TRANSMISSION MODEL OF DENGUE DISEASE WITH THE APPEARANCE OF SYMPTOM

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ABSTRACT

Dengue virus is transmitted to the human by biting of the infected *Aedes Aegypti* mosquito. After infection with dengue virus, the people may be symptomatic or asymptomatic. This fact is studied through the mathematical model. The infectious population with symptom and no symptom classes are introduced into the modified model. We compare this model with the SIR (**S**usceptible-**I**nfectious-**R**ecovered) model. The standard dynamical analysis is used to analyze the behavior of the solutions for the two models. A new expression for the basic reproduction rate is obtained. It is found that the symptomatic and asymptomatic classes reduce the periods of oscillations in the susceptible human, Infectious human and infectious vector and the tightness of the spiraling into the endemic equilibrium state.

KEYWORDS: transmission model, dengue disease, SIR model, symptomatic infection, asymptomatic infection

1. INTRODUCTION

Dengue disease is the disease which can be found in the tropical regions of the world. Three forms of this disease are dengue fever (DF), dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). The symptom of DF is headaches, bone or joint and muscular pains, leukopenia and rash. DHF is presented by high fever, hemorrhagic phenomena, hepatomegaly and signs of circulatory failure. The dengue patients may shock resulting from plasma leakage. This is called DSS. Four serotypes of dengue virus are denoted by DEN-1, DEN-2, DEN-3 and DEN-4. This disease can be transmitted to the person by biting of the infected vector. *Aedes aegypti* is one of the most efficient mosquito vectors for arboviruses, because it is highly antropophilic and thrives in close proximity to humans and often lives indoors. Any one serotype of dengue virus is transmitted to the human begins when an infectious mosquito bites a human and injects a large number of the dengue virus of one serotype into the blood of the human. The virus may be causing either a symptomatic or an asymptomatic infection in the person. The latter type of infections is more common than the former infection. The illness resulting from the former infection lasts for about one to two weeks. During this time, the infected person has the immunity by any of the four dengue virus serotypes. After the person recovers, he keeps his immunity to the infecting serotype but losses the temporary immunity he had to the other serotypes. If a susceptible mosquito bites a person while he has a high count of virus in the blood, the susceptible mosquito can become infected. It takes from three to fourteen days (the incubation period) for the virus to develop inside the mosquito before it becomes infectious, i.e., able to transmit the disease to a human by its bite.

The early outbreak of this disease seems to have appeared in the Philippines and in Thailand. In Thailand, outbreaks first occurred in Bangkok with the pattern of two-year cycle, then subsequently in irregular cycles as the disease spread throughout the country. This disease becomes endemic in many large cities of Thailand, eventually spreading to smaller towns and villages during the period of the epidemic transmission [1]. Most dengue cases occur in children less than 15 years old. Burke et al. [2] estimates that 87 % of dengue infections in one study in Thailand were either mild or asymptomatic. Within a year of DEN-1 epidemic in Cuba in 1977 [3], 44.6 % of the population in Cuba had the

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antibodies to DEN-1 virus even though the reported number of confirmed DF illness in Cuba during the year was much less.

In this paper, we compare the behaviors of the transmission of dengue disease by considering the solutions from two mathematical models. There are no symptomatic and asymptomatic classes for the first model. The second model, we include the symptomatic and asymptomatic classes. We assume that the transmission probabilities of dengue virus to symptomatic and asymptomatic classes are difference.

2. MATHEMATICAL MODELS

In 1998, Esteva and Vargas [4] proposed their SIR (**S**usceptible-**I**nfectious-**R**ecovered) model for the transmission of dengue virus. Their model is based on the following assumptions:
The human population has constant size and is divided into three groups, susceptible, infectious, and recovered persons. A susceptible person is one who is both not immune and not infectious. An infectious person is one who is both infected and can transmit the dengue virus to the mosquitoes. This occurs only during the period of viremia. A recovered person is the infected person after the viremia stage until after they recover from dengue infection. They have assumed that there is only one type of virus and disease-related death rate is negligible. The vector population has constant size and is divided into two groups, susceptible and infectious mosquitoes, with the mosquitoes never recover from infection. Let

