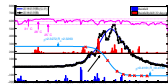Dengue Epidemics
└─Real Case

  └─Real Case

2017-04-20

Figure: 2015 Dengue Epidemics fitting results

- First, the blue line is our estimated new cases at day t; the black one is our historical data. At the middle part (the red cross), epidemic prevention were done by government. So we guess the effect contact rate should decay.

- Second part is rainfall, look at the historical data, new cases add rapidly at some date. Then we compare the rainfall data with 22 days shift, it looks match with these peak. Why we choose 22 days shift ? Because mosquito grow up from eggs to adults need about 3 weeks.

- Third part is temperature, mosquito eggs won't grow up below or over 25 and 31 degrees. So the epidemics will also decay when entering winter.

- So effect contact rate might be affected by these factor. These factors are the key to control life of mosquito, the host of dengue

- R_0 of SEIR model

$$R_0 = \frac{\sigma \beta \lambda}{\mu(\sigma + \mu)(\gamma + \mu + \delta)}$$

- The effective contact rate β and basic reproduction number R_0 decays after the epidemic prevention works by the government.
- With the help of mathematical simulation, we can realize the relationship between different factors. We can integrate them into the mathematical model in the future.

Mathematical Modeling and Computational Issues of
Dengue Epidemics
└─Real Case

  └─Conclusions

2017-04-20

Conclusions

- R_0 of SEIR model
$$R_0 = \frac{\sigma\beta\lambda}{\mu(\sigma + \mu)(\gamma + \mu + \delta)}$$
- The effective contact rate β and basic reproduction number R_0 decays after the epidemic prevention works by the government.
- With the help of mathematical simulation, we can realize the relationship between different factors. We can integrate them into the mathematical model in the future.

- I derive the basic reproduction number for SEIR model.

- With our simulation, we can analysis epidemic prevention by the government works or not.

- We can realize the relationship between rainfall, epidemic prevention, temperature and other factors. It will help us integrate these factor together into mathematical model in the future.

- In this work, let me know how computational mathematics connect with our world and solve the real problems.

Thank you for your attention !

Mathematical Modeling and Computational Issues of
Dengue Epidemics
└─Real Case

└─

Thank you for your attention !

Thank you for your attention ! Any questions ?