Modelling the spread of Dengue in Singapore

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Abstract: In this paper, we develop a simulation model that describes the spread of dengue in Singapore. The host population is divided into compartments representing disease status (susceptible, exposed, infectious and resistant). The vector population is considered as a whole because it is difficult to figure out the dengue virus status in the vector. We use the larvae density as an index of vector and set up a relationship between this index and the number of dengue cases. In our model, the flow between compartments is described by a set of differential equations and the change of vector population with time is described by means of a piece-wise function. The model is stochastic as well as deterministic. We take into account the majority of factors that are known to influence dengue epidemiology. Compared with the theoretical model developed by Newton and Reiter (1992), our model is more realistic and suitable to the local situation. The results will hopefully provide an insight into the spread of Dengue in Singapore and form a basis for further modelling studies in this area.

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. With no vaccine available, 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 Dengue fever in Singapore

Dengue fever had become 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 the 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. Vector plays an important role in transmission of dengue 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.

2. MATHEMATICAL MODEL OF DENGUE

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 (1992). Population 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 difficult to realistically determine the disease status of the mosquitoes. In our model, we take the population of vector as a whole and using real data from the Ministry of Environment (Singapore), we obtain a function as an indicator to show the change of vector population over time. These two models are represented schematically in Figure 1. 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). Hence, the change in the population of the vector has an important effect on the spread of dengue. Therefore, instead of assuming a constant vector,

an attempt is made to obtain a function to describe this change.

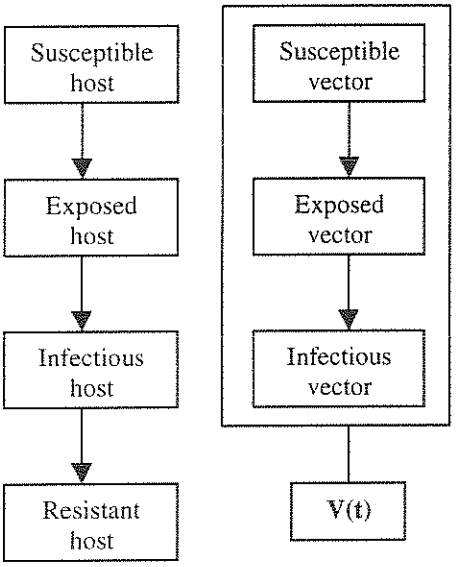

Figure 1. Flow diagram for the model of dengue fever transmission

Let S_h, E_h, I_h and R_h represent the host population which are susceptible, exposed, infectious and resistant respectively, and let V represent the vector population. Our model assumes homogenous mixing. 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:

$$\frac{dS_h}{dt} = hN - S_h\left(\frac{VPC_{vh}}{N} + \mu\right) \quad (1)$$

$$\frac{dE_h}{dt} = S_h\frac{VPC_{vh}}{N} - E_h\left(\frac{1}{T_1} + \mu\right) \quad (2)$$

$$\frac{dI_h}{dt} = \frac{E_h}{T_1} - I_h\left(\frac{1}{T_2} + \mu\right) \quad (3)$$

$$\frac{dR_h}{dt} = \frac{I_h}{T_2} - \mu R_h \quad (4)$$

$$V(t) = \text{to be obtained from data} \quad (5)$$

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. We will discuss a base set of parameters and initial values for state variables (shown in Table 1 and Table 2) below in detail.

Transmission probability (a_{vh}). 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 (h, μ_h). 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

Table 1. 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_{vh}	Transmission probability, vector to host	0.75 per bite
b	Bites per vector per day	0.25 (1.0 per e-weeks*)
C_{vh}	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 (1/30 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*
μ_h	Host mortality rate $(1/T_h)$	1/876 per e-weeks*

* e-weeks (shown in Table 3) is a period used to survey and collect data of vector. We assume one e-week is approximately 30 days.

Table 2. State variable definition and initial value used in the model

Symbol	State variable definition	Initial value
S_h	Susceptible host (no contact with the disease)	55,000
E_h	Exposed host (incubating the virus but not infectious)	0
I_h	Infectious host	0
R_h	Resistant host (immune)	0
V	Vector	$V(0)$

area of Singapore. The mid-year resident population sizes in 1996 and 1995 are 3,044,300 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 $\frac{SVPC_{vh}}{N}$ in equations (1) and (2).

Susceptible host (S_h). 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. 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.

