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# Modelling the Spread of Dengue in Singapore

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## Abstract

We have developed a simulation model that describes the spread of dengue fever in Singapore. The population of the host is divided into compartments representing disease status (susceptible, exposed, infectious and resistant) whereas the population of the vector is considered as a whole because it is difficult to determine the dengue virus status in the vector. Larvae density is used as an index of the vector population. In our model, the flow between compartments is described by a set of differential equations and the change of vector is represented by means of a piece-wise function over time. The resulting model is stochastic as well as deterministic. We took into account the majority of factors that known to influence dengue epidemiology. Compared with the deterministic model developed by Newton and Reiter (1992), our model is more realistic and suitable to the local situation. This model also demonstrates the successful use of Maple V, a commonly used computer algebra system, in such modelling techniques.

## 1. Introduction

### 1.1 Dengue fever

Dengue is the most common mosquito-borne viral infection of humans, with up to 100 million cases reported annually and some 2 billion people at risk of infection in tropical and subtropical regions of Africa, Asia, and Americas where the virus is often endemic. Dengue viruses are transmitted from viremic to susceptible human beings by various mosquitoes, notably *Aedes aegypti* and *Aedes albopictus*. Dengue fever is a severe, flu-like illness that affects infants, young children and adults but rarely causes death. There is no specific treatment for dengue fever. No vaccine available, so efforts to control the disease focus on the vector. At present, the only method of controlling or preventing dengue is to combat the vector mosquito.

### 1.2 Mathematical model of dengue fever transmission

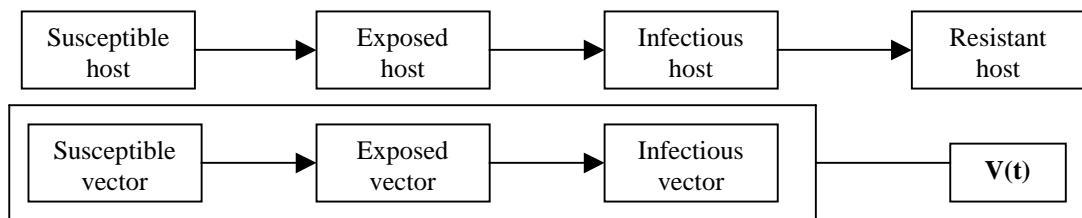
We examine a deterministic susceptible, exposed, infectious, resistant or removed (SEIR) model developed by Newton and Reiter (1992). In our model, the host population is divided into compartments representing disease status. However, because it is almost impossible to determine the disease status of the vector, it seems more appropriate to consider the vector as a whole. Also, since we are able to obtain real data on the vector population, we have incorporated it into the model. A critical element in the spread of dengue is the relationship between host and vector. Our model gives a more realistic way to reflect vector change so that we can simulate the spread more accurately.

### 1.3 Dengue fever in Singapore

Dengue fever had been endemic in Singapore with the first epidemic reported in 1901. The disease became an important public health problem with large epidemics occurring almost annually from 1961-1964 and 1966-1968. In 1973, Singapore saw a large outbreak of 1187 cases with 27 deaths. The epidemiological pattern of dengue in Singapore has shifted from one with high *Aedes* population and high dengue transmission in the 1960s to one with low *Aedes* population and low dengue transmission. Dengue control program conducted from 1960 has a significant impact on dengue transmission. The vector plays an important role in the transmission of dengue and so the focus of this program has been the suppression of dengue vector through environmental management. The aim has been to maintain the vector population at levels that are too low to sustain epidemic transmission. Singapore's Ministry of the Environment currently collects data on larvae density as an indicator of vector population at the fixed period.

