

# Mathematical Model of Dengue Disease with the Incubation Period of Virus

P. Pongsumpun

**Abstract**—Dengue virus is transmitted from person to person through the biting of infected *Aedes Aegypti* mosquitoes. DEN-1, DEN-2, DEN-3 and DEN-4 are four serotypes of this virus. Infection with one of these four serotypes apparently produces permanent immunity to it, but only temporary cross immunity to the others. The length of time during incubation of dengue virus in human and mosquito are considered in this study. The dengue patients are classified into infected and infectious classes. The infectious human can transmit dengue virus to susceptible mosquitoes but infected human can not. The transmission model of this disease is formulated. The human population is divided into susceptible, infected, infectious and recovered classes. The mosquito population is separated into susceptible, infected and infectious classes. Only infectious mosquitoes can transmit dengue virus to the susceptible human. We analyze this model by using dynamical analysis method. The threshold condition is discussed to reduce the outbreak of this disease.

**Keywords**—Transmission model, intrinsic incubation period, extrinsic incubation period, basic reproductive number, equilibrium states, local stability.

## I. INTRODUCTION

IN recent years, dengue disease has become a major public health concern [1]. This disease is found in tropical and sub-tropical regions around the world. More than 100 countries in Africa, the Americas, the Eastern Mediterranean, South-east Asia and the Western Pacific are affected due to this disease. Only nine countries had experienced dengue epidemics before 1970 but a number had increased more than four-fold by 1995. In 2001, there were more than 609,000 patients due to dengue disease. This was greater than double the number of dengue patients which were recorded in the same region in 1995. Two-fifth of the world's population is now at risk from dengue disease. WHO currently estimates there may be 50 million cases of dengue disease worldwide per year. Attack rates among susceptible are 40-50% may be reach 80-90% during epidemics of this disease. The person who be infected with this disease are classified into 3 forms, Dengue Fever (DF), Dengue hemorrhagic fever (DHF) and Dengue shock syndrome (DSS). These three forms depend on

P. Pongsumpun is with the Department of Mathematics and Computer Science, Faculty of Science, King Mongkut's Institute of Technology Ladkrabang, Chalongkrung road, Ladkrabang, Bangkok 10520, Thailand. (phone: 662-737-3000 ext. 6196; fax: 662-326-4344 ext.284; e-mail: kppuntan@kmitl.ac.th).

the symptom of each patient. DHF and DSS are severe forms of this disease. The transmission cycle of dengue virus by the mosquito *Aedes aegypti* begins with a dengue infectious person. Most of these people will have virus circulating in the blood (viremia) that lasts for about four to seven days [2,3]. During this viremic period, an uninfected female *Aedes aegypti* mosquito bites the person and ingests blood that contains dengue virus. Although there is some evidence of transovarial transmission of dengue virus in *Aedes aegypti*, usually mosquitoes are only infected by biting a viremic person. Then within the mosquito, the viruses replicate during an extrinsic incubation period of eight to twelve days. After an extrinsic incubation period of the mosquito, its salivary glands become infected and the virus is transmitted when the infectious mosquito bites and injects the salivary fluid into the wound of the human. The mosquito can bite a susceptible person and could transmit the virus to him or her, as well as to every other susceptible persons, the mosquito bites for the rest of its lifetime. The virus then replicates in the person during an intrinsic incubation period [4].

The original model used by Esteva and Vargas [5] did not include the intrinsic and extrinsic incubation periods of dengue virus in human and vector populations. Their model considered the transmission between the human and vector populations. The human population is separated into susceptible, infectious and recovered classes. The vector population is divided into susceptible and infectious classes. In our study, the length of time during the dengue virus circulating in the blood of human and vector populations are considered. The infected human and infected vector classes are included into the model. There are the difference between infected and infectious classes for the human and vector populations. The infected classes can not transmit dengue virus until they become to be infectious class.