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

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

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

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

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

The transmission model of dengue disease can be described by the following equations:

$$\begin{aligned}
\frac{d}{dt}\bar{S}_h &= \nu N_T - \frac{b\alpha_h}{N_T}\bar{S}_h\bar{I}_v - \gamma_h\bar{S}_h, \\
\frac{d}{dt}\bar{I}_h &= \frac{b\alpha_h}{N_T}\bar{S}_h\bar{I}_v - (\gamma_h + r)\bar{I}_h, \\
\frac{d}{dt}\bar{R}_h &= r\bar{I}_h - \gamma_h\bar{R}_h. \qquad (1)
\end{aligned}$$

$$\begin{aligned}
\frac{d}{dt}\bar{S}_v &= L - \frac{b\alpha_v}{N_T}\bar{S}_v\bar{I}_h - \gamma_v\bar{S}_v, \\
\frac{d}{dt}\bar{I}_v &= \frac{b\alpha_v}{N_T}\bar{S}_v\bar{I}_h - \gamma_v\bar{I}_v
\end{aligned}$$

with the conditions

$$N_T = \bar{S}_h + \bar{I}_h + \bar{R}_h \quad \text{and} \quad N_v = \bar{S}_v + \bar{I}_v \qquad (2)$$

where N_T is the total number of human population,

ν is the birth rate of the human population,

b is the biting rate of the vector population,

α_h is the transmission probability of dengue virus from vector population to human population,

α_v is the transmission probability of dengue virus from human population to vector population,

γ_h is the death rate of the human population,

r is the recover rate of the human population,

L is the constant recruitment rate of the vector population,

γ_v is the death rate of the vector population.

Because the total populations are constant, so the rates of change for the total human and vector populations are equal to zero. Thus $\nu = \gamma_h$ for the human population and $N_v = \frac{L}{\gamma_v}$ for the vector population. After normalizing (1), then the equations become

$$\frac{dS}{dt} = \gamma_h(1-S) - \xi_h S I_v,$$

$$\frac{dI}{dt} = \xi_h S I_v - (\gamma_h + r)I \qquad (3)$$

and $$\frac{dI_v}{dt} = \xi_v(1-I_v)I - \gamma_v I_v,$$

where $\xi_v = b\alpha_v$ and $\xi_h = b\alpha_h a$ with $a = \frac{(L/\gamma_v)}{N_T}$ (4)

with the conditions

$$S + I + R = 1 \quad \text{and} \quad S_v + I_v = 1 \qquad (5)$$

Because dengue patients may be symptomatic or asymptomatic, so the infectious human is separated into symptomatic and asymptomatic classes. Both asymptomatic and symptomatic infectious human can transmit dengue virus. Let $\bar{I}_{hs}(t)$ and $\bar{I}_{ha}(t)$ are the number of symptomatic and asymptomatic infectious human at time t, respectively. Then the modified mathematical model becomes:

$$\frac{d}{dt}\bar{S}_h = \nu N_T - \frac{b(\alpha_{hs}+\alpha_{ha})}{N_T}\bar{S}_h\,\bar{I}_v - \gamma_h \bar{S}_h,$$

$$\frac{d}{dt}\bar{I}_{hs} = \frac{b\alpha_{hs}}{N_T}\bar{S}_h\,\bar{I}_v - (\gamma_h + r)\bar{I}_{hs},$$

$$\frac{d}{dt}\bar{I}_{ha} = \frac{b\alpha_{ha}}{N_T}\bar{S}_h\,\bar{I}_v - (\gamma_h + r)\bar{I}_{ha}, \qquad (6)$$

$$\frac{d}{dt}\bar{R}_h = r(\bar{I}_{hs} + \bar{I}_{ha}) - \gamma_h \bar{R}_h,$$

$$\frac{d}{dt}\bar{S}_v = L - \frac{b\alpha_v}{N_T}\bar{S}_v(\bar{I}_{hs} + \bar{I}_{ha}) - \gamma_v \bar{S}_v,$$

$$\frac{d}{dt}\bar{I}_v = \frac{b\alpha_v}{N_T}\bar{S}_v(\bar{I}_{hs} + \bar{I}_{ha}) - \gamma_v \bar{I}_v$$

with the conditions

$$N_T = \bar{S}_h + \bar{I}_{hs} + \bar{I}_{ha} + \bar{R}_h \quad \text{and} \quad N_v = \bar{S}_v + \bar{I}_v \qquad (7)$$

