MATHEMATICAL MODEL OF DENGUE FEVER IN THAILAND INFLUENCED BY RAINFALL, TRANSOVARIAL TRANSMISSION, AND VACCINATION

PRATCHAYA CHANPRASOPCHAI

A THESIS SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENT FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN APPLIED MATHEMATICS

DEPARTMENT OF MATHEMATICS
FACULTY OF SCIENCE
KING MONGKUT'S INSTITUTE OF TECHNOLOGY LADKRABANG

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Thesis Title	Mathematical model of dengue fever influenced by rainfall, transovarial transmission, and vaccination
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Abstract

The actual historical data of dengue fever in Thailand is collected. The reported and death cases due to dengue disease are presented by total number, region, month, age, and occupation. Mathematical modelling is an essential tool to analyze the dengue fever behavior which the dynamical transmission of dengue virus is described by SIR (Susceptible-Infected-Recovered) and SEIR (Susceptible-Exposed-Infected-Recovered) models. The SEIR model is determined by the role of rainfall in Thailand and the possibility of vertical transmission (VT) while SIR model is analyzed by the effects of vaccination on the transmission of the disease. The stability of the solution of the model is analyzed and investigated by using the Routh-Hurwitz criteria. The numerical solutions of differential equations of the model converges to the disease free equilibrium state when the basic reproduction number R_0 is less than 1 and converges to endemic equilibrium state when R_0 is greater than 1. The trajectories of the numerical solutions for all possibilities projected onto various 2D planes and 3D spaces are presented. The main contributions are determining the effect of rainfall for the dynamical transmission model of the dengue fever in Thailand, the effect of vertical transmission of dengue virus and the role of dengue vaccination in the model.

Keywords: Dengue fever, stability, disease free equilibrium, endemic equilibrium, SIR model, SEIR model, rainfall, transovarial transmission, vaccination

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Mr. Pratchaya Chanprasopchai

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Abbreviations/Symbols

WHO: World Health Organization
DF: Dengue Fever
DV: Dengue Virus
VT: Vertical Transmission
HT: Horizontal Transmission
DEN1: Dengue Virus Serotype 1
DEN2: Dengue Virus Serotype 2
DEN3: Dengue Virus Serotype 3
DEN4: Dengue Virus Serotype 4
SIR: Susceptible-Infected-Recovered
SEIR: Susceptible-Exposed-Infected-Recovered
DHF: Dengue Hemorrhagic Fever
DSS: Dengue Shock Syndrome
MIR: Minimum Infection Rate

Chapter 1
Introduction

1.1 Research Motivation

Dengue fever (DF) is a vector born infection which is normally found in tropical and subtropical regions around the world [1]. World Health Organization (WHO) reported the distribution of global dengue risk and it is shown as in Figure 1.1 [2].

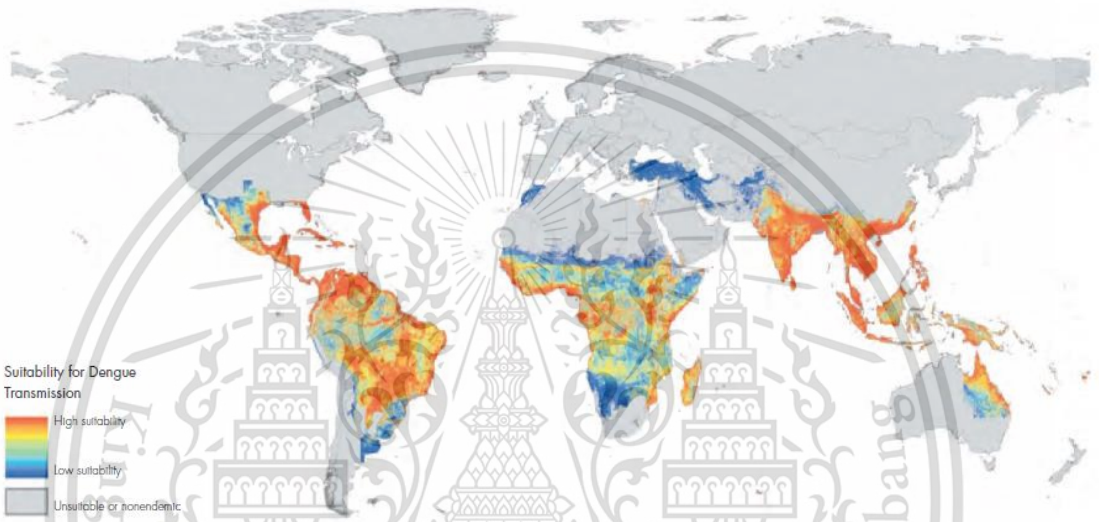


Figure 1.1 Distribution of global dengue risk [2]

DF is caused by dengue virus which is transmitted to humans by vector through the bites of infected *Aedes* mosquitoes. Dengue virus (DV) is comprising four serotypes, DEN1-4 which human is the primary host of all serotypes. Transmission of DV is circulating in blood of human during feeding of female mosquito. So, human is called host and mosquito is called vector of DF dynamical transmission cycle.

Thailand has dengue spreading nationwide including Bangkok metropolitan. Bureau of Epidemiology, Ministry of Public Health was reported dengue cases of 2016 from 77 provinces that was total 63,931 reported cases (morbidity rate 97.71/100,000 population) and 64 deaths (mortality rate 0.1 / 100,000 population). The morbidity rate / 100,000 population by region from South, North, Central, and Northeast were 190.6, 107.97, 78.79, and 72.16 respectively. The top five highest reported cases by province were from Maehongsorn, Songkla, Pattani, Pattalung, and Chiangmai which the morbidity rate / 100,000 population were 434.53, 391.20, 336.18, 282.03, and 279.11 respectively. DF of Thailand morbidity rate / 100,000 population by province of 2016 is shown as Figure 1.2.

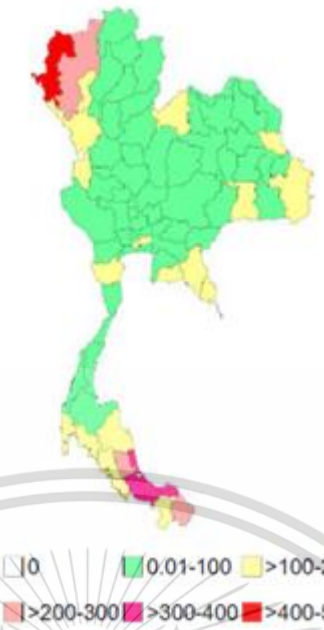


Figure 1.2 Dengue fever's Thailand morbidity rate of 2016 [3]

There are many factors influencing of the dynamical DV transmission such as environmental and climate factors, host-pathogen interactions and population immunological factors. The climate factor directly influences the biology of the vectors and distribution. This thesis focuses on the dynamical transmission of DV, which is consequently an important determinant of vector-borne disease epidemics and rainfall effect. Seecifically, it investigates and analyzes the reported data of Bureau of Epidemiology, Ministry of Public Health during 2003 – 2015. The mathematical model is formulated to analyze the behaviors of transovarial transmission, rainfall effect, and vaccination with dengue fever. The thesis's results can be supported data in order to reduce dengue epidemic.

1.2 Objectives of the study

The mathematical model is developed to analyze dengue fever transmission which is caused by rainfall, vector born infection and vaccinnation effect. The mathematical analysis is used standard dynamical modeling method in order to investigate the dynamical behaviors. The objectives of the study are:

1) To study the dynamical transmission of dengue fever by using mathematical model.

2) To formulate mathematical model of dengue fever influenced by rainfall for analyzing the epidemic of dengue disease.

3) To develop mathematical model of dengue fever with and without the effect of transovarial transmission or vertical transmission for investigating the behaviors and relationships between susceptible, infective, recovered classes.

4) To create mathematical model of dengue fever influenced by vaccination for observing the epidemic of dengue disease.

1.3 Scopes of the study

The scopes of study are as follows:

1) The data is used reported cases and annual report from Bureau of Epidemiology, Ministry of Public Health during 2003 – 2015 in order to analyze and study the behaviors of DF.

2) The mathematical model is developed to analyze the dynamical transmission of DF influenced by rainfall which assumes the constant population of each class.

3) The mathematical model is developed to analyze the dynamical transmission of DF with and without the effect of transovarial or vertical or transmission cases, which assumes the constant population of each class.

4) The mathematical model is developed to analyze the dynamical transmission of DF influences by vaccination which assumes the constant population of each class.

5) The standard dynamical modeling method is applied in order to investigate and analyze the dynamical behaviors of DF mathematical model.

1.4 Benefits of the study

This study will be benefit to related parties as follows:

1) The mathematical model will explain the behaviors in order to understand in detail of DF dynamical transmission.

2) This study will support to better understanding with and without the influence of transovarial or vertical transmission cases.

3) This study will support to better understanding DF influence by rainfall case.

4) This study will support to better understanding DF influence by vaccination case.

5) This study will be used to reduce the epidemic of DF. The results may be adopted to prevent the outbreak.

Chapter 2
Theory and Literature Reviews

This chapter will introduce background of dengue fever in order to understand the behaviors and infectious disease influence by transovarial or vertical transmission, rainfall and vaccination. The mathematical model used to analyze the dynamical transmission of dengue disease will explain the dengue infectious disease. The theoretical background and literature reviews are used in this study which discuss previous modeling related with the aims of this study.

2.1 Background of dengue fever (DF)

2.1.1 Dengue fever (DF)

Dengue fever is known as dengue which can affect humans of all age [4]. Dengue is global burden which the incidence of dengue has grown dramatically around the world in recent decades [5, 6]. The prevalence of dengue is estimated around 3.9 billion people in 128 countries, as shown in Figure. 1.1, which is indicated countries at risk of infection with dengue viruses. It is about half of the world's population that is now at risk. Normally urban and semi-urban areas is facing dengue especially tropical and sub-tropical climates. Dengue is a mosquito-borne viral disease that has rapidly spread in all regions worldwide. The infection causes flu-like illness but there is no specific treatment for dengue. Dengue prevention depends on effective vector control. The early detection and access to proper medical care will lead to lowers fatality rates.

World Health Organization divides the illnesses into 2 categories: dengue and severe dengue [6, 7]. DF infection causes flu-like illness, and occasionally develops into a potentially lethal complication called severe dengue [6]. The symptomatic dengue infection is a systemic and dynamical disease that is followed by three phases: a febrile phase, a critical phase and a recovery phase. After the incubation period, the illness begins with a febrile phase that patients typically suddenly develops a high-grade fever. It usually lasts 2–7 days which normally involves facial flushing, skin erythema, generalized body ache, myalgia, arthralgia, retro-orbital eye pain, photophobia and headache. The next phase is called the critical phase, where conditions worses when patients' temperatures drops to 37.5–38°C or less. This phase usually occurs on days 3–8 of illness which patients with increased capillary permeability may manifest with the warning signs, mostly as a result of plasma leakage. The last phase is called recovery that the patients survives the 24–48 hour critical phase. The gradual reabsorption of fluid takes place in the following 48–72 hours. At

this stage, patients' wellbeing improved, appetite returns, and gastrointestinal symptoms abate [8, 9]. The course of dengue illness is shown in Figure 2.1 [5].

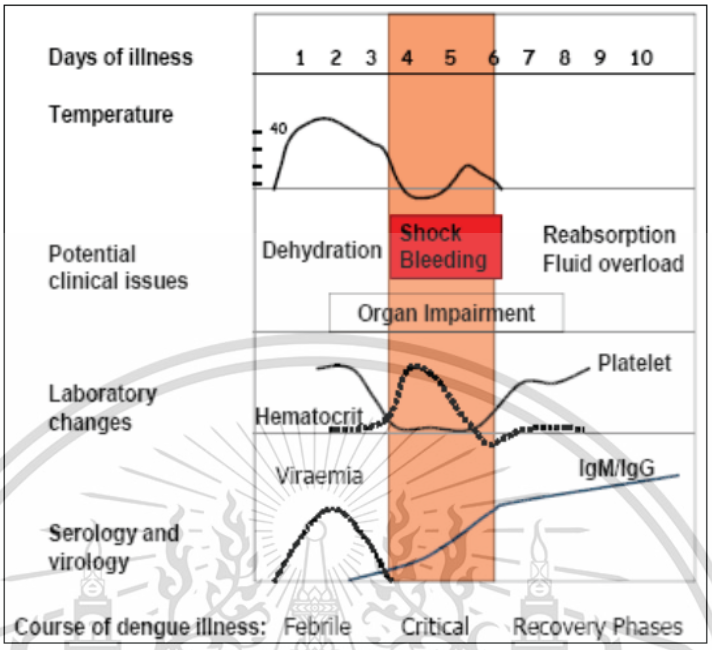


Figure 2.1 Course of dengue illness [5]

2.1.2 Dengue virus (DV)

DF is spread throughout the tropics with local variations in risk influenced by rainfall, temperature and unplanned rapid urbanization [6]. DF is an infection caused by dengue viruses which is transmitted to human through the bites of infected female mosquitoes. DV is members of the genus *Flavivirus* in the Family *Flaviviridae* which has 4 serotypes including DEN-1, DEN-2, DEN-3 and DEN-4. DV is an *Arbovirus* that is required a blood-sucking complete its life cycle. The hosts of DV normally are humans and mosquitoes [10]. The mature DV genome consists of three structural proteins including capsid protein C, membrane protein M, and envelope protein E and seven nonstructural (NS1, NS2A, NS2B, NS3, NS4A, NS4B, and NS5) proteins [11, 12] as shown in Figure 2.2. The dengue virus has approximately spherical shape with diameter of around 50 nm [12, 13]. The inner of the virus is the nucleocapsid that is made of the viral genome and C proteins. The nucleocapsid is surrounded by a membrane of viral envelope (lipid bilayer) that is taken from the host. Embedded of the viral envelope are E and M proteins that span through the lipid bilayer. The proteins form a protective outer layer to controls the entry of the virus into human cells [12, 13]. The protein E

of DV and the structural of DV are shown in Figure 2.3 [11] and Figure 2.4 [12, 13] respectively.

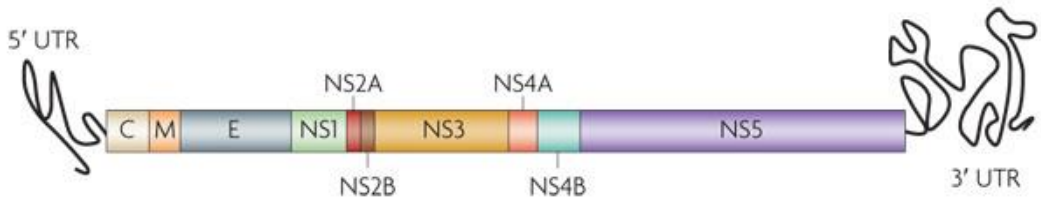


Figure 2.2 Dengue virus (DV) genome [12]

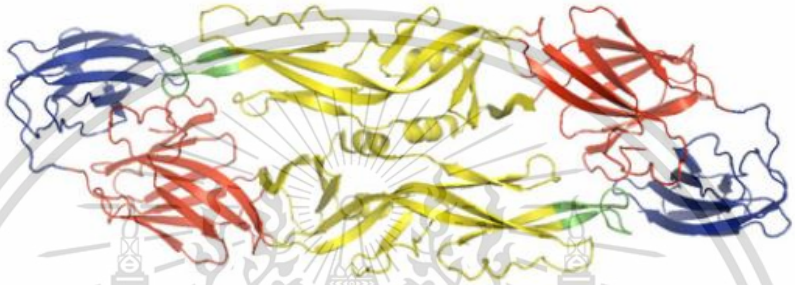


Figure 2.3 Protein E of Dengue virus (DV) [11]

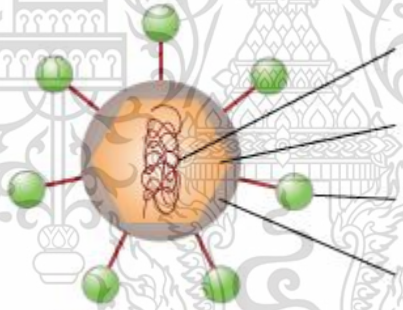


Figure 2.4 Structural of dengue virus (DV) [12, 13]

2.1.3 Dengue Vector

The vector of DF is normally *Aedes* mosquito which the female mosquitoes mainly of the species of *Aedes aegypti* and *Aedes albopictus* transmit an infection of DV to human by biting. On normal condition, the entire life cycle of *Aedes* mosquito consist of 4 stages including egg, larva, pupa, and adult mosquito stages which is normally completed within 1.5 – 3 weeks depending on environmental conditions [12]. On optimal conditions, the egg of an Aedes mosquito will develop into a larva in less than a day. The larva will develop into pupa in about four days, which develops into an adult mosquito after two days. After adult female mosquito has bitten and taken in blood of human, the mosquito will lay their eggs after 2 days. The life cycle of *Aedes* mosquito is shown in Figure 2.5 [14]. Human who is infected with DV first undergo an incubation period 4-5 days and 12 days. After this incubation period, the infected

human can now transmit DV to *Aedes* mosquito. When DV is transmitted to *Aedes* mosquito, it will take incubation period around 4-10 days. The infected *Aedes* mosquito can then transmit the DV for the remaining of its life.

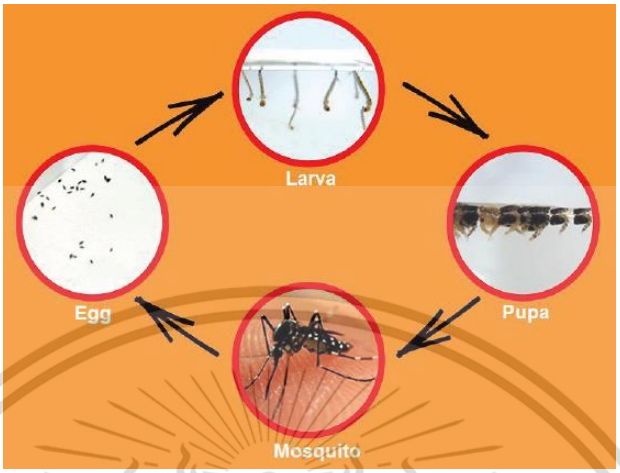


Figure 2.5 The life cycle of *Aedes* mosquito [14]

The *Aedes aegypti* mosquito is the main dengue vector which normally lives in urban area and spread in containers, both indoors and outdoors. The *Aedes albopictus* is secondary dengue vector which normally lives in thickets or arboreal vegetation and spread in used water-filled containers around or away from households mostly outdoors. *Aedes aegypti* is the day time feeder, whose peak biting time are usually in the morning and in the evening before dusk. The vector can multiple bites in one single feeding [15]. On the other hand, *Aedes albopictus* is an aggressive feeder, whose peak biting is in the morning and late afternoon. This vector is high adaptive and can survive in cooler temperate regions and spread due to the tolerance to temperatures below freezing, hibernation, and ability to shelter in microhabitats [16]. The *Aedes aegypti* and *Aedes albopictus* mosquitoes are shown in Figure 2.6 [17].

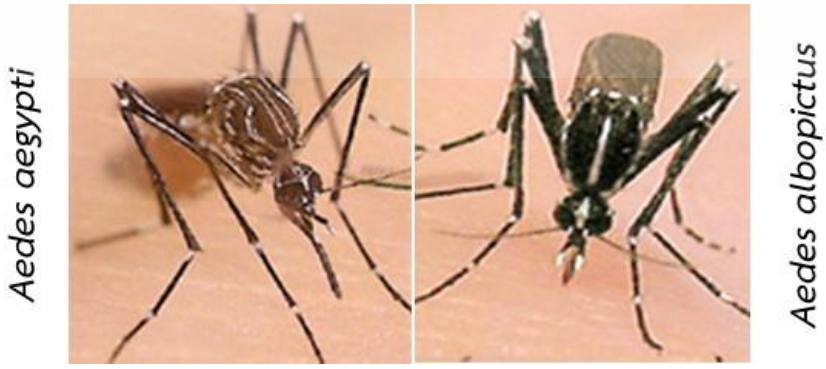


Figure 2.6 *Aedes aegypti* and *Aedes albopictus* mosquito [17]

2.2 Rainfall effect of DF

2.2.1 DV influence by rainfall

Normally, the transmission of DV is highly sensitive to environmental conditions where temperature, precipitation, humidity and rainfall are critical to mosquito survival, reproduction, and development. The patterns of rainfall can influence mosquito presence and abundance and higher temperatures reduce the time required for DV to replicate and disseminate in the mosquito. The higher temperatures associated with Thailand climate accelerates the mosquito development stages than in countries with cooler countries. The altered patterns of rainfall also produces more standing water with potentials for mosquito breedings and increases the dengue transmission. The altered patterns of rainfall and humidity are identified as a consistent, substantial weather factor to provide favorable conditions for dengue vectors [18].

2.2.2 DF and rainfall in Thailand

In Thailand, the prevalence of DF is in the raining season from June to September nationwide. The rainy season provides widely breeding habitats for *Aedes* mosquito, which the population density can increase quickly after rainfall. The disposing of solid waste, domestic water storage containers, and water storage outdoor containers are the potential breeding site which is suitable for *Aedes* mosquito egg-laying habitats. The official dengue reported case in Thailand from Y2003 to Y2015 is shown in Figure 2.7, with peak around the rainy season from June till September [3]. The patterns of rainfall in Thailand indicates its major impact to the reported cases of DF.

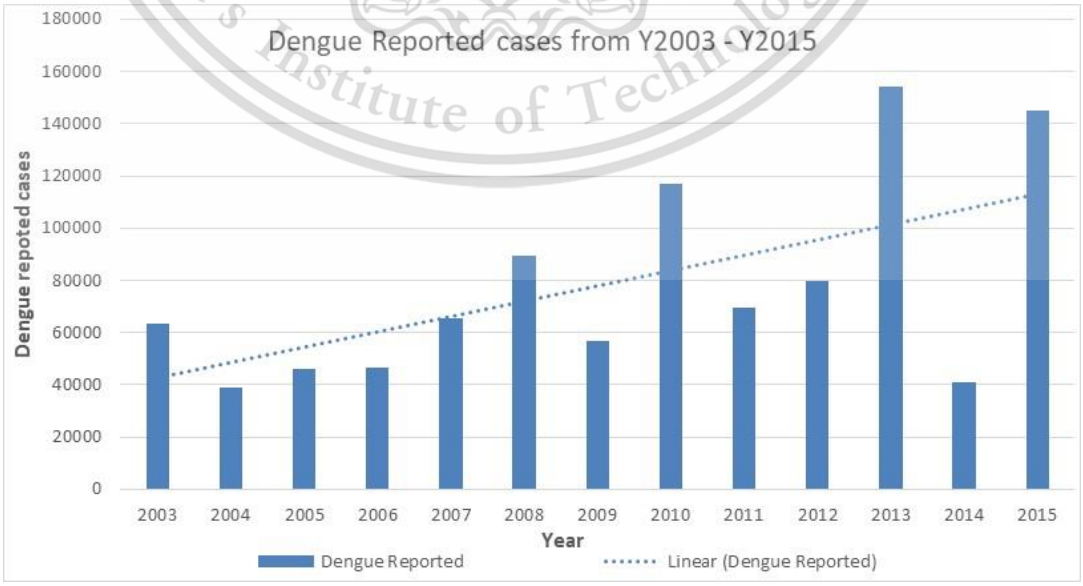


Figure 2.7 Dengue reported cases in Thailand during Y2003 to Y2015

2.3 Horizontal transmission (HT) and Vertical transmission (VT)

2.3.1 Horizontal transmission (HT)

DF is a mosquito-borne viral disease, in which the DV uses human as a host and mosquito as a vector. When an *Aedes* mosquito bites on infected human, the mosquito feeds the DV into the human blood. After the DV incubation period of around 4-10 days, the *Aedes* mosquito is now an infected mosquito and can transmit to human by biting. Human who is bitten by the infected mosquito, is an infected human. This cycle is called horizontal transmission (HT). Normally, DV generally transmits through HT (human to mosquito or mosquito to human) which refers to non-parental transmission while VT refers to parental chains transmission. Another way of DV transmission is called the transovarial or vertical transmission (VT), in which DV is transmitted by the pregnancy of infected female mosquito. The infected mosquito will lay their eggs which is including DV. Then, it will be infected eggs, infected larvae, infected pupae, and infected *Aedes* mosquito. Infected mosquito through transovarial or VT can transmit DV to human as HT. As the result, DV can spread by both horizontal and transovarial or vertical transmissions as shown in Figure 2.8.

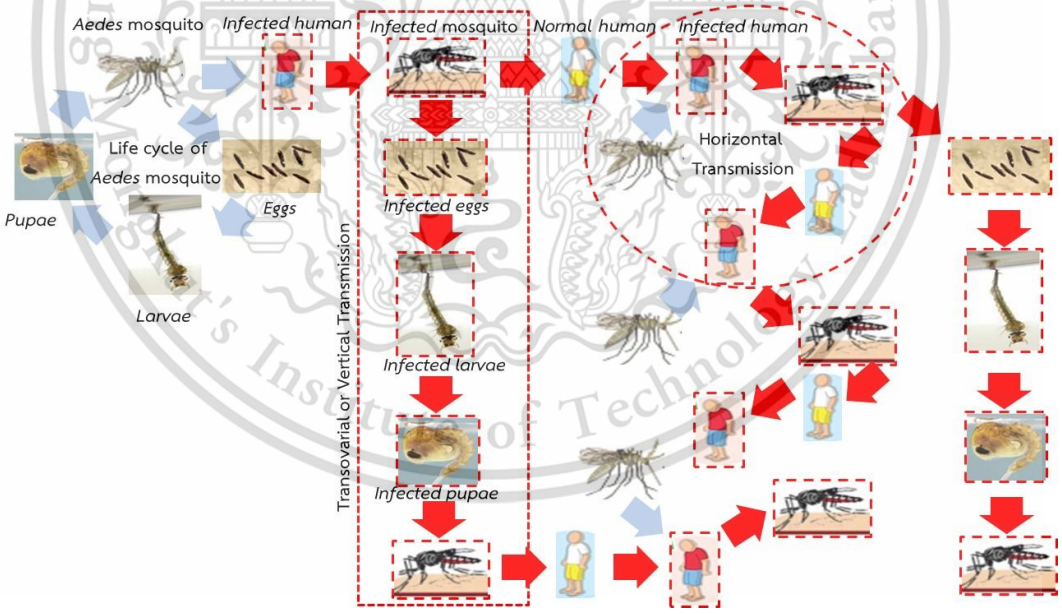


Figure 2.8 Horizontal and vertical transmission of dengue virus (DV)

2.3.2 Vertical transmission (VT)

VT provides a possible mechanism supporting DV transmission in nature by the absence of a recognized host and under unfavorable conditions for mosquito activity which can transmit from the maternal body to eggs within the ovaries. VT is the

transmitted directly to subsequent life generation within vector populations. These have been reports in which Aedes aegypti and Aedes albopictus are involved in the mosquito which is VT of the DV from experimental environments as well as from collected mosquito larvae [19, 20]. The prospective field study of transovarial dengue virus transmission in Bangkok was conducted in two forms of *Aedes aegypti* mosquitoes [21] which mosquitoes assayed for dengue virus were proceed in pool to determine dengue virus inflection status. The newly emerged adult *Aedes aegypti* were dark 98.2% and pale form 1.8%. The dark and pale form of *Aedes aegypti* are shown in Figure 2.9. The minimum infection rate (MIR) by transovarial transmission of dengue virus was ranged round 0 - 24.4/1,000 mosquitoes which increased gradually peak in April - June [21]. Transovarial transmission of dengue virus infections found in both form of *Aedes aegypti* and all dengue virus four serotypes were detected. Water temperature was affected the development of *Aedes aegypti* immature which was varied between 79% - 90% under different temperature conditions [22]. The limitation temperature for development of *Aedes aegypti* immature is around 35°C.

Figure 2.9 *Aedes aegypti* dark form (left) and pale form (right) [21]

2.4 Vaccination of dengue fever

2.4.1 Dengue vaccine worldwide

DF is a mosquito-borne viral disease where the DV uses human as a host and mosquito as a vector. Dengue vaccine is a vaccine to prevent DF in humans. WHO

reported that the first dengue vaccine, Dengvaxia (CYD-TDV), was registered in several countries in late 2015 and early 2016 [6, 23]. The vaccine can be used in individuals 9 – 45 years of age living in endemic areas. WHO only recommends the vaccine as a possible option in areas of the world where epidemiological data indicate a high burden of disease including Thailand. The vaccination schedule consists of 3 injections of 0.5 mL administered at 6-month intervals, given on a 0/6/12 month schedule, which is for the prevention of dengue illness caused by dengue virus serotypes 1, 2, 3, and 4. The lower limit of the indication at 9 years old was chosen due to a safety concern in children. It is not recommended for women in pregnancy and lactating due to lack of sufficient data in this population. There is no recommendation for vaccination of travelers or health-care workers at this time. Vaccine efficacy varies by country, with efficacy ranging from 31.3% in Mexico to 79.0% in Malaysia [23]. This variability in efficacy reflects in part the baseline seropositivity and circulating serotypes which affect the performance of the vaccine. Vaccine efficacy against dengue illness of any severity has been measured in the first and second years post dose 1 that vaccine efficacy can be evaluated 5–6 years protection post dose 1.

2.4.2 Dengue vaccine in Thailand

WHO has approved and recommended to use dengue vaccine for Thailand in 2016. The first vaccine against the four strains of DV was available in Thailand on December 2016, which is the evolution of dengue prevention in Thailand in order to reduce severity and to allow a better quality of life [24]. The launch of the first dengue vaccine in Thailand has been involved in the development to create a stable immunity against all four dengue serotypes (DEN1-4) which is complicated due to the unpredictable predominance of different serotypes at different points in time. The vaccine has efficacy 65.6% for preventing dengue, efficacy 93.2% for reducing the severity of the disease, and efficacy 80.8% for reducing hospitalization of dengue which can be taken by individuals between 9-45 years of age [24]. The live recombinant tetravalent vaccine has been registered in Thailand. The vaccine is administered as a 3-dose series on a 0/6/12 month schedule. Each person may develop immunity at different points in time, but immunity usually occurs after 2 shots.

2.5 Mathematical model to analyze dengue fever

2.5.1 Epidemic modelling

Mathematical model has long been used as a tool to analyze the epidemic of infectious disease. Mathematical modelling allows investigations into the behavior of the disease e.g. described spreading mechanism, predicting the future epidemic, controlling the spread of epidemic, etc. The popular epidemiological model is derived

from Kermack and McKendrick [25], which plays an important role in mathematical epidemiology. This model assumed a closed and constant population size that is divided into 3 classes: Susceptible-Infected-Recover, or SIR model. The susceptible class *(S)* is people who have no immunity and no infectious. The infected class *(I)* is human who are infected with capability of passing on the disease onto vectors. When the human gets well, the patient passes into the recovery class *(R).* The proportions in each class at time t is given as *s(t)*, *i(t)*, and *r(t)* respectively. The basic system epidemic of SIR model is described as Figure 2.10.

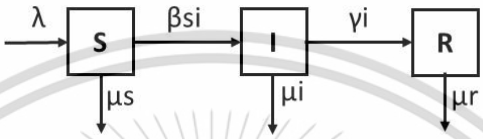


Figure 2.10 The basic SIR epidemic model [25]

The differential equations describing this system are defined:

$$\left.\begin{aligned}\frac{ds}{dt} &= \lambda - \beta si - \mu s \\ \frac{di}{dt} &= \beta si - (\gamma + \mu)i \\ \frac{dr}{dt} &= \gamma i - \mu r\end{aligned}\right\} \quad (2.1)$$

The variables are *s(t)*: number of susceptible at time t, *i(t)*: number of infected at time t and *r(t)*: number of recovery at time t respectively. The parameters are λ: birth rate, β: transmission rate, μ: death rate, and γ: recovery rate respectively. The important assumption is closed and constant population that can be defined *1 = s(t) + i (t) + r (t).* All parameters value is higher than 1. Then, it can be defined $\lambda = \mu$ and basic reproductive number, R_0. The basic reproductive number is the number of secondary infection which is produced by a case of an infection in a population of its infectious period.

$$\left.R_0 = \frac{\beta}{\mu + \gamma}\right\} \quad (2.2)$$

2.5.2 Steady state solution

The steady state can be defined by setting RHS of equation (2.1) to zero which can be rewritten os follows:

$$\left.\begin{aligned}\mu - \beta si - \mu s &= 0 \\ \beta si - \gamma i - \mu i &= 0\end{aligned}\right\} \quad (2.3)$$

Equation (2.3) admits 2 steady state solutions, namely the disease free steady state *(i=0)* and endemic steady state *(i≠0)*. It can be solved to yield both steady state as follows:

$$(s,i) = (1,0)$$
$$(s^*,i^*) = (\frac{1}{R_0}, \frac{\mu(R_0-1)}{\beta})$$

The disease free steady state exists for the value of $R_0 <1$, while the endemic steady state exists for the value of $R_0 >1$. The stability of the steady states can be calculated by linearization Equation (2.1). The Jacobian matrix is found by:

$$J = \left[\begin{matrix} -\mu-\beta i & -\beta s \\ \beta i & \beta s-\gamma-\mu \end{matrix}\right] \Bigg\} \tag{2.4}$$

Substituting both steady state values into equation (2.4), two Jacobian matrices, one for each class of steady state, can be derived:

$$\left.\begin{aligned} J_{disease-free} &= \left[\begin{matrix} -\mu & -\beta \\ 0 & \beta-(\gamma+\mu) \end{matrix}\right] \\ J_{endemic} &= \left[\begin{matrix} -\mu R_0 & -(\gamma+\mu) \\ \mu(R_0-1) & 0 \end{matrix}\right] \end{aligned}\right\} \tag{2.5}$$

2.5.3 Stability analysis of linear systems

The general form of a two-state linear system is defined:

$$\left.\begin{aligned} \frac{dX_1(t)}{dt} &= ax_1(t)+bx_2(t)+c_1 \\ \frac{dX_2(t)}{dt} &= cx_1(t)+dx_2(t)+c_2 \end{aligned}\right\} \tag{2.6}$$

The system can be solved in which the solution can be written as:

$$\left.\begin{aligned} X_1(t) &= c_{11}e^{\lambda_1 t}+c_{12}e^{\lambda_2 t} \\ X_2(t) &= c_{21}e^{\lambda_1 t}+c_{22}e^{\lambda_2 t} \end{aligned}\right\} \tag{2.7}$$

The Jacobian matrix of the linear system is constructed from equation (2.6) as shown below.

$$J = \left[\begin{matrix} \frac{\partial X_1}{\partial x_1} & \frac{\partial X_1}{\partial x_2} \\ \frac{\partial X_2}{\partial x_1} & \frac{\partial X_2}{\partial x_2} \end{matrix}\right] = \left[\begin{matrix} a & b \\ c & d \end{matrix}\right] \Bigg\} \tag{2.8}$$

The eigenvalues of the matrix are the root of the quadratic equation as shown below equation (2.8) which can be real-valued or complex-valued.

$$\left.\begin{aligned} &\lambda^2-(a+d)\lambda+(ad-bc)=0 \\ &\lambda_{1,2}=\frac{(a+d)\pm\sqrt{(a+d)^2-4(ad-bc)}}{2} \end{aligned}\right\} \tag{2.9}$$

The stability properties of steady state use three quantities as follows:

$$\left.\begin{aligned} \beta &= (a+d) \\ \gamma &= ad-bc \\ \delta &= \beta^2-4\gamma \end{aligned}\right\} \tag{2.10}$$

The root of quadratic equation can be rewritten:

$$\left.\begin{aligned} \lambda_{1,2} &= \frac{\beta\pm\sqrt{\delta}}{2}(real-valued) \\ \lambda_{1,2} &= \frac{\beta\pm i\sqrt{-\delta}}{2}(complex-valued) \end{aligned}\right\} \tag{2.11}$$

The steady state can be classified into six cases. Case 1 for $\gamma > 0$ and $\beta > 0$, the equilibrium is unstable node while case 2 for $\gamma < 0$, the equilibrium is saddle point. Case 3 for $\beta < 0$ and $\gamma > 0$, the equilibrium is stable node. Case 4 for $\beta^2 < 4\gamma$ and $\beta > 0$, the equilibrium is unstable spiral while case 5 for $\beta^2 < 4\gamma$ and $\beta = 0$, the equilibrium is natural center. Case 6 for $\beta^2 < 4\gamma$ and $\beta < 0$, the equilibrium is stable spiral. All stability type of linear systems is shown as Figure 2.11.

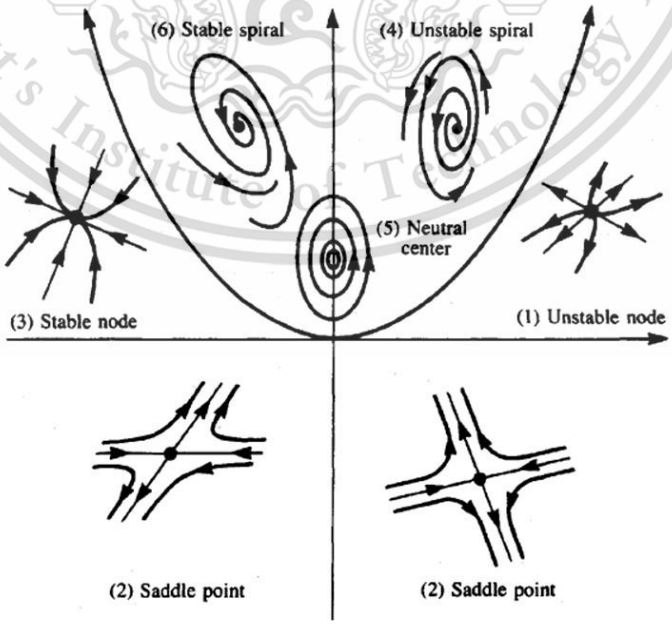


Figure 2.11 All stability type of linear systems [26]

2.5.4 Ruth-Hurwitz stability criterion

Considering the general equation and vector notation are shown as below.

$$\left.\begin{aligned}\frac{dN_i(t)}{dt} &= f_i(N_1, N_2, ..., N_k), (i = 1,2,...,k)\\ \frac{dN}{dt} &= F(N), N = (N_1, N_2, ..., N_k), F = (f_1, f_2, ..., f_k)\end{aligned}\right\} \quad (2.12)$$

The equilibrium point can be calculated by *F(N)=0*. The stability of the equilibrium point is obtained by the following equation.

$$\left.\begin{aligned}J &= \frac{\partial F}{\partial N}(\overline{N})\\ J &= \begin{pmatrix} \frac{\partial f_1}{\partial N_1} & \frac{\partial f_2}{\partial N_2} & ... & \frac{\partial f_k}{\partial N_k} \\ . & & & \\ . & & & \\ . & & & \\ \frac{\partial f_k}{\partial N_1} & \frac{\partial f_k}{\partial N_2} & ... & \frac{\partial f_k}{\partial N_k} \end{pmatrix}\end{aligned}\right\} \quad (2.13)$$

J is matrix *k x k*, and eigenvalues λ of this matrix can be determined by determinant, *det (J-* λ*I) = 0*. The characteristic equation is written in the form:

$$\lambda^k + a_1\lambda^{k-1} + a_2\lambda^{k-2} + a_3\lambda^{k-3} + ... + a_k = 0\} \quad (2.14)$$

From the coefficients of the characteristic polynomial of Equation (2.14), define the following Hurwitz matrices.

$$H_1 = (a_1), \quad (2.15)$$

$$H_2 = \begin{pmatrix} a_1 & 1 \\ a_3 & a_2 \end{pmatrix}, \quad (2.16)$$

$$H_3 = \begin{pmatrix} a_1 & 1 & 0 \\ a_3 & a_2 & a_1 \\ a_5 & a_4 & a_3 \end{pmatrix}, ..., \quad (2.17)$$

$$H_j = \begin{pmatrix} a_1 & 1 & 0 & 0 & ... & 0 \\ a_3 & a_2 & a_1 & 1 & ... & 0 \\ a_5 & a_4 & a_3 & a_2 & ... & 0 \\ a_{2j-1} & a_{2j-2} & a_{2j-3} & a_{2j-4} & ... & a_j \end{pmatrix}, ..., \quad (2.18)$$

$$H_k = \begin{pmatrix} a_1 & 1 & 0 & \dots & 0 \\ a_3 & a_2 & a_1 & \dots & 0 \\ \cdot & \cdot & \cdot & & \cdot \\ \cdot & \cdot & \cdot & & \cdot \\ \cdot & \cdot & \cdot & & \cdot \\ 0 & 0 & \dots & & a_k \end{pmatrix} \tag{2.19}$$

The *(n,m)* term in the matrix is a_{2n-m} for *0 < 2n-m < k*, 1 for *2n=m*, and 0 for *2n < m* or *2n > k+m*. Then all eigenvalues have negative real parts. The steady state is deemed stable and only if the determinants of all Hurwitz matrices are positive.

$$\det H_j > 0, (j = 1,2...,k)$$

For example, for *k=1, 2, 3, 4.*

$$k = 1 : a_1 > 0.$$
$$k = 2 : a_1 > 0, a_2 > 0.$$
$$k = 3 : a_1 > 0, a_3 > 0, a_1^2 > a_3.$$
$$k = 4 : a_1 > 0, a_3 > 0, a_4 > 0, a_1^2 a_3 > a_3^2 + a_1^2 a_4.$$

Chapter 3
Research methodology

This chapter presents data preparation, data analysis and the outline of this thesis. The historical data of dengue disease is prepared by the actual data from Bureau of vector born disease and Bureau of Epidemiology, Ministry of public health.

3.1 Data preparation

All actual data related with dengue disease are collected and analyzed to get the thesis results. The historical numbers of dengue disease in Thailand during 1958 - 2016 are shown in Table 3.1 which is including reported cases, death cases, reported rate, deaths rates, reported fatality rates (%), and population. The reported rates and death rate is per 100,000 population.

Table 3.1 Historical numbers of dengue disease in Thailand during 1958-2016. [27,28]

Remark: Reported rates and death rates are per 100,000 population						
Year	Reported Case	Death Case	Reported Rates	Death Rates	Fatality Rates	Population
1958	2,158	300	8.87	1.23	13.9	24,315,524
1959	2,706	296	10.92	1.19	10.94	24,791,025
1960	1,851	65	7.01	0.25	3.51	26,388,421
1961	561	36	2.27	0.13	6.42	27,103,450
1962	5,947	308	21.36	1.11	5.18	27,840,787
1963	2,215	173	7.74	0.6	7.81	28,601,179
1965	4,094	193	13.56	0.64	4.71	30,194,262
1966	5,816	137	18.74	0.44	2.36	31,028,584
1967	2,060	65	6.46	0.20	3.16	31,889,228
1968	6,430	71	19.62	0.22	1.10	32,777,090
1969	8,670	109	25.73	0.32	1.26	33,694,197
1970	2,767	47	7.61	0.13	1.70	36,370,000

Year	Reported Case	Death Case	Reported Rates	Death Rates	Fatality Rates	Population
1971	11,540	299	30.85	0.80	2.59	37,409,000
1972	23,782	685	61.81	1.78	2.88	38,477,000
1973	8,280	315	20.92	0.80	3.80	39,576,000
1974	8,160	328	20.05	0.81	4.02	40,707,000
1975	17,767	438	42.43	1.05	2.47	41,869,000
1976	9,616	361	22.43	0.84	3.75	42,880,000
1977	38,768	756	89.24	1.74	1.95	43,441,000
1978	12,547	308	28.22	0.69	2.54	44,455,000
1979	11,478	127	25.25	0.28	1.11	45,460,000
1980	43,382	403	93.38	0.87	0.93	46,455,000
1981	25,670	198	54.06	0.42	0.77	47,488,000
1982	22,250	159	45.89	0.33	0.71	48,490,000
1983	30,025	229	60.71	0.46	0.76	49,459,000
1984	69,101	496	137.12	0.98	0.72	50,396,000
1985	80,076	542	154.94	1.05	0.68	51,681,000
1986	27,837	236	52.88	0.54	0.85	52,646,700
1987	174,285	1,007	325.13	1.88	0.58	53,605,100
1988	26,926	179	49.37	0.33	0.66	54,534,000
1989	74,391	290	133.95	0.52	0.39	55,537,648
1990	92,005	414	163.43	0.74	0.45	56,296,817
1991	43,511	137	76.79	0.24	0.31	56,661,966
1992	41,125	136	71.16	0.24	0.33	57,788,965
1993	67,017	222	114.88	0.38	0.33	58,336,072
1994	51,688	140	87.47	0.24	0.27	59,095,419
1995	60,330	183	101.46	0.31	0.30	59,460,382

Year	Reported Case	Death Case	Reported Rates	Death Rates	Fatality Rates	Population
1996	37,929	116	63.09	0.19	0.31	60,116,182
1997	101,689	253	167.21	0.42	0.25	60,816,227
1998	129,954	424	211.42	0.68	0.33	61,466,178
1999	24,826	56	40.32	0.09	0.23	61,577,827
2000	18,617	32	30.14	0.05	0.17	61,770,259
2001	139,355	245	255.21	0.40	0.18	61,878,746
2002	114,800	176	184.24	0.28	0.15	62,308,887
2003	63,657	75	101.14	0.12	0.12	62,939,819
2004	39,135	48	62.59	0.08	0.12	62,526,710
2005	45,893	71	73.79	0.11	0.15	62,195,878
2006	46,829	59	74.78	0.09	0.13	62,623,416
2007	65,581	95	104.21	0.15	0.14	62,933,515
2008	89,626	102	141.78	0.16	0.11	63,214,022
2009	56,651	50	89.27	0.08	0.09	63,457,439
2010	116,947	139	183.59	0.22	0.12	63,701,703
2011	69,800	63	109.10	0.09	0.10	63,977,185
2012	79,593	87	123.85	0.14	0.11	64,266,405
2013	154,444	136	241.03	0.21	0.09	64,076,033
2014	41,082	49	63.25	0.08	0.12	64,955,313
2015	144,952	148	222.58	0.23	0.10	65,124,716
2016	63,931	64	97.71	0.10	0.10	65,426,907

3.2 Data analysis

All raw data should classify to analyze the data. The other related data should also be collected to achieve the thesis results e.g. amount of rainfall of Thailand and Bangkok and dengue vaccination. All data in this thesis are analyzed by Mathematica and MS-office.

3.3 Research outline

This thesis is organized as follows: Chapter one explains the research motivation, objectives of thesis, scope of the thesis, benefits of thesis and outline of the thesis. Theory and literature review are explained in Chapter two which is introduced the background of DF, rainfall effect of DF, horizontal and vertical transmission of DF, vaccination of DF, and mathematical model to analyze DF. Research methodology is presented in Chapter three. Chapter four present the dengue disease in Thailand and mathematical model for dynamical transmission of dengue disease (Paper 1). The effect of rainfall for the dynamical transmission model of the dengue disease in Thailand (Paper 2), the SEIR dynamical transmission model of dengue disease with and without the vertical transmission of the virus (Paper 3) and dynamical transmission of dengue disease based on SIR modeling influence by dengue vaccination (Paper 4) are presented in Chapter five, six and seven respectively. The conclusion and suggestion are summarized in chapter eight. All research papers for this thesis title, Mathematical model of dengue fever in Thailand influenced by rainfall, transovarial transmission, and vaccination, are shown in Figure 3.1

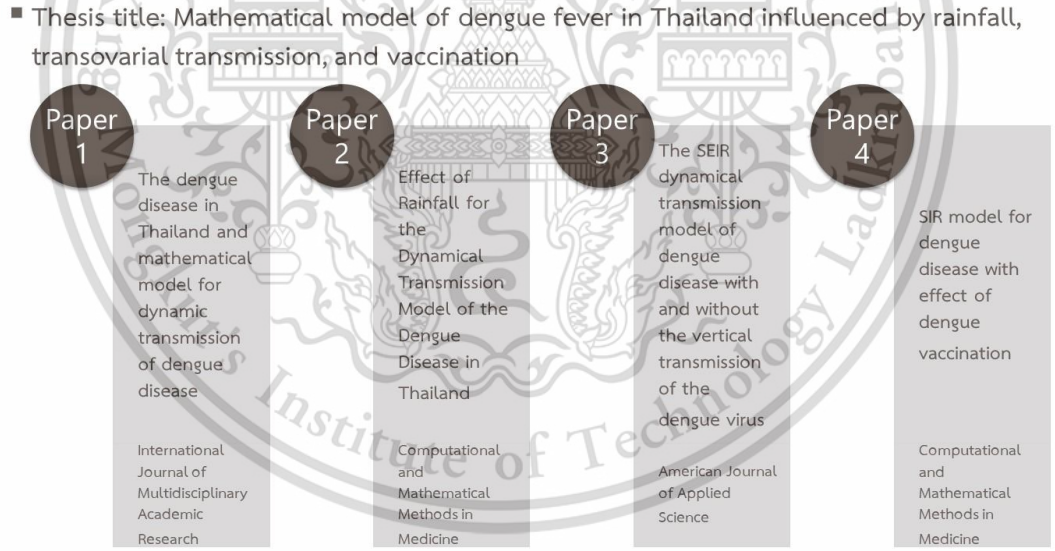


Figure 3.1 Research papers for thesis: Mathematical model of dengue fever in Thailand influenced by rainfall, transovarial transmission, and vaccination

Chapter 4

Dengue disease in Thailand and mathematical model for dynamical transmission of dengue disease

In this chapter, we proposed the historical data of dengue disease in Thailand. The reported case and death due to dengue disease are presented by total number, region, month, age, and occupation. The mathematical model is the key to analyze dengue disease which can investigate the reproductive number to control the outbreak. Currently, the best way to control the outbreak is controlling the environmental of spreading of dengue disease.

4.1 Introduction

Dengue virus is found in tropical and subtropical region around the world such as South-East Asia, the Western Pacific and Latin and Central America [1]. Dengue virus is transmitted to human by biting of *Aedes* mosquitoes. There are four serotypes: DEN1, DEN2, DEN3, and DEN4. The mosquitoes can be growth in any places that have stagnant water which can be found anywhere and anytime in home. Mosquito is the most dangerous animal on earth because of the number of people killed by mosquito per year, which is shown in Figure 4.1. Mosquitoes can carry devastating diseases, which are included malaria, yellow fever, encephalitis and dengue fever.

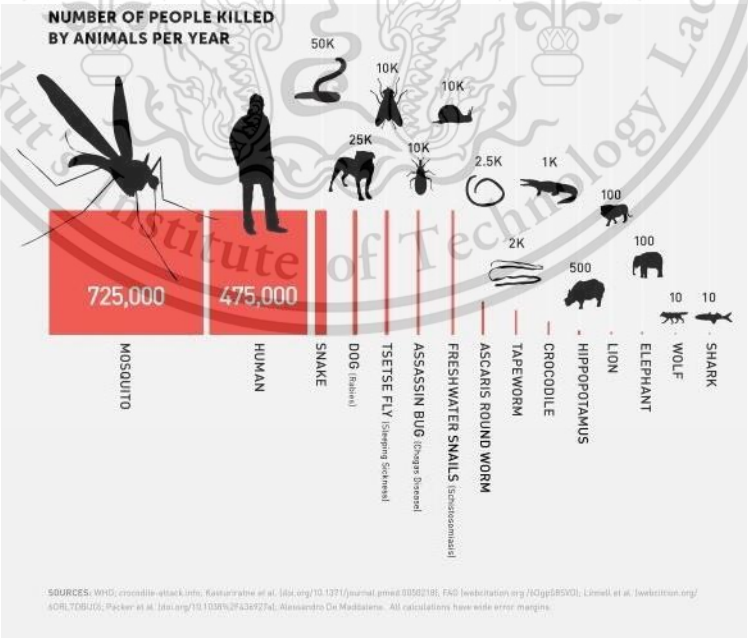


Figure 4.1 The number of people killed by animal per year [29]
Source: The Washington Post, April 29, 2014

Dengue disease is an international public health concern that has no specific treatment. There is no vaccine available that the appropriate medical care frequently survives the lives of patients. The way to control dengue disease is focused on mosquitoes spreading. Therefore, the mathematical model is an important tool to analyze the spread and control of infectious disease that can provide the dengue epidemic to better understand the mechanisms.

Dengue disease is a fastest emerging arboviral infection spread by *Aedes* mosquitos with major public health consequences in over 100 tropical and sub-tropical countries in South-East Asia, the Western Pacific and Latin and Central America which around 2.5 billion people globally live under the threat of dengue fever [1,2]. The rising level of dengue infections around the world has become seriously an international concern that has increased with increasing geographic expansion distribution as shown in Figure 1.1. The color countries are the area where dengue has been reported.

4.2 Dengue disease in Thailand

The first case of dengue disease in Thailand was observed in 1949 and continued throughout 1950 and the first major outbreak of dengue disease appeared in Bangkok in 1958 [30]. The historical reported case and death of dengue disease in Thailand during 1958-2014 is shown in Figure 4.2.

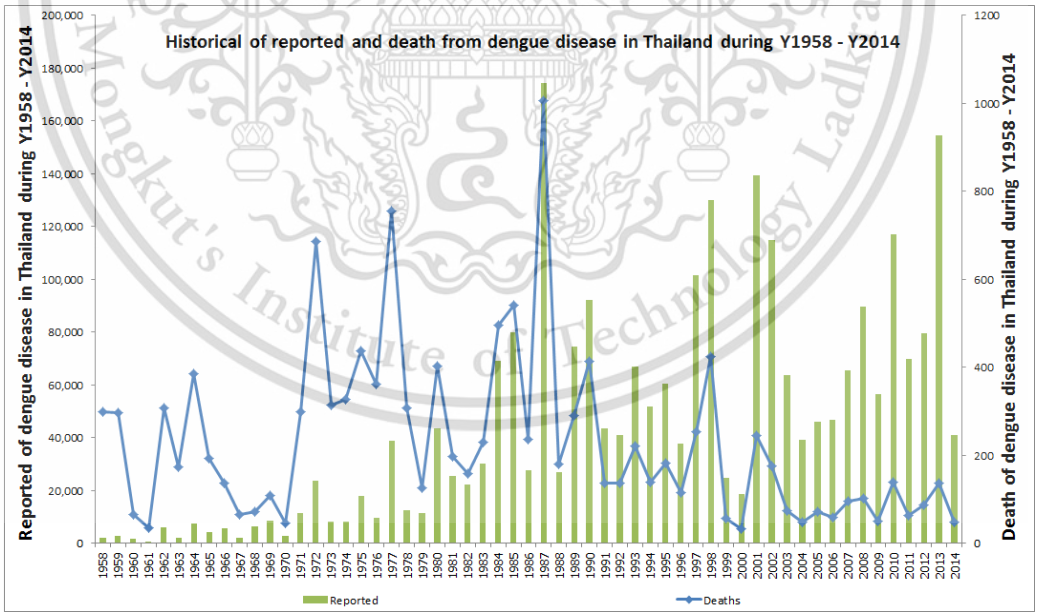


Figure 4.2 Historical reported and death of dengue disease in Thailand [27,28]

The reported case and death due to dengue disease by regions in Thailand during 2003-2014 are shown in Figure 4.3 and Figure 4.4 respectively [27, 28]. The regions are divided by geographical areas which include Bangkok, central (excluding

Bangkok), north, north east, and south area. The detail of each regional consist of central (excluding Bangkok) 24 provinces, north 18 provinces, north east 20 provinces, and south 14 provinces.

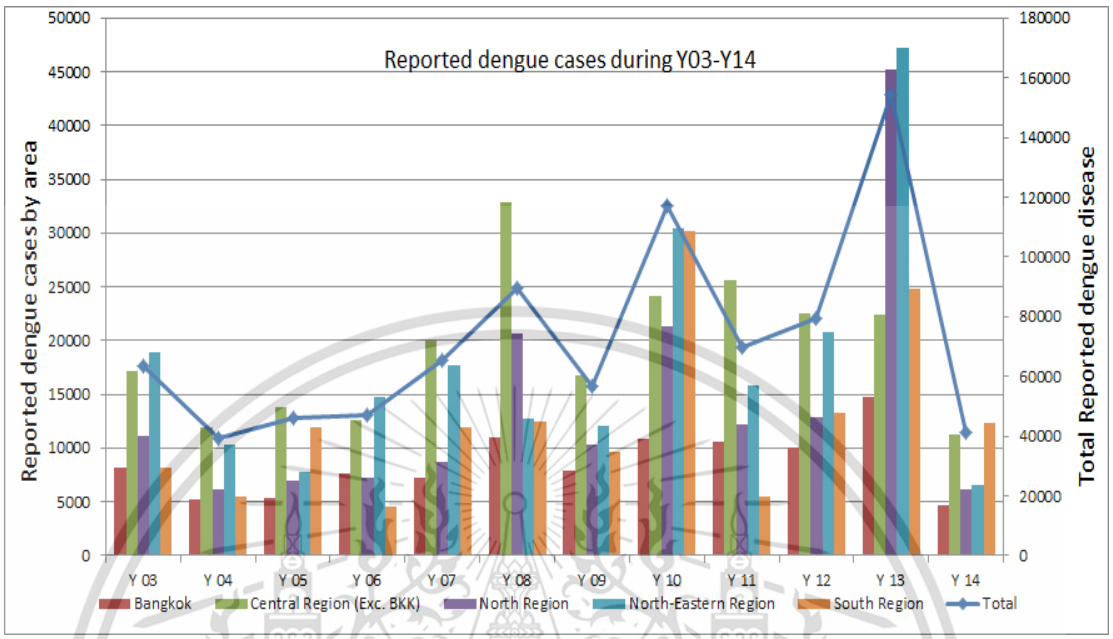


Figure 4.3 The reported of dengue disease in Thailand by regional during 2003-2014

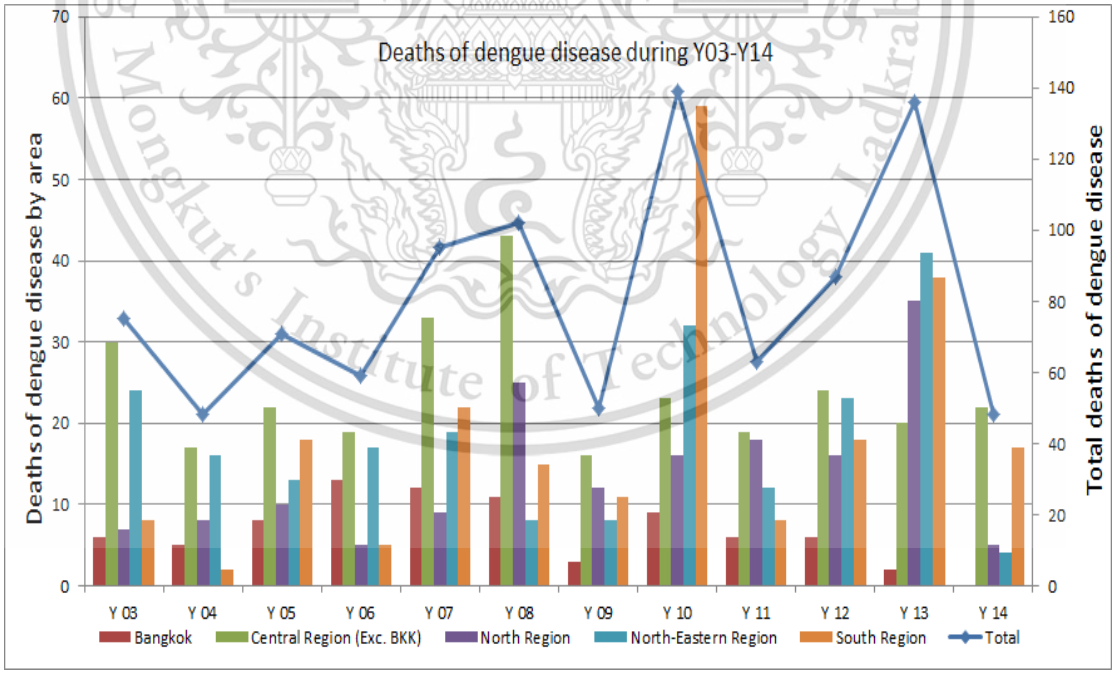


Figure 4.4 The death of dengue disease in Thailand by regional during 2003-2014

The reported case and death due to dengue disease by month in Thailand during 2003-2014 are shown in Figure 4.5 and Figure 4.6 respectively [27,28]. The peak

period for dengue reported is around rainy season in Thailand from May to September of each year which is the same pattern for death of dengue case. The dengue disease situation in Thailand has mad badly because of the unseasonably wet and warm weather which is allowing mosquitoes to reproduce at a rapid rate. Mosquitoes can breed in clear water which is usually found around housing development in urban area that is most active in daytime. As the results, seasonal is effected with mosquitoes breading and reported and deaths of dengue disease in Thailand.

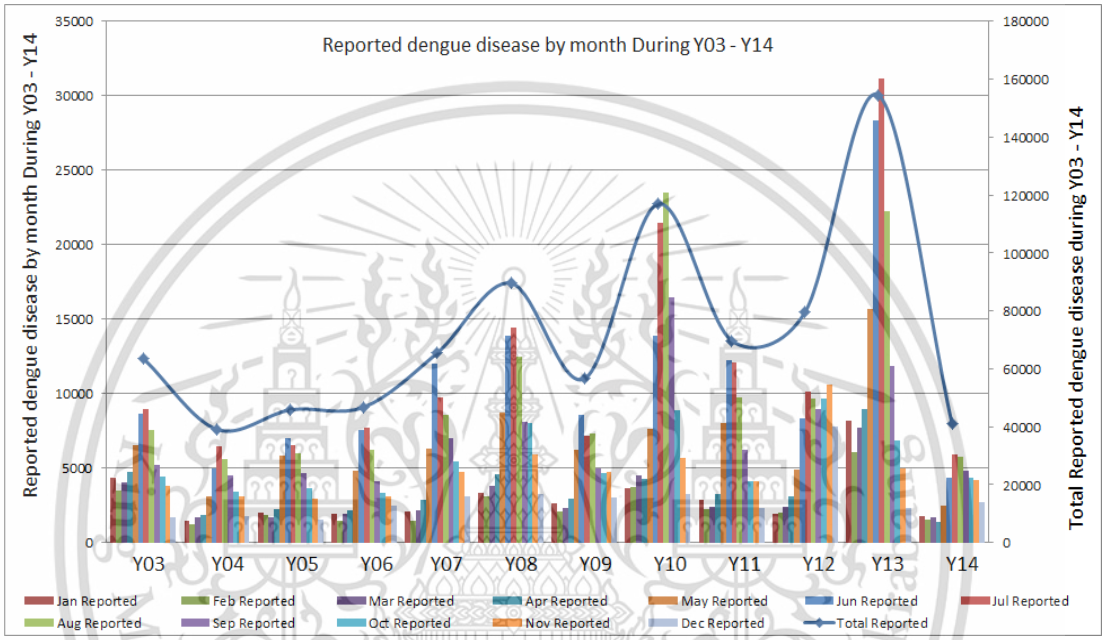


Figure 4.5 Thailand monthly reported cases of dengue disease during 2003-2014

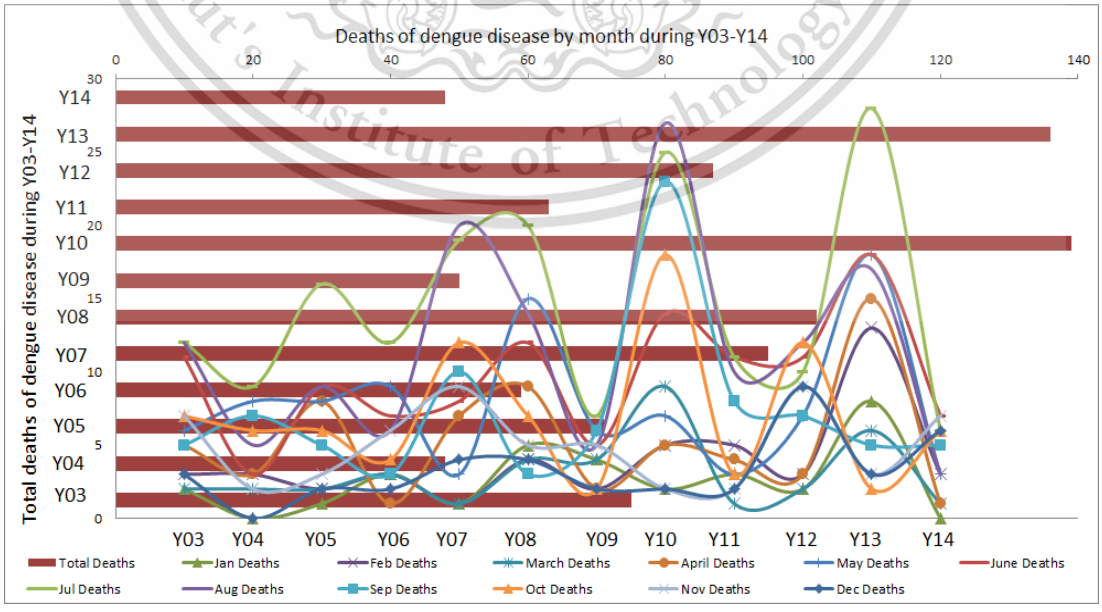


Figure 4.6 Thailand monthly death case of dengue disease during 2003-2014

The reported dengue disease by age in Thailand during 2004-2014 is shown in Figure 4.7 [27,28]. The high reported of dengue disease remains in age group 10-14 and 15-24. The highest reported changed from the age 10-14 years to 15-24 years in 2009.

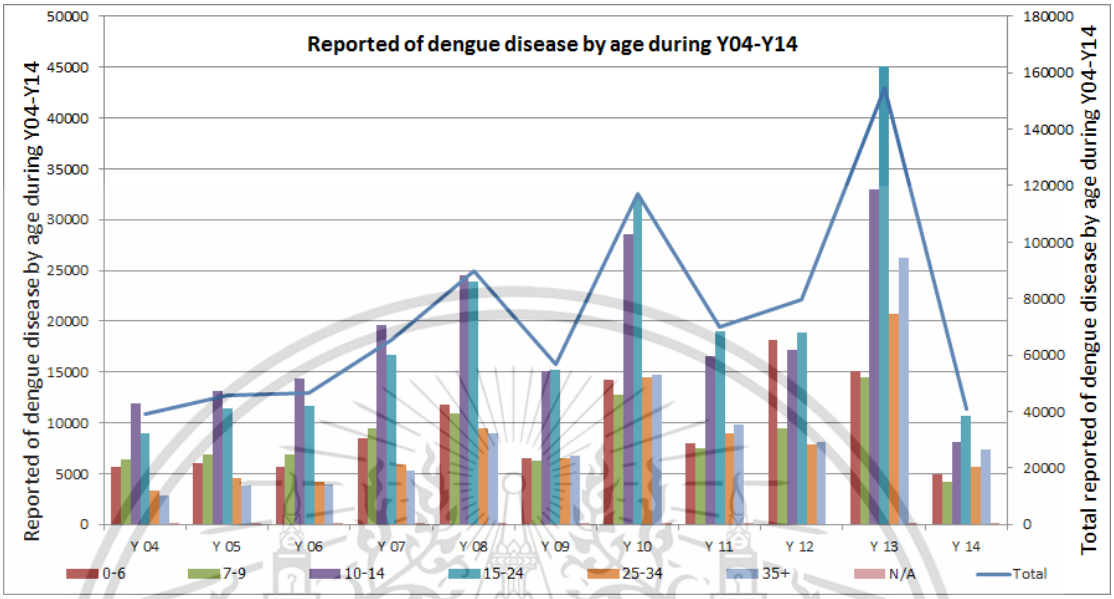


Figure 4.7 The reported of dengue disease in Thailand by age during 2004-2014

The reported dengue disease by occupation in Thailand during 2006-2014 is shown in Figure 4.8 [27,28]. The highest reported of dengue disease remains in student occupation. The second and the third main reported of dengue disease are in employee and agriculturist occupation.

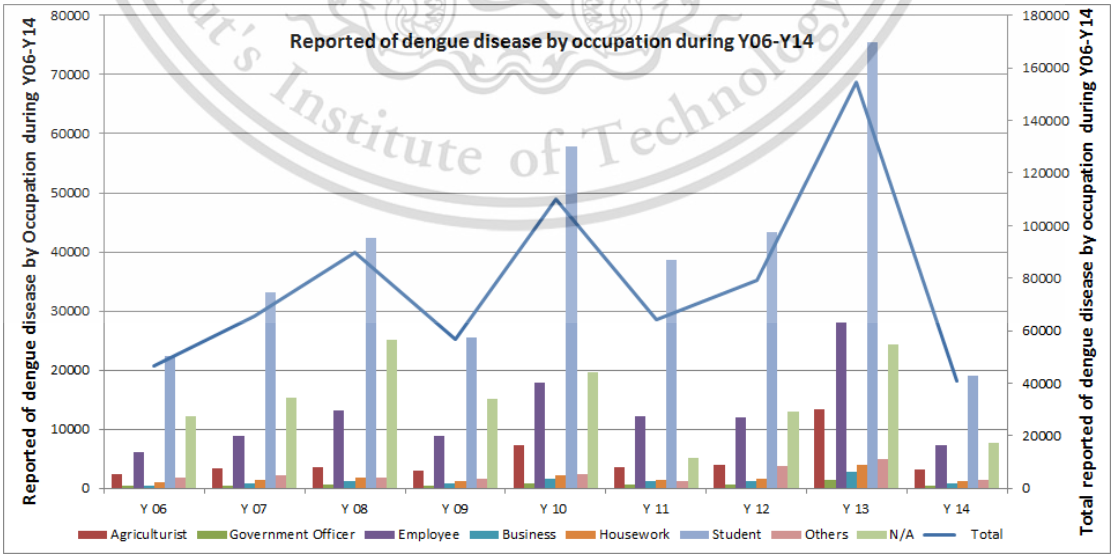


Figure 4.8 Thailand reported of dengue disease by occupation during 2004-2014

In 2015, the reported dengue disease cases as of 7 May totaled 5837 cases and 0 deaths from 77 provinces. The spread of the dengue disease situation is shown in the Figure 4.9. [27,28] The morbidity rate was 9.06 per 100,000 populations. The reported proportions of dengue disease by age group were 15-24 years old 27.17%, 10-14 years old 20.56%, and 25-34 years old 13.83%.