## II. MATHEMATICAL MODEL

Let  $\bar{S}_h(t)$  be the number of susceptible human population at time  $t$ ,

$\bar{X}_h(t)$  be the number of infected human population at time  $t$ ,

$\bar{I}_h(t)$  be the number of infectious human population at time  $t$ ,

$\bar{R}_h(t)$  be the number of recovered human population at time  $t$ ,

$\bar{S}_v(t)$  be the number of susceptible vector population at time  $t$ ,

$\bar{X}_v(t)$  be the number of infected vector population at time  $t$ ,

$\bar{I}_v(t)$  be the number of infectious vector population at time  $t$ ,

The dynamical system for human and vector populations can be described by the following equations:

$$\begin{aligned} \frac{d}{dt} \bar{S}_h &= \lambda N_T - \beta_h \bar{S}_h \bar{I}_v - \mu_h \bar{S}_h \\ \frac{d}{dt} \bar{X}_h &= \beta_h \bar{S}_h \bar{I}_v - \alpha_h \bar{X}_h - \mu_h \bar{X}_h \\ \frac{d}{dt} \bar{I}_h &= \alpha_h \bar{X}_h - r \bar{I}_h - \mu_h \bar{I}_h \\ \frac{d}{dt} \bar{R}_h &= r \bar{I}_h - \mu_h \bar{R}_h \\ \frac{d}{dt} \bar{S}_v &= C - \beta_v \bar{I}_h \bar{S}_v - \mu_v \bar{S}_v \\ \frac{d}{dt} \bar{X}_v &= \beta_v \bar{I}_h \bar{S}_v - \alpha_v \bar{X}_v - \mu_v \bar{X}_v \\ \frac{d}{dt} \bar{I}_v &= \alpha_v \bar{X}_v - \mu_v \bar{I}_v \end{aligned} \quad (1)$$

with the conditions

$$N_T = \bar{S}_h + \bar{X}_h + \bar{I}_h + \bar{R}_h \quad \text{and} \quad N_v = \bar{S}_v + \bar{X}_v + \bar{I}_v$$

where

$N_T$  is the total number of human population,

$\lambda$  is the birth rate of the human population,

$\beta_h$  is the infectious rate of dengue virus from vector to human population,

$\alpha_h$  is the rate at which the infected human change to be infectious human population,

$\beta_v$  is the infectious rate of dengue virus from human to vector population,

$\mu_h$  is the death rate of human population,

$r$  is the recovery rate of human population,

$C$  is the constant recruitment rate of the vector population,  $\alpha_v$  is the rate at which the infected vector change to be infectious vector population,

$\mu_v$  is the death rate of vector population.

The total human and vector populations are constant, thus the rate of change for both populations equal to zero. Then

$$\frac{d}{dt} N_T = 0 \quad \text{and} \quad \frac{d}{dt} N_v = 0. \quad (2)$$

From (2), we obtain  $\lambda = \mu_h$  for human population and

$$N_v = \frac{C}{\mu_v} \text{ for vector population.}$$

Normalizing (1) by letting

$$\begin{aligned} S &= \frac{\bar{S}_h}{N_T}, \quad X = \frac{\bar{X}_h}{N_T}, \quad I = \frac{\bar{I}_h}{N_T}, \\ R &= \frac{\bar{R}_h}{N_T}, \quad S_v = \frac{\bar{S}_v}{N_v}, \quad X_v = \frac{\bar{X}_v}{N_v}, \quad I_v = \frac{\bar{I}_v}{N_v}, \end{aligned}$$

then the reduced equations become

$$\begin{aligned} \frac{dS}{dt} &= \mu_h - \beta_h S I_v (C / \mu_v) - \mu_h S \\ \frac{dX}{dt} &= \beta_h S I_v (C / \mu_v) - \alpha_h X - \mu_h X \\ \frac{dI}{dt} &= \alpha_h X - r I - \mu_h I \\ \frac{dX_v}{dt} &= \beta_v I N_T (1 - X_v - I_v) - \alpha_v X_v - \mu_v X_v \\ \frac{dI_v}{dt} &= \alpha_v X_v - \mu_v I_v \end{aligned} \quad (3)$$

with the conditions  $S + X + I + R = 1$

and  $S_v + X_v + I_v = 1$ .

