An analysis of the model for dengue transmission with two strains

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Abstract: We study the SIR model of transmission of dengue fever with two pathogen strains. A model is constructed to study the effects of different factors on the course of the epidemic. The difference between the two strains is not discussed. Instead, we focus on the trends of primary infection and secondary infection. Our analysis shows that factors related to the host (such as host population) do not change the pattern the spread significantly. In contrast, factors related to the vector (such as vector population, vector life span and biting rate) have a more significant effect on the outbreak of secondary infection.

1. Introduction

Dengue fever is an acute febrile viral disease and the dengue virus exists in four antigenically distinct serological types (designated DEN-1 to DEN-4) which were first identified by plaque reduction neutralization tests (Russell and Nisalak, 1967). The dengue serotypes may have evolved in geographic isolation from one another. Today all four viruses cocirculate in many areas of Africa, Asia, and the Americas, although one serotype often dominates (Edward C.H., Lucy M.B. and Geoggrey P.G., 1998).

The initial infection leads to a moderate viremia and serotype-specific antibodies that provide long-term (perhaps lifelong) immunity to the serotype of the infecting strain. For a short time these antibodies are also able to inhibit subsequent infection with the other serotypes, but they soon decay to very low levels at which point they have little impact against geterologous strains (Halstead, S.B. *et al.*, 1980). Severity of dengue fever has been associated with secondary dengue infections. Epidemiological studies in Thailand suggest that an important risk factor for DHF-DSS is the presence of pre-existing dengue antibody at subneutralizing levels. Also, endemic DHF-DSS is found in areas where *Aedes aegypti* densities are high and dengue virus of multiple types are endemic. Moreover, DHF-DSS is associated with secondary-type dengue infections in individuals one or more years of age and with primary dengue infectious in infants born to dengue-immune mothers (Gubler, D.J., 1986; Halstead, S.B., 1984). These facts led to the formulation of the secondary infection or immune enhancement hypothesis to explain it. This hypothesis states that only those persons experiencing a second infection with heterologous dengue serotype present DHF-DSS. Not all cases of severe disease are associated with a second infection, however, and only a relatively small proportion of dual infections progress to DHF/DSS. This observation led to the proposal of a second hypothesis in which viral strains exist which have a greater probability of giving rise to DHF/DSS. Such strain differences may exist among or within serotypes. An example of serotypes differing in virulence comes from epidemiological work in Thailand where

epidemics of DHF/DSS appear to be most frequently associated with DEN-2 although it is clear that all four serotypes have the potential to cause serious disease (Burkle *et al., 1988*).

2. A model of the spread of dengue with two strains

Our model is a mathematical simulation of transmission of two serotypes of dengue virus between host and vector. The model is based on the susceptible, infectious and resistant (SIR) model of infectious disease that was adopted by Zhilan and Jorge (1995). They used the model to show the existence of an unstable endemic state that produces a long transient behavior where both dengue serotypes cocirculate. According to the spread of dengue, our model can be represented schematically in Figure 1 and Figure 2 which we describe the transmission of dengue viruses between host and vector separately. V_1 and V_2 represent infectious vector populations with strain 1 and strain 2 respectively. The populations of host and vector are divided into classes or compartments representing disease status. We do not incorporate the "exposed" compartment, but include instead the existence of a second co-circulating strain that can produce secondary infections in those individuals either susceptible or already recovered from a primary infection with a different strain.