We normalize (6), then the system becomes

$$\frac{dS}{dt} = \gamma_h(1-S) - (\xi_{hs} + \xi_{ha})S I_v,$$

$$\frac{dI_s}{dt} = \xi_{hs} S I_v - (\gamma_h + r)I_s, \qquad (8)$$

$$\frac{dI_a}{dt} = \xi_{ha} S I_v - (\gamma_h + r)I_a,$$

and $$\frac{dI_v}{dt} = \xi_v(1-I_v)I - \gamma_v I_v$$

where $\xi_v = b\alpha_v$ (9)

and $\xi_{hs} = b\alpha_{hs}a$, $\xi_{ha} = b\alpha_{ha}a$ with $a = \frac{(L/\gamma_v)}{N_T}$ (10)

with the conditions

$$S + I_s + I_a + R = 1 \text{ and } S_v + I_v = 1 \qquad (11)$$

3. ANALYSIS OF THE MATHEMATICAL MODELS

3.1 Analytical results

For the system model (3), the equilibrium solutions can be found by setting the right hand side equals to zero then we have

i) $H^0 = (1,0,0)$ is the disease free equilibrium state and

ii) $H^1 = (S', I', I_v')$ is the endemic disease equilibrium state

where
$$S' = \frac{P+\beta}{\beta+PB_0}, \tag{12}$$

$$I' = \frac{B_0-1}{\beta+PB_0}, \tag{13}$$

and
$$I_v' = \frac{\beta(B_0-1)}{B_0(\beta+P)} \tag{14}$$

where
$$\beta = \frac{b\alpha_v}{\gamma_v},\ P = \frac{\gamma_h+r}{\gamma_h}. \tag{15}$$

We can determine the local stability of the endemic equilibrium point by calculating the Jacobian matrix of the right hand side of (3). If all eigenvalues have negative real parts then the equilibrium solution is local stable. Diagonalizing the Jacobian for the *endemic equilibrium point*, the characteristic equation is given by

$$\sigma^3 + c_0\sigma^2 + c_1\sigma + c_2 = 0 \tag{16}$$

where
$$c_0 = \gamma_h\left(\frac{\beta+PB_0}{P+\beta}\right) + \gamma_h P + \gamma_v B_0\left(\frac{P+\beta}{\beta+PB_0}\right),$$

$$c_1 = \gamma_h^2 P\left(\frac{\beta+PB_0}{P+\beta}\right) + \gamma_v\gamma_h B_0 + (B_0-1)\left(\frac{\gamma_v\gamma_h\beta}{\beta+PB_0}\right)P, \tag{17}$$

$$c_2 = \gamma_v\gamma_h^2 P(B_0-1).$$

We use Routh-Hurwitz criteria [5] for determining the local stable of the endemic equilibrium point. If the coefficients c_0, c_1 and c_2 satisfy the following inequalities:

$$c_0 > 0, c_1 > 0 \text{ and } c_0c_1 > c_2 \tag{18}$$

then the equilibrium point is local stable.

It can be seen that

i) $c_0 = \gamma_h\left(\frac{\beta+PB_0}{P+\beta}\right) + \gamma_h P + \gamma_v B_0\left(\frac{P+\beta}{\beta+PB_0}\right)$ is always positive

ii) $c_1 = \gamma_h^2 P\left(\frac{\beta+PB_0}{P+\beta}\right) + \gamma_v\gamma_h B_0 + (B_0-1)\left(\frac{\gamma_v\gamma_h\beta}{\beta+PB_0}\right)P$ is positive for $B_0 > 1$

