Analysis of a dengue disease transmission model with clinical diagnosis in Thailand

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***Abstract*—**An S-I-R epidemiological model with clinical diagnosis of dengue transmission, Dengue Fever (DF), Dengue Haemorrhagic Fever (DHF), Dengue Shock Syndrome (DSS) dynamics in a population in Thailand is discussed. Our model consists of seven non-linear differential equations. The standard dynamical analysis is used for analyzing the behavior for the transmission of dengue disease. Local existence results are given for the resulting ordinary differential system. The numerical results are discussed in terms of threshold parameters and the numerical simulations are shown to confirm our results.

***Keywords*—**Clinical diagnosis, numerical simulation , ordinary differential system, S-I-R .

I. Introduction

MATHEMATICAL model have been widely used in various areas of infectious disease epidemiology. Mathematical modeling of dengue disease transmission in human and vector populations has been done since the beginning of last century. Some of the recent models could be seen in [1-6]. Several studies on infection model within human have been done for various cases [7-8]. Mathematical models are used in comparing, planning, implementing, evaluating, and optimizing various detection, prevention, therapy, and control programs. Epidemiology modeling can contribute the design and analysis of epidemiological surveys, suggest crucial data that should be collected, identify trends, make general forecasts, and estimate the uncertainty in forecasts [9-10].

The epidemiological systems often exists a peculiar equilibrium the disease free equilibrium, which corresponds to a steady state of the population without disease. The another one equilibrium is the endemic equilibrium state. It is the steady state solutions where the disease persists in the population. In the context of within host dengue viral infection, the basic reproductive number is defined as the average number of secondary infected monocytes generated by a single infected monocyte placed in an uninfected monocyte population [11].

In this paper, we are developing mathematical models to better understand the transmission and spread of dengue disease. Dengue is an acute fever caused by a *Flavivirus*. The disease can occur in three forms: Dengue Fever (DF), Dengue Haemorrhagic Fever (DHF) and Dengue Shock Syndrome (DSS).

DF is an acute viral disease manifesting with myalgias, headache, retro-orbital pain, vomiting, maculopapular rash, leucopenia and thrombocytopenia. DHF is characterized by four major clinical features: high fever, hemorrhagic phenomena, hepatomegaly and signs of impending circulatory failure. The major pathophysiological abnormality differentiating DF from DHF is the plasma leakage syndrome. The severity of disease in DHF depends on the quantum of plasma leakage. The DHF patients are presented with shock due to excessive plasma loss are labeled as dengue shock syndrome (DSS). DHF/DSS are potentially fatal conditions.

As DF, DHF, DSS are endemic in Thailand, cases are reported every years. A total of 220,885 cases of DF, 650,810 cases of DHF and 17,267 cases of DSS have been reported during twelve year review period. Between 1997 and 2008, the percentage of mortality DF, DHF and DSS cases reported 1.04%, 40.83% and 58.13% , respectively. Fig. 1, shows the percentage of cases by clinical diagnosis in Thailand between 1997 and 2008. Fig. 2, shows the percentage of deaths by clinical diagnosis in Thailand during 1997 to 2008.

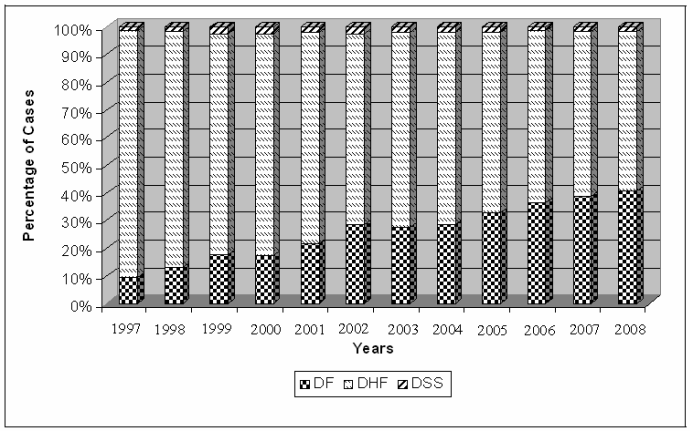


Fig. 1 The percentage of cases by clinical diagnosis in Thailand between 1997 and 2008 [12].

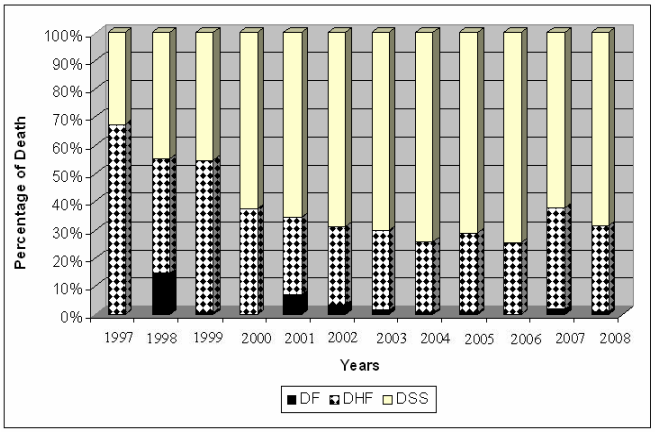


Fig. 2 The percentage of deaths by clinical diagnosis in Thailand [12].