### III. ANALYSIS OF THE MODEL

#### A. Analytical Results

Finding equilibrium states by setting right hand side of all equations in (3) equal to zero, then we obtain two equilibrium states:

i) Disease free equilibrium state:  $\bar{V}_0 = (1,0,0,0,0)$  (4)

ii) Endemic equilibrium state:

$$\bar{V}_1 = (S^*, X^*, I^*, X_v^*, I_v^*) \quad (5)$$

$$\text{where } S^* = \frac{(\alpha_v + \mu_v)(\alpha_h \gamma_v \mu_h + MN \mu_h^2 \mu_v)}{\alpha_h \gamma_v (\mu_h (\alpha_v + \mu_v) + \alpha_v \gamma_h)},$$

$$X^* = \frac{M \mu_h^2 \mu_v (\alpha_v + \mu_v) (E_0 - 1)}{\alpha_h \gamma_v (\mu_h (\alpha_v + \mu_v) + \alpha_v \gamma_h)},$$

$$I^* = \frac{\mu_h \mu_v (\alpha_v + \mu_v) (E_0 - 1)}{\gamma_v (\mu_h (\alpha_v + \mu_v) + \alpha_v \gamma_h)},$$

$$X_v^* = \frac{MN \mu_h^3 \mu_v^2 (E_0 - 1)}{\alpha_v \gamma_h (\alpha_h \gamma_v \mu_h + MN \mu_h^2 \mu_v)}$$

$$I_v^* = \frac{MN \mu_h^3 \mu_v (E_0 - 1)}{\gamma_h (\alpha_h \gamma_v \mu_h + MN \mu_h^2 \mu_v)}$$

and

$$\gamma_h = \beta_h (C / \mu_v), \quad \gamma_v = \beta_v N_T, \quad M = \frac{\mu_h + r}{\mu_h}, \quad N = \frac{\alpha_h + \mu_h}{\mu_h}$$

and

$$E_0 = \frac{\alpha_h \alpha_v \gamma_h \gamma_v}{(r + \mu_h)(\alpha_h + \mu_h) \mu_v (\alpha_v + \mu_v)}$$

The local stability for each equilibrium state can be determined by the sign of all eigenvalues. If all eigenvalues have negative real part, then that equilibrium state is local

stability. We find eigenvalues for each equilibrium state by setting

$$\det(J - \xi I) = 0 \tag{6}$$

where  $J$  is the Jacobian matrix of the right hand side of (3) calculated at the equilibrium state.

For the equilibrium state  $\bar{V}_o$ , the characteristic equation is

$$(\xi + \mu_h)(\xi^4 + w_3\xi^3 + w_2\xi^2 + w_1\xi + w_0) = 0 \tag{7}$$

where

$$\begin{aligned} w_3 &= \alpha_v + (M + N)\mu_h + 2\mu_v \\ w_2 &= MN\mu_h^2 + 2(M + N)\mu_h\mu_v + \mu_v^2 + \alpha_v(M + N)\mu_h + \mu_v \\ w_1 &= \mu_h(\alpha_v(MN\mu_h + (M + N)\mu_v) \\ &+ \mu_v(2MN\mu_h + (M + N)\mu_v)) \\ w_0 &= MN\mu_h^2\mu_v(1 - E_0)(\alpha_v + \mu_v) \end{aligned} \tag{8}$$

There are five eigenvalues corresponding to (7). We denote these five eigenvalues by  $\xi_1, \xi_2, \xi_3, \xi_4$  and  $\xi_5$ .  $\xi_1 = -\mu_h$  has negative real part. The other four eigenvalues can be obtained by solving

$$\xi^4 + w_3\xi^3 + w_2\xi^2 + w_1\xi + w_0 = 0.$$

These four eigenvalues have negative real part if they satisfy the Routh-Hurwitz criteria [6,7] :

$$w_3 > 0 \tag{9}$$

$$w_1 > 0 \tag{10}$$

$$w_0 > 0 \tag{11}$$

$$w_1w_2w_3 > w_1^2 + w_3^2w_0 \tag{12}$$

It can be easily seen that coefficients  $w_3, w_2$  and  $w_0$  satisfy (9), (10) and (11) when  $E_0 < 1$ . Evaluating

$$\begin{aligned} &w_1w_2w_3 - (w_1^2 + w_3^2w_0) \\ &= (M + N)\mu_h(M\mu_h + \mu_v)(\alpha_v + M\mu_h + \mu_v) \\ &(N\mu_h + \mu_v)(\alpha_v + N\mu_h + \mu_v)(\alpha_v + 2\mu_v) \\ &+ \alpha_h\alpha_v\gamma_h\gamma_v(\alpha_v + (M + N)\mu_h + 2\mu_v)^2 \end{aligned}$$