iii) c_0c_1

$$= \left(\gamma_h\left(\frac{\beta+PB_0}{P+\beta}\right) + \gamma_h P + \gamma_v B_0\left(\frac{P+\beta}{\beta+PB_0}\right)\right)\left(\gamma_h^2 P\left(\frac{\beta+PB_0}{P+\beta}\right) + \gamma_v\gamma_h B_0 + (B_0-1)\left(\frac{\gamma_v\gamma_h\beta}{\beta+PB_0}\right)P\right)$$

$$= \left(\gamma_h\left(\frac{\beta+PB_0}{P+\beta}\right) + \gamma_h P + \gamma_v B_0\left(\frac{P+\beta}{\beta+PB_0}\right)\right)\left(\gamma_h^2 P\left(\frac{\beta+PB_0}{P+\beta}\right) + (B_0-1)\left(\frac{\gamma_v\gamma_h\beta}{\beta+PB_0}\right)P\right)$$

$$+ \left(\gamma_h\left(\frac{\beta+PB_0}{P+\beta}\right) + \gamma_v B_0\left(\frac{P+\beta}{\beta+PB_0}\right)\right)(\gamma_v\gamma_h B_0) + \gamma_v\gamma_h^2 PB_0$$

$$> \gamma_v\gamma_h^2 PB_0 \quad \text{for} \quad B_0 > 1$$

$$> \gamma_v\gamma_h^2 P(B_0-1)$$

$\therefore\ c_0c_1 > c_2$ for $B_0 > 1$.

Therefore the endemic equilibrium state is local stable for $B_0 > 1$ where $B_0 = \dfrac{b^2\alpha_h\alpha_v a}{\gamma_v(\gamma_h + r)}$

For the system model (8), the two equilibrium states are

i) $T^0 = (1,0,0,0)$ is the disease free state

ii) $T^1 = (S', I_s', I_a', I_v')$ is the endemic disease equilibrium state

where
$$S' = \frac{\beta + P}{\beta + PG}, \tag{19}$$
$$I_s' = \frac{G_s}{G}\frac{(G-1)}{(\beta+PG)}, \tag{20}$$
$$I_a' = \frac{G_a}{G}\frac{(G-1)}{(\beta+PG)}, \tag{21}$$
$$I_v' = \frac{\beta}{G}\frac{(G-1)}{(\beta+P)} \tag{22}$$

where
$$\beta = \frac{b\alpha_v}{\gamma_v}, \qquad P = \frac{\gamma_h + r}{\gamma_h},$$
$$G_s = \frac{b^2\alpha_{hs}\alpha_v a}{\gamma_v(\gamma_h + r)},\ G_a = \frac{b^2\alpha_{ha}\alpha_v a}{\gamma_v(\gamma_h + r)} \text{ and } G = \frac{b^2(\alpha_{hs} + \alpha_{ha})\alpha_v a}{\gamma_v(\gamma_h + r)} \tag{23}$$

We determine the local stable of the endemic equilibrium state by considering the signs of all eigenvalues. The eigenvalues are found by solving the characteristic equation.
$$(\sigma + P\gamma_h)(\sigma^3 + d_0\sigma^2 + d_1\sigma + d_2) = 0 \tag{24}$$

where
$$d_0 = \frac{(\beta + P(P+G+\beta))\gamma_h}{P+\beta} + \frac{G(P+\beta)\gamma_v}{PG+\beta}$$
$$d_1 = \frac{P(PG+\beta)\gamma_h^2}{P+\beta} + \frac{(G\beta + P(G^2 + (G-1)\beta))\gamma_h\gamma_v}{PG+\beta} \tag{25}$$
$$d_2 = P(G-1)\gamma_h^2\gamma_v$$

We will see that one eigenvalue has negative real part. The other eigenvalues have negative real part if it satisfies the Routh-Hurwitz criteria, that is
$$d_0 > 0, d_1 > 0 \text{ and } d_0d_1 > d_2 \tag{26}$$

i) $d_0 = \dfrac{(\beta + P(P+G+\beta))\gamma_h}{P+\beta} + \dfrac{G(P+\beta)\gamma_v}{PG+\beta}$ is always positive.

