



Available online at <http://scik.org>

Commun. Math. Biol. Neurosci. 2023, 2023:98

<https://doi.org/10.28919/cmbn/8134>

ISSN: 2052-2541

A STABILITY AND OPTIMAL CONTROL ANALYSIS ON A DENGUE TRANSMISSION MODEL WITH MOSQUITO REPELLENT

ELIZABETH L. MEGAWATI, DIPO ALDILA*

Department of Mathematics, Faculty of Mathematics and Natural Sciences, Universitas Indonesia, Depok 16424,
Depok, Indonesia

Copyright © 2023 the author(s). This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Abstract. Dengue fever is a significant global disease that is transmitted by female mosquitoes, specifically the *Aedes aegypti* and *Aedes albopictus* species. As part of efforts to control the spread of this disease, the use of mosquito repellent has emerged as an alternative. This research presents an analysis of the stability and optimal control of a dengue transmission model incorporating the use of mosquito repellent. Dynamical analysis conducted to see the impact of the control reproduction number on the stability of the equilibrium points. We find that due to the limited treatment resources, the condition of control reproduction number less than one is not enough to guarantee the disappearance of dengue from the population. Optimal control simulation conducted to see the impact of mosquito repellent intervention to reduce dengue effectively under some specific scenario.

Keywords: dengue transmission; mosquito repellent; stability; backward bifurcation; sensitivity; optimal control.

2020 AMS Subject Classification: 00A69, 37N25, 93D20.

1. INTRODUCTION

Dengue fever is a disease that spreads through the bites of female mosquitoes, specifically the *Aedes aegypti* and *Aedes albopictus* species, carrying different strains of the dengue virus

*Corresponding author

E-mail address: aldiladipo@sci.ui.ac.id

Received July 18, 2023

(DENV) [1]. In addition to transmitting the virus from mosquitoes to humans, mosquitoes can also acquire infection from individuals who experience viremia, a phase during which the DENV virus is present in the blood, occurring 24 to 48 hours before the onset of symptoms [2, 3]. This transmission can occur in someone who is symptomatic, someone who is pre-symptomatic, or even in individuals who are asymptomatic [3]. Dengue fever predominantly occurs in tropical and subtropical regions worldwide. As of June 8, 2023, the European Centre for Disease Prevention and Control (ECDC) reported a global total of 2,162,214 cases with 974 deaths from dengue fever [4].

The clinical manifestations of dengue can vary, ranging from asymptomatic infection to severe cases with multiple organ failure [5]. It is possible for a person to experience dengue infection multiple times throughout their life. Secondary dengue infections may occur due to different serotypes of the virus and can present with more severe symptoms. In some severe cases, dengue shock syndrome (DSS) can develop, which is believed to be associated with the Antibody-Dependent Enhancement (ADE) hypothesis [6].

Although there is no specific therapy for the treatment of dengue [7, 3], the primary focus of treatment is to maintain the patient's fluid balance. Therefore, prevention plays a crucial role in avoiding dengue infection. One preventive measure is the use of various forms of mosquito repellent, such as lotions, sprays, gels, or creams. Mosquito repellent typically work by creating a vapor barrier that prevents mosquitoes from coming into contact with the skin [8]. Some commonly used active ingredients in mosquito repellent include DEET, picaridin, IR3535, Paramenthane-diol (PMD), and 2-undecanone [7, 8].

Numerous studies have explored the efficacy of natural ingredients derived from plant extracts as mosquito repellent. Examples include pineapple peel extract (*Ananas comosus*) [9], citronella extract (*Cymbopogon nardus*) [10], liquid crystal-based tea tree oil [11], lemon eucalyptus oil [8], mint extract (*Mentha spicata*) [12], Mecca basil extract (*Ocimum gratissimum*) [12], moringa leaf extract (*Moringa oleifera*) [12], among others [8]. Mosquito repellent lotions or creams can be applied to the skin to create an effective protective layer, while sprays or gels can be used on areas prone to mosquito bites. By choosing mosquito repellent that suit personal

preferences and needs, and following the provided instructions, the effectiveness of protection against mosquito bites can be maximized, reducing the risk of dengue fever transmission.

The mathematical model of dengue infection spread, considering recurrent infections, has been analyzed in several studies. Jan et al. [13] introduced a model of dengue infection with asymptomatic carriers using fractional-order derivatives, highlighting the role of memory effects and analyzing the influence of input parameters and fractional order on the basic reproduction number and infected individuals. Onyejekwe et al. [14] constructed an epidemiological model to study the dynamics of dengue fever spread in the human population and applied optimal control theory to reduce the population of infected individuals through education and therapeutic drug treatment. Ndii et al. [15] investigated the effects of vaccination on the dynamics of dengue fever transmission using mathematical models and found that vaccination of seropositive individuals can help reduce the proportion of severe dengue cases. Schäfer et al. [16] focused on qualitative estimation of the dynamics of dengue fever transmission and proposed a single-compartment vector-host model and a multi-patch model to depict seasonal effects and inter-region mobility. Shah et al. [17] developed nonlinear differential equation models to separately and jointly explain the dynamics of malaria and dengue fever transmission, emphasizing the role of control parameters and treatment. Siddik et al. [18] formulated a mathematical model that incorporates predator-prey dynamics in the mosquito larval stage to control the spread of dengue fever virus. Chamnan et al. [19] analyzed the impact of vaccination on the dynamics of dengue fever transmission in Thailand, emphasizing the importance of considering specific serotype differences for optimal intervention delivery. Sanusi et al. [20] built and analyzed an SIRS model for dengue fever, predicting the number of cases and assessing the endemic status of the disease in South Sulawesi. Bonyah et al. [21] discussed the influence of climate change on the control of dengue fever in Africa using fractional-order models. Ndii et al. [22] studied the effects of various dengue fever elimination strategies, including vector control, vaccination, and media campaigns, on seasonally varying mosquito populations. Aldila et al. [23] investigated the impact of media campaigns and case detection in controlling the spread of dengue fever in Jakarta, finding that media campaigns were more effective in reducing the basic reproduction number. In other research, Aldila et al. [24] construct their simple

dengue model considering human ignorance on dengue. They found that this ignorance may trigger the existence of backward bifurcation phenomena. Hanif et al. [25] proposed a modified fractional-order-based $S_hE_hI_hR_h - S_vI_v$ model to simulate the dynamics of dengue fever transmission, considering treatment compartments and protected travelers, and applied an optimal control approach to study the impact of control strategies.

Previously, several studies have discussed mathematical models considering mosquito repellents. Prasetyo et al. [26] showed that vaccination and the use of mosquito repellents can reduce the number of dengue fever-infected human subpopulations with minimum costs in control implementation. Khan et al. [27] revealed that the use of mosquito repellents and insecticides is the best strategy to minimize the number of infected hosts and dengue fever vectors in a population. Srivastav et al. [28] demonstrated that the use of mosquito repellents is more constructive or provides better outcomes or more effective solutions in reducing the impact of epidemics at high severity levels ($\mathcal{R}_0 > 4$). Hamid et al. [29] demonstrated that the infected and exposed population experiences a significant decline with the variable use of mosquito repellents. Hasan et al. [30] indicated that human awareness of protecting individuals from dengue fever by using bed nets and insect repellents has a greater impact than other factors in epidemic control. Saha et al. [31] revealed that protective measures (such as using mosquito repellents) combined with stronger treatment are more effective compared to human efforts in mosquito control and treatment for dengue control.

However, it is important to note that the use of mosquito repellent may have certain limitations that can reduce their effectiveness in controlling the spread of mosquito-borne diseases. Factors such as inconsistent use, inappropriate application, variations in product effectiveness, and limitations in range or duration of use can impact the overall effectiveness of control measures [32, 33, 8]. In our study, we conducted an analysis of a dengue transmission model that incorporates the use of mosquito repellent. The mathematical model takes into account the growth rates of human and mosquito populations, the transmission of viruses between mosquitoes and humans, and the impact of mosquito repellent on reducing mosquito bite rates in humans. The model includes differential equations that describe the changes in relevant variables over time.

We then performed a stability analysis to determine the equilibrium points of the model. Equilibrium points are states where the model variables remain constant over time. Using the linearization method, we examined the stability of these equilibrium points to determine whether the system tends toward a stable or unstable state. Next, we incorporated the concept of optimal control in our analysis. We considered the optimal strategy for using mosquito repellent to minimize the transmission rate of dengue fever. Within a mathematical framework, we applied the principle of optimal control to describe the interactions between human populations, mosquitoes, and mosquito repellent. By applying the Pontryagin Principle, we can determine the optimal control strategy to reduce dengue transmission. This strategy involves selecting the optimal timing and frequency of using mosquito repellent. We hope that this analysis provides a deeper understanding of the impact of mosquito repellent on dengue transmission. The results can serve as a valuable guide for designing effective interventions and control policies aimed at reducing the spread of this disease.

