MATHEMATICAL MODEL OF REPELLENT EFFECT IN DENGUE TRANSMISSION

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ABSTRACT

Dengue is a disease caused by the dengue virus, transmitted through the bite of an infected female Aedes aegypti. Dengue virus is a member of the genus Flavivirus, family Flaviviridae. Indonesia is one of the countries with the most dengue cases in Southeast Asia. Therefore, dengue transmission must be controlled to reduce the increase in dengue cases. One of the controls is by using repellents. Repellent is one of the human protection strategies to avoid mosquito bites used by spraying or smearing. This study models dengue transmission by reviewing the effect and control of repellent. A mathematical model of repellent effect and control in dengue transmission uses a SIR compartment model. The SIR model is modified by involving mosquitoes and the human population. Repellent is used in both susceptible humans, infected humans, and recovered humans. Numerical and analytical simulations are conducted to analyze the behavior of each compartment of the mosquito and human populations in dengue transmission. Analytical results show that the factors affecting the spread of infection are the transmission rate of the dengue virus and the loss of human-repellent protection. The transmission rate of dengue virus in the interval [0.200, 0.550] increases the infected human by 2.73%, while the rate of loss of human-repellent protection in the interval [0.0001, 0.01] increases the infected human by 0.03%. Optimal control is used to minimize the number of infected humans who do not use repellent. The results of numerical simulations on the optimal control problem show that an increase in the proportion of healthy humans who have campaign effect and use repellent regularly in the range of 14.67% can reduce infected individuals by 0.647%.

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1. INTRODUCTION

Dengue is a dangerous disease caused by the dengue virus, which is transmitted through the bite of an infected female Aedes aegypti mosquito. The dengue virus has four serotypes, namely DEN-1, DEN-2, DEN-3, and DEN-4 [1]. Infection with one serotype will lead to the formation of antibodies against that specific serotype [2]. Aedes aegypti mosquitoes can become infected and act as vectors for dengue when they feed on the blood of individuals who are already infected with the virus [3]. After an incubation period of approximately 8 to 12 days, the mosquitoes can transmit the dengue virus to healthy individuals [4]. Generally, female Aedes aegypti mosquitoes bite two hours after sunrise and several hours before sunset [5]. The World Health Organization has stated that the recorded dengue cases have increased by over 8-fold in the past two decades [6]. The Ministry of Health of the Republic of Indonesia reported that Indonesia has shown an increasing trend in the cumulative number of dengue cases from January to September 2022, reaching 87,501 cases, including 816 fatalities. Among these cases, 38.96% occurred in the age group of 14 - 44 years, and 35.61% occurred in the age group of 5 - 14 years [7].

The transmission of dengue must be controlled to mitigate the increase in dengue cases. A study conducted by Prasetyo et al. (2020) [8] reviewed a disease spread model on dengue with control measures involving vaccination and repellent. However, vaccination has more impact for individuals previously been infected with dengue fever [9]. Therefore, a control model can be used to study how to reduce the spread and prevent the possible occurrence of Dengue epidemics. Repellents are chemical substances or household pesticides used to avoid insect bites or disturbances, and they can be applied through sprays or lotions, offering varying durations of protection depending on their types [10].

A mathematical model of the repellent effect in dengue transmission is constructed using the SIR compartments model. The SIR model is modified to include both mosquito population and the human population. Repellents are applied to humans, whether they are healthy, infected, or have recovered from the disease. Analytical solutions and numerical simulations are conducted to analyze the behavior of each compartment, both mosquito and human population, in the transmission of dengue.

2. RESEARCH METHODS

In this section, we present the model formulation, basic reproduction number, equilibrium points, stability, and the optimal control consisting of state, costate, and stationary conditions.

2.1 Model Formulation

A control problem of repellent effect in dengue transmission involving host and vector population is discussed here. The vector population is divided into two compartments, susceptible mosquitoes, \( S_v \), and infectious mosquitoes, \( I_v \). The human population is composed of susceptible humans without repellent \( S_{hn} \), susceptible humans with repellent \( S_{hr} \), infected humans without repellent \( I_{hn} \), infected humans with repellent \( I_{hr} \), recovered humans with repellent \( R_{hn} \) and recovered humans without repellent \( R_{hr} \). Transmission diagram between mosquitoes and humans are shown in Figure 1.
Let $\mathbf{X} = (S_v, I_v, S_{hn}, S_{hr}, I_{hn}, I_{hr}, R_{hn}, R_{hr})^T$, we consider the following dynamical system:

$$
\frac{dS_v}{dt} = \mu_v N_v - \tau_v S_v - \frac{b\beta_v I_{hn} S_v}{N_h} 
$$

(1)

$$
\frac{dI_v}{dt} = \frac{b\beta_v I_{hn} S_v}{N_h} - \tau_v I_v
$$

(2)

$$
\frac{dS_{hn}}{dt} = \mu_h N_h + \varepsilon S_{hr} - \tau_h S_{hn} - \alpha S_{hn} - \frac{b\beta_h I_v S_{hn}}{N_h}
$$

(3)

$$
\frac{dS_{hr}}{dt} = \alpha S_{hn} - \varepsilon S_{hr} - \tau_h S_{hr}
$$

(4)

$$
\frac{dI_{hn}}{dt} = \frac{b\beta_h I_v S_{hn}}{N_h} + \varepsilon I_{hr} - \tau_h I_{hn} - \alpha I_{hn} - \gamma I_{hn}
$$

(5)

$$
\frac{dI_{hr}}{dt} = \alpha I_{hn} - \varepsilon I_{hr} - \tau_h I_{hr} - \gamma I_{hr}
$$