ii) $d_1 = \dfrac{P(PG+\beta)\gamma_h^2}{P+\beta} + \dfrac{(G\beta + P(G^2 + (G-1)\beta))\gamma_h\gamma_v}{PG+\beta}$ is positive for $G > 1$

iii d_0d_1
$$= \left(\frac{(\beta + P(P+G+\beta))\gamma_h}{P+\beta} + \frac{G(P+\beta)\gamma_v}{PG+\beta}\right)\left(\frac{P(PG+\beta)\gamma_h^2}{P+\beta} + \frac{(G\beta + P(G^2 + (G-1)\beta))\gamma_h\gamma_v}{PG+\beta}\right)$$
$$= \left(\frac{(\beta + P(P+G+\beta))\gamma_h}{P+\beta}\right)\left(\frac{P(PG+\beta)\gamma_h^2}{P+\beta} + \frac{(G\beta + P(G^2 + (G-1)\beta))\gamma_h\gamma_v}{PG+\beta}\right) +$$
$$\left(\frac{G(P+\beta)\gamma_v}{PG+\beta}\right)\left(\frac{(G\beta + P(G^2 + (G-1)\beta))\gamma_h\gamma_v}{PG+\beta}\right) + PG\gamma_h^2\gamma_v$$
$$> PG\gamma_h^2\gamma_v \quad \text{for } G > 1$$
$$> P(G-1)\gamma_h^2\gamma_v$$

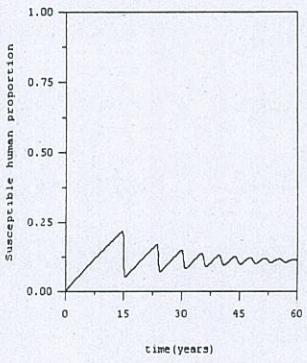
$\therefore d_0 d_1 > d_2$ for $G > 1$

It can be demonstrated that the coefficients d_0, d_1 and d_2 satisfy (26) for $G > 1$.

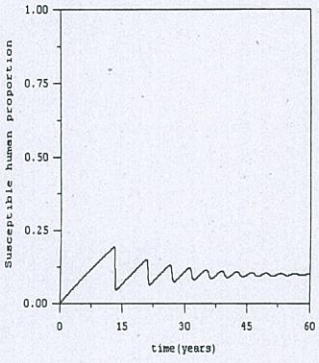
So the endemic equilibrium state is local stable if $G > 1$.

3.2 Numerical results

The numerical solutions are shown for comparing the transmission of dengue disease for the two situations. Parameters are determined corresponding to the real life observations. The values of the parameters used in the first model are $\gamma_h = 0.0000456$ per day corresponding to a life expectancy of 60 years for human. $\gamma_v = 0.071$ per day corresponding to the mean life of the vector (14 days). The biting rate of the vector is 1/3 per day. The transmission probability of dengue virus (α_h, α_v) are chosen: $\alpha_h = 1.0$, $\alpha_v = 0.75$. The recovery rate is 1/3 per day. Setting a equals to 3. The values of the parameters in the second model are $\alpha_{hs} = 0.2$, $\alpha_{ha} = 0.8$ and the other parameters are same as in the first model.



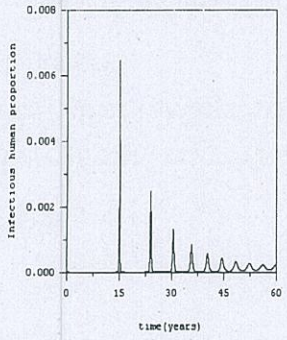
1a)



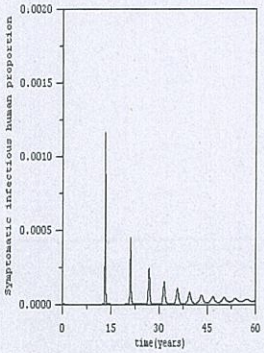
1b)

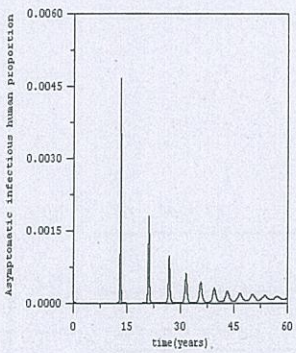
Figure 1. 1a) Numerical solutions of (3) yield the time series solutions of the susceptible human population. The values of the parameters in the model are $\gamma_h = 0.0000456\ day^{-1}$, $\gamma_v = 0.071\ day^{-1}$, $b = 1/3\ day^{-1}$, $\alpha_h = 1.0$, $\alpha_v = 0.75$, $a = 3$, $r = 1/3\ day^{-1}$, $B_0 = 10.56$.