The structure of this article is outlined as follows: We introduce our model in Section 2, followed by model analysis in Section 3. Section 4 presents the elasticity and sensitivity analysis, while Section 5 provides the characterization of optimal control and simulation. Lastly, our conclusions are presented in Section 6.

2. MODEL CONSTRUCTION

At the beginning, a compartmental model is constructed, divided into two populations: the human population N and the mosquito population M . The human population is further divided into two subpopulations: S , representing individuals susceptible to Dengue fever virus, and I , representing individuals infected with the Dengue fever virus. Meanwhile, the vector population is divided into two subpopulations: U , representing vectors susceptible to the Dengue fever virus, and V , representing vectors infected with the Dengue fever virus. Hence, the total of human and mosquito population is given by $N = S + I$ and $M = U + V$, respectively.

Before constructing the model, certain limitations or assumptions need to be made, such as:
a) the population is constant, b) the recruitment rate in subpopulations S and U is constant, c) there is no human to human transmission disease and vector to vector disease transmission, d) natural deaths occur in each subpopulation, e) there is no disease-induced mortality, f) there is

saturation of human recovery, g) after the infectious period, humans become susceptible again, and h) infected vectors do not experience recovery due to their short lifespan. Based on the compartmental model shown in Figure 1, a mathematical model can be formulated as follows:

$$(1a) \quad \frac{dS}{dt} = \Lambda_h - (1 - u + u\xi)\beta_h SV - \mu_h S + \frac{\gamma}{1 + bI} I,$$

$$(1b) \quad \frac{dI}{dt} = (1 - u + u\xi)\beta_h SV - \mu_h I - \frac{\gamma}{1 + bI} I,$$

$$(1c) \quad \frac{dU}{dt} = \Lambda_v - (1 - u + u\xi)\beta_v UI - \mu_v U,$$

$$(1d) \quad \frac{dV}{dt} = (1 - u + u\xi)\beta_v UI - \mu_v V,$$

completed with a non-negative initial conditions. Here, u represents the control variable, which is the use of mosquito repellent. The effectiveness of the control can be reduced, represented by the parameter ξ . Other parameters include Λ_h and Λ_v , which represent the recruitment rates of humans and vectors, respectively. β_h and β_v represent the transmission rates from S to I and from U to V , respectively. μ_h and μ_v represent the natural death rates for humans and vectors, respectively. γ represents the recovery rate for humans. We assume that there is a saturation on human recovery rate due to the lack of hospital bed capacity. Hence, assuming b as the saturation parameter of recovery rate, then total of recovery infected human per day is given by $\frac{\gamma}{1 + bI} I$.

In the given model, the term $(1 - u + u\xi)$ represents the reduction in control effectiveness on the spread of mosquito-borne diseases, specifically referring to the extent to which the use of mosquito repellent and control effectiveness can diminish disease transmission by mosquitoes. The term $(1 - u + u\xi)$ represents a combination of them who use mosquito repellent (uN) and who do not ($(1 - u)N$). The explanation is as follows. Let there is proportion u of N who use mosquito repellent. We assume that the efficacy of this mosquito repellent to reduce effective contact rate β_h and β_v is given by ξ . Hence, smaller ξ shows a better quality of mosquito repellent. On the other hand, if human population do not use any mosquito repellent, then the infection rate will not reduced. Hence, the total of new infection per day is given by $(1 - u + u\xi)\beta_h SV$ and $(1 - u + u\xi)\beta_v UI$ for human and mosquito population, respectively. Therefore, the larger the value of $(1 - u + u\xi)$, the smaller the impact of mosquito repellent

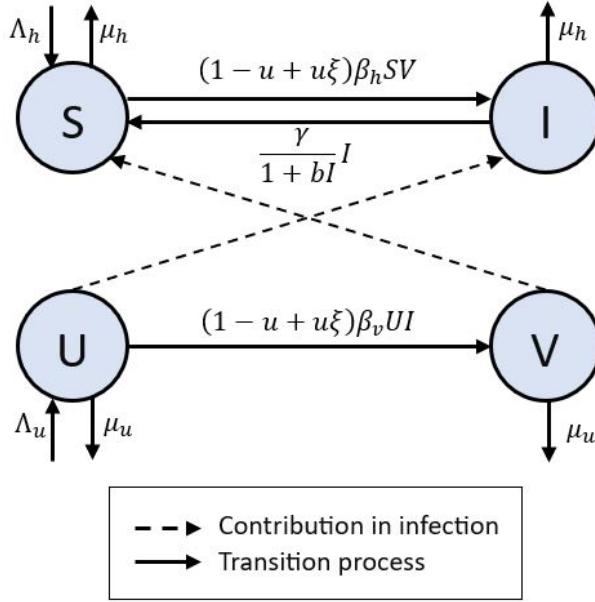


FIGURE 1. Transmission diagram of the dengue model in system (1)

usage and control effectiveness in reducing disease transmission by mosquitoes. Conversely, the smaller the value of $(1 - u + u\xi)$, the greater the impact of mosquito repellent usage in reducing disease transmission.

TABLE 1. Table of parameters in system (1).

Par.	Description	Unit
b	Saturation coefficient affecting the transfer from infected to susceptible individuals	$\frac{1}{\text{individual}}$
β_h	Transmission rate from infected vectors to susceptible individuals	$\frac{1}{\text{individual.day}}$
β_v	Transmission rate from infected individuals to susceptible vectors	$\frac{1}{\text{vector.day}}$
γ	Recovery rate of individuals	$\frac{1}{\text{day}}$
Λ_h	Natural birth rate of individuals	$\frac{\text{individual}}{\text{day}}$
Λ_v	Natural birth rate of vectors	$\frac{\text{vector}}{\text{day}}$
μ_h	Natural death rate of individuals	$\frac{1}{\text{day}}$
μ_v	Natural death rate of vectors	$\frac{1}{\text{day}}$
u	Proportion of mosquito repellent usage intervention	-
ξ	Reduced control effectiveness	-

3. MODEL ANALYSIS

Before we analyzed our model, it is necessary to show that our model solution always has a biological interpretation, which means that the solution should always be non-negative. The results are given in the following theorem.

Theorem 3.1. *System (1) is positively invariant in the following region.*

$$(2) \quad \Omega = \{(S, I, U, V) \in \mathbb{R}_{\geq 0}^4 \mid S \leq N, I \leq N, U \leq M, V \leq M, S + I \leq N, U + V \leq N\}.$$

Proof. We prove this theorem using the same approach with authors in [34]. System (1) can be rewritten as follows:

$$(3) \quad \frac{dX}{dt} = CX + D,$$

where

$$(4) \quad X = (S, I, U, V)^T, \quad C = \begin{bmatrix} d_1 & d_2 & 0 & 0 \\ d_3 & d_4 & 0 & 0 \\ 0 & 0 & d_5 & 0 \\ 0 & 0 & d_6 & -\mu_v \end{bmatrix},$$

with $d_1 = -(1 - u - u\xi)\beta_h V - \mu_h$, $d_2 = \frac{\gamma}{1+bI}$, $d_3 = (1 - u + u\xi)\beta_h V$, $d_4 = -\mu_h - \frac{\gamma}{1+bI}$, $d_5 = -(1 - u + u\xi)\beta_v I - \mu_v$, $d_6 = (1 - u + u\xi)\beta_v I$, and $D = (\Lambda_h, 0, \Lambda_v, 0)$.

Since C has non-negative values off the main diagonal, C is a Metzler matrix. With the value of $D \geq 0$, the system (3) has a positive invariant in \mathbb{R}_+^4 , which implies that any trajectory of (3) starting from an initial state in the positive orthant \mathbb{R}_+^4 will remain in \mathbb{R}_+^4 indefinitely. In other words, the system will not cross over to reach the negative regions in the 4-dimensional space and will continue to stay in the positive region forever. \square

3.1. Non-dimensionalization and Model Reduction. To reduce the number of parameters and variables, we derive the non-dimensional form of our model by setting $\Lambda_h = \mu_h N$ and $\Lambda_v = \mu_v M$, $x_1 = \frac{S}{N}$, $x_2 = \frac{I}{N}$, $y_1 = \frac{U}{M}$, and $y_2 = \frac{V}{M}$. Furthermore, let $b_1 = \frac{\beta_h}{\gamma} M$, $b_2 = \frac{\beta_v}{\gamma} N$,

$b_3 = bN$, $m_1 = \frac{\mu_h}{\gamma}$, and $m_2 = \frac{\mu_v}{\gamma}$. Thus, model in system (1) can be reduced to

$$(5) \quad \begin{aligned} \frac{dx_2}{d\tau} &= (1 - u + u\xi)b_1(1 - x_2)y_2 - m_1x_2 - \frac{x_2}{1 + b_3x_2}, \\ \frac{dy_2}{d\tau} &= (1 - u + u\xi)b_2(1 - y_2)x_2 - m_2y_2. \end{aligned}$$