(6)

$$
\frac{dR_{hn}}{dt} = \gamma (I_{hn} + I_{hr}) + \varepsilon R_{hr} - \tau_h R_{hn} - \alpha R_{hn}
$$

(7)

$$
\frac{dR_{hr}}{dt} = \alpha R_{hn} - \varepsilon R_{hr} - \tau_h R_{hr}
$$

(8)

with $N_v = S_v + I_v$ the total of mosquito population and $N_h = S_{hn} + S_{hr} + I_{hn} + I_{hr} + R_{hn} + R_{hr}$ the total of human population. For the overall mosquito population, it holds that $\frac{dN_v}{dt} = (\mu_v - \tau_v) N_v$, and for all human population, it holds that $\frac{dN_h}{dt} = (\mu_h - \tau_h) N_h$. Assuming that $N_v$ and $N_h$ will be constant all the time, we get $\mu_v = \tau_v$ and $\mu_h = \tau_h$. Description and dimension for all compartments are showed in the Table 1 and see Table 2 for further detail about parameters value.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Description</th>
<th>Dimension</th>
</tr>
</thead>
<tbody>
<tr>
<td>$S_v$</td>
<td>Number of Susceptible Mosquito</td>
<td>Mosquito</td>
</tr>
<tr>
<td>$I_v$</td>
<td>Number of Infected Mosquito</td>
<td>Mosquito</td>
</tr>
<tr>
<td>$S_{hn}$</td>
<td>Number of Susceptible Human without Repellent</td>
<td>Human</td>
</tr>
<tr>
<td>$S_{hr}$</td>
<td>Number of Susceptible Human with Repellent</td>
<td>Human</td>
</tr>
<tr>
<td>$I_{hn}$</td>
<td>Number of Infected Human without Repellent</td>
<td>Human</td>
</tr>
<tr>
<td>$I_{hr}$</td>
<td>Number of Infected Human with Repellent</td>
<td>Human</td>
</tr>
<tr>
<td>$R_{hn}$</td>
<td>Number of Recovered Human without Repellent</td>
<td>Human</td>
</tr>
<tr>
<td>$R_{hr}$</td>
<td>Number of Recovered Human with Repellent</td>
<td>Human</td>
</tr>
</tbody>
</table>
### Table 2. Parameters Description

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Description</th>
<th>Value</th>
<th>Unit</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\mu_v$</td>
<td>Mosquito birth rate</td>
<td>0.03</td>
<td>Day$^{-1}$</td>
<td>[3]</td>
</tr>
<tr>
<td>$\tau_v$</td>
<td>Mosquito death rate</td>
<td>0.03</td>
<td>Day$^{-1}$</td>
<td>[3]</td>
</tr>
<tr>
<td>$b$</td>
<td>Number of mosquito bites on humans every day</td>
<td>1</td>
<td>-</td>
<td>Assumed</td>
</tr>
<tr>
<td>$\beta_v$</td>
<td>Transmission rate of dengue virus from mosquito to mosquito</td>
<td>0.375</td>
<td>Day$^{-1}$</td>
<td>[8]</td>
</tr>
<tr>
<td>$\mu_h$</td>
<td>Average human birth rate</td>
<td>0.000042</td>
<td>Day$^{-1}$</td>
<td>[7, 8]</td>
</tr>
<tr>
<td>$\tau_h$</td>
<td>Average human death rate</td>
<td>0.000042</td>
<td>Day$^{-1}$</td>
<td>[7, 8]</td>
</tr>
<tr>
<td>$\alpha$</td>
<td>The rate of humans using repellent</td>
<td>0.01</td>
<td>Day$^{-1}$</td>
<td></td>
</tr>
<tr>
<td>$\varepsilon$</td>
<td>The rate of loss of repellent protection</td>
<td>0.001</td>
<td>Day$^{-1}$</td>
<td>Assumed</td>
</tr>
<tr>
<td>$\beta_h$</td>
<td>Transmission rate of dengue virus from mosquito to human</td>
<td>0.375</td>
<td>Day$^{-1}$</td>
<td>[3, 8]</td>
</tr>
<tr>
<td>$\gamma$</td>
<td>The rate of human recovery</td>
<td>0.3</td>
<td>Day$^{-1}$</td>
<td>[7]</td>
</tr>
</tbody>
</table>

Assuming that humans and mosquitoes are in equilibria, we could scale the human subpopulations by $N_h$ and the mosquito subpopulations by $N_v$. The proportion of each individual can be expressed as:

$$s_v = \frac{S_v}{N_v}, i_v = \frac{I_v}{N_v}, s_{hn} = \frac{S_{hn}}{N_h}, s_{hr} = \frac{S_{hr}}{N_h}, i_{hn} = \frac{I_{hn}}{N_h}, i_{hr} = \frac{I_{hr}}{N_h}, r_{hn} = \frac{R_{hn}}{N_h}, r_{hr} = \frac{R_{hr}}{N_h}$$