$w_1w_2w_3 - (w_1^2 + w_3^2w_0)$  is always positive. Therefore the disease free equilibrium state is local stability for  $E_0 < 1$ .

For the equilibrium state  $\bar{V}_1$ , the characteristic equation is

$$\xi^5 + u_4\xi^4 + u_3\xi^3 + u_2\xi^2 + u_1\xi + u_0 = 0 \tag{13}$$

where

$$\begin{aligned} u_4 &= \alpha_v + (1 + M + N)\mu_h + 2\mu_v \\ &+ \frac{(E_0 - 1)\mu_h\mu_v(\alpha_v + \mu_v)}{\alpha_v(\gamma_h + \mu_h) + \mu_h\mu_v} + \frac{(E_0 - 1)MN\mu_h^3\mu_v}{\alpha_h\gamma_v\mu_h + MN\mu_h^2\mu_v} \\ u_3 &= \mu_v^2 + \mu_h\mu_v \left( 2(1 + M + N) + \frac{(E_0 - 1)\mu_v(\alpha_v + \mu_v)}{\alpha_v(\gamma_h + \mu_h) + \mu_h\mu_v} \right) \\ &+ \mu_h^2(M + N + MN \\ &+ \frac{(1 + M + N)(E_0 - 1)\mu_v(\alpha_v + \mu_v)}{\alpha_v(\gamma_h + \mu_h) + \mu_h\mu_v}) \end{aligned}$$