3.2. Existence of Equilibria and the reproduction number. System (5) has a trivial dengue-free equilibrium which given by $\mathcal{E}_0 = (0, 0)$. Defining the transmission (F) and transition (V) matrix of system (5) as

$$F = \begin{bmatrix} 0 & (1 - u + u\xi)b_1 \\ (1 - u + u\xi)b_2 & 0 \end{bmatrix}, \quad V = \begin{bmatrix} -1 - m_1 & 0 \\ 0 & -m_2 \end{bmatrix},$$

then the next-generation matrix of system (5) is given by

$$(6) \quad NGM = \begin{bmatrix} 0 & \frac{(1 - u + u\xi)b_1}{m_2} \\ \frac{(1 - u + u\xi)b_2}{m_1 + 1} & 0 \end{bmatrix}.$$

Hence, the control reproduction number of system (5) as the spectral radius of NGM is given by

$$\mathcal{R}_c = \frac{\sqrt{(m_1 + 1)m_2 b_1 b_2}(1 - u + u\xi)}{(m_1 + 1)m_2}.$$

When no mosquito repellent is given, then the basic reproduction number of system (5) is given by

$$\mathcal{R}_0 = \frac{\sqrt{(m_1 + 1)m_2 b_1 b_2}}{(m_1 + 1)m_2}.$$

In the context of our dengue model under the impact of mosquito repellent, \mathcal{R}_c represent the expected number of secondary cases caused by one single infection during it infection period in a virgin population under the impact of dengue repellent. In many mathematical model, reproduction number play an important role to determine the endemicity of a disease in the population. Please see [35, 36, 37, 38, 39, 40] for more examples. In our model, the importance of the control reproduction number in determining the stability of the dengue-free equilibrium stated in the following theorem.

Theorem 3.2. *The equilibrium point \mathcal{E}_0 in the system (5) is locally asymptotically stable if $\mathcal{R}_c < 1$, and unstable if $\mathcal{R}_c > 1$.*

Proof. The Jacobian matrix evaluated at \mathcal{E}_0 is given by

$$(7) \quad J\mathcal{E}_0 = \begin{bmatrix} -1 - m_1 & (1 - u + u\xi)b_1 \\ (1 - u + u\xi)b_2 & -m_2 \end{bmatrix}.$$

The eigenvalues of $J\mathcal{E}_0$ are the solutions of

$$p_i(\lambda) = \lambda^2 + (m_1 + m_2 + 1)\lambda - (1 - u + u\xi)^2 b_1 b_2 + (1 + m_1)m_2 = 0.$$

The real parts of (λ) that satisfy $p_i(\lambda) = 0$ are negative if and only if $\lambda_1 + \lambda_2 < 0$ and $\lambda_1 \lambda_2 > 0$. It is easy to see that $\lambda_1 + \lambda_2 = -(m_1 + m_2 + 1) < 0$ is always satisfied. On the other hand, $\lambda_1 \lambda_2 = m_2(1 + m_1)(1 - \mathcal{R}_c^2) > 0$ only if $\mathcal{R}_c < 1$. Hence, \mathcal{E}_0 is locally asymptotically stable if $\mathcal{R}_c < 1$, and unstable if $\mathcal{R}_c > 1$. The proof is completed. \square

Next, we analyze the existence of the dengue endemic equilibrium point (\mathcal{E}_1) of system (5). Taking the right hand side of system (5) equal to zero, and solve it respect to x_2 and y_2 , we have

$$(8) \quad \mathcal{E}_1 = (x_2^*, y_2^*) = \left(x_2^*, \frac{b_2 x_2^*(1 - u + u\xi)}{x_2^* b_2 (1 - u + u\xi) + m_2} \right),$$

where x_2^* is taken from the positive roots of the following polynomial.

$$(9) \quad f(x_2) = a_2(x_2)^2 + a_1 x_2 + a_0 = 0,$$

where $a_2 = b_2 b_3 m_1 (1 - u + u\xi) + \mathcal{R}_c^2 b_3 m_2 (m_1 + 1)$, $a_1 = (m_1 + 1)(1 - u + u\xi)b_2 + b_3 m_1 m_2 - \mathcal{R}_c^2 m_2 (1 - b_3)(1 - m_1)$, and $a_0 = m_2(m_1 + 1)(1 - \mathcal{R}_c^2)$. With this expression, we have the following theorem.

Theorem 3.3. *Let \mathcal{R}_c^* is \mathcal{R}_c that satisfy $a_1^2 - 4a_0a_2 < 0$ and $\mathcal{K} = (1 + m_1 - b_3)m_2 + (1 - u + u\xi)b_2(1 + m_1)$. Dengue model in system (5) has:*

- (1) *One endemic equilibrium if $\mathcal{R}_c > 1$,*
- (2) *No endemic equilibrium for $\mathcal{R}_c < 1$ if $\mathcal{K} \geq 0$,*
- (3) *No endemic equilibrium for $\mathcal{R}_c < \mathcal{R}_c^* < 1$ if $\mathcal{K} < 0$,*
- (4) *Two endemic equilibrium for $\mathcal{R}_c^* \leq \mathcal{R}_c < 1$ if $\mathcal{K} < 0$.*

Proof. To analyze the existence of the dengue endemic equilibrium, it is necessary to guarantee the existence of a positive of polynomial (9). If the roots is positive, then y_2^* will automatically positive. From Descartes rule of signs in Table 2, it is easy to see that when $\mathcal{R}_c > 1$, then the polynomial always has a unique endemic equilibrium. Hence part (1) proofed. Furthermore, we can see that if $a_2 < 0$, then it is possible that the polynomial will have 0 or two positive roots. Hence, further analysis needed. We conduct gradient analysis of the polynomial at $\mathcal{R}_c = 1, x_2 = 0$. Using implicit differential on polynomial 9, we have

$$(10) \quad \frac{\partial x_2}{\partial \mathcal{R}_c} \Big|_{\mathcal{R}_c=1, x_2=0} = \frac{2(m_1 m_2 + m_2)}{(1+m_1-b_3)m_2 + (1-u+u\xi)b_2(1+m_1)}.$$

Hence, if $\mathcal{K} = (1+m_1-b_3)m_2 + (1-u+u\xi)b_2(1+m_1) < 0$, then we will have a negative gradient of x_2 at $\mathcal{R}_c = 1, x_2 = 0$. This indicates an existence of positive roots x_2 for $\mathcal{R}_c < 1$. Using the fact from (a) and $f(x_2)$ is a two degree polynomial, then $f(x_2)$ will have a turning point at $\mathcal{R}_c = \mathcal{R}_c^*$ where \mathcal{R}_c^* is \mathcal{R}_c that satisfy the discriminant of $f(x_2)$ equal to zero, which is $a_1^2 - 4a_0a_2 = 0$. Hence, we have (3) proofed. If $\mathcal{R}_c < \mathcal{R}_c^*$, then we will have no positive root (part 4 proofed). Lastly, if $\mathcal{K} \geq 0$, then we will have the gradient is positive which confirm part (2). The illustration of this proof is given in Figure 2. \square

TABLE 2. The maximum number of roots for x_2^* can be determined using the Descartes' Rule of Signs for equation

Case	a_2	a_1	a_0	\mathcal{R}_c	Change of Sign	Number of Possible Roots
1	+	+	+	$\mathcal{R}_c < 1$	0	0
2	+	+	-	$\mathcal{R}_c > 1$	1	1
3	+	-	+	$\mathcal{R}_c < 1$	2	0 or 2
4	+	-	-	$\mathcal{R}_c > 1$	1	1

3.3. Existence of backward bifurcation. Next, we will analyze the local stability of the dengue-endemic equilibrium around $\mathcal{R}_c = 1$ using the Castillo-Song bifurcation theorem [41].

Theorem 3.4. *Dengue model in system (5) undergoes backward bifurcation at $\mathcal{R}_c = 1$ if $\mathcal{K} < 0$, and forward bifurcation when $\mathcal{K} > 0$.*

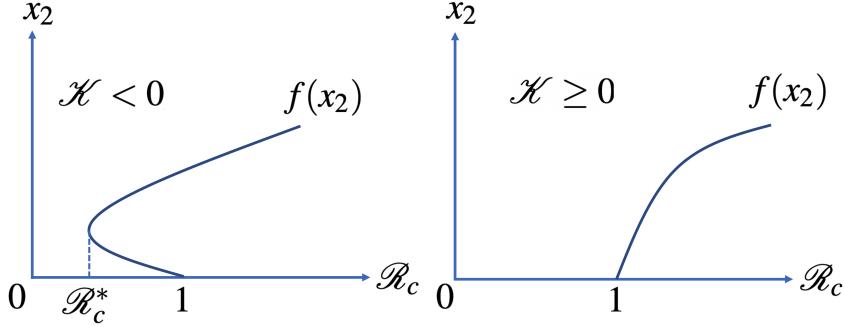


FIGURE 2. Illustration of Theorem 3.3.