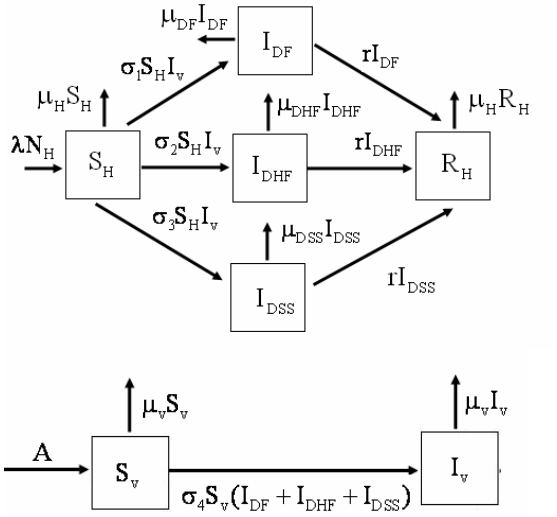


Fig. 3 Compartmental transmission model of DF, DHF, DSS system following a Susceptible-Infectious-Recovered structure in human population and Susceptible-Infectious structure in vector population.

It can be seen in the Fig. 1 that the percentage of deaths of DSS cases is higher than DHF and DF death cases.

A basic S-I-R (Susceptible-Infected-Recovered) model is used for representing DF, DHF, DSS transmission system in this study. This paper is organized as follows. In the first section, we present the introduction that guided the dengue disease and model's structure. In section 2, we present the model's equations and definition of the variables and parameters. In section 3, we deduce the basic reproductive number, which can be used for predicting all the possible behaviors of the system. Finally, the numerical solutions of this model are presented.

II. Mathematical Model

A. Model Formulation

The model describes the dynamic of dengue in the two components of transmission, namely human hosts and vector. The total human population is denoted by N_H, it is partitioned into five classes, the susceptible, infectious with DF clinical diagnosis, infectious with DHF clinical diagnosis, infectious with DSS clinical diagnosis and recovered are denoted by S_H, I_{DF}, I_{DHF}, I_{DSS} and R_H, respectively.

The total vector population is N_v and the vector population is divided into two classes, the susceptible and infectious vector are denoted by S_v and I_v,respectively.

The total human population size N_H can be determined by $N_H = S_H + I_{DF} + I_{DHF} + I_{DSS} + R_H$. The total vector population size N_v can be determined by $N_v = S_v + I_v$.

This model is shown in Fig. 1.

The parameters in our model are defined in Table 1.

Table 1. Parameter involved in the transmission of dengue, incorporated into the model shown in Fig. 1.

Symbol	Meaning
N_H	Total human population size
N_v	Total vector population size
A	The constant recruitment rate of mosquitoes
λ	Birth rate of human population
μ_H	The natural death rate of human population
μ_{DF}	Death rate of human population (with DF)
μ_{DHF}	Death rate of human population (with DHF)
μ_{DSS}	Death rate of human population (with DSS)
β_{VDF}	Transmission probability from infectious vector to human and human becomes to infectious with DF
β_{VDHF}	Transmission probability from infectious vector to human and human becomes to infectious with DHF
β_{VDSS}	Transmission probability from infectious vector to human and human becomes to infectious with DSS
β_{HV}	Transmission probability from infecious human to vector and vector becomes to infectious
σ_1	The contact rate from infectious vector to susceptible human and human becomes to infectious human with DF
σ_2	The contact rate from infectious vector to susceptible human and human becomes to infectious human with DHF
σ_3	The contact rate from infectious vector to susceptible human and human becomes to infectious human with DSS
σ_4	The contact rate from infectious human to susceptible vector and vector becomes to infectious vector
μ_v	Death rate of vector
b	Average rate of biting per vector per day
r	Human recovery rate

From the averaging of the real data in Thailand between 1997 to 2008, we have $\beta_{VDHF} > \beta_{VDF} > \beta_{VDSS}$ and

$\mu_{DSS} > \mu_{DHF} > \mu_{DF}$

B. Model Equations

When In our model, the dynamic of epidemic model is established:

$$\frac{dS_H}{dt} = \lambda N_H - (\mu_H + (\sigma_1 + \sigma_2 + \sigma_3)I_v)S_H,$$

$$\frac{dI_{DF}}{dt} = \sigma_1 S_H I_v - (\mu_{DF} + r)I_{DF},$$

$$\frac{dI_{DHF}}{dt} = \sigma_2 S_H I_v - (\mu_{DHF} + r)I_{DHF},$$

$$\frac{dI_{DSS}}{dt} = \sigma_3 S_H I_v - (\mu_{DSS} + r)I_{DSS}, \quad (1)$$

$$\frac{dR_H}{dt} = r(I_{DF} + I_{DHF} + I_{DSS}) - \mu_H R_H,$$

$$\frac{dS_v}{dt} = A - (\mu_v + \sigma_4(I_{DF} + I_{DHF} + I_{DSS}))S_v,$$

$$\frac{dI_v}{dt} = \sigma_4(I_{DF} + I_{DHF} + I_{DSS})S_v - \mu_v I_v.$$

The first five equations represent the susceptible, infectious with DF, infectious with DHF, infectious with DSS and recovered human population densities, respectively.