1b) Numerical solutions of (8) yield the time series solutions of the susceptible human population. The values of the parameters in the model are $\gamma_h = 0.0000456\ day^{-1}$, $\gamma_v = 0.071\ day^{-1}$, $b = 1/3\ day^{-1}$, $\alpha_{hs} = 0.2$, $\alpha_{ha} = 0.8$, $\alpha_v = 0.75$, $a = 3$, $r = 1/3\ day^{-1}$, $G = 10.56$.



2a)

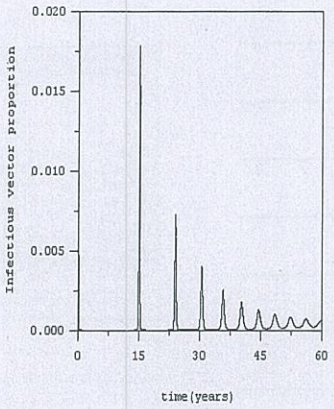




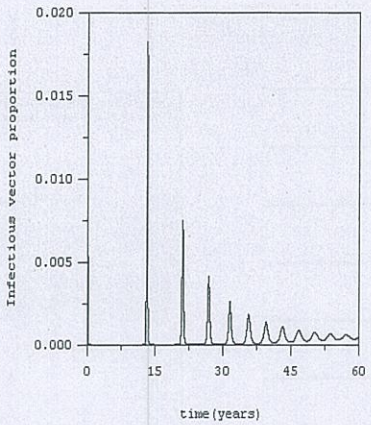
2b)

Figure 2. 2a) Numerical solutions of (3) yield the time series solutions of the Infectious human population. The values of the parameters in the model are γ_h =0.0000456 day^{-1}, γ_v = 0.071 day^{-1}, b = 1/3 day^{-1}, α_h = 1.0, α_v = 0.75, a = 3, r = 1/3 day^{-1}, B_0 =10.56.

2b) Numerical solutions of (8) yield the time series solutions of the Symptomatic and asymptomatic infectious human population. The values of the parameters in the model are γ_h = 0.0000456 day^{-1}, γ_v = 0.071 day^{-1}, b = 1/3 day^{-1}, α_{hs} = 0.2, α_{ha} = 0.8, α_v = 0.75, a = 3, r = 1/3 day^{-1}, G =10.56.



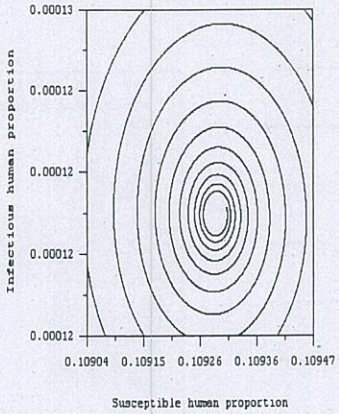
3a)



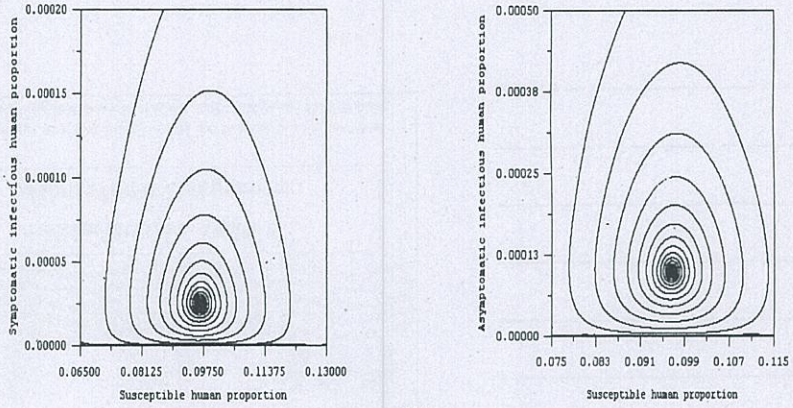
3b)

Figure 3.3a)Numerical solutions of (3) yield the time series solutions of the infectious vector population. The values of the parameters in the model are γ_h = 0.0000456 day^{-1}, γ_v = 0.071 day^{-1}, b = 1/3 day^{-1}, α_h = 1.0, α_v = 0.75, a = 3, r = 1/3 day^{-1}, B_0 =10.56.