Proof. The stability of the endemic equilibrium points is analyzed using the theory of Center Manifold [41] with the following steps. The reduced system (5) can be expressed as the following equations (11).

$$(11) \quad \begin{aligned} f_1 &= (1-u+u\xi)b_1(1-z_1)z_2 - m_1z_1 - \frac{z_1}{1+b_3z_1} \\ f_2 &= (1-u+u\xi)b_2(1-z_2)z_1 - m_2z_2 \end{aligned}$$

By setting $\mathcal{R}_c = 1$, we obtain the bifurcation point $b_1 = b_1^* = \frac{m_2(m_1+1)}{b_2(1-u+u\xi)^2}$, also known as the bifurcation parameter, then the linearized matrix around the DFE is given by

$$(12) \quad J_{|\mathcal{E}_0, b_1=b_1^*} = \begin{bmatrix} -1-m_1 & \frac{m_2(m_1+1)}{b_2(1-u+u\xi)} \\ (1-u+u\xi)b_2 & -m_2 \end{bmatrix}.$$

Equation (12) has a right eigenvector w and a left eigenvector v given by

$$\begin{aligned} w &= \begin{bmatrix} m_2 \\ b_2(1-u+u\xi) \end{bmatrix}, \\ v &= \begin{bmatrix} b_2(1-u+u\xi) & 1+m_1 \end{bmatrix}. \end{aligned}$$

The second partial derivatives of equation (11) are as follows

$$\begin{aligned} \frac{\partial^2 f_1}{\partial z_1 \partial z_1} &= \frac{2b_3}{(b_3z_1+1)^2} \left(1 - \frac{b_3z_1}{b_3z_1+1}\right), & \frac{\partial^2 f_2}{\partial z_1 \partial z_1} &= 0, \\ \frac{\partial^2 f_1}{\partial z_1 \partial z_2} &= (-1+u-u\xi)b_1, & \frac{\partial^2 f_2}{\partial z_1 \partial z_2} &= (-1+u-u\xi)b_2, \\ \frac{\partial^2 f_1}{\partial z_2 \partial z_1} &= (-1+u-u\xi)b_1, & \frac{\partial^2 f_2}{\partial z_2 \partial z_1} &= (-1+u-u\xi)b_2, \end{aligned}$$

$$\frac{\partial^2 f_1}{\partial z_2 \partial z_2} = 0, \quad \frac{\partial^2 f_2}{\partial z_2 \partial z_2} = 0.$$

The partial derivatives of equation (11) with respect to the bifurcation parameter are as follows

$$\begin{aligned} \frac{\partial^2 f_1}{\partial z_1 \partial b_1^*} &= (-1 + u - u\xi)y_2, & \frac{\partial^2 f_2}{\partial z_1 \partial b_1^*} &= 0, \\ \frac{\partial^2 f_1}{\partial z_2 \partial b_1^*} &= (1 - u + u\xi), & \frac{\partial^2 f_2}{\partial z_2 \partial b_1^*} &= 0. \end{aligned}$$

Next, we will determine the values of \mathcal{A} and \mathcal{B} .

(13)

$$\mathcal{A} = \sum_{k,i,j=1}^2 v_k w_i w_j \frac{\partial^2 f_k}{\partial z_i \partial z_j}(0,0) = -2m_2 b_2 (1 - u + u\xi) [(1 + m_1 - b_3)m_2 + (1 - u + u\xi)b_2(1 + m_1)].$$

(14)

$$\mathcal{B} = \sum_{k,i=1}^2 v_k w_i \frac{\partial^2 f_k}{\partial z_i \partial b_1^*}(0,0) = b_2^2 (1 - u + u\xi)^3.$$

From equations (13) and (14), it can be observed that \mathcal{B} always has a positive sign. On the other hand, \mathcal{A} is positive when $\mathcal{K} < 0$ and negative when $\mathcal{K} > 0$ where $\mathcal{K} = (1 + m_1 - b_3)m_2 + (1 - u + u\xi)b_2(1 + m_1)$. Therefore, system (5) undergoes backward bifurcation when $\mathcal{K} > 0$, and forward bifurcation when $\mathcal{K} < 0$. Hence the proof is complete. \square

To conduct numerical experiments on this article, the base for parameter values for system in (1) is given as follows.

$$\begin{aligned} N &= 1000, M = 2000, \Lambda_h = \frac{1000}{73.6 \times 365}, \Lambda_v = \frac{2000}{21}, \gamma = \frac{1}{21}, \mu_v = \frac{1}{21}, \\ \mu_h &= \frac{1}{73.6 \times 365}, \beta_h = \frac{0.1}{N}, \beta_v = \frac{0.2}{N}, u \in [0, 1], \xi = 3\%, b > 0. \end{aligned}$$

With this chosen parameters, we can calculate our parameter values for system (5), and use it to draw the bifurcation diagram in Figure 3. Our results in Theorem 3.4 indicates an existence of backward bifurcation if $\mathcal{K} < 0$. When backward bifurcation appears, then we have a stable dengue-free and dengue-endemic equilibrium appears together. This phenomena indicates that a condition of $\mathcal{R}_c < 1$ is not enough to guarantee the extinction of dengue from population. Figure 3 calculated when $b = 4$ (represent the lack of hospital bed capacity) such that $\mathcal{K} < 0$. Hence, we have $\mathcal{R}_c^* = 0.88$. Hence, we have no endemic equilibrium when $\mathcal{R}_c < 0.88$, two

endemic equilibrium when $\mathcal{R}_c \in (0.88, 1)$, and one endemic equilibrium when $\mathcal{R}_c > 1$. We draw the phase portrait of system (5) based on this region by choosing one example point in each region, namely P_1, P_2 , and P_3 . The Backward bifurcation diagram shown in panel (a), while the phase portrait in panel (b), (c), and (d). In panel (b), we can see that all solution will tends to a stable dengue-endemic equilibrium. Similarly in panel (c) shown that all solution tends to the dengue-free equilibrium. On the other hand, we can see from panel (b) that the trajectory of the solution depend on it initial condition, since bistability phenomena appears.

On the other hand, when the quantity of hospital bed capacity becomes better (smaller value of b_3), then Theorem 3.4 shows a bigger chance that no endemic equilibrium point appears when $\mathcal{R}_c < 1$. This phenomena illustrated in Figure 4. To conduct this simulation, we use a same parameter values in Figure 3, except $b_3 = 2$. Hence, we have $\mathcal{K} > 0$, and forward bifurcation appears. Hence, when $\mathcal{R}_c < 1 \iff u > 0.336$, then no dengue-endemic equilibrium appears, and the dengue-free equilibrium become stable. On the other hand, when $\mathcal{R}_c > 1 \iff u < 0.336$, dengue-free equilibrium becomes unstable, but the dengue-endemic equilibrium is stable.

Figure 5 shows a sensitivities of Bifurcation threshold \mathcal{K} depending on mosquito repellent use u and saturated treatment parameter b_3 due to hospital bed capacity. Smaller b_3 means a larger hospital bed capacity. We can see that a combination of u and b_3 can determine the type of bifurcation of system (5) at $\mathcal{R}_c = 1$. A smaller b_3 requires will reduce the chance $\mathcal{K} < 0$. From Theorem 3.4, smaller value of \mathcal{K} will increase the chance of Forward bifurcation.

4. SENSITIVITY AND ELASTICITY ANALYSIS

In this section, we conduct a sensitivity analysis of our model respect to it parameters. Sensitivity analysis reveals the impact of model parameters that have the greatest influence on the basic reproduction number of the dengue fever model system (1). To evaluate the sensitivity, we employ the forward sensitivity index, which is normalized with respect to the basic reproduction number \mathcal{R}_0 and is denoted as

$$(15) \quad \epsilon_{\mathcal{R}_c}^{\sigma} = \frac{\partial \mathcal{R}_c}{\partial \sigma} \times \frac{\sigma}{\mathcal{R}_c}$$