$$\begin{aligned} &+ \frac{(E_0 - 1)MN\mu_h^3\mu_v((M + N)\mu_h + 2\mu_v)}{\alpha_h\gamma_v\mu_h + MN\mu_h^2\mu_v} \\ &+ \frac{(E_0 - 1)\mu_h\mu_v(\alpha_v + \mu_v)}{\alpha_v(\gamma_h + \mu_h) + \mu_h\mu_v} \\ &+ \frac{\alpha_v(\gamma_h + \mu_h) + \mu_h\mu_v}{\alpha_h\gamma_v\mu_h + MN\mu_h^2\mu_v} \\ &+ \alpha_v \left( (1 + M + N)\mu_h + \mu_v + \frac{(E_0 - 1)\mu_h\mu_v(\alpha_v + \mu_v)}{\alpha_v(\gamma_h + \mu_h) + \mu_h\mu_v} + \frac{(E_0 - 1)MN\mu_h^3\mu_v}{\alpha_h\gamma_v\mu_h + MN\mu_h^2\mu_v} \right) \\ u_2 &= \mu_h \left( MN\mu_h^2 + 2(M + N + MN)\mu_h\mu_v + (1 + M + N)\mu_v^2 \right. \\ &+ \frac{(E_0 - 1)\mu_h\mu_v(\alpha_v + \mu_v)((M + N)\mu_h + (1 + M + N)\mu_v)}{\alpha_v(\gamma_h + \mu_h) + \mu_h\mu_v} \\ &+ \frac{(E_0 - 1)MN\mu_h^2\mu_v(MN\mu_h^2 + 2(M + N)\mu_h\mu_v + \mu_v^2)}{\alpha_h\gamma_v\mu_h + MN\mu_h^2\mu_v} \\ &+ \frac{(E_0 - 1)MN\mu_h^2\mu_v \left( \frac{(E_0 - 1)\mu_h\mu_v(\alpha_v + \mu_v)((M + N)\mu_h + \mu_v)}{\alpha_v(\gamma_h + \mu_h) + \mu_h\mu_v} \right)}{\alpha_h\gamma_v\mu_h + MN\mu_h^2\mu_v} \\ &+ \alpha_v \left( (M + N + MN)\mu_h + (1 + M + N)\mu_v + \frac{(1 + M + N)(E_0 - 1)\mu_h\mu_v(\alpha_v + \mu_v)}{\alpha_v(\gamma_h + \mu_h) + \mu_h\mu_v} \right. \\ &+ \left. \left. \frac{(E_0 - 1)MN\mu_h^2\mu_v \left( (M + N)\mu_h + \mu_v + \frac{(E_0 - 1)\mu_h\mu_v(\alpha_v + \mu_v)}{\alpha_v(\gamma_h + \mu_h) + \mu_h\mu_v} \right)}{\alpha_h\gamma_v\mu_h + MN\mu_h^2\mu_v} \right) \right) \\ u_1 &= \mu_h^2 \left( \frac{MN(E_0 - 1)\mu_h^2\mu_v(\alpha_v + \mu_v) \left( 1 + \frac{(E_0 - 1)N\mu_h^2\mu_v}{\alpha_h\gamma_v\mu_h + N\mu_h^2\mu_v} \right)}{\alpha_v(\gamma_h + \mu_h) + \mu_h\mu_v} \right. \\ &+ \mu_v^2 \left( M + N + MN + \frac{(M + N)(E_0 - 1)N\mu_h^2\mu_v}{\alpha_h\gamma_v\mu_h + N\mu_h^2\mu_v} \right) \\ &+ \mu_h\mu_v \left( 2MN + \frac{(M + N + MN)(E_0 - 1)\mu_v(\alpha_v + \mu_v)}{\alpha_v(\gamma_h + \mu_h) + \mu_h\mu_v} \right. \\ &+ \left. \left. \frac{(E_0 - 1)N\mu_h^2\mu_v \left( 2MN + \frac{(M + N)(E_0 - 1)\mu_v(\alpha_v + \mu_v)}{\alpha_v(\gamma_h + \mu_h) + \mu_h\mu_v} \right)}{\alpha_h\gamma_v\mu_h + N\mu_h^2\mu_v} \right) \right) \\ &+ \alpha_v(MN\mu_h + (M + N + MN)\mu_v) \\ &+ \frac{(M + N + MN)(E_0 - 1)\mu_h\mu_v(\alpha_v + \mu_v)}{\alpha_v(\gamma_h + \mu_h) + \mu_h\mu_v} \end{aligned}$$

$$+ \frac{(E_0 - 1)N\mu_h^2\mu_v \left( MN\mu_h + (M+N)\mu_v + \frac{(M+N)(E_0 - 1)\mu_h\mu_v(\alpha_v + \mu_v)}{\alpha_v(\gamma_h + \mu_h) + \mu_h\mu_v} \right)}{\alpha_h\gamma_v\mu_h + N\mu_h^2\mu_v} \Bigg)$$

$$u_0 = \mu_h\mu_v(\alpha_v + \mu_v)$$

$$\left( MN\mu_h^2 \left( 1 + \frac{(E_0 - 1)N\mu_h^2\mu_v}{\alpha_h\gamma_v\mu_h + N\mu_h^2\mu_v} \right) \left( 1 + \frac{(E_0 - 1)\mu_h(\alpha_v + \mu_v)}{\alpha_v(\gamma_h + \mu_h) + \mu_h\mu_v} \right) \right)$$

There are five eigenvalues corresponding to (13). We denote these five eigenvalues by  $\xi_1, \xi_2, \xi_3, \xi_4$  and  $\xi_5$ . These four eigenvalues have negative real parts if they satisfy the Routh-Hurwitz criteria, that is [6,7]

$$u_i > 0; \quad \text{for } i = 1, 2, 3, 4, 5 \quad (14)$$

$$u_2u_3u_4 - u_2^2 - u_4^2u_1 > 0 \quad (15)$$

$$(u_1u_4 - u_0)(u_4u_3u_2 - u_2^2 - u_4^2u_1) - u_0(u_4u_3 - u_2^2) - u_4u_0^2 > 0 \quad (16)$$

It can be easily seen that the coefficients  $u_i$  for  $i = 1, 2, 3, 4, 5$  are satisfied (14) for  $E_0 > 1$ . From our evaluations, we found that conditions (15) and (16) are satisfied for  $E_0 > 1$  also.