## 2. Mathematical Model of Dengue Fever

Our model is a mathematical simulation of transmission of one serotype of dengue virus between host and vector. The model is based on the susceptible, exposed, infectious, resistant or removed (SEIR) models of infectious disease epidemiology, which was adopted by Newton and Reiter in their model in 1992. Populations of host and vector are divided into classes or compartments representing disease status. These classes are referred to as state variable. Compartments for host are susceptible (no contact with the disease), exposed (incubating the virus but not infectious), infectious and resistant (immune). Newton and Reiter also divided population of vector into susceptible, exposed and infectious. Once infected, mosquitoes are assumed to remain so until death. However, it is almost impossible to determine the disease status of mosquitoes in real situation. Therefore, in our model, we consider the population of vector as a whole and use real data as an indicator of the change of vector over time. These two models are represented schematically in Figure1. There is concern that changing densities of mosquito populations may result in the occurrence of future epidemics in localities which currently have low dengue incidence (Gubler, 1988; Monath, 1994; Rodriguez-Figueroa *et al.*, 1995). Change of population of vector has the important effect on spread of dengue.



**Figure 1** Flow diagram for the model of dengue fever transmission

Let  $S$ ,  $E$ ,  $I$  and  $R$  represent the host population which are susceptible, exposed, infectious and resistant respectively, and let  $V$  represent the vector population. State variable definitions and initial values are shown on Table 1 and parameters are shown on Table 2. Our model assumes homogenous mixing within each compartment of the population. The populations are confined to a particular geographic area, small enough that each bite has an equal probability of being taken from any particular human. The equations representing the relationship between these populations are given as:

$$\frac{dS}{dt} = hN - S\left(\frac{VPC}{N} + \mu\right) \quad (1)$$

$$\frac{dE}{dt} = S\frac{VPC}{N} - E\left(\frac{1}{T_1} + \mu\right) \quad (2)$$

$$\frac{dI}{dt} = \frac{E}{T_1} - I\left(\frac{1}{T_2} + \mu\right) \quad (3)$$

$$\frac{dR}{dt} = \frac{I}{T_2} - \mu R \quad (4)$$

$$V(t) = \text{function\_to\_be\_fitted\_from\_data} \quad (5)$$

The transmission of dengue virus between compartments is described by differential equations.  $V(t)$  is represented by a piece-wise function obtained from the real data. This will be discussed in the next section.

**Table 1** State variable definition and initial value used in the model

Symbol	State variable definition	Initial value
$S$	Susceptible host (no contact with the disease)	55,000
$E$	Exposed host (incubating the virus but not infectious)	0
$I$	Infectious host	0
$R$	Resistant host (immune)	0
$V$	Vector	$V(0)$

### 3. Parameters and initial values

The epidemiological pattern of dengue infections and disease is dependent on geographic location. The virus is hyperendemic in many tropical areas and particularly Southeast Asia, South Asia and Africa, whereas other areas of the world only experience occasional dengue epidemics. Furthermore, there is concern that values of parameters used in the model are dependent of locality. The parameters and initial values used here present problems due to a lack of detailed field data. Therefore, some of the values rely on somewhat reasonable guess as well as information from the literature. We shall discuss a base set of parameters and initial values (shown in Table 2) below in detail.

**Table 2** Parameter definition and values used in the model

Symbol	Parameter definition	Value
$N$	Population of sensitive area	55000
$P$	Percent of infectious mosquitoes	9%
$a$	Transmission probability, vector to host	0.75 per bite
$b$	Bites per vector per day	0.25 (1.0 per e-weeks*)
$C$	Effective contact rate, vector to host ( $a_{vh}b$ )	0.75
$T_1$	Intrinsic incubation time	6 days ( 1/5 per e-weeks*)
$T_2$	Host infection duration	4 days ( 4/30 per e-weeks*)
$T_h$	Life span of host	73 years( 876 e-weeks*)
$h$	Birth rate of host ( $1/T_h$ )	1/876 per e-weeks*
$\mu$	Host mortality rate( $1/T_h$ )	1/876 per e-weeks*

\* *e-weeks* is a period used to survey and collect data of vector. We assume one *e-weeks* is equal to 30 days approximately.

**Transmission probability ( $a$ ).** We have evidence for much variation in the virulence of viruses and the susceptibility of mosquitoes to these viruses, both of which will affect transmission probabilities (Guber DJ, 1988). We take a value of 0.75 based on the study of Watts *et al* (1987).