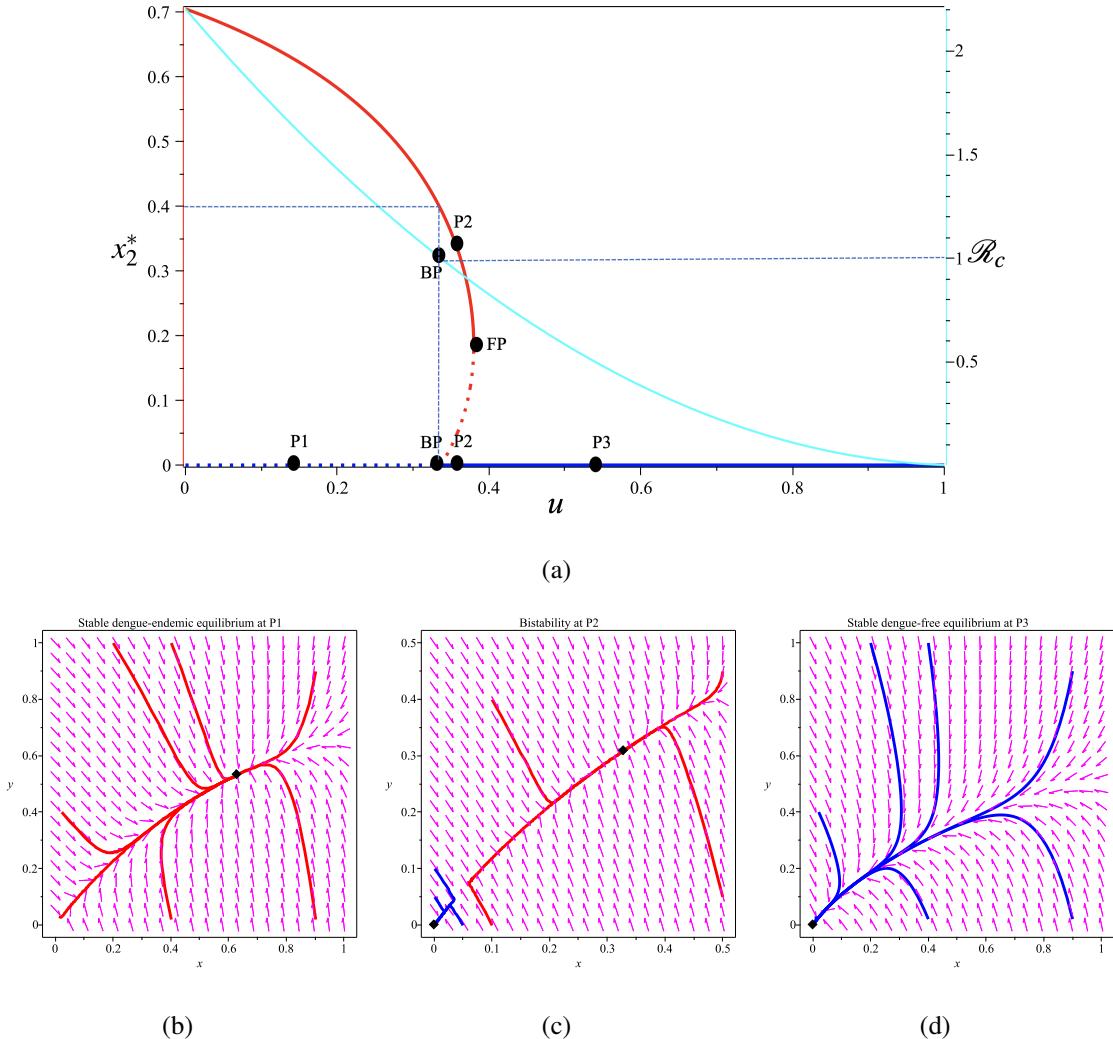


FIGURE 3. A backward bifurcation diagram of system (5) with respect to u given in panel (a). Parameter values are: $b_1 = 1.05, b_2 = 2.1, b_3 = 4, m_1 = 0.000752, m_2 = 1, \xi = 0.03$, while u varying. The Branching Point BP is when $\mathcal{R}_c(u = 0.336) = 1$, and the Fold point FP is when $\mathcal{R}_c(u = 0.379) = \mathcal{R}_c^* = 0.88$. Panels (b), (c) and (d) show the phase portrait of system (5) at $P1$ when only dengue-endemic equilibrium stable, at $P2$ when bistability appears, and at $P3$ when only dengue-free equilibrium stable, respectively. Blue and red curve present the solution which tends to dengue-free and dengue-endemic equilibrium, respectively.

We calculate elasticities indices of \mathcal{R}_c respect to all parameter values to see the results of relative changes of \mathcal{R}_c respect to parameter change. Using above formula, then we have the

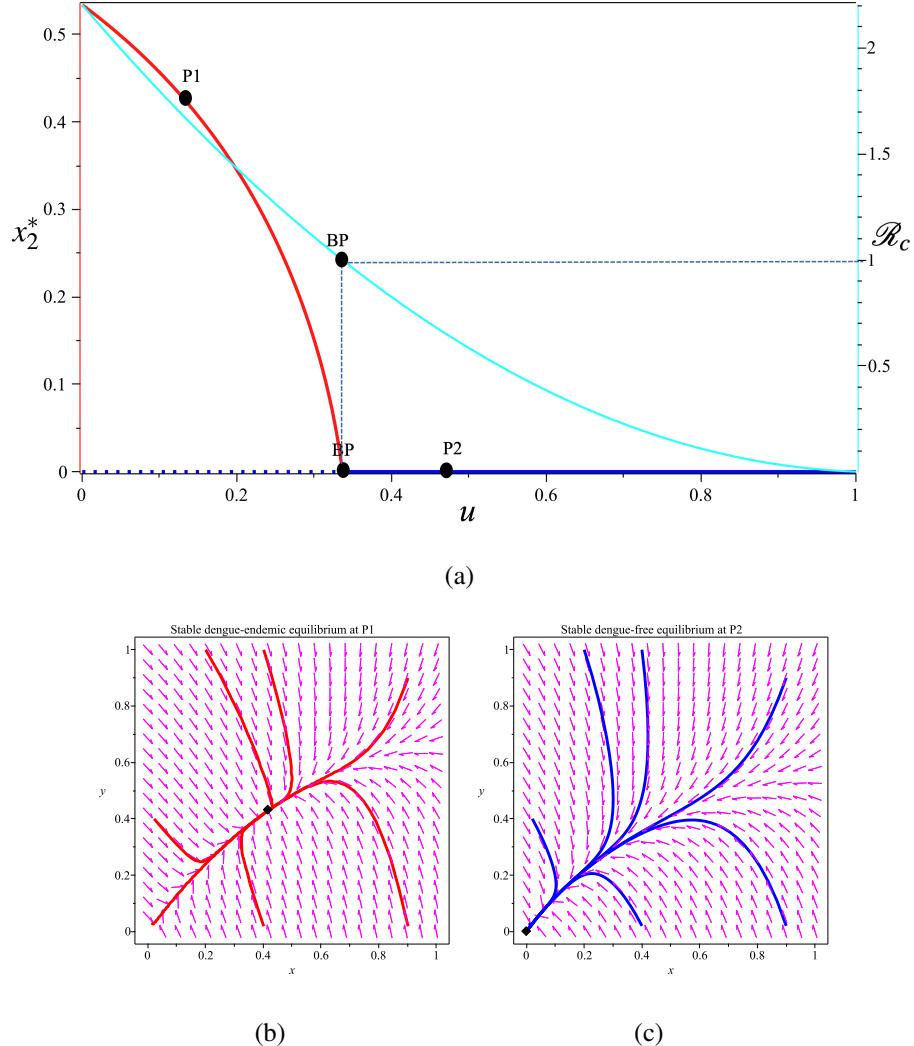


FIGURE 4. A Forward bifurcation diagram of system (5) with respect to u given in panel (a). Parameter values are: $b_1 = 1.05, b_2 = 2.1, b_3 = 2, m_1 = 0.000752, m_2 = 1, \xi = 0.03$, while u varying. The Branching Point BP is when $\mathcal{R}_c(u = 0.336) = 1$. No Fold Point appears. Panels (b) and (c) show the phase portrait of system (5) at $P1$ when only dengue-endemic equilibrium stable and at $P2$ when only dengue-free equilibrium stable, respectively. Blue and red curve present the solution which tends to dengue-free and dengue-endemic equilibrium, respectively.

following results.

$$(16) \quad \begin{aligned} \varepsilon_{\mathcal{R}_c}^{b_1} &= \frac{(1-u+u\xi)b_2}{2G} > 0, & \varepsilon_{\mathcal{R}_c}^{b_2} &= \frac{(1-u+u\xi)b_1}{2G} > 0, & \varepsilon_{\mathcal{R}_c}^{m_1} &= -\frac{(1-u+u\xi)b_1b_2}{2(1+m_1)G} < 0, \\ \varepsilon_{\mathcal{R}_c}^{m_2} &= -\frac{(1-u+u\xi)b_1b_2}{2m_2G} < 0, & \varepsilon_{\mathcal{R}_c}^u &= -\frac{(1-\xi)G}{(1+m_1)m_2} < 0, & \varepsilon_{\mathcal{R}_c}^\xi &= \frac{uG}{(1+m_1)m_2} > 0, \end{aligned}$$

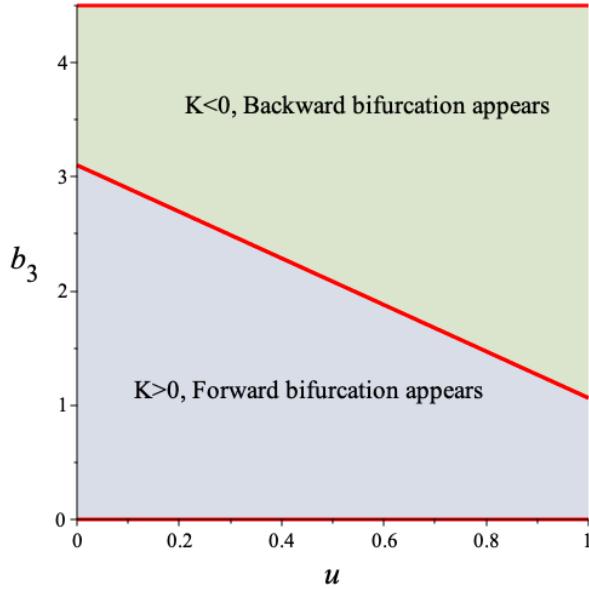


FIGURE 5. Sensitivity area of bifurcation type at $\mathcal{R}_c = 1$ depend on u and b_3 .

where, $G = \sqrt{(1+m_1)m_2b_1b_2}$. Using parameter values as in Figure 3 except b_1 varying from 0.9 to 1.4 (10 sample values) and $u = 0.336$, then the average value of elasticity index for each parameter to \mathcal{R}_c is given in Table 3.