Before we apply this data to in the model, we need to use a spline curve fitting technique to approximate the curve representing the data. We obtain a piecewise function $V(t)$, shown on Figure 2. The resulting function is smooth and differentiable everywhere. Also, this

Table 3. Larvae density in 1995 and 1996*

	e-weeks	Larvae density		e-weeks	Larvae density		e-weeks	Larvae density
1	1-4	4280	**9**	36-39	4899	**17**	70-74	9273
2	5-8	5321	**10**	40-43	5662	**18**	75-78	6781
3	9-13	5503	**11**	44-48	9469	**19**	79-83	6497
4	14-17	3224	**12**	49-52	4274	**20**	84-87	6870
5	18-22	5559	**13**	53-57	6393	**21**	88-91	9057
6	23-26	4425	**14**	58-61	3399	**22**	92-96	12974
7	27-30	5330	**15**	62-65	2519	**23**	97-100	10191
8	31-35	10999	**16**	66-69	6183	**24**	101-104	7208

* Data from the Ministry of Environment, Singapore.

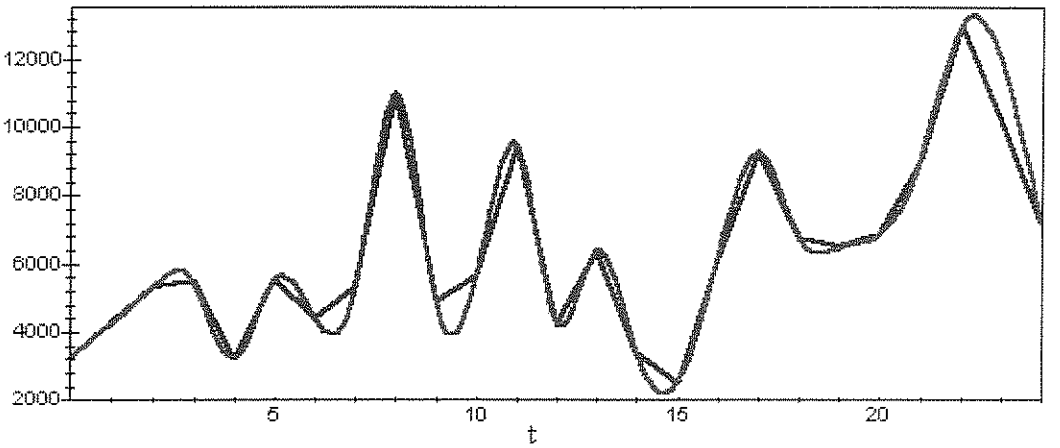

Figure 2. Larvae density and spline curve fitting function

function approximately describes the change of vector very well. 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. All calculations are performed and graphs obtained by using Maple V Release 4.

3. RESULTS AND DISCUSSION

Based on our model and the set of parameters and initial values mentioned above, we simulate an epidemic in an immunologically naïve population. 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 vectors. 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 and vice versa (Figures 5 and 6).

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 an epidemic of dengue.