The sixth and seventh equations represent the susceptible and infectious vector population densities.

Before we analyze the system (1), we reduce the number of parameters by introducing

$$\hat{S}_H = (S_H/N_H), \hat{I}_{DF} = (I_{DF}/N_H), \hat{I}_{DHF} = (I_{DHF}/N_H),$$

$$\hat{I}_{DSS} = (I_{DSS}/N_H), \hat{R}_H = (R_H/N_H), \hat{S}_v = (S_v/N_v),$$

$$\hat{I}_v = (I_v/N_v).$$

We get the following model

$$\frac{d\hat{S}_H}{dt} = \mu_H - (\mu_H + (\sigma_1 + \sigma_2 + \sigma_3)\hat{I}_v N_v)\hat{S}_H,$$

$$\frac{d\hat{I}_{DF}}{dt} = \sigma_1 N_v \hat{S}_H \hat{I}_v - \varepsilon_1 \hat{I}_{DF},$$

$$\frac{d\hat{I}_{DHF}}{dt} = \sigma_2 N_v \hat{S}_H \hat{I}_v - \varepsilon_2 \hat{I}_{DHF}, \quad (2)$$

$$\frac{d\hat{I}_{DSS}}{dt} = \sigma_3 N_v \hat{S}_H \hat{I}_v - \varepsilon_3 \hat{I}_{DSS},$$

$$\frac{d\hat{I}_v}{dt} = \sigma_4 N_H(\hat{I}_{DF} + \hat{I}_{DHF} + \hat{I}_{DSS})(1 - \hat{I}_v) - \mu_v \hat{I}_v$$

where $\varepsilon_1 = \mu_{DF} + r$, $\varepsilon_2 = \mu_{DHF} + r$ and $\varepsilon_3 = \mu_{DSS} + r$.

For the biological interest, the region of system (2) is restricted to

$$\Omega = \{(\hat{S}_H, \hat{I}_{DF}, \hat{I}_{DHF}, \hat{I}_{DSS}, \hat{I}_v): 0 \le \hat{S}_H, \hat{I}_{DF}, \hat{I}_{DHF}, \hat{I}_{DSS}, \hat{I}_v \le 1\},$$

and all of the parameters used in system (2) are positive.

III. Mathematical Analysis

A. Analysis of Models

The local stability of an equilibrium state is determined from the Jacobian matrix of the right hand side of (2) evaluated at the equilibrium point. We obtain the Jacobian matrix

$$\begin{bmatrix} -\mu_H - \mu_H\phi_1 I_v^* & 0 & 0 & 0 & -\mu_H\phi_1 S_H^* \\ \varepsilon_1\eta_1 I_v^* & -\varepsilon_1 & 0 & 0 & \varepsilon_1\eta_1 S_H^* \\ \varepsilon_2\eta_2 I_v^* & 0 & -\varepsilon_2 & 0 & \varepsilon_2\eta_2 S_H^* \\ \varepsilon_3\eta_3 I_v^* & 0 & 0 & -\varepsilon_3 & \varepsilon_3\eta_3 S_H^* \\ 0 & \sigma_4 N_H(1-I_v^*) & \sigma_4 N_H(1-I_v^*) & \sigma_4 N_H(1-I_v^*) & -\sigma_4 N_H(I_{DF}^* + I_{DHF}^* + I_{DSS}^*) - \mu_v \end{bmatrix}$$

The equilibrium states $(S_H^*, I_{DF}^*, I_{DHF}^*, I_{DSS}^*, I_v^*)$ are found by setting the right hand side of (2) to zero, then we obtain:

$$S_H^* = \frac{1}{1+\phi_1 I_v^*}, \quad I_{DF}^* = \frac{\eta_1 I_v^*}{1+\phi_1 I_v^*}, \quad I_{DHF}^* = \frac{\eta_2 I_v^*}{1+\phi_1 I_v^*},$$

$I_{DSS}^* = \frac{\eta_3 I_v^*}{1+\phi_1 I_v^*}$, and $I_v^* = 0$ for the disease free state or