TABLE 3. Average value of sensitivity indices of \mathcal{R}_c to the parameter values of the model for 11 set of data.

Parameter	b_1	b_2	m_1	m_2	u	ξ
Sensitivity index	0.459	0.249	-0.522	-0.522	-1.503	0.521

Sensitivity analysis reveals that the most sensitive parameter is the use of mosquito repellent, denoted as u . Positive sensitivity indices indicate that \mathcal{R}_c increases with an increase in this parameter. Conversely, negative sensitivity indices indicate that \mathcal{R}_c decreases with an increase in this parameter. In summary, \mathcal{R}_c increases due to an increase in the mosquito-to-human transmission rate b_1 , the human-to-mosquito transmission rate b_2 , and a decrease in the effectiveness of control measures ξ . On the other hand, \mathcal{R}_c decreases due to an increase in the mosquito death rate m_1 , the human death rate m_2 , and the use of mosquito repellent u . Sensitivity of \mathcal{R}_c respect to u is -1.503, which means that by increasing u for 1% will reduce \mathcal{R}_c for 1.503%. Furthermore, we can since the elasticity of mosquito repellent efficacy is 0.521, then increasing ξ for

1% will increase \mathcal{R}_c for 0.521%. With this findings, we suggest that the most effective mitigation strategy for reducing \mathcal{R}_c is the use of an effective mosquito control measure, such as mosquito repellent u .

5. OPTIMAL CONTROL

System (1) considers a single control variable (u), which represents the human effort to protect themselves from mosquito bites using mosquito repellent. We assume that mosquito repellent use is depend on time t and are applied as needed. The main objective of the researchers is to minimize the total losses caused by mosquitoes and infected individuals, as well as the costs associated with implementing the control. Therefore, the researchers formulate the objective function that needs to be minimized as follows

$$(17) \quad J = \int_0^T \omega_1 x_2 + \omega_2 y_2 + \omega_u u^2 dx, \quad \text{with} \quad U = \{u(t) : 0 \leq u(t) \leq 1, \forall t \in [0, T]\}.$$

Here, the constants ω_1 and ω_2 represent the per-individual losses caused by the presence of infected individuals and infected mosquitoes, respectively. The constant ω_u represents the cost associated with awareness efforts to protect individuals from mosquito bites, specifically the use of mosquito repellent.

Next, we form the Hamiltonian H which consists of the cost function components and the right-hand side of the state system (5) through the adjoint variables λ_i , where $i = 1, 2$. Thus, H is defined as

$$\begin{aligned} H(x_2, y_2) &= \omega_1 x_2 + \omega_2 y_2 + \omega_u u^2 \\ &\quad + \lambda_1 \left((1 - u + u\xi) b_1 (1 - x_2) y_2 - m_1 x_2 - \frac{x_2}{1 + b_3 x_2} \right) \\ &\quad + \lambda_2 ((1 - u + u\xi) b_2 (1 - y_2) x_2 - m_2 y_2). \end{aligned}$$

To determine the adjoint equations and transversality conditions, the researchers utilize the Pontryagin's maximum principle [42], which gives

$$\begin{aligned} \frac{d\lambda_1(t)}{dt} &= -\frac{\partial H}{\partial x_2} \\ &= -\omega_1 - \lambda_1 \left(-(u\xi - u + 1) b_1 y_2 - m_1 - \frac{1}{b_3 x_2 + 1} + \frac{x_2 b_3}{(b_3 x_2 + 1)^2} \right) \dots \end{aligned}$$

$$\begin{aligned}
& -\lambda_2(u\xi - u + 1)b_2(1 - y_2), \\
(18) \quad \frac{d\lambda_2(t)}{dt} &= -\frac{\partial H}{\partial y_2} \\
&= -\omega_2 - \lambda_1(u\xi - u + 1)b_1(1 - x_2) - \lambda_2(-(u\xi - u + 1)b_2x_2 - m_2),
\end{aligned}$$

subject to the transversality conditions $\lambda_i(T) = 0, i = 1, 2$. Now, using the optimality condition $\frac{\partial H}{\partial u} = 0$, we obtain

$$u = \frac{(((b_1\lambda_1 + b_2\lambda_2)y_2 - b_2\lambda_2)x_2 - b_1\lambda_1y_2)(\xi - 1)}{2\omega_u}.$$

Therefore, the optimal control for the minimum value of the optimal problem is given by

$$(19) \quad u^* = \max \left\{ 0, \min \left\{ \frac{(((b_1\lambda_1 + b_2\lambda_2)y_2 - b_2\lambda_2)x_2 - b_1\lambda_1y_2)(\xi - 1)}{2\omega_u}, 1 \right\} \right\}.$$

From the above explanation, our optimal control problem consists of a state system in system (5) with the initial condition given, cost function J in (17) adjoint system in (18) with transversality condition $\lambda_i(T) = 0$, and optimality condition u^* in (19). To solve this problem, we use a forward-backward iterative method as in [43]. At first, we give an initial condition for u for all time t . With this initial guess, we find $x_i(t)$ forward in time and use the result to find $\lambda_i(t)$ for all time t . With this result, we update our optimal u using the formula in (19). This iteration is terminated when the cost function in (17) converges or the maximum iteration is achieved.

We conduct our numerical simulation for the optimal control problem in several scenarios as follows.

5.1. Effect of mosquito repellent efficacy. In this numerical experiment, we want to understand the impact of mosquito repellent efficacy on the dynamics of the control. To analyze this, we run our simulation for four different values of ξ , while the other parameter values are the same with in Figure 3. The dynamic result of system (5) and its optimal control trajectories are given in Figure 6, while the comparison of the cost and reduced infected are given in Table 4. We can see clearly that when the efficacy of mosquito repellent is better (smaller ξ), then the proportion of human who uses mosquito repellent reach its maximum value over a longer period

(see panel (a)). As a result, we can see that the proportion of infected humans reduced better compared to the other result.