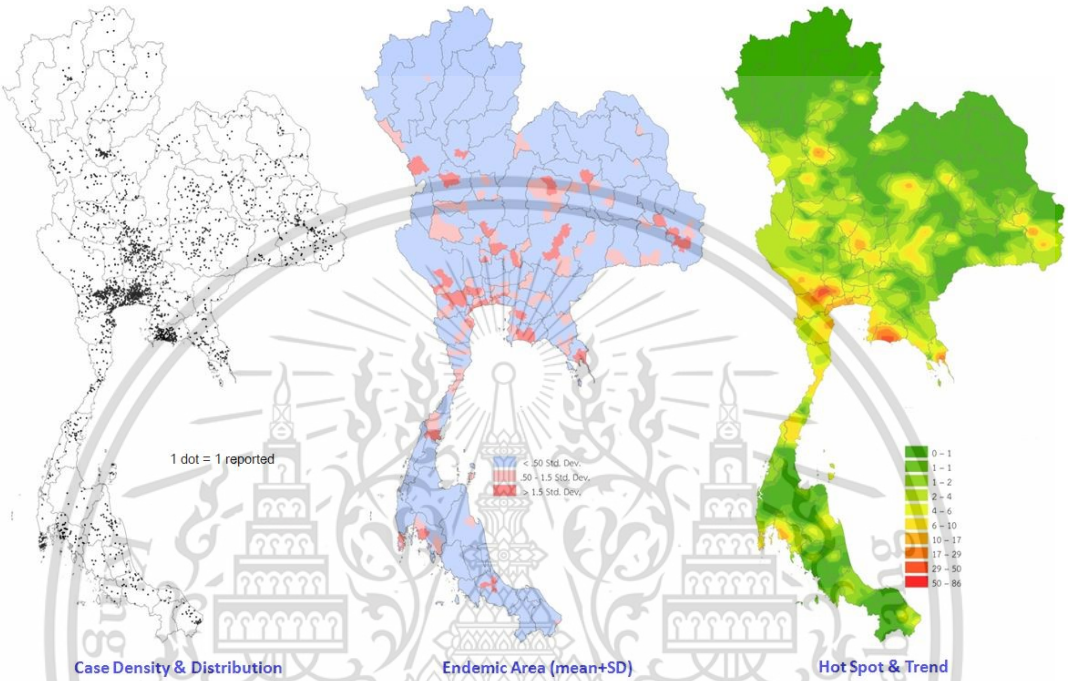


Figure 4.9 Dengue disease situation as of 7 May 2015 in Thailand [3]

Dengue disease is an important mosquito-borne viral infection found in tropical and sup-tropical climates around the world especially urban and semi urban area. The widespread of dengue disease is throughout the tropic which local variation in risk is influenced by rainfall, temperature, and unplanned rapid urbanization. The current decade dengue disease situation in Thailand is shown in Figure 4.2-4.9. The highest reported cases and deaths were 154,444 cases in 2013 and 139 cases in 2010, during which the morbidity and mortality rate per 100,000 populations were 241.03 in 2013 and 0.22 in 2010 respectively. In regional level, north-eastern region was reported to the highest cases in 2013 while the highest deaths were from the southern region in 2010. The highest reported by age group was 15-24 years in 2013, with the student occupation being the most prevalent. The peak period reported each year appeared during rainy season in May through September. The total reported, total death, trend of total reported, and trend of total death during 2003 - 2014 are shown in Figure 4.10 [27,28].

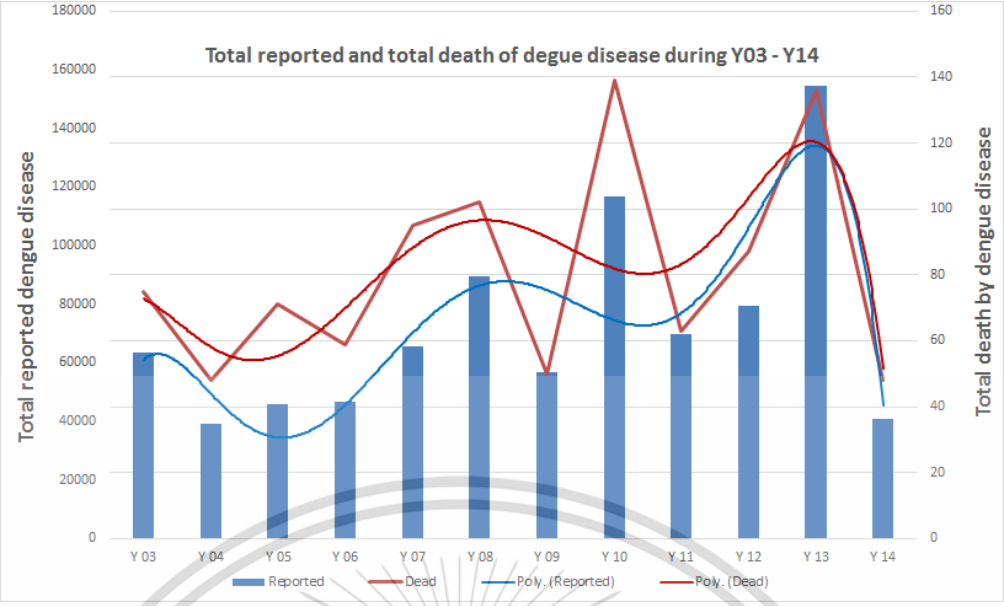


Figure 4.10 Dengue disease in Thailand during 2003 – 2014 [3]

4.3 Mathematical model for transmission of dengue disease

The vector of dengue disease is *Aedes* mosquitoes which transmits the dengue virus to human by biting infected female mosquitoes. Incubation of dengue virus is around 4-10 days, during which the infected mosquito can transmit dengue virus for its entire life. When human received the dengue virus from infected mosquitoes, an infected human is the source of dengue virus for uninfected mosquito. The patients infected with dengue virus from an infected mosquito can transmit the dengue virus to mosquitoes for 4-12 days after the first symptoms occur. The transmission cycle is completed when uninfected mosquitoes feed on a human with dengue infection.

There are several mathematical models to develop the transmission mechanism of dengue disease, which the appropriated models can provide a qualitative risk assessment of the spread of dengue disease. Esteva and Vargas [31] proposed a model for the transmission of dengue fever in a constant human population and variable vector population. The global analysis was presented to establish the global stability of the endemic equilibrium. Naowarat, S. et al. [32] proposed the dynamical model for determining human susceptibility to dengue fever. The standard method was proposed to analyze the dynamical of dengue disease system. They have proposed and analyzed the dynamical transmission of Dengue fever by considering the role played without immunity in human population. They found that there are two equilibrium states, a disease-free state and endemic state. When the reproductive number is lower than one, the disease-free state is locally asymptotically stable. If reproductive number is more than one, the endemic equilibrium state is locally asymptotically stable. As the

result, if the basic reproductive number decreases below one, it can reduce the human susceptibility to the disease and can reduce the outbreak of the disease.

The works of Pongsumpun P. [33, 34, 35, and 36] proposed the mathematical models for dengue disease. The dynamical transmission with the effect of extrinsic incubation period was presented. The standard dynamical analysis to a modified Susceptible-Infected-Recovered (SIR) model included an annual variation in the length of the extrinsic incubation period was investigated [33]. It was found that the dynamical behavior of the endemic state changes as influence of the seasonal variation of the incubation period. If the influence is increased, the trajectory exhibits sustained oscillations. The dynamical transmission model for dengue disease with and without the effect of extrinsic incubation period was compared in [34]. Here, it was found that the dynamical behaviors of the endemic state changes while the influence of the seasonal variation of the incubation period become stronger. The modified mathematical model of dengue disease with effect of incubation period of virus was considered in [35] that were formulated by separating the human population into susceptible, infected, infectious and recovered classes. The vector population was divided into susceptible, infected and infectious classes. It was found in this work that the infected class reduces the periods of the oscillations in the population. The seasonal transmission model of dengue virus infection in Thailand was presented in [36]. This work concluded that the basic reproductive number in high endemic season is higher than the normalized susceptible classes decrease. And the basic reproductive number in lower endemic season is higher than normalized inflected classes increase. This behavior occurs because there is enough susceptible human to be infected from infectious mosquitoes.

Chanprasopchai P. and Pongsumpun P. [37] proposed the transmission dynamical of SIR modeling for dengue fever with vector-born infection. The infected vectors caused by both biting of infected human and vector-born infection are proposed. This work applies the standard dynamical system method to analyze the mathematical model. The stability of the model is analyzed by Routh – Hurwitz criteria. Numerical solutions show that the dynamical behaviors converge to the endemic equilibrium state and the relation between each individual variable with the biting rate of mosquito are presented. The work also found that if the mosquito biting is increased, the values basic reproductive number and susceptible human will increase while infected human and infected vector will increase.

Pongsumpun, P. and Kongnuy, R. [38, 39] presented the mathematical model to describe the transmission of dengue disease for pregnant and non-pregnant. In cases where the basic reproductive is higher, the period of oscillation is shorter. The endemic

equilibrium points for proportion of susceptible pregnant and non-pregnant decrease and proportion of infective pregnant and non-pregnant and infective vector decrease. These behaviors occur when there is enough of susceptible pregnant and non-pregnant to be infected from infectious vector. Application of an ultra-low volume amount of insecticide could reduce the basic reproductive number lower than one and the basic reproductive number would return to above one once the application is stopped. Since the endemic state is local stable, the dengue disease would return. So, the eradication program would have to be a continued one which can increase the outbreak of dengue disease.

Mathematical model is used to analyze and investigate the dengue disease. The basic reproductive number from mathematical analysis is applied to control the outbreak of dengue disease. The outbreak will spread when the basic reproductive number value is lower than one. On another hand, when the basic reproductive number is lower than one, it can control the outbreak. As the current, there is no specific treatment and vaccination for dengue disease. The best way to control the outbreak is to control spreading of infected mosquitoes.

4.4 Discussion and conclusion

Dengue disease is one of the diseases of international concern affecting human around the world, especially in tropical and sup-tropical area. Dengue disease is caused by mosquito which is more dangerous as shown in Figure 4.1. Global incidence of dengue disease has increased dramatically in the current decade, and around half of world's population is living in risk area which has reported of dengue disease as detail in Figure 1.1. It is not only the number of reported increasing but also the dengue disease spreads to new area that the dengue disease is endemic in more than 100 countries. Thailand had reported the dengue disease cases since 1950 with the first outbreak in 1958. The historical dengue disease cases in Thailand is shown in Figure 4.2. Figure 4.3 and Figure 4.4 show the reported cases and death of dengue disease by region. The monthly report cases and death are presented in Figure 4.5 and Figure 4.6. The reported dengue disease occurrences by age is shown in Figure 4.7 while Figure 4.8 presents the reported dengue disease occurrences by occupation. The dengue disease situation in year, 2015, is shown in figure 4.9, while the trend of occurrences and death of dengue disease is also proposed in Figure 10.

The mathematical model of dengue disease has developed for a long time. The popular one was proposed by Esteva, L. and C. Vargas in 1999 [31]. Many researchers developed different mathematical models to find the way to control the outbreak.

The reproductive number is used to control the outbreak. It is generally known that if the reproductive number below one, the outbreak would decrease. At present, the method to control the transmission of dengue disease is mainly through the control of the spread, such as environmental management of egg laying, waste disposing, and water storage. The community participation and mobilization will improve the sustained mosquito control and the insecticides spraying during outbreak is the one of emergency vector control. Active monitoring of mosquitoes should continue to control the outbreak [1,2].

Chapter 5

The effect of rainfall for the dynamical transmission model of the dengue disease in Thailand

In this chapter, the SEIR (Susceptible-Exposed-Infected-Recovered) model is used to describe the transmission of dengue virus. The main contribution is determining the role of the rainfall in Thailand in the model. The transmission of dengue disease is assumed to depend on the nature of the rainfall in Thailand. We analyze the dynamical transmission of dengue disease. The stability of the solution of the model is analyzed. It is investigated by using the Routh-Hurwitz criteria. We find two equilibrium states: a disease free state and an endemic equilibrium state. The basic reproductive number (R_0) is obtained, indicating the stability of each equilibrium state. Numerical results taking into account the rainfall is obtained and they are seen to correspond to the analytical results.

5.1 Introduction

Dengue disease is caused by the dengue virus that is transmitted to human by the bite of a mosquito. The mosquito is the vector of this disease. The spread of dengue disease depends on the contact between the human and the mosquitoes. Therefore, the way to control dengue virus transmission is to either control the mosquito vectors or interrupt the human-vector contact [1]. Outbreaks of dengue disease often occur in most tropical countries around the world, with close to 75% of the global population exposed to the disease living in the Asia-Pacific region [2]. Four serotypes of the dengue virus, DEN1–DEN4, are responsible for the disease in humans. They are all transmitted to human through the bites of infected *Aedes aegypti* and *Aedes albopictus* mosquitoes. When the mosquitoes are in immature or lava stages, they are usually found in water-filled habitats such as water containers close to dwellings of humans. In the adult stages, the mosquitoes may spend most of their lifetimes around the homes of humans. This would lead to the mosquitoes being able to transmit the dengue virus rapidly between the communities.

In Thailand, dengue disease has been reported nationwide in all parts of Thailand, including the Bangkok metropolitan area in which three forms of dengue disease, dengue fever (DF), dengue hemorrhagic fever (DHF), and dengue shock syndrome (DSS), were reported. The three categories are based on the clinical presentation of patients. The most severe form of dengue disease is DSS [1, 2]. It reappears on a regular basis every year with the peak during the rainy season, June–August. The amount of rainfall is the single most important factor for dengue virus

transmission, since this condition is most suitable for mosquitoes to lay their eggs and for the humans and mosquito to come into contact. The historical data in Thailand indicates that the number of reported cases correlates with the average amount of rainfall. The relationships between average monthly dengue reported cases and average monthly amount of rainfall during 2003–2015 in Thailand and Bangkok metropolitan area are presented in Figures 5.1 and 5.2, respectively [40].

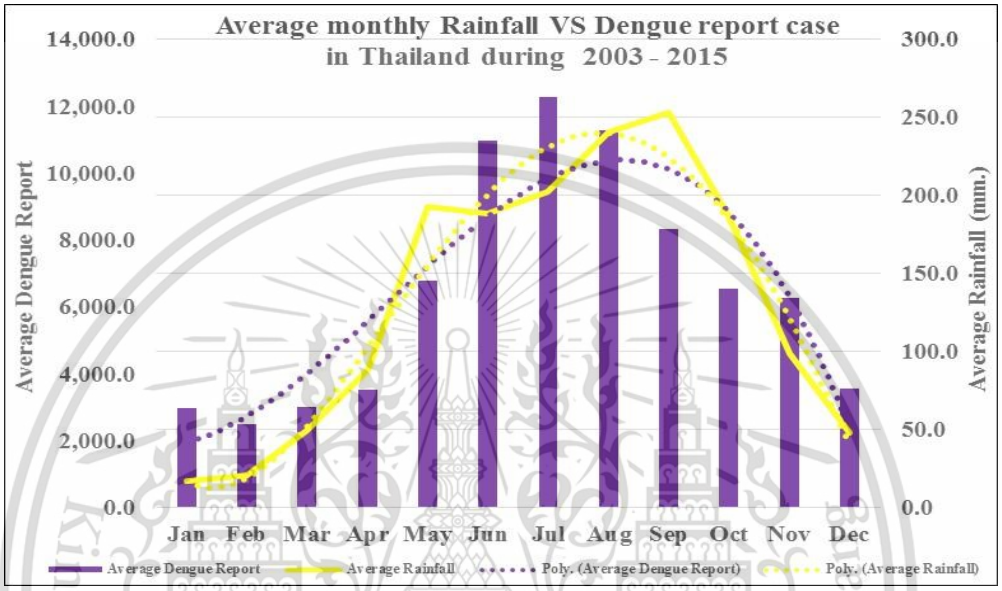


Figure 5.1 Average monthly rainfall and dengue reported cases during 2003–2015 in Thailand [40].

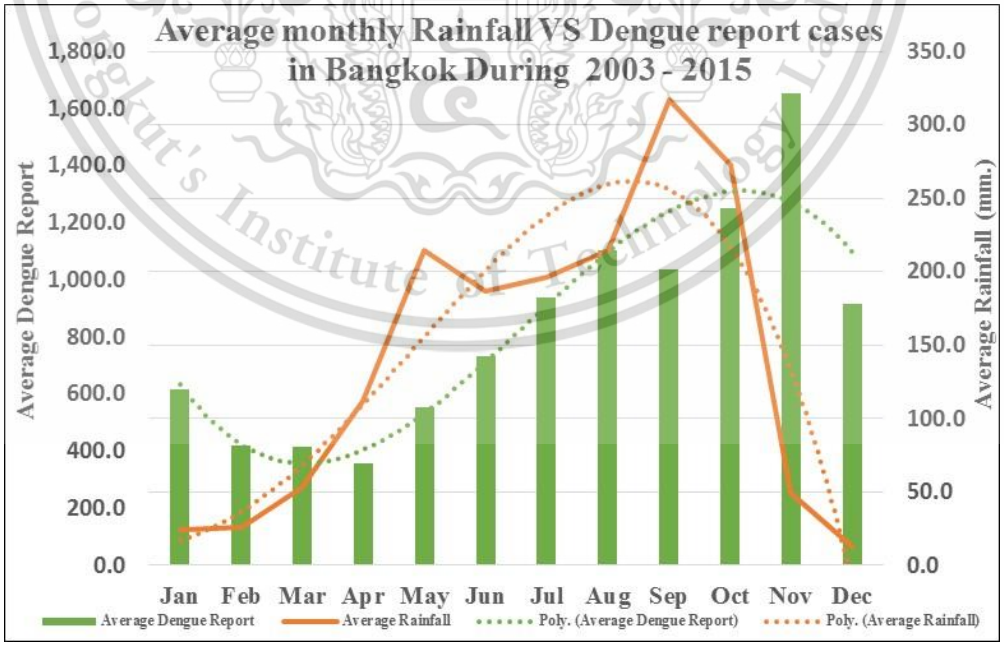


Figure 5.2 Average monthly rainfall and dengue reported cases during 2003–2015 in Bangkok [40].

As we can see from Figures 1 and 2, the correlation between the amount of rainfall and the number of reported cases of dengue disease in the period of this study is cosine function dependence corresponding to the study of Stolwijk et al. [41]. When mosquito bites an infectious human being, the mosquito will be feeding on the infected blood. As a consequence, the mosquito receives the dengue viruses and will be a vector for the transmission of the dengue viruses. The dengue disease epidemic can then be analyzed in order to determine a set of parameter values that will allow a strategy to control the spread of the disease when other factors are taken into account. The mathematical model to be developed will be a SEIR (Susceptible-Exposed-Infected-Recovered) mathematical model. Mathematical models have long been used to describe the dengue transmission.

Esteva and Vargas [31] proposed a model with a constant human population and variable vector population model to describe the transmission of dengue disease and studied the global stability of the endemic equilibrium. Polwiang [42] presented a mathematical model for general vector-host infectious disease and used the reproduction number as a means to evaluate the potential, severity, and persistence of dengue infection. The dengue infection will depend on the seasonal variation of the climate and the rainfall which will affect the breeding pool for the mosquitoes to lay their eggs and to develop into the adult stage. Rodrigues et al. [43] presented disease transmission with the effects of seasonality on the vectorial capacity and, consequently, on the disease development. Using entomological information of the mosquito's behavior under different temperatures and rainfall, the time development of the epidemics was simulated and analyzed. Chompoosri et al. [44] introduced seasonal dengue infection rates in the *Aedes aegypti* mosquitoes to study the dengue infection in suspected patients in 4 central provinces of Thailand. Dengue morbidity rates used for the patients in all 4 provinces were taken to be the highest in rainy season. Kesorn et al. [45] discovered that the *Aedes aegypti* female and larvae mosquito infection rates significantly positively associated with the morbidity rate, where the increasing infection rate of female mosquitoes and larvae led to a higher number of dengue cases. This result supports regarding the largest female populations to be present in the rainy season (May-June) in Thailand, in which the biting activity rate of female mosquito increases and more dengue cases occur. Siriyasatien et al. [46] found that female mosquitoes and seasons were strongly correlated with dengue cases in Thailand in which infected female mosquitos together with season are directly correlated to the number of dengue cases. Pongsumpun and Tang [47] analyzed a model when a seasonal variation in the incubation period of the virus while it was developing in the mosquito was included in the model. The annual variation in the length of the extrinsic incubation period was considered by using standard dynamical

modeling method to analyze the Susceptible-Exposed-Infected-Recovered (SEIR) model. Chanprasopchai and Pongsumpun [37] used a mathematical model for transmission dynamical of dengue based on the Susceptible-Infected-Recovered (SIR) model. The standard dynamical modeling techniques were used to analyze that model. Relations between each individual variable in the model and the biting rate of mosquito were obtained. Sungchasit et al. [48] later proposed a transmission model of dengue virus in which there were two mosquito species, *Aedes aegypti* and *Aedes albopictus,* causing the infection. Separate SIR (Susceptible-Infected-Recovered) models were proposed to describe the dengue virus transmission by two mosquito species. Pongsumpun and Tang [49] proposed the transmission of dengue hemorrhagic fever by Susceptible-Infected-Recovered model considering the influence of age structure in human population. Human population was divided into two groups, adult and juvenile groups, in order to analyze the dengue disease transmission and the equilibrium state, stability, and numerical calculation were presented. Adams et al. [50] proposed the epidemic pattern observed in Bangkok regarding the result of cross-protective immunity and presented significantly altered changes in the interserotypic immune reaction. They used records of the annual number of confirmed cases of dengue in Bangkok between 1977 and 2000 and used a mathematical model based on standard SIR formulation forced with an annually periodic transmission rate cosine function representing seasonal fluctuations in the vector population.

In this study, we consider the transmission of dengue disease by using mathematical model to investigate the dengue disease mechanism with the effect of rainy season taken into account. The transmission rates of dengue virus vary during the season. The Routh-Hurwitz criteria are applied to analyze the system stability of the SEIR model and the dynamical transmission model of dengue disease is proposed. The equilibrium state and stability, numerical simulation and results, and conclusion are presented.

5.2 Materials and Methods

5.2.1 Mathematical Model

The SEIR mathematical model consists of two population compartments, human's population and mosquito's population. Human's population includes four epidemiological states, Susceptible human $(\overline{S_H})$, Exposed human $(\overline{E_H})$, Infected human $(\overline{I_H})$, and Recovered human $(\overline{R_H})$, whereas mosquito's population is divided into 3 epidemiological states, Susceptible vector $(\overline{S_V})$, Exposed vector $(\overline{E_V})$, and Infected vector $(\overline{I_V})$. The mosquito's population cannot recover from infection which

has no recovery epidemiological states. The dynamical transmission between human's population and mosquito's populations is shown in Figure 5.3.

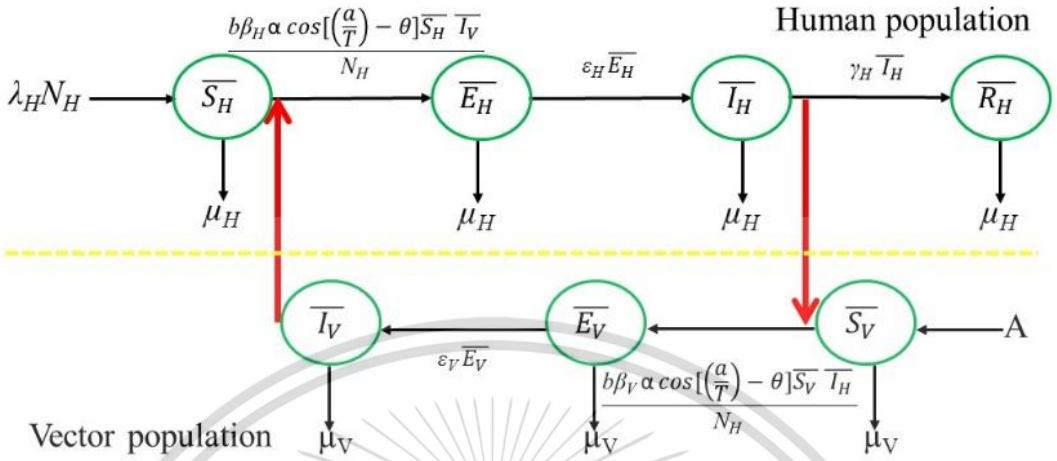


Figure 5.3 The dynamical transmission of dengue disease.

In the figure,

$\overline{S_H}(t)$ =Number of susceptible humans at any time t,

$\overline{S_V}(t)$ =Number of susceptible vector at any time t,

$\overline{E_H}(t)$ =Number of exposed humans at any time t,

$\overline{E_V}(t)$ =Number of exposed vector at any time t,

$\overline{I_H}(t)$ =Number of infected humans at any time t,

$\overline{I_V}(t)$ = Number of infected vector at any time t,

$\overline{R_H}(t)$ = Number of recovered humans at any time t,

β_H = Transmission probability of dengue virus from vector to human,

β_V = Transmission probability of dengue virus from human to vector

ε_H = Intrinsic incubation rate,

ε_V = Extrinsic incubation rate,

μ_H = Death rate of human,

μ_V = Death rate of vector,

γ_H = Recovery rate of human,

λ_H = Birth rate of human,

A = Constant recruitment rate,

b = Biting rate,

α = Amplitude,

θ = Horizontal shift of the cosine function,

a = Time period, and

T = Number of time periods.

To simplify the model, we assume that both the human and mosquito populations are constant and there is no vertical transmission; that is, the eggs cannot be infected by sexual contacts between the male and female mosquitoes. It means that total human population is $N_H = \overline{S_H} + \overline{E_H} + \overline{I_H} + \overline{R_H}$ and total mosquito population is $N_V = \overline{S_V} + \overline{E_V} + \overline{I_V}$. The mathematical descriptions of the processes shown in Figure 5.3 are the seven differential equations given as follows:

$$\left.\begin{aligned}
\frac{d\overline{S_H}}{dt} &= \lambda_H N_H - \mu_H \overline{S_H} - \frac{b\beta_H \alpha \cos[(\frac{a}{T}) - \theta]}{N_H} \overline{S_H}\,\overline{I_V} \\
\frac{d\overline{E_H}}{dt} &= \frac{b\beta_H \alpha \cos[(\frac{a}{T}) - \theta]}{N_H} \overline{S_H}\,\overline{I_V} - \varepsilon_H \overline{E_H} + \mu_H \overline{E_H} \\
\frac{d\overline{I_H}}{dt} &= \varepsilon_H \overline{E_H} - \mu_H \overline{I_H} - \gamma_H \overline{I_H} \\
\frac{d\overline{R_H}}{dt} &= \gamma_H \overline{I_H} - \mu_H \overline{R_H}
\end{aligned}\right\} \tag{5.1}$$

$$\left.\begin{aligned}
\frac{d\overline{I_V}}{dt} &= \varepsilon_V \overline{E_V} - \mu_V \overline{I_V} \\
\frac{d\overline{E_V}}{dt} &= \frac{b\beta_V \alpha \cos[(\frac{a}{T}) - \theta]}{N_H} \overline{S_V}\,\overline{I_H} - \varepsilon_V \overline{E_V} + \mu_V \overline{E_V} \\
\frac{d\overline{S_V}}{dt} &= A - \frac{b\beta_V \alpha \cos[(\frac{a}{T}) - \theta]}{N_H} \overline{S_V}\,\overline{I_H} - \mu_V \overline{S_V}
\end{aligned}\right\} \tag{5.2}$$

Since we have assumed that the total human and mosquito populations are constant, we have

$$\left.\begin{aligned}
\frac{d\overline{S_H}}{dt} + \frac{d\overline{E_H}}{dt} + \frac{d\overline{I_H}}{dt} + \frac{d\overline{R_H}}{dt} &= 0 \\
\frac{d\overline{I_V}}{dt} + \frac{d\overline{E_V}}{dt} + \frac{d\overline{S_V}}{dt} &= 0
\end{aligned}\right\} \tag{5.3}$$

with

$$\left.\begin{aligned}
N_V &= A/\mu_V \\
\lambda_H &= \mu_H
\end{aligned}\right\} \tag{5.4}$$

Equations (5.1) and (5.2) can be normalized as follows: we first define the normalized variables as

$$\left.\begin{aligned}
S_H = \frac{\overline{S_H}}{N_H}, E_H = \frac{\overline{E_H}}{N_H}, I_H = \frac{\overline{I_H}}{N_H}, R_H = \frac{\overline{R_H}}{N_H}, \\
S_V = \frac{\overline{S_V}}{N_V}, E_V = \frac{\overline{E_V}}{N_V}, I_V = \frac{\overline{I_V}}{N_V}
\end{aligned}\right\} \tag{5.5}$$

with

$$\left.\begin{aligned}
S_H + E_H + I_H + R_H &= 1 \\
S_V + E_V + I_V &= 1
\end{aligned}\right\} \tag{5.6}$$

Then, there are only five independent variables and only five differential equations are needed. We pick them to be:

$$\left.\begin{aligned}
\frac{dS_H}{dt} &= \mu_H - \mu_H S_H - \frac{b\beta_H \alpha \cos[(\frac{a}{T}) - \theta]}{N_H} S_H I_V N_V \\
\frac{dE_H}{dt} &= \frac{b\beta_H \alpha \cos[(\frac{a}{T}) - \theta]}{N_H} S_H I_V N_V - \varepsilon_H E_H - \mu_H E_H \\
\frac{dI_H}{dt} &= \varepsilon_H E_H - \mu_H I_H - \gamma_H I_H \\
\frac{dE_V}{dt} &= b\beta_V \alpha \cos[(\frac{a}{T}) - \theta] S_V I_H - \varepsilon_V E_V - \mu_V E_V \\
\frac{dI_V}{dt} &= \varepsilon_V E_V - \mu_V I_V
\end{aligned}\right\} \quad (5.7)$$

We now have five differential equations involving five independent normalized population groups $(S_V, E_H, I_H, S_V, I_V)$. We can set the RHS of equation (5.7) to zero and find the equilibrium (time-independent) populations. There will be two equilibrium states for each population group, a disease-free equilibrium point and an endemic equilibrium point (one with $I_V^{1(2)} = 0$ and the other $\neq 0$). Calling the five equilibrium points for the five populations X_i *(i=1, 2, ... ,5)* and letting each of the independent population groups be equal to the equilibrium point plus a perturbation V_i which is time-dependent, we insert these new forms of the solution into equation (5.7) and expand the RHS about the equilibrium populations. Doing this, we get the 5x5 matrix equation.

$$\frac{\mathrm{dV}}{\mathrm{dt}} = \mathrm{JV} \quad (5.8)$$

Where *J* is the gradient matrix evaluated at the equilibrium points or "the Jacobian matrix."

5.2.2 Mathematical Analysis for equilibrium point

The stability of the solutions of equation (5.7) will be considered for 2 cases, one where $\theta \neq a/T$ and one where $\theta = a/T$. It should be noted when $\theta = a/T$, equation (5.7) will be the standard case of SEIR model, where no effects of rainfall are taken into account. For $\theta \neq a/T$, the value of cosine function will change during the rainy season and will vary according to the amount of rainfall, meaning that the rate of transmission will change during the rainy season. The change in rate could be due to the fact that more eggs can be laid or developed quicker or slower depending on the amount of rain that has fallen. It is also well known that climatic factors control the development of the mosquitoes and of the dengue virus.

In either case, the equilibrium points must first be determined. This is done by setting the right-hand side of equation (5.7) to zero. Doing this, we obtain two solutions: one will be the disease-free equilibrium point (E_1) and the other will be the endemic

equilibrium point (E_2). The two possible solutions depend on whether we take $I_V = 0$ or $I_V \neq 0$. After much work, we find that

$$E_1(t) = (S_H^1 = 1, E_H^1 = 0, I_H^1 = 0, E_V^1 = 0, I_V^1 = 0),$$
$$E_2(t) = (S_H^{2*}(t), E_H^{2*}(t), I_H^{2*}(t), E_V^{2*}(t), I_V^{2*}(t)) \quad (5.9)$$

where

$$S_H^{2*}(t) = \frac{\sec[a/T-\theta](\varepsilon_V+\mu_V)(b\alpha\cos[a/T-\theta]N_H\beta_V\varepsilon_H\mu_H + (\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V)}{b\alpha\beta_V\varepsilon_H(b\alpha\cos[a/T-\theta]N_V\beta_H\varepsilon_V + N_H\mu_H(\varepsilon_V+\mu_V))},$$

$$E_H^{2*}(t) = -\frac{\sec[a/T-\theta]\mu_H\left(-2b^2\alpha^2\cos[a/T-\theta]^2 N_V\beta_H\beta_V\varepsilon_H\varepsilon_V + 2(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V(\varepsilon_V+\mu_V)\right)}{2b\alpha\beta_V\varepsilon_H(\varepsilon_H+\mu_H)(b\alpha\cos[a/T-\theta]N_V\beta_H\varepsilon_V + N_H\mu_H(\varepsilon_V+\mu_V))},$$

$$I_H^{2*}(t) = -\frac{\sec[a/T-\theta]\mu_H\left(-2b^2\alpha^2\cos[a/T-\theta]^2 N_V\beta_H\beta_V\varepsilon_H\varepsilon_V + 2(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V(\varepsilon_V+\mu_V)\right)}{2b\alpha\beta_V(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)(b\alpha\cos[a/T-\theta]N_V\beta_H\varepsilon_V + N_H\mu_H(\varepsilon_V+\mu_V))}, \quad (5.10)$$

$$E_V^{2*}(t) = -\frac{\sec[a/T-\theta]N_H\mu_H\mu_V\left(-2b^2\alpha^2\cos[a/T-\theta]^2 N_V\beta_H\beta_V\varepsilon_H\varepsilon_V + 2(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V(\varepsilon_V+\mu_V)\right)}{2b\alpha N_V\beta_H\varepsilon_V(\varepsilon_V+\mu_V)(b\alpha\cos[a/T-\theta]N_H\beta_V\varepsilon_H\mu_H + (\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V)},$$

$$I_V^{2*}(t) = -\frac{\sec[a/T-\theta]N_H\mu_H\left(-2b^2\alpha^2\cos[a/T-\theta]^2 N_V\beta_H\beta_V\varepsilon_H\varepsilon_V + 2(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V(\varepsilon_V+\mu_V)\right)}{2b\alpha N_V\beta_H(\varepsilon_V+\mu_V)(b\alpha\cos[a/T-\theta]N_H\beta_V\varepsilon_H\mu_H + (\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V)}.$$

All parameters in the system should be positive definite and the epidemic region of system will be restricted to the region of interest given by

$$\Omega = \left\{E_1, E_2 : 0 \le S_H^1, S_H^{2*}, E_H^1, E_H^{2*}, I_H^1, I_H^{2*}, E_V^1, E_V^{2*}, I_V^1, I_V^{2*} \le 1\right\} \quad (5.11)$$

5.2.3 Mathematical Analysis for local stability

The equilibrium states are locally asymptotically stable if all the eigenvalues obtained by solving the eigenvalues equation Det $|J-\lambda I| = 0$ have negative imaginary parts. This will be true if the characteristic equation has coefficients which satisfy the Routh-Hurwitz criteria. Performing the calculations, we find that the Jacobian matrix for equation (5.7) is just

$$J = \begin{bmatrix} -\mu_H - \frac{b\beta_H\alpha\cos[(\frac{a}{T})-\theta]}{N_H}I_V N_V & 0 & 0 & 0 & -\frac{b\beta_H\alpha\cos[(\frac{a}{T})-\theta]}{N_H}S_H N_V \\ \frac{b\beta_H\alpha\cos[(\frac{a}{T})-\theta]}{N_H}I_V N_V & -(\varepsilon_H+\mu_H) & 0 & 0 & \frac{b\beta_H\alpha\cos[(\frac{a}{T})-\theta]}{N_H}S_H N_V \\ 0 & \varepsilon_H & -(\mu_H+r_H) & 0 & 0 \\ 0 & 0 & b\beta_V\alpha\cos[(\frac{a}{T})-\theta](1-I_V-E_V) & -(\varepsilon_V+\mu_V) & 0 \\ 0 & 0 & 0 & \varepsilon_V & -\mu_V \end{bmatrix} \quad (5.12)$$

The stability is usually expressed in terms of what is known as the basic reproduction number. This is the number of secondary infections which is produced by a case of an infection in a population of its infectious period ($\sqrt{R_0}$). This number is the best indicator of the potential for disease transmission.

Proposition 5.1. The equilibrium state E_1 is asymptotically stable when R_0 is lower than 1; that is, $R_0 < 1$ and $\theta \neq a/T$.

Proof. The local stability of E_1 is governed by linearization of equation (5.7). The R_0 is shown below. Rearranging the expressions for the equilibrium values of I_H or E_H. So that they would be in a form α *R-1*, we find that R_0 will be of the following form:

$$R_0 = \frac{b^2\alpha^2 \mathrm{Cos}[\frac{2\pi t}{T} - \theta]^2 N_V \beta_H \beta_V \varepsilon_H \varepsilon_V}{N_H \mu_V (\gamma_H + \mu_H)(\varepsilon_H + \mu_H)(\varepsilon_V + \mu_V)} \tag{5.13}$$

The eigenvalues of equation (5.12) are used to evaluate the disease-free equilibrium point which is determined by solving

$$\text{Det } |J - \lambda I| = 0, \tag{5.14}$$

where JE_1 is the Jacobian matrix at the equilibrium point E_1, λ are eigenvalues, and I_5 is identity 5 × 5 matrix.

Evaluating the determinant of equation (5.12), we obtain the following characteristic equation:

$$(\lambda + \mu_H)(\lambda^4 + e_1\lambda^3 + e_2\lambda^2 + e_3\lambda^1 + e_4) = 0 \tag{5.15}$$

where

$$\begin{aligned}
e_1 &= \gamma_H + \varepsilon_H + \varepsilon_V + 2(\mu_H + \mu_V) \\
e_2 &= \varepsilon_H(\gamma_H + \varepsilon_V + \mu_H + 2\mu_V) + \varepsilon_V(\gamma_H + 2\mu_H + \mu_V) + \quad (\gamma_H\mu_H + \mu_H^2 + 2\gamma_H\mu_V + 4\mu_H\mu_V + \mu_V^2) \\
e_3 &= \varepsilon_H(\gamma_H\varepsilon_V + \varepsilon_V\mu_H + 2\gamma_H\mu_V + \varepsilon_V\mu_V + 2\mu_H\mu_V + \mu_V^2) + \varepsilon_V(\gamma_H\mu_H + \mu_H^2 + \gamma_H\mu_V + 2\mu_H\mu_V) + \mu_H\mu_V(\mu_H + \mu_V) + \\
&\gamma_H(2\mu_H\mu_V + \mu_V^2) \\
e_4 &= \left(b^2\alpha^2 \mathrm{Cos}\left[\frac{2\pi t}{T} - \theta\right]^2 N_V\beta_H\beta_V\varepsilon_H\varepsilon_V\right) + \quad (\gamma_H + \mu_H)(\varepsilon_H + \mu_H)\mu_V(\varepsilon_V + \mu_V)
\end{aligned} \tag{5.16}$$

Routh-Hurwitz criteria required for all of the eigenvalues (solutions) defined by equation (5.12) are negative real parts and the coefficients must satisfy all conditions given as follows:

$$\left.\begin{aligned} &e_1 > 0, e_3 > 0, e_4 > 0 \\ &e_1e_2e_3 > e_3^2 + e_1^2e_4 \end{aligned}\right\} \tag{5.17}$$

When this happens and for $R_0 < 1$, disease-free equilibrium will be stable as is seen in Figure 5.4.

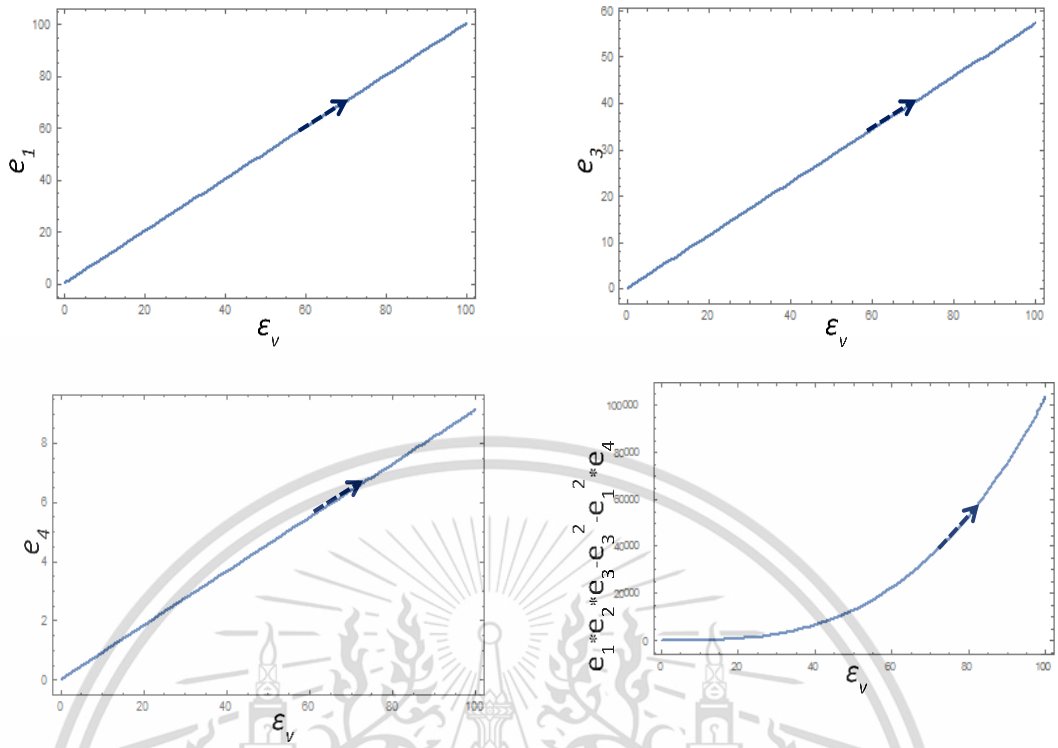


Figure 5.4 All parameters spaces of disease free equilibrium of E_1 are satisfied the Routh-Hurwitz criteria. All parameter value are N_H= 9,200, b=1/3, μ_H =1/(70*365), λ_H =1/3, β_H =0.1, β_V =0.1 μ_V =1/14, ε_V =0.1428, ε_H =0.1667 and A=500.

Proposition 5.2. The equilibrium state E_2 is asymptotically stable when R_0 is higher than 1; that is, $R_0 > 1$ and $\theta \neq a/T$.

Proof. The local stability of E_2 is governed by linearization of equation (5.7). The characteristic equation is now

$$(\lambda^5 + e_1\lambda^4 + e_2\lambda^3 + e_3\lambda^2 + e_4\lambda^1 + e_5) = 0 \tag{5.18}$$

where

$$\begin{aligned}
e_1 &= (-\eta_1\eta_2\eta_3\eta_4\eta_5 + \eta_1(\eta_4\eta_5(\eta_9\eta_3 - \mu_V\eta_8) + \eta_3(\eta_8\eta_4\eta_5 + \eta_4\eta_7))) / (\eta_1\eta_3\eta_4\eta_5)\\
e_2 &= (-\eta_1\eta_2(\eta_4\eta_5(\eta_9\eta_3 - \mu_V\eta_8) + \eta_3(\eta_8\eta_4\eta_5 + \eta_4\eta_7)) + \eta_1(-\eta_9\mu_V\eta_8\eta_4\eta_5 + \eta_3\eta_8\eta_4\eta_7(\eta_9\eta_3 - \mu_V\eta_8)\\
&\quad + \eta_3(\eta_8\eta_4\eta_5 + \eta_4\eta_7))) / (\eta_1\eta_3\eta_4\eta_5)\\
e_3 &= (\eta_1(\eta_8\eta_4\eta_7(\eta_9\eta_3 - \mu_V\eta_8) - \eta_9\mu_V\eta_8(\eta_3(\eta_8\eta_4\eta_5 + \eta_4\eta_7)) - \eta_1\eta_2(-\eta_9\mu_V\eta_8\eta_4\eta_5 + \eta_3\eta_8\eta_4\eta_7 + (\eta_9\eta_3 - \mu_V\eta_8)\\
&\quad + \eta_3(\eta_8\eta_4\eta_5 + \eta_4\eta_7))) / (\eta_1\eta_3\eta_4\eta_5)\\
e_4 &= (-\eta_1\eta_9\mu_V\eta_8^2\eta_4\eta_7 + (\eta_1\eta_8^2\eta_4\eta_5\eta_6 - \eta_1\eta_2(\eta_8\eta_4\eta_7(\eta_9\eta_3 - \mu_V\eta_8) - \eta_9\mu_V\eta_8(\eta_8\eta_4\eta_5 + \eta_4\eta_7)))) / (\eta_1\eta_3\eta_4\eta_5)\\
e_5 &= (N_H\mu_H(\gamma_H + \mu_H)(\varepsilon_H + \mu_H)\mu_V(b^2\alpha^2\mathrm{Cos}[\tfrac{2\pi t}{T} - \theta]^2 N_V\beta_H\beta_V\varepsilon_H\varepsilon_V\\
&\quad - (\gamma_H + \mu_H)(\varepsilon_H + \mu_H)\mu_V(\varepsilon_V + \mu_V))) / b\alpha\mathrm{Cos}[\tfrac{2\pi t}{T} - \theta]N_H\beta_V\varepsilon_H\mu_H + (\gamma_H + \mu_H)(\varepsilon_H + \mu_H)\mu_V
\end{aligned} \tag{5.19}$$

where

$$\eta_1 = N_V \beta_H \beta_V^2 \varepsilon_H^2 \varepsilon_V$$
$$\eta_2 = (-\gamma_H - \mu_H)$$
$$\eta_3 = (-\varepsilon_V - \mu_V)$$
$$\eta_4 = \left(b\alpha \mathrm{Cos}\left[\frac{2\pi t}{T} - \theta\right] N_V \beta_H \varepsilon_V + N_H \varepsilon_V \mu_H + N_H \mu_H \mu_V\right)^2 (b\alpha \mathrm{Cos}[\frac{2\pi t}{T} - \theta] N_H \beta_V \varepsilon_H \mu_H + \gamma_H \varepsilon_H \mu_V + \gamma_H \mu_H \mu_V + \varepsilon_H \mu_H \mu_V + \mu_H^2 \mu_V)^2$$
$$\eta_5 = (b\alpha \mathrm{Cos}[\frac{2\pi t}{T} - \theta] N_H \beta_V \varepsilon_H \varepsilon_V \mu_H + \gamma_H \varepsilon_H \varepsilon_V \mu_V + b\alpha \mathrm{Cos}[\frac{2\pi t}{T} - \theta] N_H \beta_V \varepsilon_H \mu_H \mu_V + \gamma_H \varepsilon_V \mu_H \mu_V + \varepsilon_H \varepsilon_V \mu_H \mu_V + \varepsilon_V \mu_H^2 \mu_V + \gamma_H \varepsilon_H \mu_V^2 + \gamma_H \mu_H \mu_V^2 + \varepsilon_H \mu_H \mu_V^2 + \mu_H^2 \mu_V^2)$$
$$\eta_6 = (b\alpha \mathrm{Cos}[\frac{2\pi t}{T} - \theta] N_V \beta_H \gamma_H \varepsilon_H \varepsilon_V \mu_V +$$
$$b\alpha \mathrm{Cos}\left[\frac{2\pi t}{T} - \theta\right] N_V \beta_H \gamma_H \varepsilon_V \mu_H \mu_V + b\alpha \mathrm{Cos}\left[\frac{2\pi t}{T} - \theta\right] N_V \beta_H \varepsilon_H \varepsilon_V \mu_H \mu_V + N_H \gamma_H \varepsilon_H \varepsilon_V \mu_H \mu_V$$
$$+ b\alpha \mathrm{Cos}\left[\frac{2\pi t}{T} - \theta\right] N_V \beta_H \varepsilon_V \mu_H^2 \mu_V + N_H \gamma_H \varepsilon_V \mu_H^2 \mu_V N_H \varepsilon_H \varepsilon_V \mu_H^2 \mu_V + N_H \varepsilon_V \mu_H^3 \mu_V + N_H \gamma_H \varepsilon_H \mu_H \mu_V^2 \quad (5.20)$$
$$+ N_H \gamma_H \mu_H^2 \mu_V^2 + N_H \varepsilon_H \mu_H^2 \mu_V^2 + N_H \mu_H^3 \mu_V^2)$$
$$\eta_7 = (b^2 \alpha^2 \mathrm{Cos}\left[\frac{2\pi t}{T} - \theta\right]^2 N_H N_V \beta_H \beta_V \varepsilon_H \varepsilon_V \mu_H + \quad b\alpha \mathrm{Cos}[\frac{2\pi t}{T} - \theta] N_H \beta_V \varepsilon_H \varepsilon_V \mu_H^2 + \gamma_H \varepsilon_H \varepsilon_V \mu_H \mu_V$$
$$- N_H \gamma_H \varepsilon_H \varepsilon_V \mu_H \mu_V + b\alpha \mathrm{Cos}\left[\frac{2\pi t}{T} - \theta\right] N_H \beta_V \varepsilon_H \mu_H^2 \mu_V + \gamma_H \varepsilon_V \mu_H^2 \mu_V - N_H \gamma_H \varepsilon_V \mu_H^2 \mu_V + \varepsilon_H \varepsilon_V \mu_H^2 \mu_V$$
$$- N_H \varepsilon_H \varepsilon_V \mu_H^2 \mu_V + \varepsilon_V \mu_H^3 \mu_V - N_H \varepsilon_V \mu_H^3 \mu_V + \gamma_H \varepsilon_H \mu_H \mu_V^2 - N_H \gamma_H \varepsilon_H \mu_H \mu_V^2 + \gamma_H \mu_H^2 \mu_V^2 - N_H \gamma_H \mu_H^2 \mu_V^2$$
$$+ \varepsilon_H \mu_H^2 \mu_V^2 - N_H \varepsilon_H \mu_H^2 \mu_V^2 + \mu_H^3 \mu_V^2 - N_H \mu_H^3 \mu_V^2))))$$
$$\eta_8 = (\varepsilon_V + \mu_V), \text{ and}$$
$$\eta_9 = (\varepsilon_H + \mu_H)$$

The endemic equilibrium point of local stability of the system will have negative real parts when the coefficients in the characteristic equation (5.18) satisfy the Routh-Hurwitz conditions now given by

$$\left.\begin{aligned} & e_1 > 0, e2 > 0, e_3 > 0, e_4 > 0, e5 > 0 \\ & e_1 e_2 e_3 - e_3^2 - e_1^2 e_4 > 0 \\ & (e_1 e_4 - e_5)(e_1 e_2 e_3 - e_3^2 - e_1^2 e_4) - e_5 (e_1 e_2 - e_3)^2 - e_1 e_5^2 > 0 \end{aligned}\right\} \quad (5.21)$$

All conditions of equation (5.21) are satisfied for endemic equilibrium point as is evident by the behaviors seen in Figure 5.5. Next, we consider the case of $\theta = a/T$; equation (5.7) will be the standard case of SEIR model, where no effects of rainfall are taken into account. As a result, the mathematical equations describing the model are

$$\left.\begin{aligned} \frac{dS_H}{dt} &= \mu_H - \mu_H S_H - \frac{b\beta_H}{N_H} S_H I_V N_V \\ \frac{dE_H}{dt} &= \frac{b\beta_H}{N_H} S_H I_V N_V - \varepsilon_H E_H - \mu_H E_H \\ \frac{dI_H}{dt} &= \varepsilon_H E_H - \mu_H I_H - \gamma_H I_H \\ \frac{dE_V}{dt} &= b\beta_V S_V I_H - \varepsilon_V E_V - \mu_V E_V \\ \frac{dI_V}{dt} &= \varepsilon_V E_V - \mu_V I_V \end{aligned}\right\} \quad (5.22)$$

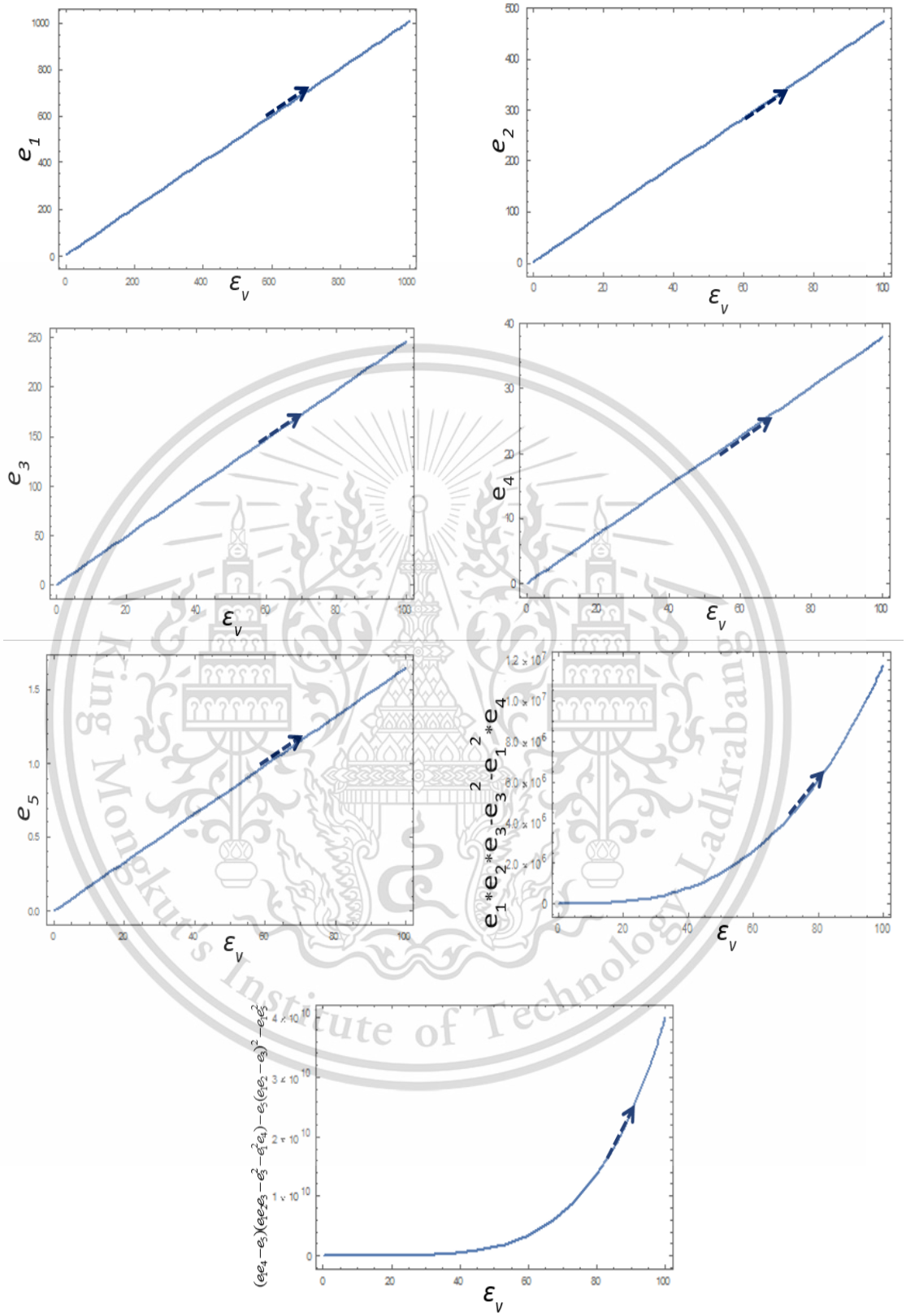


Figure 5.5 All parameters spaces of disease free equilibrium of E_2 are satisfied the Routh-Hurwitz criteria. All parameter value are N_H= *9,200*, *b=1/3*, μ_H *=1/(70*365),* λ_H *=1/3,* β_H *=0.5,* β_V *=0.3* μ_V *=1/14,* ε_V *=0.1428,* ε_H *=0.1667* and *A=500*.

R_0 obtained from equation (5.22) is as follows:

$$R_0 = \frac{b^2 N_V \beta_H \beta_V \varepsilon_H \varepsilon_V}{N_H \mu_V (\gamma_H + \mu_H)(\varepsilon_H + \mu_H)(\varepsilon_V + \mu_V)}. \quad (5.23)$$

5.3 Numerical Results

The transmission of dengue disease in this study is based on the SEIR model. The susceptible class will be people who have no immunity and who are not infectious. Human beings infected are people who are infectious, that is, able to pass on the virus onto the mosquitoes. The infectious period will be taken to be the period during which the person appears to be sick, a period of one to two weeks. When human gets well, the patient passes into the recovery class with lifelong immunity to the virus. In this study, the numerical simulations assume the following values of the parameters; $\mu_H = 1/(70 * 365)$ per day corresponding to a life expectancy of 70 years in Thai people, $A = 5{,}000$ corresponding to constant recruitment rate, $N_H = 92{,}000$ corresponding to total number of human population, and $b = 1/3$ corresponding to biting rate of vector population.

For case 1, the values of the parameters of case 1 for disease-free equilibrium are $\mu_V = 1/14$, $\gamma_H = 1/3$, $\beta_H = 0.1$, $\beta_V = 0.1$, $\varepsilon_V = 0.1428$, and $\varepsilon_H = 0.1667$ which will lead to $R_0 < 1$, while the set of values of the parameters of case 2 are $\mu_V = 1/14$, $\gamma_H = 1/3$, $\beta_H = 0.5$, $\beta_V = 0.3$, $\varepsilon_V = 0.1428$, and $\varepsilon_H = 0.1667$ which will lead to $R_0 > 1$. The trajectories of the numerical solutions for case 1 and for case 2 of S_H, E_H, I_H, E_V, and I_V are shown in the Figures 5.6 and 5.7, respectively. The trajectories of the numerical solutions for case 1 and case 2 plotted in the 2D (S_H, E_H), (S_H, I_H), (S_H, E_V), and (S_H, I_V) planes are shown in Figures 5.8 and 5.9, respectively. The trajectories of the numerical solutions for case 1 and case 2 in the 3D (S_H, E_H, I_H), (S_H, E_H, E_V), (S_H, E_H, I_V), (S_H, E_V, I_V), (E_H, E_V, I_V), and (I_H, E_V, I_V) spaces are shown in Figures 5.10 and 5.11, respectively.

5.4 Discussion and Conclusion

The effect of rainfall on the dynamical transmission of dengue disease in Thailand has been studied using the SEIR model to model the dynamical of the dengue epidemic in Thailand. The analysis is based on using the Routh-Hurwitz criteria to establish the local asymptotic stability of the equilibrium points. Two equilibrium points were found: a disease-free equilibrium point and an endemic equilibrium point. The disease-free equilibrium point, E_1, is locally asymptotically stable for $R_0 < 1$ and $\theta \neq a/T$. The set of differential equations for the SEIR model of the dengue infections were solved for different sets of numerical values of the parameters to obtain the

different trajectories of the different population groups in the model. The trajectories were projected into the 2D (S_H, E_H), (S_H, I_H), (S_H, E_V), and (S_H, I_V) planes and onto the 3D (S_H, E_H, I_H), (S_H, E_H, E_V), (S_H, E_H, I_V), (S_H, E_V, I_V), (E_H, E_V, I_V), and (I_H, E_V, I_V) spaces. These trajectories are shown in Figures 5.4, 5.6, 5.8, and 5.10, respectively. When the values of the parameters are such that $R_0 >$ and $\theta \neq a/T$, then the trajectories ending at the endemic equilibrium point, E_2, are described in Figures 5.5, 5.7, 5.9, and 5.11, respectively. The numerical results correspond to Propositions 1 and 2.

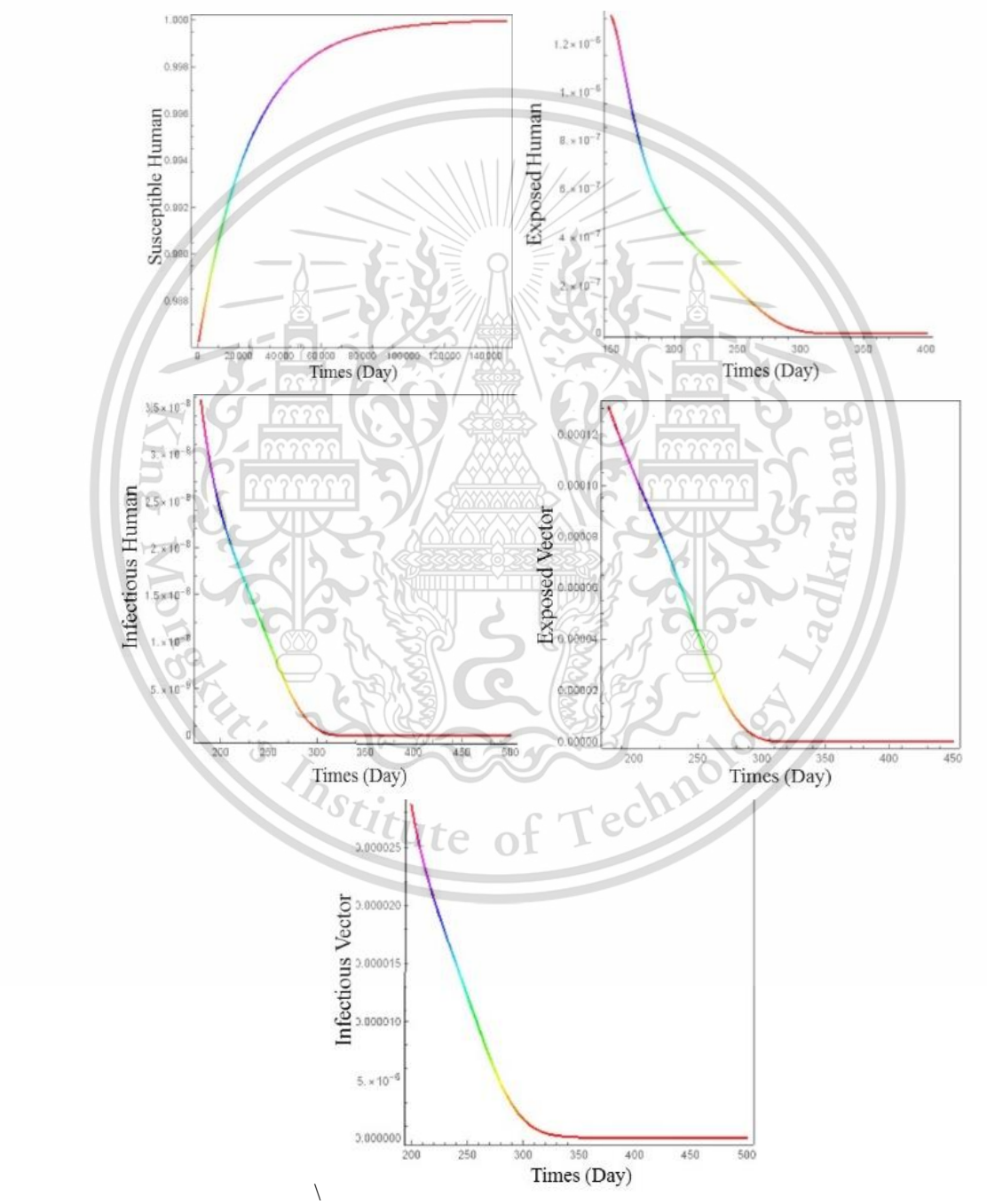


Figure 5.6 The trajectories of the time evolutions of the five population groups, S_H, E_H, I_H, E_V, and I_V towards the disease-free equilibrium.

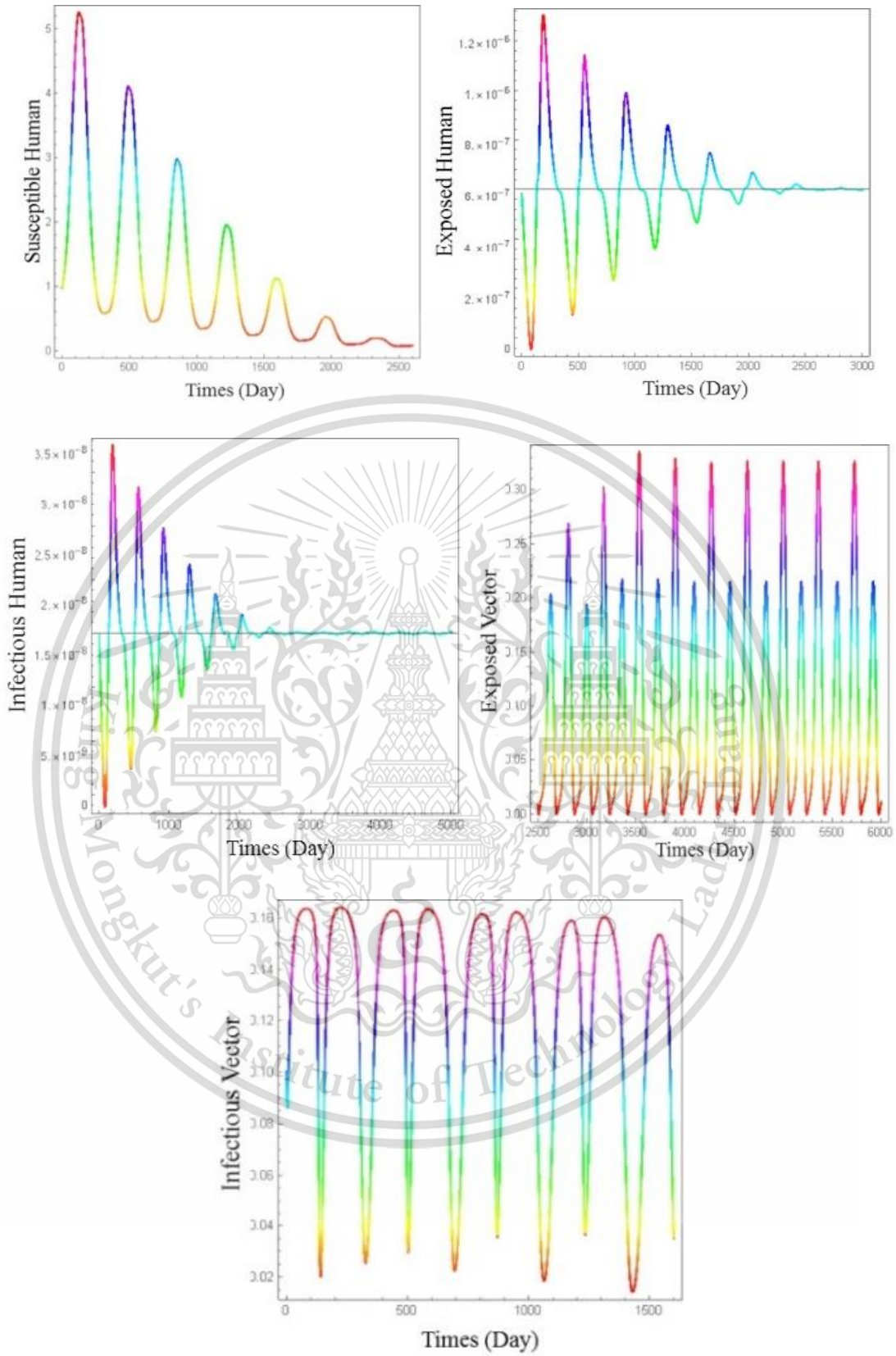


Figure 5.7 The trajectories of the time evolution of S_H, E_H, I_H, E_V, and I_V based on numerical solving.

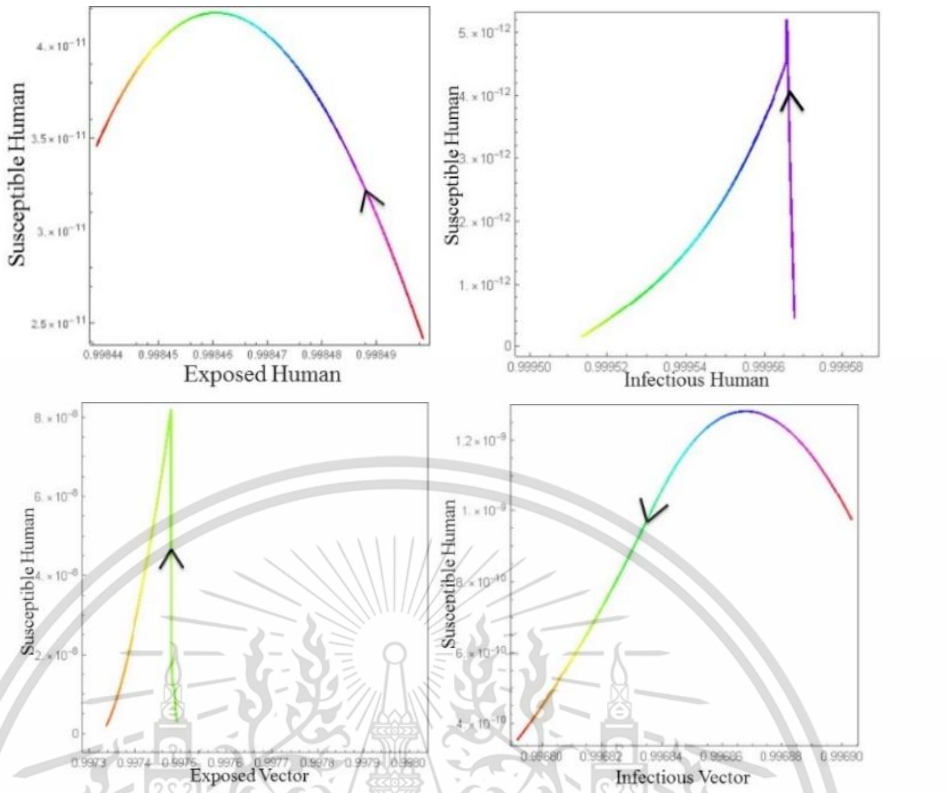


Figure 5.8 The trajectories of the numerical solutions of dengue disease for disease-free equilibrium projected onto (S_H, E_H), (S_H, I_H), (S_H, E_V), and (S_H, I_V).

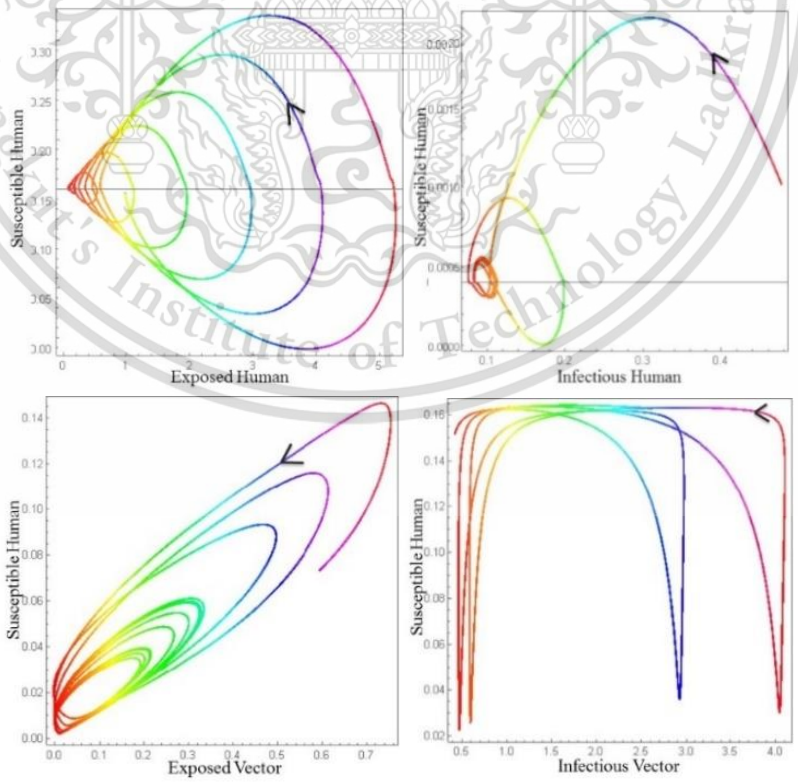


Figure 5.9 The trajectories of the numerical solutions of dengue disease for endemic equilibrium projected onto (S_H, E_H), (S_H, I_H), (S_H, E_V), and (S_H, I_V).