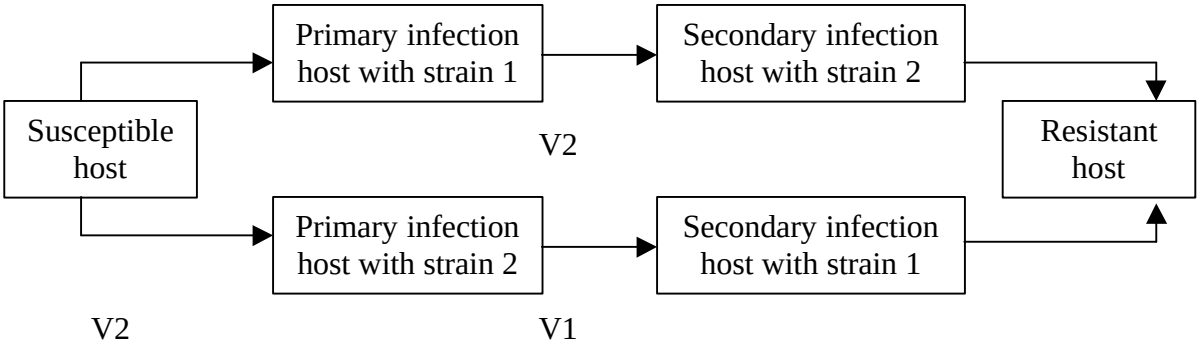

Figure 1 Flow diagram for dengue transmission in host population

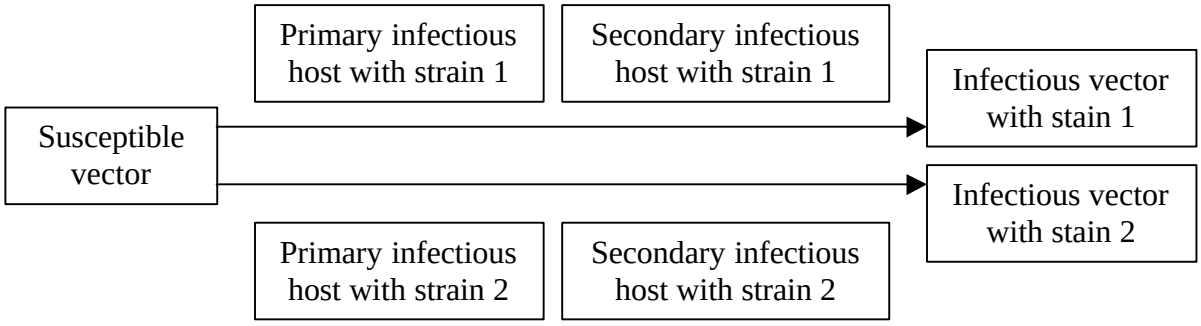

Figure 2 Flow diagram for dengue transmission in vector population

These classes are referred to as state variables shown on Table 1 and parameter definition is shown on Table 2 in detail. Recruitment is assumed to occur only into the susceptible

compartments. Deaths occur form all compartments, with a fractional death rate of 1/life span. Disease status does not affect death rates. The populations of host and vector are assumed to be in a steady state so that in general recruitment equals deaths.

Table 1 State variables for the model of dengue fever transmission with two strains

Symbol	*Variable definition*
S_h	Susceptible host
I_1	Primary infectious host with strain 1
I_2	Secondary infectious host with strain 1
Y_1	Primary infectious host with strain 2
Y_2	Secondary infectious host with strain 2
R_h	Resistant host
M	Susceptible vector
V_1	Infectious vector with strain 1
V_2	Infectious vector with strain 2

Table 2 Parameter definitions and initial values

Symbol	*Parameter definition*	*Initial value*
N	Population of host	50000
T	Population of vector	10000
a_{vh}	Transmission probability, vector to host	0.75
a_{hv}	Transmission probability, host to vector	1
b	Biting rate	0.5
C_{vh}	Effect contact rate, vector to host ($a_{vh}b$)	0.375
C_{hv}	Effect contact rate, host to vector ($a_{hv}b$)	0.5
T_d	Host infection duration	4 days
p	Birth rate of vector	1/7
q	Vector mortality rate	1/7
h	Birth rate of host	1/25000
m_h	Host mortality rate	1/25000