**Bites per vector per day ( $b$ ).** It is difficult to estimate the biting rate of mosquitoes. The size of the initial blood meal, availability of sugar, temperature and many other factors may influence biting rate frequency (Klowden MJ, Lea AO, 1978). A figure of 0.25 bites per day obtained from observation by Yasuno and Tonn (1977) is probably more realistic. Given the vector control programme taken, we assume the mean life span of the vector to be about four days. This also corresponds to the study by Sheppard *et al.* (1969). So we use 1.0 per *e-weeks* in our model.

**Intrinsic incubation time ( $T_1$ ).** Intrinsic incubation time is the average period of time from the point of infection to the point when the host becomes infectious. The symptomatic viremia period is 4-5 days, but may be as long as 12 days (Gubler *et al.*, 1981). We take six days as our base value.

**Host infection duration ( $T_2$ ).** Gulber *et al.* found that during an explosive epidemic associated with severe disease and high viremia, most hospitalized patients had detectable circulating virus for 4-5 days. Moreover, in any epidemic, a major portion of cases is subclinical, probably with low viremia of short duration (Newton and Reiter, 1992). Therefore, we use four days in our model.

**Life span of host ( $T_h$ ).** According to Singapore's 1995 and 1996 census (Singapore 1995; Singapore 1996), it is reported that average life span of Singaporean is 72-74 years. So we use 73 years as the value of this parameter.

**Birth rate and death rate of host ( $b, \mu$ ).** Because we consider the entire population of the host as a constant, in our model we assume the birth rate and the death rate have the same value of  $1/T_h$ .

**Population of sensitive area ( $N$ ).** A sensitive area refers to the particular area with a high incidence of disease cases. There are many areas identified as "sensitive" in Singapore. Because of the frequent flow of population between sensitive areas and neighboring areas, it is not possible to obtain accurate statistical data of each sensitive area. We hence assumed that the population in Singapore is evenly distributed and estimate the population of these sensitive areas using their area sizes. The total sensitive area surveyed in this study is about 1.8% of the total area of Singapore. The mid-year resident population sizes in 1996 and 1995 are 3,044,30 and 2,986,500 respectively. In our model, we take 55000 as an estimated value of this parameter.

**Percent of infectious mosquitoes ( $P$ ).** As mentioned above, it is difficult to figure out the dengue virus status of the mosquito. However, L.K.Lim, *et al* (1999) managed to estimate the infection rates in adult mosquitoes caught between April 1997 to March 1998 in Singapore. These include *Aedes aegypti* and *Aedes albopictus*, which are two major vectors of dengue in Singapore. The infection rates are 12.3% and 5.9% respectively. We shall assume an average infectious rate of 9% in our model and factor it into the term  $\frac{SVPC}{N}$  in equations (1) and (2).

**Susceptible host ( $S$ ).** A population of 55,000 as initial value represents all sensitive areas included in our model. The assumption here is an even distribution of population in Singapore and a homogenous mixing in population.

**Population of vector ( $V$ ).** The vector population used in our model is not the actual number of mosquitoes but larvae density. The larval and adult biology of *Aedes aegypti* is now well known but rather variable according to local conditions and to the characteristics of the local mosquito population. We assume more eggs are laid because there are more gravid female mosquitoes around. Higher larvae density means there are more eggs in the breeding spot that were laid, hatched and grew into larvae. It is hence reasonable to take larvae density as a measurement of the quantity of mosquitoes. In our model, we set up a direct relationship between dengue cases and actual surveillance data of the vector's larvae density. The data used in our model is shown in Table 3.

**Table 3** Larvae density in 1995 and 1996\*

e-weeks	Larvae density	e-weeks	Larvae density	e-weeks	Larvae density
1	4280	9	4899	17	9273
2	5321	10	5662	18	6781
3	5503	11	9469	19	6497
4	3224	12	4274	20	6870
5	5559	13	6393	21	9057
6	4425	14	3399	22	12974
7	5330	15	2519	23	10191
8	10999	16	6183	24	7208

(\* Data from the Ministry of the Environment, Singapore)