$I_v^* = \frac{\sigma_4 N_H(\eta_1+\eta_2+\eta_3) - \mu_v}{\sigma_4 N_H(\eta_1+\eta_2+\eta_3) + \mu_v\phi_1}$ for the endemic disease state where

$$\phi_1 = \frac{(\sigma_1+\sigma_2+\sigma_3)N_v}{\mu_H}, \quad \eta_1 = \frac{\sigma_1 N_v}{\varepsilon_1}, \quad \eta_2 = \frac{\sigma_2 N_v}{\varepsilon_2}, \quad \eta_3 = \frac{\sigma_3 N_v}{\varepsilon_3}.$$

For this case there are two equilibrium states, those are, the disease free equilibrium $E_1 = (1,0,0,0,0)$ when $I_v^* = 0$ which always exists and the endemic equilibrium $E_2 = (S_H^*, I_{DF}^*, I_{DHF}^*, I_{DSS}^*, I_V^*)$ when $I_v^* = \dfrac{\sigma_4 N_H(\eta_1+\eta_2+\eta_3)-\mu_v}{\sigma_4 N_H(\eta_1+\eta_2+\eta_3)+\mu_v\phi_1}$.

B. Analysis of Stability

The local stability of an equilibrium state is determined from the above Jacobian matrix evaluated at equilibrium state around $I_v^* = 0$ and $I_v^* = \dfrac{\sigma_4 N_H(\eta_1+\eta_2+\eta_3)-\mu_v}{\sigma_4 N_H(\eta_1+\eta_2+\eta_3)+\mu_v\phi_1}$.

The local stability property of those equilibrium state is given in the following proposition.

Proposition 1 If $R_0 < 1$, the equilibrium E_1 is locally asymptotically stable. If $R_0 > 1$, the equilibrium E_1 is unstable and E_2 is locally asymptotically stable when

$$R_0 = \frac{(\eta_1+\eta_2+\eta_3)N_H\sigma_4}{\mu_v} \le 1.$$

Proof The local stability of E_1 is governed by the linearization of system (2) at E_1. The eigenvalue of the disease free state is $\lambda = -\mu_H$ and the other eigenvalues are the roots of

$$\lambda^4 + a_3\lambda^3 + a_2\lambda^2 + a_1\lambda + a_0 = 0 \qquad (3)$$

where

$$a_3 = \varepsilon_1 + \varepsilon_2 + \varepsilon_3 + \mu_v, \qquad (4)$$

$$a_2 = -N_H\sigma_4(\eta_1\varepsilon_1 + \eta_2\varepsilon_2 + \eta_3\varepsilon_3) + \varepsilon_2(\varepsilon_1+\varepsilon_3) + (\varepsilon_1+\varepsilon_2+\varepsilon_3)\mu_v, \qquad (5)$$

$$a_1 = -(-\varepsilon_1\varepsilon_2 + \eta_3 N_H\sigma_4(\varepsilon_1+\varepsilon_2))\varepsilon_3 - N_H\sigma_4(\eta_2\varepsilon_2(\varepsilon_1+\varepsilon_3) + \eta_1\varepsilon_1(\varepsilon_2+\varepsilon_3))(\varepsilon_2\varepsilon_2 + \varepsilon_1(\varepsilon_2+\varepsilon_3))\mu_v, \qquad (6)$$

$$a_0 = \varepsilon_1\varepsilon_2\varepsilon_3(-(\eta_1+\eta_2+\eta_3)N_H\sigma_4 + \mu_v). \qquad (7)$$

By the Hurwitz Criterion [13], all the roots of the polynomial order four have negative real part when

i) $a_3 > 0$, (8)

ii) $a_1 > 0$, (9)

iii) $a_0 \ge 0$, (10)

iv) $a_3a_2a_1 > a_1^2 + a_3^2a_0$. (11)

It can be seen a_3 is always positive. $a_0 \ge 0$ when

$$\frac{(\eta_1+\eta_2+\eta_3)N_H\sigma_4}{\mu_v} \le 1.$$

For the second and fourth conditions, we show the map by putting the regions in $a_1 - \beta_{VDSS}$ phase space and $(a_3a_2a_1 - a_1^2 - a_3^2a_0) - \beta_{VDSS}$ phase space to confirm two conditions in Fig. 4.

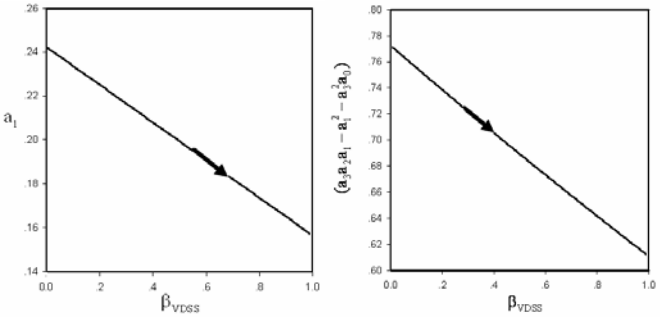


Fig. 4 The second and fourth conditions which satisfies the Routh-Hurwitz criteria. The value of parameters are defined in Table 2.