The equations for the model are given:

$$\frac{dS_h}{dt} = hN - (\frac{V_1 C_{vh}}{N} + \frac{V_2 C_{vh}}{N}) S_h - m_h S_h \qquad (1)$$

$$\frac{dI_1}{dt} = \frac{V_1 C_{vh}}{N} S_h - \frac{V_2 C_{vh}}{N} I_1 - m_h I_1 \qquad (2)$$

$$\frac{dI_2}{dt} = \frac{V_2 C_{vh}}{N} S_h - \frac{V_1 C_{vh}}{N} I_2 - m_h I_2 \qquad (3)$$

$$\frac{dY_1}{dt} = \frac{V_1 C_{vh}}{N} I_2 - (m_h + \frac{1}{T_d}) Y_1 \qquad (4)$$

$$\frac{dY_2}{dt} = \frac{V_2 C_{vh}}{N} I_1 - (m_h + \frac{1}{T_d}) Y_2 \qquad (5)$$

$$\frac{dR_h}{dt} = \frac{1}{T_d}(Y_1 + Y_2) - mR_h \qquad (6)$$

$$\frac{dM}{dt} = qT - (I_1 + I_2 + Y_1 + Y_2) \frac{C_{hv} M}{N} - pM \qquad (7)$$

$$\frac{dV_1}{dt} = (I_1 + Y_1) \frac{C_{hv} M}{N} - pV_1 \qquad (8)$$

$$\frac{dV_2}{dt} = (I_2 + Y_2) \frac{C_{hv} M}{N} - pV_2 \qquad (9)$$

We assume that once a mosquito is infected it never recovers and it cannot be reinfected with a different strain of virus. Secondary infection, therefore, may take place only in the host. The parameters for the vector (such as biting rate and transmission probability) have been assumed to take the same value for both stain 1 and strain 2 and we focus on the effect by different factors on primary and secondary infections themselves. Hence, in the discussion to follow, we shall only consider the primary and secondary infections with strain 1 only.

The equations in the model are solved by using Maple V* (Release 4) on a personal computer running Windows 98. Figures 3 and 4 show numbers of susceptible and resistant persons. We define the *peak value* as the maximum number of infectious host reached within the period considered in the simulation. The corresponding time at which this peak value occurs is termed the *peak time* (see Figures 5 and 6). A sample Maple worksheet for the two strain model for dengue transmission is provided in Appendix A.

Some model parameters are then varied to examine their effects on the peak values and peak times in both the primary and secondary infections. The results from these comparisons allow us to study quantitatively the factors which influence dengue transmission. The factors considered here include host population, vector population, vector life span and vector biting rate. Since variations in the biting rate of the vector (b) and transmission probabilities (a_{vh} and a_{hv}) are similar in effect

according to the effect rates (C_{vh} and C_{hv}) in our model, the values of the transmission probabilities are kept constant here.