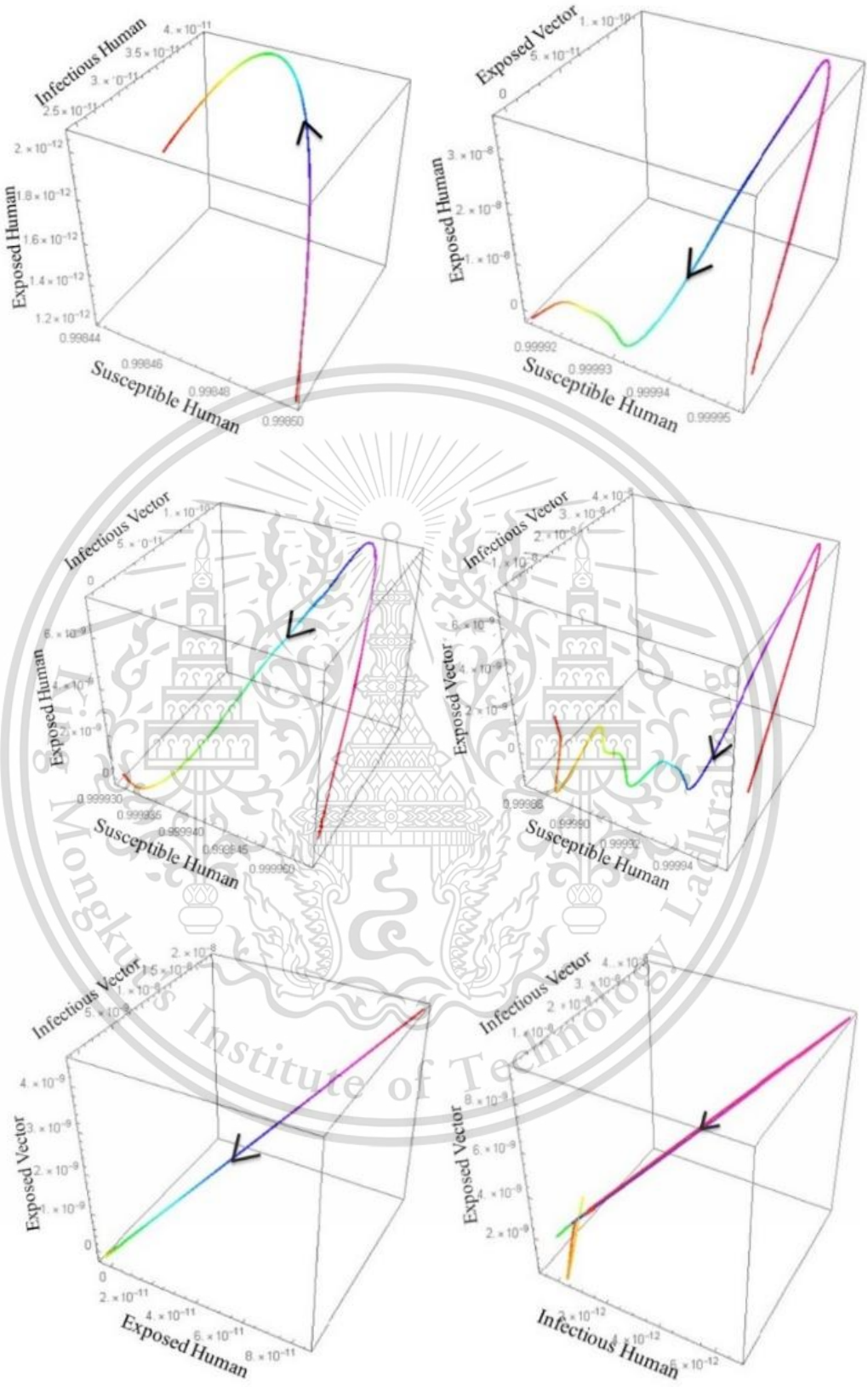


Figure 5.10 The trajectories of the numerical solutions of dengue disease for disease-free equilibrium projected onto (S_H, E_H, I_H), (S_H, E_H, E_V), (S_H, E_H, I_V), (S_H, E_V, I_V), (E_H, E_V, I_V), and (I_H, E_V, I_V).

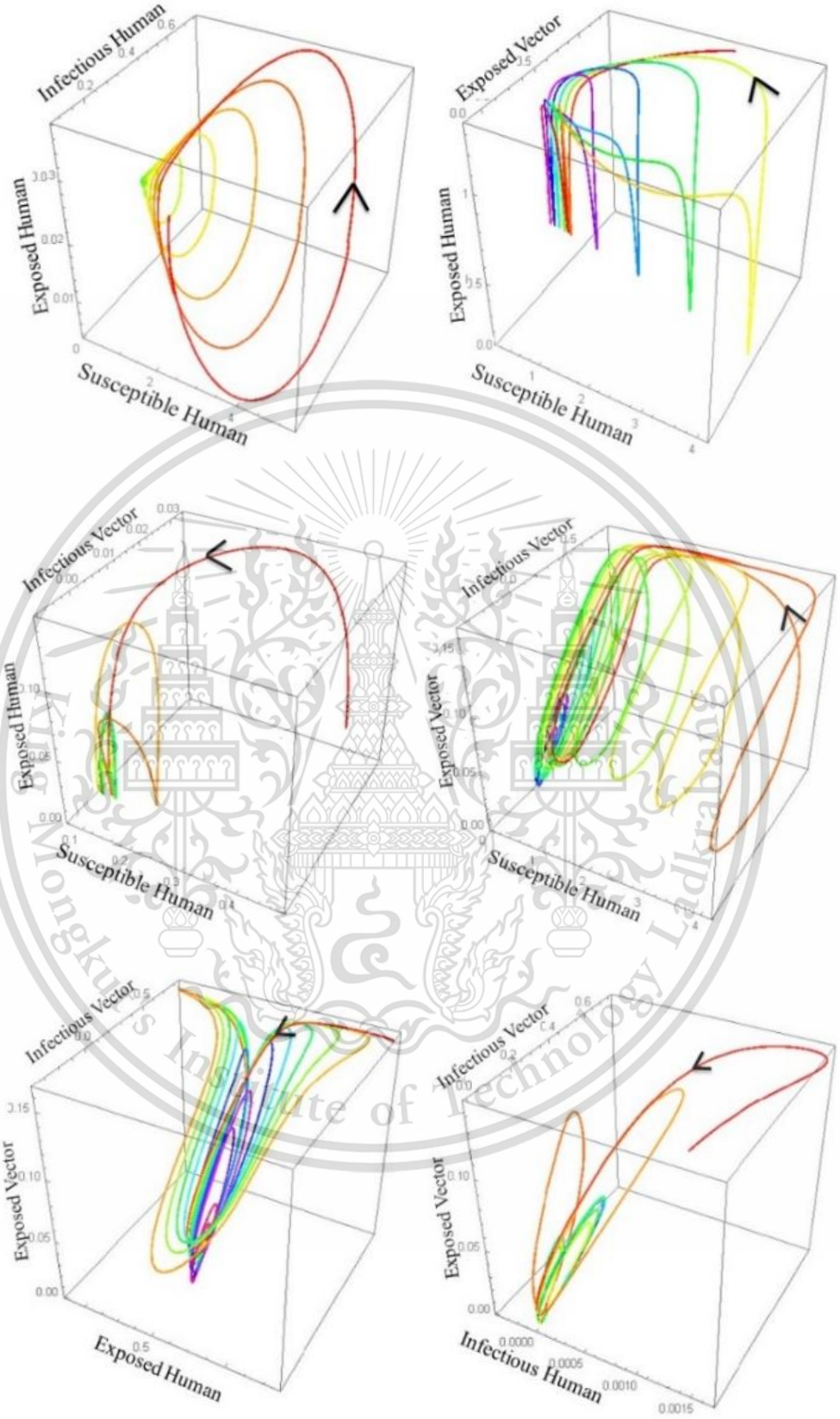


Figure 5.11 The trajectories of the numerical solutions of dengue disease for endemic equilibrium projected onto (S_H, E_H, I_H), (S_H, E_H, E_V), (S_H, E_H, I_V), (S_H, E_V, I_V), (E_H, E_V, I_V), and (I_H, E_V, I_V).

Looking at the figures, we see that everything is determined by whether $R_0 < 1$ or $R_0 > 1$; in the first case, the equilibrium state is the disease-free state, while in the second case, it is the endemic equilibrium state. Everything depends on the form of the expression for R_0. In summary, R_0 in SEIR model which includes the effect of rainfall is given by equation (5.24), while R_0 in SEIR model which ignores the effect of rainfall is given by expression equation (5.25). R_0 value of the SIR model of Esteva and Vargas [31] is given by equation (5.26) and the simplest expression is given by Rodrigues et al. [43] in equation (5.27).

$$R_0 = \frac{b^2\alpha^2 \cos\left[2\pi t/T - \theta\right]^2 N_V \beta_H \beta_V \varepsilon_H \varepsilon_V}{N_H \mu_V (\gamma_H + \mu_H)(\varepsilon_H + \mu_H)(\varepsilon_V + \mu_V)}, \tag{5.24}$$

$$R_0 = \frac{b^2 N_V \beta_H \beta_V \varepsilon_H \varepsilon_V}{N_H \mu_V (\gamma_H + \mu_H)(\varepsilon_H + \mu_H)(\varepsilon_V + \mu_V)}, \tag{5.25}$$

$$R_0 = \frac{b^2 \beta_H \beta_V N_H (A/\mu_V)}{(N_H + m)^2 \mu_V (\gamma_H + \mu_H)}, \tag{5.26}$$

$$R_0 = \frac{b^2 \beta_H \beta_V N_V}{N_H \mu_V (\gamma_H + \mu_H)}. \tag{5.27}$$

In expression equation (5.26), m is the number of alternative sources of blood, that is, other animals.

In equation (5.24), R_0 value is considered the effect of rainfall, where Thailand has correlation between rainfall and the prevalence of clinical cases of dengue [51]. Thailand's historical data indicate that rainfall was associated with dengue in many regions, for example, southern [52], northern [53], northeastern [54], and central [55] regions. Dengue disease fluctuation is related to climate variability and seasonal factor is taken into account [46, 56-60] in which the dengue virus transmission is considered as a cosine function [50, 61]. When $R_0 > 1$, this will increase the opportunity of the outbreak situation. R_0 is an important indicator, where the realistic controlling of the value of R_0 will improve the way to control the outbreak. The value of R_0 simulation of endemic equilibrium state and the average amount of rainfall are shown in Figure 5.12. It is indicated that there is a relation between the value of R_0 and the average amount of rainfall.

In addition, the suitable ways to control the dengue disease are environmental management to prevent mosquitoes from laying their eggs and breeding and using of personal household protection to prevent contact between human and mosquito [1, 2]. In the present paper, we did not explicitly take into account the egg and aquatic stages of the mosquito development (see equation (5.2)) as was done by Erickson et

al. [62] and Moulay et al. [63]. The lack of these classes precludes any discussion of the vertical transmission of the disease, since the "sexual" transmission (evidenced by the presence of the DNA fragments of the dengue virus in the larvae and pupae [64]) occurs at these stages.

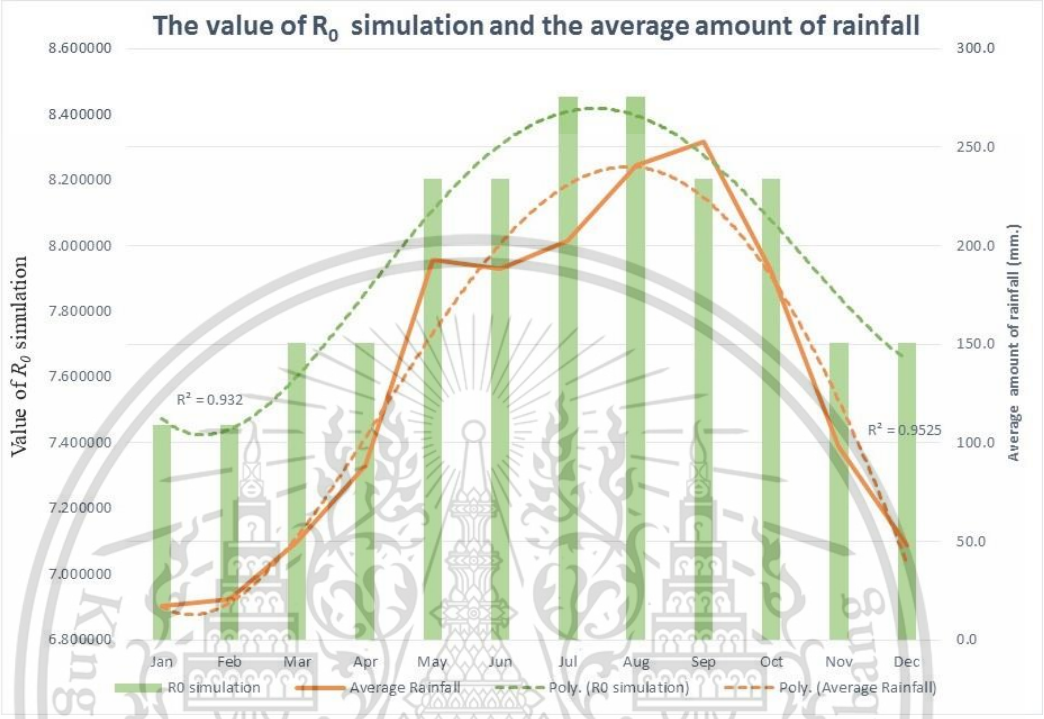


Figure 5.12 The value of R_0 simulation of endemic equilibrium state and the average amount of rainfall

Chapter 6

The SEIR dynamical transmission model of dengue disease with and without the vertical transmission of the dengue virus

In this chapter, the transmission of dengue disease when there is a possibility of vertical transmission (VT) is studied using mathematical modeling. In the normal case, the mosquito is infected by the dengue virus when it bites an infectious human being. Evidence is gathering that the mosquitoes can also be infected through sexual contact with infected male mosquito. To see the possible consequence of having this addition mode of transmission, a SEIR, Susceptible-Exposed-Infected-Recovery, model is constructed. The Routh – Hurwitz criteria are applied to the model in order establish the stability of the infection. It is seen that the model without the VT model has 2 equilibrium points, a disease-free equilibrium and an endemic equilibrium points, while the model with the VT has only an endemic equilibrium point. The numerical solutions of differential equations of the model without the VT mode exhibit dynamical behaviors that converges to the disease-free equilibrium state when basic reproduction time R_0 is less than 1 and converges to endemic equilibrium state when $R_0 > 1$. The trajectories of the numerical solutions for all possibilities (with and without VT mode) projected onto various 2D planes and 3D spaces able are presented.

6.1 Introduction

Dengue disease is found in the tropical and subtropical areas around the world such as in South-East Asia, the Western Pacific, America, African, Eastern Mediterranean, and others [1]. Dengue infection is estimated to infect 50-100 million populations with almost half of world' population living in dengue endemic countries [2]. Dengue virus has four serotypes; i.e. DEN1, DEN2, DEN3, and DEN4 and cannot transmit from human to human directly. Dengue virus is transmitted to human by the bite of infected *Aedes* mosquitoes. It means that human is the main host of the dengue virus and mosquito are the vectors of the transmission. The mosquitoes can be found around houses and be infected when they bite an infectious human. This leads to the dengue virus moving within and between communities. The way to control dengue disease is focused on the spreading of the mosquitoes.

In Thailand, dengue has been reported in from all regions including the Bangkok metropolitan area. The reported cases and death cases from 2003 to 2015 are shown in Figure 6.1. In 2015, the reported cases and deaths cases were 144,952 and 148 respectively [3]. The historical reported data is indicated that dengue disease has

potential to spread quickly with the country experiencing large epidemic in both reported cases and death. There is a high-risk potential for the spread of the dengue disease when there is a high rate of contact between the host and vector in a large population of human and mosquito (as in the Bangkok metropolitan). Rainy season is suitable for mosquito to lay their eggs and Figure 6.2 shows that there is high number of reported cases during the rainy season. Female mosquitoes will become the vector for the disease when they feed on the blood of infectious human. As the results, the mosquito will be able to transmit the virus to an uninfected human when she bites him.

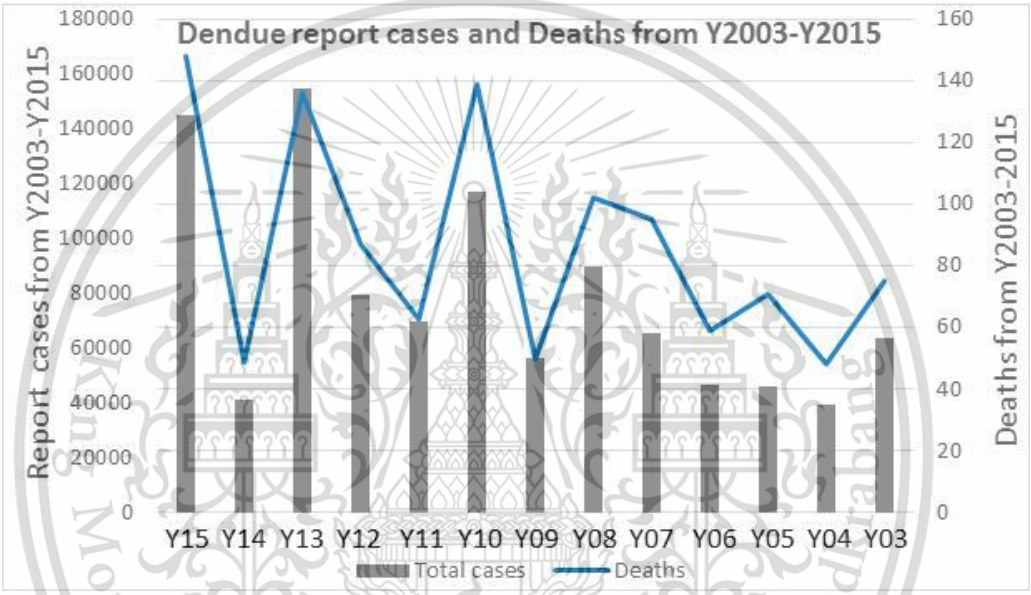


Figure 6.1 Thailand dengue reported historical data from 2003 - 2015

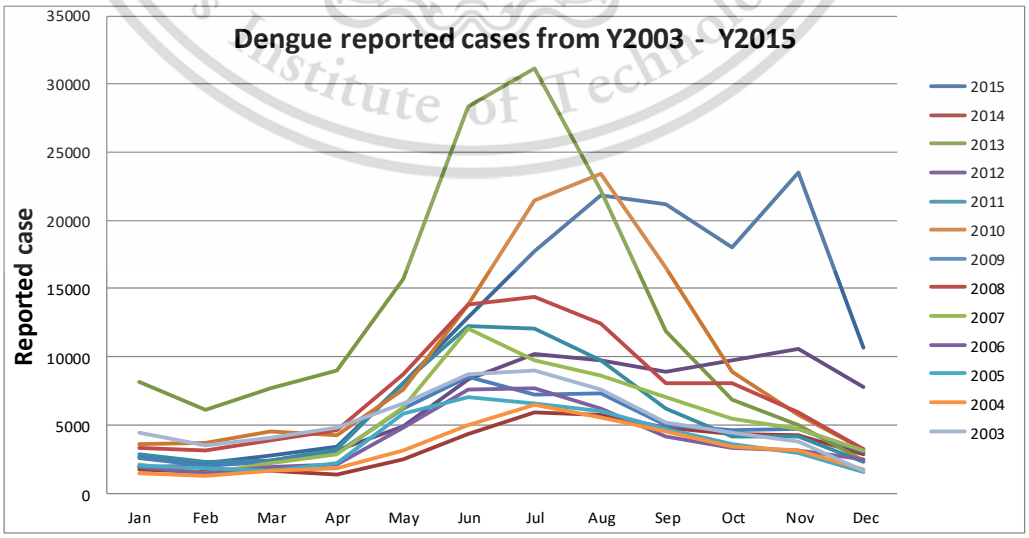


Figure 6.2 Thailand dengue reported cases from 2003 to 2015 (month by month)

A model of the dengue epidemic is necessary to better understand the mechanism and behavior in order to analyze the spread and control the spread of the disease. Mathematical models are often developed to describe the transmission of dengue disease. Esteva and Vargas [31] proposed a model for the transmission of dengue fever where the human population is constant but mosquito population varies. They provided a global analysis to establish the global stability of the endemic equilibrium. Naowarat, et al. [32] proposed a dynamical model to determine the human susceptibility to dengue fever. The standard method was used to analyze the dynamical of dengue disease system. Pongsumpun and co-workers [33, 34, 35, and 36] proposed mathematical models for dengue disease which took into account additional features of the disease. The dynamical transmission with the effect of extrinsic incubation period was included. A standard dynamical analysis was applied to a modified Susceptible-Infected-Recovered (SIR) model included an annual variation in the length of the extrinsic incubation period in the mosquito [33]. The dynamical transmission behaviors of dengue disease in the presence and absence of an extrinsic incubation period were compared [34]. In other study, the effects of there being an incubation period in the virus was studied in a SEIR model [35]. The vector populations in this model were divided into susceptible, infected and infectious classes. In a further study, a seasonal change was introduced into the transmission model used describe the dengue virus infection in Thailand [36].

Hiroshi [65] proposed a new SIR model to clarify the relative contributions of a mathematical approach and of a statistical approach to the dengue epidemiology without having to delve into the mathematical details. He introduced a new method to determine the basic reproductive number which did not involve extensive mathematical manipulations. Erickson et al. [66] used a SEIR model to examine the role of temperature in driving the vector dynamical. Their model used the Aedes albopictus mosquitoes as the transmitting vector. Bakach I. and Braselton J. [67] looked at different mathematical models and compared their predicted behaviors with each other. The evaluation of each model under different scenarios allowed one to identify the strengths and weakness of each of the model. The effect of the spreading and progression of the disease were studied in order to determine what the values of the parameters were. Rodrigues et al. [68] has also studied the transmission of dengue fever. They used their results to explain outbreak of the disease in Cape Verde. Aldila et al. [69] a host-vector dengue transmission model to determine what the optimal control strategy should be. The strategy was based on using different amounts of mosquito repellent on different segments of the human population.

In another paper, Esteva and Vargas [70] included the possibility of vertical or transovarial transmission. In this type of transmission, one does not need the host;

one can pass the virus from mosquito to mosquito without the need of a human or from human to human without the need of a mosquito. These types of transmission are vary. The rarity is seen in the report in 2010 of the first putative case of vertical transmission in China [71]. Thenozhi et al. [72] reported that they had collected mosquitoes (both male and female) in Kerala State and examined for dengue virus DNA in them. They found that some of the male mosquitoes in them. Since the males do not need human blood for the purpose of generating eggs, the most likely way would be through sexual contact. This has happened in the most recent ZIKA epidemic [73]. The ZIKA disease is also an airborne disease where the same mosquito transmitting the virus is the same virus specie transmitting the dengue fever virus. The latest report is that the ZIKA disease has become a STD (sexually transmitted disease) which needs a different form of disease control strategy. Whatever the reasons, two recent reviews have appeared in 2016 on the vertical transmission of spread of dengue fever [74 and 75].

In this chapter, it will be reconsidering the transmission of dengue virus in the case where vertical transmission of the virus between the mosquitoes is possible. We will be using the SEIR model (Susceptible, Exposed, Infected and Recovered) is used to investigate the dynamical of the disease. We will be analyzing the stability of the model using standard dynamical analysis. We will consider the dynamical transmission model of dengue disease for the cases where vertical transmission is or is not possible. The equilibrium state and stability are considered both behaviors. The numerical simulation, results and conclusion are presented.

6.2 Material and Methods

6.2.1 Mathematical Model

The mathematical model is for two populations, human and mosquito. In the SEIR model, the human is divided into four compartments, susceptible human ($\widetilde{S_H}$), exposed human ($\widetilde{E_H}$), infected human ($\widetilde{I_H}$), and re-denoted as covered human ($\widetilde{R_H}$). The vector population is partitioned into 3 compartments: susceptible vector ($\widetilde{S_V}$), exposed vector ($\widetilde{E_V}$), and infected vector ($\widetilde{I_V}$). In this model, we assumed that the total number of members of each population is constant. For the vector population, we further assume that the rate at which the number of susceptible vectors entering into mosquito population is A per unit time and M is the number of infected mosquitoes that enter directly by vertical (transovarial) infection if this type of transmission is possible. As we have mentioned, this transmission mode is rare or nonexistent. We consider the different behaviors of dynamical transmission of dengue disease with and without the effect of vertical transmission taken into account ($M \neq 0$ and $M = 0$). The

dynamical transmission of dengue disease when both modes of transmissions are possible is shown schematically in Figure 6.3.

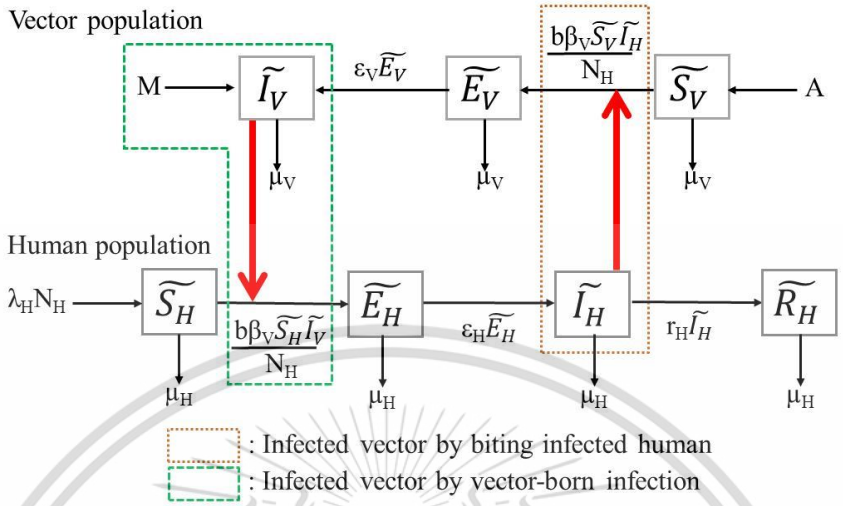


Figure 6.3 The dynamical transmission of dengue disease by both biting infected human and vector born infection

Let:

$\widetilde{S_H}$ (t) = Number of susceptible human population at time t,
$\widetilde{E_H}$ (t) = Number of exposed human population at time t,
$\widetilde{I_H}$ (t) = Number of infected human population at time t,
$\widetilde{R_H}$ (t) = Number of recovered human population at time t,
$\widetilde{S_V}$ (t) = Number of susceptible vector population at time t,
$\widetilde{E_V}$ (t) = Number of exposed vector population at time t,
$\widetilde{I_V}$ (t) = Number of vertically infected population at time t,
A = Constant recruitment rate,
M = Number of mosquitoes which were infected transovarially.

The mathematical representations of the processes shown schematically in Figure 6.3 are given by equations (6.1) to (6.7). The dynamical change of the human and mosquito populations is given by equation (6.1) to (6.4) and (6.5) to (6.7) respectively.

$$\frac{d\widetilde{S}_H}{dt} = \lambda_H N_H - \frac{b\beta_H}{N_H}\widetilde{S}_H\widetilde{I}_V - \mu_H\widetilde{S}_H \tag{6.1}$$

$$\frac{d\widetilde{E}_H}{dt} = \frac{b\beta_H}{N_H}\widetilde{S}_H\widetilde{I}_V - (\varepsilon_H + \mu_H)\widetilde{E}_H \tag{6.2}$$

$$\frac{d\widetilde{I}_H}{dt} = \varepsilon_H\widetilde{E}_H - (\mu_H + r_H)\widetilde{I}_H \tag{6.3}$$

$$\frac{d\widetilde{R}_H}{dt} = r_H\widetilde{I}_H - \mu_H\widetilde{R}_H \tag{6.4}$$

$$\frac{d\widetilde{S}_V}{dt} = A - \frac{b\beta_V}{N_H}\widetilde{S}_V\widetilde{I}_H - \mu_V\widetilde{S}_V \tag{6.5}$$

$$\frac{d\widetilde{E}_V}{dt} = \frac{b\beta_V}{N_H}\widetilde{S}_V\widetilde{I}_H - (\varepsilon_V + \mu_V)\widetilde{E}_V \tag{6.6}$$

$$\frac{d\widetilde{I}_V}{dt} = M + \varepsilon_V\widetilde{E}_V - \mu_V\widetilde{I}_V \tag{6.7}$$

We have assumed that

$$N_H = \widetilde{S}_H + \widetilde{E}_H + \widetilde{I}_H + \widetilde{R}_H \tag{6.8}$$

$$N_V = \widetilde{S}_V + \widetilde{E}_V + \widetilde{I}_V \tag{6.9}$$

Where

N_H = Total number of human population,

N_V = Total number of vector population,

λ_H = Birth rate of human population,

b = Biting rate of vector population,

β_H = Transmission probability of dengue virus from vector population to human,

β_V = Transmission probability of dengue virus from human population to vector,

ε_H = Intrinsic incubation rate,

ε_V = Extrinsic incubation rate,

μ_H = Death rate of human population,

μ_V = Death rate of vector population,

r_H = Recovery rate of the human population.

The assumption of our model is the total human and vector populations are constant. This leads to the rate of change for human and vector population being zero, i.e.,

$$\frac{d\widetilde{S}_H}{dt} + \frac{d\widetilde{E}_H}{dt} + \frac{d\widetilde{I}_H}{dt} + \frac{d\widetilde{R}_H}{dt} = 0 \tag{6.10}$$

$$\frac{d\widetilde{S}_V}{dt} + \frac{d\widetilde{E}_V}{dt} + \frac{d\widetilde{I}_V}{dt} = 0 \tag{6.11}$$

From the above equations, we can obtain the following equations:

$$N_V = (A+M)/\mu_V \tag{6.12}$$

$$\lambda_H = \mu_H \tag{6.13}$$

We now normalized equations (6.1) – (6.9) as following:

$$S_H = \frac{\widetilde{S}_H}{N_H}, E_H = \frac{\widetilde{E}_H}{N_H}, I_H = \frac{\widetilde{I}_H}{N_H}, R_H = \frac{\widetilde{R}_H}{N_H}, \tag{6.14}$$

$$S_V = \frac{\widetilde{S}_V}{N_V}, E_H = \frac{\widetilde{E}_V}{N_V}, I_V = \frac{\widetilde{I}_V}{N_V} \quad (6.15)$$

We also have

$$1 = S_H + E_H + I_H + R_H \quad (6.16)$$

$$1 = S_V + E_H + I_V \quad (6.17)$$

The mathematical model of equation (6.1) – (6.7) is now reduced to the following 5 equations:

$$\frac{dS_H}{dt} = \mu_H(1 - S_H) - \frac{b\beta_H}{N_H} S_H I_V N_V \quad (6.18)$$

$$\frac{dE_H}{dt} = \frac{b\beta_H}{N_H} S_H I_V N_V - (\varepsilon_H + \mu_H)E_H \quad (6.19)$$

$$\frac{dI_H}{dt} = \varepsilon_H E_H - (\mu_H + r_H)I_H \quad (6.20)$$

$$\frac{dE_V}{dt} = b\beta_V S_V I_H - (\varepsilon_V + \mu_V)E_V \quad (6.21)$$

$$\frac{dI_V}{dt} = \frac{M}{N_V} + \varepsilon_V E_V - \mu_V I_V \quad (6.22)$$

6.2.2 Mathematical Analysis for equilibrium point

The mathematical model is now analyzed and investigated in order to find the equilibrium points and system stability. The equilibrium point is determined by setting the right-hand side of equation (6.18) – (6.22) to zero. The system stability is determined by its eigenvalues and R0. After we solved equation (6.18) – (6.22), we only obtain the endemic disease equilibrium points E_1 given by

$$E_1 = (S_H^{1*}, E_H^{1*}, I_H^{1*}, E_V^{1*}, I_V^{1*}) \quad (6.23)$$

Where

$$\begin{aligned} S_H^{1*} = {} & (b^2 N_V^2 \beta_H \beta_V \varepsilon_H \varepsilon_V \mu_H + \\ & N_V(N_H \mu_H(\varepsilon_V + \mu_V)(2b\beta_V \varepsilon_H \mu_H + (\gamma_H + \mu_H)(\varepsilon_H + \mu_H)\mu_V) \\ & + bM\beta_H(\gamma_H(\varepsilon_H + \mu_H)(\varepsilon_V + \mu_V) + \mu_H(b\beta_V \varepsilon_H + (\varepsilon_H + \mu_H)(\varepsilon_V + \mu_V)))) \\ & - \sqrt{(N_V^2(4bMN_H\beta_H\mu_H(\gamma_H + \mu_H)(\varepsilon_H + \mu_H)(\varepsilon_V + \mu_V)^2(b\beta_V\varepsilon_H\mu_H} \\ & + (\gamma_H + \mu_H)(\varepsilon_H + \mu_H)\mu_V) + (N_H\mu_H(\gamma_H + \mu_H)(\varepsilon_H + \mu_H)\mu_V(\varepsilon_V + \mu_V) - \\ & b\beta_H(M\gamma_H(\varepsilon_H + \mu_H)(\varepsilon_V + \mu_V) + \mu_H(b\beta_V\varepsilon_H(M + N_V\varepsilon_V) + M(\varepsilon_H + \\ & \mu_H)(\varepsilon_V + \mu_V))))^2)))/ \\ & (2bN_V\beta_V\varepsilon_H\mu_H(b\beta_H(M + N_V\varepsilon_V) + N_H\mu_H(\varepsilon_V + \mu_V))) \end{aligned} \quad (6.24)$$

$$\begin{aligned} E_H^{1*} = {} & (b^2 N_V^2 \beta_H \beta_V \varepsilon_H \varepsilon_V \mu_H + N_V(-N_H\mu_H(\gamma_H + \mu_H)(\varepsilon_H + \mu_H)\mu_V(\varepsilon_V + \mu_V) \\ & + bM\beta_H(-\gamma_H(\varepsilon_H + \mu_H)(\varepsilon_V + \mu_V) - \mu_H(-b\beta_V\varepsilon_H + (\varepsilon_H + \mu_H)(\varepsilon_V + \mu_V)))) \\ & + \sqrt{(N_V^2(4bMN_H\beta_H\mu_H(\gamma_H + \mu_H)(\varepsilon_H + \mu_H)(\varepsilon_V + \mu_V)^2(b\beta_V\varepsilon_H\mu_H} \\ & + (\gamma_H + \mu_H)(\varepsilon_H + \mu_H)\mu_V) + (N_H\mu_H(\gamma_H + \mu_H)(\varepsilon_H + \mu_H)\mu_V(\varepsilon_V + \mu_V) \\ & - b\beta_H(M\gamma_H(\varepsilon_H + \mu_H)(\varepsilon_V \\ & + \mu_V) + \mu_H(b\beta_V\varepsilon_H(M + N_V\varepsilon_V) + M(\varepsilon_H + \mu_H)(\varepsilon_V + \mu_V))))^2))) / \\ & (2bN_V\beta_V\varepsilon_H(\varepsilon_H + \mu_H)(b\beta_H(M + N_V\varepsilon_V) + N_H\mu_H(\varepsilon_V + \mu_V))) \end{aligned} \quad (6.25)$$

$$
\begin{aligned}
I_H^{1*} =& (b^2N_V^2\beta_H\beta_V\varepsilon_H\varepsilon_V\mu_H + N_V(-N_H\mu_H(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V(\varepsilon_V+\mu_V)\\
&+bM\beta_H(-\gamma_H(\varepsilon_H+\mu_H)(\varepsilon_V+\mu_V) - \mu_H(-b\beta_V\varepsilon_H + (\varepsilon_H+\mu_H)(\varepsilon_V+\mu_V))))\\
&+\sqrt{(N_V^2(4bMN_H\beta_H\mu_H(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)(\varepsilon_V+\mu_V)^2(b\beta_V\varepsilon_H\mu_H}\\
&+(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V) + (N_H\mu_H(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V(\varepsilon_V+\mu_V)\\
&-b\beta_H(M\gamma_H(\varepsilon_H+\mu_H)(\varepsilon_V+\mu_V)\\
&\quad+\mu_H(b\beta_V\varepsilon_H(M+N_V\varepsilon_V) + M(\varepsilon_H+\mu_H)(\varepsilon_V+\mu_V))))^2)))/\\
&(2bN_V\beta_V(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)(b\beta_H(M+N_V\varepsilon_V) + N_H\mu_H(\varepsilon_V+\mu_V)))
\end{aligned}
\tag{6.26}
$$

$$
\begin{aligned}
E_V^{1*} =& (-bMN_V\beta_H(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V(\varepsilon_V+\mu_V)\\
&-N_HN_V\mu_H(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V^2(\varepsilon_V+\mu_V)\\
&+b^2N_V\beta_H\beta_V\varepsilon_H\mu_H(-M\mu_V+\varepsilon_V(-2M+N_V\mu_V))\\
&+\mu_V\sqrt{(N_V^2(4bMN_H\beta_H\mu_H(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)(\varepsilon_V+\mu_V)^2(b\beta_V\varepsilon_H\mu_H}\\
&+(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V) + (N_H\mu_H(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V(\varepsilon_V+\mu_V)\\
&\quad-b\beta_H(M\gamma_H(\varepsilon_H+\mu_H)(\varepsilon_V+\mu_V)\\
&+\mu_H(b\beta_V\varepsilon_H(M+N_V\varepsilon_V) + M(\varepsilon_H+\mu_H)(\varepsilon_V+\mu_V))))^2))) /\\
&\left(2bN_V^2\beta_H\varepsilon_V(\varepsilon_V+\mu_V)(b\beta_V\varepsilon_H\mu_H + (\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V)\right)
\end{aligned}
\tag{6.27}
$$

$$
\begin{aligned}
I_V^{1*} =& (b^2N_V^2\beta_H\beta_V\varepsilon_H\varepsilon_V\mu_H + N_V(-N_H\mu_H(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V(\varepsilon_V+\mu_V)\\
&+bM\beta_H(\gamma_H(\varepsilon_H+\mu_H)(\varepsilon_V+\mu_V) + \mu_H(b\beta_V\varepsilon_H + (\varepsilon_H+\mu_H)(\varepsilon_V+\mu_V))))\\
&+\sqrt{(N_V^2(4bMN_H\beta_H\mu_H(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)(\varepsilon_V+\mu_V)^2}\\
&(b\beta_V\varepsilon_H\mu_H + (\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V) + (N_H\mu_H(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V(\varepsilon_V+\mu_V)\\
&-b\beta_H(M\gamma_H(\varepsilon_H+\mu_H)(\varepsilon_V+\mu_V)\\
&+\mu_H(b\beta_V\varepsilon_H(M+N_V\varepsilon_V) + M(\varepsilon_H+\mu_H)(\varepsilon_V+\mu_V))))^2)))/\\
&(2bN_V^2\beta_H(\varepsilon_V+\mu_V)(b\beta_V\varepsilon_H\mu_H + (\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V))
\end{aligned}
\tag{6.28}
$$

All parameters used in system equation (6.24) – (6.28) are positive and the epidemic region is

$$\Omega = \left\{(S_H^{1*}, E_H^{1*}, I_H^{1*}, E_V^{1*}, I_V^{1*}) : 0 \le S_H^{1*}, E_H^{1*}, I_H^{1*}, E_V^{1*}, I_V^{1*} \le 1\right\}$$

6.2.3 Mathematical analysis for local stability

The local stability of the equilibrium point determined from equation (6.18) – (6.22) is analyzed by first obtaining an expression for the basic reproduction number R_0 and the Jacobian matrix. After these are done, we then solve the eigenvalues equation which involves the Jacobian matrix. The Jacobian matrix of system equation (6.18) – (6.22) is as follows:

$$
J = \begin{bmatrix}
-\mu_H - \frac{b\beta_H}{N_H} I_V^{1*} N_V & 0 & 0 & 0 & -\frac{b\beta_H}{N_H} S_H^{1*} N_V \\
\frac{b\beta_H}{N_H} I_V^{1*} N_V & -(\varepsilon_H+\mu_H) & 0 & 0 & \frac{b\beta_H}{N_H} S_H^{1*} N_V \\
0 & \varepsilon_H & -(\mu_H+r_H) & 0 & 0 \\
0 & 0 & b\beta_V(1-I_V^{1*}-E_V^{1*}) & -(\varepsilon_V+\mu_V) & 0 \\
0 & 0 & 0 & \varepsilon_V & -\mu_V
\end{bmatrix}
\tag{6.29}
$$

The basic reproductive number, $\sqrt{R_0}$, is the number of secondary infection produced by a typical case of an infection in a population of its infectious period. R_0

can be indicated the transmission potential of disease. In case of $R_0>1$, the transmission has potential to spread between people. The requirement for local stability at the equilibrium state is stated in proposition 1 given below.

Proposition 6.1. The equilibrium state E_1 is asymptotically stable when R_0 is higher than 1, $R_0 > 1$.

Proof. The local stability of E_1 is governed by linearization of system equation (6.18) - (6.22). The R_0 is given as.

$$R_0 = (\alpha_1 + N_V M\alpha_2(\gamma_H\alpha_3 + \mu_{\mathrm{H}}(\alpha_4 + \alpha_3))) + \sqrt{\frac{(N_V^2(\alpha_5\alpha_2\alpha_6\alpha_3^2(\alpha_4\mu_{\mathrm{H}} + \alpha_6\alpha_7\mu_{\mathrm{V}}) + (\alpha_8\alpha_6\alpha_3 - \alpha_2(\mathrm{M}\gamma_{\mathrm{H}}\alpha_3 + \mu_{\mathrm{H}}(\alpha_4\alpha_9 + \mathrm{M}\alpha_3)))^2)))}{N_V\alpha_8\alpha_6\alpha_3}} \quad (6.30)$$

Where

$\alpha_1 = b^2N_V^2\beta_H\beta_V\varepsilon_H\varepsilon_V\mu_H$

$\alpha_2 = b\beta_H$

$\alpha_3 = (\varepsilon_H + \mu_H)(\varepsilon_V + \mu_V)$

$\alpha_4 = b\beta_V\varepsilon_H$

$\alpha_5 = 4N_H\mu_H M$

$\alpha_6 = (\gamma_H + \mu_H)$

$\alpha_7 = (\varepsilon_H + \mu_H)$

$\alpha_8 = N_H\mu_H\mu_V$

$\alpha_9 = (M + N_V\varepsilon_V)$

The characteristic of equation (29) which determines the eigenvalues is the eigenvalue equation obtained by solving det $|J_{E_1} - \lambda I_5| = 0$, where

J_{E1} = The Jacobian matrix at the equilibrium point E1,

λ = The eigenvalues,

I_5= The identity 5x5 matrix.

Evaluating the determinant, we get the following characteristic equation

$$(\lambda^5 + e_1\lambda^4 + e_2\lambda^3 + e_3\lambda^2 + e_4\lambda^1 + e_5) = 0 \quad (6.31)$$

where

$e_1 = [-F(-\gamma_H - \mu_H)\mu_H^2GH + F(-GHJ - \mu_H^2GH\ (-\mu_H - KL))]/N$

$e_2 = [(-F(-\gamma_H - \mu_H)GHJ - \mu_H^2GH(-\mu_H - K + L))$
$+F(-GHP + GHJ(-\mu_H - K + L)))]/N$

$e_3 = [-F(-\gamma_H - \mu_H)GHP + GHJ(-\mu_H - K + L)$
$+FOGH + GHP(-\mu_H - K + L)]/N$

$e_4 = [-FOGH(-\mu_H - K + L) + (QH(-K + R))(1 - K + S) - F((-\gamma_H -$
$\mu_H)\ OGH + GHP(-\mu_H - K + L))\ ] / F\mu_H^2GH$

$e_5 = (1/2N_HN_V(b\beta_V\varepsilon_H\mu_H + (\gamma_H + \mu_H)(\varepsilon_H + \mu_H)\mu_V))T$

where

$F = 8N_H^2N_V^4\beta_H\beta_V^2\varepsilon_H^2\varepsilon_V$

$G = (\varepsilon_V + \mu_V)^2$

$H = (bM\beta_H + bN_V\beta_H\varepsilon_V + N_H\varepsilon_V\mu_H + N_H\mu_H\mu_V)^2(b\beta_V\varepsilon_H\mu_H + \gamma_H\varepsilon_H\mu_V +$
$\gamma_H\mu_H\mu_V + \varepsilon_H\mu_H\mu_V + \mu_H^2\mu_V)^3$

$$J = \left((-\varepsilon_H - \mu_H)\mu_H^2 - \mu_H^2(\varepsilon_V + 2\mu_V)\right)$$

$$K = (b^2 N_V^2 \beta_H \beta_V \varepsilon_H \varepsilon_V \mu_H + N_V(-N_H \mu_H(\gamma_H + \mu_H)(\varepsilon_H + \mu_H)\mu_V(\varepsilon_V + \mu_V) + bM\beta_H(\gamma_H(\varepsilon_H + \mu_H)(\varepsilon_V + \mu_V) + \mu_H(b\beta_V\varepsilon_H + (\varepsilon_H + \mu_H)(\varepsilon_V + \mu_V))))$$

$$L = \sqrt{(N_V^2(4bMN_H\beta_H\mu_H(\gamma_H + \mu_H)(\varepsilon_H + \mu_H)(\varepsilon_V + \mu_V)^2 (b\beta_V\varepsilon_H\mu_H + (\gamma_H + \mu_H)(\varepsilon_H + \mu_H)\mu_V) + (N_H\mu_H(\gamma_H + \mu_H)(\varepsilon_H + \mu_H)\mu_V(\varepsilon_V + \mu_V) - b\beta_H(M\gamma_H(\varepsilon_H + \mu_H)(\varepsilon_V + \mu_V) + \mu_H(b\beta_V\varepsilon_H(M + N_V\varepsilon_V) + M(\varepsilon_H + \mu_H)(\varepsilon_V + \mu_V))))^2))) / (2N_H N_V(\varepsilon_V + \mu_V)(b\beta_V\varepsilon_H\mu_H + (\gamma_H + \mu_H)(\varepsilon_H + \mu_H)\mu_V)))}$$

$$N = (8N_H^2 N_V^4 \beta_H \beta_V^2 \varepsilon_H^2 \varepsilon_V \mu_H^2(\varepsilon_V + \mu_V)^2(bM\beta_H + bN_V\beta_H\varepsilon_V + N_H\varepsilon_V\mu_H + N_H\mu_H\mu_V)^2(b\beta_V\varepsilon_H\mu_H + \gamma_H\varepsilon_H\mu_V + \gamma_H\mu_H\mu_V + \varepsilon_H\mu_H\mu_V + \mu_H^2\mu_V)^3)$$

$$O = (-\varepsilon_H - \mu_H)\mu_H^2(-\varepsilon_V - \mu_V)\mu_V$$

$$P = \left(\mu_H^2(-\varepsilon_V - \mu_V)\mu_V + (-\varepsilon_H - \mu_H)\mu_H^2(\varepsilon_V + 2\mu_V)\right)$$

$$Q = 1/\left(b\beta_H(M + N_V\varepsilon_V) + N_H\mu_H(\varepsilon_V + \mu_V)\right)\ 4bN_H N_V^4 \beta_H^2 \beta_V^2 \varepsilon_H^2 \varepsilon_V^2 \mu_H(\varepsilon_V + \mu_V)^2$$

$$S = \sqrt{(N_V^2(4bMN_H\beta_H\mu_H(\gamma_H + \mu_H)(\varepsilon_H + \mu_H)(\varepsilon_V + \mu_V)^2(b\beta_V\varepsilon_H\mu_H + (\gamma_H + \mu_H)(\varepsilon_H + \mu_H)\mu_V) + (N_H\mu_H(\gamma_H + \mu_H)(\varepsilon_H + \mu_H)\mu_V(\varepsilon_V + \mu_V) - b\beta_H(M\gamma_H(\varepsilon_H + \mu_H)(\varepsilon_V + \mu_V) + \mu_H(b\beta_V\varepsilon_H(M + N_V\varepsilon_V) + M(\varepsilon_H + \mu_H)(\varepsilon_V + \mu_V))))^2))) / \left(2bN_V^2\beta_H(\varepsilon_V + \mu_V)(b\beta_V\varepsilon_H\mu_H + (\gamma_H + \mu_H)(\varepsilon_H + \mu_H)\mu_V)\right)}$$

$$T = (-b^3 N_V^2 \beta_H \beta_V^2 \varepsilon_H^2 \varepsilon_V \mu_H^2 + bN_V\beta_V\varepsilon_H\mu_H(N_H\mu_H(\gamma_H + \mu_H)(\varepsilon_H + \mu_H)\mu_V(\varepsilon_V + \mu_V) + bM\beta_H(-\gamma_H(\varepsilon_H + \mu_H)(\varepsilon_V + \mu_V) - \mu_H(b\beta_V\varepsilon_H + (\varepsilon_H + \mu_H)(\varepsilon_V + \mu_V)))) + (b\beta_V\varepsilon_H\mu_H + 2(\gamma_H + \mu_H)(\varepsilon_H + \mu_H)\mu_V)\sqrt{(N_V^2(N_H^2\mu_H^2(\gamma_H + \mu_H)^2(\varepsilon_H + \mu_H)^2\mu_V^2(\varepsilon_V + \mu_V)^2 + 2bN_H\beta_H\mu_H(\gamma_H + \mu_H)(\varepsilon_H + \mu_H)(\varepsilon_V + \mu_V)(M(\gamma_H + \mu_H)(\varepsilon_H + \mu_H)\mu_V(\varepsilon_V + \mu_V) + b\beta_V\varepsilon_H\mu_H(2M\varepsilon_V + (M - N_V\varepsilon_V)\mu_V) + b^2\beta_H^2(M\gamma_H(\varepsilon_H + \mu_H)(\varepsilon_V + \mu_V) + \mu_H(b\beta_V\varepsilon_H(M + N_V\varepsilon_V) + M(\varepsilon_H + \mu_H)(\varepsilon_V + \mu_V)))^2)))}$$

$$R = \sqrt{(N_V^2(4bMN_H\beta_H\mu_H(\gamma_H + \mu_H)(\varepsilon_H + \mu_H)(\varepsilon_V + \mu_V)^2(b\beta_V\varepsilon_H\mu_H + (\gamma_H + \mu_H)(\varepsilon_H + \mu_H)\mu_V) + (N_H\mu_H(\gamma_H + \mu_H)(\varepsilon_H + \mu_H)\mu_V(\varepsilon_V + \mu_V) - b\beta_H(M\gamma_H(\varepsilon_H + \mu_H)(\varepsilon_V + \mu_V) + \mu_H(b\beta_V\varepsilon_H(M + N_V\varepsilon_V) + M(\varepsilon_H + \mu_H)(\varepsilon_V + \mu_V))))^2)))}$$

The solution of equation (31) is solved through use of the Routh-Hurwitz criteria. The equilibrium point will be local stability when all eigenvalues have negative real parts. This will happen if all the coefficients satisfy the following conditions:

$$e_1 > 0, e_2 > 0, e_3 > 0, e_4 > 0, e_5 > 0 \tag{6.32}$$

$$e_1 e_2 e_3 > e_3^2 + e_1^2 e_4 \tag{6.33}$$

$$(e_1 e_4 - e_5)(e_1 e_2 e_3 - e_3^2 - e_1^2 e_4) > e_5(e_1 e_2 - e_3)^2 + e_1 e_5^2 \tag{6.34}$$

All conditions of equation (32) - (34) are satisfied for endemic equilibrium point as seen in Figure 6.4.

The dynamical transmission of dengue disease without a vertical mode of transmission (*M = 0*) is described by equations (6.18) to (6.21) which are the same as the case where vertical transmission is possible except that equation (6.22) has been replaced by the equation below

$$\frac{dI_V}{dt} = \varepsilon_V E_V - \mu_V I_V \tag{6.35}$$

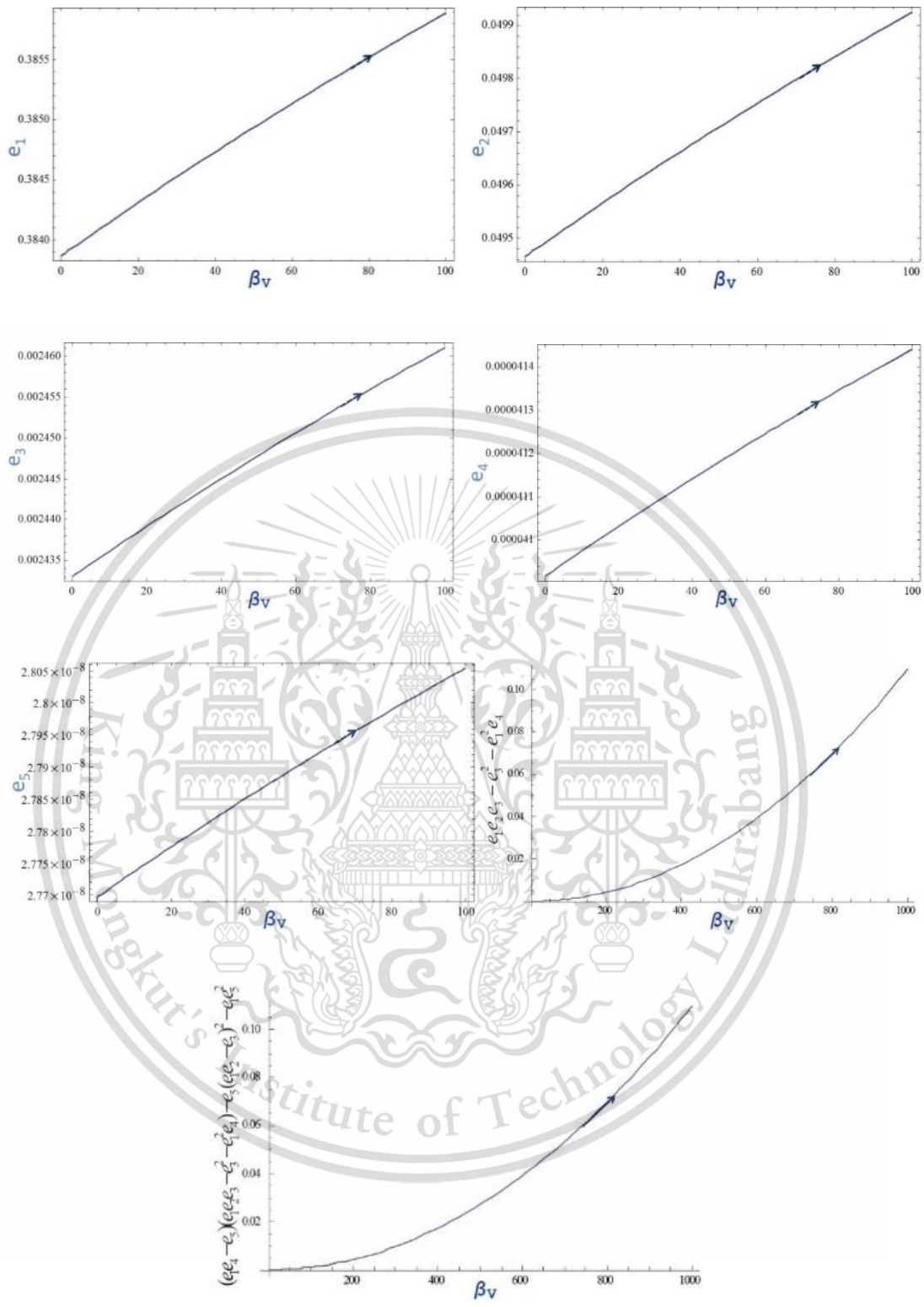


Figure 6.4 All parameters spaces of endemic disease equilibrium of E_1 are satisfied the Routh-Hurwitz criteria. The parameters value are N_H=92,000, b=1/5, μ_H=1/ (70*365), γ_H=0.1428, β_H=0.95, β_V=0.75, μ_V=1/24, ε_V=0.1428, ε_H=0.1667, A=5,000 and M=400

Reanalyzing the new set of equations in the same way as before, we now arrive at two equilibrium points, a disease-free equilibrium and an endemic disease equilibrium points defined as.

i. Disease free equilibrium point

$$E_0 = (1,0,0,0,0) \tag{6.36}$$

ii. Endemic disease equilibrium point

$$E_2 = (S_H^{2*}, E_H^{2*}, I_H^{2*}, E_V^{2*}, I_V^{2*}) \tag{6.37}$$

where;

$$S_H^{2*} = [N_H(\varepsilon_V + \mu_V)(b\beta_V\varepsilon_H\mu_H + (\gamma_H + \mu_H)(\varepsilon_H + \mu_H)\mu_V)] / [b\beta_V\varepsilon_H\big(bN_V\beta_H\varepsilon_V + N_H\mu_H(\varepsilon_V + \mu_V)\big)] \tag{6.38}$$

$$E_H^{2*} = -[\mu_H(-b^2N_V\beta_H\beta_V\varepsilon_H\varepsilon_V + N_H(\gamma_H + \mu_H)(\varepsilon_H + \mu_H)\mu_V(\varepsilon_V + \mu_V))] / [b\beta_V\varepsilon_H(\varepsilon_H + \mu_H)\big(bN_V\beta_H\varepsilon_V + N_H\mu_H(\varepsilon_V + \mu_V)\big)] \tag{6.39}$$

$$I_H^{2*} = [\mu_H(b^2N_V\beta_H\beta_V\varepsilon_H\varepsilon_V - N_H(\gamma_H + \mu_H)(\varepsilon_H + \mu_H)\mu_V(\varepsilon_V + \mu_V))] / b\beta_V(\gamma_H + \mu_H)(\varepsilon_H + \mu_H)(bN_V\beta_H\varepsilon_V + N_H\mu_H(\varepsilon_V + \mu_V)) \tag{6.40}$$

$$E_V^{2*} = -[\mu_H\mu_V(-b^2N_V\beta_H\beta_V\varepsilon_H\varepsilon_V + N_H(\gamma_H + \mu_H)(\varepsilon_H + \mu_H)\mu_V(\varepsilon_V + \mu_V))] / bN_V\beta_H\varepsilon_V(\varepsilon_V + \mu_V)(b\beta_V\varepsilon_H\mu_H + (\gamma_H + \mu_H)(\varepsilon_H + \mu_H)\mu_V) \tag{6.41}$$

$$I_V^{2*} = -[\mu_H(-b^2N_V\beta_H\beta_V\varepsilon_H\varepsilon_V + N_H(\gamma_H + \mu_H)(\varepsilon_H + \mu_H)\mu_V(\varepsilon_V + \mu_V))] / bN_V\beta_H(\varepsilon_V + \mu_V)(b\beta_V\varepsilon_H\mu_H + (\gamma_H + \mu_H)(\varepsilon_H + \mu_H)\mu_V) \tag{6.42}$$

The Jacobian matrix used to determine the stability of eigenvalues at $E_0 = (1,0,0,0,0)$ has the form.

$$J = \begin{bmatrix} -\mu_H & 0 & 0 & 0 & -\frac{b\beta_H}{N_H}N_V \\ 0 & -(\varepsilon_H + \mu_H) & 0 & 0 & \frac{b\beta_H}{N_H}N_V \\ 0 & \varepsilon_H & -(\mu_H + r_H) & 0 & 0 \\ 0 & 0 & b\beta_V & -(\varepsilon_V + \mu_V) & 0 \\ 0 & 0 & 0 & \varepsilon_V & -\mu_V \end{bmatrix} \tag{6.43}$$

Proposition 2. The equilibrium state E_0 is asymptotically stable when R_0 is less than 1, $R_0 < 1$.

Proof. The local stability of E_0 is governed by linearization of system equation (6.18) - (6.21) and (6.35). The R_0 will be of the form

$$R_0 = \frac{b^2N_V\beta_H\beta_V\varepsilon_H\varepsilon_V}{N_H\mu_V(\gamma_H + \mu_H)(\varepsilon_H + \mu_H)(\varepsilon_V + \mu_V)}$$

The characteristic equation obtained same by solving the determinant equation, Equation (6.43) is given by

$$(\lambda^5 + e_1\lambda^4 + e_2\lambda^3 + e_3\lambda^2 + e_4\lambda^1 + e_5) = 0$$

Where;

$$e_1 = [N_H\gamma_H + N_H\varepsilon_H + N_H\varepsilon_V + 3N_H\mu_H + 2N_H\mu_V]/N_H$$

$$e_2 = [N_H\gamma_H\varepsilon_H + N_H\gamma_H\varepsilon_V + N_H\varepsilon_H\varepsilon_V + 2N_H\gamma_H\mu_H + 2N_H\varepsilon_H\mu_H + 3N_H\varepsilon_V\mu_H + 3N_H\mu_H^2 + 2N_H\gamma_H\mu_V + 2N_H\varepsilon_H\mu_V + N_H\varepsilon_V\mu_V + 6N_H\mu_H\mu_V + N_H\mu_V^2]/N_H$$

$$e_3 = [(N_H\gamma_H\varepsilon_H\varepsilon_V + N_H\gamma_H\varepsilon_H\mu_H + 2N_H\gamma_H\varepsilon_V\mu_H + 2N_H\varepsilon_H\varepsilon_V\mu_H + N_H\gamma_H\mu_H^2 + N_H\varepsilon_H\mu_H^2 + 3N_H\varepsilon_V\mu_H^2 + N_H\mu_H^3 + 2N_H\gamma_H\varepsilon_H\mu_V + N_H\gamma_H\varepsilon_V\mu_V + N_H\varepsilon_H\varepsilon_V\mu_V + 4N_H\gamma_H\mu_H\mu_V + 4N_H\varepsilon_H\mu_H\mu_V + 3N_H\varepsilon_V\mu_H\mu_V + 6N_H\mu_H^2\mu_V + N_H\gamma_H\mu_V^2 + N_H\varepsilon_H\mu_V^2 + 3N_H\mu_H\mu_V^2)]/N_H$$

$$e_4 = [-b^2N_V\beta_H\beta_V\varepsilon_H\varepsilon_V + N_H\gamma_H\varepsilon_H\varepsilon_V\mu_H + N_H\gamma_H\varepsilon_V\mu_H^2 + N_H\varepsilon_H\varepsilon_V\mu_H^2 + N_H\varepsilon_V\mu_H^3 + N_H\gamma_H\varepsilon_H\varepsilon_V\mu_V + 2N_H\gamma_H\varepsilon_H\mu_H\mu_V + 2N_H\gamma_H\varepsilon_V\mu_H\mu_V + 2N_H\varepsilon_H\varepsilon_V\mu_H\mu_V + 2N_H\gamma_H\mu_H^2\mu_V + 2N_H\varepsilon_H\mu_H^2\mu_V + 3N_H\varepsilon_V\mu_H^2\mu_V + 2N_H\mu_H^3\mu_V + N_H\gamma_H\varepsilon_H\mu_V^2 + 2N_H\gamma_H\mu_H\mu_V^2 + 2N_H\varepsilon_H\mu_H\mu_V^2 + 3N_H\mu_H^2\mu_V^2)]/N_H$$

$$e_5 = [\mu_H(-b^2N_V\beta_H\beta_V\varepsilon_H\varepsilon_V + N_H(\gamma_H + \mu_H)(\varepsilon_H + \mu_H)\mu_V(\varepsilon_V + \mu_V))]/N_H$$

All conditions of equation (6.32) - (6.34) are satisfied for disease free equilibrium point as seen in Figure 6.5.

The Jacobian matrix at $E_2 = (S_H^{2*}, E_H^{2*}, I_H^{2*}, E_V^{2*}, I_V^{2*})$ is

$$J = \begin{bmatrix} -\mu_H - \frac{b\beta_H}{N_H} I_V^{2*} N_V & 0 & 0 & 0 & -\frac{b\beta_H}{N_H} S_H^{2*} N_V \\ \frac{b\beta_H}{N_H} I_V^{2*} N_V & -(\varepsilon_H + \mu_H) & 0 & 0 & \frac{b\beta_H}{N_H} S_H^{2*} N_V \\ 0 & \varepsilon_H & -(\mu_H + r_H) & 0 & 0 \\ 0 & 0 & b\beta_V(1 - I_V^{2*} - E_V^{2*}) & -(\varepsilon_V + \mu_V) & 0 \\ 0 & 0 & 0 & \varepsilon_V & -\mu_V \end{bmatrix} \quad (6.44)$$

Proposition 3. The equilibrium state E_2 is asymptotically stable when R_0 is higher than 1, $R_0 > 1$.

Proof. The local stability of E_2 is established through the linearization of equations (6.18) - (6.21) and (6.35) which leads to the determinant equation previously obtained. Solving the eigenvalue equation, we get a similar characteristic equation, i.e.,

$$(\lambda^5 + e_1\lambda^4 + e_2\lambda^3 + e_3\lambda^2 + e_4\lambda^1 + e_5) = 0$$

Except that the coefficients are now

Where:

$$e_1 = [-(-UH + GH(-\mu_H + V)] / GH$$

$$e_2 = [-(-GH(W_1 - W_2 + W_3\ W_4) + GUH(-\mu_H + V)] / GH$$

$$e_3 = [-(-UH(-W_3\ W_2 + W_1\ W_4) + GH(W_1 - W_2 + W_3\ W_4)(-\mu_H + V)] / GH$$

$$e_4 = [(1/Y_1HY_2)(1 + V + \mu_V V) - Y_3(W_1W_2GH + GH(-W_3W_2 + W_1W_4))(-\mu_H + V)] / GHY_3$$

$$e_5 = [-\mu_H(\gamma_H + \mu_H)(\varepsilon_H + \mu_H)\mu_V(-b^2 N_V \beta_H \beta_V \varepsilon_H \varepsilon_V + N_H(\gamma_H + \mu_H)(\varepsilon_H + \mu_H)\mu_V(\varepsilon_V + \mu_V))] / N_H(b\beta_V \varepsilon_H \mu_H + (\gamma_H + \mu_H)(\varepsilon_H + \mu_H)\mu_V)$$

Where:

$$U = (\gamma_H + \varepsilon_H + \varepsilon_V + 2\mu_H + 2\mu_V)$$

$$V = \left[\mu_H\left(-b^2 N_V \beta_H \beta_V \varepsilon_H \varepsilon_V + N_H(\gamma_H + \mu_H)(\varepsilon_H + \mu_H)\mu_V(\varepsilon_V + \mu_V)\right)\right] / [N_H(\varepsilon_V + \mu_V)(b\beta_V \varepsilon_H \mu_H + (\gamma_H + \mu_H)(\varepsilon_H + \mu_H)\mu_V)]$$

$$W_1 = (-\gamma_H - \mu_H)(-\varepsilon_H - \mu_H)$$

$$W_2 = (-\varepsilon_V - \mu_V)\mu_V$$

$$W_3 = (\gamma_H + \varepsilon_H + 2\mu_H)$$

$$W_4 = (\varepsilon_V + 2\mu_V)$$

$$Y_1 = (bN_V \beta_H \varepsilon_V + N_H \mu_H(\varepsilon_V + \mu_V))\, bN_H^2 N_V^2 \beta_H^2 \beta_V^2 \varepsilon_H^2 \varepsilon_V^2 (\varepsilon_V + \mu_V)^3$$

$$Y_2 = (b\beta_V \varepsilon_H \mu_H + (\gamma_H + \mu_H)(\varepsilon_H + \mu_H)\mu_V)),$$

$$Y_3 = N_H^2 N_V \beta_H \beta_V^2 \varepsilon_H^2 \varepsilon_V$$

These coefficients of this new characteristic equation will also satisfy the Routh-Hurwitz criteria, equation (6.32) - (6.34) for the coefficients defined above (See Figure 6.6) and so the eigenvalues by the characteristic equation above will all have negative imaginary parts and the endemic disease equilibrium point will be stable.

6.3 Numerical Results

The numerical analysis in this study considers the transmission of dengue disease in models where the values of the parameter values are listed in Table 6.1, which gives different values for three sets of parameters which leads to the three cases we are looking at case 1 are the values when vertical transmission occurs and the equilibrium state is the endemic state. Case 2 are the values when there is no vertical transmission is possible but the equilibrium state will be the disease-free state. Finally, case 3 are the values when there is no vertical transmission but the equilibrium state will be the endemic state.

The trajectories of the numerical solutions case 1, case 2, and case 3 projected onto S_H, E_H, I_H, E_V and I_V are shown in the Figure 6.7, Figure 6.8, and Figure 6.9 respectively. The trajectory of the numerical solutions case 1, case 2, and case 3 projected onto (S_H, E_H), (S_H, I_H), (S_H, E_V), (S_H, I_V), (E_H, E_V) and (I_H, I_V) are shown in the Figure 6.10, Figure 6.11, and Figure 6.12 respectively. The trajectory of the numerical solutions case 1, case 2, and case 3 projected onto (S_H, E_H, I_H), (S_H, E_H, E_V), (S_H, E_H, I_V), (S_H, E_V, I_V), (E_H, E_V, I_V), and (I_H, E_V, I_V) are shown in the Figure 6.13, Figure 6.14, and Figure 6.15 respectively.