By letting $\phi_S = \frac{s_v}{N_h}$ and $\phi_I = \frac{i_v}{N_h}$, we could obtain the normalized system of [Equation (1)] - [Equation (8)] is given by

\[
\begin{align*}
\frac{ds_v}{dt} &= \mu_v - \tau_v s_v - b \beta_v i_{hn} \phi_S \\
\frac{di_v}{dt} &= b \beta_v i_{hn} \phi_S - \tau_v i_v \\
\frac{ds_{hn}}{dt} &= \mu_h + \varepsilon s_{hr} - \tau_h s_{hn} - \alpha s_{hn} - b \beta_h \phi_I s_{hn} \\
\frac{ds_{hr}}{dt} &= \alpha s_{hn} - \varepsilon s_{hr} - \tau_h s_{hr} \\
\frac{di_{hn}}{dt} &= b \beta_h \phi_I s_{hn} + \varepsilon i_{hr} - \tau_h i_{hn} - \alpha i_{hn} - \gamma i_{hn} \\
\frac{di_{hr}}{dt} &= \alpha i_{hn} - \varepsilon i_{hr} - \tau_h i_{hr} - \gamma i_{hr} \\
\frac{dr_{hn}}{dt} &= \gamma (i_{hn} + i_{hr}) + \varepsilon r_{hr} - \tau_h r_{hn} - \alpha r_{hn} \\
\frac{dr_{hr}}{dt} &= \alpha r_{hn} - \varepsilon r_{hr} - \tau_h r_{hr}
\end{align*}
\]

#### 2.2 Basic Reproduction Ratio ($R_0$)

The basic reproduction ratio $R_0$ represents the expected number of secondary cases produced by a typical infected individual during its entire period of infectiousness in a completely susceptible population [11]. If $R_0 < 1$, the virus will not spread. If $R_0 > 1$, the virus will spread [12]. In this model, the value of $R_0$ is determined by defining the Next Generation Matrix [13] from the constructed compartments of the infected population.
where

\[ NGM_r = \begin{bmatrix} 0 & 0 & b\beta_h\mu_v(e+\tau_h) \\ \frac{b\beta_v\mu_e(e+\tau_h)}{N_h\tau_d(e+\tau_h)-\alpha e} & 0 & \frac{b\beta_h\mu_u(e+\tau_h)}{N_h\tau_d(e+\tau_h)-e} \\ \frac{b\beta_v\mu_e(\alpha+\varepsilon+\tau_h)}{N_h\tau_d(\alpha+\varepsilon+\tau_h)-\alpha e} & \frac{b\beta_h\mu_u(\alpha+e+\tau_h)}{N_h\tau_d(\alpha+e+\tau_h)-e} & 0 \end{bmatrix}. \]

Furthermore, the largest eigenvalue of the \( NGM_r \) is the basic reproduction number with repellent

\[ R_{0r} = \frac{b^2\beta_h\beta_v\mu_e(e+\tau_h)(\varepsilon+\gamma+\tau_h)}{(\gamma+\tau_h)(\alpha+\varepsilon+\tau_h)(\alpha+\varepsilon+\gamma+\tau_h)}. \]  

(17)

\( R_{0r} \) is the basic reproduction ratio \( R_0 \), which is reviewed with the effect of repellent and is expressed as Equation (17). This parameter \( R_{0r} \) can be used to estimate whether a new infection may end up in an epidemic and to estimate the severity of the epidemic when no treatment takes place.

### 2.3 Equilibrium Points

The equilibrium point is where the system stays stable, without any changes in subpopulation over time [14]. There are two types of the equilibriums, namely disease-free equilibrium and endemic equilibrium.

#### Disease-Free Equilibrium

This condition occurs when there is no infection [15], so \( i_{hn}(t) = i_{hr}(t) = i_v(t) = 0 \). Then the Equation (9) - Equation (16) has a disease-free equilibrium

\[ P_0 = \left( \frac{\mu_h(e+\tau_h)}{\tau_h(\alpha+\varepsilon+\tau_h)}, \frac{\alpha\mu_h}{\tau_h(\alpha+\varepsilon+\tau_h)}, 0, 0, 0, 0, \frac{\mu_v}{\omega_v}, 0 \right). \]  

(18)

To analyze the stability of the disease-free equilibrium, the Jacobi matrix from the model, which is evaluated around the point \( P_0 \), is defined as

\[ J_0 = \begin{bmatrix} -\alpha - \tau_h & \varepsilon & 0 & 0 & 0 & 0 & 0 & -\frac{b\beta_h\mu_u(e+\tau_h)}{\tau_h(\alpha+\varepsilon+\tau_h)} \\ \alpha & -\varepsilon - \tau_h & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & -\alpha - \gamma - \tau_h & \varepsilon & 0 & 0 & 0 & 0 \\ 0 & 0 & \alpha & -\varepsilon - \gamma - \tau_h & 0 & 0 & 0 & 0 \\ 0 & 0 & \gamma & \gamma & -\alpha - \tau_h & \varepsilon & 0 & 0 \\ 0 & 0 & 0 & 0 & \alpha & -\varepsilon - \tau_h & 0 & 0 \\ 0 & 0 & -\frac{b\beta_v\mu_e}{\omega_v} & 0 & 0 & 0 & -\tau_v & 0 \\ 0 & 0 & \frac{b\beta_v\mu_e}{\omega_v} & 0 & 0 & 0 & 0 & -\tau_v \end{bmatrix}. \]

(19)

The disease-free equilibrium point in Equation (18) will be locally asymptotically stable if all the real part of eigen values matrix in Equation (19) are negative and this condition is satisfied when

\[ R_{0r} < \tau_v \text{ and } R_{0r} < \sqrt{\tau_v(\varepsilon+\gamma+\tau_h)} \left( \frac{\tau_v}{\alpha+\varepsilon+\gamma+\tau_h} + \frac{\alpha+\varepsilon+\gamma+\tau_h}{\gamma+\tau_h} \right). \]

#### Endemic Equilibrium

This situation occurs when the infection spreads in population [15] so that \( i_{hn}(t) \neq 0, i_{hr}(t) \neq 0 \), and \( i_v(t) \neq 0 \). Let \( P_E \) is the endemic equilibrium point of model in Equation (9) - Equation (16). Then, \( P_E \) can be expressed as:

\[ P_E = \left( S_{hn}^E, S_{hr}^E, i_{hn}^E, i_{hr}^E, r_{hn}^E, r_{hr}^E, S_v^E, i_v^E \right) \]  