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

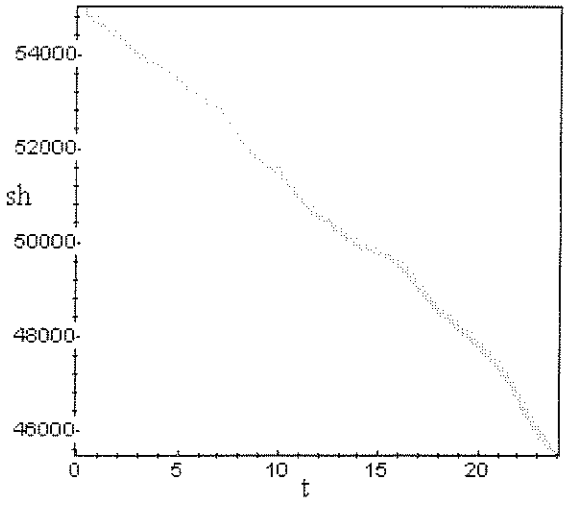

Figure 3. Susceptible host

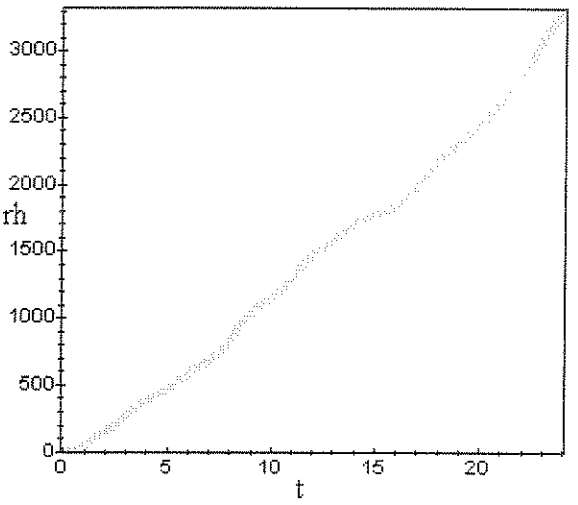

Figure 4. Resistant host

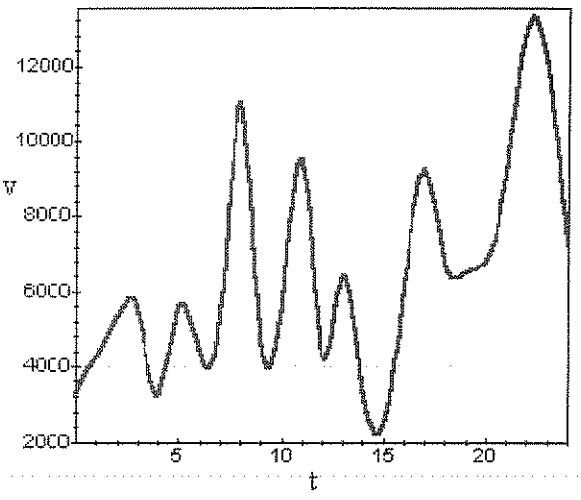

Figure 5. Vector (Larvae density)

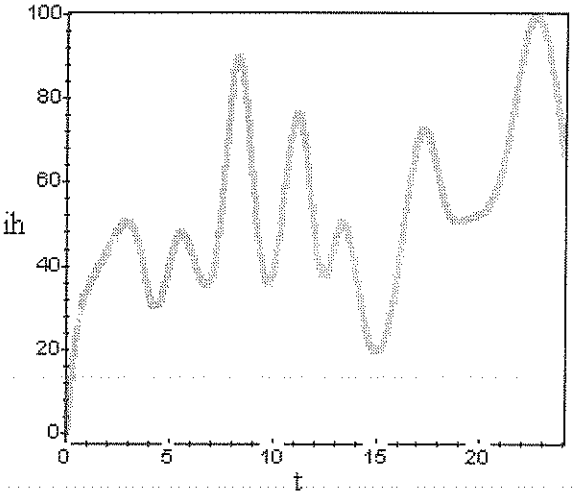

Figure 6. Infectious host in the model

epidemic. Due to the lack of relevant data, we are not able to test our model in detail and make more comparison with real data. Such studies will enable us to improve our current model. Nevertheless, the model presented in this paper may serve as a theoretical base for the control of dengue fever and surveillance of vector.

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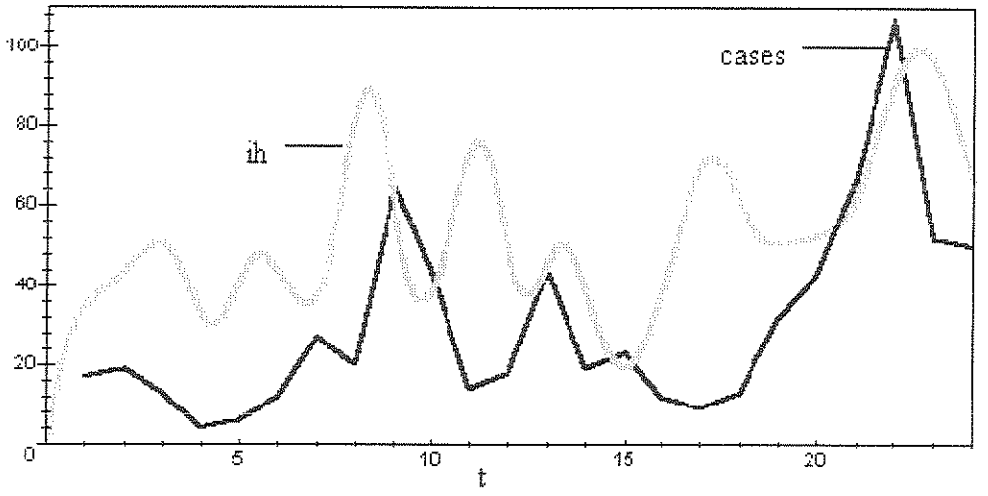

Figure 7. Infectious host in the model and real data of dengue cases

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