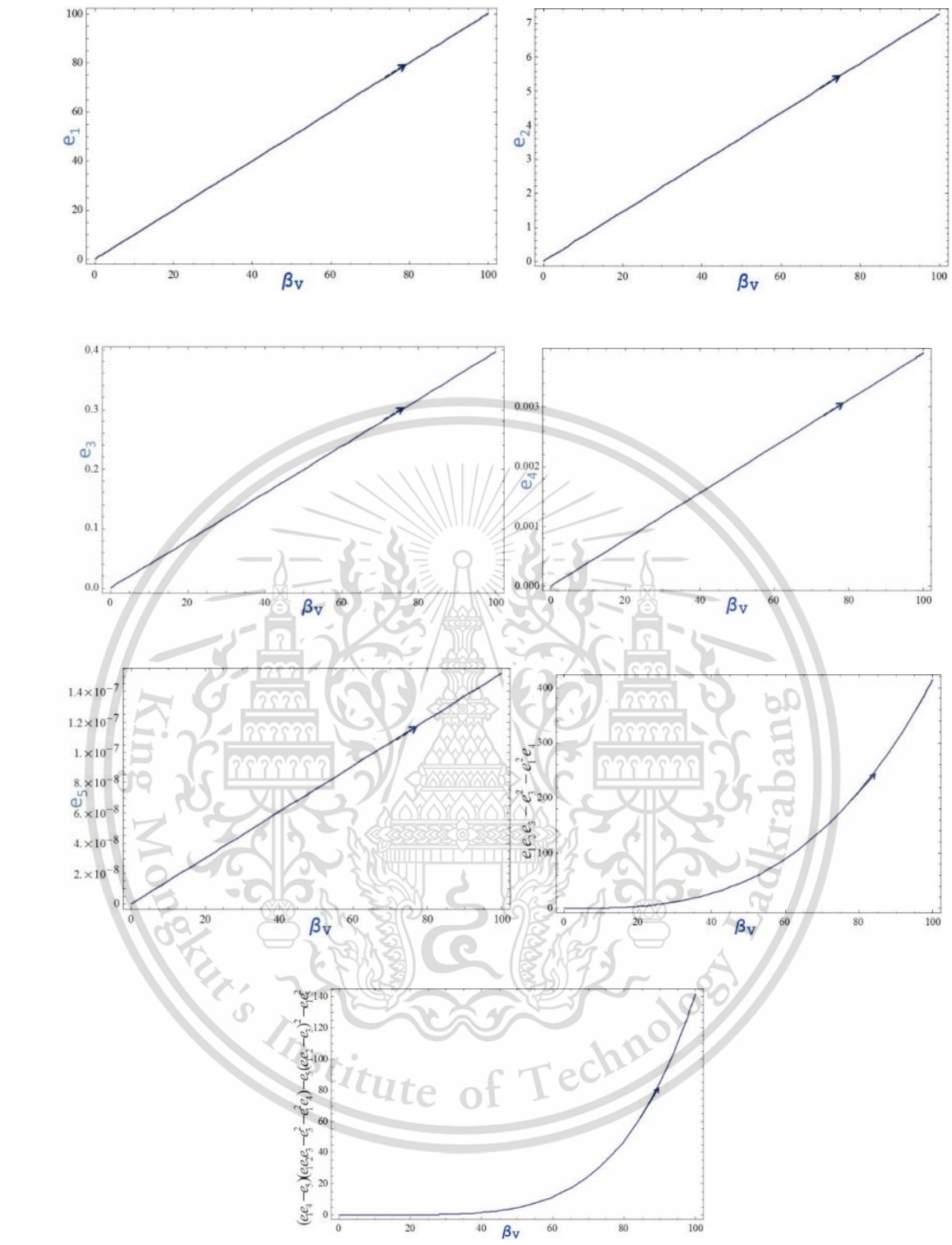


Figure 6.5 All parameters spaces of disease free equilibrium of E_0 are satisfied the Routh-Hurwitz criteria. The parameters value are N_H=92,000, b=1/5, μ_H=1/ (70*365), γ_H=0.01428, β_H=0.65, β_V=0.65, μ_V=1/24, ε_V=0.01428, ε_H=0.01667, A=5,000 and M=0

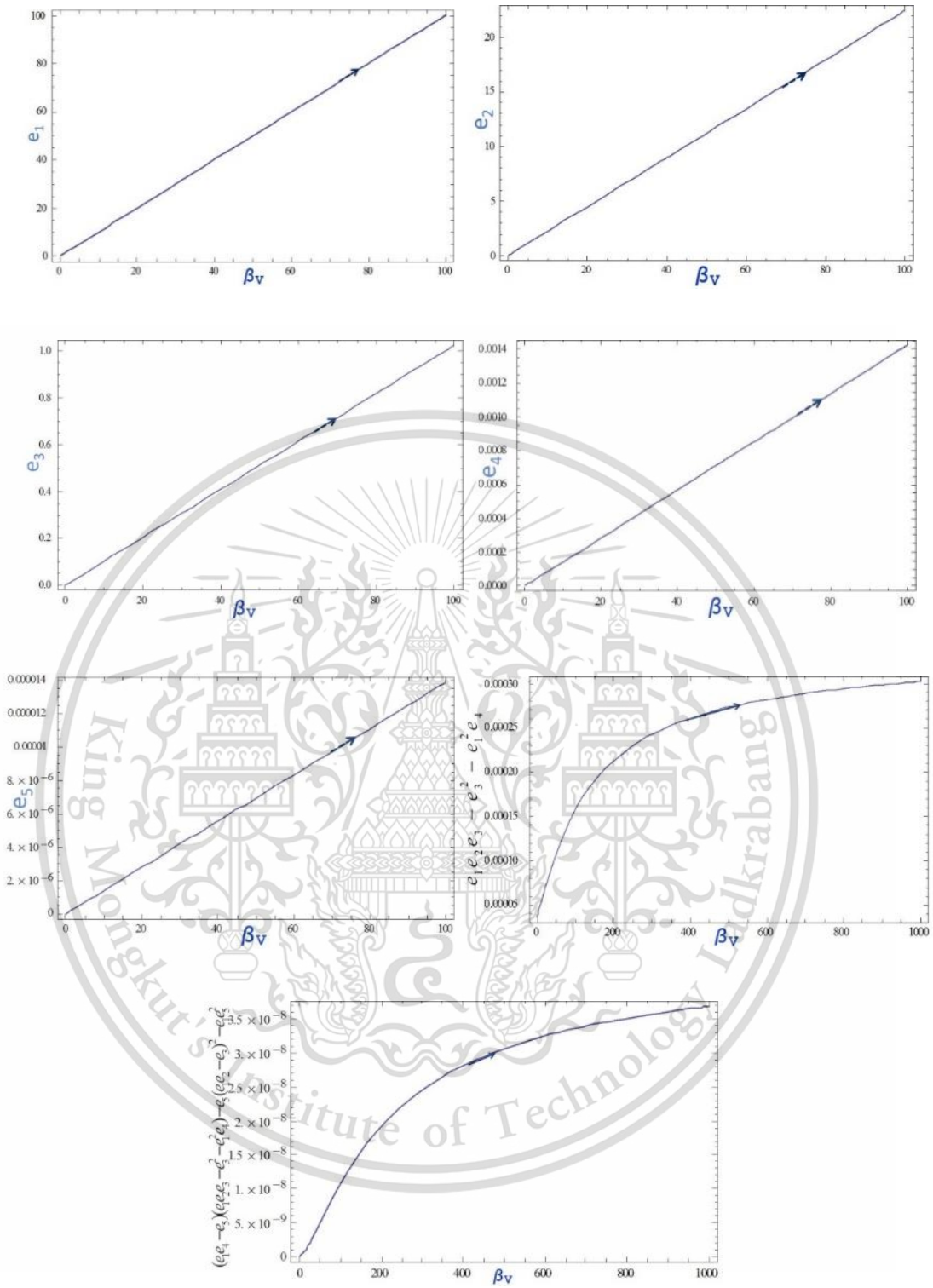


Figure 6.6 All parameters spaces of endemic disease equilibrium of E_2 are satisfied the Routh-Hurwitz criteria. The parameters value are N_H=92,000, b=1/5, μ_H=1/ (70*365), γ_H=0.1428, β_H=0.65, β_V=0.65, μ_V=1/24, ε_V=0.1428, ε_H=0.1667, A=5,000 and M=0

Table 6.1 Parameter are used involved in the transmission of dengue disease

Parameters	Case 1	Case 2	Case 3
μ_H	1/(70*365)	1/(70*365)	1/(70*365)
N_H	92,000	92,000	92,000
b	1/5	1/5	1/5
A	5,000	5,000	5,000
μ_V	1/24	1/24	1/24
M	400	0	0
γ_H	0.1428	0.01428	0.01428
β_H	0.95	0.65	0.65
β_V	0.75	0.65	0.65
ε_V	0.1428	0.01428	0.1428
ε_H	0.1667	0.01667	0.1667

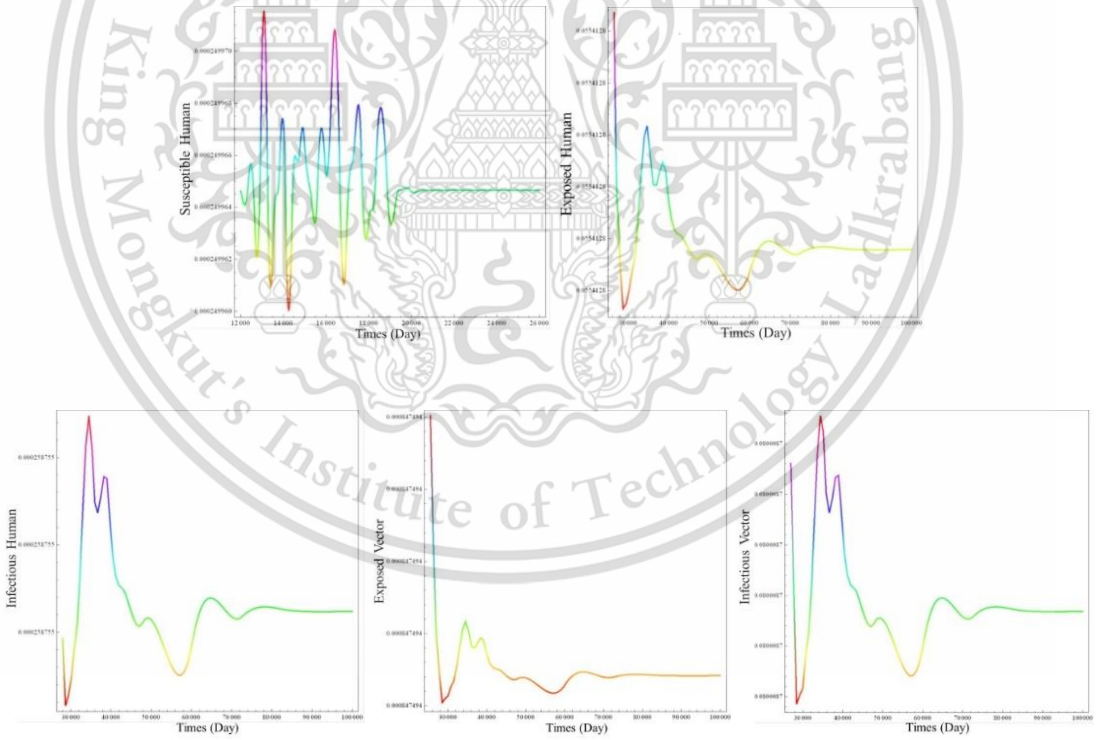


Figure 6.7 The time trajectories of the numerical solutions of the model when vertical transmission occurs for S_H, E_H, I_H, E_V and I_V are shown.

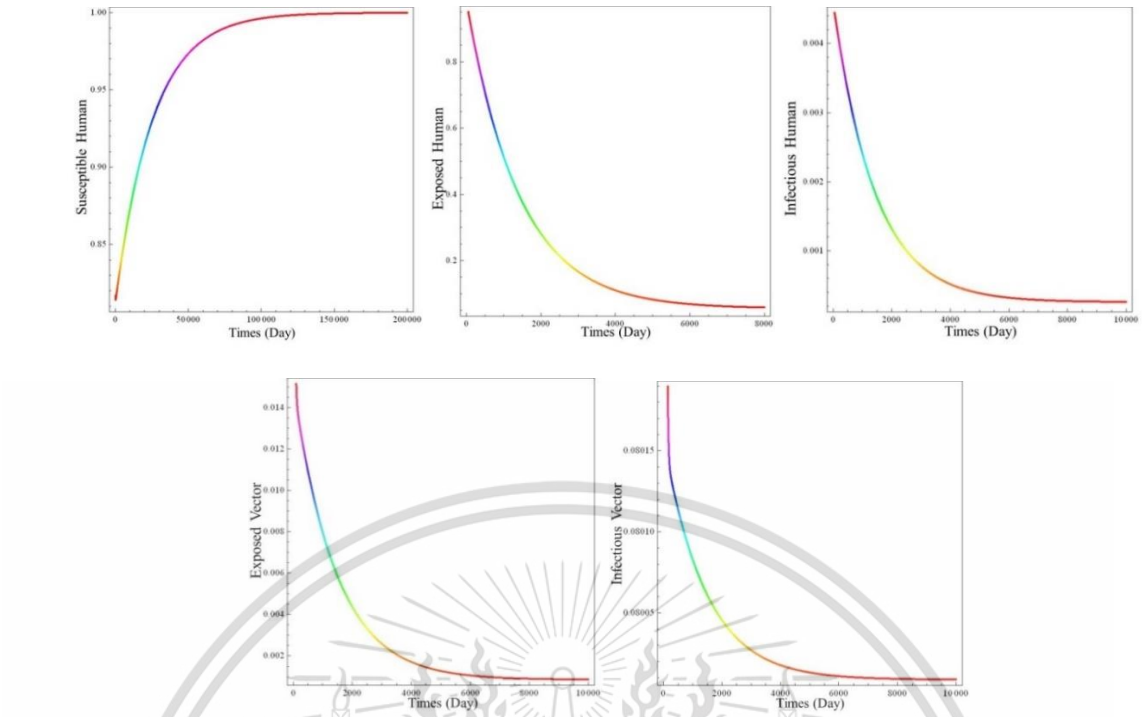


Figure 6.8 The time trajectories of the numerical solutions of the model when there is no vertical transmission of the virus of S_H, E_H, I_H, E_V and I_V lead to the equilibrium state being the disease-free state.

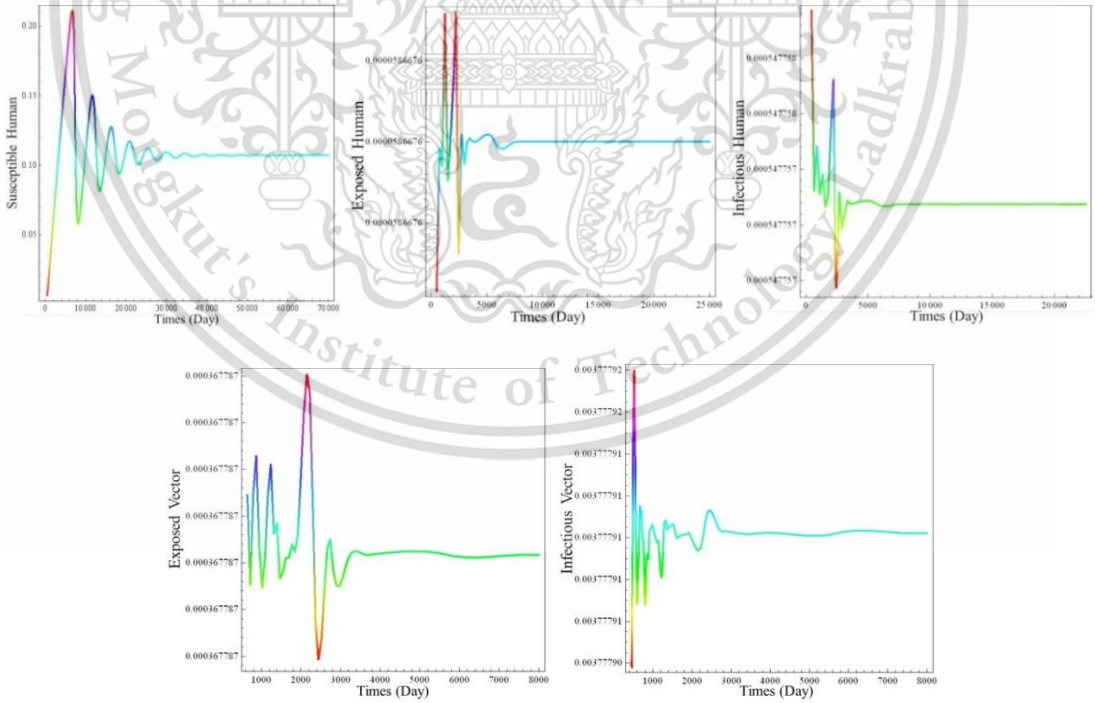


Figure 6.9 The time trajectories of the numerical solutions of dengue disease of S_H, E_H, I_H, E_V and I_V when there is no vertical transmission of the virus and the values of the parameters lead the equilibrium state being the endemic disease state.

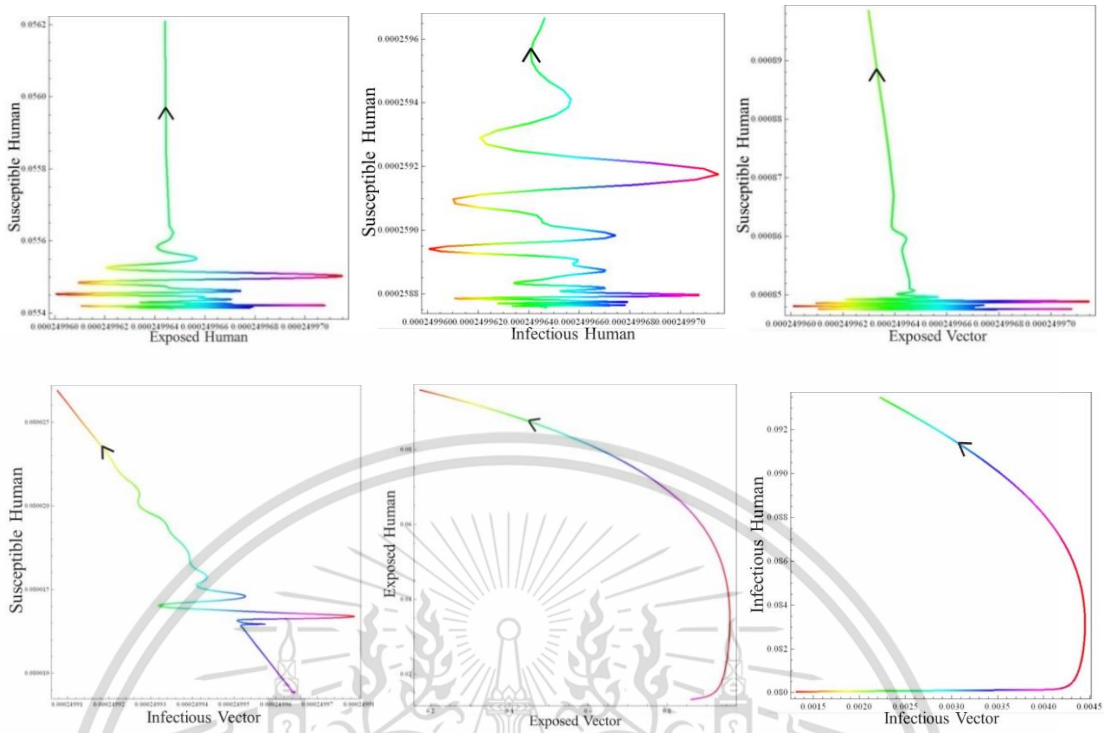


Figure 6.10 The trajectories of the numerical solutions projected onto the 2D (S_H, E_H), (S_H, I_H), (S_H, E_V), (S_H, I_V), (E_H, E_V) and (I_H, I_V) planes when vertical transmission occurs.

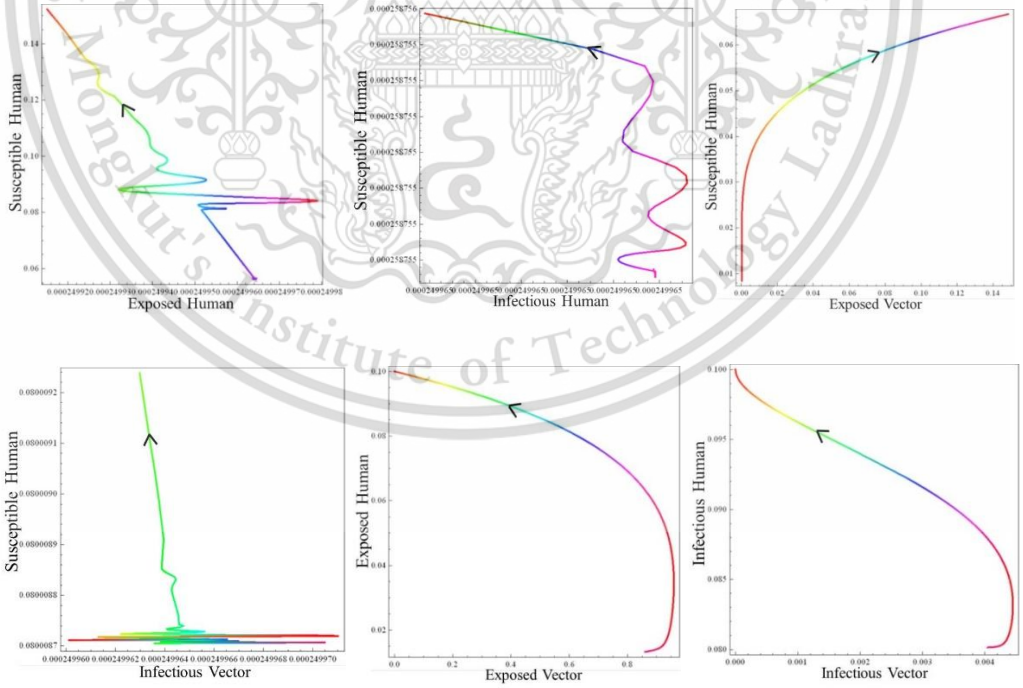


Figure 6.11 The trajectories of the numerical solutions projected onto the 2D (S_H, E_H), (S_H, I_H), (S_H, E_V), (S_H, I_V), (E_H, E_V) and (I_H, I_V) planes when there is no vertical transmission and equilibrium state is the disease-free state.

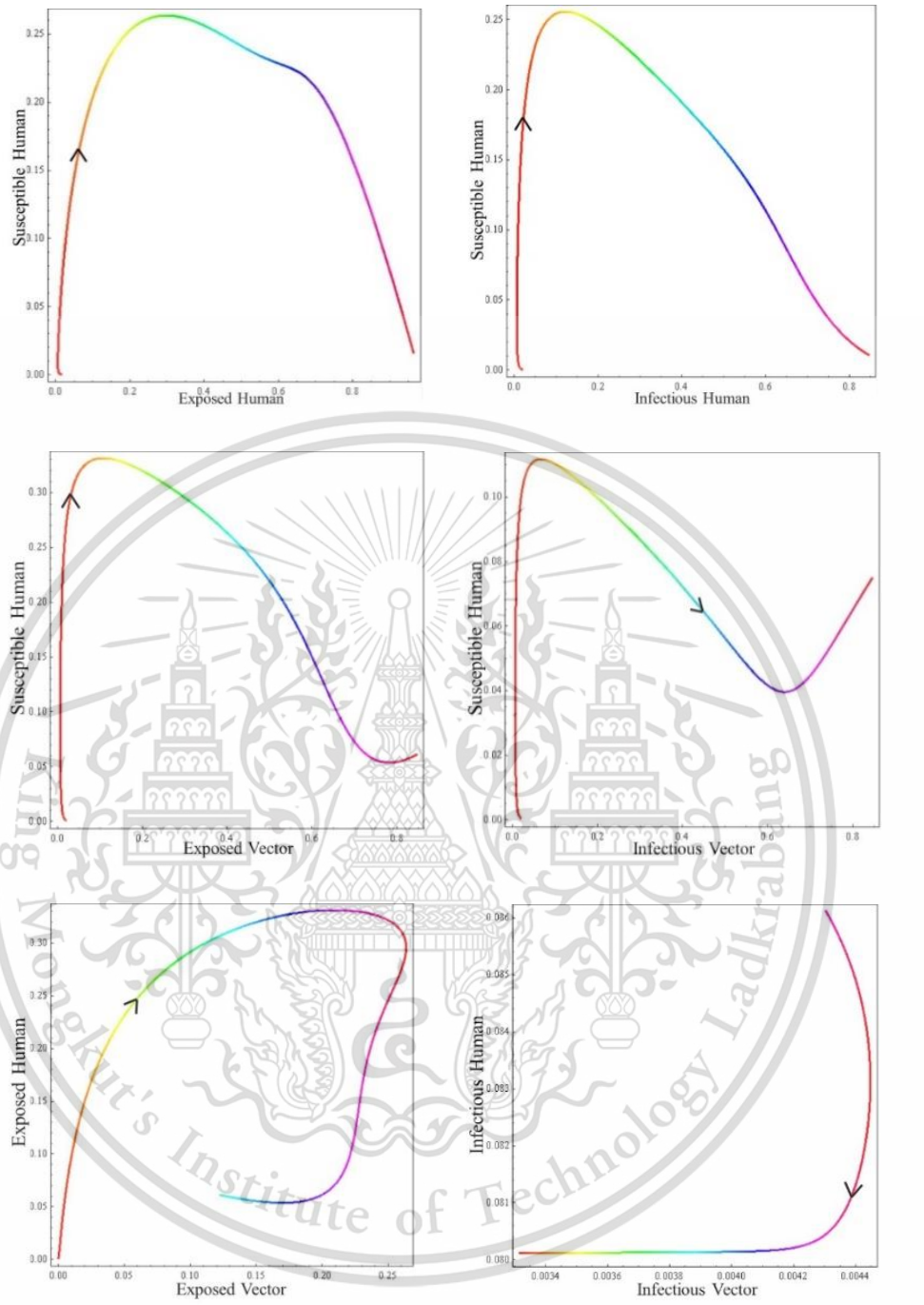


Figure 6.12 The trajectories of the numerical solutions projected onto the 2D (S_H, E_H), (S_H, I_H), (S_H, E_V), (S_H, I_V), (E_H, E_V) and (I_H, I_V) planes when there is no vertical transmission and the equilibrium state is endemic state

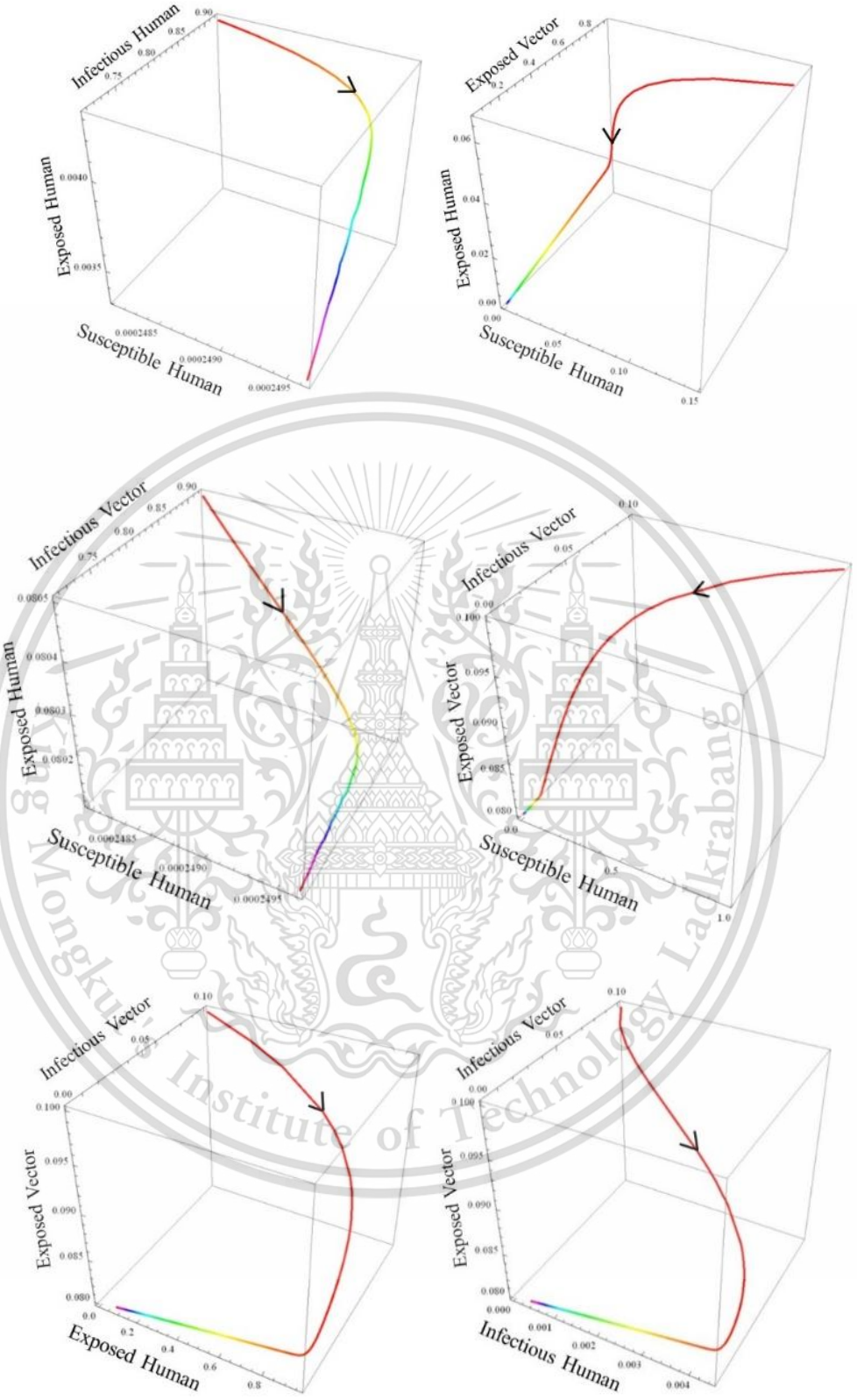


Figure 6.13 The trajectories of the numerical solutions of the model when vertical transmission occurs into the 3D (S_H, E_H, I_H), (S_H, E_H, E_V), (S_H, E_H, I_V), (S_H, E_V, I_V), (E_H, E_V, I_V), and (I_H, E_V, I_V) space.

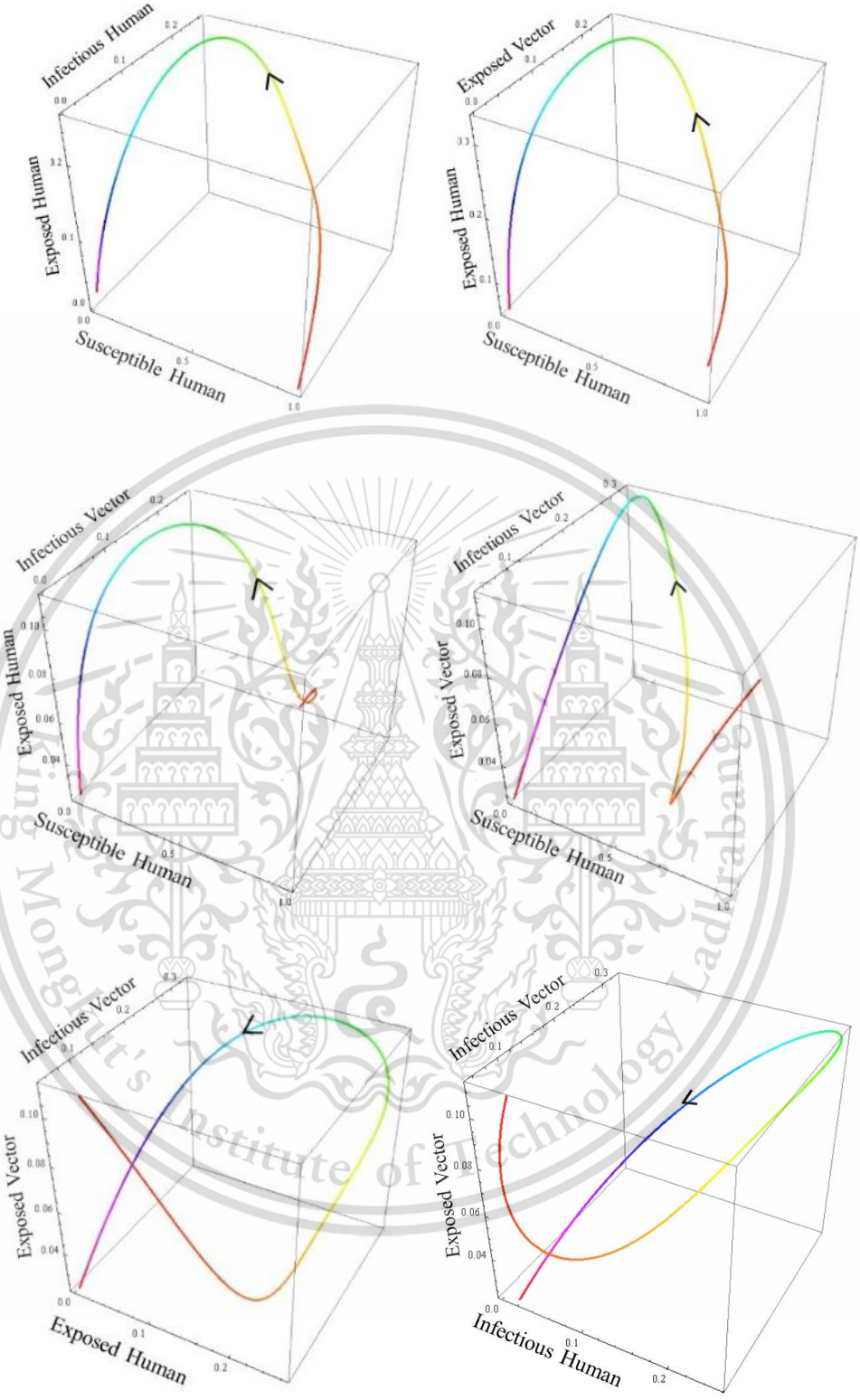


Figure 6.14 The trajectories of the numerical solutions into the 3D (S_H, E_H, I_H), (S_H, E_H, E_V), (S_H, E_H, I_V), (S_H, E_V, I_V), (E_H, E_V, I_V), and (I_H, E_V, I_V) space when there is no vertical transmission and the values of the parameters are such that the equilibrium state is the disease-free state.

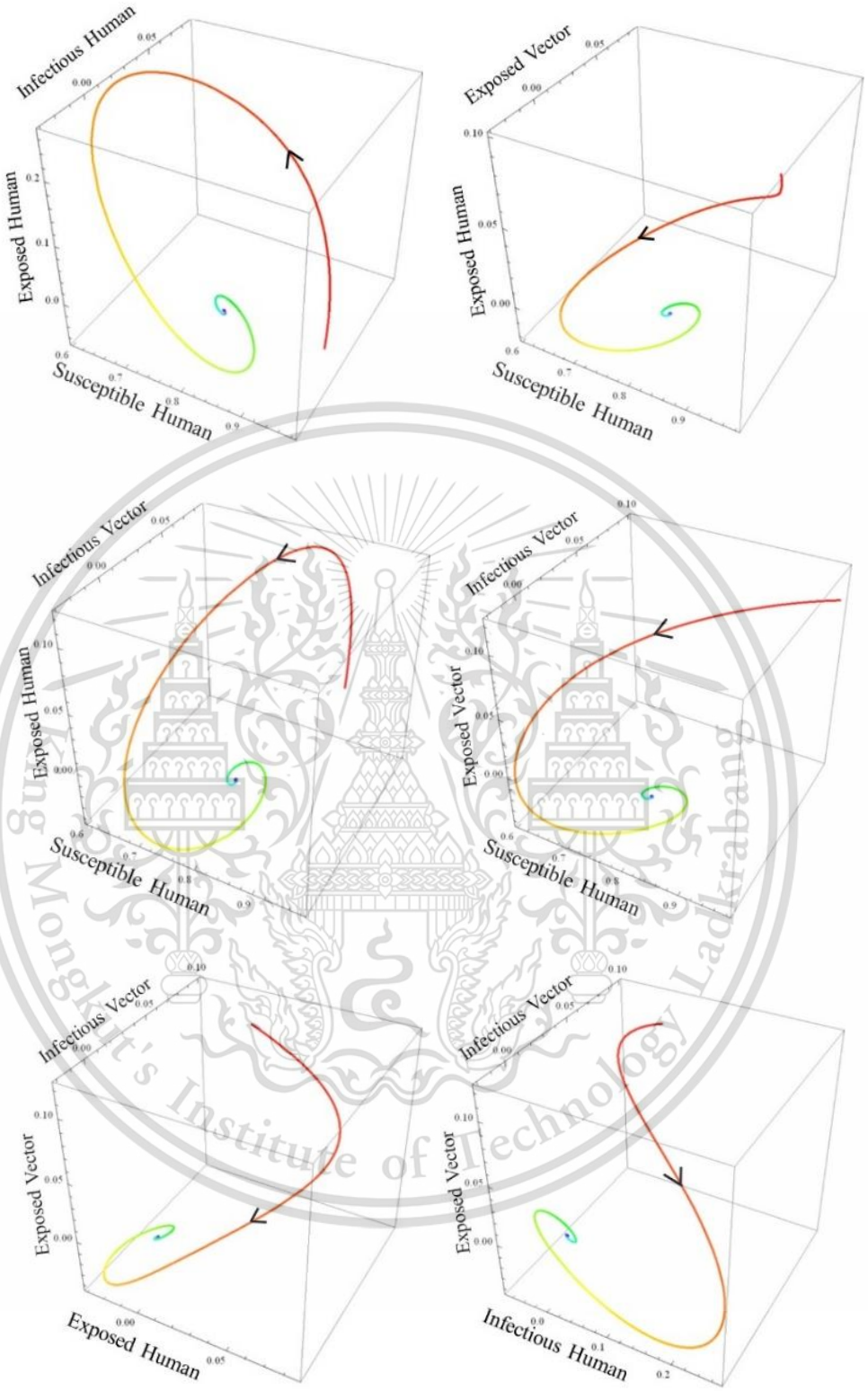


Figure 6.15 The trajectories of the numerical solutions into the 3D (S_H, E_H, I_H), (S_H, E_H, E_V), (S_H, E_H, I_V), (S_H, E_V, I_V), (E_H, E_V, I_V), and (I_H, E_V, I_V) space when there is no vertical transmission and the values of the parameters are such that the equilibrium state is the endemic disease state.

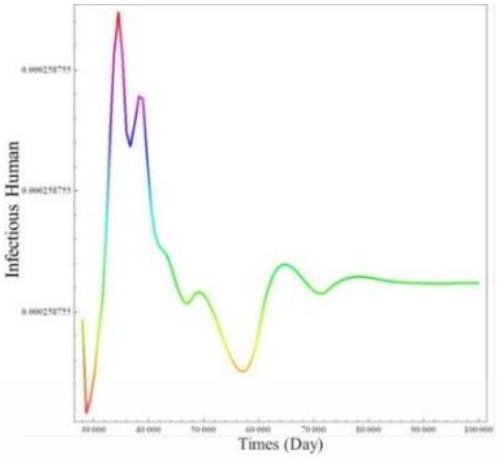
6.4 Discussion and Conclusion

In this paper, the dynamical transmission of dengue disease using SEIR mathematical models which focus on the transmission of the virus in the mosquito by its being bitten by an infected human or by vertical transmission mode, i.e., through sexual contact with a male mosquito is studied. It is shown that the presence of vertical transmission insures that the endemic equilibrium state is the only possible outcome. In the absence of vertical transmission, the model leads to two possible outcomes, a disease-free equilibrium state and an endemic equilibrium state which depend on whether $R_0 < 1$ or $R_0 > 1$. The Routh-Hurwitz criteria for the coefficients of the characteristics equations for the system are used to determine whether all the eigenvalues have negative imaginary parts.

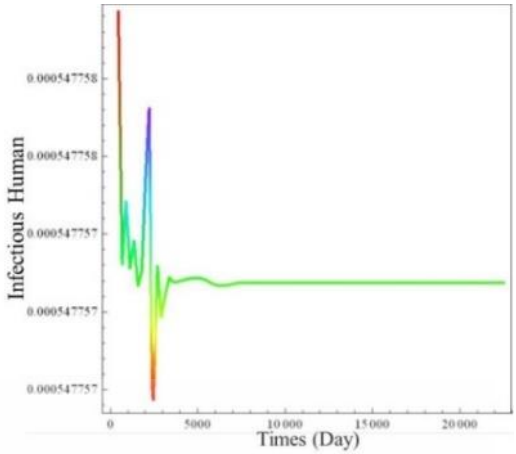
When there is vertical transmission of the virus in the mosquito and the values of the parameters are such that $R_0 > 1$, the only equilibrium state is the endemic equilibrium point, E_1, and it is local asymptotically stable as can be seen from Figure 6.4 which shows the values of the parameters satisfy the Routh-Hurwitz criteria. The time trajectories of S_H, E_H, I_H, E_V and I_V are plotted on Figure 6.7. The trajectories of the numerical solutions are plotted on the 2D (S_H, E_H), (S_H, I_H), (S_H, E_V), (S_H, I_V), (E_H, E_V) and (I_H, I_V) planes and in the 3D (S_H, E_H, I_H), (S_H, E_H, E_V), (S_H, E_H, I_V), (S_H, E_V, I_V), (E_H, E_V, I_V), and (I_H, E_V, I_V) spaces seen in Figure 6.10 and Figure 6.13 respectively.

In the absence of vertical transmission, the disease-free equilibrium point, E_0, will be local asymptotically stable when $R_0 < 1$. The range of values of the parameters for which the coefficients of the characteristic equation for eigenvalues satisfy the Routh-Hurwitz criteria for the disease-free state to be local asymptotical stable are shown in Figure 6.5. Picking the values (the ones listed for case 2 in Table 6.1 and given in figure caption), the time dependences of S_H, E_H, I_H, E_V and I_V are plotted in Figure 6.8. The trajectories of the numerical solutions are plotted in the 2D (S_H, E_H), (S_H, I_H), (S_H, E_V), (S_H, I_V), (E_H, E_V) and (I_H, I_V) and the 3D (S_H, E_H, I_H), (S_H, E_H, E_V), (S_H, E_H, I_V), (S_H, E_V, I_V), (E_H, E_V, I_V), and (I_H, E_V, I_V) space in Figures 6.11 and 6.14 respectively. The endemic equilibrium point, E_2, is local asymptotically stable for $R_0 > 1$. The behaviors of the populations for this case (case 3) are shown in Figures 6.9, 6.12, and 6.15.

To see the influence of vertical transmission in the mosquitoes on the human and mosquito populations, we have plotted on Figures 6.16(a) and 6.16(b) the time dependence of the infectious humans and mosquitoes in the presence or absence of vertical transmission of the virus in the mosquitoes of I_H and I_V. In both cases, the equilibrium state was the endemic state. We see that the equilibrium states were reached slower when vertical transmission of the virus in the mosquito occurs.

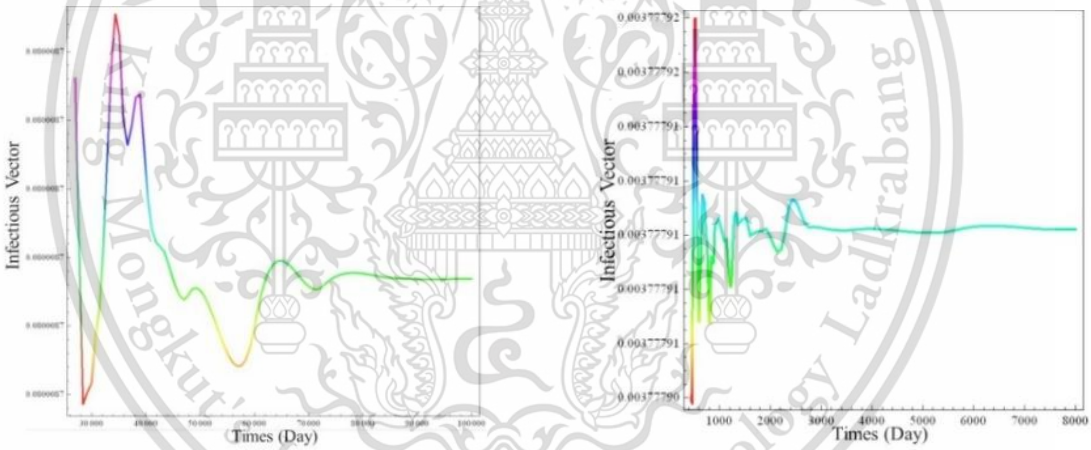


In the presence of vertical transmission of the virus.



In the absence of vertical transmission of the virus.

Figure 6.16 (a) The time series comparison of dengue disease with and without the effect of vertical transmission for infectious human, I_H.



Behavior when vertical transmission is possible

Behavior when no vertical transmission is possible

Figure 6.16 (b) The time series comparison of dengue disease with and without the effect of vector born infection projected onto infectious vector, I_V.

Chapter 7

SIR model for dengue disease with effect of dengue vaccination

The dengue disease is caused by dengue virus and there is no specific treatment. The medical care by an experienced physicians and nurses will save life and will lower the mortality rate. A dengue vaccine to control the disease has been available in Thailand since late 2016. Mathematical model would be an important way to analyze the effects of the vaccination on the transmission of the disease. We have formulated a SIR (Susceptible-Infected-Recovered) model of the transmission of the disease which includes the effect of vaccination and used standard dynamical modeling methods to analyze the effects. The equilibrium states and their stabilities are investigated. The trajectories of the numerical solutions plotted into the 2D planes and 3D spaces are presented. The main contribution is determining the role of dengue vaccination in the model. From the analysis, we find that there is a significant reduction in the total hospitalization time needed to treat the illness.

7.1 Introduction

Dengue disease is a mosquito-borne viral infection caused by 4 serotypes of dengue virus, DEN-1, DEN-2, DEN-3, and DEN-4. Dengue disease is widely spread in tropical and sub-tropical region of the world. Dengue virus is transmitted to human by the bite of the female mosquito of the species, Aedes aegypti and Aedes albopictus [1]. An estimated 3.9 billion people in 128 countries are at risk to this disease. The countries at danger to infection by the dengue viruses around the world are shown on Figure 1.1 [2].

Thailand is located in tropical region where dengue virus is widely circulating. Dengue is spreading nationwide in Thailand including the Bangkok metropolitan area. Thailand is in special danger since three of the four species of the dengue virus have been found in Thailand and both of the *Aedes* vector species are present. The Bureau of Epidemiology, Ministry of Public Health has reported dengue cases in all provinces in 2016, a total of 63,931 cases with 64 deaths [3]. At the present time, there is no special treatment for dengue disease but early detection and the appropriated medical care will decrease the fatality rates. A dengue vaccine would be another way to reduce the fatality rates. WHO reported the first dengue vaccine, called as Dengvaxia (CYD-TDV). It was registered in several countries in late 2015 and early 2016. It was recommended for use only in high dengue disease burden countries such as Thailand [1]. Dengue vaccine against four strains of the dengue virus was first launched in

Thailand in late 2016. The vaccine would be suitable for use in individuals between 9-45 years of age living in endemic areas. Since the reported incidence of dengue peaks in the rainy season between June to September, the vaccination should in advance of the peak period in order for the immunity to develop.

There were many mathematical models for describing and analyzing the behaviors of dengue disease. Esteva and Vargas [31] proposed a SIR (susceptible-Infected-Recovery) model to describe the transmission of dengue disease with constant human and vector populations while Chanprasopchai et al. [76] proposed a SEIR (Susceptible-Exposed-Infected-Recovered) model for Thailand to deter-mine the effect of the rainfall on the spread of dengue in Thailand model. The transmission of dengue disease is assumed to depend on the nature of the rainfall in different countries. The stability of the solution of the model was then analyzed. Numerical results taking into account the rainfall was obtained and they were seen to correspond to the analytical results. Using standard dynamical analysis techniques, Chanprasopchai and Pongsumpun [37] established relations between the different variables in a SIR model of the dengue transmission model in which the biting rate of mosquito became as factor. Pongsumpun and Tang [49] analyzed the transmission of dengue hemorrhagic fever in a SIR model which included an age structure in human population.

Recently, Shim [77] studied the recently approved dengue vaccination program in the Philippines and showed that with appropriated pricing of dengue vaccination, reduction of the burden of the dengue disease in the Philippines and a significant potential to confer excellent value were possible. Aguiar et al. [78] has proposed a mathematical modeling for investigating the impact of the newly licensed dengue vaccine using different scenarios and presented the results for achieving significant reduction in disease burden. The vaccination program is most effective when only individuals have been already been exposed to at least one dengue virus. Recker et al. [79] reported that the availability of epidemiological and clinical data from the trials of vaccine provided a great opportunity for formulating mathematical models in which the vaccine efficacy depends on the serotype, age, host immune status, and severity. Mathematical modelling becomes a valuable tool in the policy-making process to estimate what the consequences of any decisions taken could be.

In this study, we propose a SIR mathematical model to analyze the behaviors of the transmission of dengue disease with vaccination effect and apply it to Thailand. The standard analysis method using Routh – Hurwitz criteria is applied to investigate the system stability which the dynamical transmission model of dengue disease, equilibrium state, stability, numerical simulation, results and conclusion are presented.

7.2 Methodology

In our SIR model, the population is divided into 2 populations, a human and a vector populations. The human population consists of three epidemiological states; susceptible humans $(\overline{S_H})$, infected humans $(\overline{I_H})$, and recovered humans $(\overline{R_H})$, while the vector population has two epidemiological states; susceptible vector $(\overline{S_V})$ and infected vector $(\overline{I_V})$.Mosquito has no recovery state since the mosquito dies before it can recover from the disease. Susceptible mosquito state is un-immune and un-infected while in the infected state, it is infected with dengue virus and can transmit the virus. Recovery state in the human population is a person who has recovered from an infection by the dengue virus. We assumed that the human and vector populations are constant. The dynamical transmission of human and mosquito population with effect of vaccination is shown in Figure 7.1.

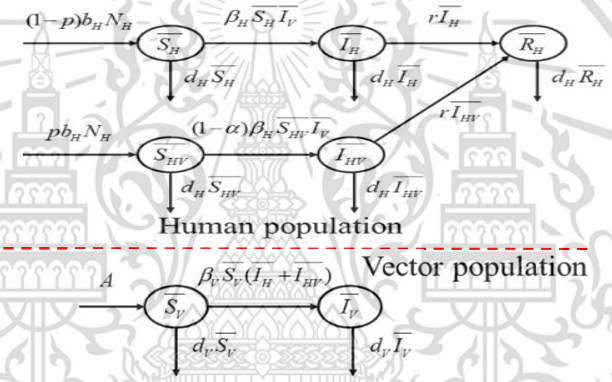


Figure 7.1 Dynamical transmission of human and mosquito with effect of vaccination

where;

$\overline{S_H}(t)$ = Number of susceptible humans population who has unvaccinated at time t,

$\overline{I_H}(t)$ = Number of infected humans population who has unvaccinated at time t,

$\overline{R_H}(t)$ = Number of recovered humans population who has unvaccinated at time t,

$\overline{S_{HV}}(t)$ = Number of susceptible humans population who has vaccinated at time t,

$\overline{I_{HV}}(t)$ = Number of infected humans population who has vaccinated at time t,

$\overline{S_V}(t)$ = Number of susceptible vector population at time t,

$\overline{I_V}(t)$ = Number of infected vector population at time t,

d_H, d_V = Death rate of human population, Vector population,

N_H, N_V = Total human population, total vector population,

β_H, β_V = Transmission rate of dengue virus from vector to human, human to vector,

b_H = Birth rate of human population,

A = Constant recruitment rate of vector population,

α = Vaccine efficacy, and

p = fraction of newborns vaccinated.

The transmission model of dengue disease with effect of vaccination can be described by the following differential equations:

$$\left.\begin{aligned}
\frac{d\overline{S_H}}{dt} &= (1-p)b_H N_H - \beta_H \overline{S_H}\,\overline{I_V} - d_H \overline{S_H} \\
\frac{d\overline{I_H}}{dt} &= \beta_H \overline{S_H}\,\overline{I_V} - \gamma \overline{I_H} - d_H \overline{I_H} \\
\frac{d\overline{R_H}}{dt} &= \gamma(\overline{I_H} + \overline{I_{HV}}) - d_H \overline{R_H} \\
\frac{d\overline{S_{HV}}}{dt} &= pb_H N_H - (1-\alpha)\beta_H \overline{S_{HV}}\,\overline{I_V} - d_H \overline{S_{HV}} \\
\frac{d\overline{I_{HV}}}{dt} &= (1-\alpha)\beta_H \overline{S_{HV}}\,\overline{I_V} - \gamma \overline{I_{HV}} - d_H \overline{I_{HV}} \\
\frac{d\overline{S_V}}{dt} &= A - \beta_V \overline{S_V}(\overline{I_H} + \overline{I_{HV}}) - d_V \overline{S_V} \\
\frac{d\overline{I_V}}{dt} &= \beta_V \overline{S_V}(\overline{I_H} + \overline{I_{HV}}) - d_V \overline{I_V}
\end{aligned}\right\} \quad (7.1)$$

The total human and vector populations are assumed to be governed by the following conditions:

$$\left.\begin{aligned}
\overline{S_H} + \overline{I_H} + \overline{R_H} + \overline{S_{HV}} + \overline{I_{HV}} &= N_H \\
\overline{S_V} + \overline{I_V} &= N_V
\end{aligned}\right\} \quad (7.2)$$

where:

N_H = Total number the human population, and

N_V = Total number the vector population

If total human and vector populations are constants, then the rates of change for total human and vector populations are 0. As the results, we will have the following equations:

$$\left.\begin{aligned}
\frac{d\overline{S_H}}{dt} + \frac{d\overline{I_H}}{dt} + \frac{d\overline{R_H}}{dt} + \frac{d\overline{S_{HV}}}{dt} + \frac{d\overline{I_{HV}}}{dt} &= 0 \\
\frac{d\overline{S_V}}{dt} + \frac{d\overline{I_V}}{dt} &= 0
\end{aligned}\right\} \quad (7.3)$$

$$\left.\begin{aligned}
N_V &= A/\mu_V \\
b_H &= d_H
\end{aligned}\right\} \quad (7.4)$$

Normalizing the equations by introducing the following normalized variables:

$$\left.\begin{aligned}
S_H = \frac{\overline{S_H}}{N_H}, I_H = \frac{\overline{I_H}}{N_H}, R_H = \frac{\overline{R_H}}{N_H}, S_{HV} = \frac{\overline{S_{HV}}}{N_H}, I_{HV} = \frac{\overline{I_{HV}}}{N_H} \\
S_V = \frac{\overline{S_V}}{N_V}, I_V = \frac{\overline{IV}}{N_V}
\end{aligned}\right\} \quad (7.5)$$

Introducing these normalized variables into equations (7.1) we get the new set of equations of states:

$$\left.\begin{aligned}
\frac{dS_H}{dt} &= (1-p)b_H - \beta_H S_H I_V N_V - d_H S_H \\
\frac{dI_H}{dt} &= \beta_H S_H I_V N_V - \gamma I_H - d_H I_H \\
\frac{dS_H}{dt} &= pb_H - (1-\alpha)\beta_H S_{HV} I_V N_V - d_H S_{HV} \\
\frac{dI_{HV}}{dt} &= (1-\alpha)\beta_H S_{HV} I_V N_V - \gamma I_{HV} - d_H I_{HV} \\
\frac{dI_V}{dt} &= \beta_V S_V (I_H + I_{HV}) N_H - d_V I_V
\end{aligned}\right\} \quad (7.6)$$

The equilibrium states are obtained by setting the right-hand side of equations (7.6) to be 0. Doing this, we obtain an expression for something known as the basic production number R_0. This number is defined as

$$R_0 = \frac{\varepsilon_1(-(-2+\alpha)\varepsilon_2 d_V + N_H((1-p\alpha)d_H + \varepsilon_3 N_V \beta_H)\beta_V)}{\sqrt{\varepsilon_1^2(\alpha^2\varepsilon_2^2 d_V^2 + 2\alpha\varepsilon_2 d_V N_H((1+p(-2+\alpha))d_H + (-1+2p)\varepsilon_3 N_V \beta_H)\beta_V + N_H^2((-1+p\alpha)d_H + \varepsilon_3 N_V \beta_H)^2 \beta_V^2)}}$$

When *Ro ≤ 1*, the equilibrium state will be the disease free state *E1* defined as

$E_1(t) = (S_H = 1-p, I_H = 0, S_{HV} = p, I_{HV} = 0, I_V = 0),$

and when $R_0 > 1$, the equilibrium state is the endemic state defined as

$E_2(t) = (S_H^*(t), I_H^*(t), S_{HV}^*(t), I_{HV}^*(t), I_V^*(t))$

where;

$$S_H^*(t) = \frac{\varepsilon_1(\alpha\varepsilon_2 d_V + \varepsilon_3\varepsilon_4) + \varepsilon_5}{2\alpha d_H \varepsilon_6}$$

$$I_H^*(t) = \frac{\varepsilon_1(-\alpha\varepsilon_2 d_V + (1+\alpha-2p\alpha)\varepsilon_4) - \varepsilon_5}{2\alpha\varepsilon_2\varepsilon_6}$$

$$S_{HV}^*(t) = \frac{\varepsilon_1(-\alpha\varepsilon_2 d_V + \varepsilon_3\varepsilon_4) + \varepsilon_5}{2\varepsilon_3\alpha d_H \varepsilon_6}$$

$$I_{HV}^*(t) = \frac{\varepsilon_1(\alpha\varepsilon_2 d_V + \varepsilon_3(-1+2p\alpha)\varepsilon_4) - \varepsilon_5}{2\varepsilon_3\alpha\varepsilon_2\varepsilon_6} \text{ and}$$

$$I_V^*(t) = \frac{\varepsilon_1(-(-2+\alpha)\varepsilon_2 d_V + \varepsilon_3\varepsilon_4) - \varepsilon_5}{2\varepsilon_3\varepsilon_2 d_V N_V^2 \beta_H^2},$$

with

$\varepsilon_1 = d_H N_V \beta_H$

$\varepsilon_2 = (\gamma + d_H)$

$\varepsilon_3 = (-1+\alpha)$

$\varepsilon_4 = N_H N_V S_V \beta_H \beta_V$

$$\varepsilon_5 = \sqrt{d_H^2 N_V^2 \beta_H^2 (\alpha^2(\gamma+d_H)^2 d_V^2} + \sqrt{2(-1+2p)(-1+\alpha)\alpha(\gamma+d_H)d_V N_H N_V S_V \beta_H \beta_V}$$
$$+ \sqrt{(-1+\alpha)^2 N_H^2 N_V^2 S_V^2 \beta_H^2 \beta_V^2}$$

$\varepsilon_6 = N_H N_V^2 S_V \beta_H^2 \beta_V.$

The equilibrium states are local asymptotically stable if all the eigenvalues have negative real parts. The eigenvalues ($\boldsymbol{\lambda}$) are obtained by solving the eigenvalue matrix equation

$$\boldsymbol{Det|J - \lambda I| = 0} \qquad (7.7)$$

where

J is the Jacobian matrix of each equilibrium point,

$\boldsymbol{\lambda}$ is the eigenvalue and

I is the identity matrix.

Constructing the Jacobian matrix from equation (7.6) and evaluating it at the two equilibrium points, we obtain the eigenvalue equation

$$(-\lambda - \gamma - d_H)(\lambda^4 + e_1\lambda^3 + e_2\lambda^2 + e_3\lambda^1 + e_4) = 0 \qquad (7.8)$$

For the disease free state E_1 and the eigenvalue equation

$$(\lambda^5 + e_1\lambda^4 + e_2\lambda^3 + e_3\lambda^2 + e_4\lambda^1 + e_5) = 0 \quad (7.9)$$

For the endemic state E_2.

The eigenvalues of disease free equilibrium state will have negative real parts when the coefficients of equation (7.8) have values satisfying the Routh-Hurwitz criteria

$$\left.\begin{aligned} &e_1 > 0, e_3 > 0, e_4 > 0 \\ &e_1e_2e_3 > e_3^2 + e_1^2e_4 \end{aligned}\right\} \quad (7.10)$$

The eigenvalues of endemic equilibrium state will have negative real parts when the coefficients of equation (7.9) have values which satisfy a different Routh-Hurwitz criteria

$$\left.\begin{aligned} &e_1 > 0, e_2 > 0, e_3 > 0, e_4 > 0, e_5 > 0 \\ &e_1e_2e_3 - e_3^2 - e_1^2e_4 > 0 \\ &(e_1e_4 - e_5)(e_1e_2e_3 - e_3^2 - e_1^2e_4) - e_5(e_1e_2 - e_3)^2 - e_1e_5^2 > 0 \end{aligned}\right\} \quad (7.11)$$

7.3 Results and discussion

The transmission of dengue disease in this study is based on the SIR model with vaccination. The non-zero values of α and p are the parameters are the parameters pertaining to the vaccination program. The numerical simulations were done using the following values of parameters; d_H=1/(65*365) per day corresponding to a life expectancy of 65 years for the Thai people, d_V=1/12 corresponding to a life expectancy of 12 days of mosquito population. For disease free equilibrium state, the parameter values were A=1,000, N_H=1,000, γ_H =1/3, β_H =0.000012, β_V =0.000012, p=0.8, and α=0.8 while the parameters value of endemic equilibrium state, were A=500, N_H=500, γ_H =0.03, β_H =0.000045, β_V =0.000045, p=0.75, and α=0.75. These numerical values in the first set gave $R_0 < 1$ while the values in the second set gave $R_0 > 1$. The trajectories of the numerical simulations for disease free and endemic states of S_H, I_H, S_{HV}, I_{HV}, and I_V are shown in the Figure 7.2 and Figure 7.3, respectively. The trajectories of the numerical simulation for disease free and endemic states plotted in the 2D planes (S_H, I_H), (S_H, S_{HV}), (S_H, I_{HV}), (S_H, I_V), (I_H, S_{HV}), (I_H, I_{HV}), (I_H, I_V), (S_{HV}, I_{HV}), (S_{HV}, I_V) and (I_{HV}, I_V) planes are shown in the Figure 7.4 and Figure 7.5, respectively. The trajectories of the numerical solutions for disease free and endemic states plotted in the 3D spaces (S_H, I_H, S_{HV}), (S_H, I_H, I_{HV}), (S_H, I_H, I_V), (S_H, S_{HV}, I_{HV}), (S_H, S_{HV}, I_V) and (S_H, I_{HV}, I_V) spaces are shown in the Figure 7.6 and Figure 7.7, respectively.

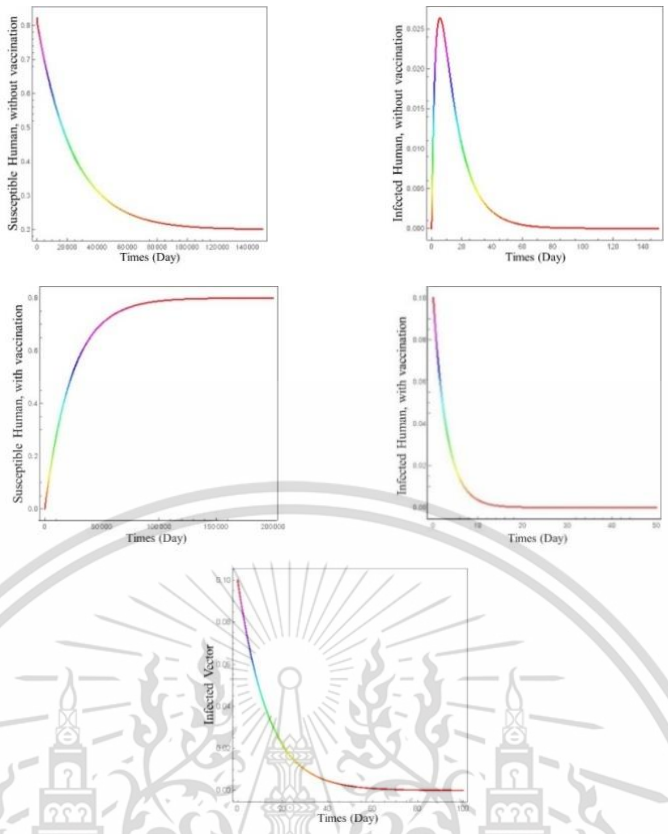


Figure 7.2 The trajectory of S_H, I_H, S_{HV}, I_{HV}, and I_V towards the disease-free equilibrium

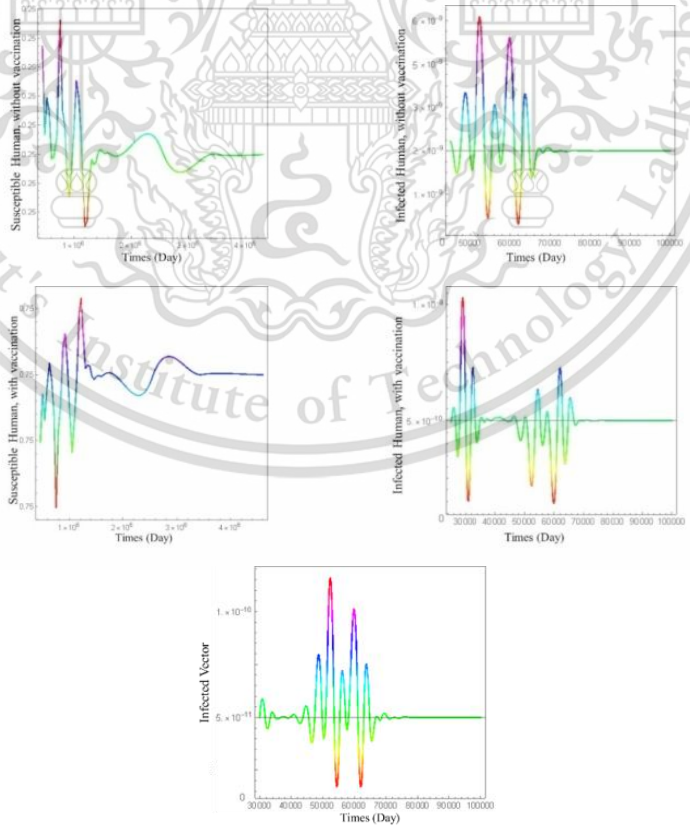


Figure 7.3 The trajectory of S_H, I_H, S_{HV}, I_{HV}, and I_V towards the endemic equilibrium

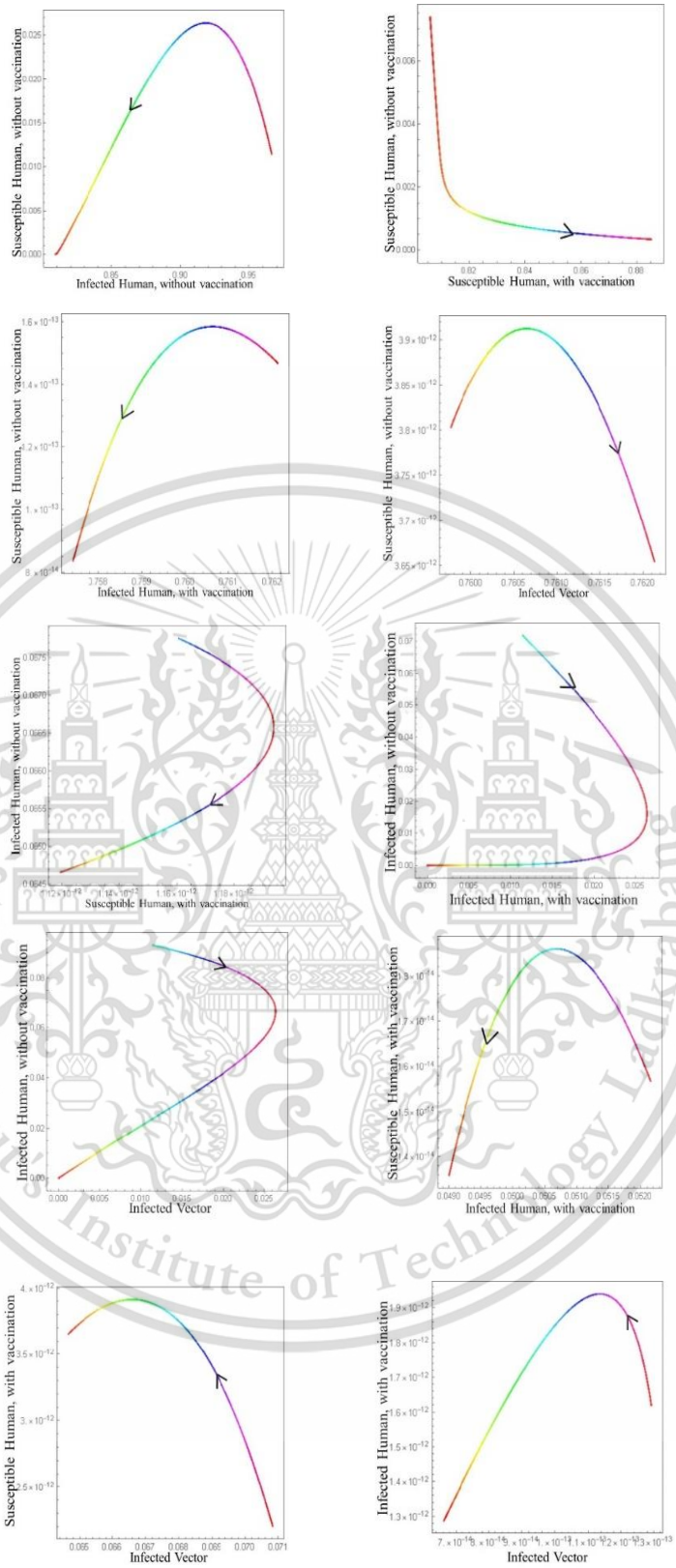


Figure 7.4 Trajectories of dengue disease for disease free equilibrium projected onto (S_H, I_H), (S_H, S_{HV}), (S_H, I_{HV}), (S_H, I_V), (I_H, S_{HV}), (I_H, I_{HV}), (I_H, I_V), (S_{HV}, I_{HV}), (S_{HV}, I_V) and (I_{HV}, I_V)

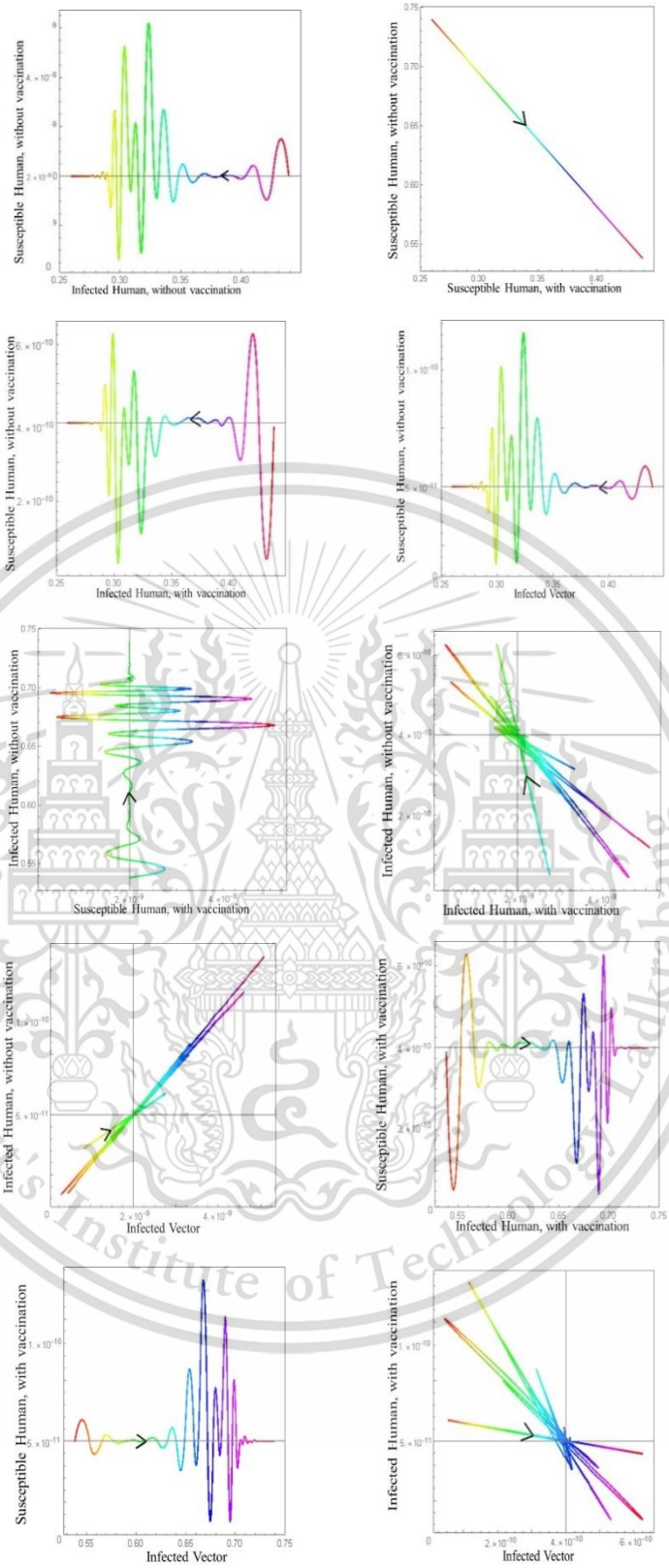


Figure 7.5 Trajectories of dengue disease for endemic equilibrium projected onto (S_H, I_H), (S_H, S_{HV}), (S_H, I_{HV}), (S_H, I_V), (I_H, S_{HV}), (I_H, I_{HV}), (I_H, I_V), (S_{HV}, I_{HV}), (S_{HV}, I_V) and (I_{HV}, I_V)

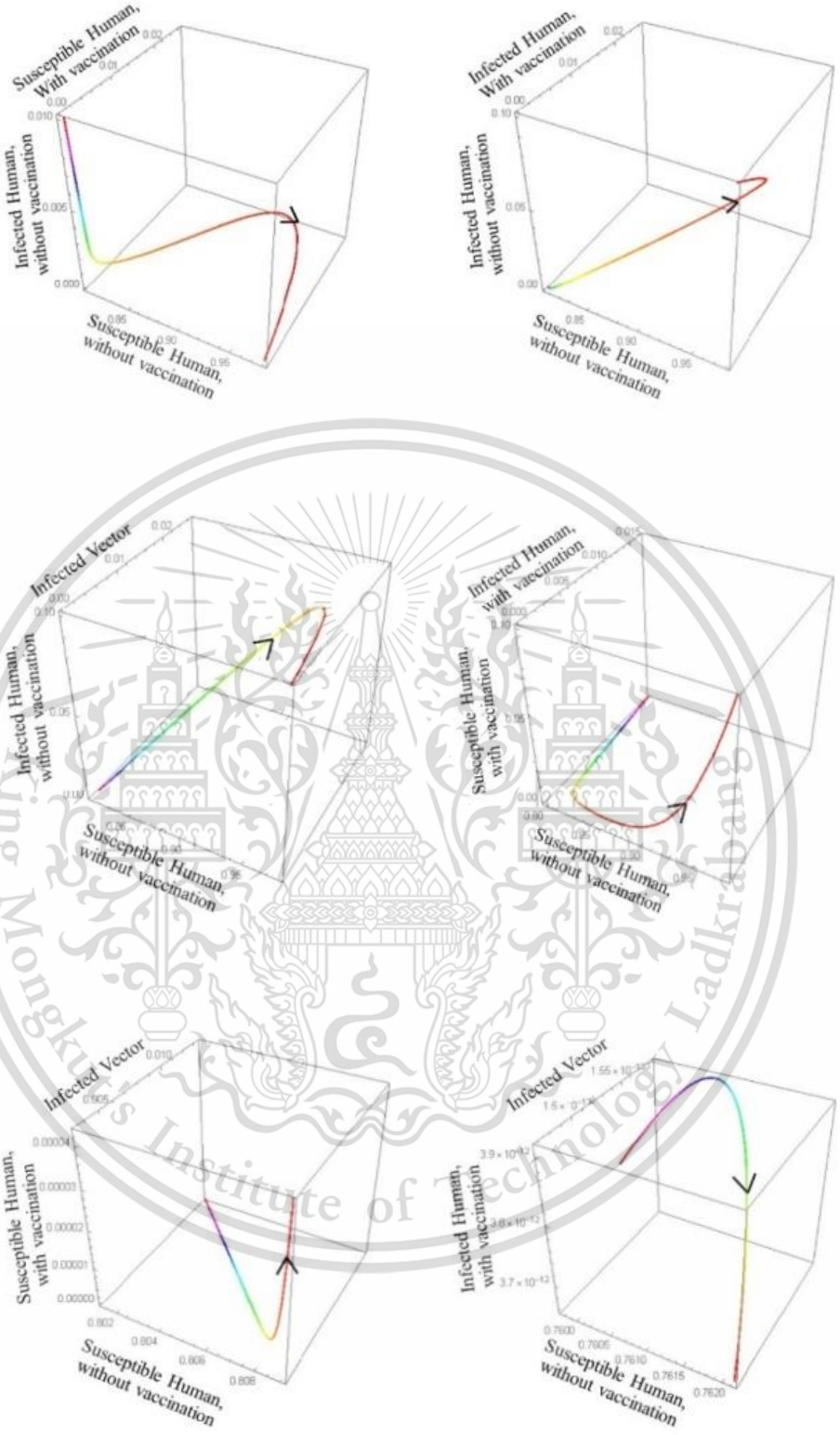


Figure 7.6 Trajectories of dengue disease for disease free equilibrium projected onto (S_H, I_H, S_{HV}), (S_H, I_H, I_{HV}), (S_H, I_H, I_V), (S_H, S_{HV}, I_{HV}), (S_H, S_{HV}, I_V) and (S_H, I_{HV}, I_V)

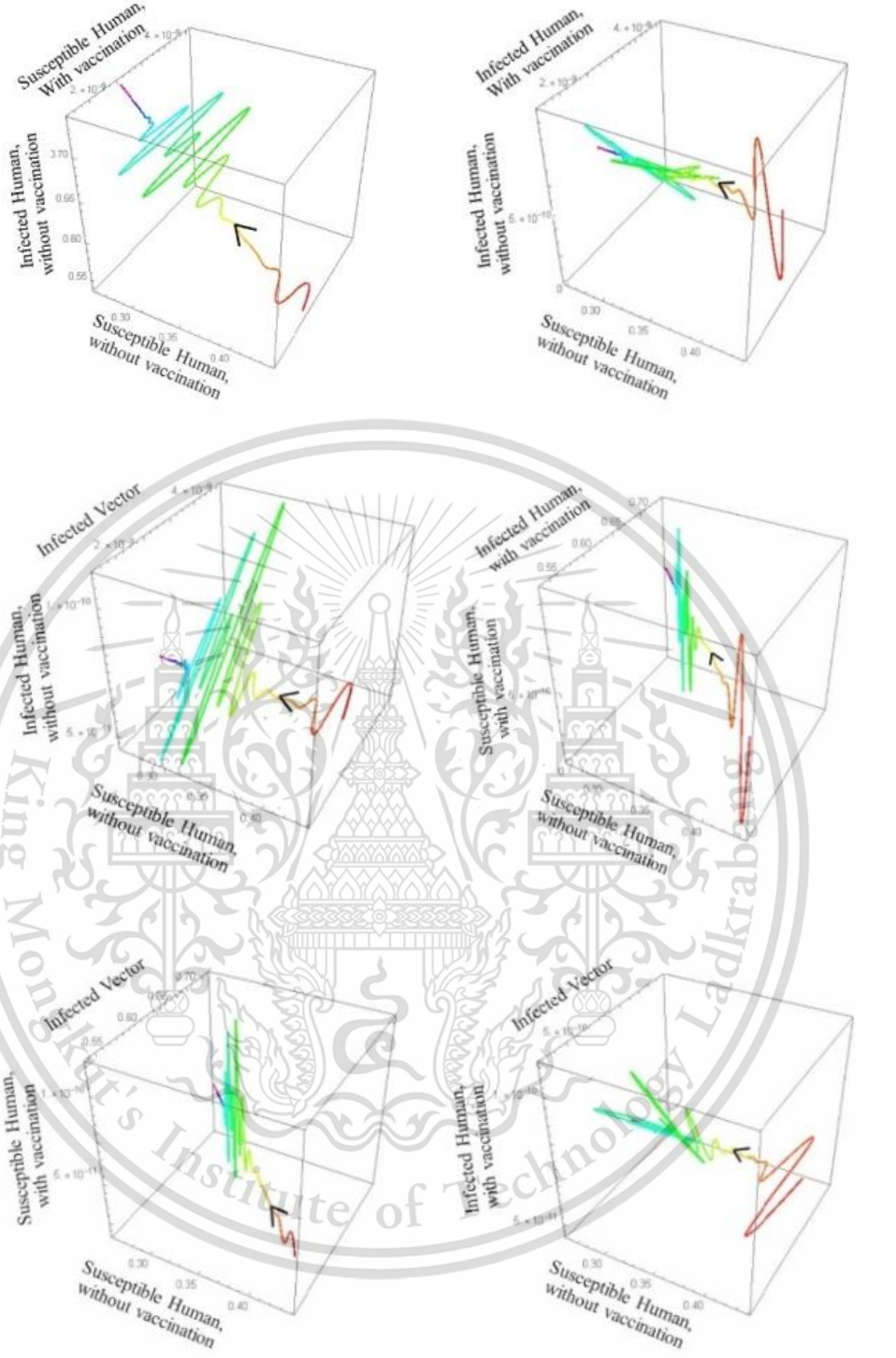
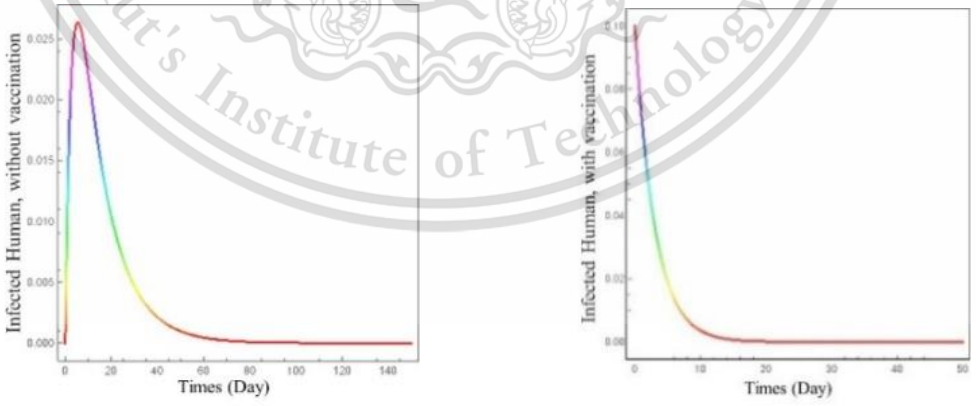


Figure 7.7 Trajectories of dengue disease for endemic equilibrium projected onto (S_H, I_H, S_{HV}), (S_H, I_H, I_{HV}), (S_H, I_H, I_V), (S_H, S_{HV}, I_{HV}), (S_H, S_{HV}, I_V) and (S_H, I_{HV}, I_V)

7.4 Conclusion

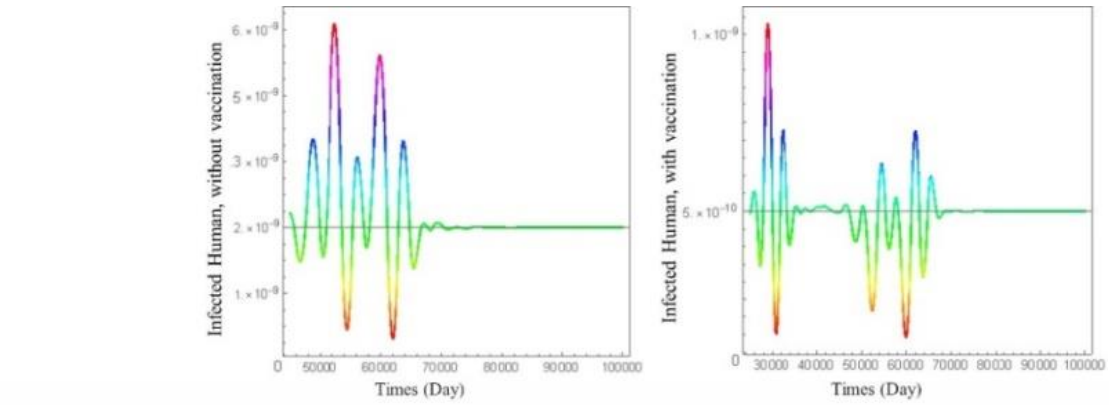
In this study, the dynamical transmission of dengue disease based on a SIR model where a dengue vaccination campaign in the human population has occurred is studied. Again, it is found that the model system has two equilibrium points, a disease free and an endemic states. The occurrence of the two equilibrium states depend on whether $R_0 < 1$ and $R_0 > 1$ where R_0 is the basic reproduction number or number of secondary infection caused by an initial infection. The conditions for the stability of disease free and endemic equilibrium states were established. The time series solution of disease free and endemic equilibrium states are presented in Figure 7.2 and 7.3 respectively. The trajectories of disease free and endemic equilibrium projected onto 2D planes are showed in Figure 7.4 and 7.5 while the trajectories of disease free and endemic equilibrium projected onto 3D planes are showed in Figure 7.6 and 7.7, respectively.