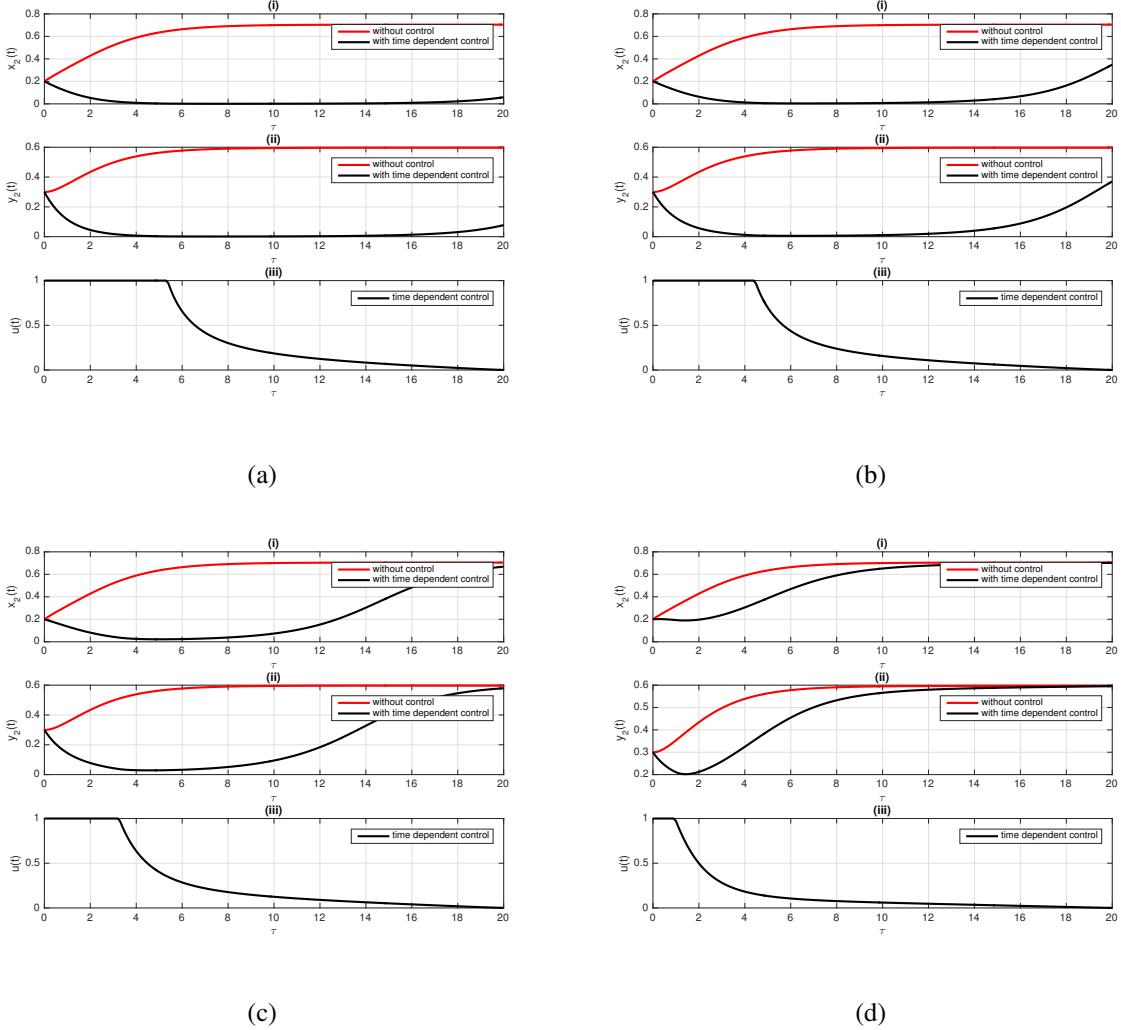


FIGURE 6. Effect of ξ to the trajectory of $u(t)$. The value of ξ is 0.03, 0.1, 0.2, and 0.5 for panel (a) to (d), respectively. The x -axis represent the time scale τ where $\tau = \gamma t$, while y -axis represent the proportion of infected human and mosquitoes in panel (i) and (ii) and control in (iii).

Table 4 shows a better quality of mosquito repellent could give a smaller cost of intervention, more infected averted, and a larger Infected Averted Ratio (IAR). This IAR represent the average cost needed for each 1% Infected averted. For example, we can see that when the efficacy of

mosquito repellent is 97% ($\xi = 0.03$), then infected averted reach 61% compared when $u = 0$. Hence, IAR for the case $\xi = 0.03$ is 0.716.

Scenario	ξ	J	Infected averted	IAR
(a)	0.03	0.854	61% of N	0.716
(b)	0.1	1.162	57.2% of N	0.492
(c)	0.2	2.646	41.3% of N	0.156
(d)	0.5	5.616	9.3% of N	0.016

TABLE 4. Comparison of the cost function for each scenario in Figure 6.

5.2. Effect of the different initial condition of population. In this section, we run our simulation for two different initial conditions of the infected population. The first scenario is when the number of infected individuals and mosquitoes is relatively small, i.e. $(x_2(0), y_2(0)) = (0.05, 0.05)$. We called this scenario as the endemic prevention scenario since the purpose of control is to avoid further infection or even an outbreak. On the other hand, the second scenario is called endemic reduction since the purpose of the control is to reduce the spread of dengue that already occur. The initial condition for this scenario is $(x_2(0), y_2(0)) = (0.5, 0.5)$. All parameter values are the same as in scenario (a) in Figure 6, and the results are given in Figure 7. The optimal cost for the endemic prevention scenario is 0.837, which is smaller than the endemic reduction scenario ($J=1.774$). This results means that it is better to implement the intervention of mosquito repellent at the begining of disease spread rather than wait it until it reach high number of infected individuals.

6. CONCLUSION

In this paper, we analyze the stability and optimal control of the dengue transmission model $SIS - UV$ considering the use of mosquito repellent. Mathematical analysis of the equilibrium points, local stability of the equilibrium points, and the basic reproduction number have been shown analytically. We show that the model may exhibits forward or backward bifurcations at $\mathcal{R}_c = 1$, indicating that a control reproduction number less than one alone is not always sufficient

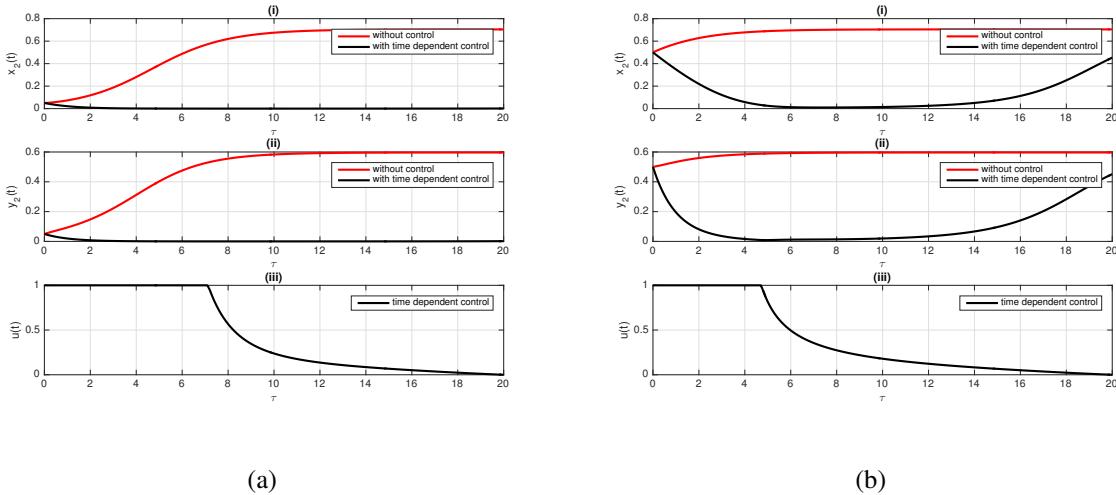


FIGURE 7. Effect of different initial conditions to the trajectory of $u(t)$. Panel (a) and (b) shows the result for endemic prevention and endemic reduction scenario, respectively. The infected averted ratio for scenario (a) is 0.634 while scenario (b) is 0.317.

to guarantee the eradication of dengue from the population. Sensitivity analysis reveals that the use of mosquito repellent is promising to help to control the spread of dengue.

Furthermore, we consider an optimal control problem aiming to minimize the total loss caused by mosquitoes and infected individuals, as well as the cost associated with the implementation of control u with effectiveness $1 - \xi$. To minimize the intervention cost, we treat u as a time-dependent variable. The Pontryagin's Minimum Principle is used to formulate the optimal control problem. Numerical simulations of the optimal control illustrate the contribution of the control parameter in the dynamics of the infection, highlighting the importance of not only using mosquito repellent but also ensuring its high effectiveness for significant impact. Furthermore, we show that it is better to give an intervention to the spread of dengue using mosquito repellent at the beginning of dengue spread, instead of wait the dengue incidence increases.

ACKNOWLEDGEMENT

This research is funded by Faculty of Mathematics and Natural Sciences (FMIPA), Universitas Indonesia, through Article Publication Grant 2023.

CONFLICT OF INTERESTS

The author(s) declare that there is no conflict of interests.

REFERENCES

- [1] W.H. Wang, A.N. Urbina, M.R. Chang, et al. Dengue hemorrhagic fever - A systemic literature review of current perspectives on pathogenesis, prevention and control, *J. Microbiol. Immunol. Infect.* 53 (2020), 963-978. <https://doi.org/10.1016/j.jmii.2020.03.007>.
- [2] T.J. Schaefer, P.K. Panda, R.W. Wolford, Dengue fever, in: StatPearls [Internet], StatPearls Publishing, Treasure Island, Florida, (2022). <https://www.ncbi.nlm.nih.gov/books/NBK430732>.
- [3] WHO, Dengue and severe dengue, (2023). <https://www.who.int/news-room/fact-sheets/detail/dengue-and-severe-dengue>.
- [4] European Centre for Disease Prevention and Control, Dengue worldwide overview, (2023). <https://www.ecdc.europa.eu/en/dengue-monthly>.
- [5] S.A. Kularatne, C. Dalugama, Dengue infection: Global importance, immunopathology and management, *Clin. Med.* 22 (2022), 9–13. <https://doi.org/10.7861/clinmed.2021-0791>.
- [6] B. Wibowo, Hubungan infeksi dengue sekunder dengan derajat keparahan infeksi dengue, *J. Med. Hutama.* 2 (2020), 327–331.
- [7] Centers for Disease Control and Prevention, Avoid dengue by preventing mosquito bites, (2023). <https://www.cdc.gov/ncezid/dvbd/media/avoid-dengue.html>.
- [8] H.F. Khater, A.M. Selim, G.A. Aboueella, et al. Commercial mosquito repellents and their safety concerns, in: F. H. Kasenga (Ed.), *Malaria*, IntechOpen, 2019. <https://doi.org/10.5772/intechopen.87436>.
- [9] Rafiqi, Y. Nindia, The effectiveness of pineapple peel extract (*ananas comosus*) as a mosquito repellent for *aedes aegypti*, *ASJo: Aceh Sanitation J.* 1 (2022), 34–38.
- [10] N.L. Arpiwi, I.K. MUksin, N.L. Kartini, Essential oil from *Cymbopogon nardus* and repellent activity against *Aedes aegypti*, *Biodiversitas.* 21 (2020), 3873-3878. <https://doi.org/10.13057/biodiv/d210857>.
- [11] B. Fonseca-Santos, C. Del Nero Pacheco, M.C. Pinto, M. Chorilli, An effective mosquito-repellent topical product from liquid crystal-based tea tree oil, *Ind. Crops Products.* 128 (2019), 488–495. <https://doi.org/10.1016/j.indcrop.2018.11.020>.
- [12] M.E. Ojewumi, O.R. Obanla, D.M. Atauba, A review on the efficacy of *Ocimum gratissimum*, *Mentha spicata*, and *Moringa oleifera* leaf extracts in repelling mosquito, *Beni-Suef Univ. J. Basic Appl. Sci.* 10 (2021), 87. <https://doi.org/10.1186/s43088-021-00176-x>.