(20)

where

\[ S_{hn}^E = \frac{m_1(\varepsilon+\tau_h)}{w_1(\varepsilon+\gamma+\tau_h)}. \]
\[
\begin{align*}
s^*_h &= \frac{am_1}{w_1(\epsilon + \gamma + \tau_h)} \\
i^*_h &= \frac{m_2}{w_1(\gamma + \tau_h)(\epsilon + \alpha + \gamma + \tau_h)} \\
i^*_r &= \frac{am_2}{w_1(\epsilon + \tau_h)(\alpha + \epsilon + \gamma + \tau_h)} \\
s^*_h &= \frac{ym_2(\epsilon + \tau_h)}{w_1(\gamma + \tau_h)(\alpha + \epsilon + \gamma + \tau_h)(\epsilon + \gamma + \tau_h)} \\
i^*_r &= \frac{m_2\alpha}{w_1(\gamma + \tau_h)(\alpha + \epsilon + \gamma + \tau_h)(\epsilon + \gamma + \tau_h)} \\
s^*_v &= \frac{w_1(\gamma + \tau_h)(\alpha + \epsilon + \gamma + \tau_h)}{b\beta_1w_2} \\
i^*_v &= \frac{m_2}{\tau_1w_2}
\end{align*}
\]

and
\[
\begin{align*}
m_1 &= \tau_v(b\beta_1\mu_h(\epsilon + \gamma + \tau_h) + \tau_v(\gamma + \tau_h)(\alpha + \epsilon + \gamma + \tau_h)) \\
m_2 &= b^2\beta_1\beta_2\mu_h\mu_v(\epsilon + \gamma + \tau_h)(\epsilon + \gamma + \tau_h) - \tau_h\tau_v(\gamma + \tau_h)(\alpha + \epsilon + \gamma + \tau_h)(\alpha + \epsilon + \gamma + \tau_h) \\
w_1 &= b\beta_1(b\beta_1\mu_h(\epsilon + \tau_h) + \tau_h\tau_v(\alpha + \epsilon + \gamma + \tau_h)) \\
w_2 &= b\beta_1(\epsilon + \tau_h)(\beta_1\mu_h(\epsilon + \gamma + \tau_h) + \tau_v(\alpha + \epsilon + \gamma + \tau_h)).
\end{align*}
\]

To analyze the stability of the endemic equilibrium, the Jacobi matrix from the model, which is evaluated around the point \(P_\epsilon\), is defined as:
\[
J_\epsilon = \begin{pmatrix}
\frac{-bf_hm_2}{\tau_1w_2} - \alpha - \tau_h & \epsilon & 0 & 0 & 0 & 0 & 0 & -\frac{\tau_tw_2}{w_1(\epsilon + \gamma + \tau_h)} \\
\alpha & -\epsilon - \tau_h & 0 & 0 & 0 & 0 & 0 & \frac{\tau_tw_2}{w_1(\epsilon + \gamma + \tau_h)} \\
\frac{bf_2m_2}{\tau_1w_2} & 0 & -\alpha - \gamma - \tau_h & \epsilon & 0 & 0 & 0 & 0 \\
0 & 0 & \alpha & -\epsilon - \gamma - \tau_h & 0 & 0 & 0 & 0 \\
0 & 0 & \gamma & \gamma & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & \alpha & -\epsilon - \tau_h & 0 & 0 \\
0 & 0 & -\frac{\rho}{w_2} & 0 & 0 & 0 & -\frac{m_2}{\rho} - \tau_v & 0 \\
0 & 0 & \frac{\rho}{w_2} & 0 & 0 & 0 & \frac{m_2}{\rho} & -\tau_v
\end{pmatrix}
\]

where \(\rho = w_1(\gamma + \tau_h)(\alpha + \epsilon + \gamma + \tau_h)\). The endemic equilibrium in Equation (20) will be locally asymptotically stable if all the real parts of eigen values matrix in Equation (21) are negative, and this condition is satisfied when
\[
\frac{\tau_v}{\sqrt{(\gamma + \tau_h)(\alpha + \epsilon + \gamma + \tau_h)}} < R_{0r} < \frac{\tau_v}{\sqrt{\frac{(\epsilon + \tau_h)(\alpha + \epsilon + 2\tau_h)}{(\gamma + \tau_h)(\alpha + \epsilon + \tau_h)(\alpha + \epsilon + \gamma + \tau_h)}}}
\]

2.4 Optimal Control

Given the disease model Equation (9-16), we want to design the repellent treatment rate \(u_1\) for the human population and the proportion of providing a campaign \(u_2\) about the importance of mosquito repellent for susceptible humans \(s_{nh}\), such that we minimize the number of infected humans without repellent \(i_{hn}\). Assuming that healthy humans who receive the campaign immediately become aware of the need to use mosquito repellent regularly, this population is classified as a recovered population.
Let \( \bar{x} = (s_v, i_v, s_h, s_{hr}, i_h, i_{hr}, r_h, r_{hr})^T \) and the dynamical model with repellent control is expressed as \( \dot{\bar{x}} = (f_1(\bar{x}), f_2(\bar{x}), f_3(\bar{x}), f_4(\bar{x}), f_5(\bar{x}), f_6(\bar{x}), f_7(\bar{x}), f_8(\bar{x})) \) and defined as:

\[
\begin{align*}
\frac{ds_v}{dt} &= f_1(\bar{x}) = \mu_v - \tau_v s_v - b \beta_v i_{hn} s_v N_v / N_h \\
\frac{di_v}{dt} &= f_2(\bar{x}) = b \beta_v i_{hn} s_v N_v / N_h - \tau_v i_v \\
\frac{ds_{hn}}{dt} &= f_3(\bar{x}) = \mu_h (1 - u_2) + \varepsilon s_{hr} - \tau_h s_{hn} - \alpha s_{hn} u_1 - b \beta_h s_{hn} / N_h \\
\frac{di_{hn}}{dt} &= f_5(\bar{x}) = b \beta_h s_{hn} / N_h + \varepsilon i_{hr} - \tau_h i_{hn} - \alpha i_{hn} u_1 - \gamma i_{hn} \\
\frac{di_{hr}}{dt} &= f_6(\bar{x}) = \alpha i_{hn} u_1 - \varepsilon i_{hr} - \tau_h i_{hr} - \gamma i_{hr} \\
\frac{dr_{hn}}{dt} &= f_7(\bar{x}) = \gamma (i_{hn} + i_{hr}) + \varepsilon r_{hr} - \tau_h r_{hn} - \alpha r_{hn} u_1 \\
\frac{dr_{hr}}{dt} &= f_8(\bar{x}) = \alpha r_{hn} u_1 + \mu u_2 - \varepsilon r_{hr} - \tau_h r_{hr} 
\end{align*}
\]

To find a suitable compromise between the minimal number of infected individuals and the costs of the campaign, we consider the following cost-functional

\[
J(u_1, u_2) = \min_{u_1, u_2} \int_{t_0}^{t_{end}} [A i_{hn} + Bu_1^2 + Cu_2^2] dt
\]

where feasible control input set is written as \( \bar{u} = \{(u_1, u_2) : 0 \leq u_1 \leq 1 \text{ and } 0 \leq u_2 \leq 1 \} \). The weighting parameter \( A \) is used for the state variables \( \bar{x} \) in Equation (22) - Equation (29) and the weighting parameters \( B \) and \( C \) are used for the control variables \( \bar{u} = (u_1, u_2) \). Since we are mainly interested in minimizing the number of the infected human \( i_{hn} \), we set \( A > 0 \). On the other hand, we want to minimize the costs of repellent and campaign. The costs of the treatment use are more-or-less proportional to the repellent rates hence we also choose \( B, C > 0 \) as usual. According to Equation (30) and \( \bar{\lambda} = (\lambda_1, \lambda_2, \lambda_3, \lambda_4, \lambda_5, \lambda_6, \lambda_7, \lambda_8)^T \) as costate or adjoint variables, we define the Hamiltonian function as:

\[
H(\bar{x}, \bar{u}, \bar{\lambda}, t) = A i_{hn} + Bu_1^2 + Cu_2^2 + \bar{\lambda}^T \bar{\dot{x}}
\]

**Proposition 1.** Consider \( \bar{x} = (s_v, i_v, s_h, s_{hr}, i_h, i_{hr}, r_h, r_{hr})^T \) as state variables and \( \bar{u} = (u_1, u_2)^T \) as control variables. If the objective function is defined as in Equation (30), then the optimal control solution must exist, such that \( J(u_1^*, u_2^*) = \min J(u_1, u_2) \).

**Proof.** Optimal control solution exists if these four conditions hold:

1. The state variables and the corresponding control variables are non-empty sets.
2. Suppose that \( \Gamma = \{(u_1, u_2) | 0 \leq u_1 \leq u_1^{max}, 0 \leq u_2 \leq u_2^{max}\} \). Hence, \( \Gamma \) is closed and convex.
3. The model Equation (22-29) are nonlinear and depend on the control variables.
4. Suppose that the objective function of system is defined as follows

\[
J(u) = \int_{t_0}^{T} L(x(t), u(t), t) dt = \int_{t_0}^{t_{end}} [A i_{hn} + Bu_1^2 + Cu_2^2] dt
\]

with \([t_0, T]\) is a time interval and \( L(x(t), u(t), t) \) is a weight function that depends on the state and the input at time interval \([t_0, T] \). Then, there are nonnegative constants \( l_1, l_2 \) and \( n > 1 \) so that the weight function \( L(x(t), u(t), t) \) is convex and satisfies

\[
L(x(t), u(t), t) \geq l_1 + l_2 (|u_1|^2 + |u_2|^2)^{\frac{n}{2}}
\]
Condition 1 is satisfied since the state and control variables are nonempty and finite with $s_v, s_{hn}, s_{hr} > 0$, $i_v, i_{hn}, i_{hr}, r_{vn}, r_{vh} > 0$, $0 \leq u_1 \leq 1$, and $0 \leq u_2 \leq 1$. Condition 2 is satisfied by the definition of $\Gamma$. From Condition 1, $u_1^{\max} = u_2^{\max} = 1$ and we can get $\Gamma = \{(u_1, u_2) | 0 \leq u_1 \leq 1, 0 \leq u_2 \leq 1\}$. Condition 3 is clearly satisfied, and the system in Equation (22) - Equation (29) depends on the control variables $u$. It will be shown that Condition 4 is satisfied. Note that, $L$ is clearly convex and depends on the control variables $u$. We have to choose nonnegative constants $l_1$ and $l_2$. Suppose that $l_1 = \min Al_{hn} \leq Al_{hn}$, with $l_{hn} > 0$ and $l_2 = \min (B, C)$ with $B, C > l_2$. With $n = 2 > 1$, we can get

$$L(x(t), u(t), t) = Al_{hn} + Bu_1^2 + Cu_2^2 \geq l_1 + l_2 (|u_1|^2 + |u_2|^2)$$

Consequently, $L$ is finite and Condition 4 is satisfied. The optimal control solution $u^*(t)$ must exist.