In order to analyze the effect of dengue vaccination, we have investigated both the disease free and endemic states using different values of parameters which would give $R_0 < 1$ and $R_0 > 1$. These same set of numerical values were used for numerical simulation with and without the influence of dengue vaccination campaign. $\alpha = 0$ and $p = 0$ were used in the simulation to get the trajectories in the case where there was no vaccine administrated. The influence of dengue vaccination is seen in Figures 7.8 and 7.9. Figure 7.8 show that the disease free state is sooner when there are dengue viruses vaccines administrated than when there was not vaccines administrated. This means that the hospitalization time can be reduced. Figure 7.9 shows the effects of the vaccine when the parameters are such that the endemic state is equilibrium state.



(a) Without vaccination (b) With vaccination

Figure 7.8 Infected human without vaccination (a) and with vaccination (b) comparison by time series to disease free equilibrium point



(a) Without vaccination (b) With vaccination

Figure 7.9 Infected human without vaccination (a) and with vaccination (b) comparison by time series to endemic equilibrium point

The presence of oscillations around the endemic equilibrium E_2 means that the imaginary part of the eigenvalue is not zero. For the simulation shown in Figure 7.3, the imaginary part of the complex roots is approximately 0.000238428. This leads to an estimate of the period of the oscillations or $T_{period} = 2\pi/\omega$ where ω = imaginary part of λ or $2\pi/0.000238428 \approx 72.20$ years. This value is the approximation to the period of the solutions [31].

In any vaccination campaigns, one must take into account the difference in the efficacy of the vaccine. It may not be the same for all age groups. Since one is not sure about the safety of the vaccine to children, the vaccination has been recommended only for people between the ages of 9 and 45. As of now, the vaccination schedule consists of 3 injections of 0.5 mL administered at 6-month intervals, given on a 0/6/12 month schedule [80].

The campaign in Thailand began in December 2016 and information on efficacy of the vaccine against the different serotypes and the difference in the efficacy for different age groups is being collected. Dengue disease in Thailand occurs in urban and suburban area [52, 53, 54, 55] with peak transmission rates during the rainy season [42, 76]. Seasonal and climate are affect the dengue fluctuation [43, 56, 57, 61]. At present, it is not recommended to give dengue vaccination to pregnant women and travelers or health-care workers at this time due to lack of sufficient data.

Chapter 8
Conclusions and Suggestions

8.1 Conclusions

DF is caused by dengue virus which is transmitted to humans through the bites of infected *Aedes* mosquitoes vector. Transmission of DV is circulating in blood of human during feeding of female mosquito. In this respect the human is called host and the mosquito is called vector of DF dynamical transmission cycle. Dengue fever is regarded one of the most important arboviral infections in the world, whose global incidence has increased dramatically in the current decade. In fact, around half of world's population, including Thailand is living at risk area, and the dengue fever spreads more than 100 countries.

Thailand had reported the dengue fever since 1950 with the first outbreak in 1958. The dynamical transmission of DV is consequently an important determinant of vector-borne disease epidemics and rainfall effect. This investigation and analysis used reported data from the Bureau of Epidemiology, Ministry of Public Health during 2003 – 2015. The mathematical model is formulated to analyze the behaviors of vector born infection and rainfall effect with dengue fever. The classic mathematical model was proposed by Esteva, L. and C. Vargas in 1999 [31]. Many researchers developed various the mathematical models to find the way to control the outbreak and the reproductive number is used to control the outbreak.

The effect of rainfall on the dynamical transmission of dengue disease in Thailand has been studied using the SEIR model to model the dynamical of the dengue epidemic in Thailand. The analysis is based on application of the Routh-Hurwitz criteria to establish the local asymptotic stability of the equilibrium points. Two equilibrium points were found: a disease-free equilibrium point and an endemic equilibrium point. The disease-free equilibrium point, E_1, is locally asymptotically stable for $R_0 < 1$ and $\theta \neq a/T$. When the values of the parameters are such that $R_0 > 1$ and $\theta \neq a/T$, the trajectories ending at the endemic equilibrium point, E_2, is locally asymptotically stable. Everything depends on the form of the basic reproduction number R_0, and whether $R_0 < 1$, yielding the disease-free equilibrium, or $R_0 > 1$ for the endemic equilibrium. Thailand's historical data indicates that rainfall is associated with dengue, where the dengue fever fluctuation is seen to relate to climate variability and seasonal factor. R_0 is an important indicator, where the realistic controlling of the value of R_0 will improve the way to control the outbreak.

The SEIR mathematical models considering the transmission of the virus in the mosquito through being bitten by an infected human and by vertical transmission

mode, i.e., through sexual contact with a male mosquito are studied. The presence of vertical transmission ensures that the endemic equilibrium state is the only possible outcome. In the absence of vertical transmission, the model leads to two possible outcomes, a disease-free equilibrium state and an endemic equilibrium state, both of which depending on whether $R_0 < 1$ or $R_0 > 1$. When there is vertical transmission of the virus in the mosquito and the values of the parameters are such that $R_0 > 1$, the only equilibrium state is the endemic equilibrium point. In the absence of vertical transmission, the disease-free equilibrium point, will be asymptotically stable locally when $R_0 < 1$. The endemic equilibrium point is asymptotically stable clocally for $R_0 > 1$. The influence of vertical transmission in the mosquitoes on the human and mosquito populations, is such that, the equilibrium states are reached slower when vertical transmission of the virus in the mosquito occurs.

The dynamical transmission of dengue disease based on a SIR model with dengue vaccination campaign in the human population is studied. The model system has two equilibrium points, a disease free and an endemic states. The occurrence of the two equilibrium states again depends on whether $R_0 < 1$ and $R_0 > 1$. To analyze the effect of dengue vaccination, both the disease free and endemic states are investigated using different parameter values which would give $R_0 < 1$ and $R_0 > 1$. These same set of numerical values were used for numerical simulation with and without the influence of dengue vaccination campaign. The influence of dengue vaccination shows that the disease free state is reach sooner under the administration of the viruses vaccines, than under the absence of such administration. This revelation means that the hospitalization time can be reduced. In any vaccination campaigns, one must take into account the difference in the efficacy of the vaccine. The campaign in Thailand began in December 2016 and information on efficacy of the vaccine against the different serotypes and the difference in the efficacy for different age groups is being collected. At present, it is not recommended to give dengue vaccination to pregnant women and travelers or health-care workers at this time due to lack of sufficient data.

8.2 Suggestions

The presence of vertical transmission can reduce the time of convergence to the equilibrium state when we decrease the number of transovarially infected mosquitoes (M), the transmission probability of dengue virus from vector population to human (β_H) and the transmission probability of dengue virus from human population to vector (β_V). The effect of reducing these parameters in the vertical transmission i.e. $M=100$, $\beta_H = 0.65$ and $\beta_V = 0.65$ to determine the equilibrium state which the trajectories of the numerical solutions projected onto S_H, E_H, I_H, E_V and I_V are shown in the Figure 8.1. The

vertical transmission of the virus in the mosquito yields only the endemic equilibrium point ($R_0 > 1$). Figure 8.2 show the relationship between M and R_0. Note also that our chosen M value effectively guarantees the endemic equilibrium point.

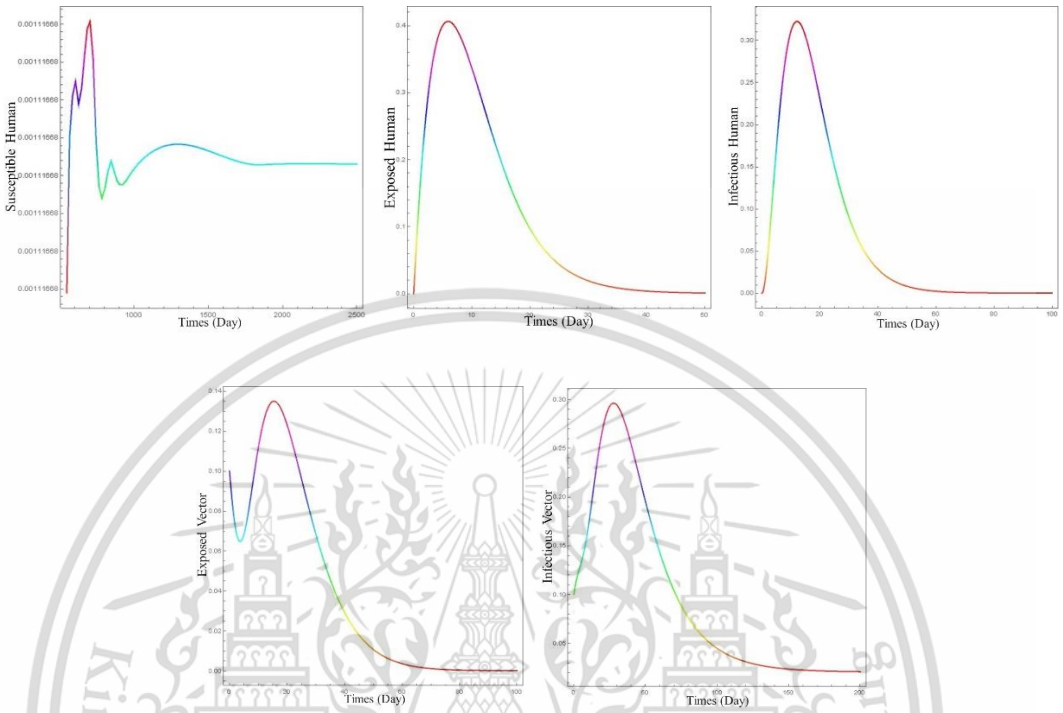


Figure 8.1 The time trajectories of the reduced parameters value ($M=100$, $\beta_H = 0.65$, and $\beta_V = 0.65$) involved in the vertical transmission for S_H, E_H, I_H, E_V and I_V are shown.

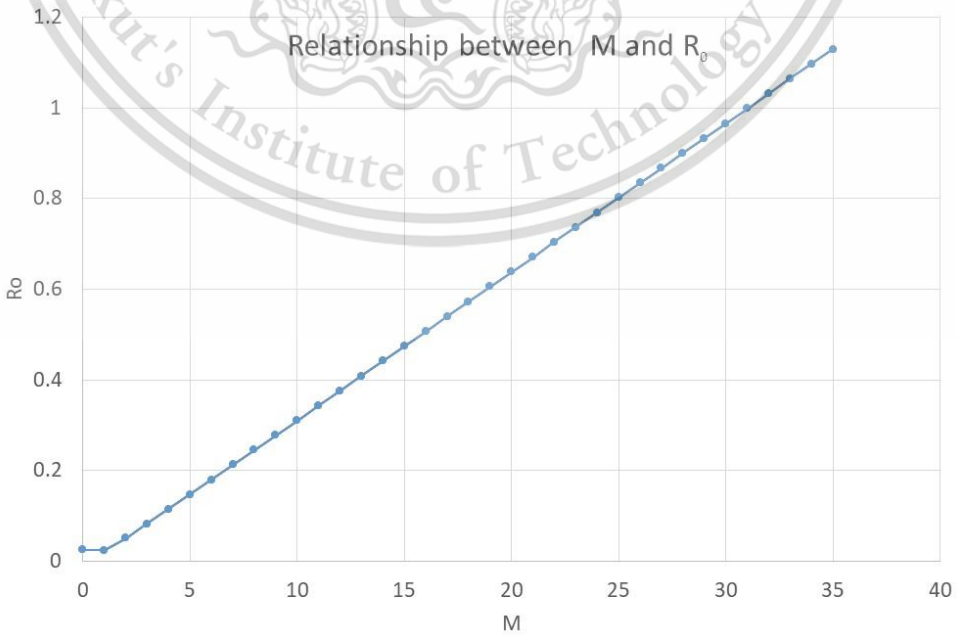


Figure 8.2 The relationship between M and R_0 is shown.

Department of Disease Control (DDC) reported that the available Dengvaxia dengue vaccine contains some side effects for people who have not previously been infected [80]. People should have a medical consultation before administering the vaccine, even though no ill effects had yet been detected in Thailand [80]. Althrough, the Ministry of Public Health retains the registration of the Dengvaxia dengue vaccine, they will however adjust some wordings on the drug label, and will advise doctors to exercise caution in vaccination [81]. People have not been infected with dengue may still suffer severe dengue fever if inoculated with the vaccine, but the dengue vaccine works well with people who are used to contract the disease [81].

At present, the traditional method to control the transmission of dengue fever is controlling the spread of mosquitoes such as environmental management of egg laying, waste disposing, and water storage. In addition, the suitable ways to control the dengue disease are environmental management to prevent mosquitoes from laying their eggs and breeding and using of personal household protection to prevent contact between human and mosquitoes [1, 2].

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Appendices

Appendix A

Paper 1

Dengue disease in Thailand and mathematical model for dynamical transmission of dengue disease

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DENGUE DISEASE IN THAILAND AND MATHEMATICAL MODEL FOR DYNAMICAL TRANSMISSION OF DENGUE DISEASE

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ABSTRACT

In this paper, we proposed the historical data of dengue disease in Thailand. The reported case and death due to dengue disease are presented by total number, region, month, age, and occupation. The mathematical model is the key to analyze dengue disease which can investigate the reproductive number in order to control the outbreak. At the current, the best way to control the outbreak is controlling the environmental of spreading of dengue disease.

Keywords: Basic reproductive number, dengue disease, endemic equilibrium state, mathematical model, outbreak.

INTRODUCTION

Dengue virus is found in tropical and subtropical region around the world such as South-East Asia, the Western Pacific and Latin and Central America [1]. Dengue virus is transmitted to human by biting of *Aedes* mosquitoes. There is four serotypes: DEN1, DEN2, DEN3, and DEN4. The mosquitoes can be growth in any places that have stagnant water which can be found anywhere and anytime in home. Mosquito is the most dangerous animal on earth because of the number of people killed by mosquito per year. The Washington Post, April 29, 2014, stated that mosquito is the animal that can kill most of people. Mosquitoes can carry devastating diseases, which are included malaria, yellow fever, encephalitis and dengue fever. Dengue disease is an international public health concern that is no specific treatment. There is no vaccine available that the appropriate medical care frequently survives the lives of patients. The way to control dengue disease is focused on mosquitoes spreading. Therefore, the mathematical model is an important tool in order to analyze the spread and control of infectious disease that can provide the dengue epidemic in order to better understand the mechanisms.

Dengue disease is a fastest emerging arboviral infection spread by *Aedes* mosquitos with major public health consequences in over 100 tropical and sub-tropical countries in South-East Asia, the Western Pacific and Latin and Central America which around 2.5 billion people globally live under the threat of dengue fever (WHO, 2013). The rising level of dengue infections around the world has become seriously an international concern that has increased with increasing geographic expansion distribution [1].

DENGUE DISEASE IN THAILAND

The first case of dengue disease in Thailand observed in 1949 and continued throughout 1950 and the first major outbreak of dengue disease was appeared in Bangkok in 1958 [2]. The

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historical reported case and death of dengue disease in Thailand during 1958-2014 are shown in Figure 1.

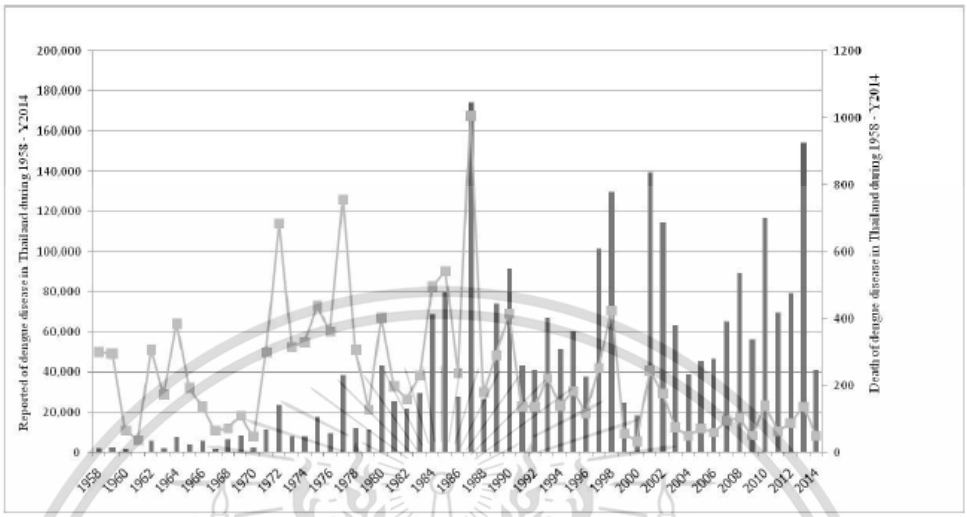

Figure 1: Historical reported and death of dengue disease in Thailand
Source: The Bureau of vector born disease, Thai ministry of public health [3]

The reported of deaths, reported rates, deaths rates, reported fatality rates (%), and population of dengue disease are presented[3]. The reported case and death due to dengue disease by regional in Thailand during 2003-2014 are shown in Figure 2 and Figure 3 respectively. The regional are divided by geographical areas which include Bangkok, central (excluding Bangkok), north, north east, and south area. The detail of each regional consist of central (excluding Bangkok) 24 provinces, north 18 provinces, north east 20 provinces, and south 14 provinces.

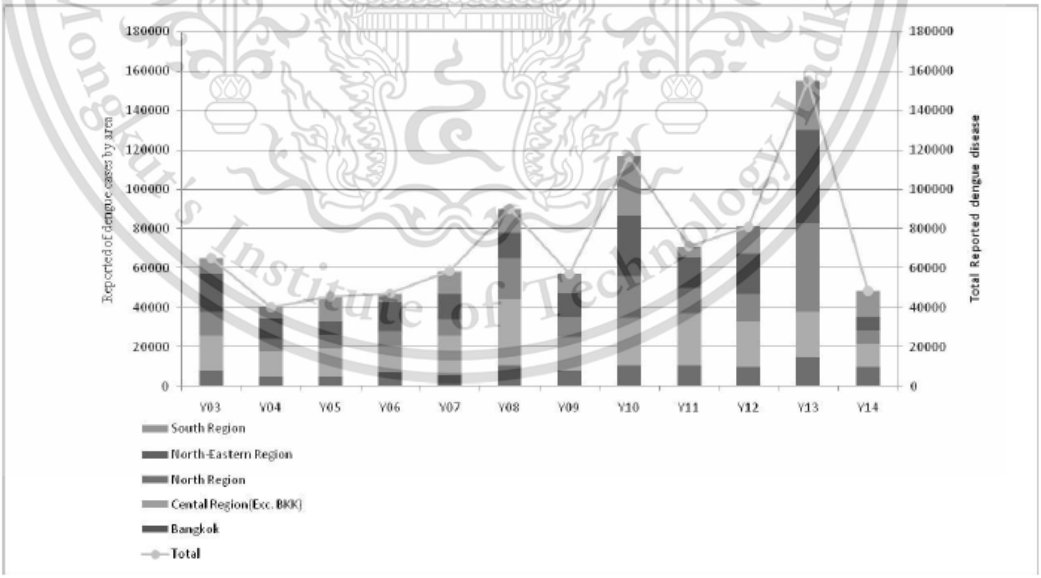

Figure 2: The reported of dengue disease in Thailand by regional during 2003-2014
Source: The Bureau of Epidemiology, Thai ministry of public health [4]

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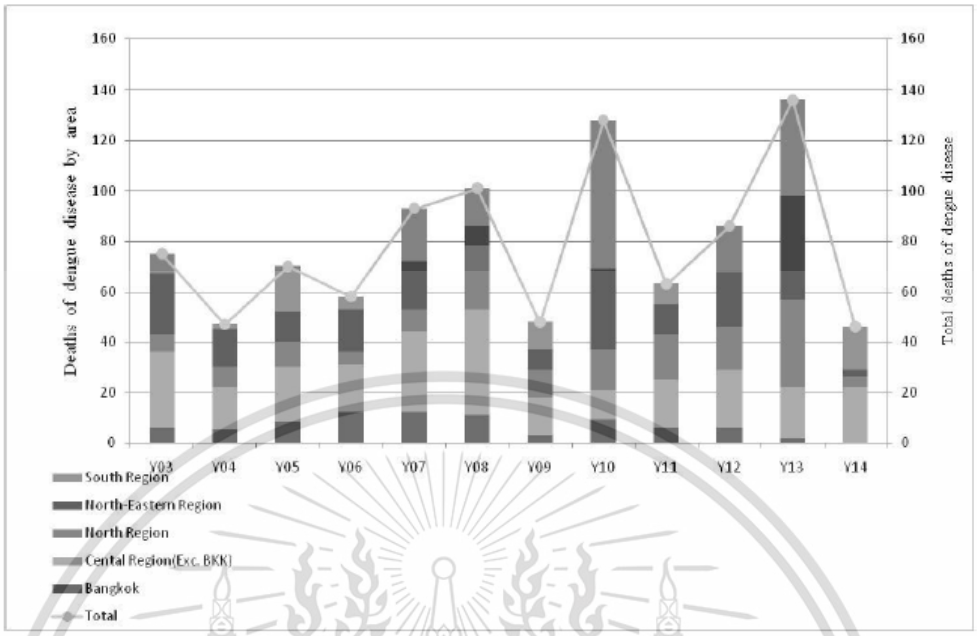

Figure 3: The death of dengue disease in Thailand by regional during 2003-2014
Source: The Bureau of Epidemiology, Thai ministry of public health [4]

The reported case and death due to dengue disease by month in Thailand during 2003-2014 are shown in Figure 4 and Figure 5 respectively. The peak period for dengue reported is around rainy season in Thailand from May to September of each year which is the same pattern for death of dengue case. The dengue disease situation in Thailand has mad badly because of the unseasonably wet and warm weather which is allowing mosquitoes to reproduce at a rapid rate. Mosquitoes can breed in clear water which is usually found around housing development in urban area that is most active in daytime. As the results, seasonal is effected with mosquitoes breading and also reported and deaths of dengue disease in Thailand.

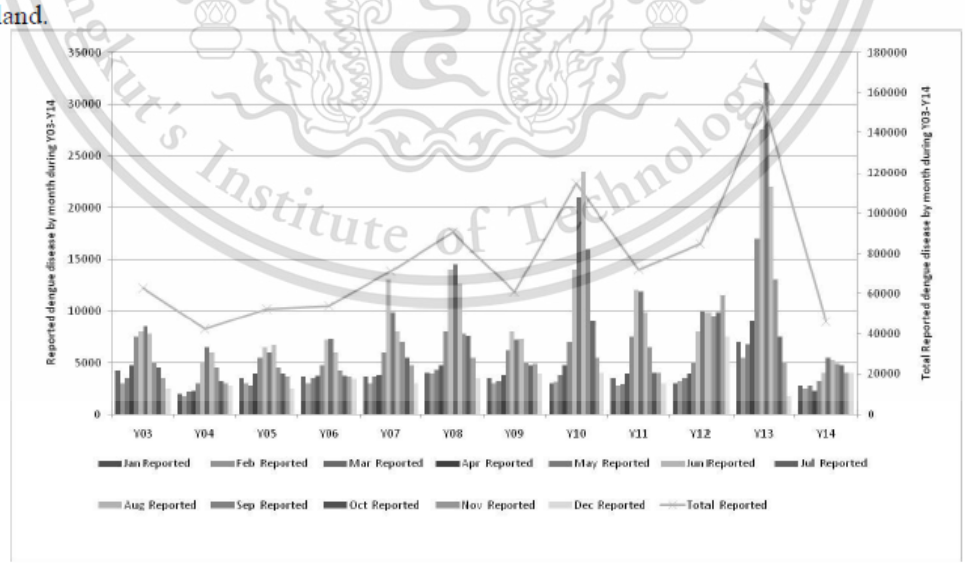

Figure 4: The reported cases of dengue disease in Thailand by month during 2003-2014
Source: The Bureau of Epidemiology, Thai ministry of public health [4]

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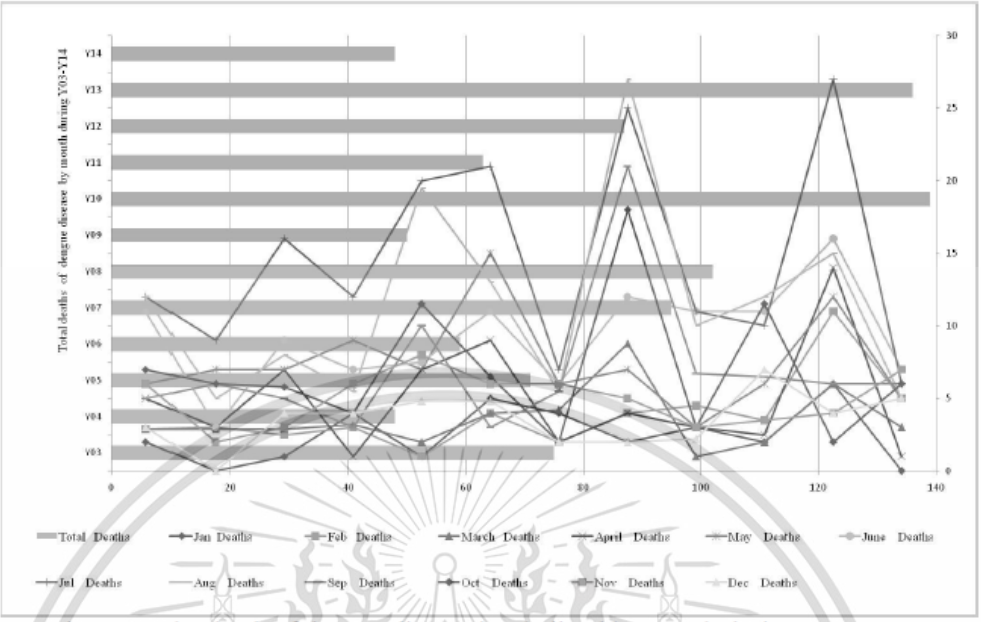

Figure 5. The death of dengue disease in Thailand by month during 2003-2014
Source: The Bureau of Epidemiology, Thai ministry of public health [4]

The reported dengue disease by age in Thailand during 2004-2014 is shown in Figure 6. The high reported of dengue disease remains in age group 10-14 and 15-24. The highest reported changed from the age 10-14 years to 15-24 years in 2009.

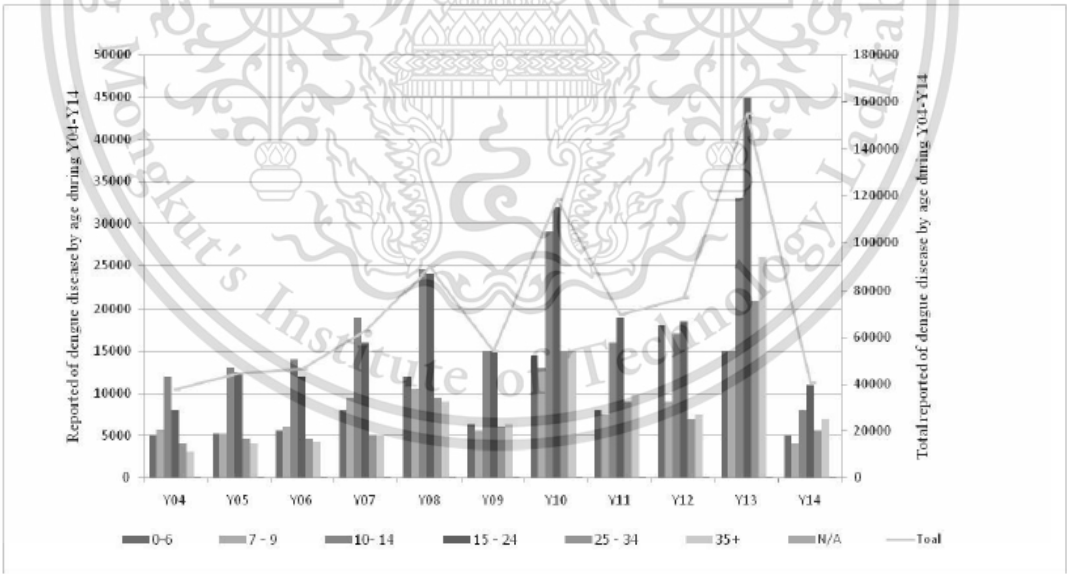

Figure 6: The reported of dengue disease in Thailand by age during 2004-2014
Source: The Bureau of Epidemiology, Thai ministry of public health [13]

The reported dengue disease by occupation in Thailand during 2006-2014 is shown in Figure 7. The highest reported of dengue disease remains in student occupation. The second and the third main reported of dengue disease are in employee and agriculturist occupation.

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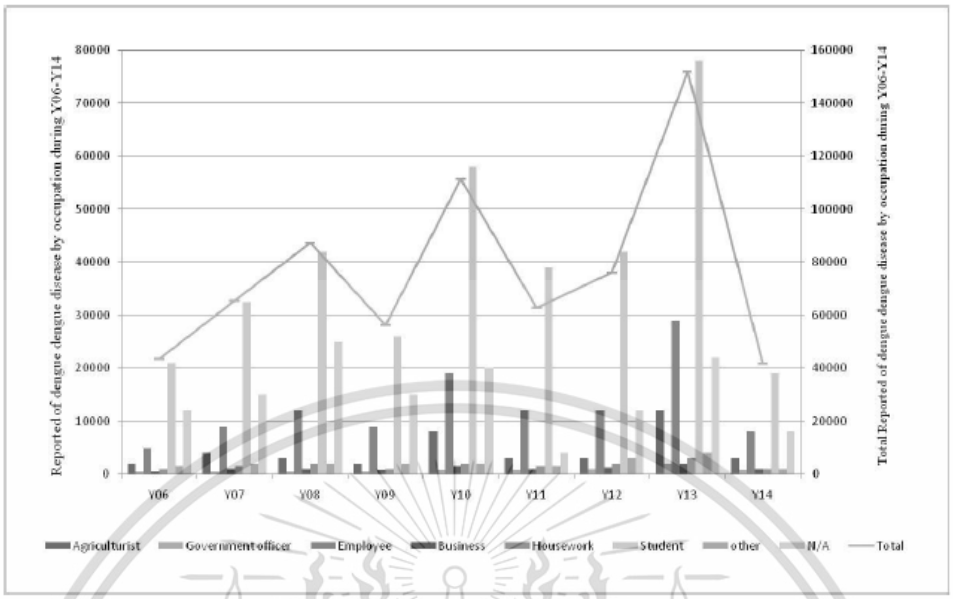

Figure 7: The reported of dengue disease in Thailand by occupation during 2004-2014
Source: The Bureau of Epidemiology, Thai ministry of public health [4]

In 2015, the reported of dengue disease as of 7 May was total 5837 reported cases and 0 deaths from 77 provinces which dengue disease situation is shown in the Figure 10. The morbidity rate was 9.06 per 100,000 populations. The reported proportions of dengue disease by age group were 15-24 years old 27.17%, 10-14 years old 20.56%, and 25-34 years olds 13.83%.

Dengue disease is an important mosquito-borne viral infection found in tropical and sup-tropical climates around the world especially urban and semi urban area. The widespread of dengue disease is throughout the tropic which local variation in risk is influenced by rainfall, temperature, and unplanned rapid urbanization. The current decade dengue disease situation in Thailand is shown in Figure 1 – 7. The highest reported and deaths were 154,444 cases in 2013 and 139 cases in 2010 which the morbidity and mortality rate per 100,000 populations were 241.03 in 2013 and 0.22 in 2010 respectively. In regional level, north-eastern region was reported the highest cases in 2013 while the highest deaths was south region in 2010. The highest reported by age group was aged 15-24 years in 2013 and main reported of occupation was student. The peak period reported each year was appeared during rainy season in May through September. The total reported, total death, trend of total reported, and trend of total death during 2003 - 2014 are shown in Figure 8.

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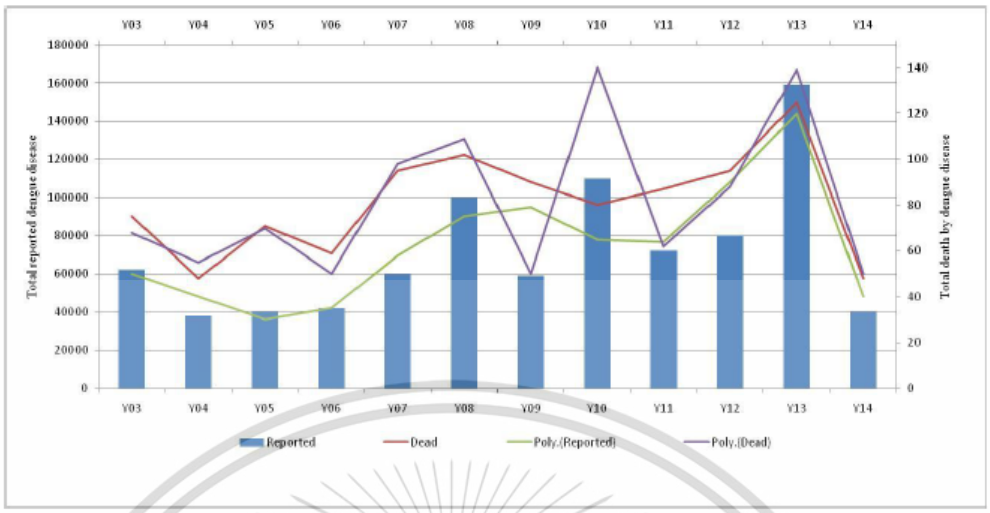

Figure 8: Dengue disease in Thailand during 2003 - 2014

MATHEMATICAL MODEL FOR TRANSMISSION OF DENGUE DISEASE

Aedes mosquito is vector of dengue disease. It can transmit dengue virus to human through biting of infected female mosquitoes. Incubation of dengue virus is around 4-10 days that infected mosquito is able to transmit dengue virus for the whole life. When human got dengue virus from infected mosquitoes, an infected human is the source of dengue virus for uninfected mosquito. The patients who got dengue virus from infected mosquito can transmit dengue virus to mosquitoes for 4-12 days after the first symptoms occur. The transmission cycle is completed when uninfected mosquitoes feed on a human with dengue infection.

There are several mathematical models to develop the transmission mechanism of dengue disease, the appropriated models can provide a qualitative risk assessment of the spread of dengue disease. Esteva and Vargas [5] proposed a model for the transmission of dengue fever in a constant human population and variable vector population. The global analysis was present to establish the global stability of the endemic equilibrium. Naowarat, S. et al. [6] proposed the dynamical model for determining human susceptibility to dengue fever. The standard method was proposed to analyze the dynamic of dengue disease system. They have proposed and analyzed the dynamical transmission model of Dengue fever by taking into account the role played without immunity in human population. They found that there are two equilibrium states, a disease-free state and endemic state. When the reproductive number is lower than one, the disease-free state is locally asymptotically stable. If reproductive number is more than one, the endemic equilibrium state is locally asymptotically stable. As the results, if the basic reproductive number decreases below one, it can reduce the human susceptibility to the disease and can reduce the outbreak of the disease.

Pongsumpun P. [7, 8, 9, and 10] proposed the mathematical models for dengue disease. The dynamical transmission model with the effect of extrinsic incubation period was present and the standard dynamical analysis to a modified Susceptible-Infected-Recovered (SIR) model included an annual variation in the length of the extrinsic incubation period was investigated [7]. They found that the dynamic behavior of the endemic state changes as influence of the seasonal variation of the incubation period. If the influence is increased, the trajectory exhibits sustained oscillations. The dynamic transmission model for dengue disease with and

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without the effect of extrinsic incubation period was compared [8]. The found that the dynamic behaviors of the endemic state changes while the influence of the seasonal variation of the incubation period become stronger. The modified mathematical model of dengue disease with effect of incubation period of virus was considered [9] that were formulated by separating the human population into susceptible, infected, infectious and recovered classes. The vector population was divided into susceptible, infected and infectious classes. She found that the infected class reduces the periods of the oscillations in the population. The seasonal transmission model of dengue virus infection in Thailand was presented [10]. She found that the basic reproductive number in high endemic season is higher than the normalized susceptible classes decrease. The basic reproductive number in lower endemic season is higher than normalized infected human classes increase. This behavior occurs because there is enough susceptible human to be infected from infectious mosquitoes.

Chanprasopchai P. and Pongsumpun P. [11] proposed the transmission dynamic of SIR model for dengue fever with vector-born infection. The infected vectors caused by both biting of infected human and vector-born infection are proposed. We apply standard dynamic modeling method to analysis our mathematical model and the stability of the model is analyzed by Routh – Hurwitz criteria. The numerical solutions show that the dynamical behaviors converge to the endemic equilibrium state and the relation between each individual variable with the biting rate of mosquito are presented. We found that if the mosquito biting is increased, the values basic reproductive number and susceptible human will increase while infected human and infected vector will increase.

Pongsumpun, P. and Kongnuy, R. [12, 13] presented the mathematical model to describe the transmission of dengue disease for pregnant and non-pregnant. In case of the basic reproductive is higher, the period of oscillation is shorter. The endemic equilibrium points for proportion of susceptible pregnant and non-pregnant decrease and proportion of infective pregnant and non-pregnant and infective vector decrease. These behaviors occur when there is enough of susceptible pregnant and non-pregnant to be infected from infectious vector. Application of an ultra-low volume amount of insecticide could reduce the basic reproductive number lower than one and the basic reproductive number would return to above one once the application is stopped. Since the endemic state is local stable, the dengue disease would return. So, the eradication program would have to be a continued one which can increase the outbreak of dengue disease.

Mathematical model is used to analyze and investigate the dengue disease. The basic reproductive number from mathematical analysis is applied to control the outbreak of dengue disease. The outbreak will spread when the basic reproductive number value is lower than one. On another hand, when the basic reproductive number is lower than one, it can control the outbreak. As the current, there is no specific treatment and vaccination for dengue disease. The best way to control the outbreak is to control spreading of infected mosquitoes.

CONCLUSION AND DISCUSSION

Dengue disease is an international concern disease affecting human around the world especially tropical and sup-tropical area. Dengue disease is caused by mosquito which is more dangerous. Global incidence of dengue disease has increased dramatically in the current decade and around half of world' population is living at risk area which has reported of dengue disease. It is not only the numbers of reported cases are increasing but also the dengue disease spreads to new area that the dengue disease is endemic in more than 100

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countries. Thailand had reported of dengue disease since 1950 and the first outbreak in 1958. The historical reported of dengue disease in Thailand are shown in Figure 1. Figure 2 and 3 show the reported and death of dengue disease by regional. The report and death of dengue disease by month are presented in Figure 4 and Figure 5. The reported of dengue disease by age is shown in Figure 6 while Figure 7 presented the reported of dengue disease by occupation. The dengue disease situation in this year, 2015, is shown in figure 8 while the trend of reported and death of dengue disease is also proposed in Figure 5.

The mathematical model of dengue disease has developed for long time. The popular one was proposed by Esteva, L. and C. Vargus in 1999. Many researchers developed the mathematical model to find the way to control the outbreak. The reproductive number is used to control the outbreak. The reproductive number is lower than one will decrease the outbreak. At the present, the method to control the transmission of dengue disease is controlled the spreading of mosquitoes such as environmental management of egg laying, waste disposing, and water storage. The community participation and mobilization will improve the sustained mosquito control and the insecticides spraying during outbreak is the one of emergency vector control. The active monitoring of mosquitoes should be continued to control the outbreak [14].

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Appendix B

Paper 2

The effect of rainfall for the dynamical transmission model of the dengue disease in Thailand

Hindawi
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Research Article

Effect of Rainfall for the Dynamical Transmission Model of the Dengue Disease in Thailand

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The SEIR (Susceptible-Exposed-Infected-Recovered) model is used to describe the transmission of dengue virus. The main contribution is determining the role of the rainfall in Thailand in the model. The transmission of dengue disease is assumed to depend on the nature of the rainfall in Thailand. We analyze the dynamic transmission of dengue disease. The stability of the solution of the model is analyzed. It is investigated by using the Routh-Hurwitz criteria. We find two equilibrium states: a disease-free state and an endemic equilibrium state. The basic reproductive number (R_0) is obtained, which indicates the stability of each equilibrium state. Numerical results taking into account the rainfall are obtained and they are seen to correspond to the analytical results.

1. Introduction

Dengue disease is caused by the dengue virus that is transmitted to human by the bite of a mosquito. The mosquito is the vector of this disease. The spread of dengue disease depends on the contact between the human and the mosquitoes. Therefore, the way to control dengue virus transmission is to either control the mosquito vectors or interrupt the human-vector contact [1]. Outbreaks of dengue disease often occur in most tropical countries around the world, with close to 75% of the global population exposed to the disease living in the Asia-Pacific region [2]. Four serotypes of the dengue virus, DEN1–DEN4, are responsible for the disease in humans. They are all transmitted to human through the bites of infected *Aedes aegypti* and *Aedes albopictus* mosquitoes. When the mosquitoes are in immature or lava stages, they are usually found in water-filled habitats such as water containers close to dwellings of humans. In the adult stages, the mosquitoes may spend most of their lifetimes around the homes of humans. This would lead to the mosquitoes being able to transmit the dengue virus rapidly between the communities.

In Thailand, dengue disease has been reported nationwide in all parts of Thailand, including the Bangkok metropolitan area in which three forms of dengue disease, dengue fever (DF), dengue hemorrhagic fever (DHF), and dengue shock syndrome (DSS), were reported. The three categories are based on the clinical presentation of patients. The most severe form of dengue disease is DSS [1, 2]. It reappears on a regular basis every year with the peak during the rainy season, June–August. The amount of rainfall is the single most important factor for dengue virus transmission, since this condition is most suitable for mosquitoes to lay their eggs and for the humans and mosquito to come into contact. The historical data in Thailand indicates that the number of reported cases correlates with the average amount of rainfall. The relationships between average monthly dengue reported cases and average monthly amount of rainfall during

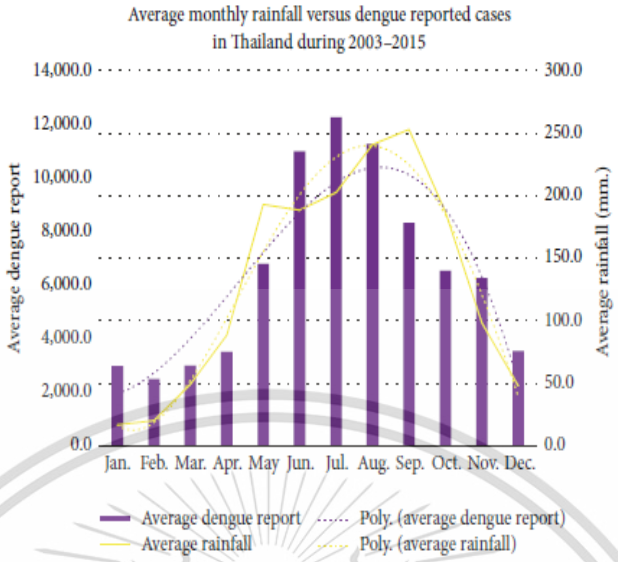

FIGURE 1: Average monthly rainfall and dengue reported cases during 2003–2015 in Thailand [3].

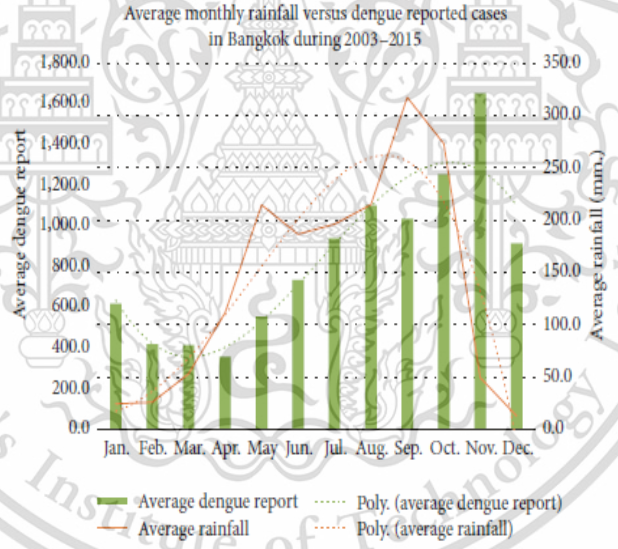

FIGURE 2: Average monthly rainfall and dengue reported cases during 2003–2015 in Bangkok [3].

2003–2015 in Thailand and Bangkok metropolitan area are presented in Figures 1 and 2, respectively [3].

As we can see from Figures 1 and 2, the correlation between the amount of rainfall and the number of reported cases of dengue disease in the period of this study is cosine function dependence corresponding to the study of Stolwijk et al. [4]. When mosquito bites an infectious human being, the mosquito will be feeding on the infected blood. As a consequence, the mosquito receives the dengue viruses and will be a vector for the transmission of the dengue viruses. The dengue disease epidemic can then be analyzed in order to determine a set of parameter values that will allow a strategy to control the spread of the disease when other factors are taken into account. The mathematical model to be developed will be a SEIR (Susceptible-Exposed-Infected-Recovered) mathematical model. Mathematical models have long been used to describe the dengue transmission.

Esteva and Vargas [5] proposed a model with a constant human population and variable vector population model to describe the transmission of dengue disease and studied the global stability of the endemic equilibrium. Polwiang [6] presented a mathematical model for general vector-host infectious disease and used the reproduction number as a means to evaluate the potential, severity, and persistence of dengue infection. The dengue infection will depend on the seasonal variation of the climate and the rainfall which will affect the breeding pool for the mosquitoes to lay their eggs and to develop into the adult stage. Rodrigues

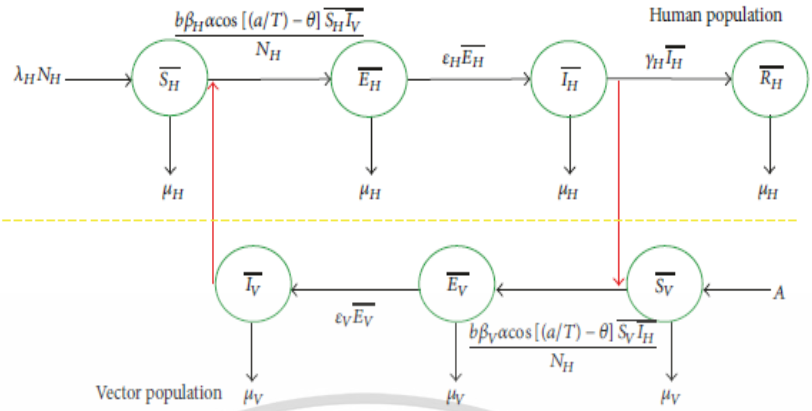

FIGURE 3: The dynamical transmission of dengue disease.

et al. [7] presented disease transmission with the effects of seasonality on the vectorial capacity and, consequently, on the disease development. Using entomological information of the mosquito's behavior under different temperatures and rainfall, the time development of the epidemics was simulated and analyzed. Chompoosri et al. [8] introduced seasonal dengue infection rates in the *Aedes aegypti* mosquitoes to study the dengue infection in suspected patients in 4 central provinces of Thailand. Dengue morbidity rates used for the patients in all 4 provinces were taken to be the highest in rainy season. Kesorn et al. [9] discovered that the *Aedes aegypti* female and larvae mosquito infection rates significantly positively associated with the morbidity rate, where the increasing infection rate of female mosquitoes and larvae led to a higher number of dengue cases. This result supports regarding the largest female populations to be present in the rainy season (May-June) in Thailand, in which the biting activity rate of female mosquitoes increases and more dengue cases occur. Siriyasatien et al. [10] found that female mosquitoes and seasons were strongly correlated with dengue cases in Thailand in which infected female mosquitos together with season are directly correlated to the number of dengue cases. Pongsumpun and Tang [11] analyzed a model when a seasonal variation in the incubation period of the virus while it was developing in the mosquito was included in the model. The annual variation in the length of the extrinsic incubation period was considered by using standard dynamical modeling method to analyze the Susceptible-Exposed-Infected-Recovered (SEIR) model. Chanprasopchai and Pongsumpun [12] used a mathematical model for transmission dynamics of dengue based on the Susceptible-Infected-Recovered (SIR) model. The standard dynamical modeling techniques were used to analyze that model. Relations between each individual variable in the model and the biting rate of mosquito were obtained. Sungchasit et al. [13] later proposed a transmission model of dengue virus in which there were two mosquito species, *Aedes aegypti* and *Aedes albopictus*, causing the infection. Separate SIR (Susceptible-Infected-Recovered) models were proposed to describe the dengue virus transmission by two mosquito species. Pongsumpun and Tang [14] proposed the transmission of dengue hemorrhagic fever by Susceptible-Infected-Recovered model considering the influence of age structure in human population. Human population was divided into two groups, adult and juvenile groups, in order to analyze the dengue disease transmission and the equilibrium state, stability, and numerical calculation were presented. Adams et al. [15] proposed the epidemic pattern observed in Bangkok regarding the result of cross-protective immunity and presented significantly altered changes in the interserotypic immune reaction. They used records of the annual number of confirmed cases of dengue in Bangkok between 1977 and 2000 and used a mathematical model based on standard SIR formulation forced with an annually periodic transmission rate cosine function representing seasonal fluctuations in the vector population.

In this study, we consider the transmission of dengue disease by using mathematical model to investigate the dengue disease mechanism with the effect of rainy season taken into account. The transmission rates of dengue virus vary during the season. The Routh-Hurwitz criteria are applied to analyze the system stability of the SEIR model and the dynamical transmission model of dengue disease is proposed. The equilibrium state and stability, numerical simulation and results, and conclusion are presented.

2. Materials and Methods

2.1. Mathematical Model. The SEIR mathematical model consists of two population compartments, human's population and mosquito's population. Human's population includes four epidemiological states, Susceptible human ($\overline{S_H}$), Exposed human ($\overline{E_H}$), Infected human ($\overline{I_H}$), and Recovered human ($\overline{R_H}$), whereas mosquito's population is divided into 3 epidemiological states, Susceptible vector ($\overline{S_V}$), Exposed vector ($\overline{E_V}$), and Infected vector ($\overline{I_V}$). The mosquito's population cannot recover from infection which has no recovery epidemiological states. The dynamical transmission between human's population and mosquito's populations is shown in Figure 3.

In the figure, $\overline{S_H}(t)$ is number of susceptible humans at any time t, $\overline{S_V}(t)$ is number of susceptible vectors at any time t, $\overline{E_H}(t)$ is number of exposed humans at any time t, $\overline{E_V}(t)$ is number of exposed vectors at any time t, $\overline{I_H}(t)$ is number of infected humans at any time t, $\overline{I_V}(t)$ is number of infected vectors at any time t, $\overline{R_H}(t)$ is number of recovered humans at any time t, β_H, β_V are transmission probabilities of dengue virus from vector to human and from human to vector, ε_H is intrinsic incubation rate, ε_V is extrinsic incubation rate, μ_H, μ_V are death rates of human and vector, λ_H, γ_H are birth rate of human and recovery rate of human, respectively, A, b are constant recruitment rate and biting rate, respectively, α, θ are amplitude and horizontal shift of the cosine function, and a, T are time period and number of time periods.

To simplify the model, we assume that both the human and mosquito populations are constant and there is no vertical transmission; that is, the eggs cannot be infected by sexual contacts between the male and female mosquitoes. It means that total human population is $N_H = \overline{S_H} + \overline{E_H} + \overline{I_H} + \overline{R_H}$ and total mosquito population is $N_V = \overline{S_V} + \overline{E_V} + \overline{I_V}$. The mathematical descriptions of the processes shown in Figure 3 are the seven differential equations given as follows:

$$\begin{aligned}
\frac{d\overline{S_H}}{dt} &= \lambda_H N_H - \mu_H \overline{S_H} - \frac{b\beta_H \alpha \cos[(a/T) - \theta]}{N_H} \overline{S_H}\,\overline{I_V}, \\
\frac{d\overline{E_H}}{dt} &= \frac{b\beta_H \alpha \cos[(a/T) - \theta]}{N_H} \overline{S_H}\,\overline{I_V} - \varepsilon_H \overline{E_H} + \mu_H \overline{E_H}, \\
\frac{d\overline{I_H}}{dt} &= \varepsilon_H \overline{E_H} - \mu_H \overline{I_H} - \gamma_H \overline{I_H}, \\
\frac{d\overline{R_H}}{dt} &= \gamma_H \overline{I_H} - \mu_H \overline{R_H}, \\
\frac{d\overline{I_V}}{dt} &= \varepsilon_V \overline{E_V} - \mu_V \overline{I_V}, \\
\frac{d\overline{E_V}}{dt} &= \frac{b\beta_V \alpha \cos[(a/T) - \theta]}{N_H} \overline{S_V}\,\overline{I_H} - \varepsilon_V \overline{E_V} + \mu_V \overline{E_V}, \\
\frac{d\overline{S_V}}{dt} &= A - \frac{b\beta_V \alpha \cos[(a/T) - \theta]}{N_H} \overline{S_V}\,\overline{I_H} - \mu_V \overline{S_V}.
\end{aligned} \tag{1}$$

Since we have assumed that the total human and mosquito populations are constant, we have

$$\begin{aligned}
\frac{d\overline{S_H}}{dt} + \frac{d\overline{E_H}}{dt} + \frac{d\overline{I_H}}{dt} + \frac{d\overline{R_H}}{dt} &= 0, \\
\frac{d\overline{I_V}}{dt} + \frac{d\overline{E_V}}{dt} + \frac{d\overline{S_V}}{dt} &= 0
\end{aligned} \tag{3}$$

with

$$\begin{aligned}
N_V &= \frac{A}{\mu_V}, \\
\lambda_H &= \mu_H.
\end{aligned} \tag{4}$$

Equations (1) and (2) can be normalized as follows: we first define the normalized variables as

$$\begin{aligned}
S_H &= \frac{\overline{S_H}}{N_H}, \\
E_H &= \frac{\overline{E_H}}{N_H}, \\
I_H &= \frac{\overline{I_H}}{N_H}, \\
R_H &= \frac{\overline{R_H}}{N_H}, \\
S_V &= \frac{\overline{S_V}}{N_V}, \\
E_V &= \frac{\overline{E_V}}{N_V}, \\
I_V &= \frac{\overline{I_V}}{N_V}
\end{aligned} \tag{5}$$

with

$$\begin{aligned}
S_H + E_H + I_H + R_H &= 1, \\
S_V + E_V + I_V &= 1.
\end{aligned} \tag{6}$$

Then, there are only five independent variables and only five differential equations are needed. We pick them to be

$$\begin{aligned}
\frac{dS_H}{dt} &= \mu_H - \mu_H S_H - \frac{b\beta_H \alpha \cos[(a/T) - \theta]}{N_H} S_H I_V N_V, \\
\frac{dE_H}{dt} &= \frac{b\beta_H \alpha \cos[(a/T) - \theta]}{N_H} S_H I_V N_V - \varepsilon_H E_H \\
&\quad - \mu_H E_H, \\
\frac{dI_H}{dt} &= \varepsilon_H E_H - \mu_H I_H - \gamma_H I_H, \\
\frac{dE_V}{dt} &= b\beta_V \alpha \cos\left[\left(\frac{a}{T}\right) - \theta\right] S_V I_H - \varepsilon_V E_V - \mu_V E_V, \\
\frac{dI_V}{dt} &= \varepsilon_V E_V - \mu_V I_V.
\end{aligned} \tag{7}$$

We now have five time differential equations involving five independent normalized population groups $(S_H, E_H, I_H, S_V, I_V)$. We can set the RHS of (7) to zero and find the equilibrium (time-independent) populations. There will be two equilibrium states for each population group, a disease-free equilibrium point and an endemic equilibrium point (one with $I_V^{1(2)} = 0$ and the other $\neq 0$). Calling the five equilibrium points for the five populations X_i $(i = 1, 2, \ldots, 5)$ and letting each of the independent population groups be equal to the equilibrium point plus a perturbation V_i which is time-dependent, we insert these new forms of the solution into (7) and expand the RHS about

the equilibrium populations. Doing this, we get the 5 × 5 matrix equation.

$$\frac{dV}{dt} = JV, \tag{8}$$

where J is the gradient matrix evaluated at the equilibrium points or "the Jacobian matrix."

2.2. Mathematical Analysis for Equilibrium Point. The stability of the solutions of (7) will be considered for 2 cases, one where $\theta \neq a/T$ and one where $\theta = a/T$. It should be noted that when $\theta = a/T$, the argument of the cosine function will be zero, meaning that there are no changes in the rate of infection due to increasing or decreasing rainfall. For $\theta \neq a/T$, the value of cosine function will change during the rainy season and will vary according to the amount of rainfall, meaning that the rate of transmission will change during the rainy season. The change in rate could be due to the fact that more eggs can be laid or developed quicker or slower depending on the amount of rain that has fallen. It is also well known that climatic factors control the development of the mosquitoes and of the dengue virus.

In either case, the equilibrium points must first be determined. This is done by setting the right-hand side of (7) to zero. Doing this, we obtain two solutions: one will be the disease-free equilibrium point (E_1) and the other will be the endemic equilibrium point (E_2). The two possible solutions depend on whether we take $I_V = 0$ or $I_V \neq 0$. After much work, we find that

$$\begin{aligned} E_1(t) &= \left(S_H^1 = 1, E_H^1 = 0, I_H^1 = 0, E_V^1 = 0, I_V^1 = 0\right), \\ E_2(t) &= \left(S_H^{2*}(t), E_H^{2*}(t), I_H^{2*}(t), E_V^{2*}(t), I_V^{2*}(t)\right), \end{aligned} \tag{9}$$

where

$$\begin{aligned} S_H^{2*}(t) &= \frac{\sec[a/T-\theta](\varepsilon_V+\mu_V)(b\alpha\cos[a/T-\theta]N_H\beta_V\varepsilon_H\mu_H+(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V)}{b\alpha\beta_V\varepsilon_H(b\alpha\cos[a/T-\theta]N_V\beta_H\varepsilon_V+N_H\mu_H(\varepsilon_V+\mu_V))}, \\ E_H^{2*}(t) &= -\frac{\sec[a/T-\theta]\mu_H\left(-2b^2\alpha^2\cos[a/T-\theta]^2N_V\beta_H\beta_V\varepsilon_H\varepsilon_V+2(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V(\varepsilon_V+\mu_V)\right)}{2b\alpha\beta_V\varepsilon_H(\varepsilon_H+\mu_H)(b\alpha\cos[a/T-\theta]N_V\beta_H\varepsilon_V+N_H\mu_H(\varepsilon_V+\mu_V))}, \\ I_H^{2*}(t) &= -\frac{\sec[a/T-\theta]\mu_H\left(-2b^2\alpha^2\cos[a/T-\theta]^2N_V\beta_H\beta_V\varepsilon_H\varepsilon_V+2(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V(\varepsilon_V+\mu_V)\right)}{2b\alpha\beta_V(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)(b\alpha\cos[a/T-\theta]N_V\beta_H\varepsilon_V+N_H\mu_H(\varepsilon_V+\mu_V))}, \\ E_V^{2*}(t) &= -\frac{\sec[a/T-\theta]N_H\mu_H\mu_V\left(-2b^2\alpha^2\cos[a/T-\theta]^2N_V\beta_H\beta_V\varepsilon_H\varepsilon_V+2(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V(\varepsilon_V+\mu_V)\right)}{2b\alpha N_V\beta_H\varepsilon_V(\varepsilon_V+\mu_V)(b\alpha\cos[a/T-\theta]N_H\beta_V\varepsilon_H\mu_H+(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V)}, \\ I_V^{2*}(t) &= -\frac{\sec[a/T-\theta]N_H\mu_H\left(-2b^2\alpha^2\cos[a/T-\theta]^2N_V\beta_H\beta_V\varepsilon_H\varepsilon_V+2(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V(\varepsilon_V+\mu_V)\right)}{2b\alpha N_V\beta_H(\varepsilon_V+\mu_V)(b\alpha\cos[a/T-\theta]N_H\beta_V\varepsilon_H\mu_H+(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V)}. \end{aligned} \tag{10}$$

All parameters in the system should be positive definite and the epidemic region of system will be restricted to the region of interest given by

$$\begin{aligned} \Omega = \{&E_1, E_2 : 0 \\ &\leq S_H^1, S_H^{2*}, E_H^1, E_H^{2*}, I_H^1, I_H^{2*}, E_V^1, E_V^{2*}, I_V^1, I_V^{2*} \leq 1\}. \end{aligned} \tag{11}$$

2.3. Mathematical Analysis for Local Stability. The equilibrium states are locally asymptotically stable if all the eigenvalues obtained by solving the eigenvalues equation $\mathrm{Det}|J - \lambda I| = 0$ have negative imaginary parts. This will be true if the characteristic equation has coefficients which satisfy the Routh-Hurwitz criteria. Performing the calculations, we find that the Jacobian matrix for (7) is just

$$J(t) = \begin{bmatrix} -\mu_H - \frac{b\beta_H\alpha\cos[(a/T)-\theta]}{N_H}I_VN_V & 0 & 0 & 0 & -\frac{b\beta_H\alpha\cos[(a/T)-\theta]}{N_H}S_HN_V \\ \frac{b\beta_H\alpha\cos[(a/T)-\theta]}{N_H}I_VN_V & -(\varepsilon_H+\mu_H) & 0 & 0 & \frac{b\beta_H\alpha\cos[(a/T)-\theta]}{N_H}S_HN_V \\ 0 & \varepsilon_H & -(\mu_H+r_H) & 0 & 0 \\ 0 & 0 & b\beta_V\alpha\cos\left[\left(\frac{a}{T}\right)-\theta\right](1-I_V-E_V) & -(\varepsilon_V+\mu_V) & 0 \\ 0 & 0 & 0 & \varepsilon_V & -\mu_V \end{bmatrix}. \tag{12}$$

The stability is usually expressed in terms of what is known as the basic reproduction number. This is the number of secondary infections which is produced by a case of an infection in a population of its infectious period ($\sqrt{R_0}$). This number is the best indicator of the potential for disease transmission.