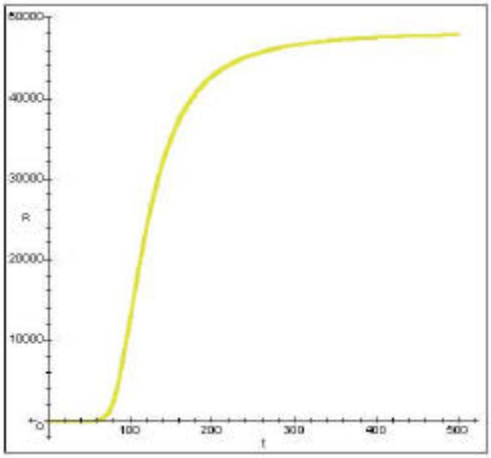

Figure 3 Susceptible host

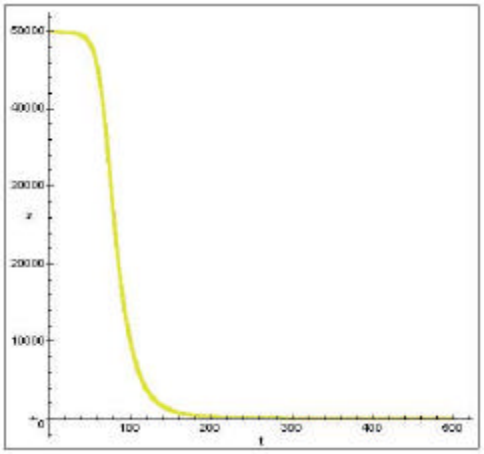

Figure 4 Resistant host

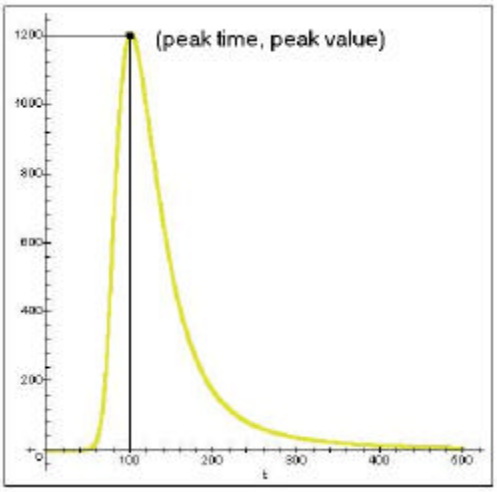

Figure 5 Primary infectious host

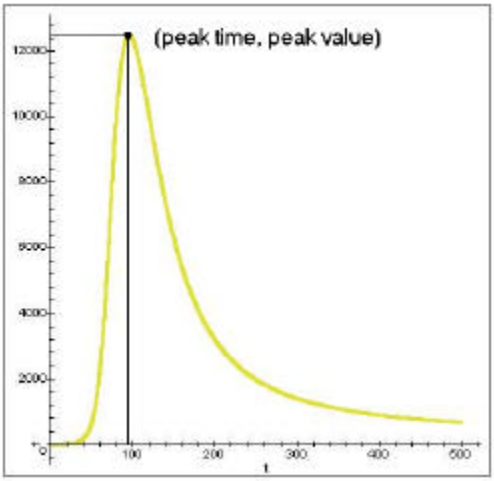

Figure 6 Secondary infectious host

3. Results

There are many factors that influence the spread of dengue. Tables 3 and 4 show the effect of the host and vector populations respectively. Higher human: mosquito ratio increases the peak time. However, when we increase the population of host by as much as 10000 every time, the percentage of primary infectious remains at around 24.9% even though the number of primary infectious host increases correspondingly. Comparatively, the vector population has a less

significant effect on the primary infectious host. Altering the vector population mainly influences the secondary infection. Secondary infectious host population increases as the number of vector increases.

Table 3 Effect of host population on the course of epidemic

	Primary infection		Secondary infection	
Host population	Peak time	Peak value	Peak time	Peak value
30000	64	7480 24.93%	70	1186
40000	80	9968 24.92%	86	1199
50000*	95	12452 24.90%	101	1203
60000	111	14935 24.89%	116	1201
70000	127	17411 24.87%	132	1187

Table 4 Effect of vector population on the course of epidemic

	Primary infection		Secondary infection	
Vector population	Peak time	Peak value	Peak time	Peak value
5000	162	12419	167	598 1.19%
7500	118	12441	123	902 1.84%
10000*	95	12452	101	1203 2.41%
12500	81	12460	87	1498 2.99%
15000	72	12465	77	1787 3.97%

Our results indicate that a higher human:mosquito ratio delays the peak time as shown in Figures 7 and 8. However, as vector population increases, the effect on peak time becomes less and less significant.