Moreover, for $R_0 > 1$, we have the characteristic equation

$$\lambda^5 + b_1\lambda^4 + b_2\lambda^3 + b_3\lambda^2 + b_4\lambda + b_5 = 0. \qquad (11)$$

By the Hurwitz Criterion [13], all the roots of the polynomial order five have negative real part when

i) $b_i > 0 \quad [i = 1,2,3,4,5]$, (12)

ii) $b_1b_2b_3 > b_3^2 + b_1^2b_4$, (13)

iii) $(b_1b_4 - b_5)(b_1b_2b_3 - b_3^2 - b_1^2b_4) > b_5(b_1b_2 - b_3)^2 + b_1b_5^2$. (14)

The roots of polynomial (11) have negative real parts when they are corresponding above three conditions. We now map the regions in $b_i - \beta_{VDSS}$ phase space, $(b_1b_2b_3 - b_3^2 - b_1^2b_4) - \beta_{VDSS}$ phase space and $((b_1b_4 - b_5)(b_1b_2b_3 - b_3^2 - b_1^2b_4) - b_5(b_1b_2 - b_3)^2 - b_1b_5^2) - \beta_{VDSS}$ phase space in which the three above conditions are met and $R_0 > 1$. These are shown in the following figures.

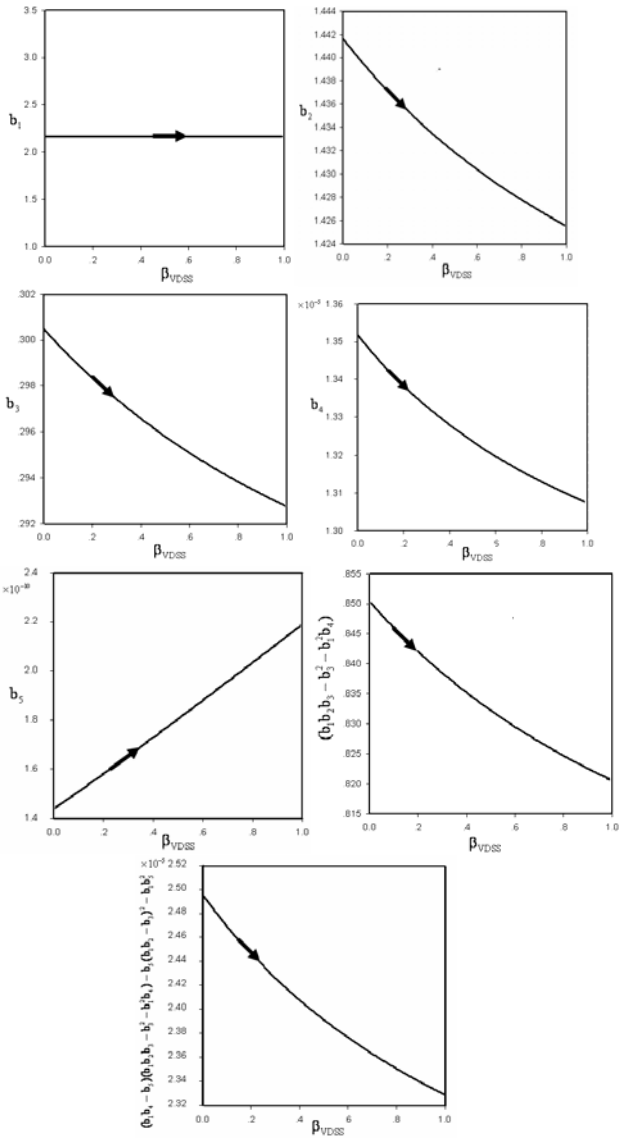


Fig. 5 The three above conditions which satisfies the Routh-Hurwitz criteria. The value of parameters are defined in Table 2.

From the above figure, Routh-Hurwitz Criterion are satisfied for $R_0 > 1$. Thus, the endemic equilibrium state is locally stable when $R_0 > 1$
with

$$R_0 = \frac{(\eta_1 + \eta_2 + \eta_3) N_H \sigma_4}{\mu_v} . \qquad (15)$$

Table 2. Parameter involved in the transmission of dengue, they are used in Fig. 4, 5, 6 and 7.