Thus, the endemic equilibrium state is local stability for  $E_0 > 1$ .

**B. Numerical Results**

In this study, we are interested in the incubation period of dengue virus in human and vector populations. After each susceptible person is bitten by infectious vector, that person can not transmit dengue virus immediately. We call this person in this period as an infected human. Intrinsic incubation period of dengue virus in human is about 5 days [2]. When the susceptible vector bites the infectious person, it will be infected vector before it become to be infectious vector. Extrinsic incubation period of dengue virus in vector population is about 10 days [2]. The susceptible person is the person who has no immunity and not infected. The recovered person is the person who has immunity after infected with dengue virus. The parameters are determined by real life observations.  $\mu_h = 0.0000391$  corresponds to the real life expectancy of 70 years for human.  $\beta_h$  and  $\beta_v$  are arbitrarily chosen.  $\alpha_h = 1/5$  corresponds to the extrinsic incubation period of 5 days.  $\alpha_v = 1/10$  corresponds to the intrinsic incubation period of 10 days.  $r = 1/14$  corresponds to the length of 14 days for illness.  $\mu_v = 1/14$  corresponds to the mean life of 14 days for vector population.  $C$  is the constant recruitment rate of vector population; this parameter is arbitrarily chosen.

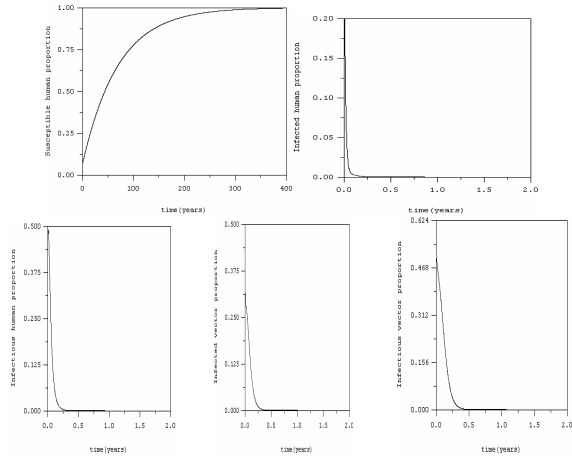


Fig. 1 Time series of susceptible human, infected human, infectious human, infected vector and infectious vector proportions. The values of the parameters are  $\mu_h = 0.0000391$ ,  $\beta_h = 0.00005$ ,  $\alpha_h = \frac{1}{5}$ ,

$$r = \frac{1}{14}, N_T = 5,000, \beta_v = 0.00008, \mu_v = \frac{1}{14}, \alpha_v = \frac{1}{10}, C = 30, E_0 = 0.95$$

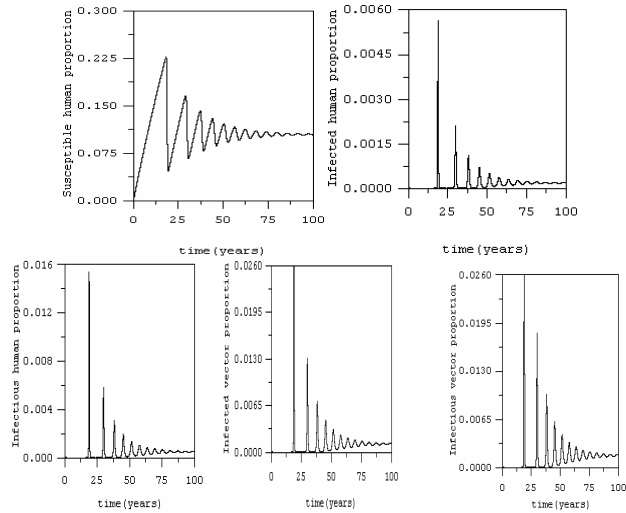


Fig. 2 Time series of susceptible human, infected human, infectious human, infected vector and infectious vector proportions. The values of the parameters are  $\mu_h = 0.0000391$ ,  $\beta_h = 0.00005$ ,  $\alpha_h = \frac{1}{5}$ ,

$$r = \frac{1}{14}, N_T = 5,000, \beta_v = 0.00008, \mu_v = \frac{1}{14}, \alpha_v = \frac{1}{10}, C = 300, E_0 = 9.5$$