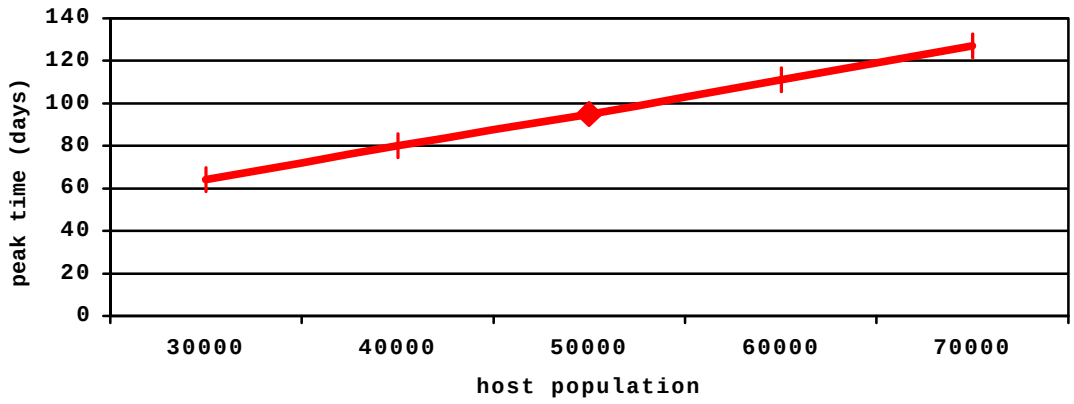

Figure 7 Peak time of secondary infection against host population

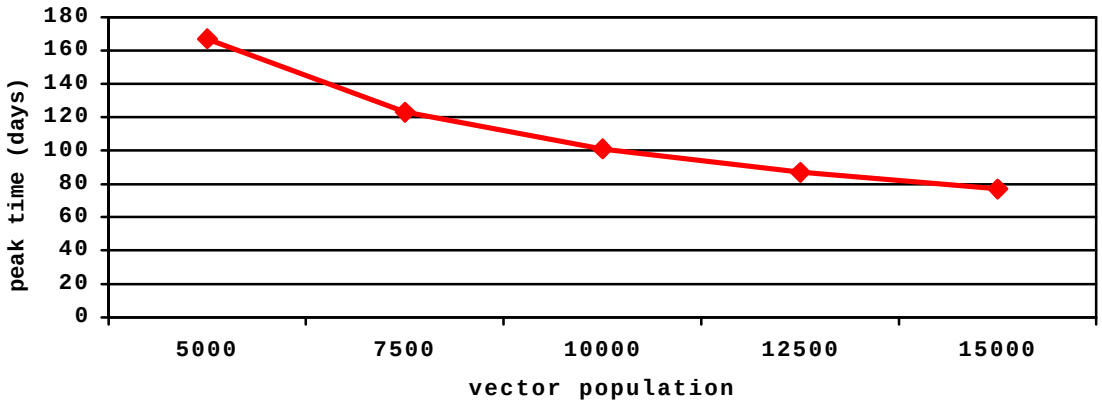

Figure 8 Peak time of secondary infection against vector population

Table 5 Effect of vector life span on the course of epidemic

	Primary infection		Secondary infection	
Vector life span	Peak time	Peak value	Peak time	Peak value
3	147	12426	152	817 1.63%
5	110	12444	115	1056 2.11%
7*	95	12452	101	1203 2.41%
9	88	12456	93	1301 2.60%
11	83	12458	89	1372 2.74%

Table 5 shows the effect of vector life span on the primary and secondary infections. Vector life span varies according to geographical and meteorological conditions. From Table 5 and Figure 9, compared with the longer vector life span, the changes on the shorter vector life span are going to cause more significant influence on both peak time and secondary infectious population.