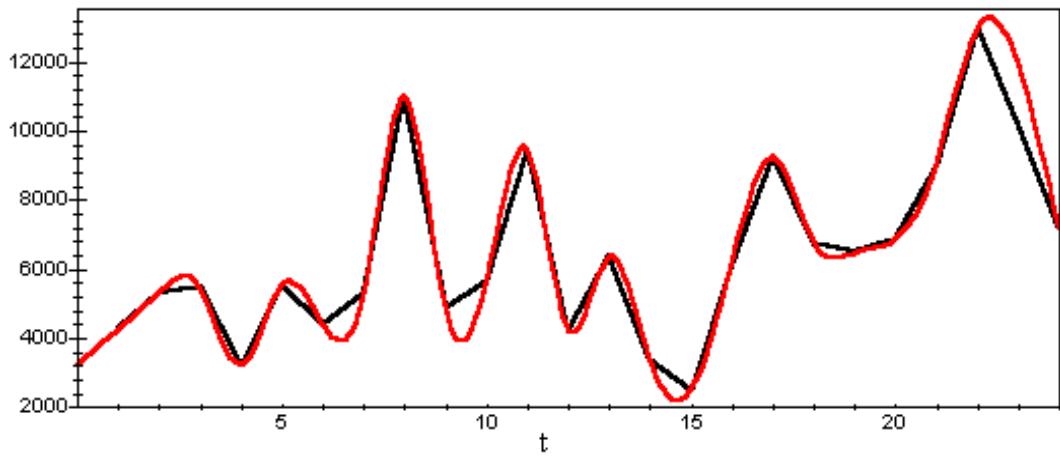
#### 4. Solution of the Model using Maple V

The model was solved using Maple V (Release 5.1). Because we are using real data in our model, we need to split the solution process into two parts. In the first part, we use Maple's curve fitting features to fit a function to the known values of vector numbers to obtain a closed form function for  $V(t)$ . The next part involves the use of Maple's ODE (Ordinary Differential Equations) solver to solve the system of differential equations governing the dengue spread as presented in the preceding sections.

To fit a curve through the data values, the following set of Maple commands were used:

```
> readlib(spline): with(plots):
> f := spline(
[1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21,22,23,24],
[4280.0,5321.0,5503.0,3224.0,5559.0,4425.0,5330.0,10999.0,4899.0,
5662.0,9469.0,4274.0,6393.0,3399.0,2519.0,6183.0,9273.0,6781.0,
6497.0,6870.0,9057.0,12974.0,11974.0,7208.0],t,cubic);
```

The second line in the command basically consists of information on the larvae density (from Table 3). The result of this command is a set of piece-wise cubic spline functions  $V(t)$ , shown on Figure 2. The resulting function is smooth and differentiable everywhere. Also, this function approximately describes the change of vector very well.



**Figure 2** Larvae density and spline curve fitting function

Once we have obtained  $V(t)$ , we may then proceed to use the ODE solver in Maple to solve the system of equations. A typical set of commands used for the solution is given below:

```
> with(DEtools):
> with(plots):
> N:=55000.0:h:=1/876.0:t1:=1.0/5:t2:=4.0/30:p:=1.227e-6:uh:=1.0/876:
> M1:={diff(sh1(t),t)=h*N-sh1*(v1*p+uh),
      diff(eh1(t),t)=sh1*v1*p-eh1*(1/t1+uh),
      diff(ih1(t),t)=eh1/t1-ih1*(1/t2+uh),
      diff(rh1(t),t)=ih1/t2-uh*rh1,
      diff(v1(t),t)=1146.832075-317.4962262*t+158.7481131*t^2}:
> p1:=DEplot(M1,[sh1,eh1,ih1,rh1,v1],t=0..2,
             {[sh1(0)=55000.0,eh1(0)=0.0,ih1(0)=0.0,rh1(0)=0.0,v1(0)=3239.0]},
             scene=[t,ih1],stepsize=0.1,linecolor=black);
```

This set of commands produces the solution curve for the susceptible host, exposed host, infectious host and resistant host for  $t = 0.2$  since only one “piece” of  $V(t)$  is used. The commands are repeated for subsequent time intervals and the resulting solution curves are then collected and pieced together.