Proposition 1. *The equilibrium state E_1 is asymptotically stable when R_0 is lower than 1; that is, $R_0 < 1$ and $\theta \neq a/T$.*

Proof. The local stability of E_1 is governed by linearization of (7). Rearranging the expressions for the equilibrium values of I_H or E_H so that they would be in a form $\propto R - 1$, we find that R_0 will be of the following form:

$$R_0 = \frac{b^2\alpha^2 \cos\left[2\pi t/T - \theta\right]^2 N_V \beta_H \beta_V \varepsilon_H \varepsilon_V}{N_H \mu_V \left(\gamma_H + \mu_H\right)\left(\varepsilon_H + \mu_H\right)\left(\varepsilon_V + \mu_V\right)}. \tag{13}$$

The eigenvalues of (12) are used to evaluate the disease-free equilibrium point which is determined by solving

$$\mathrm{Det}\left|J - \lambda I\right| = 0, \tag{14}$$

where J_{E_1} is the Jacobian matrix at the equilibrium point E_1, λ are eigenvalues, and I_5 is identity 5×5 matrix.

Evaluating the determinant of (12), we obtain the following characteristic equation:

$$\left(\lambda + \mu_H\right)\left(\lambda^4 + e_1\lambda^3 + e_2\lambda^2 + e_3\lambda^1 + e_4\right) = 0, \tag{15}$$

where

$$e_1 = \gamma_H + \varepsilon_H + \varepsilon_V + 2\left(\mu_H + \mu_V\right),$$

$$e_2 = \varepsilon_H\left(\gamma_H + \varepsilon_V + \mu_H + 2\mu_V\right) + \varepsilon_V\left(\gamma_H + 2\mu_H + \mu_V\right) + \left(\gamma_H\mu_H + \mu_H^2 + 2\gamma_H\mu_V + 4\mu_H\mu_V + \mu_V^2\right),$$

$$e_3 = \varepsilon_H\left(\gamma_H\varepsilon_V + \varepsilon_V\mu_H + 2\gamma_H\mu_V + \varepsilon_V\mu_V + 2\mu_H\mu_V + \mu_V^2\right) + \varepsilon_V\left(\gamma_H\mu_H + \mu_H^2 + \gamma_H\mu_V + 2\mu_H\mu_V\right) + \mu_H\mu_V\left(\mu_H + \mu_V\right) + \gamma_H\left(2\mu_H\mu_V + \mu_V^2\right),$$

$$e_4 = \left(b^2\alpha^2 \cos\left[\frac{2\pi t}{T} - \theta\right]^2 N_V\beta_H\beta_V\varepsilon_H\varepsilon_V\right) + \left(\gamma_H + \mu_H\right)\left(\varepsilon_H + \mu_H\right)\mu_V\left(\varepsilon_V + \mu_V\right). \tag{16}$$

Routh-Hurwitz criteria required for all of the eigenvalues (solutions) defined by (12) are negative real parts and the coefficients must satisfy all conditions given as follows:

$$\begin{aligned} e_1 &> 0, \\ e_3 &> 0, \\ e_4 &> 0, \\ e_1e_2e_3 &> e_3^2 + e_1^2e_4. \end{aligned} \tag{17}$$

When this happens and for $R_0 < 1$, disease-free equilibrium will be stable as is seen in Figure 4. □

Proposition 2. *The equilibrium state E_2 is asymptotically stable when R_0 is higher than 1; $R_0 > 1$ and $\theta \neq a/T$.*

Proof. The local stability of E_2 is governed by linearization of (7). The characteristic equation is now

$$\left(\lambda^5 + e_1\lambda^4 + e_2\lambda^3 + e_3\lambda^2 + e_4\lambda^1 + e_5\right) = 0, \tag{18}$$

where

$$e_1 = \frac{\left(-\eta_1\eta_2\eta_3\eta_4\eta_5 + \eta_1\left(\eta_4\eta_5\left(\eta_9\eta_3 - \mu_V\eta_8\right) + \eta_3\left(\eta_8\eta_4\eta_5 + \eta_4\eta_7\right)\right)\right)}{\left(\eta_1\eta_3\eta_4\eta_5\right)},$$

$$e_2 = \frac{\left(-\eta_1\eta_2\left(\eta_4\eta_5\left(\eta_9\eta_3 - \mu_V\eta_8\right) + \eta_3\left(\eta_8\eta_4\eta_5 + \eta_4\eta_7\right)\right) + \eta_1\left(-\eta_9\mu_V\eta_8\eta_4\eta_5 + \eta_3\eta_8\eta_4\eta_7\left(\eta_9\eta_3 - \mu_V\eta_8\right) + \eta_3\left(\eta_8\eta_4\eta_5 + \eta_4\eta_7\right)\right)\right)}{\left(\eta_1\eta_3\eta_4\eta_5\right)},$$

$$e_3 = \frac{\left(\eta_1\left(\eta_8\eta_4\eta_7\left(\eta_9\eta_3 - \mu_V\eta_8\right) - \eta_9\mu_V\eta_8\left(\eta_3\left(\eta_8\eta_4\eta_5 + \eta_4\eta_7\right)\right) - \eta_1\eta_2\left(-\eta_9\mu_V\eta_8\eta_4\eta_5 + \eta_3\eta_8\eta_4\eta_7 + \left(\eta_9\eta_3 - \mu_V\eta_8\right) + \eta_3\left(\eta_8\eta_4\eta_5 + \eta_4\eta_7\right)\right)\right)\right)}{\left(\eta_1\eta_3\eta_4\eta_5\right)}, \tag{19}$$

$$e_4 = \frac{\left(-\eta_1\eta_9\mu_V\eta_8{}^2\eta_4\eta_7 + \left(\eta_1\eta_8{}^2\eta_4\eta_5\eta_6 - \eta_1\eta_2\left(\eta_8\eta_4\eta_7\left(\eta_9\eta_3 - \mu_V\eta_8\right) - \eta_9\mu_V\eta_8\left(\eta_8\eta_4\eta_5 + \eta_4\eta_7\right)\right)\right)\right)}{\left(\eta_1\eta_3\eta_4\eta_5\right)},$$

$$e_5 = \frac{\left(N_H\mu_H\left(\gamma_H + \mu_H\right)\left(\varepsilon_H + \mu_H\right)\mu_V\left(b^2\alpha^2\cos\left[2\pi t/T - \theta\right]^2 N_V\beta_H\beta_V\varepsilon_H\varepsilon_V - \left(\gamma_H + \mu_H\right)\left(\varepsilon_H + \mu_H\right)\mu_V\left(\varepsilon_V + \mu_V\right)\right)\right)}{b\alpha\cos\left[2\pi t/T - \theta\right]N_H\beta_V\varepsilon_H\mu_H + \left(\gamma_H + \mu_H\right)\left(\varepsilon_H + \mu_H\right)\mu_V},$$

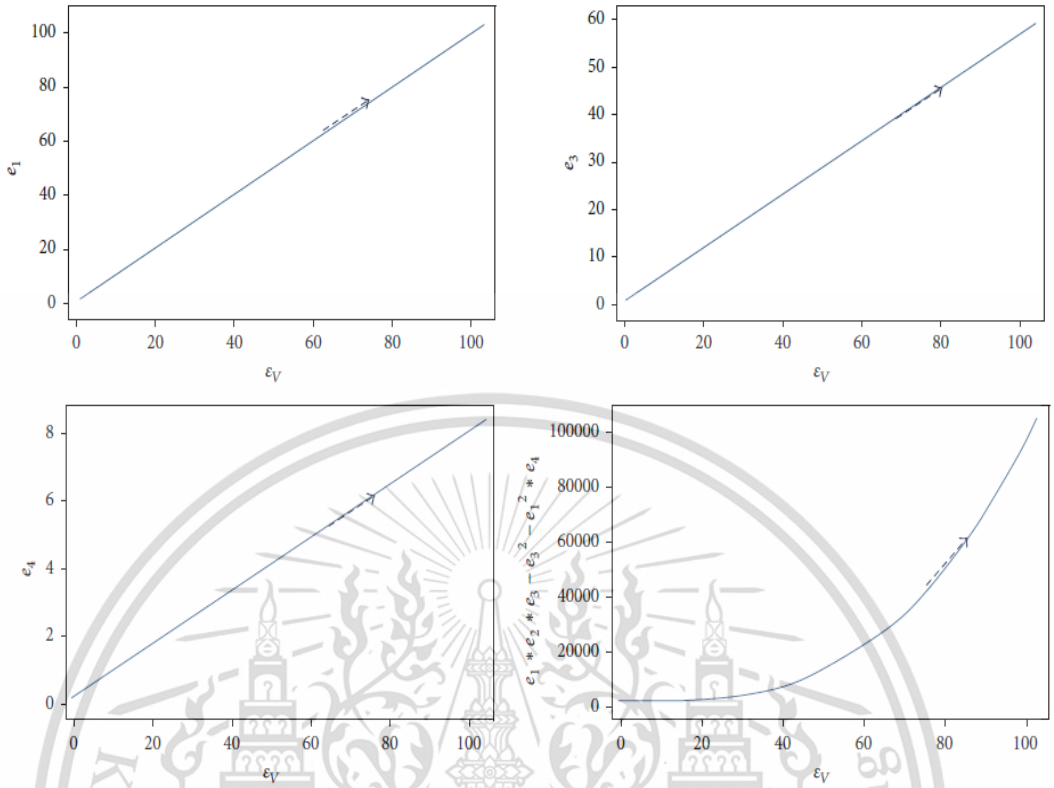

FIGURE 4: All parameters spaces of disease-free equilibrium of E_1 satisfy the Routh-Hurwitz criteria. All parameter values are $N_H = 9{,}200$, $b = 1/3$, $\mu_H = 1/(70 * 365)$, $\gamma_H = 1/3$, $\beta_H = 0.1$, $\beta_V = 0.1$, $\mu_V = 1/14$, $\varepsilon_V = 0.1428$, $\varepsilon_H = 0.1667$, and $A = 500$.

where

$$\eta_1 = N_V\beta_H\beta_V^2\varepsilon_H^2\varepsilon_V,$$

$$\eta_2 = (-\gamma_H - \mu_H),$$

$$\eta_3 = (-\varepsilon_V - \mu_V),$$

$$\eta_4 = \left(b\alpha\cos\left[\frac{2\pi t}{T} - \theta\right]N_V\beta_H\varepsilon_V + N_H\varepsilon_V\mu_H + N_H\mu_H\mu_V\right)^2 \left(b\alpha\cos\left[\frac{2\pi t}{T} - \theta\right]N_H\beta_V\varepsilon_H\mu_H + \gamma_H\varepsilon_H\mu_V + \gamma_H\mu_H\mu_V + \varepsilon_H\mu_H\mu_V + \mu_H^2\mu_V\right)^2,$$

$$\eta_5 = \left(b\alpha\cos\left[\frac{2\pi t}{T} - \theta\right]N_H\beta_V\varepsilon_H\varepsilon_V\mu_H + \gamma_H\varepsilon_H\varepsilon_V\mu_V + b\alpha\cos\left[\frac{2\pi t}{T} - \theta\right]N_H\beta_V\varepsilon_H\mu_H\mu_V + \gamma_H\varepsilon_V\mu_H\mu_V + \varepsilon_H\varepsilon_V\mu_H\mu_V + \varepsilon_V\mu_H^2\mu_V + \gamma_H\varepsilon_H\mu_V^2 + \gamma_H\mu_H\mu_V^2 + \varepsilon_H\mu_H\mu_V^2 + \mu_H^2\mu_V^2\right),$$

$$\eta_6 = \left(b\alpha\cos\left[\frac{2\pi t}{T} - \theta\right]N_V\beta_H\gamma_H\varepsilon_H\varepsilon_V\mu_V + b\alpha\cos\left[\frac{2\pi t}{T} - \theta\right]N_V\beta_H\gamma_H\varepsilon_V\mu_H\mu_V + b\alpha\cos\left[\frac{2\pi t}{T} - \theta\right]N_V\beta_H\varepsilon_H\varepsilon_V\mu_H\mu_V + N_H\gamma_H\varepsilon_H\varepsilon_V\mu_H\mu_V + b\alpha\cos\left[\frac{2\pi t}{T} - \theta\right]N_V\beta_H\varepsilon_V\mu_H^2\mu_V + N_H\gamma_H\varepsilon_V\mu_H^2\mu_V N_H\varepsilon_H\varepsilon_V\mu_H^2\mu_V + N_H\varepsilon_V\mu_H^3\mu_V + N_H\gamma_H\varepsilon_H\mu_H\mu_V^2 + N_H\gamma_H\mu_H^2\mu_V^2 + N_H\varepsilon_H\mu_H^2\mu_V^2 + N_H\mu_H^3\mu_V^2\right),$$

$$\eta_7 = \left(b^2\alpha^2\cos\left[\frac{2\pi t}{T} - \theta\right]^2 N_H N_V\beta_H\beta_V\varepsilon_H\varepsilon_V\mu_H + b\alpha\cos\left[\frac{2\pi t}{T} - \theta\right]N_H\beta_V\varepsilon_H\varepsilon_V\mu_H^2 + \gamma_H\varepsilon_H\varepsilon_V\mu_H\mu_V - N_H\gamma_H\varepsilon_H\varepsilon_V\mu_H\mu_V + b\alpha\cos\left[\frac{2\pi t}{T} - \theta\right]N_H\beta_V\varepsilon_H\mu_H^2\mu_V + \gamma_H\varepsilon_V\mu_H^2\mu_V\right)$$

$$
\begin{aligned}
&- N_H\gamma_H\varepsilon_V\mu_H^2\mu_V + \varepsilon_H\varepsilon_V\mu_H^2\mu_V - N_H\varepsilon_H\varepsilon_V\mu_H^2\mu_V \\
&+ \varepsilon_V\mu_H^3\mu_V - N_H\varepsilon_V\mu_H^3\mu_V + \gamma_H\varepsilon_H\mu_H\mu_V^2 \\
&- N_H\gamma_H\varepsilon_H\mu_H\mu_V^2 + \gamma_H\mu_H^2\mu_V^2 - N_H\gamma_H\mu_H^2\mu_V^2 \\
&+ \varepsilon_H\mu_H^2\mu_V^2 - N_H\varepsilon_H\mu_H^2\mu_V^2 + \mu_H^3\mu_V^2 - N_H\mu_H^3\mu_V^2\Big), \\
\eta_8 &= (\varepsilon_V + \mu_V), \\
\eta_9 &= (\varepsilon_H + \mu_H).
\end{aligned} \tag{20}
$$

The endemic equilibrium point of local stability of the system will have negative real parts when the coefficients in the characteristic equation (18) satisfy the Routh-Hurwitz conditions now given by

$$
\begin{aligned}
&e_1 > 0, \\
&e_2 > 0, \\
&e_3 > 0, \\
&e_4 > 0, \\
&e_5 > 0, \\
&e_1e_2e_3 - e_3^2 - e_1^2e_4 > 0, \\
&(e_1e_4 - e_5)(e_1e_2e_3 - e_3^2 - e_1^2e_4) - e_5(e_1e_2 - e_3)^2 \\
&\quad - e_1e_5^2 > 0.
\end{aligned} \tag{21}
$$

All conditions of (21) are satisfied for endemic equilibrium point as is evident by the behaviors seen in Figure 5. Next, we consider the case of $\theta = a/T$; (7) will be the standard case of SEIR model, where no effects of rainfall are taken into account. As a result, the mathematical equations describing the model are

$$
\begin{aligned}
\frac{dS_H}{dt} &= \mu_H - \mu_H S_H - \frac{b\beta_H}{N_H} S_H I_V N_V, \\
\frac{dE_H}{dt} &= \frac{b\beta_H}{N_H} S_H I_V N_V - \varepsilon_H E_H - \mu_H E_H, \\
\frac{dI_H}{dt} &= \varepsilon_H E_H - \mu_H I_H - \gamma_H I_H, \\
\frac{dE_V}{dt} &= b\beta_V S_V I_H - \varepsilon_V E_V - \mu_V E_V, \\
\frac{dI_V}{dt} &= \varepsilon_V E_V - \mu_V I_V.
\end{aligned} \tag{22}
$$

R_0 obtained from (22) is as follows:

$$
R_0 = \frac{b^2 N_V \beta_H \beta_V \varepsilon_H \varepsilon_V}{N_H \mu_V (\gamma_H + \mu_H)(\varepsilon_H + \mu_H)(\varepsilon_V + \mu_V)}. \tag{23}
$$

□

3. Numerical Results

The transmission of dengue disease in this study is based on the SEIR model. The susceptible class will be people who have no immunity and who are not infectious. Human beings infected are people who are infectious, that is, able to pass on the virus onto the mosquitoes. The infectious period will be taken to be the period during which the person appears to be sick, a period of one to two weeks. When human gets well, the patient passes into the recovery class with lifelong immunity to the virus. In this study, the numerical simulations assume the following values of the parameters; $\mu_H = 1/(70 * 365)$ per day corresponding to a life expectancy of 70 years in Thai people, $A = 5{,}000$ corresponding to constant recruitment rate, $N_H = 92{,}000$ corresponding to total number of human population, and $b = 1/3$ corresponding to biting rate of vector population.

For case 1, the values of the parameters of case 1 for disease-free equilibrium are $\mu_V = 1/14$, $\gamma_H = 1/3$, $\beta_H = 0.1$, $\beta_V = 0.1$, $\varepsilon_V = 0.1428$, and $\varepsilon_H = 0.1667$ which will lead to $R_0 < 1$, while the set of values of the parameters of case 2 are $\mu_V = 1/14$, $\gamma_H = 1/3$, $\beta_H = 0.5$, $\beta_V = 0.3$, $\varepsilon_V = 0.1428$, and $\varepsilon_H = 0.1667$ which will lead to $R_0 > 1$. The trajectories of the numerical solutions for case 1 and for case 2 of S_H, E_H, I_H, E_V, and I_V are shown in the Figures 6 and 7, respectively. The trajectories of the numerical solutions for case 1 and case 2 plotted in the 2D (S_H, E_H), (S_H, I_H), (S_H, E_V), and (S_H, I_V) planes are shown in Figures 8 and 9, respectively. The trajectories of the numerical solutions for case 1 and case 2 in the 3D (S_H, E_H, I_H), (S_H, E_H, E_V), (S_H, E_H, I_V), (S_H, E_V, I_V), (E_H, E_V, I_V), and (I_H, E_V, I_V) spaces are shown in Figures 10 and 11, respectively.

4. Discussion and Conclusion

The effect of rainfall on the dynamic transmission of dengue disease in Thailand has been studied using the SEIR model to model the dynamics of the dengue epidemic in Thailand. The analysis is based on using the Routh-Hurwitz criteria to establish the local asymptotic stability of the equilibrium points. Two equilibrium points were found: a disease-free equilibrium point and an endemic equilibrium point. The disease-free equilibrium point, E_1, is locally asymptotically stable for $R_0 < 1$ and $\theta \neq a/T$. The set of differential equations for the SEIR model of the dengue infections were solved for different sets of numerical values of the parameters to obtain the different trajectories of the different population groups in the model. The trajectories were projected into the 2D (S_H, E_H), (S_H, I_H), (S_H, E_V), and (S_H, I_V) planes and onto the 3D (S_H, E_H, I_H), (S_H, E_H, E_V), (S_H, E_H, I_V), (S_H, E_V, I_V), (E_H, E_V, I_V), and (I_H, E_V, I_V) spaces. These trajectories are shown in Figures 4, 6, 8, and 10, respectively. When the values of the parameters are such that $R_0 > 1$ and $\theta \neq a/T$, then the trajectories ending at the endemic equilibrium point, E_2, are described in Figures 5, 7, 9, and 11. The numerical results correspond to Propositions 1 and 2.

Looking at the figures, we see that everything is determined by whether $R_0 < 1$ or $R_0 > 1$; in the first case, the equilibrium state is the disease-free state, while in the second

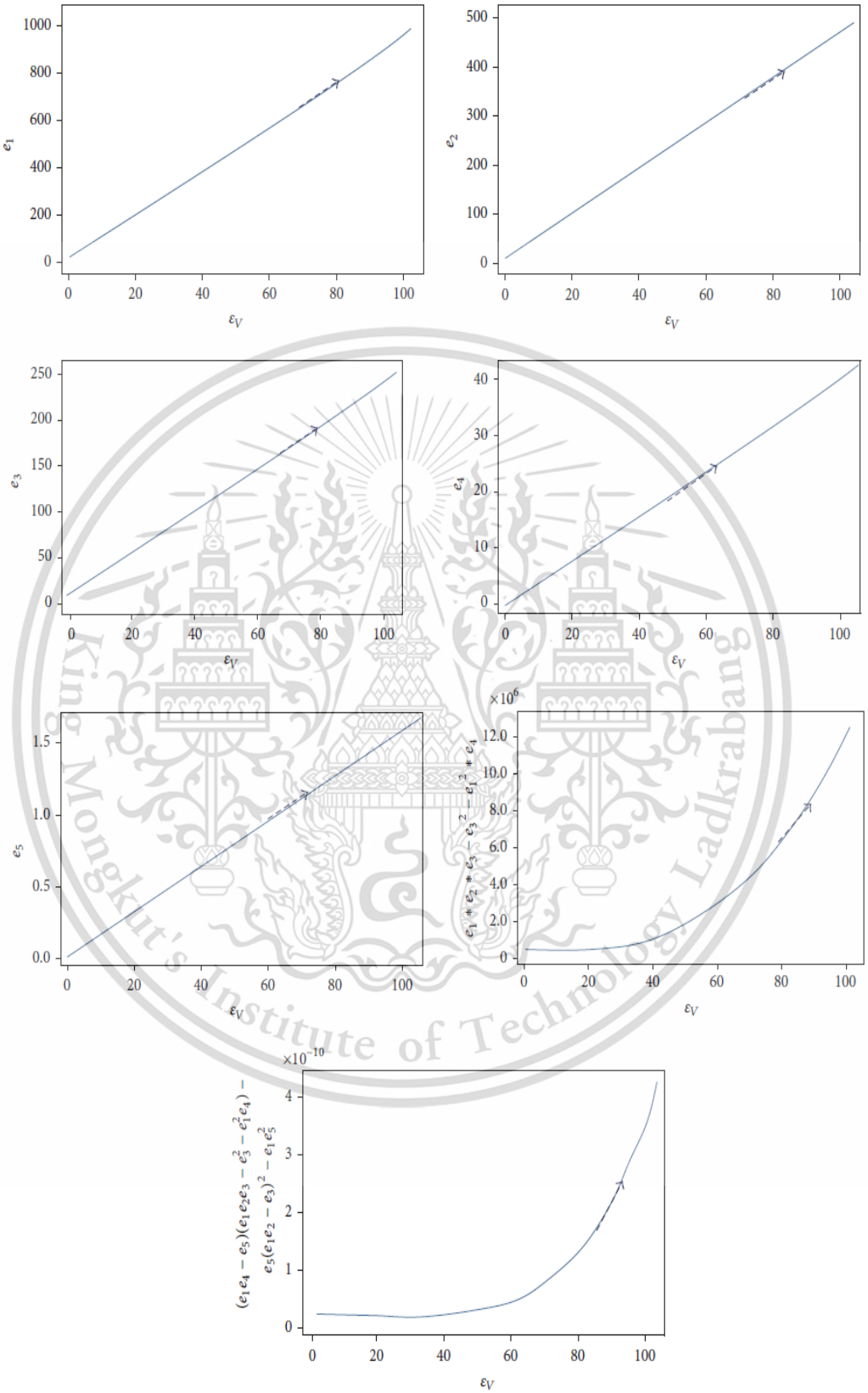

FIGURE 5: All parameters spaces of endemic equilibrium of E_2 satisfy the Routh-Hurwitz criteria. All parameter values are $N_H = 9{,}200$, $b = 1/3$, $\mu_H = 1/(70 * 365)$, $\gamma_H = 1/3$, $\beta_H = 0.5$, $\beta_V = 0.3$, $\mu_V = 1/14$, $\varepsilon_V = 0.1428$, $\varepsilon_H = 0.1667$, and $A = 500$.

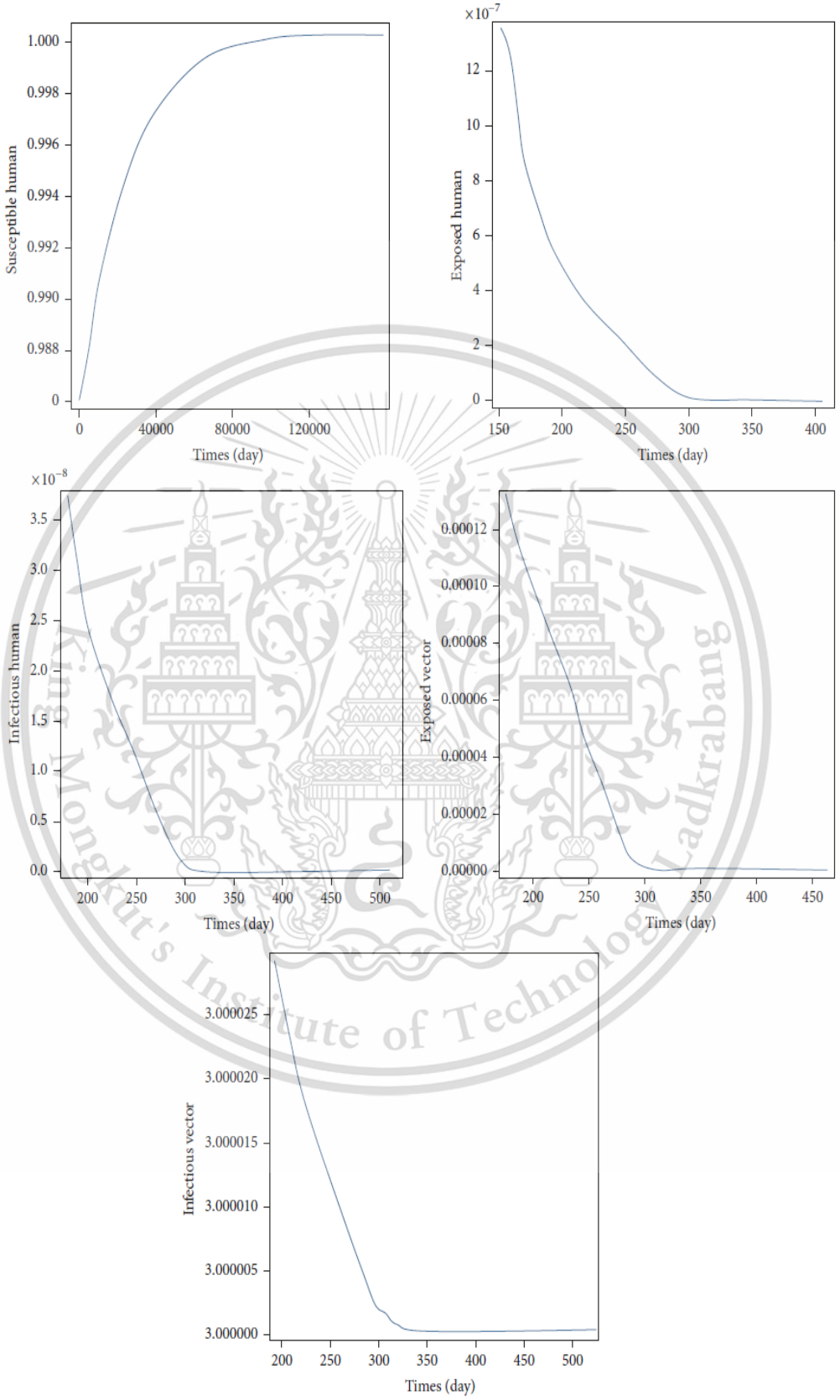

FIGURE 6: The trajectories of the time evolutions of the five population groups, S_H, E_H, I_H, E_V, and I_V, towards the disease-free equilibrium.

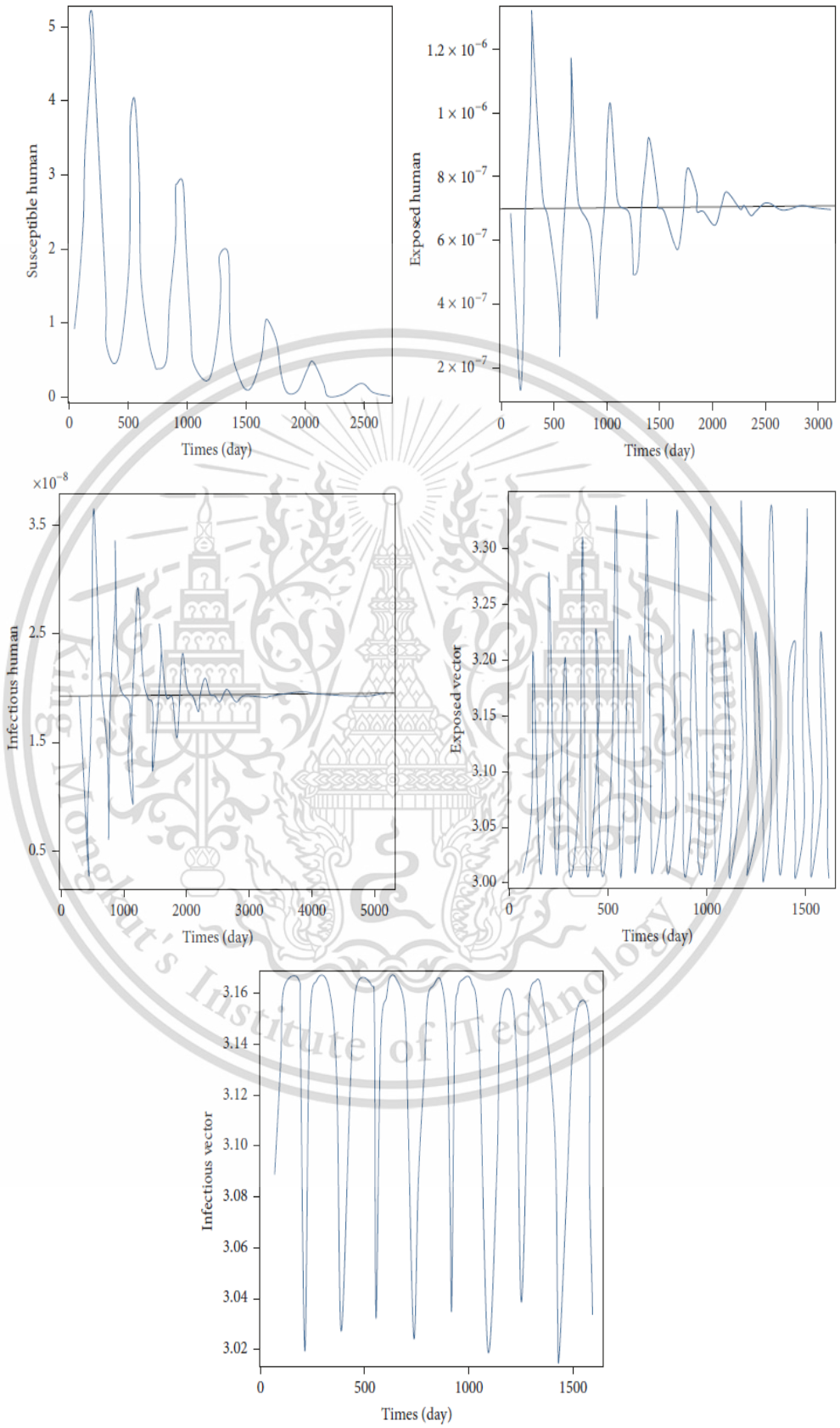

FIGURE 7: The trajectories of the time evolution of S_H, E_H, I_H, E_V, and I_V based on numerical solving.

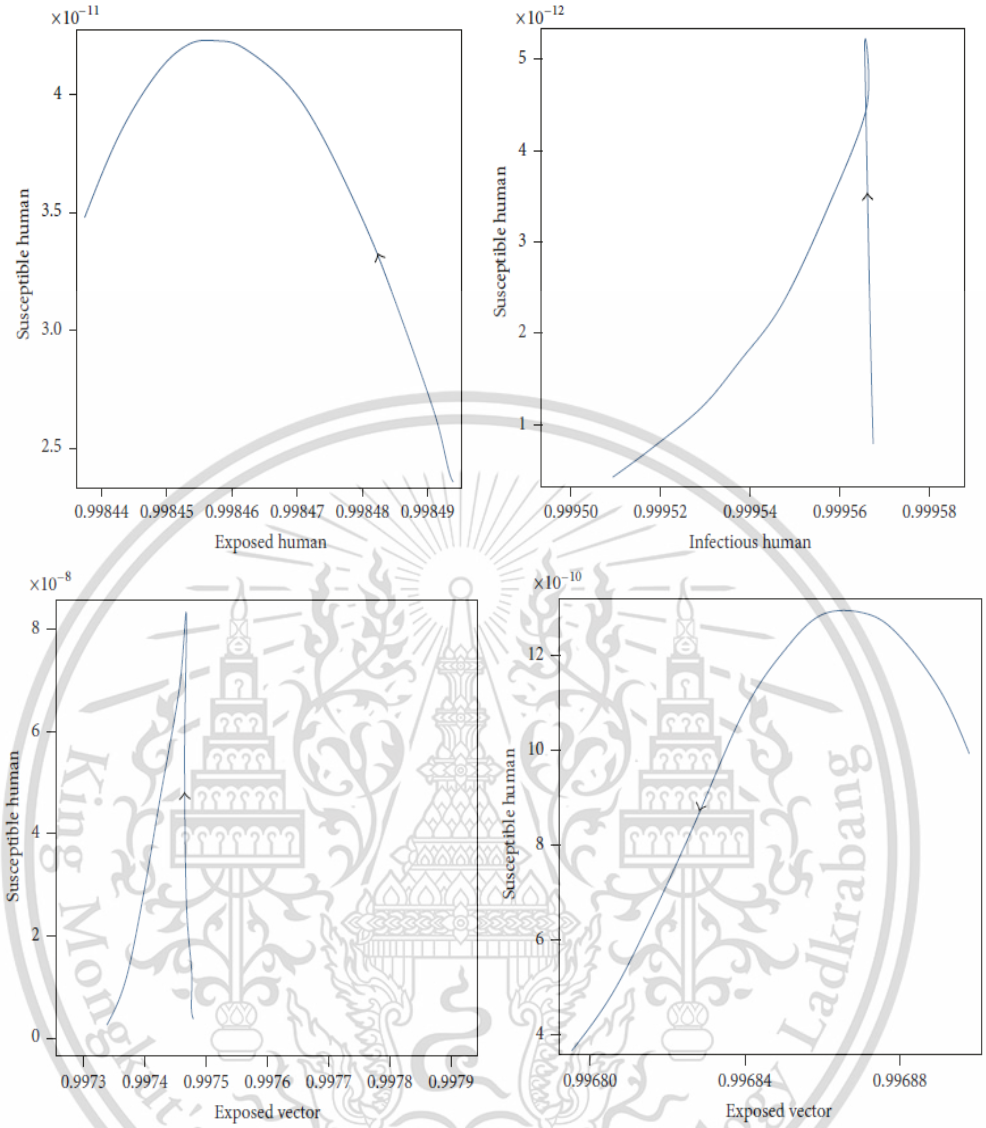

FIGURE 8: The trajectories of the numerical solutions of dengue disease for disease-free equilibrium projected onto (S_H, E_H), (S_H, I_H), (S_H, E_V), and (S_H, I_V).

case, it is the endemic equilibrium state. Everything depends on the form of the expression for R_0. In summary, R_0 in SEIR model which includes the effect of rainfall is given by (24), while R_0 in SEIR model which ignores the effect of rainfall is given by expression (25). R_0 value of the SIR model of Esteva and Vargas [5] is given by (26) and the simplest expression is given by Rodrigues et al. [7] in (27).

$$R_0 = \frac{b^2\alpha^2 \cos[2\pi t/T - \theta]^2 N_V \beta_H \beta_V \varepsilon_H \varepsilon_V}{N_H \mu_V (\gamma_H + \mu_H)(\varepsilon_H + \mu_H)(\varepsilon_V + \mu_V)}, \quad (24)$$

$$R_0 = \frac{b^2 N_V \beta_H \beta_V \varepsilon_H \varepsilon_V}{N_H \mu_V (\gamma_H + \mu_H)(\varepsilon_H + \mu_H)(\varepsilon_V + \mu_V)}, \quad (25)$$

$$R_0 = \frac{b^2 \beta_H \beta_V N_H (A/\mu_V)}{(N_H + m)^2 \mu_V (\gamma_H + \mu_H)}, \quad (26)$$

$$R_0 = \frac{b^2 \beta_H \beta_V N_V}{N_H \mu_V (\gamma_H + \mu_H)}. \quad (27)$$

In expression (26), m is the number of alternative sources of blood, that is, other animals.

In (24), R_0 value is considered the effect of rainfall, where Thailand has correlation between rainfall and the prevalence of clinical cases of dengue [16]. Thailand's historical data indicate that rainfall was associated with dengue in

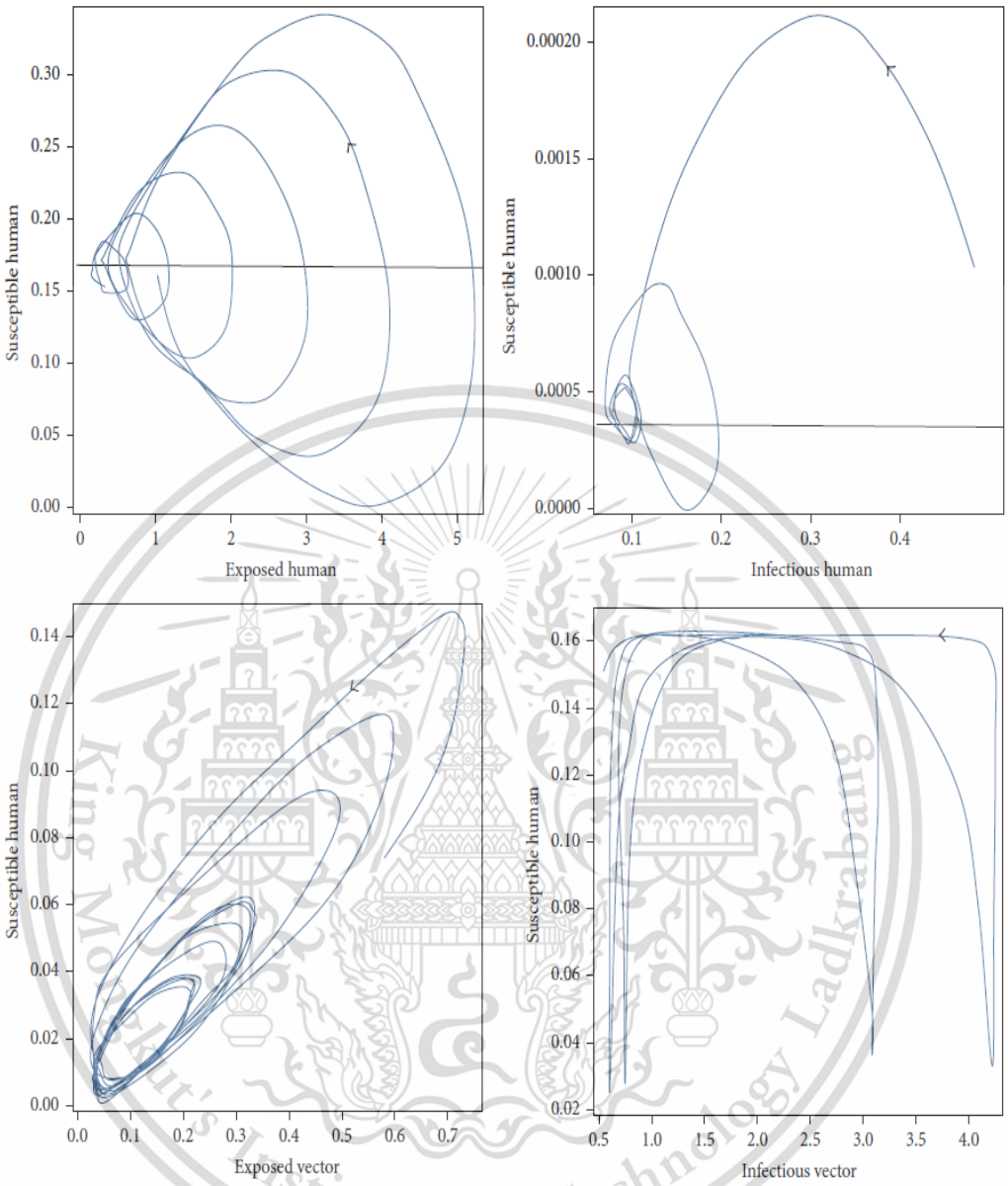

FIGURE 9: The trajectories of the numerical solutions of dengue disease for endemic equilibrium projected onto (S_H, E_H), (S_H, I_H), (S_H, E_V), and (S_H, I_V).

many regions, for example, southern [17], northern [18], northeastern [19], and central [20] regions. Dengue disease fluctuation is related to climate variability and seasonal factor is taken into account [10, 21–25] in which the dengue virus transmission is considered as a cosine function [15, 26]. When $R_0 > 1$, this will increase the opportunity of the outbreak situation. R_0 is an important indicator, where the realistic controlling of the value of R_0 will improve the way to control the outbreak. The value of R_0 simulation of endemic equilibrium state and the average amount of rainfall are shown in Figure 12. It is indicated that there is a relation between the value of R_0 and the average amount of rainfall.

In addition, the suitable ways to control the dengue disease are environmental management to prevent mosquitoes from laying their eggs and breeding and using of personal household protection to prevent contact between human and mosquito [1, 2]. In the present paper, we did not explicitly take into account the egg and aquatic stages of the mosquito development (see (2)) as was done by Erickson et al. [27] and Moulay et al. [28]. The lack of these classes precludes any discussion of the vertical transmission of the disease, since the "sexual" transmission (evidenced by the presence of the DNA fragments of the dengue virus in the larvae and pupae [29]) occurs at these stages.

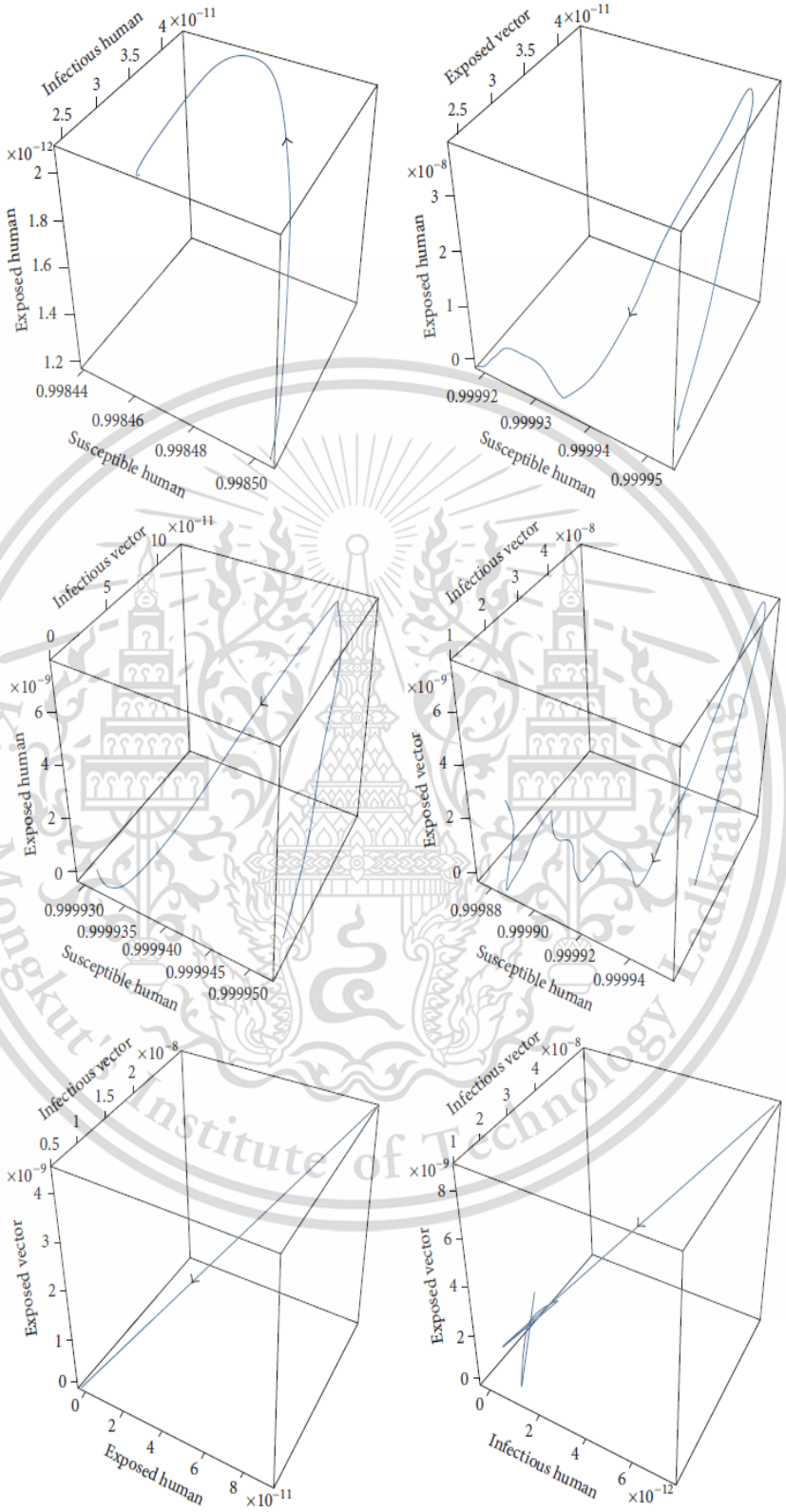

FIGURE 10: The trajectories of the numerical solutions of dengue disease for disease-free equilibrium projected onto (S_H, E_H, I_H), (S_H, E_H, E_V), (S_H, E_H, I_V), (S_H, E_V, I_V), (E_H, E_V, I_V), and (I_H, E_V, I_V).

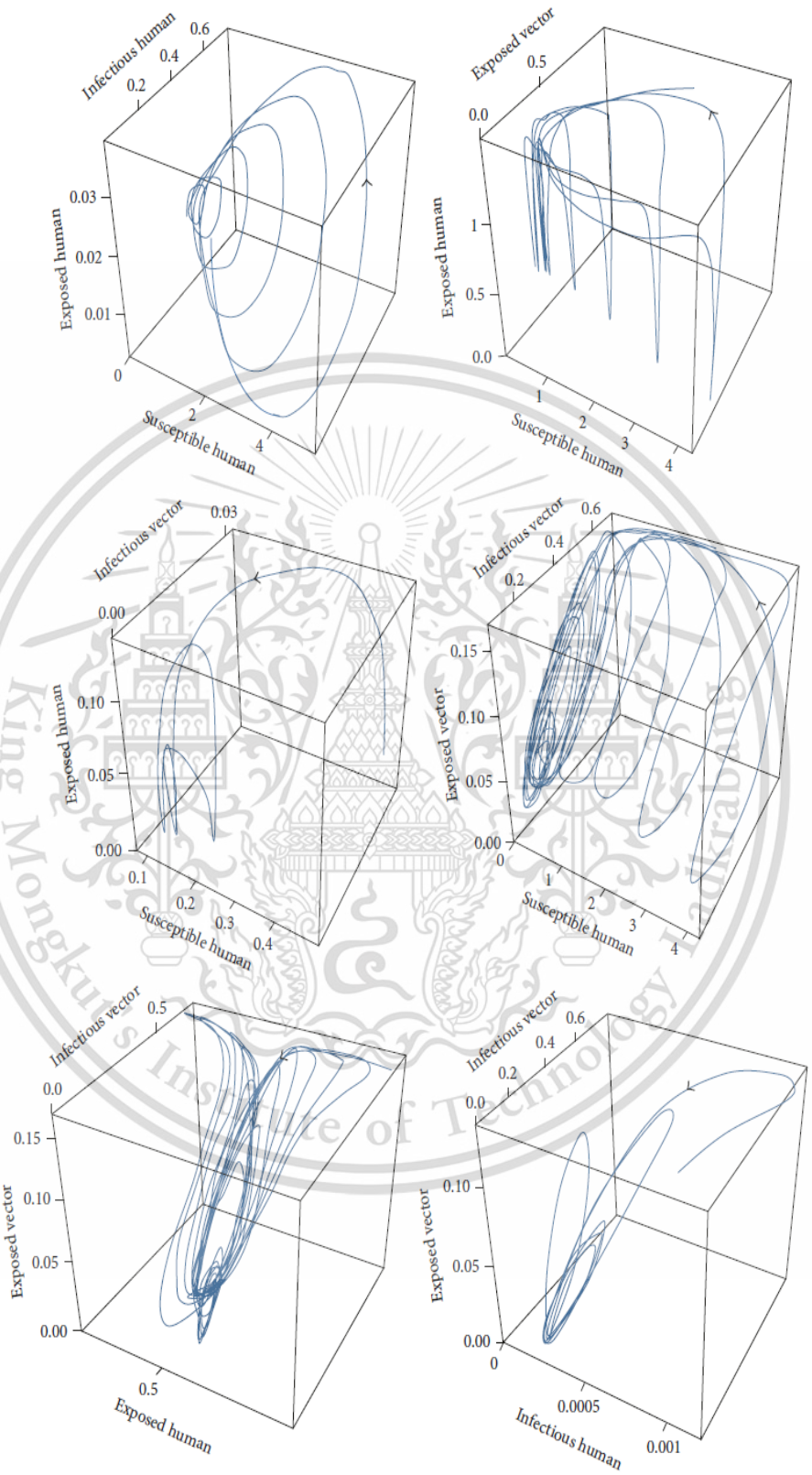

FIGURE 11: The trajectories of the numerical solutions of dengue disease for endemic equilibrium projected onto (S_H, E_H, I_H), (S_H, E_H, E_V), (S_H, E_H, I_V), (S_H, E_V, I_V), (E_H, E_V, I_V), and (I_H, E_V, I_V).

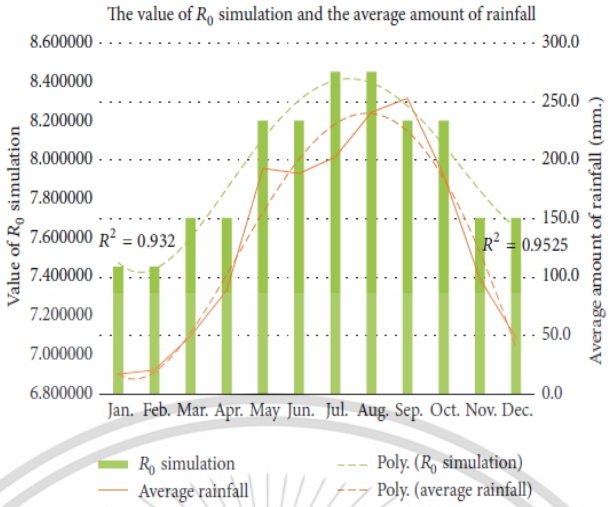

FIGURE 12: The value of R_0 simulation of endemic equilibrium state and the average amount of rainfall.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

Acknowledgments

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Appendix C

Paper 3

The SEIR dynamical transmission model of dengue disease with and without the vertical transmission of the dengue virus

American Journal of Applied Sciences

Original Research Paper

The SEIR Dynamical Transmission Model of Dengue Disease with and Without the Vertical Transmission of the Virus

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Abstract: The transmission of dengue disease when there is a possibility of Vertical Transmission (VT) is studied using mathematical modeling. In the normal case, the mosquito is infected by the dengue virus when it bites an infectious human being. Evidence is gathering that the mosquitoes can also be infected through sexual contact with infected male mosquito. To see the possible consequence of having this addition mode of transmission, a SEIR, Susceptible-Exposed-Infected-Recovery, model is constructed. The Routh – Hurwitz criteria are applied to the model in order to establish the stability of the infection. It is seen that the model without the VT model has 2 equilibrium points, a disease free equilibrium point and an endemic equilibrium point, while the model with the VT has only an endemic equilibrium point. The numerical solutions of differential equations of the model without the VT mode exhibit dynamical behaviors that converges to the disease free equilibrium state when basic reproduction time R_0 is less than 1 and converges to endemic equilibrium state when R_0>1. The trajectories of the numerical solutions for all possibilities (with and without VT mode) projected onto various 2D planes and 3D spaces are presented.

Keywords: Dengue Disease, Vertical Transmission Infection Mode, SEIR Model, Disease Free and Endemic Equilibrium State, Routh – Hurwitz Criteria, Basic Reproductive Number

Introduction

Dengue disease is found in the tropical and subtropical areas around the world such as in South-East Asia, the Western Pacific, America, African, Eastern Mediterranean and others (WHO, 2011). Dengue infection is estimated to infect 50-100 million populations with almost half of world' population living in dengue endemic countries (WHO, 2012). Dengue virus has four serotypes; i.e., DEN1, DEN2, DEN3 and DEN4 and cannot transmit from human to human directly. Dengue virus is transmitted to human by the bite of infected *Aedes* mosquitoes. It means that human is the main host of the dengue virus and mosquito are the vectors of the transmission. The mosquitoes can be found around houses and are infected when they bite an infectious human. This leads to the dengue virus moving within and between communities. The way to control dengue disease is focused on the spreading of the mosquitoes.

In Thailand, dengue has been reported from all regions including the Bangkok metropolitan area. The reported cases and death cases from 2003 to 2015 are shown in Fig. 1. In 2015, the reported cases and deaths cases were 144,952 and 148 respectively (Bureau of Epidemiology, 2015). The historical reported data is indicated that dengue disease has potential to spread quickly with the country experiencing large epidemic in both reported cases and death. There is a high risk potential for the spread of the dengue disease when there is a high rate of contact between the host and vector in a large population of human and mosquito (as in the Bangkok metropolitan). Rainy season is suitable for mosquito to lay their eggs and Fig. 2 shows that there is high number of reported cases during the rainy season. Female mosquitoes will become the vector for the disease when they feed on the blood of infectious human. As the results, the mosquito will be able to transmit the virus to an uninfected human when she bites him.

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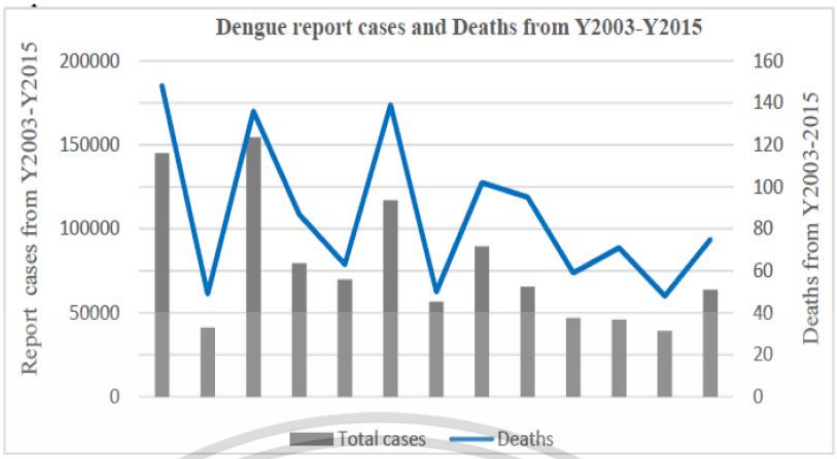

Fig. 1: Thailand dengue reported historical data from 2003 to 2015

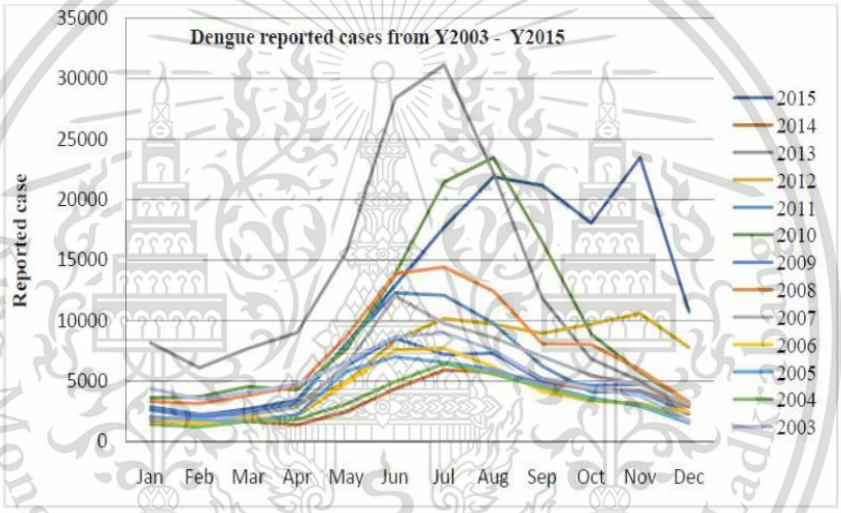

Fig. 2: Thailand dengue reported cases from 2003 to 2015 (month by month)

A model of the dengue epidemic is necessary to better understand the mechanism and behavior in order to analyze the spread and control the spread of the disease. Mathematical models are often developed to describe the transmission of dengue disease. Esteva and Vargas (1999) proposed a model for the transmission of dengue fever where the human population is constant but mosquito population varies. They provided a global analysis to establish the global stability of the endemic equilibrium. Naowarat *et al.* (2011) proposed a dynamical model to determine the human susceptibility to dengue fever. The standard method was used to analyze the dynamic of dengue disease system. Pongsumpun and co-workers proposed mathematical models for dengue disease which took into account additional features of the disease. The dynamic transmission with the effect of extrinsic incubation period was included. An standard dynamic analysis was applied to a modified Susceptible-Infected-Recovered (SIR) model included an annual variation in the length of the extrinsic incubation period in the mosquito (Pongsumpun, 2006a). The dynamic transmission behaviors of dengue disease in the presence and absence of an extrinsic incubation period were compared (Pongsumpun, 2006b). In other study, the effects of there being an incubation period in the virus was studied in a SEIR model (Pongsumpun, 2007). The vector populations in this model were divided into susceptible, infected and infectious classes. In a further study, a seasonal change was introduced into the transmission model used describe the dengue virus infection in Thailand (Pongsumpun, 2011).

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Hiroshi (2006) proposed a new SIR model to clarify the relative contributions of a mathematical approach and of a statistical approach to the dengue epidemiology without having to delve into the mathematical details. He introduced a new method to determine the basic reproductive number which did not involve extensive mathematical manipulations. Erickson *et al*. (2010) used a SEIR model to examine the role of temperature in driving the vector dynamics. Their model used the Aedes albopictus mosquitoes as the transmitting vector. Bakach and Braselton (2015) looked at different mathematical models and compared their predicted behaviors with each other. The evaluation of each model under different scenarios allowed one to identify the strengths and weakness of each of the model. The effect of the spreading and progression of the disease were studied in order to determine what the values of the parameters were. Rodrigues *et al*. (2011) has also studied the transmission of dengue fever. They used their results to explain outbreak of the disease in Cape Verde. Aldila *et al*. (2013) a host-vector dengue transmission model to determine what the optimal control strategy should be. The strategy was based on using different amounts of mosquito repellent on different segments of the human population.

In another paper, Esteva and Vargas (2000) included the possibility of vertical or transovarial transmission. In this type of transmission, one does not need the host; one can pass the virus from mosquito to mosquito without the need of a human or from human to human without the need of a mosquito. These types of transmission are very. The rarity is seen in the report in 2010 of the first putative case of vertical transmission in China (Yin *et al*., 2010) Thenmozhi *et al*. (2007) reported that they had collected mosquitoes (both male and female) in Kerala State and examined for dengue virus DNA in them. They found that some of the male mosquitoes in them. Since the males do not need human blood for the purpose of generating eggs, the most likely way would be through sexual contact. This has happen in the most recent ZIKA epidemic (Lequime *et al*., 2016). The ZIKA disease is also an airborne disease where the same mosquito transmitting the virus is the same virus specie transmitting the dengue fever virus. The latest report is that the ZIKA disease has become a STD (sexually transmitted disease) which needs a different form of disease control strategy. Whatever the reasons, two recent reviews have appeared in 2016 on the vertical transmission of spread of dengue fever (Grunnil and Boots, 2016; D'Ortenzio *et al*., 2016).

In this study, we will be reconsidering the transmission of dengue virus in the case where vertical transmission of the virus between the mosquitoes is possible. We will be using the SEIR model (Susceptible, Exposed, Infected and Recovered) is used to investigate the dynamics of the disease. We will be analyzing the stability of the model using standard dynamic analysis. We will consider the dynamical transmission model of dengue disease for the cases where vertical transmission is or is not possible. The equilibrium state and stability are considered both behaviors. The numerical simulation, results and conclusion are presented.

Materials and Methods

Mathematical Model

The mathematical model is for two populations, human and mosquito. In the SEIR model, the human is divided into four compartments, susceptible human $(\tilde{S}H)$, exposed human $(\tilde{E}H)$, infected human $(\tilde{I}H)$ and re-denoted as covered human $(\tilde{R}H)$. The vector population is partitioned into 3 compartments: Susceptible vector susceptible vector $(\tilde{S}V)$, exposed vector $(\tilde{E}V)$ and infected vector $(\tilde{I}_V)$. In this model, we assumed that the total number of members of each population is constant. For the vector population, we further assume that the rate at which the number of susceptible vectors entering into mosquito population is A per unit time and M is the number of infected mosquitoes that enter directly by vertical (transovarial) infection if this type of transmission is possible. As we have mentioned, this transmission mode is rare or nonexistent. We consider the different behaviors of dynamical transmission of dengue disease with and without the effect of vertical transmission taken into account ($M \neq 0$ and $M = 0$). The dynamic transmission of dengue disease when both modes of transmissions are possible is shown schematically in Fig. 3.

Let:

$(\tilde{S}H)$ = Number of susceptible humans population at time t
$(\tilde{E}H)$ = Number of exposed humans population at time t
$(\tilde{I}H)$ = Number of infected humans population at time t
$(\tilde{R}H)$ = Number of recovered humans population at time t
$(\tilde{S}V)$ = Number of susceptible vector population at time t
$(\tilde{E}V)$ = Number of exposed vector population at time t
$(\tilde{I}_V)$ = Number of vertically infected population at time t
A = Constant recruitment rate
M = Number of mosquitoes which were infected transovarially

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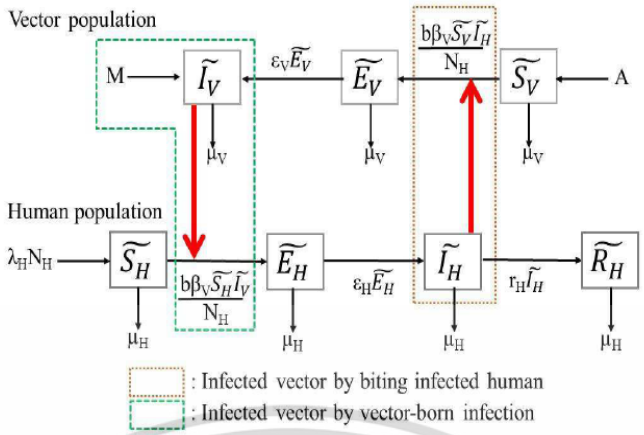

Fig. 3: The dynamic transmission of dengue disease by both biting infected human and vector born infection

The mathematical representations of the processes shown schematically in Fig. 3 are given by equations (1) to (7). The dynamic change of the human and mosquito populations are given by Equation (1) to (4) and (5) to (7) respectively:

$$\frac{d\tilde{S}_H}{dt} = \lambda_H N_H - \frac{b\beta_H}{N_H}\tilde{S}_H\tilde{I}_V - \mu_H\tilde{S}_H \quad (1)$$

$$\frac{d\tilde{E}_H}{dt} = \frac{b\beta_H}{N_H}\tilde{S}_H\tilde{I}_V - (\varepsilon_H + \mu_H)\tilde{E}_H \quad (2)$$

$$\frac{d\tilde{I}_H}{dt} = \varepsilon_H\tilde{E}_H - (\mu_H + r_H)\tilde{I}_H \quad (3)$$

$$\frac{d\tilde{I}_H}{dt} = r_H\tilde{I}_H - \mu_H\tilde{R}_H \quad (4)$$

$$\frac{d\tilde{S}_V}{dt} = A - \frac{b\beta_V}{N_H}\tilde{S}_V\tilde{I}_H - \mu_V\tilde{S}_V \quad (5)$$

$$\frac{d\tilde{E}_V}{dt} = \frac{b\beta_V}{N_H}\tilde{S}_V\tilde{I}_H - (\varepsilon_V + \mu_V)\tilde{E}_V \quad (6)$$

$$\frac{d\tilde{I}_V}{dt} = M + \varepsilon_V\tilde{E}_V - \mu_V\tilde{I}_V \quad (7)$$

We have assumed that:

$$N_H = \tilde{S}_H + \tilde{E}_H + \tilde{I}_H + \tilde{R}_H \quad (8)$$

$$N_V = \tilde{S}_V + \tilde{E}_V + \tilde{I}_V \quad (9)$$

Where:

N_H = Total number of human population
N_V = Total number of vector population
λ_H = Birth rate of human population
b = Biting rate of vector population
β_H = Transmission probability of dengue virus from vector population to human
β_V = Transmission probability of dengue virus from human population to vector
ε_H = Intrinsic incubation rate
ε_V = Extrinsic incubation rate
μ_H = Death rate of human population
μ_V = Death rate of vector population
r_H = Recovery rate of the human population

The assumption of our model is the total human and vector populations are constant. This leads to the rate of change for human and vector population being zero, i.e.:

$$\frac{d\tilde{S}_H}{dt} + \frac{d\tilde{E}_H}{dt} + \frac{d\tilde{I}_H}{dt} + \frac{d\tilde{R}_H}{dt} = 0 \quad (10)$$

$$\frac{d\tilde{S}_V}{dt} + \frac{d\tilde{E}_V}{dt} + \frac{d\tilde{I}_V}{dt} = 0 \quad (11)$$

From the above equations, we can obtain the following equations:

$$N_V = (A + M)/\mu_V \quad (12)$$

$$\lambda_H = \mu_H \quad (13)$$

We now normalized equations (1) – (9) as following:

$$S_H = \frac{\tilde{S}_H}{N_H}, E_H = \frac{\tilde{E}_H}{N_H}, I_H = \frac{\tilde{I}_H}{N_H}, R_H = \frac{\tilde{R}_H}{N_H}, \quad (14)$$

$$S_V = \frac{\tilde{S}_V}{N_V}, E_H = \frac{\tilde{E}_V}{N_V}, I_V = \frac{\tilde{I}_V}{N_V} \quad (15)$$

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We also have:

$$1 = S_H + E_H + I_H + R_H \tag{16}$$

$$1 = S_V + E_H + I_V \tag{17}$$

The mathematical model of Equation (1) – (7) is now reduced to the following 5 Equations:

$$\frac{dS_H}{dt} = \mu_H(1 - S_H) - \frac{b\beta_H}{N_H} S_H I_V N_V \tag{18}$$

$$\frac{dE_H}{dt} = \frac{b\beta_H}{N_H} S_H I_V N_V - (\varepsilon_H + \mu_H)E_H \tag{19}$$

$$\frac{dI_H}{dt} = \varepsilon_H E_H - (\mu_H + r_H)I_H \tag{20}$$

$$\frac{dE_V}{dt} = b\beta_V S_V I_H - (\varepsilon_V + \mu_V)E_V \tag{21}$$

$$\frac{dI_V}{dt} = \frac{M}{N_V} + \varepsilon_V E_V - \mu_V I_V \tag{22}$$

Mathematical Analysis for Equilibrium Point

The mathematical model is now analyzed and investigated in order to find the equilibrium points and system stability. The equilibrium point is determined by setting the right hand side of Equation (18) – (22) to zero. The system stability is determined by its eigenvalues and R_0. After we solved Equation (18) – (22), we only obtain the endemic disease equilibrium points E_1 given by:

$$E_1 = (S_H^{1*}, E_H^{1*}, I_H^{1*}, E_V^{1*}, I_V^{1*}) \tag{23}$$

Where:

$$\begin{aligned}
S_H^{1*} &= (b^2N_V^2\beta_H\beta_V\varepsilon_H\varepsilon_V\mu_H + \\
&N_V(N_H\mu_H(\varepsilon_V+\mu_V)(2b\beta_V\varepsilon_H\mu_H + \\
&(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V) \\
&+bM\beta_H(\gamma_H(\varepsilon_H+\mu_H(\varepsilon_V+\mu_V) \\
&+\mu_H(b\beta_V\varepsilon_H+(\varepsilon_H+\mu_H)(\varepsilon_V+\mu_V)))) \\
&-\sqrt{(N_V^2(4bMN_H\beta_H\mu_H(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)(\varepsilon_V+\mu_V)^2} \\
&(b\beta_V\varepsilon_H\mu_H+(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V)+ \\
&N_H\mu_H(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V(\varepsilon_V+\mu_V) \\
&-b\beta_H(M\gamma_H(\varepsilon_H+\mu_H)(\varepsilon_V+\mu_V)+ \\
&\mu_H(b\beta_V\varepsilon_H(M+N_V\varepsilon_V)+M(\varepsilon_H+\mu_H)(\varepsilon_V+\mu_V))))^2))) / \\
&(2bN_V\beta_V\varepsilon_H\mu_H(b\beta_H(M+N_V\varepsilon_V)+N_H\mu_H(\varepsilon_V+\mu_V)))
\end{aligned} \tag{24}$$

$$\begin{aligned}
E_H^{1*} &= (b^2N_V^2\beta_H\beta_V\varepsilon_H\varepsilon_V\mu_H \\
&+N_V(-N_H\mu_H(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V(\varepsilon_V+\mu_V) \\
&+bM\beta_H(-\gamma_H(\varepsilon_H+\mu_H)(\varepsilon_V+\mu_V) \\
&-\mu_H(-b\beta_V\varepsilon_H+(\varepsilon_H+\mu_H)(\varepsilon_V+\mu_V)))) \\
&+\sqrt{(N_V^2(4bMN_H\beta_H\mu_H(\gamma_H+\mu_H)} \\
&(\varepsilon_H+\mu_H)(\varepsilon_V+\mu_V)^2(b\beta_V\varepsilon_H\mu_H \\
&+(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V)+ \\
&N_H\mu_H(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V(\varepsilon_V+\mu_V) \\
&-b\beta_H(M\gamma_H(\varepsilon_H+\mu_H)(\varepsilon_V+\mu_V) \\
&+\mu_H(b\beta_V\varepsilon_H(M+N_V\varepsilon_V)+M(\varepsilon_H+\mu_H)(\varepsilon_V+\mu_V))))^2))) / \\
&(2bN_V\beta_V\varepsilon_H(\varepsilon_H+\mu_H)(b\beta_H(M+N_V\varepsilon_V)+N_H\mu_H(\varepsilon_V+\mu_V)))
\end{aligned} \tag{25}$$

$$\begin{aligned}
I_H^{1*} &= (b^2N_V^2\beta_H\beta_V\varepsilon_H\varepsilon_V\mu_H + \\
&N_V(-N_H\mu_H(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V(\varepsilon_V+\mu_V)+ \\
&+bM\beta_H(-\gamma_H(\varepsilon_H+\mu_H)(\varepsilon_V+\mu_V) \\
&-\mu_H(-b\beta_V\varepsilon_H+(\varepsilon_H+\mu_H)(\varepsilon_V+\mu_V)))) \\
&+\sqrt{(N_V^2 4bMN_H\beta_H\mu_H(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)(\varepsilon_V+\mu_V)^2} \\
&(b\beta_V\varepsilon_H\mu_H+(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V) \\
&+(N_H\mu_H(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V(\varepsilon_V+\mu_V) \\
&-b\beta_H(M\gamma_H(\varepsilon_H+\mu_H)(\varepsilon_V+\mu_V) \\
&+\mu_H(b\beta_V\varepsilon_H(M+N_V\varepsilon_V)+M(\varepsilon_H+\mu_H)(\varepsilon_V+\mu_V))))^2)))) / \\
&(2bN_V\beta_V(\gamma_H+\mu_H)(\varepsilon_H+\mu_H) \\
&(b\beta_H(M+N_V\varepsilon_V)+N_H\mu_H(\varepsilon_V+\mu_V)))
\end{aligned} \tag{26}$$

$$\begin{aligned}
E_V^{1*} &= (-bMN_V\beta_H(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V(\varepsilon_V+\mu_V) \\
&-N_HN_V\mu_H(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V^2(\varepsilon_V+\mu_V) \\
&+b^2N_V\beta_H\beta_V\varepsilon_H\mu_H(-M\mu_V+\varepsilon_V(-2M+N_V\mu_V)) \\
&+\mu_V\sqrt{(N_V^2(4bMN_H\beta_H\mu_H(\gamma_H+\mu_H)} \\
&(\varepsilon_H+\mu_H)(\varepsilon_V+\mu_V)^2(b\beta_V\varepsilon_H\mu_H \\
&+(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V)+ \\
&(N_H\mu_H(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V)(\varepsilon_V+\mu_V) \\
&-b\beta_H(M\gamma_H(\varepsilon_H+\mu_H)(\varepsilon_V+\mu_V) \\
&+\mu_Hb\beta_V\varepsilon_H(M+N_V\varepsilon_V)+M(\varepsilon_H+\mu_H)(\varepsilon_V+\mu_V))))^2))) / \\
&(2bN_V^2\beta_H\varepsilon_V(\varepsilon_V+\mu_V)(b\beta_V\varepsilon_H\mu_H+(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V))
\end{aligned} \tag{27}$$

$$\begin{aligned}
I_V^{1*} &= (b^2N_V^2\beta_H\beta_V\varepsilon_H\varepsilon_V\mu_H+N_V \\
&(-N_H\mu_H(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V(\varepsilon_V+\mu_V) \\
&+bM\beta_H(\gamma_H(\varepsilon_H+\mu_H)(\varepsilon_V+\mu_V) \\
&+\mu_H(b\beta_V\varepsilon_H+(\varepsilon_H+\mu_H)(\varepsilon_V+\mu_V)))) \\
&+\sqrt{(N_H^2(4bMN_H\beta_H\mu_H(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)(\varepsilon_V+\mu_V)^2} \\
&(b\beta_V\varepsilon_H\mu_H+(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V) \\
&+(N_H\mu_H(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V(\varepsilon_V+\mu_V) \\
&-b\beta_H(M\gamma_H(\varepsilon_H+\mu_H)(\varepsilon_v+\mu_v) \\
&+\mu_H(b\beta_V\varepsilon_H(M+N_V\varepsilon_V)+M(\varepsilon_H+\mu_H)(\varepsilon_V+\mu_V))))^2))) / \\
&(2bN_V^2\beta_H(\varepsilon_V+\mu_V)(b\beta_V\varepsilon_H\mu_H+(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V))
\end{aligned} \tag{28}$$

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All parameters used in system (24) – (28) are positive and the epidemic region is:

$$\Omega = \left\{(S_H^{1*}, E_H^{1*}, I_H^{1*}, E_V^{1*}, I_V^{1*},) : 0 \le S_H^{1*}, E_H^{1*}, I_H^{1*}, E_V^{1*}, I_V^{1*} \le 1\right\}$$

Mathematical Analysis for Local Stability

The local stability of the equilibrium point determined from Equation (18) – (22) is analyzed by first obtaining an expression for the basic reproduction number R_0 and the Jacobian matrix. After these are done, we then solve the eigenvalues equation which involves the Jacobian matrix. The Jacobian matrix of system (18) – (22) is as follows:

$$J = \begin{bmatrix} -\mu_H - \frac{b\beta_H}{N_H} I_V^{1*} N_V & 0 & 0 & 0 & -\frac{b\beta_H}{N_H} S_H^{1*} N_V \\ \frac{b\beta_H}{N_H} I_V^{1*} N_V & -(\varepsilon_H + \mu_H) & 0 & 0 & \frac{b\beta_H}{N_H} S_H^{1*} N_V \\ 0 & \varepsilon_H & -(\mu_H + \gamma_H) & 0 & 0 \\ 0 & 0 & b\beta_V (1 - I_V^{1*} - E_V^{1*}) & -(\varepsilon_V + \mu_V) & 0 \\ 0 & 0 & 0 & \varepsilon_V & -\mu_V \end{bmatrix} \quad (29)$$

The basic reproductive number, $\sqrt{R_0}$, is the number of secondary infection produced by a typical case of an infection in a population of its infectious period. R_0 can be indicated the transmission potential of disease. In case of $R_0>1$, the transmission has potential to spread between people. The requirement for local stability at the equilibrium state is stated in proposition 1 given below.