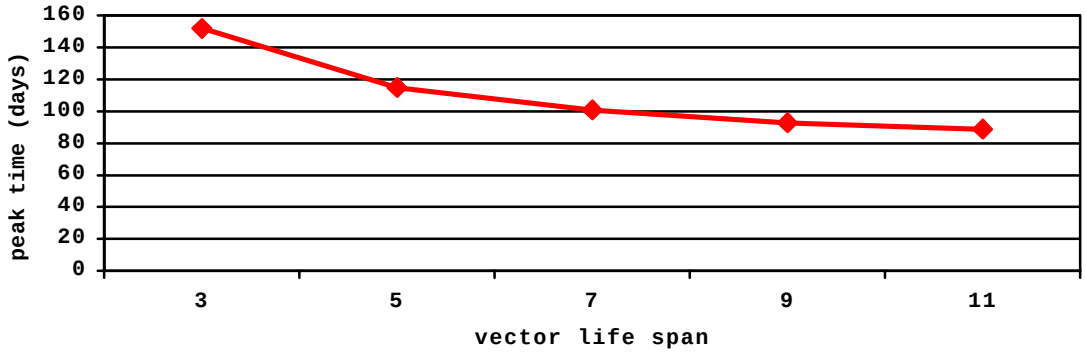

Figure 9 Peak time of secondary infection against vector life span

The size of the initial blood meal, availability of sugar, and many other factors may influence biting frequency (Klowden M.J. *et al*., 1978). Similar to the effect of vector population, biting rate has a less significant effect on primary infectious host. The change on the lower biting rate has a more significant influence on peak time. However, when biting rate goes up by as much as 0.1 every time, the population of secondary infectious host increases at the same rate around 0.6%. The results are shown on Table 6 and Figure 10.

Table 6 Effect of biting rate on the course of epidemic**

	Primary infection		Secondary infection	
Biting rate	Peak time	Peak value	Peak time	Peak value
0.3	201	12400	206	579 1.16%
0.4	130	12435	136	883 1.77%
0.5*	95	12452	101	1203 2.41%
0.6	75	12462	80	1582 3.16%
0.7	61	12470	67	1852 3.70%
0.8	52	12474	57	2171 4.34%
0.9	45	12480	50	2485 4.97%
1.0	39	12482	45	2788 5.58%