**Proposition 2.** If $(\dot{x}^*(t), \ddot{u}^*(t))$ is the optimal control solution with $x^* = (s_v^*, i_v^*, s_{hn}^*, s_{hr}^*, i_{hn}^*, i_{hr}^*, r_{vn}^*, r_{vh}^*)^T$ and $\ddot{u}^* = (u_1^*, u_2^*)^T$, then there is an adjoint variable $\ddot{x}^*(t)$ that satisfies the costate equations \( \ddot{x} = -\frac{\partial H}{\partial \dot{x}} \) with $\ddot{x} = (\lambda_1, \lambda_2, \lambda_3, \lambda_4, \lambda_5, \lambda_6, \lambda_7, \lambda_8)^T$ and expressed as:

\[
\begin{align*}
\lambda_1 &= -\frac{\partial H}{\partial s_v} = \lambda_1 \left( \tau_v + b\beta_v i_{hn} \frac{N_v}{N_h} \right) - \lambda_2 b\beta_v i_{hn} \frac{N_v}{N_h} \quad (31) \\
\lambda_2 &= -\frac{\partial H}{\partial i_v} = \lambda_2 \tau_v + \lambda_3 b\beta_h s_{hn} \frac{N_v}{N_h} - \lambda_5 b\beta_h s_{hn} \frac{N_v}{N_h} \quad (32) \\
\lambda_3 &= -\frac{\partial H}{\partial s_{hn}} = \lambda_3 \left[ \tau_h s_{hn} + au_1 - b\beta_h i_v \frac{N_v}{N_h} \right] - \lambda_4 a\mu u_1 - \lambda_5 b\beta_h i_v \frac{N_v}{N_h} \quad (33) \\
\lambda_4 &= -\frac{\partial H}{\partial s_{hr}} = -\lambda_3 \epsilon + \lambda_4 [a + \tau_h] \quad (34) \\
\lambda_5 &= -\frac{\partial H}{\partial i_{hn}} = \lambda_1 b\beta_v \frac{s_v N_v}{N_h} - \lambda_2 b\beta_v \frac{s_v N_v}{N_h} + \lambda_5 \left[ \tau_h + au_1 + \gamma \right] - \lambda_6 a\mu u_1 - \lambda_7 \gamma - A \quad (35) \\
\lambda_6 &= -\frac{\partial H}{\partial i_{hr}} = -\lambda_5 \epsilon + \lambda_6 [a + \tau_h + \gamma] - \lambda_7 \gamma \quad (36) \\
\lambda_7 &= -\frac{\partial H}{\partial r_{vn}} = \lambda_7 \left[ \tau_h + au_1 \right] - \lambda_9 a\mu u_1 \quad (37) \\
\lambda_8 &= -\frac{\partial H}{\partial r_{vh}} = -\lambda_7 \epsilon + \lambda_9 [a + \tau_h] \quad (38)
\end{align*}
\]

with $\dot{x}(T) = 0$ and the stationary the conditions $\frac{\partial H}{\partial \dot{u}} = 0$ satisfies

$$2Bu_1^* + s_{hn}(\lambda_4 - \lambda_3) + i_{hn}(\lambda_6 - \lambda_5) + r_{hn}(\lambda_8 - \lambda_7) = 0$$

$$2Cu_2^* - \lambda_3 \mu_1 + \lambda_8 \mu_1 = 0.$$

Then, we can obtain the optimal control solution

\[
\lambda_1^* = \max \left\{ \min \left\{ \frac{\alpha s_{hn}(\lambda_4 - \lambda_3) + i_{hn}(\lambda_6 - \lambda_5) + r_{hn}^*(\lambda_8 - \lambda_7)}{2B}, 0 \right\} \right\},
\]

\[
\lambda_2^* = \max \left\{ \min \left\{ \frac{(\lambda_3 - \lambda_8) \mu_1}{2C}, 1 \right\} \right\}.
\]

**Proof.** Note that the Hamiltonian function is used to determine $\dot{\ddot{x}}(t)$ that satisfies Equation (31-38) by considering $\dot{x}(t) = \ddot{x}(t)$, then the Hamiltonian function is differentiated against $\ddot{x}$. Afterward, the optimal control $\ddot{u}^*$ is obtained from these following steps:

First, substitute the values of $u_1^*$ and $u_2^*$ in Equation (39) - Equation (40) to the system in Equation (22) - Equation (29). Thus, a new Hamiltonian function $H^*$ at $(\ddot{x}, \ddot{u}, \lambda, t)$ is obtained as follows
\[ H^* = A i_{hn}^* + B \left( \max \left\{ \min \left\{ \frac{\alpha [s_{hn}(\lambda_3 - \lambda_4) + i_{hn}(\lambda_5 - \lambda_6) + r_{hn}(\lambda_7 - \lambda_8)]}{2B}, 1 \right\}, 0 \right\} \right)^2 \]

\[ + C \left( \max \left\{ \min \left\{ \frac{(\lambda_3 - \lambda_5)\mu_h}{2C}, 1 \right\}, 0 \right\} \right)^2 + \lambda_1 \frac{ds_v^*}{dt} + \lambda_2 \frac{di_v^*}{dt} + \lambda_3 \frac{ds_{hn}}{dt} + \lambda_4 \frac{ds_{hr}}{dt} + \lambda_5 \frac{di_{hn}}{dt} + \lambda_6 \frac{di_{hr}}{dt} + \lambda_7 \frac{dr_{hn}}{dt} + \lambda_8 \frac{dr_{hr}}{dt}. \]

3. RESULTS AND DISCUSSION

In this model, the endemic status of the disease depends on the transmission toward incoming viruses to the individual from mosquito bites. The larger the invasion rate \( \beta_h \) and the loss of repellent protection \( \epsilon \), the chance is higher to catch the disease. On the contrary, with the increase in the rate of using repellent for human populations, the risk of infection is lower. Based on the model in Equation (9) - Equation (16) with parameter values from Table 2 and initial values of \( s_{hn} = 0.60, s_{hr} = 0.30, i_{hn} = 0.06, i_{hr} = 0.03, s_v = 0.67, \) and \( i_v = 0.33 \), the variation for \( \alpha, \beta_h \) and \( \epsilon \) shows in Figure 2, Figure 3 and Figure 4.