Symbol	For Fig. 4 and 5	For Fig. 6	For Fig. 7
N_H	62,226,009	62,226,009	62,226,009
N_v	10,000	10,000	10,000
λ	1/(365x70)	1/(365x70)	1/(365x70)
b	1/3	1/3	1/3
μ_H	1/(365x70)	1/(365x70)	1/(365x70)
μ_v	1/14	1/14	1/14
μ_{DF}	0.1	0.1	0.1
μ_{DHF}	0.2	0.2	0.2
μ_{DSS}	0.8	0.8	0.8
β_{VDF}	0.3	0.3	0.3
β_{VDHF}	0.5	0.5	0.5
β_{VDSS}	$0 \le \beta_{VDSS} \le 1$	0.1	0.1
β_{HV}	0.01	0.01	0.5
σ_1	$(\beta_{VDF} \times b)/N_H$	$(\beta_{VDF} \times b)/N_H$	$(\beta_{VDF} \times b)/N_H$
σ_2	$(\beta_{VDHF} \times b)/N_H$	$(\beta_{VDHF} \times b)/N_H$	$(\beta_{VDHF} \times b)/N_H$
σ_3	$(\beta_{VDSS} \times b)/N_H$	$(\beta_{VDSS} \times b)/N_H$	$(\beta_{VDSS} \times b)/N_H$
σ_4	$(\beta_{HV} \times b)/N_H$	$(\beta_{HV} \times b)/N_H$	$(\beta_{HV} \times b)/N_H$
r	1/3	1/3	1/3
R_0	-	0.0267251	1.33626
$\sqrt{R_0}$	-	0.163478	1.15597

C. Numerical Results

In this study, we consider the transmission of dengue disease when consider follow by the clinical diagnosis by using data in Thailand between 1997 and 2008. The value of the parameters used in this study are $\mu_H = 1/(365\times 70)$ per day, this corresponds to a life expectancy of 70 years in Thai people. The mean life of vector is 14 days so $\mu_v = 1/14$ per day. R_0 is defined in (15). $\sqrt{R_0}$ is the basic reproductive number.

The trajectories of the numerical solutions of system (2) are shown in the following figures.

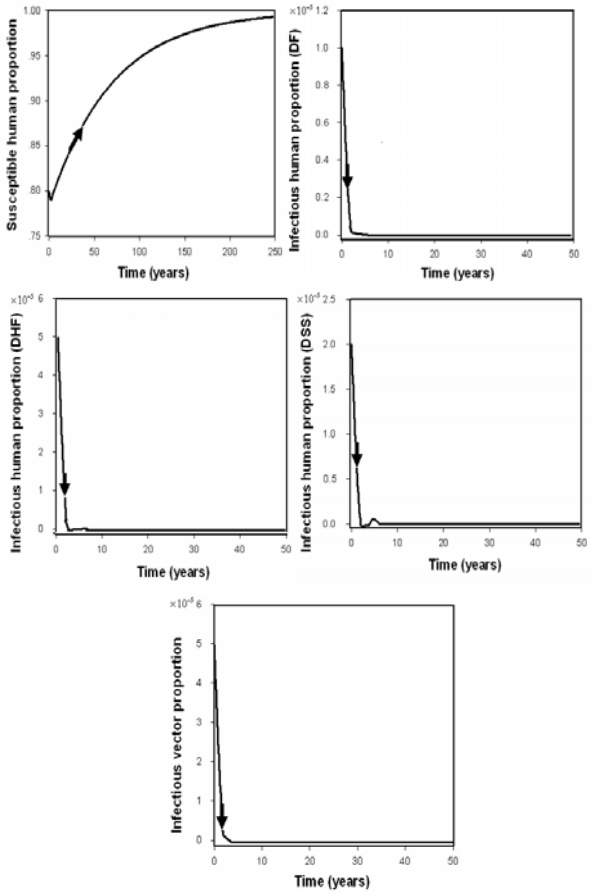
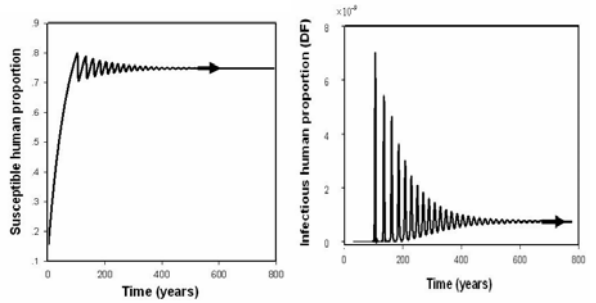


Fig. 6 Numerical solutions demonstrate time series when $R_0 < 1$. The value of parameters are defined in Table 2.