**Variations of biting rate and transmission probabilities are similar in effect.

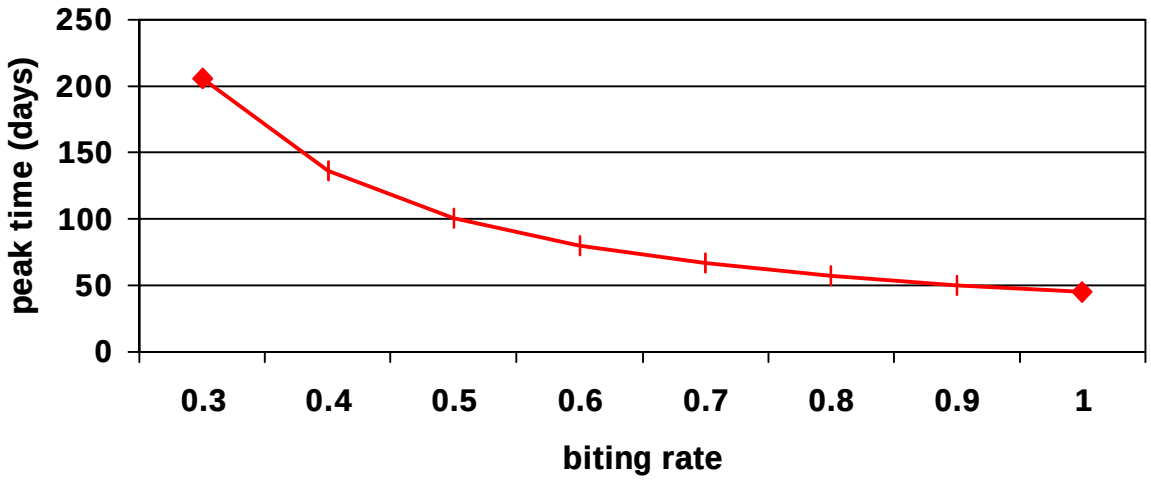

Figure 10 Peak time of secondary infection against biting rate

4. Discussion

By varying certain parameters in the model, we are able to examine the sensitivity of parameters and their effects on the course of epidemic. The ratio of host and vector population influences the peak time of epidemic but this effect becomes less significant when the vector population increases. Although increasing the host population causes more primary infectious cases, the percentage of primary infectious host changes only slightly. Also, the change in the most population has a less significant effect on the infectious host. Compared with host population, factors related to vector, such as vector population, vector life span and biting rate, mainly influence secondary infectious host. As for peak time, when increasing vector population, vector life span and biting rate, it would speed up the coming of peak time of epidemic. Vector plays a significant role on the spread of dengue and those factors related to vector are able to change the pattern of the transmission much more.

The model adopted here does not consider the difference of parameters between strain 1 and strain 2. Some factors related to virus strain may differ according to geographical or meteorological situations. Viral traits that have been recognized to modulate transmission of arboviral diseases include variations in capacity to enter and replicate in specific target cells in the vector (Gulber *et. al.,* 1979) as well as in the vertebrate host, survival mechanism in nature virulence and transmissibility between hosts. Moreover, infection by any dengue virus strain produces long lasting immunity but only temporary cross-immunity to other serotypes. It means individual with immunity to strain 1 can be resistant for both strains for a while on the course of epidemic. They all have an effect on the pattern of the spread of dengue with two strains. The assumption of constant host population size is relatively valid for diseases of short duration with limited effects on mortality. However, this assumption fails to hold for diseases that are endemic in communities with changing population size, and for diseases which raise the mortality rate. In this situation, the effects of the change population size and induced mortality may not be negligible (Lourdes E. and Cristobal V., 1998).

5. Conclusion

We have analyzed a model for dengue disease with two strains. In this model, we assume that both the host population and the vector population are constant. For each strain, all parameters related to the vector have been taken the same values. We use computer simulation to compare the effects of different parameters on the course of epidemic. The results indicate that if we increase the number of host population, it has a less significant effect on the outbreak of secondary infection while the number of primary infection increases apparently. However, the percentage of primary infection in the whole host population remains at around 24%. When the number of vector population increases, it is a high possibility to result in more serious outbreak of secondary infection which means higher peak value and earlier peak time in the model. Those factors related to vector, such as vector life span and biting rate, varied according to geographical and meteorological situations have different influences on virus infection (Kuno, 1995). Our simulations indicate that the other factors related to vector such as vector life span and biting rate have more influence on the secondary infection.

The model analyzed here does not incorporate the effects of variable host population and vector population. Because disease spread is a function the probability of contact between human, virus

and mosquito, transmission is facilitated in dengue-infected location where people congregate or mosquitoes are abundant. It is clear that many ecologic disturbances linked with human activities or natural conditions, such as rapid and uncontrolled urbanization, effective vector control program and rainfall every year, resulted in a large fluctuation of vector population and changed the contact of the mosquito with human. In those areas where are with rapid changing host and vector population sizes, the assumptions that consider both populations as constants are far from negligible, and in fact, may have a crucial influence on the dynamics of the disease. The need for the model that incorporates variable host and vector populations into the dengue spread dynamics is thus justified.

In addition, this model demonstrated the effective use of technology, namely, Maple V, in such modelling studies. Through the use of this simple but powerful tool, we have provided new insights into dengue transmission with two strains. The long term application of such models and simulations, together with the power of computer algebra systems like Maple, will continue to be important and crucial in our search for more appropriate models for the spread of dengue.