The variation of the parameter will measure how sensitive or influential the parameter is in the spread of the disease for dynamics of \( s_{hn} \) and \( i_{hn} \). Figure 2 shows the dynamics of \( s_{hn} \) and \( i_{hn} \) for different rate of using repellent, \( \alpha \). An increase in \( \alpha \) leads to a decline in the dynamic of \( s_{hn} \). The behavior of \( i_{hn} \) increases until maximum value and after the peak of infection occurs, \( i_{hn} \) will decrease more significantly as \( \alpha \) increases.

(a) Susceptible Human without Repellent, (b) Infected Human without Repellent
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Figure 3 shows the dynamics of $s_{hn}$ and $i_{hn}$ for different contact rate between susceptible human without repellent with infected mosquitoes, $\beta_h$. An increase of $\beta_h$ will decrease $s_{hn}$ more rapidly. For high value of $\beta_h$, there is a high value of $i_{hn}$ in early, but it also will decrease $i_{hn}$ more rapidly. The rate of loss of repellent protection, $\epsilon$, represents the duration for which repellents provide protection against mosquito bites. A lower rate implies an extended period of effectiveness. As observed in Figure 4, a longer duration of repellent protection leads to increase $s_{hn}$ and $i_{hn}$.

Numerical simulations of the optimal control problem are carried out for two scenarios, namely, the case of prevention to control the campaign rate for healthy humans and the case of epidemic reduction to control the usage rate of repellent. The case of prevention occurs at the early state of transmission, i.e., when the number of infected people is still relatively small before the start of the repellent treatment. In the case of epidemic reduction, the repellent treatment starts during the outbreak period, i.e., when the number of infected people is significantly large. As an initial condition, we assume that in the field, the ratio between the mosquito and human population is almost the same. With this ratio, the corresponding basic reproductive ratio is about 1.44 before the start of the repellent treatment. This condition leads the population to endemic equilibrium.

Figure 5 - Figure 7 shows the results for controlling repellent treatment rate ($u_1$) for human populations. Figure 5 shows the dynamic of $s_{hn}$ and $s_{hr}$ with and without control $u_1$. From Figure 5(a), $s_{hn}$ with control decreases slower by 1.425% than without control. While in Figure 5(b), $s_{hr}$ with control...
decreases to 6.066% compared to without control. Therefore, with control of repellent treatment rate \((u_1)\), the potential for transmission in healthy human populations will tend to have a small chance.

**Figure 5. Numerical Simulation Result of Controlling the Usage Rate of Repellent**

(a) Susceptible Human without Repellent, (b) Susceptible Human with Repellent

**Figure 6. Numerical Simulation Result of Controlling the Usage Rate of Repellent**

(a) Infected Human without Repellent, (b) Infected Human with Repellent

Figure 6 shows the dynamic of \(i_{hn}\) and \(i_{hr}\) with and without control \(u_1\). Figure 6(a) shows that after the peak of infection, \(i_{hn}\) without control decreases faster by about 0.443% than the \(i_{hn}\) with control. Meanwhile, Figure 6(b) shows \(i_{hr}\) with control decreases to 0.146% compared to the \(i_{hr}\) without control.

**Figure 7.** shows the dynamic of \(r_{hn}\) and \(r_{hr}\) with and without control \(u_1\). From Figure 7(a), \(r_{hn}\) with control increases to 23.965% compared to the \(r_{hn}\) without control. Meanwhile, Figure 7(b) shows \(r_{hr}\) with control decreases to 19.420% from \(r_{hr}\) without control and as time goes by, the decrease will be even greater. Therefore, control of repellent treatment rate \((u_1)\) can work effectively to minimize the infected population and to maximize the recovered population.
Figure 7. Numerical Simulation Result of Controlling the Usage Rate of Repellent
(a) Recovered Human without Repellent, (b) Recovered Human with Repellent

Figure 8 - Figure 10 shows the dynamics for human population if the control campaign applied and implies the repellent used regularly ($u_2$) since early of infection period. Figure 8 shows the dynamic of $s_{hn}$ and $s_{hr}$ without and with control $u_2$. From Figure 8(a), $s_{hn}$ with control increases slower by 2.613% than $s_{hn}$ without control. And Figure 8(b) shows that $s_{hr}$ with control decreases quite large by 9.381% compared to the $s_{hr}$ without control. As a result, the successful campaign to use repellent in the early infection period is effective in reducing the potential for transmission. Therefore, the number of healthy humans who use repellents will increase.