Proposition 1.

The equilibrium state E_1 is asymptotically stable when R_0 is higher than 1, $R_0>1$.

Proof.

The local stability of E_1 is governed by linearization of system (18)-(22). The R_0 is given as:

$$R_0 = (\alpha_1 + N_V M \alpha_2 (\gamma_H \alpha_3 + \mu_H (\alpha_4 + \alpha_3))) + \sqrt{\frac{N_V^2 (\alpha_5 \alpha_2 \alpha_6 \alpha_3^2 (\alpha_4 \mu_H + \alpha_6 \alpha_7 \mu_V) + (\alpha_8 \alpha_6 \alpha_3 - \alpha_2 (M \gamma_H \alpha_3 + \mu_H (\alpha_4 \alpha_9 + M \alpha_3)))^2))}{N_V \alpha_8 \alpha_6 \alpha_3}} \quad (30)$$

Where:

a_1 = $b^2 N_V^2 \beta_H \beta_V \varepsilon_H \varepsilon_V \mu_H$
a_2 = $b\beta_H$
a_3 = $(\varepsilon_H+\mu_H)$ $(\varepsilon_V+\mu_V)$
a_4 = $b\beta_V\varepsilon_H$
a_5 = $4N_H\mu_H M$
a_6 = $(\gamma_H+\mu_H)$
a_7 = $(\varepsilon_H+\mu_H)$
a_8 = $N_H\mu_H\mu_V$
a_9 = $(M+N_V\varepsilon_V)$

The characteristic of equation (29) which determines the eigenvalues is the eigenvalue equation obtained by solving det:

$$\left|J_{E_1} - \lambda I_5\right| = 0$$

Where:
J_{E1} = The Jacobian matrix at the equilibrium point E_1
λ = The eigenvalues
I_5 = The identity 5×5 matrix

Evaluating the determinant, we get the following Evaluating the determinant, we get the following:

$$(\lambda^5 + e_1\lambda^4 + e_2\lambda^3 + e_3\lambda^2 + e_4\lambda^1 + e_5) = 0 \quad (31)$$

Where:

$$e_1 = \begin{bmatrix} -F(-\gamma_H - \mu_H)\mu_H^2 GH \\ +F(-GHJ - \mu_H^2 GH(-\mu_H - KL)) \end{bmatrix} / N$$

$$e_2 = \begin{bmatrix} (-F(-\gamma_H - \mu_H)GHJ - \mu_H^2 GH(-\mu_H - K + L)) \\ +F(-GHP + GHJ(-\mu_H - K + L))) \end{bmatrix} / N$$

$$e_3 = \begin{bmatrix} -F(-\gamma_H - \mu_H)GHP + GHJ(-\mu_H - K + L) \\ +FOGH + GHP(-\mu_H - K + L) \end{bmatrix} / N$$

$$e_4 = \begin{bmatrix} -FOGH(-\mu_H - K + L) + (QH(-K + R))(1 - K + S) \\ -F((-\gamma_H - \mu_H)\, OGH + GHP(-\mu_H - K + L)) \end{bmatrix} / F\mu_H^2 GH$$

e_5 = $(1/2N_H N_V (b\beta_1\varepsilon_H\mu_H + (\gamma_H + \mu_H)\ (\varepsilon_H + \mu_H)\mu_V))T$

Where:

F = $8N_H^2 N_V^4 \beta_H \beta_V^2 \varepsilon_H^2 \varepsilon_V$
G = $(\varepsilon_V + \mu_V)^2$
H = $(bM\beta_H + bN_V\beta_H\varepsilon_V) + N_H\varepsilon_V\mu_H + N_H\mu_H\mu_V)^2$ $(b\beta_V\varepsilon_H\mu_H + \gamma_H\varepsilon_H\mu_V + \gamma_H\mu_H\mu_V + \varepsilon_H\mu_H\mu_V + \mu_H^2\mu_V)^3$
J = $\left((-\varepsilon_H - \mu_H)\mu_H^2 - \mu_H^2(\varepsilon_V + 2\mu_V)\right)$
K = $\left(b^2 N_V^2 \beta_H \beta_V \varepsilon_H \varepsilon_V \mu_H\right.$ $+N_V(-N_H\mu_H(\gamma_H + \mu_H)(\varepsilon_H + \mu_H)\mu_V(\varepsilon_V + \mu_V)$ $+bM\beta_H(\gamma_H(\varepsilon_H + \mu_H)(\varepsilon_V + \mu_V)$ $\left.+\mu_H(b\beta_V\varepsilon_H + (\varepsilon_H + \mu_H)(\varepsilon_V + \mu_V))\right)$ $\sqrt{(N_V^2(4bMN_H\beta_H\mu_H(\gamma_H + \mu_H)(\varepsilon_H + \mu_H)(\varepsilon_V + \mu_V)^2}$ $(b\beta_V\varepsilon_H\mu_H + (\gamma_H + \mu_H)(\varepsilon_H + \mu_H)\mu_V) +$
L = $(N_H\mu_H(\gamma_H + \mu_H)(\varepsilon_H + \mu_H)\mu_V(\varepsilon_V + \mu_V) -$ $b\beta_H(M\gamma_H(\varepsilon_H + \mu_H)(\varepsilon_V + \mu_V)$ $+\mu_H(b\beta_V\varepsilon_H(M + N_V\varepsilon_V) + M(\varepsilon_H + \mu_H)(\varepsilon_V + \mu_V))))^2))) /$ $(2N_HN_V(\varepsilon_V + \mu_V)(b\beta_V\varepsilon_H\mu_H + (\gamma_H + \mu_H)(\varepsilon_H + \mu_H)))))$
N = $(8N_H^2N_V^4\beta_V\beta_V^2\varepsilon_H^2\varepsilon_H^2(\varepsilon_V + \mu_V)^2$ $(bM\beta_H + bN_V\beta_H\varepsilon_V + N_H\varepsilon_V\mu_H + N_H\mu_H\mu_V)^2$ $(b\beta_V\varepsilon_H\mu_H + \gamma_H\varepsilon_H\mu_V + \gamma_H\mu_H\mu_V + \varepsilon_H\mu_H\mu_V + \mu_H^2\mu_V)^3)$
O = $(-\varepsilon_H - \mu_H)\mu_H^2(-\varepsilon_V - \mu_V)\mu_V$

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$$P = \left(\mu_H^2(-\varepsilon_V-\mu_V)\mu_V+(-\varepsilon_H-\mu_H)\mu_H^2(\varepsilon_V+2\mu_V)\right)$$

$$Q = 1/\left(b\beta_H(M+N_V\varepsilon_V)+N_H\mu_H(\varepsilon_V+\mu_V)\right)$$

$$S = 4bN_HN_V^4\beta_H^2\beta_V^2\varepsilon_H^2\varepsilon_V^2\mu_H(\varepsilon_V+\mu_V)^2$$
$$\sqrt{(N_V^2(4bMN_H\beta_H\mu_H(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)(\varepsilon_V+\mu_V)^2}$$
$$b\beta_V\varepsilon_H\mu_H+(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V)$$
$$+(N_H\mu_H(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V(\varepsilon_V+\mu_V)$$
$$-b\beta_H(M\gamma_H(\varepsilon_H+\mu_H)(\varepsilon_V+\mu_V)$$
$$+\mu_H(b\beta_V\varepsilon_H(M+N_V\varepsilon_V)+M(\varepsilon_H+\mu_H)(\varepsilon_V+\mu_V))))^2)))$$
$$/\left(2bN_V^2\beta_H(\varepsilon_V+\mu_V)(b\beta_V\varepsilon_H\mu_H+(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V)\right)$$

$$T = (-b^3N_V^2\beta_H\beta_V^2\varepsilon_H^2\varepsilon_V\mu_H^2$$
$$+bN_V\beta_V\varepsilon_H\mu_H(N_H\mu_H(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V(\varepsilon_V+\mu_V)$$
$$+bM\beta_H(-\gamma_H(\varepsilon_H+\mu_H)(\varepsilon_V+\mu_V)$$
$$-\mu_H(b\beta_V\varepsilon_H+(\varepsilon_H+\mu_H)(\varepsilon_V+\mu_V))))$$
$$+(b\beta_V\varepsilon_H\mu_H+2(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V)$$

$$R = \sqrt{(N_V^2(N_H^2\mu_H^2(\gamma_H+\mu_H)^2(\varepsilon_H+\mu_H)^2\mu_V^2(\varepsilon_V+\mu_V)^2}$$
$$+2bN_H\beta_H\mu_H(\gamma_H+\mu_H(\varepsilon_H+\mu_H)(\varepsilon_V+\mu_V)$$
$$(M(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V(\varepsilon_V+\mu_V)$$
$$+b\beta_V\varepsilon_H\mu_H(2M\varepsilon_V+(M-N_V\varepsilon_V)\mu_V)$$
$$+b^2\beta_H^2(M\gamma_H(\varepsilon_H+\mu_H)(\varepsilon_V+\mu_V)$$
$$+\mu_H(b\beta_V\varepsilon_H(M+N_V\varepsilon_V)+M(\varepsilon_H+\mu_H)(\varepsilon_V+\mu_V)))^2)))$$
$$\sqrt{(N_V^2(4bMN_H\beta_H\mu_H(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)(\varepsilon_V+\mu_V)^2}$$
$$(b\beta_V\varepsilon_H\mu_H+(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V)$$
$$+(N_H\mu_H(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V(\varepsilon_V+\mu_V)$$
$$-b\beta_H(M\gamma_H(\varepsilon_H+\mu_H)(\varepsilon_V+\mu_V)$$
$$+\mu_H(b\beta_V\varepsilon_H(M+N_V\varepsilon_V)+M(\varepsilon_H+\mu_H)(\varepsilon_V+\mu_V)))^2)))$$

The solution of equation (31) is solved through use of the Routh-Hurwitz criteria. The equilibrium point will be local stability when all eigenvalues have negative real parts. This will happen if all the coefficients satisfy the following conditions:

$$e_1>0, e_2>0, e_3>0, e_4>0, e_5>0 \quad (32)$$

$$e_1e_2e_3>e_3^2+e_1^2e_4 \quad (33)$$

$$(e_1e_4-e_5)(e_1e_2e_3-e_3^2-e_1^2e_4)>e_5(e_1e_2-e_3)^2+e_1e_5 \quad (34)$$

All conditions of equation (32) - (34) are satisfied for endemic equilibrium point as seen in Fig. 4.

The dynamic transmission of dengue disease without a vertical mode of transmission ($M = 0$) is described by equations (18) to (21) which are the same as the case where vertical transmission is possible except that Equation (22) has been replaced by the equation below:

$$\frac{dI_V}{dt}=\varepsilon_VE_V-\mu_VI_V \quad (35)$$

Reanalyzing the new set of equations in the same way as before, we now arrive at two equilibrium points, a disease free equilibrium point and an endemic disease equilibrium point defined as.

i. Disease free equilibrium point

$$E_0=(1,0,0,0,0) \quad (36)$$

ii. Endemic disease equilibrium point:

$$E_2=(S_H^{2*},E_H^{2*},I_H^{2*},E_V^{2*},I_V^{2*}) \quad (37)$$

Where:

$$S_H^{2*}=[N_H(\varepsilon_V+\mu_V)(b\beta_V\varepsilon_H\mu_H+(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V)] /[b\beta_V\varepsilon_H(bN_V\beta_H\varepsilon_V+N_H\mu_H(\varepsilon_V+\mu_V))] \quad (38)$$

$$E_H^{2*}= -\left[\mu_H(-b^2N_V\beta_H\beta_V\varepsilon_H\varepsilon_V+N_H(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V(\varepsilon_V+\mu_V))\right] /\left[b\beta_V\varepsilon_H(\varepsilon_H+\mu_H)(bN_V\beta_H\varepsilon_V+N_H\mu_H(\varepsilon_V+\mu_V))\right] \quad (39)$$

$$I_H^{2*}=\begin{bmatrix}\mu_H(b^2N_V\beta_H\beta_V\varepsilon_H\varepsilon_V\\ -N_H(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V(\varepsilon_V+\mu_V))\end{bmatrix} /b\beta_V(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)(bN_V\beta_H\varepsilon_V+N_H\mu_H(\varepsilon_V+\mu_V)) \quad (40)$$

$$E_V^{2*}=-[\mu_H\mu_V(-b^2N_V\beta_H\beta_V\varepsilon_H\varepsilon_V +N_H(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V(\varepsilon_V+\mu_V))] /bN_V\beta_H\varepsilon_V(\varepsilon_V+\mu_V)(b\beta_V\varepsilon_H\mu_H+(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V) \quad (41)$$

$$I_V^{2*}= -[\mu_H(-b^2N_V\beta_H\beta_V\varepsilon_H\varepsilon_V+N_H(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V(\varepsilon_V+\mu_V))] /bN_V\beta_H(\varepsilon_V+\mu_V)(b\beta_V\varepsilon_H\mu_H+(\gamma_H+\mu_H)(\varepsilon_H+\mu_H)\mu_V) \quad (42)$$

The Jacobian matrix used to determine the stability of eigenvalues at $E_0 = (1.0,0.0,0)$ has the form:

$$J=\begin{bmatrix}-\mu_H & 0 & 0 & 0 & -\frac{b\beta_H}{N_H}N_V\\ 0 & -(\varepsilon_H+\mu_H) & 0 & 0 & \frac{b\beta_H}{N_H}N_V\\ 0 & \varepsilon_H & -(\mu_H+r_H) & 0 & 0\\ 0 & 0 & b\beta_V & -(\varepsilon_V+\mu_V) & 0\\ 0 & 0 & 0 & \varepsilon_V & -\mu_V\end{bmatrix} \quad (43)$$

Proposition 2.

The equilibrium state E_0 is asymptotically stable when R_0 is less than 1, $R_0 < 1$.

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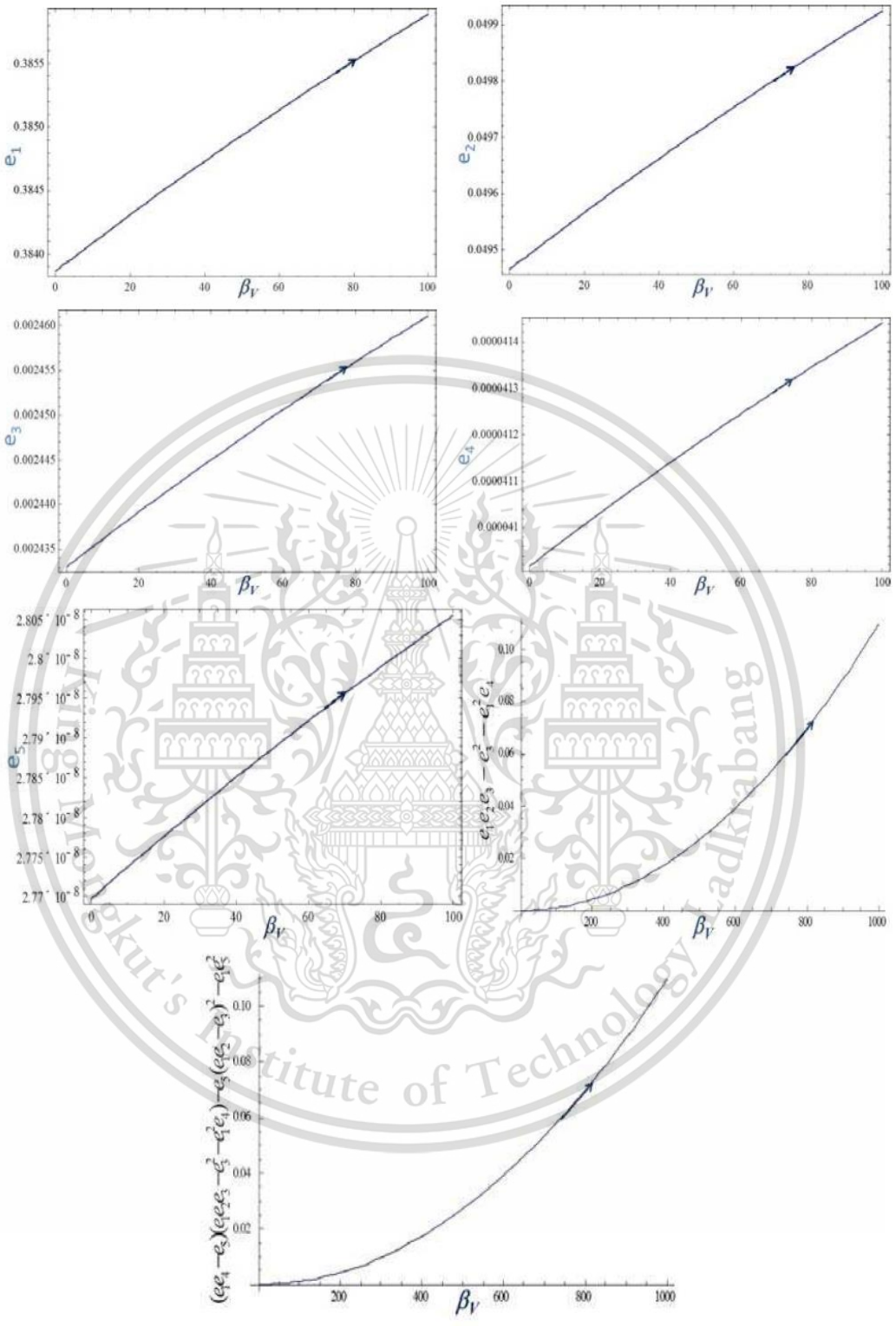

Fig. 4: The All parameters spaces of endemic disease equilibrium of E_1 are satisfied the Routh-Hurwitz criteria. The parameter value are N_H = 92,000, b = 1/5, μ_H = 1/(70*365) γ_H = 0.1428, β_H = 0.95, β_V = 0.75, μ_V = 1/24, ε_V = 0.1428, ε_H = 0.1667, A = 5,000 and M = 400

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Proof.

The local stability of E_0 is governed by linearization of system (18) - (21) and (35). The R_0 will be of the form:

$$R_0 = \frac{b^2 N_V \beta_H \beta_V \varepsilon_H \varepsilon_V}{N_H \mu_V (\gamma_H + \mu_H)(\varepsilon_H + \mu_H)(\varepsilon_V + \mu_V)}$$

The characteristic equation obtained same by solving the determinant equation, Equation (43) is given by:

$$(\lambda^5 + e_1\lambda^4 + e_2\lambda^3 + e_3\lambda^2 + e_4\lambda^1 + e_5) = 0$$

Where:

$$e_1 = [N_H\gamma_H + N_H\varepsilon_H + N_H\varepsilon_V + 3N_H\mu_H + 2N_H\mu_V]/N_H$$

$$e_2 = [N_H\gamma_H\varepsilon_H + N_H\gamma_H\varepsilon_V + N_H\varepsilon_H\varepsilon_V + 2N_H\gamma_H\mu_H + 2N_H\varepsilon_H\mu_H + 3N_H\varepsilon_V\mu_H + 3N_H\mu_H^2 + 2N_H\gamma_H\mu_V + 2N_H\varepsilon_H\mu_V + N_H\varepsilon_V\mu_V + 6N_H\mu_H\mu_V + N_H\mu_V^2]/N_H$$

$$e_3 = [(N_H\gamma_H\varepsilon_H\varepsilon_V + N_H\gamma_H\varepsilon_H\mu_H + 2N_H\gamma_H\varepsilon_V\mu_H + 2N_H\varepsilon_H\varepsilon_V\mu_H + N_H\gamma_H\mu_H^2 + N_H\varepsilon_H\mu_H^2 + 3N_H\varepsilon_V\mu_H^2 + N_H\mu_H^3 + 2N_H\gamma_H\varepsilon_H\mu_V + N_H\gamma_H\varepsilon_V\mu_V + N_H\varepsilon_H\varepsilon_V\mu_V + 4N_H\gamma_H\mu_H\mu_V + 4N_H\varepsilon_H\mu_H\mu_V + 3N_H\varepsilon_V\mu_H\mu_V + 6N_H\mu_H^2\mu_V + N_H\gamma_H\mu_V^2 + N_H\varepsilon_H\mu_V^2 + 3N_H\mu_H\mu_V^2] + [-b^2N_V\beta_H\beta_V\varepsilon_H\varepsilon_V + N_H\gamma_H\varepsilon_H\varepsilon_V\mu_H + N_H\gamma_H\varepsilon_V\mu_H^2 + N_H\varepsilon_H\varepsilon_V\mu_H^2 + N_H\varepsilon_V\mu_H^3 + N_H\gamma_H\varepsilon_H\varepsilon_V\mu_V + 2N_H\gamma_H\varepsilon_H\mu_H\mu_V + 2N_H\gamma_H\varepsilon_V\mu_H\mu_V + 2N_H\varepsilon_H\varepsilon_V\mu_H\mu_V + 2N_H\gamma_H\mu_H^2\mu_V + 3N_H\varepsilon_V\mu_H^2\mu_V + 2N_H\mu_H^3\mu_V + N_H\gamma_H\varepsilon_H\mu_V^2 + 2N_H\gamma_H\mu_H\mu_V^2 + 2N_H\varepsilon_H\mu_H\mu_V^2 + 3N_H\mu_H^2\mu_V^2)]/N_H$$

$$e_4 = [\mu_H(-b^2N_V\beta_H\beta_V\varepsilon_H\varepsilon_V + N_H(\gamma_H + \mu_H)(\varepsilon_H + \mu_H)\mu_V(\varepsilon_V + \mu_V))]/N_H$$

$$e_5 = [\mu_H(-b^2N_V\beta_H\beta_V\varepsilon_H\varepsilon_V + N_H(\gamma_H + \mu_H)(\varepsilon_H + \mu_H)\mu_V(\varepsilon_V + \mu_V))]/N_H$$

All conditions of equation (32)-(34) are satisfied for disease free equilibrium point as seen in Fig. 5.

The Jacobian matrix at $E_2 = (S_H^{2*}, E_H^{2*}, I_H^{2*}, E_V^{2*}, I_V^{2*})$ is:

$$J = \begin{bmatrix} -\mu_H - \frac{b\beta_H}{N_H} I_V^{2*} N_V & 0 & 0 & 0 & -\frac{b\beta_H}{N_H} S_H^{2*} N_V \\ \frac{b\beta_H}{N_H} I_V^{2*} N_V & -(\varepsilon_H + \mu_H) & 0 & 0 & \frac{b\beta_H}{N_H} S_H^{2*} N_V \\ 0 & \varepsilon_H & -(\mu_H + \gamma_H) & 0 & 0 \\ 0 & 0 & b\beta_V(1 - I_V^{2*} - E_V^{2*}) & -(\varepsilon_V + \mu_V) & 0 \\ 0 & 0 & 0 & \varepsilon_V & -\mu_V \end{bmatrix} \quad (44)$$

Proposition 3.

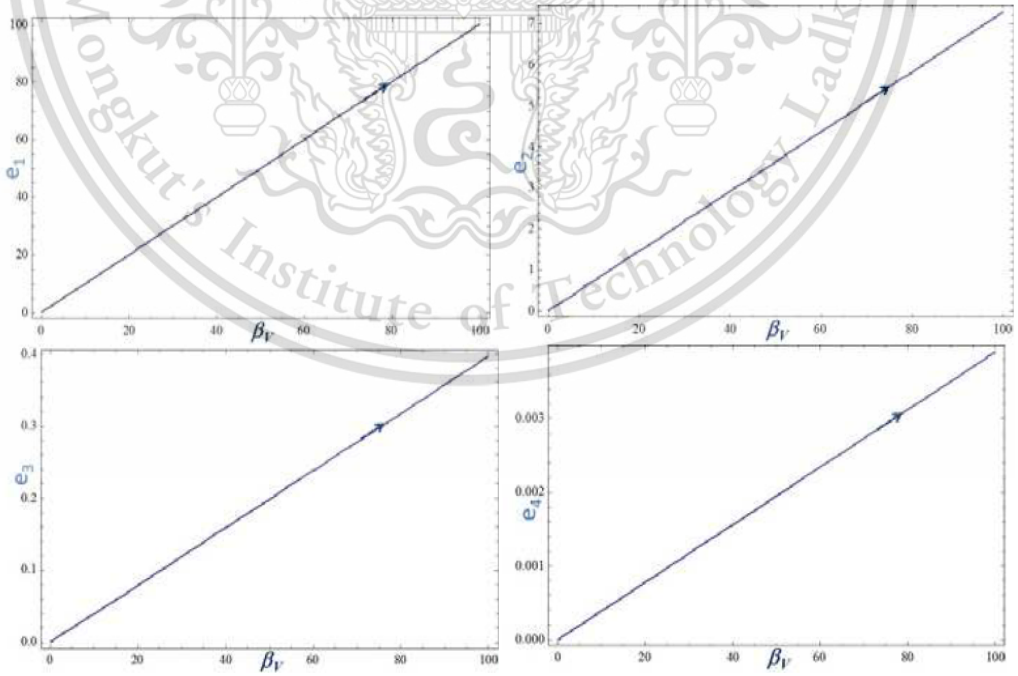
The equilibrium state E_2 is asymptotically stable when R_0 is higher than 1, R_0>1.

Proof.

The local stability of E2 is established through the linearization of equations (18) - (21) and (35) which leads to the determinant equation previously obtained. Solving the eigen value equation, we get a similar characteristic equation, i.e:

$$(\lambda^5 + e_1\lambda^4 + e_2\lambda^3 + e_3\lambda^2 + e_4\lambda^1 + e_5) = 0$$

Except that the coefficients are now.



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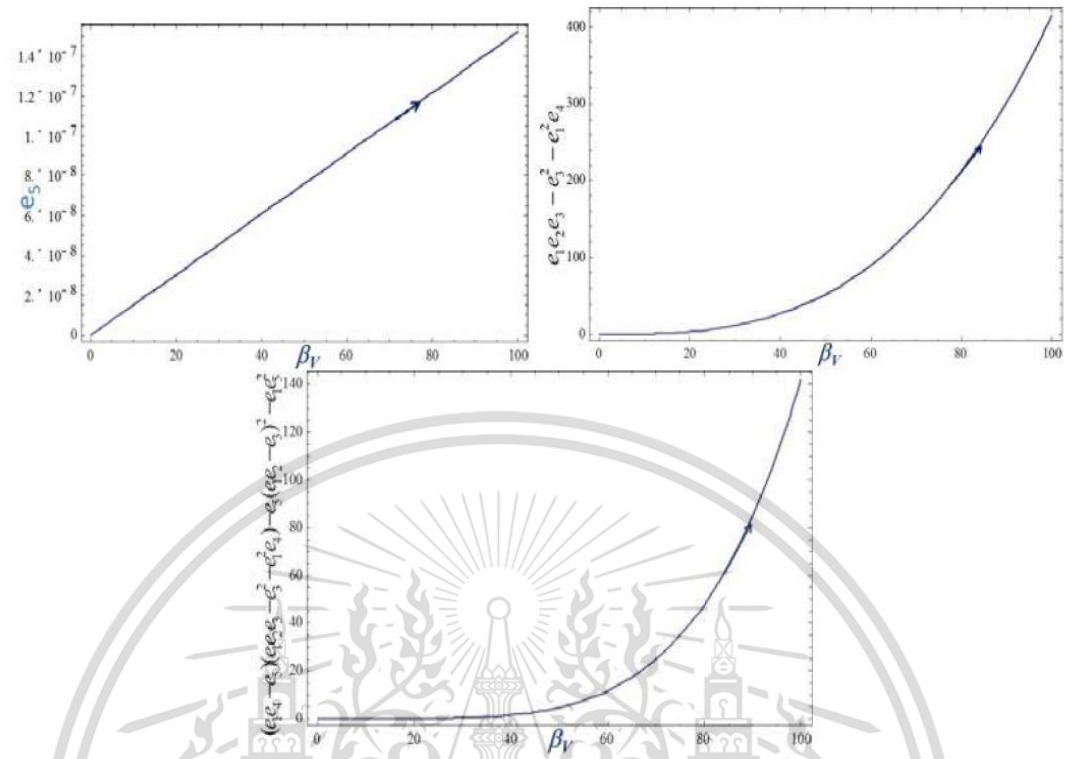
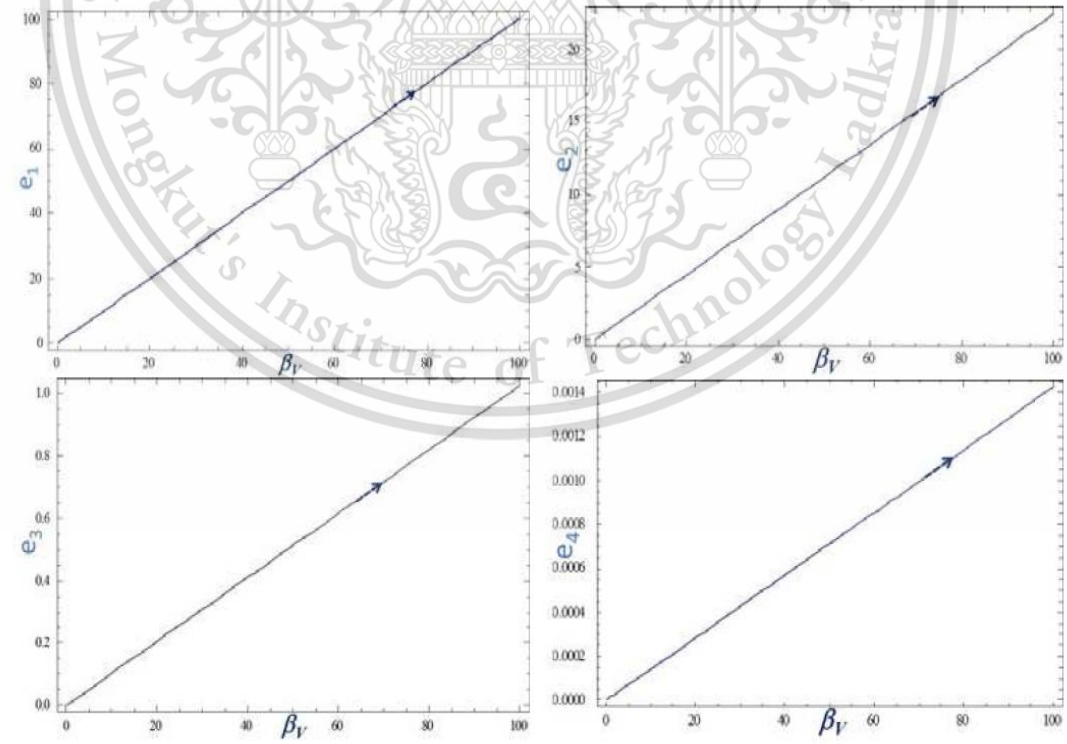


Fig. 5: The All parameters spaces of endemic disease equilibrium of E0 are satisfied the Routh-Hurwitz criteria. The parameter value are N_H = 92.000, b = 1/5, μ_H = 1/(70*365), γ_H = 0.01428, β_H = 0.65, β_V = 0.65, μ_V = 1/24, ε_V = 0.01428, ε_H = 0.1667, A = 5,000 and M = 400



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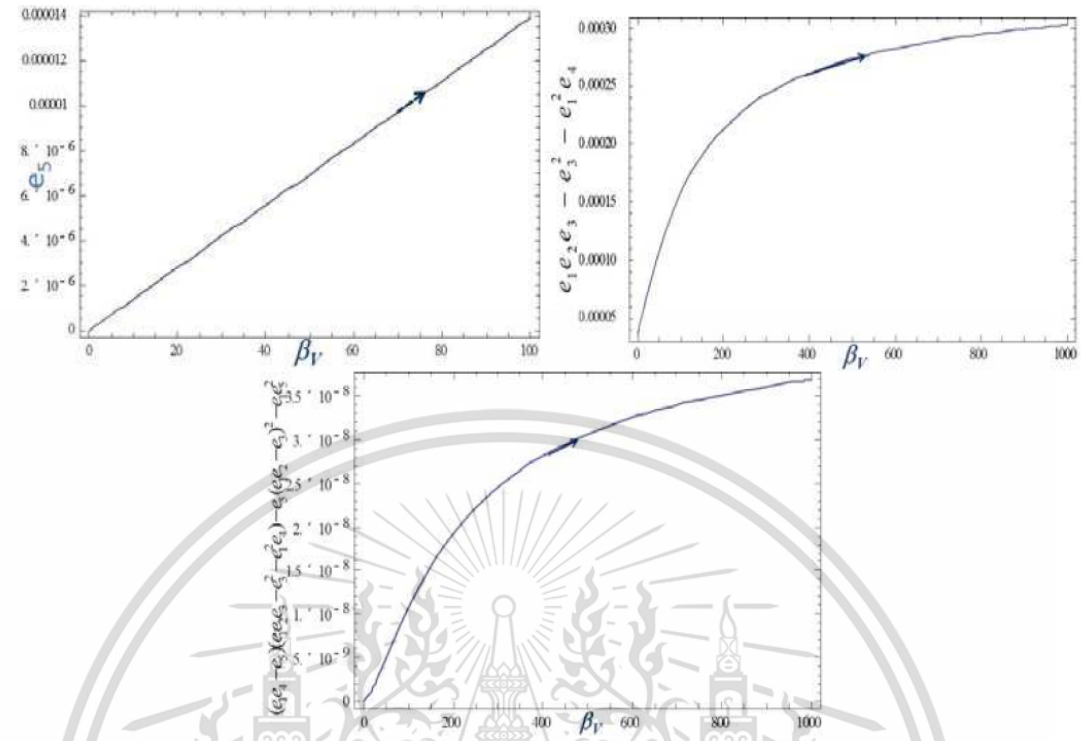

Fig. 6: The All parameters spaces of endemic disease equilibrium of E2 are satisfied the Routh-Hurwitz criteria. The parameter value are N_H = 92.000, b = 1/5, μ_H = 1/(70*365), γ_H = 0.01428, β_H = 0.65, β_V = 0.65, μ_V = 1/24, ε_H = 0.1428, ε_H = 0.1667, A = 5.000 and M = 0

Where:

$$e_1 = [-(-UH + GH(-\mu_H + V)] / GH$$

$$e_2 = [-(-GH(W_1 - W_2 + W_3W_4) + GUH(-\mu_H + V)] / GH$$

$$e_3 = [-(-UH(-W_3W_2 + W_1W_4) + GH(W_1 - W_2 + W_3W_4)(-\mu_H + V)] / GH$$

$$e_4 = [(1/Y_1HY_2)(1 + V + \mu_V V) - Y_3(W_1W_2GH + GH(-W_3W_2 + W_1W_4))(-\mu_H + V)] / GHY_3$$

$$e_5 = [-\mu_H(\gamma_H + \mu_H)(\varepsilon_H + \mu_H)\mu_V(-b^2N_V\beta_H\beta_V\varepsilon_H\varepsilon_V + N_H(\gamma_H + \mu_H)(\varepsilon_H + \mu_H)\mu_V(\varepsilon_V + \mu_V))] / N_H(b\beta_V\varepsilon_H\mu_H + (\gamma_H + \mu_H)(\varepsilon_H + \mu_H)\mu_V)$$

Where:

$$U = (\gamma_H + \varepsilon_H + \varepsilon_V + 2\mu_H + 2\mu_V)$$

$$V = [\mu_H(-b^2N_V\beta_H\beta_V\varepsilon_H\varepsilon_V + N_H(\gamma_H + \mu_H)(\varepsilon_H + \mu_H)\mu_V(\varepsilon_V + \mu_V))] / [N_H(\varepsilon_V + \mu_V)(b\beta_V\varepsilon_H\mu_H + (\gamma_H + \mu_H)(\varepsilon_H + \mu_H)\mu_V)]$$

$$W_1 = (-\gamma_H - \mu_H)(-\varepsilon_H - \mu_H)$$

$$W_2 = (-\varepsilon_V - \mu_V)\mu_V$$

$$W_3 = (\gamma_H + \varepsilon_H + 2\mu_H)$$

$$W_4 = (\varepsilon_V + 2\mu_V)$$

$$Y_1 = (bN_V\beta_H\varepsilon_V + N_H\mu_H(\varepsilon_V + \mu_V)) \; bN_H^2N_V^2\beta_H^2\beta_V^2\varepsilon_H^2\varepsilon_V^2(\varepsilon_V + \mu_V)^3$$

$$Y_2 = (b\beta_V\varepsilon_H\mu_H + (\gamma_H + \mu_H)(\varepsilon_H + \mu_H)\mu_V)),$$

$$Y_3 = N_H^2N_V\beta_H\beta_V^2\varepsilon_H^2\varepsilon_V$$

These coefficients of this new characteristic equation will also satisfy the Routh-Hurwitz criteria. Equation (32) - (34) for the coefficients defined above (Fig. 6) and so the eigenvalues by the characteristic equation above will all have negative imaginary parts and the endemic disease equilibrium point will be stable.

Numerical Results

The numerical analysis in this study considers the transmission of dengue disease in models where the values of the parameter values are listed in Table 1, which gives different values for three sets of parameters which leads to the three cases we are looking at. Case 1 are the values when vertical transmission occurs and the equilibrium state is the endemic state. Case 2 are the values when there is no vertical transmission is possible but the equilibrium state will be the disease free state. Finally, case 3 are the values when there is no vertical transmission but the equilibrium state will be the endemic state.

The trajectories of the numerical solutions case 1, case 2 and case 3 projected onto S_H, E_H, I_H, E_V and I_V are shown in the Fig. 7-9 respectively. The trajectory of the numerical solutions case 1, case 2 and case 3 projected onto (S_H, E_H), (S_H, I_H), (S_H, E_V), (S_H, I_V), (E_H, E_V) and (I_H, I_V) are shown in the Fig. 10-12 respectively.

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Table 1: Parameter are used involved in the transmission of dengue disease

Parameter	Case 1	Case 2	Case 3
μ_H	1/(70*365)	1/(70*365)	1/(70*365)
N_H	92,000	92,000	92,000
b	1/5	1/5	1/5
A	5,000	5,000	5,000
μ_V	1/24	1/24	1/24
M	400	0	0
γ_H	0.1428	0.01428	0.01428
β_H	0.95	0.65	0.65
β_V	0.75	0.65	0.65
ε_V	0.1428	0.01428	0.1428
ε_H	0.1667	0.01667	0.1667

The trajectory of the numerical solutions case 1, case 2 and case 3 projected onto (S_H, E_H, I_H), (S_H, E_H, E_V), (S_H, E_H, I_V), (S_H, E_V, I_V), (E_H, E_V, I_V) and (I_H, E_V, I_V) are shown in the Fig. 13-15 respectively.

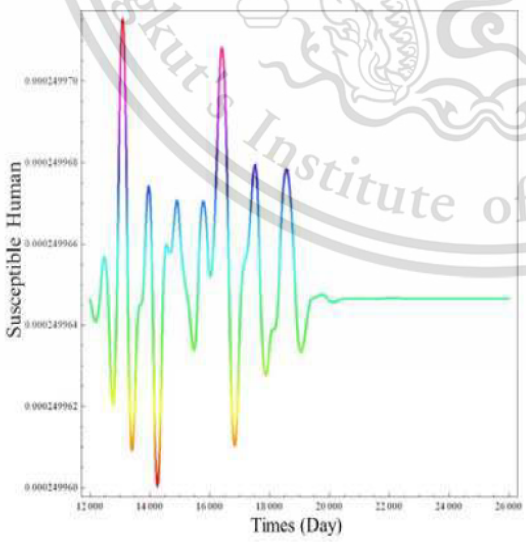
Discussion

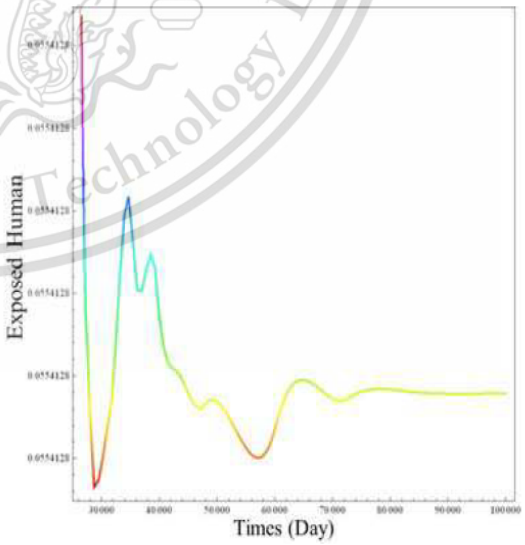
In this study, the dynamic transmission of dengue disease using SEIR mathematical models which focus on the transmission of the virus in the mosquito by its being bitten by an infected human or by vertical transmission mode, i.e., through sexual contact with a male mosquito is studied. It is shown that the presence of vertical transmission insures that the endemic equilibrium state is the only possible outcome. In the absence of vertical transmission, the model leads to two possible outcomes, a disease free equilibrium state and an endemic equilibrium state which depend on whether $R_0<1$ or $R_0>1$. The Routh-Hurwitz criteria for the coefficients of the characteristics equations for the system are used to determine whether all the eigenvalues have negative imaginary parts.

When there is vertical transmission of the virus in the mosquito and the values of the parameters are such that $R_0>1$, the only equilibrium state is the endemic equilibrium point, E_1 and it is local asymptotically stable as can be seen from Fig. 4 which shows the values of the parameters satisfy the Routh-Hurwitz criteria. The time trajectories of S_H, E_H, I_H, E_V and I_V are plotted on Fig. 7. The trajectories of the numerical solutions are plotted on the 2D (S_H, E_H), (S_H, I_H), (S_H, E_V), (S_H, I_V), (E_H, E_V) and (I_H, I_V) planes and in the 3D (S_H, E_H, I_H), (S_H, E_H, E_V), (S_H, E_H, I_V), (S_H, E_V, I_V), (E_H, E_V, I_V) and (I_H, E_V, I_V) spaces seen in Fig. 10 and 13 respectively.

In the absence of vertical transmission, the disease free equilibrium point, E_0, will be local asymptotically stable when $R_0<1$. The range of values of the parameters for which the coefficients of the characteristic equation for eigenvalues satisfy the Routh-Hurwitz criteria for the disease free state to be local asymptotical stable are shown in Fig. 5.

Picking the values (the ones listed for case 2 in Table 1 and given in figure caption), the time dependences of S_H, E_H, I_H, E_V and I_V are plotted in Fig. 8. The trajectories of the numerical solutions are plotted in the 2D (S_H, E_H), (S_H, I_H), (S_H, E_V), (S_H, I_V), (E_H, E_V) and (I_H, I_V) and the 3D (S_H, E_H, I_H), (S_H, E_H, E_V), (S_H, E_H, I_V), (S_H, E_V, I_V), (E_H, E_V, I_V) and (I_H, E_V, I_V) space in Fig. 11 and 14 respectively. The endemic equilibrium point, E_2, is local asymptotically stable for $R_0>1$. The behaviors of the populations for this case (case 3) are shown in Fig. 6, 9 and 15.





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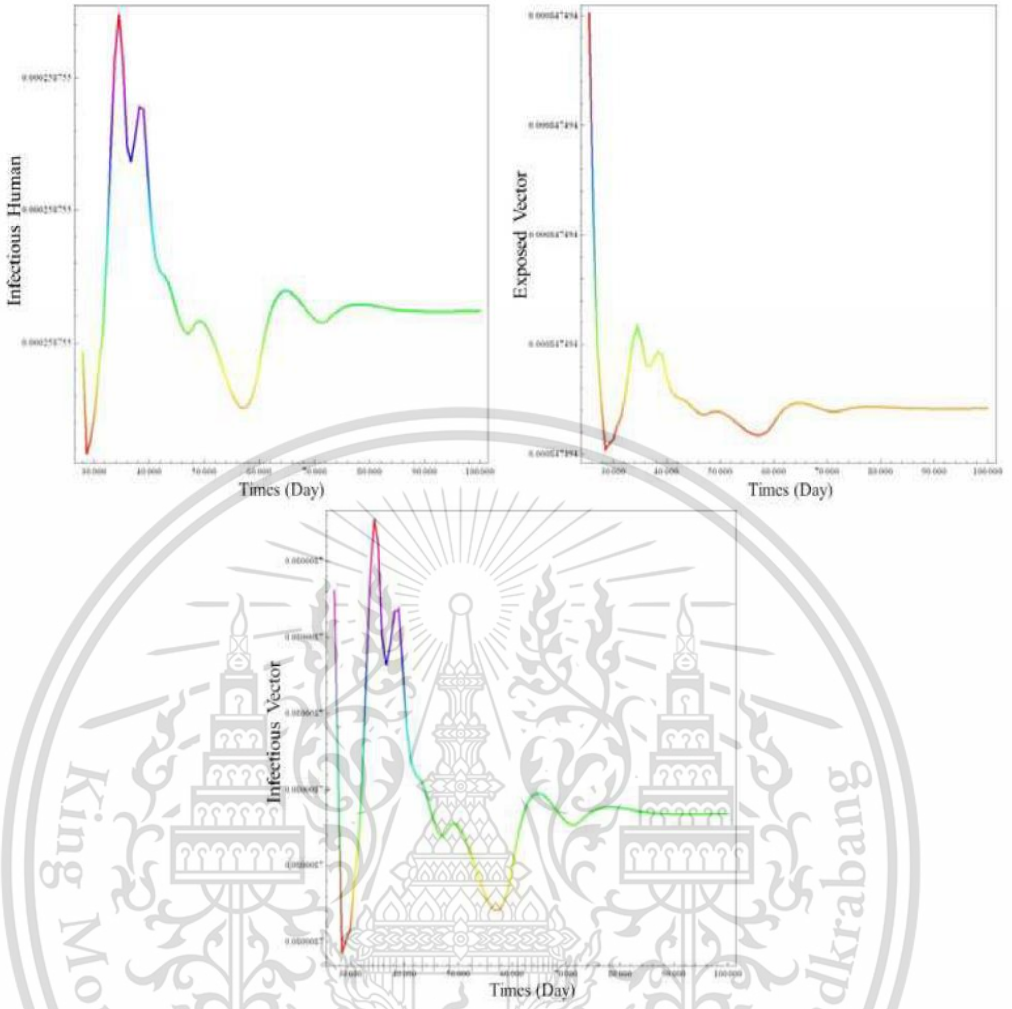
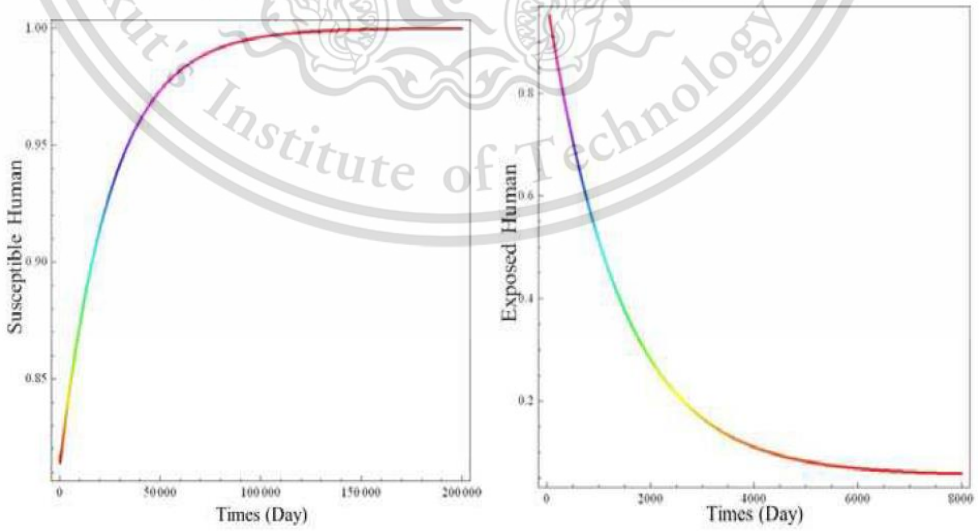


Fig. 7: The time trajectories of the numerical solutions of the model when vertical transmission occurs for S_H, E_H, I_H, E_V and I_V are shown



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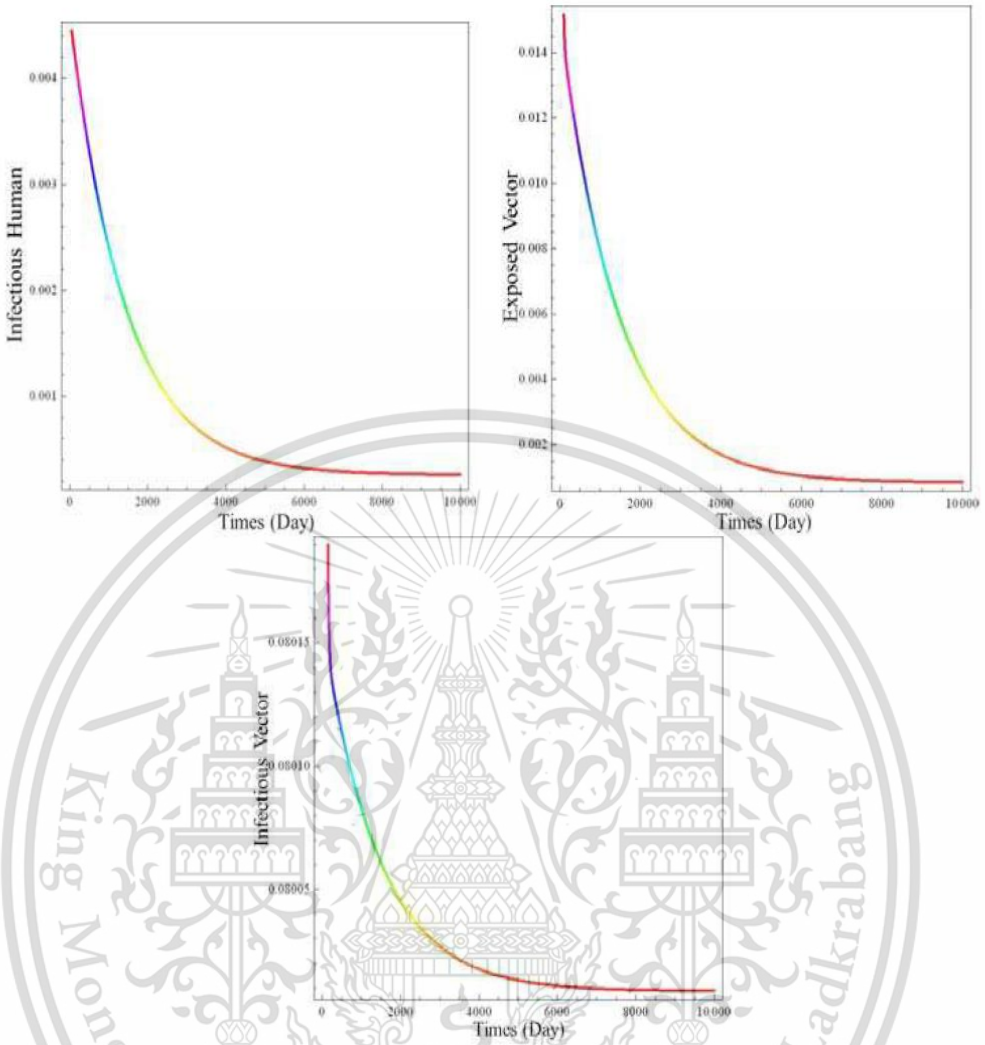
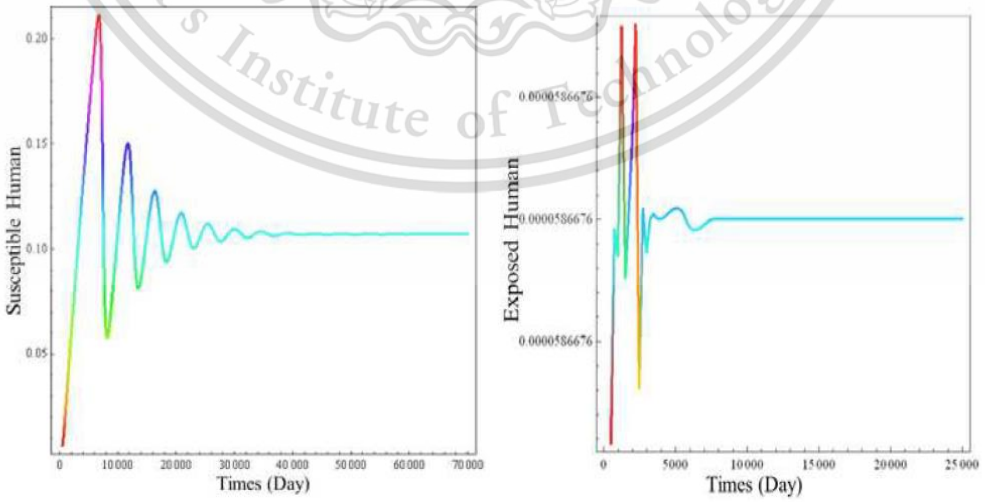


Fig. 8: The time trajectories of the numerical solutions of the model when there is no vertical transmission of the virus of S_H, E_H, I_H, E_V and I_V lead to the equilibrium state being the disease free state



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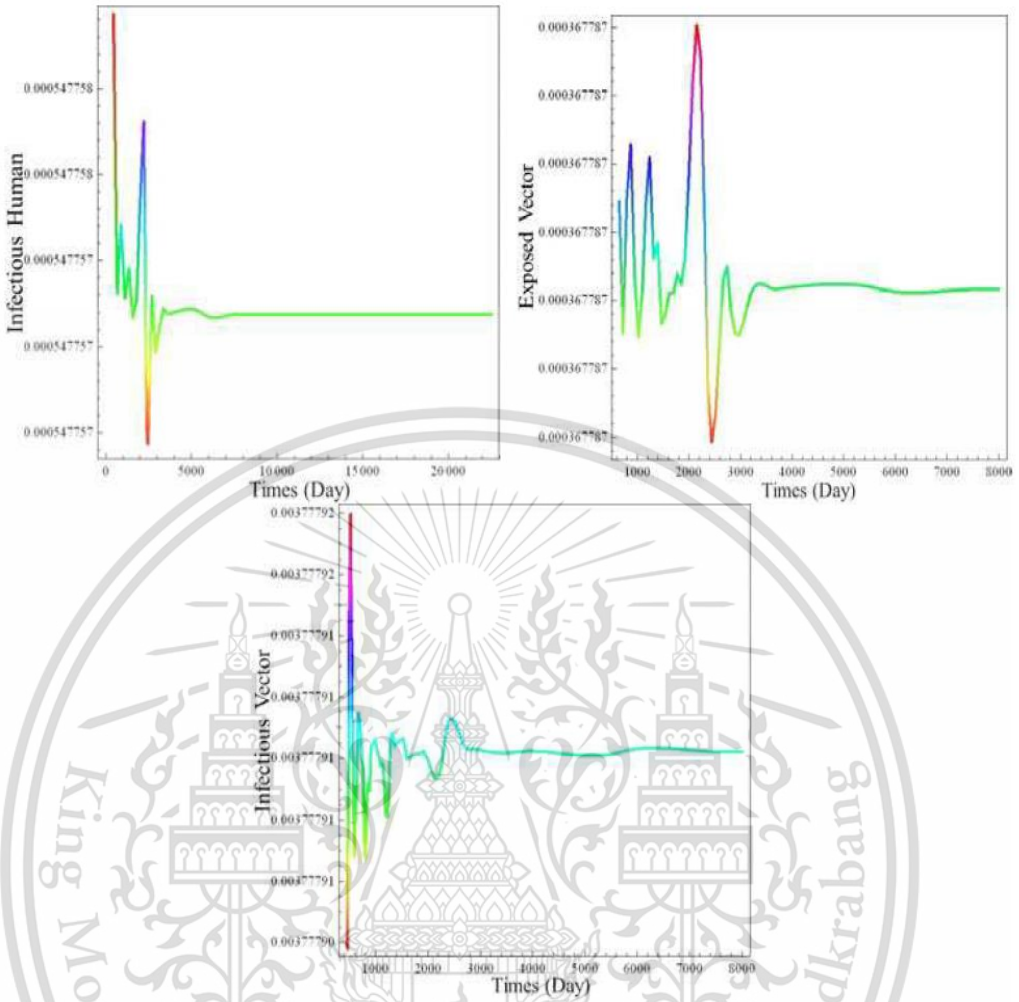
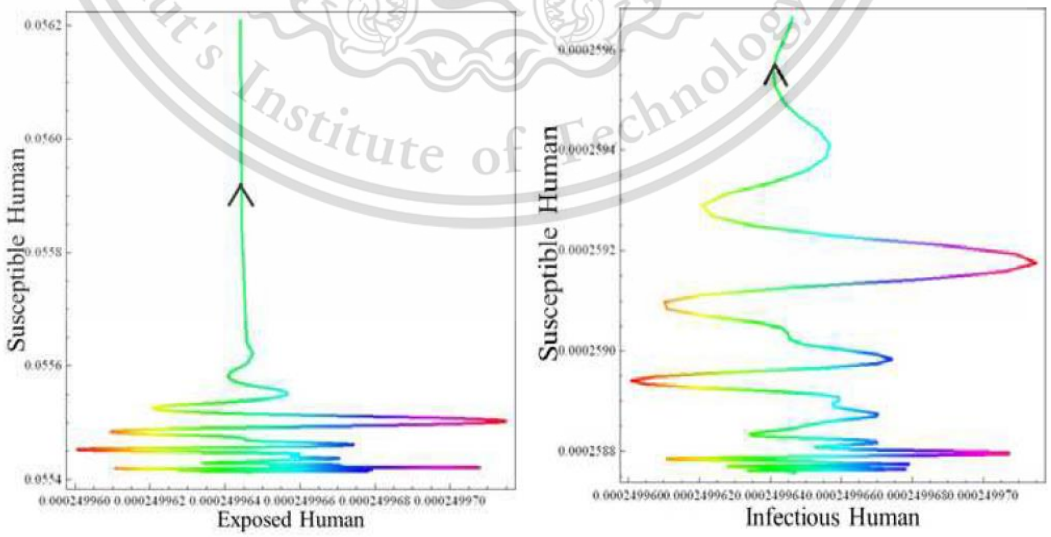


Fig. 9: The time trajectories of the numerical solutions of the model when there is no vertical transmission of the virus of S_H, E_H, I_H, E_V and I_V lead to the equilibrium state being the endemic disease state



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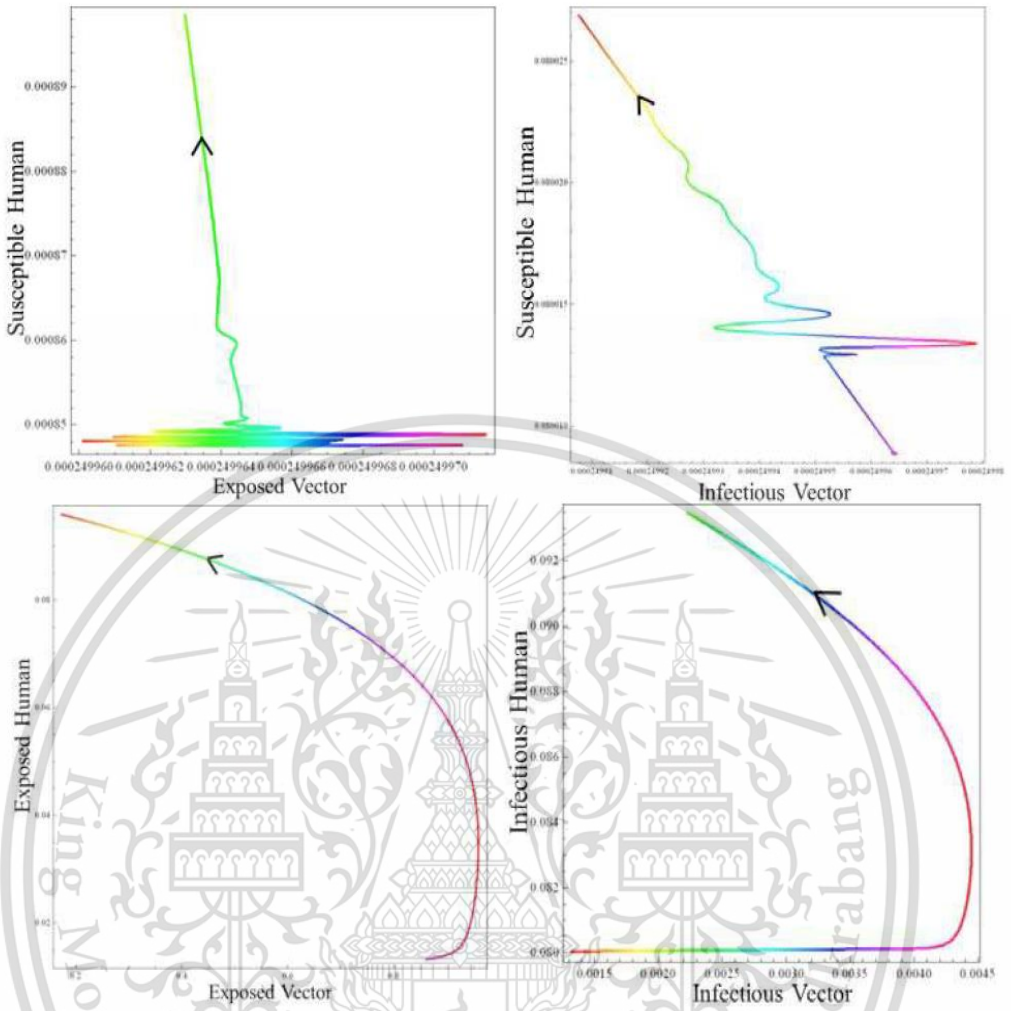
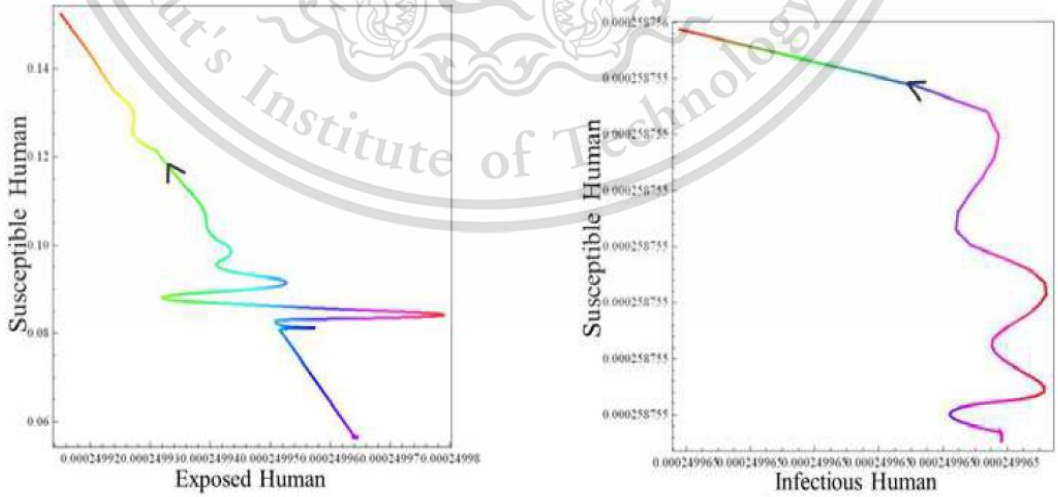


Fig. 10: The trajectories of the numerical solutions projected onto the 2D (S_H, E_H), (S_H, I_H), (S_H, E_V), (S_H, I_V), (E_H, E_V) and (I_H, I_V) planes when vertical transmission occurs



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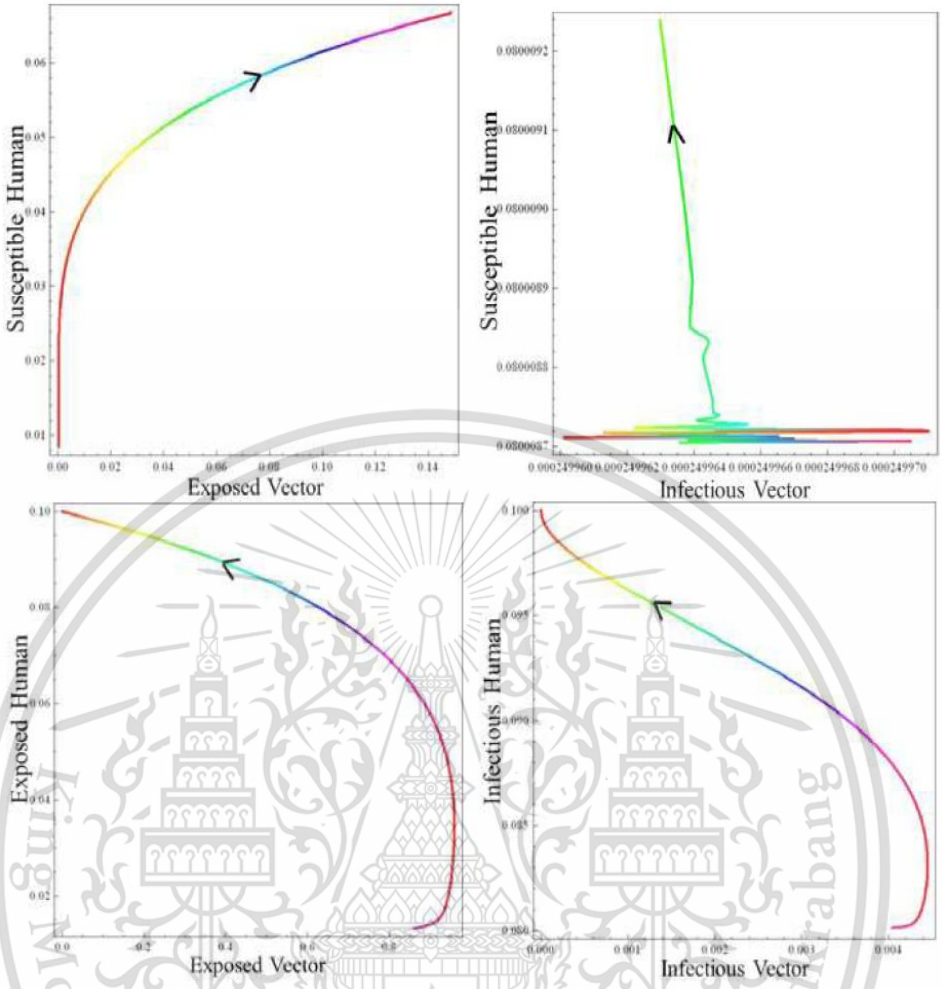
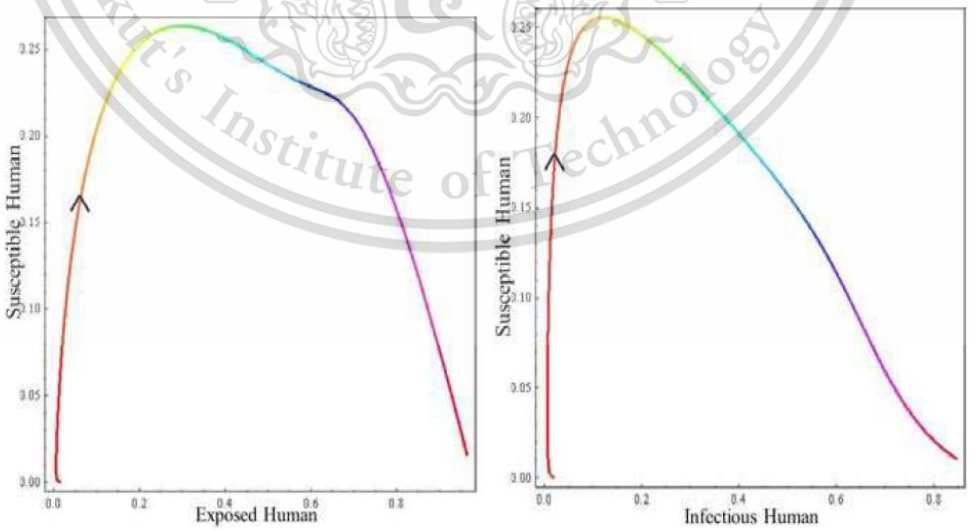