Fig. 1 and Fig. 2 show time development of human and vector classes. Fig. 1 shows numerical solutions for  $E_0 < 1$ . Fig. 2 shows numerical solutions for  $E_0 > 1$ . The solutions converge to the disease free equilibrium state as shown in Fig. 1. Fig. 2, the solutions oscillate to the endemic equilibrium

state (0.104486, 0.000175039, 0.00048984, 0.00113983, 0.00159577).

IV. DISCUSSION AND CONCLUSION

We formulate the transmission model of dengue disease by considering the incubation period of dengue virus in human and vector populations. The basic reproductive number is  $E' = \sqrt{E_0}$  where

$$E_0 = \frac{\alpha_h \alpha_v \gamma_h \gamma_v}{(r + \mu_h)(\alpha_h + \mu_h)\mu_v(\alpha_v + \mu_v)} \tag{17}$$

$E'$  represents the number of secondary cases that one case can produce if introduced into a susceptible person.  $E_0$  is the threshold condition. The threshold condition and the stability of the solutions are shown in Fig. 3.

results in the previous section. The behavior of solutions can be described in terms of the basic reproductive number; if this number is less than or equal to one, thus an infective replace itself with less than one new infective, the disease die out. Furthermore, the susceptible fraction approaches one since everyone is susceptible when the disease has vanished. If the basic reproductive number is greater than one, the normalized susceptible human decreases. The normalized infected human, infectious human populations increase. These subsequent behaviors occur because there are enough susceptible human to be infected from infectious vector.

The basic reproductive numbers are used for controlling the diseases [8, 9, 10,11]. The human population should protect themselves from infected with dengue virus by using bed-nets to reduce the infection rate of the vector population. This will cause the basic reproductive number to decrease below one. Consequently, we can reduce the outbreak of the disease.

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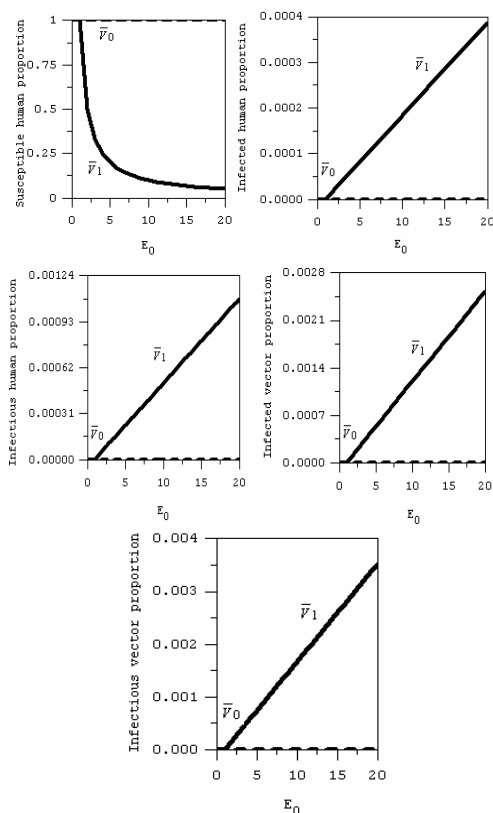


Fig. 3 Bifurcation diagrams of system (3), demonstrate the equilibrium solutions of susceptible, infected, infectious human and infected, infectious vector population respectively. — represents the stable solutions and --- represents the unstable solutions. For  $E_0 < 1$ ,  $\bar{V}_0$  will be stable. For  $E_0 > 1$ ,  $\bar{V}_1$  will be stable

The basic reproductive number for the endemic equilibrium state will prevail if and only if the basic reproductive number exceeds one. The disease free equilibrium state exists and is local stability if the basic reproductive number is less than one and become unstable when the basic reproductive number is more than one. The numerical simulations are used to confirm