3b) Numerical solutions of (8) yield the time series solutions of the infectious vector population. The values of the parameters in the model are $\gamma_h = 0.0000456$ day^{-1}, $\gamma_v = 0.071$ day^{-1}, b = 1/3 day^{-1}, $\alpha_{hs} = 0.2$, $\alpha_{ha} = 0.8$, $\alpha_v = 0.75$, a = 3, r = 1/3 day^{-1}, G = 10.56.



4a)



4b)

Figure4. 4a) Numerical solutions of (3) yield the solution trajectory, projected onto susceptible-infectious plane. The values of the parameters in the model are $\gamma_h = 0.0000456$ day^{-1}, $\gamma_v = 0.071$ day^{-1}, b = 1/3 day^{-1}, $\alpha_h = 1.0$, $\alpha_v = 0.75$, a = 3, r = 1/3 day^{-1}, $B_0 = 10.56$.

4b) Numerical solutions of (8) yield the solution trajectory, projected onto susceptible-symptomatic infectious and susceptible-asymptomatic infectious planes of the human population. The values of the parameters in the model are $\gamma_h = 0.0000456$ day^{-1}, $\gamma_v = 0.071$ day^{-1}, b = 1/3 day^{-1}, $\alpha_{hs} = 0.2$, $\alpha_{ha} = 0.8$, $\alpha_v = 0.75$, a = 3, r = 1/3 day^{-1}, G = 10.56.

4. CONCLUSION

The number of secondary infections results from primary infections, this number can be found from the square root of the basic reproduction rate [6]. If this number greater than one then the disease can be capable of invading and establishing itself. Every successive generation will diminish in size until its number approaches zero. For the modified mathematical model, we observe that symptomatic and asymptomatic infectious human will be bitten by $\frac{ba}{\gamma_h + r}$ mosquitoes during the time symptomatic and asymptomatic is infectious. Of these mosquitoes, a proportion of them will become infected, this number is given by $\alpha_v \frac{ba}{\gamma_h + r}$. One of these infected mosquitoes will in turn bite $\frac{b}{\gamma_v}$ symptomatic and asymptomatic infectious human during its life time. We assume that the transmission probabilities of dengue virus from vector to human then become symptomatic and asymptomatic infectious human are difference. These two probabilities are denoted by α_{hs} and α_{ha}, respectively. Multiplying $\frac{b}{\gamma_v}$ by α_{hs} and α_{ha}, we obtain the number of symptomatic and asymptomatic infected by an infectious vector. Multiplying the number of symptomatic and asymptomatic infected by the number of mosquitoes infected during the life time of the infectious symptomatic and asymptomatic human, adding these two numbers together, then we get the basic reproduction rate

$$G = \frac{b^2(\alpha_{hs} + \alpha_{ha})\alpha_v a}{\gamma_v(\gamma_h + r)} \qquad (27)$$

In similar manner, the basic reproduction rate of SIR model is given by

$$B_0 = \frac{b^2 \alpha_h \alpha_v a}{\gamma_v(\gamma_h + r)}. \qquad (28)$$

If the infectious humans are not divided up into symptomatic and asymptomatic classes, there is no need to separate the transmission probability of dengue virus into two parameters. It can be seen that if we change $\alpha_{hs} + \alpha_{ha}$ to α_h then the expression (27) changes to expression (28). From the numerical results for the two models, we will see that the period of oscillations in the number of individuals in each class is shorter in the absence of symptomatic and asymptomatic classes. The spiraling is more severe in the absence of the appearance of the symptom of the infectious class. The appearance of the symptom for the patients seems to calm down the fluctuations.

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