## 5. Results and Discussion

Based on our model and the set of parameters and initial values mentioned above, we attempt to solve the model for an immunologically native population. At time  $t$ , we use the corresponding  $V(t)$  as equation (5) in our model and then obtain  $S(t), E(t), I(t)$  and  $R(t)$  respectively by numerical computation. For all values of  $t$ ,  $S(t), E(t), I(t)$  and  $R(t)$  are kept smooth and differentiable.

Figures 3 and 4 show the number of susceptible and immunologically resistant persons respectively. The number of susceptibles decreases with time but number of resistants increases with time. More importantly, we obtain a curve for the infectious host in our model. We note that the graph for the infectious host is very similar to that for the vector. This indicates that the mosquitoes have a significant impact on the spread and outbreak of dengue fever. As the vector population increases, dengue cases increase correspondingly. Similarly, as the vector population decreases, dengue cases decrease (in Figures 5 and 6).

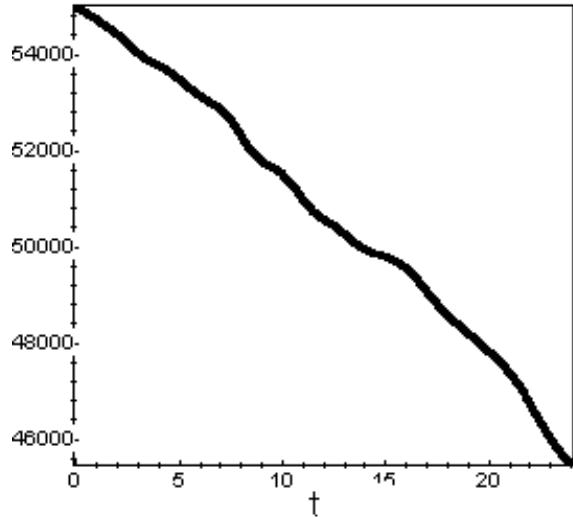


Figure 3 Susceptible host

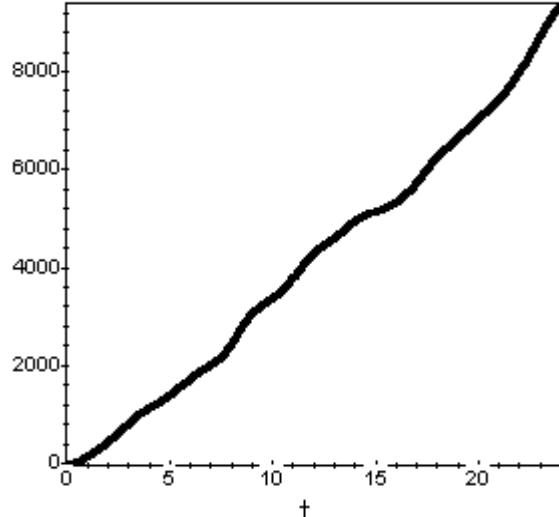


Figure 4 Resistant host

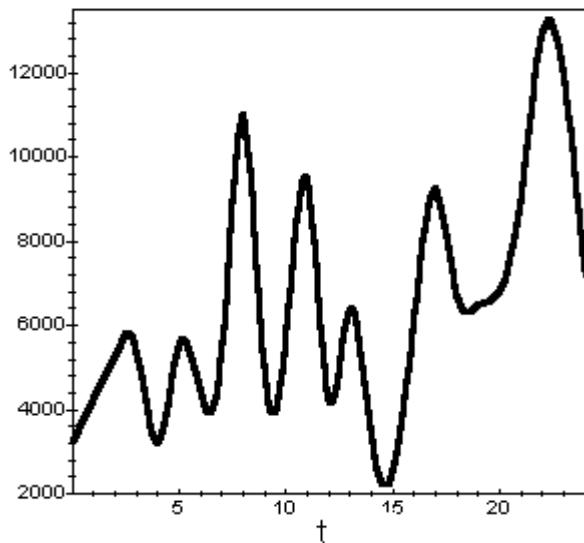


Figure 5 Vector (Larvae density)