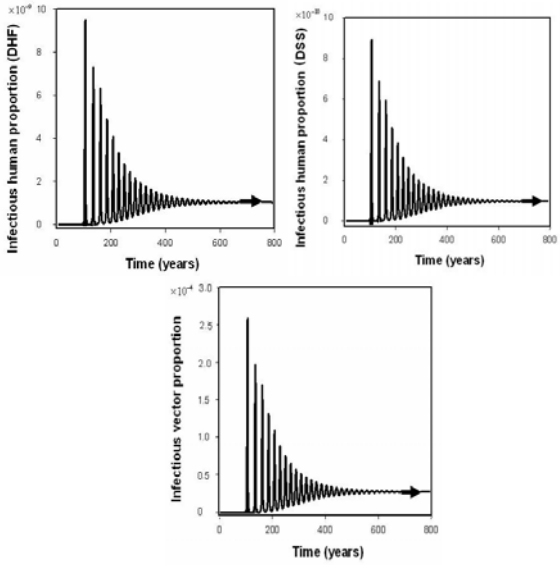
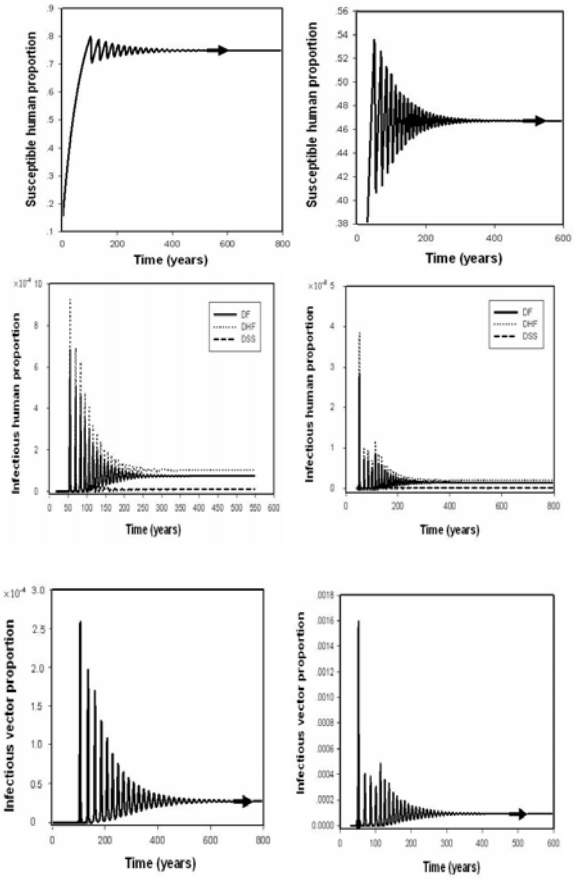


Fig. 7 Numerical solutions demonstrate time series when $R_0 > 1$. The values of parameters are defined in Table 2.



8a) 8b)

Fig. 8 Numerical solutions demonstrate time series when R_0 are different. The value of parameters are defined in Table 3.

Table 3. The value of parameters which we used for Fig. 8 and 9.

Symbol	For Fig.8a)	For Fig. 8b)	For Fig. 9
N_H	62,226,009	62,226,009	62,226,009
N_v	10,000	10,000	10,000
λ	1/(365x70)	1/(365x70)	1/(365x70)
b	1/3	1/3	1/3
μ_H	1/(365x70)	1/(365x70)	1/(365x70)
μ_v	1/14	1/14	1/14
μ_{DF}	0.1	0.1	0.1
μ_{DHF}	0.2	0.2	0.2
μ_{DSS}	0.8	0.8	0.8
β_{VDF}	0.3	0.3	0.3
β_{VDHF}	0.5	0.5	$0 \le \beta_{VDHF} \le 1$ for Fig. 9a), β_{VDHF} =0.5 for Fig. 9b)
β_{VDSS}	0.1	0.1	β_{VDSS} =0.1 for Fig. 9a), $0 \le \beta_{VDSS} \le 1$ for Fig. 9b).
β_{HV}	0.5	0.8	0.8
σ_1	(β_{VDF} x b)/ N_H	(β_{VDF} x b)/ N_H	(β_{VDF} x b)/ N_H
σ_2	(β_{VDHF} x b)/ N_H	(β_{VDHF} x b)/ N_H	(β_{VDHF} x b)/ N_H
σ_3	(β_{VDSS} x b)/ N_H	(β_{VDSS} x b)/ N_H	(β_{VDSS} x b)/ N_H
σ_4	(β_{HV} x b)/ N_H	(β_{HV} x b)/ N_H	(β_{HV} x b)/ N_H
r	1/3	1/3	1/3
R_0	1.33626	2.13801	-
$\sqrt{R_0}$	1.15597	1.46219	-

IV. DISCUSSION AND CONCLUSION

In this model, we have used, it is assumed that the human population is constants. The epidemiological data from the Division of Epidemiology, Ministry of Public Health, Thailand between 1997 and 2008 are used.