Fig. 11: The trajectories of the numerical solutions projected onto the 2D (S_H, E_H), (S_H, I_H), (S_H, E_V), (S_H, I_V), (E_H, E_V) and (I_H, I_V) planes when there is no vertical transmission and equilibrium state is the disease free state



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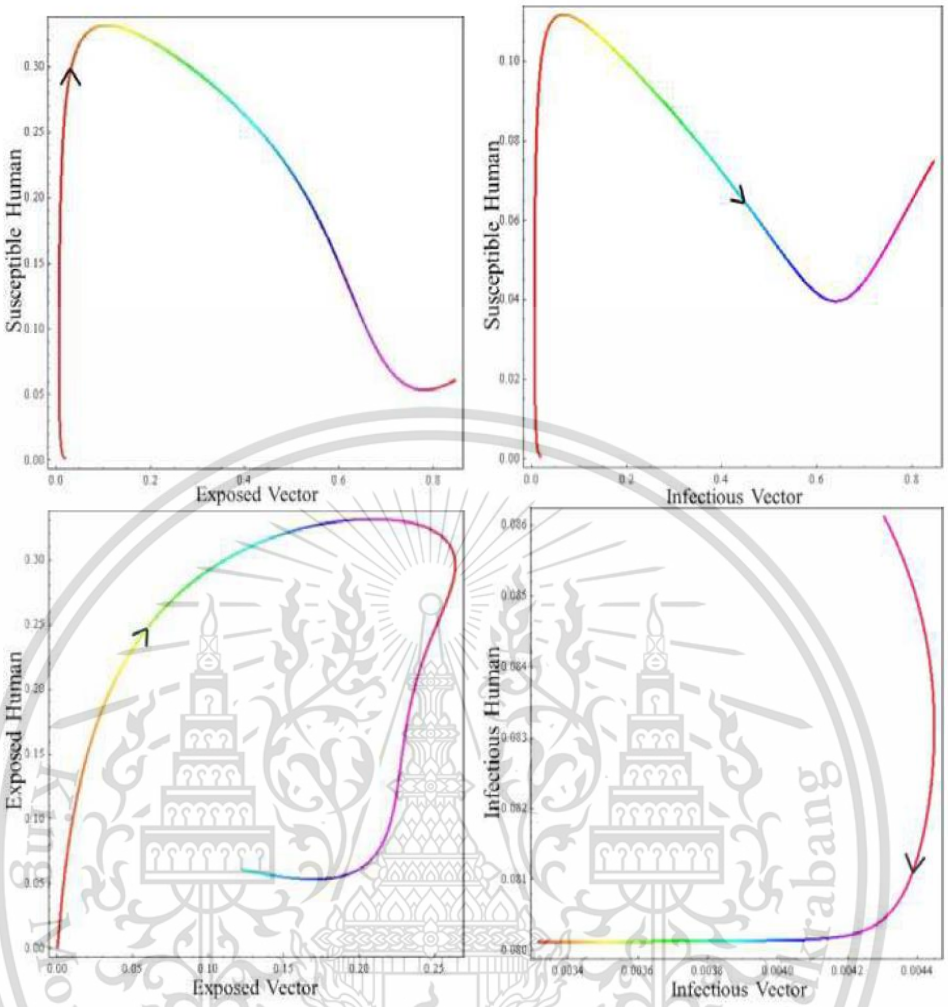
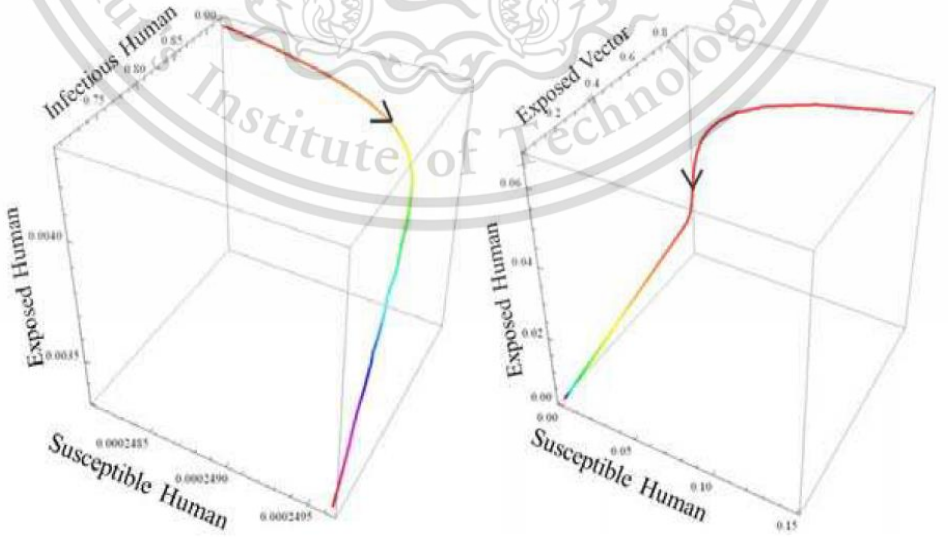


Fig. 12: The trajectories of the numerical solutions projected onto the 2D (S_H, E_H), (S_H, I_H), (S_H, E_V), (S_H, I_V), (E_H, E_V) and (I_H, I_V) planes when there is no vertical transmission and equilibrium state is the endemic state



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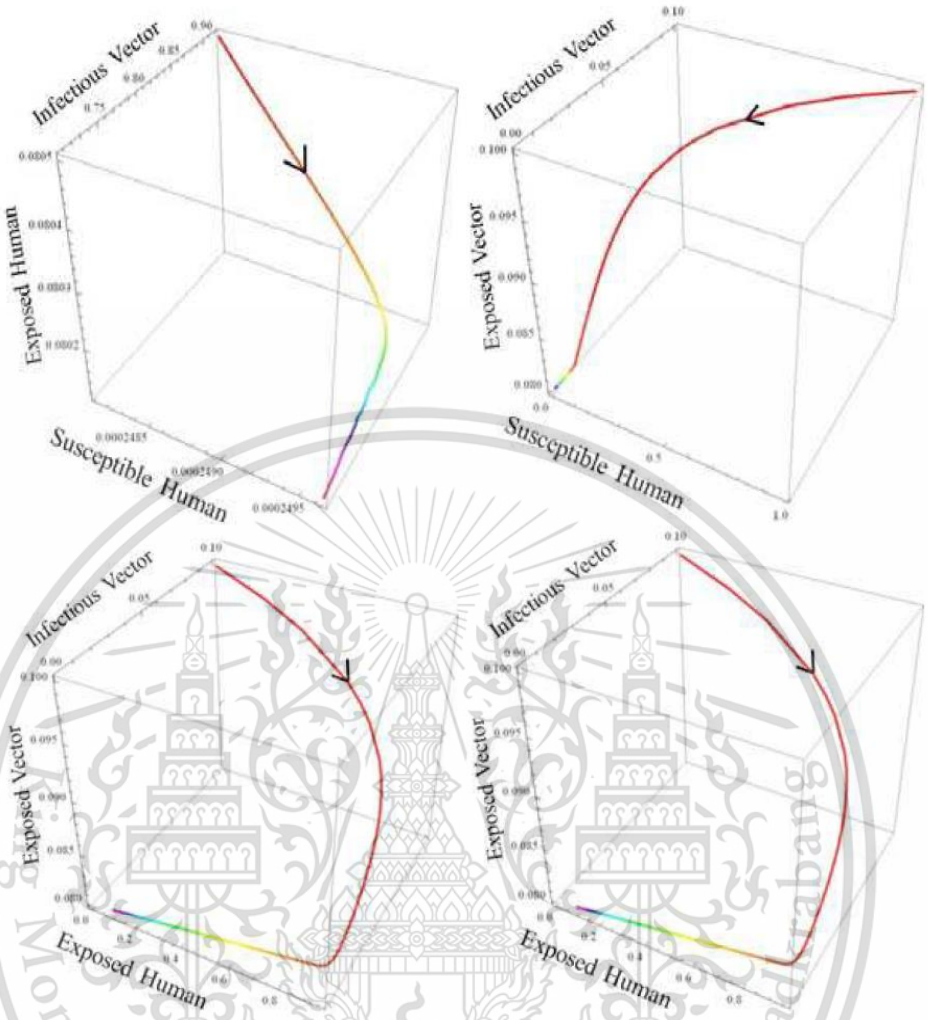
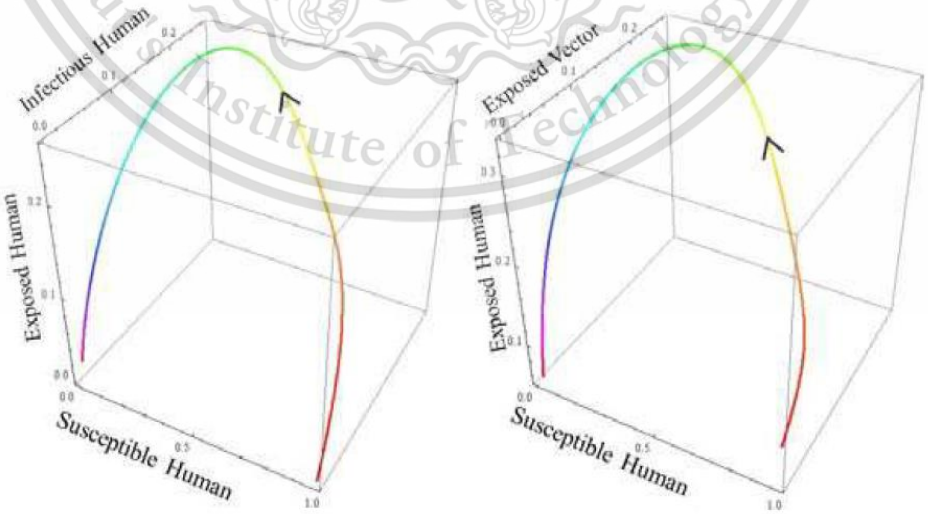


Fig. 13: The trajectories of the numerical solutions of the model when vertical transmission occurs into the 3D (S_H, E_H, I_H), (S_H, E_H, E_V), (S_H, E_H, I_V), (S_H, E_V, I_V), (E_H, E_V, I_V) and (I_H, E_V, I_V) spaces



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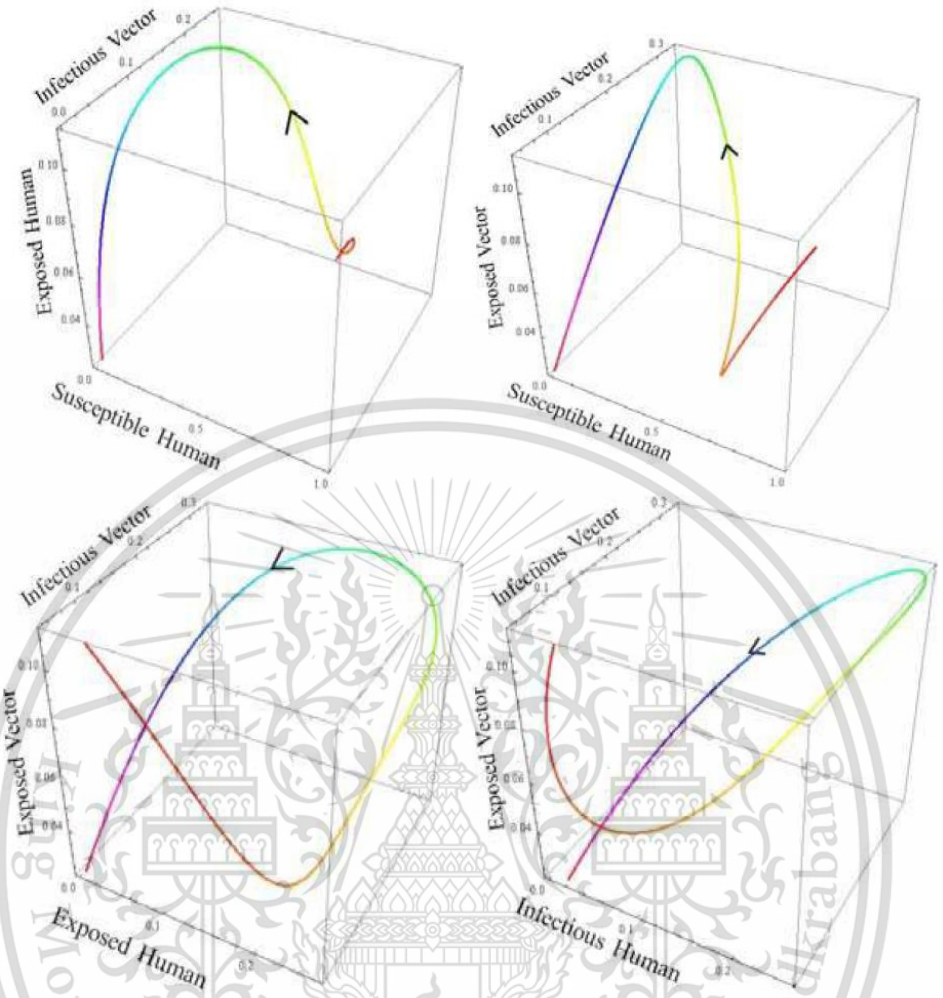
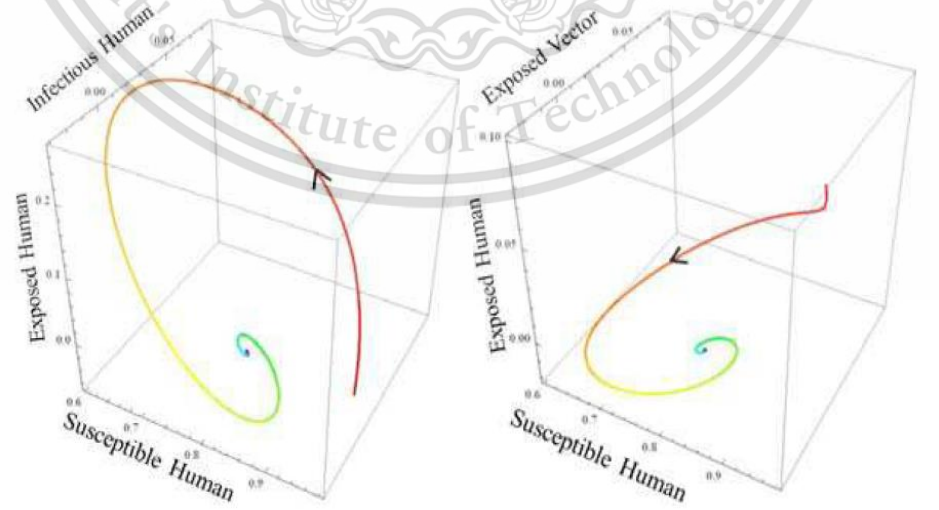


Fig. 14: The trajectories of the numerical solutions into the 3D (S_H, E_H, I_H), (S_H, E_H, E_V), (S_H, E_H, I_V), (S_H, E_V, I_V), (E_H, E_V, I_V) and (I_H, E_V, I_V) spaces when there is no vertical transmission and the values of the parameters are such that the equilibrium state is the disease free state



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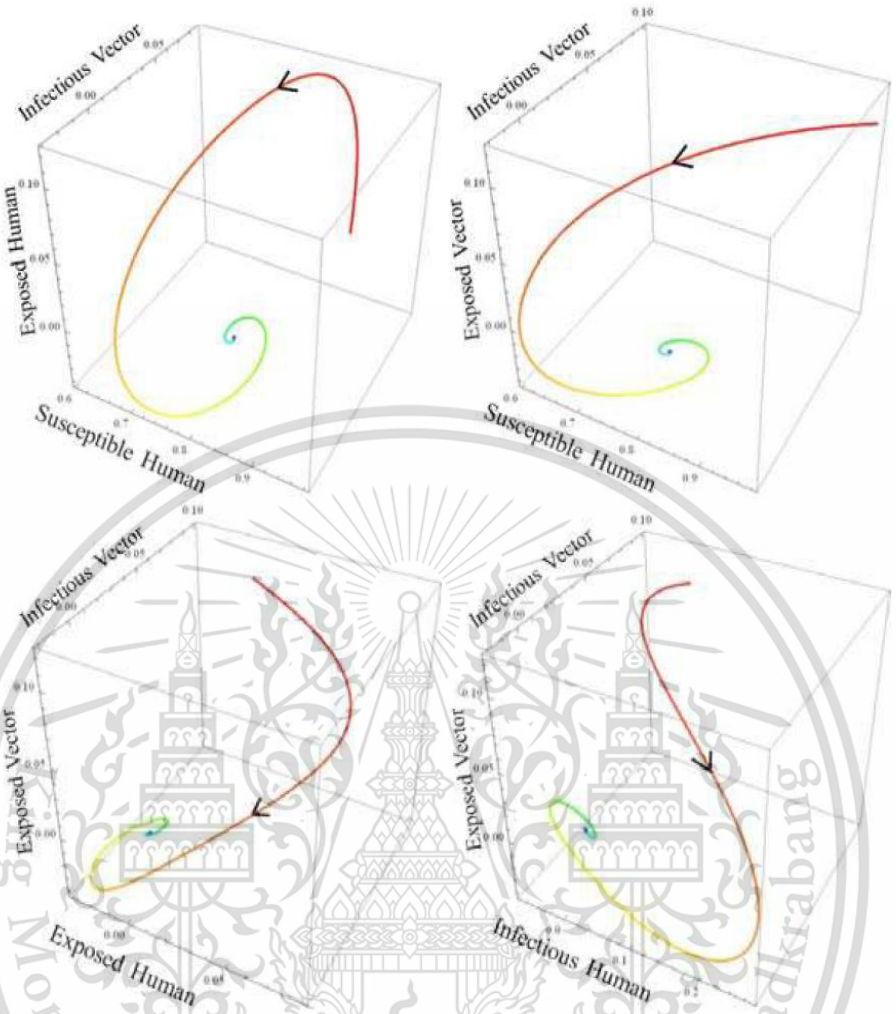
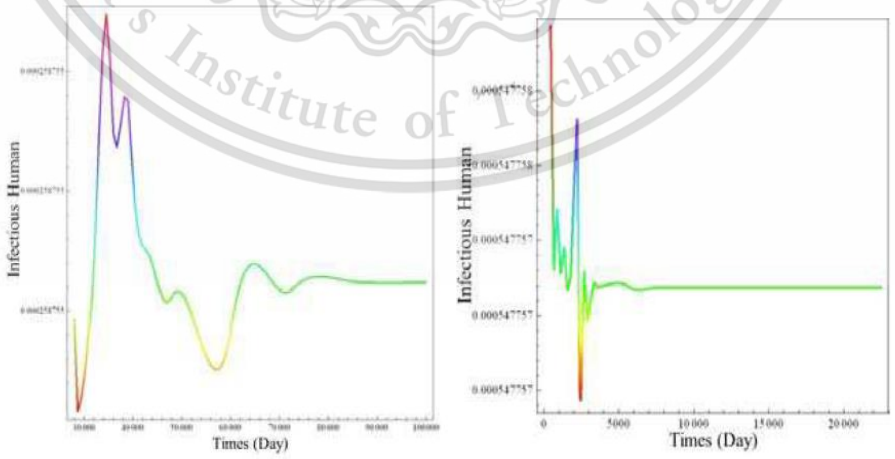


Fig. 15: The trajectories of the numerical solutions into the 3D (S_H, E_H, I_H), (S_H, E_H, E_V), (S_H, E_H, I_V), (S_H, E_V, I_V), (E_H, E_V, I_V) and (I_H, E_V, I_V) spaces when there is no vertical transmission and the values of the parameters are such that the equilibrium state is the endemic disease state



In the presence of vertical transmission of the virus (a) In the absence of vertical transmission of the virus

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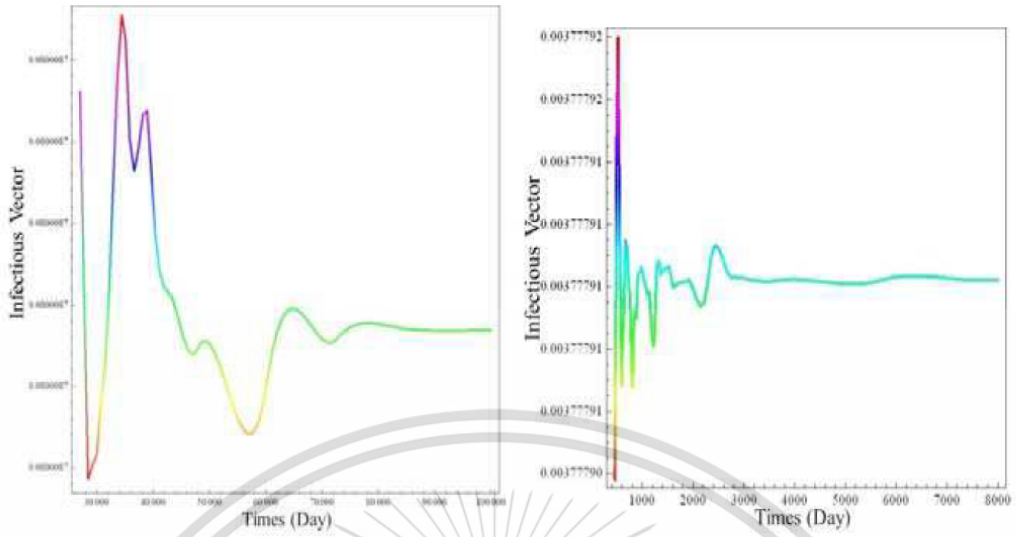

Behavior when vertical transmission is possible

(b) Behavior when no vertical transmission is possible

Fig. 16: (a) The time series comparison of dengue disease with and without the effect of vertical transmission for infectious human, IH (b) the time series comparison of dengue disease with and without the effect of vector born infection projected onto infectious vector, I_V

Conclusion

To see the influence of vertical transmission in the mosquitoes on the human and mosquito populations, we have plotted on Fig. 16(a) and 16(b) the time dependence of the infectious humans and mosquitoes in the presence or absence of vertical transmission of the virus in the mosquitoes of I_H and I_V. In both cases, the equilibrium state was the endemic state. We see that the equilibrium states were reached slower when vertical transmission of the virus in the mosquito occurs.

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Author's Contributions

Pratchaya Chanprasopchai: Make considerable contributions to conception and design and acquisition of data, analysis and interpretation of data.

I Ming Tang: Give the ideal of the problem and give final approval of the version to be submitted and any revised version.

Puntani Pongsumpun: Make considerable contributions to conception and design or acquisition of data and/or Analysis and interpretation of data and contribute in drafting the article or reviewing it critically for significant intellectual content.

Conflict of Interests

The authors declare that there is no conflict of interest regarding this research.

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Appendix D
Paper 4
SIR model for dengue disease with effect of dengue vaccination

Research Article

SIR model for dengue disease with effect of dengue vaccination

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In this paper, the dengue disease is caused by dengue virus and there is no specific treatment. The medical care by an experienced physicians and nurses will save life and will lower the mortality rate. A dengue vaccine to control the disease has been available in Thailand since late 2016. Mathematical model would be an important way to analyze the effects of the vaccination on the transmission of the disease. We have formulated a SIR (Susceptible-Infected-Recovered) model of the transmission of the disease which includes the effect of vaccination and used standard dynamical modeling methods to analyze the effects. The equilibrium states and their stabilities are investigated. The trajectories of the numerical solutions plotted into the 2D planes and 3D spaces are presented. The main contribution is determining the role of dengue vaccination in the model. From the analysis, we find that there is a significant reduction in the total hospitalization time needed to treat the illness.

1. Introduction

Dengue disease is a mosquito-borne viral infection caused by 4 serotypes of dengue virus, DEN-1, DEN-2, DEN-3, and DEN-4. Dengue disease is widely spread in tropical and sub-tropical region of the world. Dengue virus is transmitted to human by the bite of the female mosquito of the species, *Aedes aegypti* and *Aedes albopictus* [1]. An estimated 3.9 billion people in 128 countries are at risk to this disease. The countries at danger to infection by the dengue viruses around the world are shown on Figure 1 [2].

Thailand is located in tropical region where dengue virus is widely circulating. Dengue is speading nationwide in Thailand including the Bangkok metropolitan area. Thailand is in special danger since three of the four species of the dengue virus have been found in Thailand and both of the *Aedes* vector species are present. The Bureau of Epidemiology, Ministry of Public Health has reported dengue cases in all provinces in 2016, a total of 63,931 cases with 64 deaths [3]. At the present time, there is no special treatment for dengue disease but early detection and the appropriated medical care will decrease the fatality rates. A dengue vaccine would be another way to reduce the fatality rates. WHO reported the first dengue vaccine, called as Dengvaxia (CYD-TDV). It was registered in several countries in late 2015 and early 2016. It was recommended for use only in high dengue disease burden countries such as Thailand [1]. Dengue vaccine against four strains of the dengue virus was first launched in Thailand in late 2016. The vaccine would be suitable for use in individuals between 9-45 years of age living in endemic areas. Since the reported incidence of dengue peaks in the rainy season between June to September, the vaccination should in advance of the peak period in order for the immunity to develop.

There were many mathematical models for describing and analyzing the behaviors of dengue disease. Esteva and Vargus [4] proposed a SIR (susceptible-Infected-Recovery) model to describe the transmission of dengue disease with constant human and vector populations while Chanprasopchai et al. [5] proposed a SEIR (Susceptible-Exposed-Infected-Recovered) model for Thailand to deter-mine the effect of the rainfall on the spread of dengue in Thailand model. The transmission of dengue disease is assumed to depend on the nature of the rainfall in different countries. The stability of the solution of the model was then analyzed. Numerical results taking into account the rainfall was obtained and they were seen to correspond to the analytical results. Using standard dynamical analysis techniques, Chanprasopchai and Pongsumpun [6] established relations between the different variables in a SIR model of the dengue transmission model in which the biting rate of mosquito became as factor. Pongsumpun and Tang [7] analyzed the transmission of dengue hemorrhagic fever in a SIR model which included an age structure in human population.

Recently, Shim [8] studied the recently approved dengue vaccination program in the Philippines and showed that with appropriated pricing of dengue vaccination, reduction of the burden of the dengue disease in the Philippines and a significant potential to confer excellent value were possible. Aguiar et al. [9] has proposed a mathematical modeling for investigating the impact of the newly licensed dengue vaccine using different scenarios and presented the results for achieving significant reduction in disease burden. The vaccination program is most effective when only individuals have been already been exposed to at least one dengue virus.

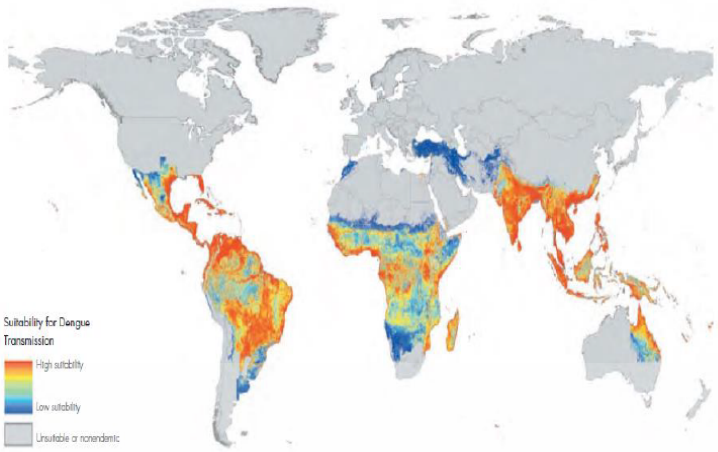

FIGURE 1: Distribution of global dengue risk [2]

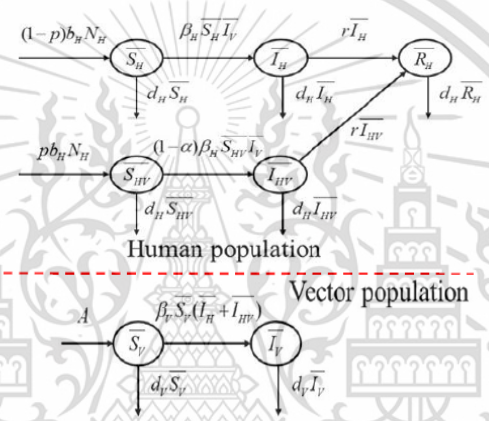

FIGURE 2: Dynamical transmission of human and mosquito with effect of vaccination

Recker et al. [10] reported that the availability of epidemiological and clinical data from the trials of vaccine provided a great opportunity for formulating mathematical models in which the vaccine efficacy depends on the serotype, age, host immune status, and severity. Mathematical modelling becomes a valuable tool in the policy-making process to estimate what the consequences of any decisions taken could be.

In this study, we propose a SIR mathematical model to analyze the behaviors of the transmission of dengue disease with vaccination effect and apply it to Thailand. The standard analysis method using Routh – Hurwitz criteria is applied to investigate the system stability which the dynamical transmission model of dengue disease, equilibrium state, stability, numerical simulation, results and conclusion are presented.

2. Material and Method

In our SIR model, the population is divided into 2 populations, a human and a vector population. The human population consists of three epidemiological states; susceptible humans ($\overline{S_H}$), infected humans ($\overline{I_H}$), and recovered humans ($\overline{R_H}$) while the vector population has two epidemiological states; susceptible vector ($\overline{S_V}$) and infected vector ($\overline{I_V}$). Mosquito has no recovery state since the mosquito dies before it can recover from the disease. Susceptible mosquito state is un-immune and un-infected while in the infected state, it is infected with dengue virus and can transmit the virus. Recovery state in the human population is a person who has recovered from an infection by the dengue virus. We assumed that the human and vector populations are constant. The dynamical transmission of human and mosquito population with effect of vaccination is shown in Figure 2.

In the figure,

$\overline{S_H}(t)$ =Number of susceptible human population who has unvaccinated at time t,

$\overline{I_H}(t)$ = Number of infected humans population who has unvaccinated at time t,

$\overline{R_H}(t)$ = *Number of recovered humans population who has unvaccinated at time t,*

$\overline{S_{HV}}(t)$ =Number of susceptible human population who has vaccinated at time t,

$\overline{I_{HV}}(t)$ = Number of infected humans population who has vaccinated at time t,

$\overline{S_V}(t)$ = Number of susceptible vector at any time t,

$\overline{I_V}(t)$ = Number of infected vector at any time t,

d_H, d_V = Death rat of human and vector population,

N_H, N_V = Total human and vector population,
β_H, β_V = Transmission rate of dengue virus from vector to human, human to vector,
b_H = Birth rate of human population,
A = Constant recruitment rate of vector population
a = Vaccine efficacy, and
p = Fraction of newborns vaccinated.

The transmission model of dengue disease with effect of vaccination can be described by the following differential equations:

$$\left.\begin{aligned}
\frac{d\overline{S_H}}{dt} &= (1-p)b_H N_H - \beta_H \overline{S_H} I_V - d_H \overline{S_H} \\
\frac{d\overline{I_H}}{dt} &= \beta_H \overline{S_H} \overline{I_V} - \gamma \overline{I_H} - d_H \overline{I_H} \\
\frac{d\overline{R_H}}{dt} &= \gamma(\overline{I_H} + \overline{I_{HV}}) - d_H \overline{R_H} \\
\frac{d\overline{S_{HV}}}{dt} &= pb_H N_H - (1-\alpha)\beta_H \overline{S_{HV}} I_V - d_H \overline{S_{HV}} \\
\frac{d\overline{I_{HV}}}{dt} &= (1-\alpha)\beta_H \overline{S_{HV}} I_V - \gamma \overline{I_{HV}} - d_H \overline{I_{HV}} \\
\frac{d\overline{S_V}}{dt} &= A - \beta_V \overline{S_V}(\overline{I_H} + \overline{I_{HV}}) - d_V \overline{S_V} \\
\frac{d\overline{I_V}}{dt} &= \beta_V \overline{S_V}(\overline{I_H} + \overline{I_{HV}}) - d_V \overline{I_V}
\end{aligned}\right\} \quad (1)$$

The total human and vector populations are assumed to be governed by the following conditions:

$$\left.\begin{aligned}
\overline{S_H} + \overline{I_H} + \overline{R_H} + \overline{S_{HV}} + \overline{I_{HV}} &= N_H \\
\overline{S_V} + \overline{I_V} &= N_V
\end{aligned}\right\} \quad (2)$$

If total human and vector populations are constants, then the rates of change for total human and vector populations are 0. As the results, we will have the following equations:

$$\left.\begin{aligned}
\frac{d\overline{S_H}}{dt} + \frac{d\overline{I_H}}{dt} + \frac{d\overline{R_H}}{dt} + \frac{d\overline{S_{HV}}}{dt} + \frac{d\overline{I_{HV}}}{dt} &= 0 \\
\frac{d\overline{S_V}}{dt} + \frac{d\overline{I_V}}{dt} &= 0
\end{aligned}\right\} \quad (3)$$

and

$$\left.\begin{aligned}
N_V &= A/\mu_V \\
b_H &= d_H
\end{aligned}\right\} \quad (4)$$

Normalizing the equations by introducing the follow-ing normalized variables:

$$\left.\begin{aligned}
S_H &= \frac{\overline{S_H}}{N_H}, I_H = \frac{\overline{I_H}}{N_H}, R_H = \frac{\overline{R_H}}{N_H}, S_{HV} = \frac{\overline{S_{HV}}}{N_H}, I_{HV} = \frac{\overline{I_{HV}}}{N_H} \\
S_V &= \frac{\overline{S_V}}{N_V}, I_V = \frac{\overline{IV}}{N_V}
\end{aligned}\right\} \quad (5)$$

Introducing these normalized variables into equation (1) we get the new set of equations of states:

$$\left.\begin{aligned}
\frac{dS_H}{dt} &= (1-p)b_H - \beta_H S_H I_V N_V - d_H S_H \\
\frac{dI_H}{dt} &= \beta_H S_H I_V N_V - \gamma I_H - d_H I_H \\
\frac{dS_H}{dt} &= pb_H - (1-\alpha)\beta_H S_{HV} I_V N_V - d_H S_{HV} \\
\frac{dI_{HV}}{dt} &= (1-\alpha)\beta_H S_{HV} I_V N_V - \gamma I_{HV} - d_H I_{HV} \\
\frac{dI_V}{dt} &= \beta_V S_V (I_H + I_{HV}) N_H - d_V I_V
\end{aligned}\right\} \quad (6)$$

The equilibrium states are obtained by setting the right-hand side of equation (6) to be 0. Doing this, we obtain an expression for something known as the basic production number R_0 This number is defined as

$$R_0 = \frac{\varepsilon_1(-(-2+\alpha)\varepsilon_2 d_V + N_H((1-p\alpha)d_H + \varepsilon_3 N_V \beta_H)\beta_V)}{\sqrt{\varepsilon_1^2(\alpha^2\varepsilon_2^2 d_V^2 + 2\alpha\varepsilon_2 d_V N_H((1+p(-2+\alpha))d_H + (-1+2p)\varepsilon_3 N_V \beta_H)\beta_V + N_H^2((-1+p\alpha)d_H + \varepsilon_3 N_V \beta_H)^2\beta_V^2)}}$$

When $R_0 \leq 1$, the equilibrium state will be the disease-free state E1 defined as

$$E_1(t) = (S_H = 1-p, I_H = 0, S_{HV} = p, I_{HV} = 0, I_V = 0),$$

and when $R_0 > 1$, the equilibrium state is the endemic state defined as

$$E_2(t) = (S_H^*(t), I_H^*(t), S_{HV}^*(t), I_{HV}^*(t), I_V^*(t)$$

Where;

$$S_H^*(t) = \frac{\varepsilon_1(\alpha\varepsilon_2 d_V + \varepsilon_3\varepsilon_4) + \varepsilon_5}{2\alpha d_H \varepsilon_6}$$

$$I_H^*(t) = \frac{\varepsilon_1(-\alpha\varepsilon_2 d_V + (1+\alpha-2p\alpha)\varepsilon_4) - \varepsilon_5}{2\alpha\varepsilon_2\varepsilon_6}$$

$$S_{HV}^*(t) = \frac{\varepsilon_1(-\alpha\varepsilon_2 d_V + \varepsilon_3\varepsilon_4) + \varepsilon_5}{2\varepsilon_3\alpha d_H \varepsilon_6}$$

$$I_{HV}^*(t) = \frac{\varepsilon_1(\alpha\varepsilon_2 d_V + \varepsilon_3(-1+2p\alpha)\varepsilon_4) - \varepsilon_5}{2\varepsilon_3\alpha\varepsilon_2\varepsilon_6}$$

and

$$I_V^*(t) = \frac{\varepsilon_1(-(-2+\alpha)\varepsilon_2 d_V + \varepsilon_3\varepsilon_4) - \varepsilon_5}{2\varepsilon_3\varepsilon_2 d_V N_V^2 \beta_H^2},$$

with

$$\varepsilon_1 = d_H N_V \beta_H$$

$$\varepsilon_2 = (\gamma + d_H)$$

$$\varepsilon_3 = (-1+\alpha)$$

$$\varepsilon_4 = N_H N_V S_V \beta_H \beta_V$$

$$\varepsilon_5 = \sqrt{d_H^2 N_V^2 \beta_H^2 (\alpha^2(\gamma + d_H)^2 d_V^2 + \sqrt{2(-1+2p)(-1+\alpha)\alpha(\gamma+d_H)d_V N_H N_V S_V \beta_H \beta_V} + \sqrt{(-1+\alpha)^2 N_H^2 N_V^2 S_V^2 \beta_H^2 \beta_V^2}}$$

$$\varepsilon_6 = N_H N_V^2 S_V \beta_H^2 \beta_V.$$

The equilibrium states are local asymptotically stable if all the eigenvalues have negative real parts. The eigenvalues (λ) are obtained by solving the eigen-value matrix equation

$$Det|J - \lambda I| = 0 \quad (7)$$

where
J is the Jacobian matrix of each equilibrium point,
λ is the eigenvalue and
I is the identity matrix.

Constructing the Jacobian matrix from equation (6) and evaluating it at the two equilibrium points, we obtain the eigenvalue equation

$$(-\lambda-\gamma-d_H)(\lambda^4+e_1\lambda^3+e_2\lambda^2+e_3\lambda^1+e_4)=0 \quad (8)$$

for the disease-free state E_1 and the eigenvalue equation

$$(\lambda^5+e_1\lambda^4+e_2\lambda^3+e_3\lambda^2+e_4\lambda^1+e_5)=0 \quad (9)$$

for the endemic state E_2.

The eigenvalues of disease free equilibrium state will have negative real parts when the coefficients of equation (8) have values satisfying the Routh-Hurwitz criteria

$$\left.\begin{aligned} &e_1>0, e_3>0, e_4>0 \\ &e_1e_2e_3>e_3^2+e_1^2e_4 \end{aligned}\right\} \quad (10)$$

The eigenvalues of endemic equilibrium state will have negative real parts when the coefficients of equation (9) have values which satisfy a different Routh-Hurwitz criterion

$$\left.\begin{aligned} &e_1>0, e_2>0, e_3>0, e_4>0, e_5>0 \\ &e_1e_2e_3-e_3^2-e_1^2e_4>0 \\ &(e_1e_4-e_5)(e_1e_2e_3-e_3^2-e_1^2e_4)-e_5(e_1e_2-e_3)^2-e_1e_5^2>0 \end{aligned}\right\} \quad (11)$$

3. Numerical Results

The transmission of dengue disease in this study is based on the SIR model with vaccination. The non-zero values of α and p are the parameters are the parameters pertaining to the vaccination program. The numerical simulations were done using the following values of parameters: $d_H=1/(65*365)$ per day corresponding to a life expectancy of 65 years for the Thai people, $d_V=1/12$ corresponding to a life expectancy of 12 days of mosquito population. For disease free equilibrium state, the parameter values were $A=1,000$, $N_H=1,000$, $\gamma_H=1/3$, $\beta_H=0.000012$, $\beta_V=0.000012$, $p=0.8$, and $\alpha=0.8$ while the parameters value of endemic equilibrium state, were $A=500$, $N_H=500$, $\gamma_H=0.03$, $\beta_H=0.000045$, $\beta_V=0.000045$, $p=0.75$, and $\alpha=0.75$. These numerical values in the first set gave $R_0<1$ while the values in the second set gave $R_0>1$. The trajectories of the numerical simulations for disease free and endemic states of S_H, I_H, S_{HV}, I_{HV}, and I_V are shown in the Figure 3 and Figure 4, respectively. The trajectories of the numerical simulation for disease free and endemic states plotted in the 2D planes (S_H, I_H), (S_H, S_{HV}), (S_H, I_{HV}), (S_H, I_V), (I_H, S_{HV}), (I_H, I_{HV}), (I_H, I_V), (S_{HV}, I_{HV}), (S_{HV}, I_V) and (I_{HV}, I_V) planes are shown in the Figure 5 and Figure 6, respectively. The trajectories of the numerical solutions for disease free and endemic states plotted in the 3D spaces (S_H, I_H, S_{HV}), (S_H, I_H, I_{HV}), (S_H, I_H, I_V), (S_H, S_{HV}, I_{HV}), (S_H, S_{HV}, I_V) and (S_H, I_{HV}, I_V) spaces are shown in the Figure 7 and Figure 8, respectively.

4. Discussion and Conclusion

In this study, the dynamical transmission of dengue disease based on a SIR model where a dengue vaccination campaign in the human population has occurred is studied. Again, it is found that the model system has two equilibrium points, a disease free and an endemic state. The occurrence of the two equilibrium states depend on whether $R_0<1$ and $R_0>1$ where R_0 is the basic reproduction number or number of secondary infection caused by an initial infection. The conditions for the stability of disease free and endemic equilibrium states were established. The time series solution of disease free and endemic equilibrium states is presented in Figure 3 and 4 respectively. The trajectories of disease free and endemic equilibrium projected onto 2D planes are showed in Figure 5 and 6 while the trajectories of disease free and endemic equilibrium projected onto 3D planes are showed in Figure 7 and 8, respectively.

In order to analyze the effect of dengue vaccination, we have investigated both the disease free and endemic states using different values of parameters which would give $R_0<1$ and $R_0>1$. These same set of numerical values were used for numerical simulation with and without the influence of dengue vaccination campaign. $\alpha=0$ and $p=0$ were used in the simulation to get the trajectories in the case where there was no vaccine administrated. The influence of dengue vaccination is seen in Figures 9 and 10. Figure 9 show that the disease-free state is sooner when there is dengue virus vaccines administrated than when there was not vaccines administrated. This means that the hospitalization time can be reduced. Figure 10 shows the effects of the vaccine when the parameters are such that the endemic state is equilibrium state.

The presence of oscillations around the endemic equilibrium E_2 means that the imaginary part of the eigenvalue is not zero. For the simulation shown in Figure 4, the imaginary part of the complex roots is approximately 0.000238428. This leads to an estimate of the period of the oscillations or $T_{period}=2\pi/\omega$ where ω = imaginary part of λ or $2\pi/0.000238428\approx 72.20$ years. This value is the approximation to the period of the solutions [4].

In any vaccination campaigns, one must take into account the difference in the efficacy of the vaccine. It may not be the same for all age groups. Since one is not sure about the safety of the vaccine to children, the vaccination has been recommended only for people between the ages of 9 and 45. As of now, the vaccination schedule consists of 3 injections of 0.5 mL administered at 6-month intervals, given on a 0/6/12 month schedule [11].

The campaign in Thailand began in December 2016 and information on efficacy of the vaccine against the different serotypes and the difference in the efficacy for different age groups is being collected. Dengue disease in Thailand occurs in urban and suburban area [12, 13, 14, 15] with peak transmission rates during the rainy season [5, 16]. Seasonal and climate are affect the dengue fluctuation [17, 18, 19, 20]. At present, it is not recommended to give dengue vaccination to pregnant women and travelers or health-care workers at this time due to lack of sufficient data.

Acknowledgment

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Conflict of Interests

The authors declare that there is no conflict of interest regarding the publication of this paper.

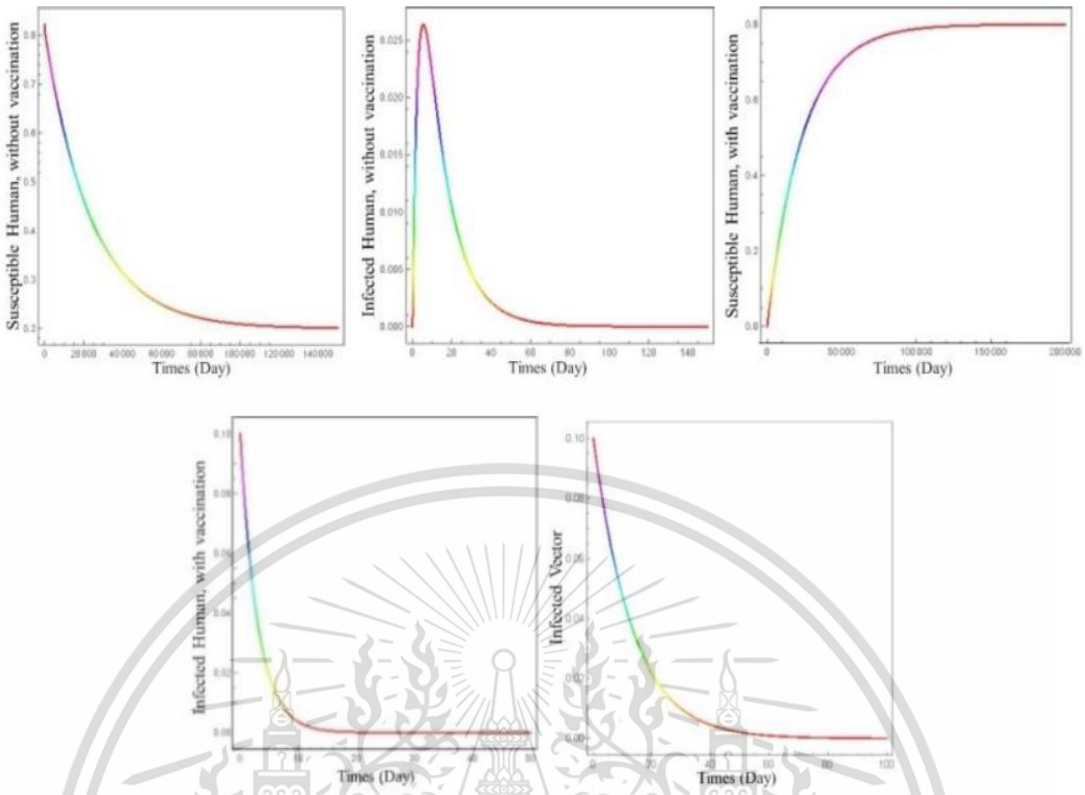


FIGURE 3: The trajectory of S_H, I_H, S_{HV}, I_{HV}, and I_V towards the disease-free equilibrium state (E_1)

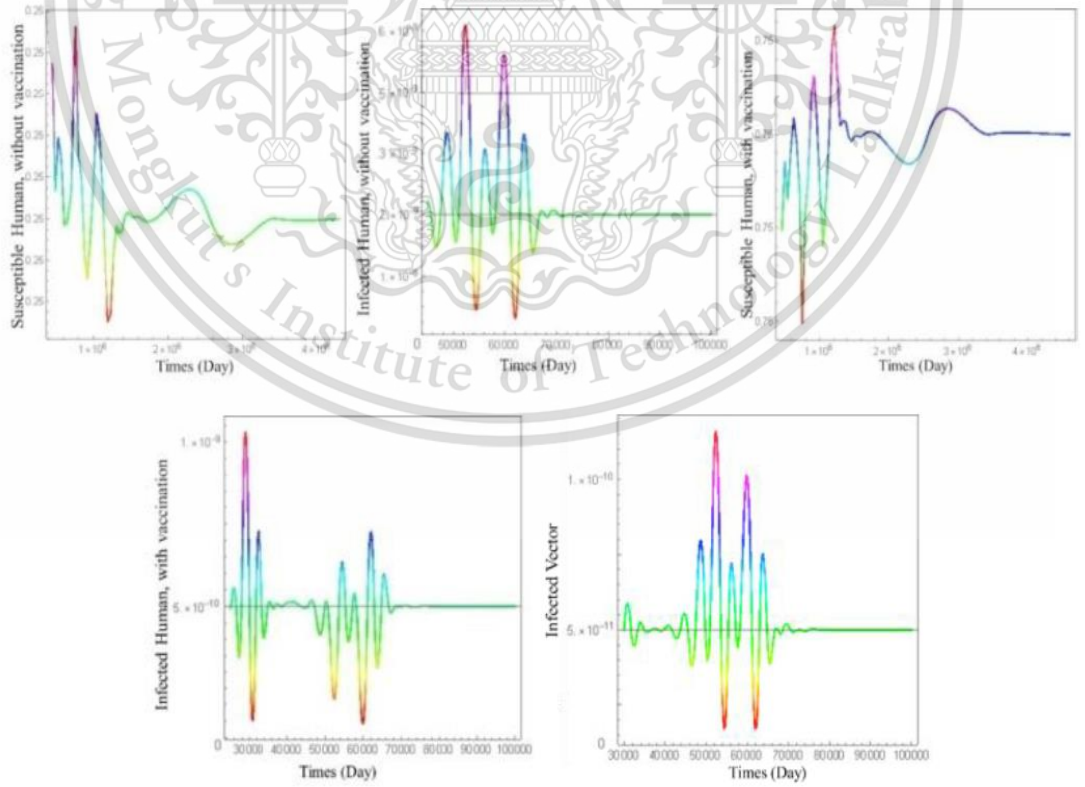


FIGURE 4: The trajectory of S_H, I_H, S_{HV}, I_{HV}, and I_V towards the endemic equilibrium state (E_2)

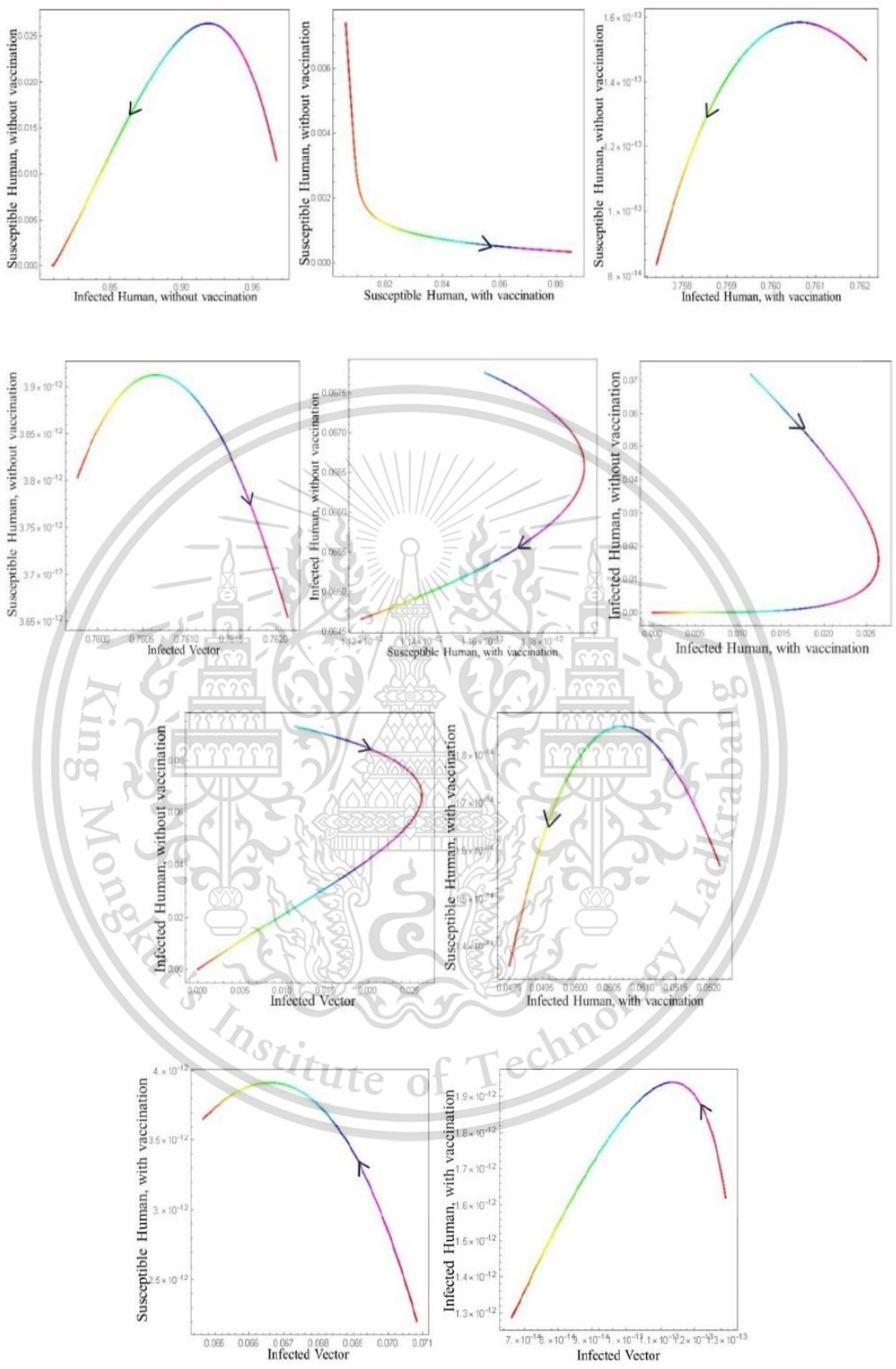


FIGURE 5: The trajectories of dengue disease for disease free equilibrium projected onto (S_H, I_H), (S_H, S_{HV}), (S_H, I_{HV}), (S_H, I_V), (I_H, S_{HV}), (I_H, I_{HV}), (I_H, I_V), (S_{HV}, I_{HV}), (S_{HV}, I_V) and (I_{HV}, I_V) planes

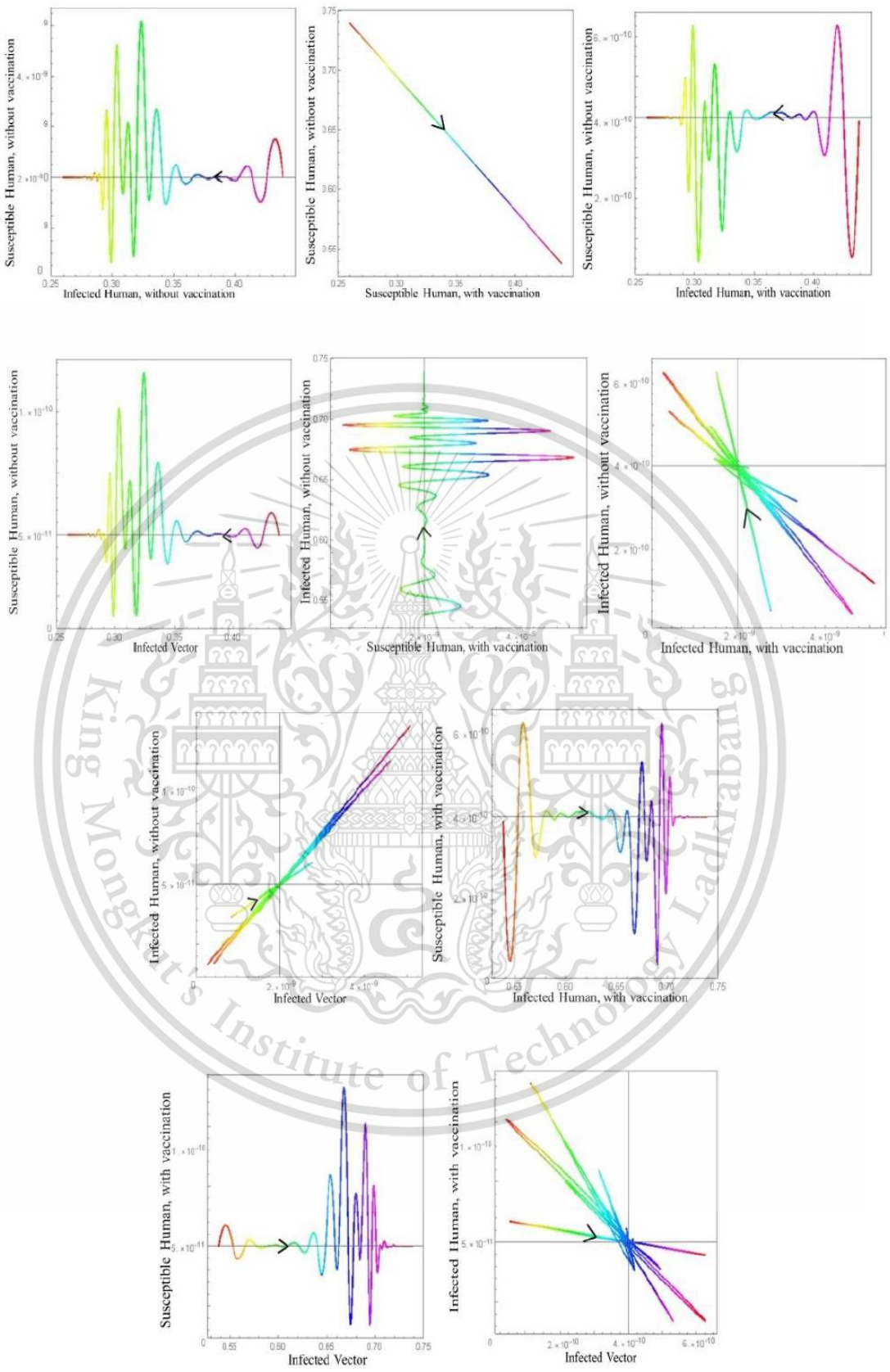


FIGURE 6: The trajectories of dengue disease for endemic equilibrium projected onto (S_H, I_H), (S_H, S_{HV}), (S_H, I_{HV}), (S_H, I_V), (I_H, S_{HV}), (I_H, I_{HV}), (I_H, I_V), (S_{HV}, I_{HV}), (S_{HV}, I_V) and (I_{HV}, I_V) planes

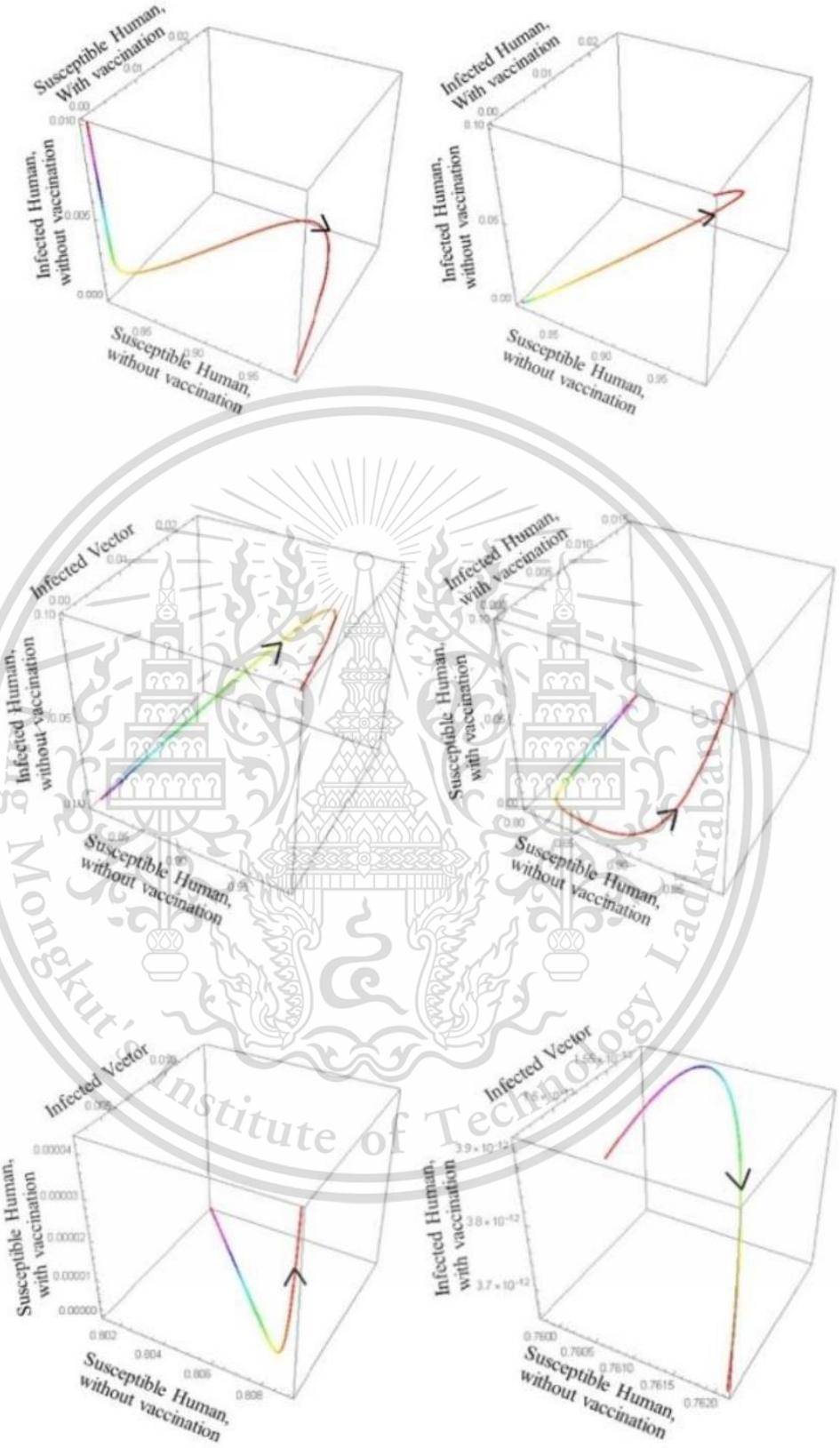


FIGURE 7: The trajectories of dengue disease for disease free equilibrium projected onto (S_H, I_H, S_{HV}), (S_H, I_H, I_{HV}), (S_H, I_H, I_V), (S_H, S_{HV}, I_{HV}), (S_H, S_{HV}, I_V) and (S_H, I_{HV}, I_V) spaces

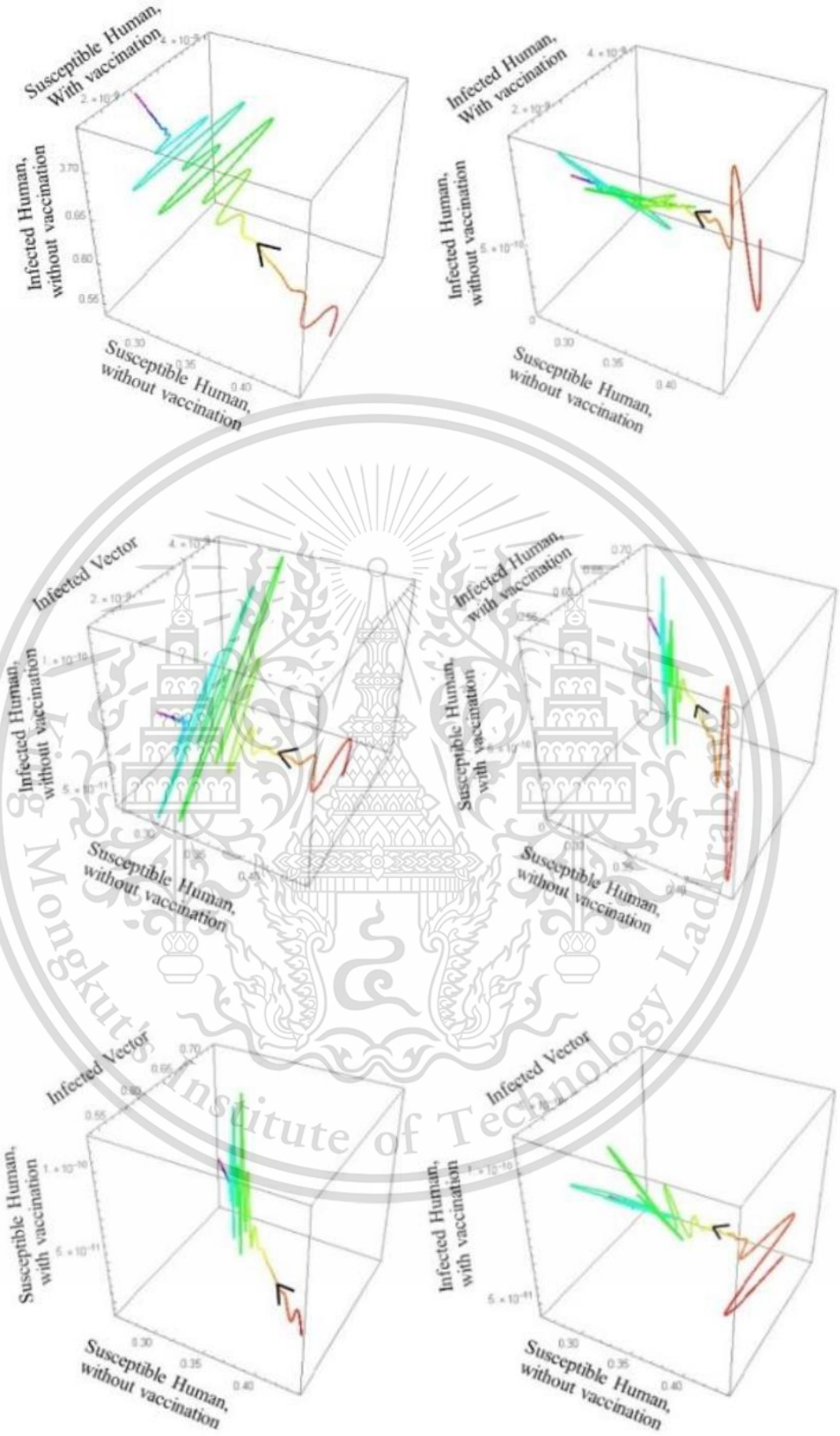
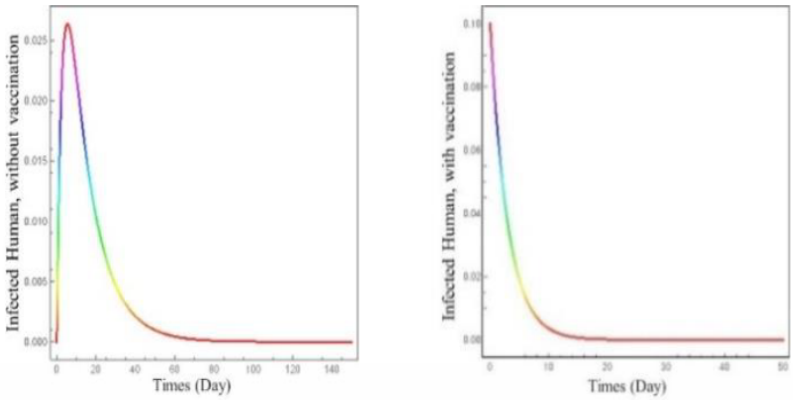
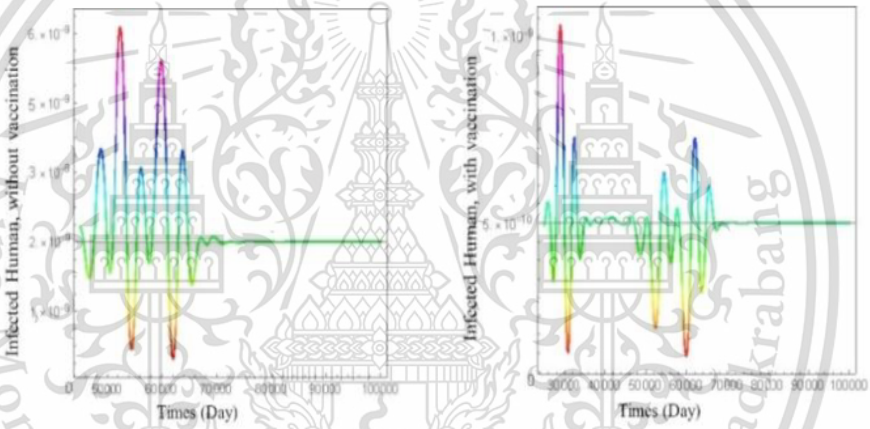


FIGURE 8: The trajectories of dengue disease for endemic equilibrium projected onto (S_H, I_H, S_{HV}), (S_H, I_H, I_{HV}), (S_H, I_H, I_V), (S_H, S_{HV}, I_{HV}), (S_H, S_{HV}, I_V) and (S_H, I_{HV}, I_V) spaces



(a) Without vaccination (b) With vaccination

FIGURE 9: The Infected human without vaccination (a) and with vaccination (b) comparison by time series to disease free equilibrium point



(a) Without vaccination (b) With vaccination

FIGURE 10: Infected human without vaccination (a) and with vaccination (b) comparison by time series to endemic equilibrium point

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SIIT, Thammasat University
Bachelor of Art (Public Administration)
Ramkhamhaeng University
Master of Science (Applied Statistics)
King Mongkut's Institute of Technology Ladkrabang
Master of Business Administration (Marketing)
Ramkhamhaeng University
Doctor of Philosophy (Applied Mathematics)
King Mongkut's Institute of Technology Ladkrabang

Scholarship
M.Sc. tuition fee – Faculty of Science, KMITL
Ph.D. tuition fee – Faculty of Science, KMITL

Academic Publications

1. Dengue disease in Thailand and mathematical model for dynamical transmission of dengue disease, International Journal of Multidisciplinary Academic Research, Vol. 5, No. 1, 2017, ISSN 2309-3218, pp. 31-39
2. Effect of Rainfall for the Dynamical Transmission Model of the Dengue Disease in Thailand, Computational and Mathematical Methods in Medicine, Volume 2017, Article ID 2541862, 17 pages, https://doi.org/10.1155/2017/2541862
3. The SEIR dynamical transmission model of dengue disease with and without the vertical transmission of the dengue virus, American Journal of Applied Science, 2017, Volume 14, Issue 12, Pages 1123-1145, DOI: 10.3844/ajassp.2017.1123.1145
4. SIR model for dengue disease with effect of dengue vaccination, Computational and Mathematical Methods in Medicine, Volume 2018, Article ID 9861572