- [13] R. Jan, M.A. Khan, P. Kumam, P. Thounthong, Modeling the transmission of dengue infection through fractional derivatives, *Chaos Solitons Fractals.* 127 (2019), 189–216. <https://doi.org/10.1016/j.chaos.2019.07.002>.
- [14] O.O. Onyejekwe, A. Tigabie, B. Ambachew, et al. Application of optimal control to the epidemiology of dengue fever transmission, *J. Appl. Math. Phys.* 07 (2019), 148–165. <https://doi.org/10.4236/jamp.2019.71013>.
- [15] M.Z. Ndii, A.R. Mage, J.J. Messakh, et al. Optimal vaccination strategy for dengue transmission in Kupang city, Indonesia, *Heliyon.* 6 (2020), e05345. <https://doi.org/10.1016/j.heliyon.2020.e05345>.
- [16] M. Schäfer, T. Götz, Modelling dengue fever epidemics in Jakarta, *Int. J. Appl. Comput. Math.* 6 (2020), 84. <https://doi.org/10.1007/s40819-020-00834-1>.
- [17] N.H. Shah, A.H. Suthar, E.N. Jayswal, Dynamics of malaria-dengue fever and its optimal control, *Int. J. Optim. Control, Theor. Appl.* 10 (2020), 166–180. <https://doi.org/10.11121/ijocata.01.2020.00828>.
- [18] S.B. Mohamed Siddik, F.A. Abdullah, A.I. Md. Ismail, Mathematical model of dengue virus with predator-prey interactions, *Sains Malays.* 49 (2020), 1191–1200. <https://doi.org/10.17576/jsm-2020-4905-24>.
- [19] A. Chamnan, P. Pongsumpun, I.M. Tang, et al. Local and global stability analysis of dengue disease with vaccination and optimal control, *Symmetry.* 13 (2021), 1917. <https://doi.org/10.3390/sym13101917>.
- [20] W. Sanusi, N. Badwi, A. Zaki, et al. Analysis and simulation of SIRS model for dengue fever transmission in South Sulawesi, Indonesia, *J. Appl. Math.* 2021 (2021), 2918080. <https://doi.org/10.1155/2021/2918080>.
- [21] E. Bonyah, M.L. Juga, C.W. Chukwu, et al. A fractional order dengue fever model in the context of protected travelers, *Alexandria Eng. J.* 61 (2022), 927–936. <https://doi.org/10.1016/j.aej.2021.04.070>.
- [22] M.Z. Ndii, The effects of vaccination, vector controls and media on dengue transmission dynamics with a seasonally varying mosquito population, *Results Phys.* 34 (2022), 105298. <https://doi.org/10.1016/j.rinp.2022.105298>.
- [23] D. Aldila, M.Z. Ndii, N. Anggriani, et al. Impact of social awareness, case detection, and hospital capacity on dengue eradication in Jakarta: A mathematical model approach, *Alexandria Eng. J.* 64 (2023), 691–707. <https://doi.org/10.1016/j.aej.2022.11.032>.
- [24] D. Aldila, C.A. Puspadi, R. Rusin, Mathematical analysis of the impact of community ignorance on the population dynamics of dengue, *Front. Appl. Math. Stat.* 9 (2023), 1094971. <https://doi.org/10.3389/fams.2023.1094971>.
- [25] A. Hanif, A.I.K. Butt, Atangana-Baleanu fractional dynamics of dengue fever with optimal control strategies, *AIMS Math.* 8 (2023), 15499–15535. <https://doi.org/10.3934/math.2023791>.
- [26] T.A. Prasetyo, R. Saragih, D. Handayani, Optimal control on the mathematical models of dengue epidemic by giving vaccination and repellent strategies, *J. Phys.: Conf. Ser.* 1490 (2020), 012034. <https://doi.org/10.1088/1742-6596/1490/1/012034>.

- [27] M.A. Khan, Fatmawati, Dengue infection modeling and its optimal control analysis in East Java, Indonesia, *Heliyon.* 7 (2021), e06023. <https://doi.org/10.1016/j.heliyon.2021.e06023>.
- [28] A.K. Srivastav, A. Kumar, P.K. Srivastava, et al. Modeling and optimal control of dengue disease with screening and information, *Eur. Phys. J. Plus.* 136 (2021), 1187. <https://doi.org/10.1140/epjp/s13360-021-02164-7>.
- [29] A. Hamid, P. Sinha, Vaccination and control measures on vector transmission dynamics: Modeling and simulation, *Int. J. Nonlinear Anal. Appl.* 13 (2022), 2999–3015. <https://doi.org/10.22075/ijnaa.2022.25189.2946>.
- [30] M.R. Hasan, A.H.A. Alshehri, Dynamic vector-host dengue epidemic model with vector control and sensitivity analysis, *Adv. Dyn. Syst. Appl.* 18 (2023), 1–21.
- [31] P. Saha, G.C. Sikdar, J.K. Ghosh, et al. Disease dynamics and optimal control strategies of a two serotypes dengue model with co-infection, *Math. Computers Simul.* 209 (2023), 16–43. <https://doi.org/10.1016/j.matcom.2023.02.011>.
- [32] I.H. Putri, T. Tutik, S. Marcellia, Efektivitas formulasi spray ekstrak kulit bawang merah (*Allium cepa L.*) sebagai repellent terhadap nyamuk *Aedes aegypti*, *J. Kedokteran Kesehatan.* 9 (2022), 934–944.
- [33] R. Beever, Mosquito repellent effectiveness: A placebo controlled trial comparing 95% DEET, Avon Skin So Soft, and a “special mixture”, *BC Med. J.* 48 (2006), 226–231.
- [34] A. Abate, A. Tiwari, S. Sastry, Box invariance in biologically-inspired dynamical systems, *Automatica.* 45 (2009), 1601–1610. <https://doi.org/10.1016/j.automatica.2009.02.028>.
- [35] P. van den Driessche, J. Watmough, Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission, *Math. Biosci.* 180 (2002), 29–48. [https://doi.org/10.1016/s0025-5564\(02\)00108-6](https://doi.org/10.1016/s0025-5564(02)00108-6).
- [36] D. Aldila, B.D. Handari, A. Widyah, et al. Strategies of optimal control for HIV spreads prevention with health campaign, *Commun. Math. Biol. Neurosci.* 2020 (2020), 7. <https://doi.org/10.28919/cmbn/4332>.
- [37] D. Aldila, N. Nuraini, E. Soewono, Optimal control problem in preventing of swine flu disease transmission, *Appl. Math. Sci.* 8 (2014), 3501–3512.
- [38] B.D. Handari, D. Aldila, E. Tamalia, et al. Assessing the impact of medical treatment and fumigation on the superinfection of malaria: a study of sensitivity analysis, *Commun. Biomath. Sci.* 6 (2023), 51–73. <https://doi.org/10.5614/cbms.2023.6.1.5>.
- [39] D. Aldila, J.P. Zhavez, K.P. Wijaya, et al. A tuberculosis epidemic model as a proxy for the assessment of the novel *M72/AS01_E* vaccine, *Commun. Nonlinear Sci. Numer. Simul.* 120 (2023), 107162. <https://doi.org/10.1016/j.cnsns.2023.107162>.
- [40] D. Aldila, N. Awdinda, Fatmawati, et al. Optimal control of pneumonia transmission model with seasonal factor: Learning from Jakarta incidence data, *Heliyon.* 9 (2023), e18096. <https://doi.org/10.1016/j.heliyon.2023.e18096>.

- [41] C. Castillo-Chavez, B. Song, Dynamical models of tuberculosis and their applications, *Math. Biosci. Eng.* 1 (2004), 361–404.
- [42] L.S. Pontryagin, Mathematical theory of optimal processes, CRC Press, Boca Raton, (1987).
- [43] S. Lenhart, J.T. Workman, Optimal control applied to biological models, CRC Press, Boca Raton, (2007).