Figure 8. Numerical Simulation Result of Controlling the Proportion Healthy Humans Who Have Impacted by Campaign and Used Repellent Regularly
(a) Susceptible Human without Repellent, (b) Susceptible Human with Repellent
Figure 9. Numerical Simulation Result of Controlling the Proportion Healthy Humans Who Have Impacted by Campaign and Used Repellent Regularly
(a) Infected Human without Repellent, (b) Infected Human with Repellent

Figure 9 shows the dynamic of \( i \) and \( i_{hr} \) without and with control \( u_2 \). Figure 9(a) shows that \( i_{hn} \) with control increases to 0.389% at the peak of infection. After that, \( i_{hn} \) with control decreased slower by 0.647% compared to \( i_{hn} \) without control. While Figure 9(b) shows that \( i_{hr} \) with control decreases to 0.255% compared to \( i_{hr} \) without control. With the decreasing of \( i_{hr} \), the control of campaign rate for using repellent in the early of infection period will reduce the potential of virus transmission.

Figure 10 shows the dynamic of \( r_{hn} \) and \( r_{hr} \) without and with control \( u_2 \). From Figure 10(a), \( r_{hn} \) with control increases to 28.961% compared to \( r_{hn} \) without control. While Figure 10(b) shows that \( r_{hr} \) with control decreases to 21.201% until the proportion limit to zero. The control of campaign rate implies the repellent used regularly \((u_2)\) since early of infection period is more work effectively to minimize the infected population and maximize the recovered population.

Figure 11- Figure 13 shows the dynamic for a human population when the combination of control \( u_1 \) and control \( u_2 \) applied to the systems. Combination control is applied to compare which strategy can provide optimal effectiveness in reducing the infected human population for both prevention and treatment control scenarios. However, combination control will result in a larger cost function compared to implementing a single control \( u_1 \) and \( u_2 \) respectively.
Figure 11 shows the dynamic of $s_{hn}$ and $s_{hr}$ without and with combination control $(u_1, u_2)$. From Figure 11(a), $s_{hn}$ with control increases slower by 1.434% than the $s_{hn}$ without control. Meanwhile, Figure 11(b) shows that the combination control $(u_1, u_2)$ causes the $s_{hr}$ with control decreases quite large by 5.881% compared to the $s_{hr}$ without control. Combination control $(u_1, u_2)$ which applied to susceptible human population has the same dynamics with single control $u_1$ and $u_2$. The potential for transmission in healthy human populations will also tend to have a small chance. However, the effect of combination control $(u_1, u_2)$ causes the smallest decreasing compared to single control $u_1$ and $u_2$.

Figure 12 shows the dynamic of $i_{hn}$ and $i_{hr}$ without and with combination control $(u_1, u_2)$. From Figure 12(a), $i_{hn}$ with control increases to 0.075% at the peak of infection. After that, $i_{hn}$ decreases slower by 0.438% than the $i_{hn}$ without controls. Meanwhile, Figure 12(b) shows that the combination control $(u_1, u_2)$ cause the $i_{hr}$ with control decreases to 0.131% compared to the $i_{hr}$ without controls. Figure 13 shows the dynamic of $r_{hn}$ and $r_{hr}$ without and with combination control $(u_1, u_2)$. Figure 13(a) shows that $r_{hn}$ with control increases to 23.611% compared to the $r_{hn}$ without controls. While Figure 13(b) shows that the combination control $(u_1, u_2)$ causes the $r_{hr}$ with control decreases to 19.186%. Dynamic of infected and recovered population with combination control $(u_1, u_2)$ has the almost same percentage effect with dynamic of infected and recovered population with single control $u_1$. 

Figure 11. Numerical Simulation Result of Controlling the Usage Rate of Repellent and the Proportion of Healthy Humans Who Have Impacted by Campaign and Used Repellent Regularly
(a) Susceptible Human without Repellent, (b) Susceptible Human with Repellent

Figure 12. Numerical Simulation Result of Controlling the Usage Rate of Repellent and the Proportion of Healthy Humans Who Have Impacted by Campaign and Used Repellent Regularly
(a) Infected Human without Repellent, (b) Infected Human with Repellent
Figure 13. Numerical Simulation Result of Controlling the Usage Rate of Repellent and the Proportion of Healthy Humans Who Have Impacted by Campaign and Used Repellent Regularly
(a) Recovered Human without Repellent, (b) Recovered Human with Repellent

Table 3. Comparison of Objective Function Values for Three Strategies

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Objective Function Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controlling the Rate of Repellent Treatment $u_1$</td>
<td>2.9936</td>
</tr>
<tr>
<td>Controlling the Proportion of Healthy Humans Who Have Impacted by Campaign and Used Repellent Regularly $u_2$</td>
<td>2.2695</td>
</tr>
<tr>
<td>Combination Control $u_1$ and $u_2$</td>
<td>3.0808</td>
</tr>
</tbody>
</table>

Table 3 shows the accumulative objective function for each control strategy, both single control $u_1$ and $u_2$ and combination control ($u_1$, $u_2$). Based on the value of the objective function in Table 3, control $u_1$, i.e. the proportion of healthy humans who have been impacted by the campaign and used repellent regularly is the most effective strategy to suppress the spread of dengue fever with an accumulative cost is 2.2695.

4. CONCLUSIONS

Based on the analysis and numerical simulations, we can conclude the effect of parameters on the dengue fever spread model and the most effective strategy to suppress the spread of dengue fever. First, a higher transmission rate of dengue leads to a faster spread of the disease. Second, a faster recovery rate from the disease slows down its transmission. Third, increased human use of repellent results in a slower rate of dengue transmission. Fourth, a longer duration of repellent protection also contributes to a slower rate of dengue spread. Fifth, controlling the proportion of healthy people who have the campaign's effect and use repellent regularly is the most effective strategy to suppress the spread of dengue fever. This implies that using repellents with long-lasting protection can serve as a control strategy to reduce or manage the spread of dengue.

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