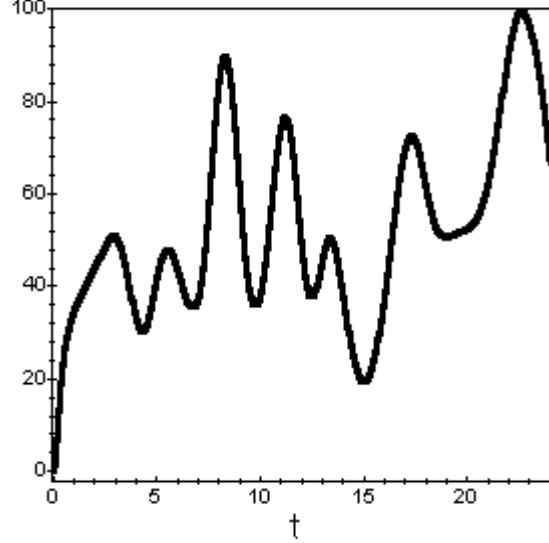
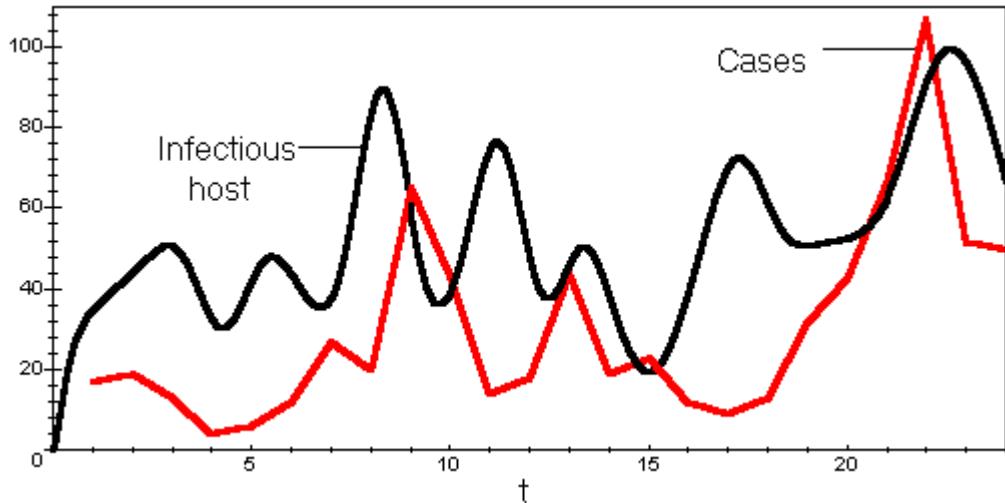


Figure 6 Infectious host in the model

Also, we note the difference between the real data of dengue cases and number of infectious host from our model in Figure 7. It can be seen that as long as the vector population reaches its local maximum, there is a corresponding outbreak of dengue. It follows that the higher the larvae density, the higher the possibility of an outbreak. In practice, the definition of a start and end of an epidemic is not obvious because of many undetected or unreported cases. However, it would not be unreasonable to presume that a local maximum in the infectious host graph indicates a possible period of dengue epidemic.



**Figure 7** Infectious host in the model and real data of dengue cases

Compared with the real data of dengue cases, we find that the number of infectious host in our model is relatively high. This is because we have used larvae density instead of the actual number of mosquitoes and some parameter values that may not be very suitable for the local situation. Surveillance is rarely good enough to provide detailed information on the progress of an epidemic. Because of insufficient real data we need in the model, we have to make some reasonable guesses about parameters and initial values.

It is obvious that the reliability of our model is directly linked to the accuracy and availability of the values of the variable parameters. It is not within the scope of this study to discuss and analysis the errors involved, although it is acknowledged that the model is not perfect. Nevertheless, in spite of these drawbacks, the model may still be used to provide some information on the spread of dengue. In particular, valuable information on the point of an impending epidemic and the duration of it may be obtained.

## 6. Conclusion

In this paper, we have developed a model for the spread of dengue in Singapore. While the model itself is deterministic, we have used relevant and real data in the model, thus making the model more realistic.

In addition, we have demonstrated how Maple V may be successfully used and exploited in such modelling techniques. Through the use of this simple but powerful tool, we have provided new insights into dengue models. It is our belief that the long term application of such models, together with the power of computer algebra systems like Maple, will provide an essential means to aid dengue control programs.

## Acknowledgement

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