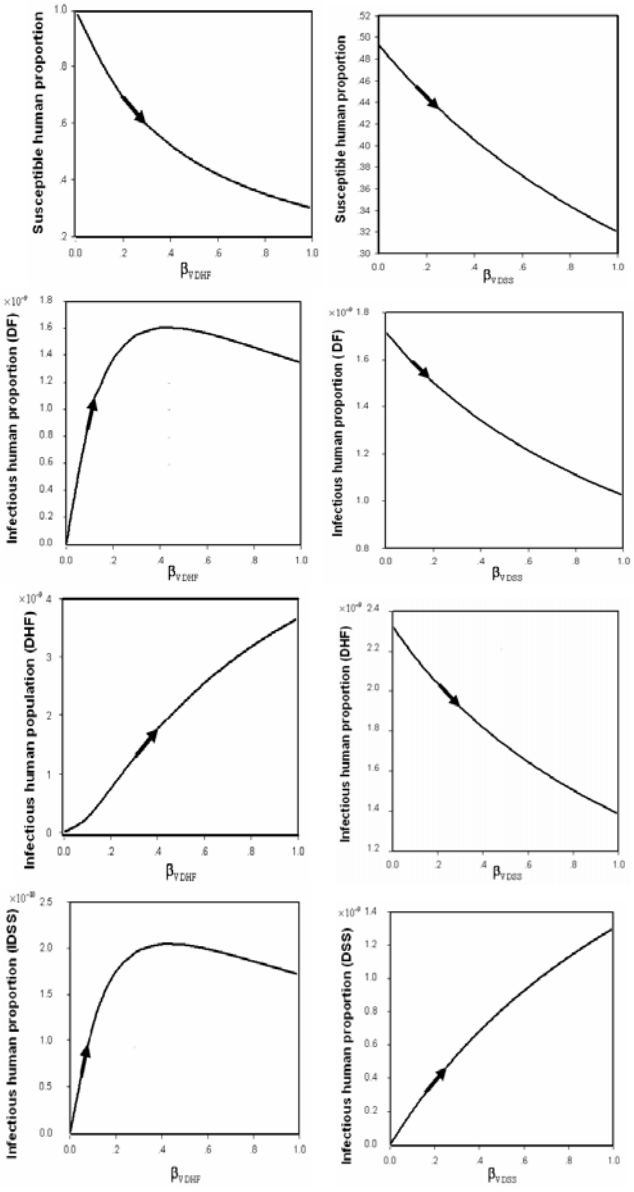
From our analysis, we obtain the following threshold number

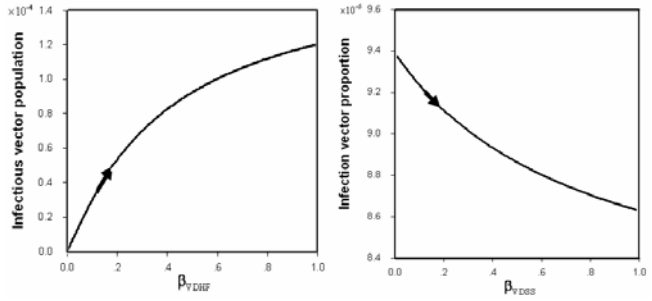
$$R_0 = \frac{(\eta_1 + \eta_2 + \eta_3)N_H\sigma_4}{\mu_v}$$

$$= \frac{b^2\beta_{HV}\beta_{VDF}}{(r+\mu_{DF})\mu_v} + \frac{b^2\beta_{HV}\beta_{VDHF}}{(r+\mu_{DHF})\mu_v} + \frac{b^2\beta_{HV}\beta_{VDSS}}{(r+\mu_{DSS})\mu_v}. \qquad (16)$$

The square root of (16) is the basic reproductive number. We can see from Fig. 6, $\hat{S}_H$, $\hat{I}_{DF}$, $\hat{I}_{DHF}$, $\hat{I}_{DSS}$ and $\hat{I}_v$ approach to the disease free equilibrium state (1,0,0,0,0) respectively for $R_0 < 1$. From Fig. 7, the fraction of populations spiral to the endemic disease state (0.74838021536, 0.00000000076, 0.00000000103, 0.00000000010, 0.00002729495). Moreover we compare the numerical solutions when R_0 is difference. We see the trajectories spiraling toward the different endemic disease states (0.74838021536, 0.00000000076, 0.00000000103, 0.00000000010, 0.00002729495) in Fig. 8a) and (0.46776807538, 0.00000000160, 0.00000000217, 0.00000000020, 0.00009236983) in Fig. 8b).

Fig. 9, shows all proportions of population when the transmission probability from infectious vector to human and human becomes to infectious with DHF (β_{VDHF}) and transmission probability from infectious vector to human and human becomes to infectious with DSS (β_{VDSS}) are difference.





9a) 9b)

Fig. 9 Numerical solutions demonstrate time series when β_{VDHF} and β_{VDSS} are different. The value of parameters are defined in Table 3.

When β_{VDHF} is higher, we can see the trajectories spiraling towards to the different endemic disease state, $\hat{S}_H$ decreases. While $\hat{I}_{DF}$, $\hat{I}_{DHF}$, $\hat{I}_{DSS}$ and $\hat{I}_v$ increases. When β_{VDSS} is higher, $\hat{S}_H$, $\hat{I}_{DF}$, $\hat{I}_{DHF}$ and $\hat{I}_v$ decrease while $\hat{I}_{DSS}$ increase.

In this study, it is assumed that the human population is constant. The effect of the non-constant human population is not taken into mathematical model. So on the further research, the non-constant human population should also be considered in this model.

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