References:

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Appendix A: Sample Maple worksheet for Two Strain Dengue Model

```
> with(DEtools):

> model:={diff(s(t),t)=h*N-(b1*v1+b2*v2)*s-u*s,
          diff(i1(t),t)=b1*v1*s-b2*v2*i1-u*i1,
          diff(i2(t),t)=b2*v2*s-b1*v1*i2-u*i2,
          diff(y1(t),t)=b1*v1*i2-(u+r1)*y1,
          diff(y2(t),t)=b2*v2*i1-(u+r1)*y2,
          diff(R(t),t)=r1*(y1+y2)-u*R,
          diff(m(t),t)=q*T-(a1*i1+a1*y1+a2*i2+a2*y2)*m-p*m,
          diff(v1(t),t)=a1*(i1+y1)*m-p*v1,
          diff(v2(t),t)=a2*(i2+y2)*m-p*v2};


model := {d
          -- s(t) = h N - (b1 v1 + b2 v2) s - u s,
          dt
         d
         -- i1(t) = b1 v1 s - b2 v2 i1 - u i1,
         dt
         d
         -- i2(t) = b2 v2 s - b1 v1 i2 - u i2,
         dt
         d
         -- y1(t) = b1 v1 i2 - (u + r1) y1,
         dt
         d
         -- y2(t) = b2 v2 i1 - (u + r1) y2,
         dt
         d
         -- R(t) = r1 (y1 + y2) - u R,
         dt
         d
         -- m(t) = q T - (a1 i1 + a1 y1 + a2 i2 + a2 y2) m - p m,
         dt
         d
         -- v1(t) = a1 (i1 + y1) m - p v1,
         dt
         d
         -- v2(t) = a2 (i2 + y2) m - p v2}
         dt


> h:=0.00004:N:=50000:u:=0.00004:p:=1/7.0:q:=1/7.0:b1:=0.0000075:
  b2:=0.0000075:a1:=0.00001:a2:=0.00001:r1:=1/4.0:T:=10000:
```

```
> DEplot(model,[s,i1,i2,y1,y2,R,m,v1,v2],t=0..500,
  {[s(0)=50000,i1(0)=0,i2(0)=0,y1(0)=0,y2(0)=0,R(0)=0,m(0)=10000,
   v1(0)=1,v2(0)=1]},scene=[t,i1],stepsize=0.1,linecolor=black);
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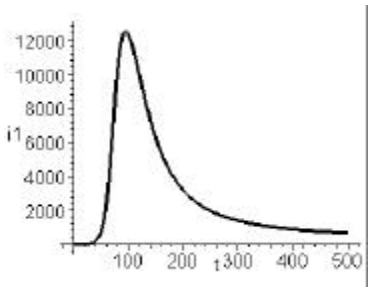


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> DEplot(model,[s,i1,i2,y1,y2,R,m,v1,v2],t=0..500,
  {[s(0)=50000,i1(0)=0,i2(0)=0,y1(0)=0,y2(0)=0,R(0)=0,m(0)=10000,
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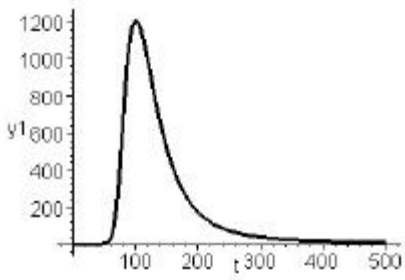


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   v1(0)=1,v2(0)=1]},scene=[t,s],stepsize=0.1,linecolor=black);
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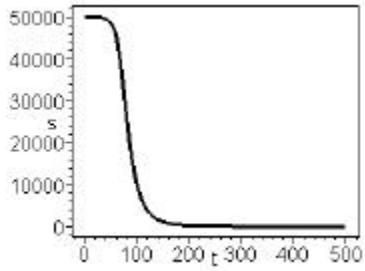


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> DEplot(model,[s,i1,i2,y1,y2,R,m,v1,v2],t=0..500,
  {[s(0)=50000,i1(0)=0,i2(0)=0,y1(0)=0,y2(0)=0,R(0)=0,m(0)=10000,
   v1(0)=1,v2(0)=1]},scene=[t,R],stepsize=0.1,linecolor=black);
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