Optimal control on the mathematical models of dengue epidemic by giving vaccination and repellent strategies

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Abstract. Dengue is a very dangerous disease in the tropic and subtropic areas. This disease is transmitted through the bite of an infected female Aedes Aegypti. In this study, optimal control of the dengue model will be discussed by applying 3 strategies, there are vaccination, repellent, and both of them. A dengue epidemic model was built without control with assumptions given by facts obtained by researchers. Then from the model, the equilibrium point is formulated and the equilibrium point stability of the model is evaluated. The next discussion is to determine the optimal control of the dengue epidemic model and minimize the costs of implementing controls. Numerical simulation results showed that 3rd strategy, which is vaccination and repellent, can reduce the subpopulations number of humans infected by dengue with the minimum cost of implementing control.

1. Introduction
Dengue is a very dangerous disease in the tropic and subtropic areas. This disease is transmitted through the bite of an infected female Aedes Aegypti. There are 4 dengue virus serotypes, there are DEN 1-DEN 4. Afterward, dengue also strongly influenced by rainfall, temperature, and the distribution of Aedes Aegypti mosquitoes [3]. In general, female Aedes Aegypti bit during the day (9:00-10:00) and in the afternoon (16:00-17:00). During fever, between 2-10 days, there is viremia (a virus in the blood). If the Aedes Aegypti is vulnerable to bite an infected person at the viremia stage, the mosquito will be infected.

Many researchers have tried to create drugs that are suitable for treating dengue but they have not succeeded yet [1]. The most effective way to overcome the mosquito bites is through vaccination (immunity) and repellent. The Possibility of an individual being vaccinated in background from flavivirus immunity [7]. Cell CD8+T is the forerunner to dengue vaccination [6]. There is an increased need for improved and affordable insect repellents to reduce transmission of dengue [8]. Repellent is a type of household pesticide used to protect the body from mosquito bites that containing DEET (N, N-diethyl-meta-toluamide). DEET is a synthetic chemical that firstly used by the United States Department of Agriculture in 1946 to protect workers from mosquito bites [2]. DEET can damage the central nervous system of insects such as mosquitoes [4]. The spray-on repellents DEET is effective in repelling Aedes Aegypti [5].

Optimal Control Theory is a method to determine control of the dynamic systems for a certain period by minimizing the performance index. The dengue epidemic model is built without control with the assumptions given to the facts obtained by researchers. The ultimate purpose of control is to find minimum time and with minimum cost of the control effort [9]. Then in this study, the dengue model will be given optimal control with vaccination and repellent strategies. The next discussion will be model analysis, determination of optimal control and numerical simulation.
2. Mathematical Model

The mathematical model of the dengue epidemic was built by the researchers based on the following assumptions. First, human populations of all ages are assumed to be uniformly distributed. Third, the human population using repellent will be separated in special compartments which will not have contact with mosquitoes at all. Fourth, the changes in the increase in the human population and mosquito constant are not influenced by environmental factors. Fifth, there is vaccination in vulnerable humans. Sixth, the use of repellent is only done once a day and it is given regularly. Seventh, the use of repellent is applied to the parts of the body that are vulnerable to being bitten by mosquitoes and under the instructions for using mosquito repellent. Eighth, there is no death due to dengue virus. Finally, there is only one DEN-3 virus, so the individual who has recovered will be immune to the virus. The mathematical model is based on the transmission diagram shown in Figure 1. Table 1 shows the variables and parameters. The dengue epidemic model of mathematics is given in Eq. (1).

\[ \text{Equation 1} \]

Table 1. Variables and Parameters Description

| Symbol   | Description                                                      | Dimension / Value |
|----------|------------------------------------------------------------------|-------------------|
| \( S_{hn}(t) \) | Number of Susceptible Human Non Repellent                        | Human             |
| \( S_{hr}(t) \) | Number of Susceptible Human With Repellent                       | Human             |
| \( I_{hn}(t) \) | Number of Infected Human Non Repellent                           | Human             |
| \( I_{hr}(t) \) | Number of Infected Human With Repellent                          | Human             |
| \( R_{hn}(t) \) | Number of Recovery Human Non Repellent                           | Human             |
| \( R_{hr}(t) \) | Number of Recovery Human With Repellent                          | Human             |
| \( S_v(t) \) | Number of Susceptible Mosquitos                                  | Mosquitos         |
| \( I_v(t) \) | Number of Infected Mosquitos                                     | Mosquitos         |
| \( \mu_h \) | The assumed proportion of mosquitoes is equal to the proportion of natural deaths in the mosquito | 0.000042          |
| \( \mu_v \) | The proportion of natural deaths in the mosquito                  | 0.03              |
| \( b \) | Average mosquito bites in humans per day                         | 1                 |
| \( \beta_v \) | Proportion of dengue virus transmission from humans to mosquitoes | 0.375             |
| \( \beta_h \) | Proportion of dengue virus transmission from mosquitoes to humans | 0.375             |
| \( \alpha \) | The proportion of humans using repellent per day                  | 0.01              |
| \( \epsilon \) | The proportion of drop out is repellent in humans per day         | 0.001             |
| \( \gamma_h \) | The proportion of humans recovered per day                        | 0.3               |
To simplify the equation system (1) it can be done by normalizing with assuming the proportion number of the individuals in each group can be expressed as, so the normalized population means $s_{hn} + s_{hr} + i_{hn} + i_{hr} + r_{hn} + r_{hr} = 1$ and $s_s + i_s = 1$. Then with $\phi = \frac{I_s}{N_p}$, the new equation systems obtained as follows.

3. Analysis of The Model
3.1. Equilibrium Point
The equilibrium point is a situation where a system is balanced or in a situation that not changes from time to time. The system of the equilibrium point (2) can be obtained when $\frac{ds_{hn}}{dr} = 0, \frac{ds_{hr}}{dr} = 0, \frac{di_{hn}}{dr} = 0, \frac{di_{hr}}{dr} = 0, \frac{dr_{hn}}{dr} = 0, \frac{dr_{hr}}{dr} = 0, \frac{ds_s}{dr} = 0, \frac{di_s}{dr} = 0$, and $\frac{ds_i}{dr} = 0$. 

\[
\begin{aligned}
\frac{dS_{hn}}{dr} &= (1 - p) \mu_h N_h + \alpha S_{hr} - \left( \mu_h + \frac{b \beta_h I_{hn}}{N_h} + \varepsilon \right) S_{hn} \\
\frac{dS_{hr}}{dr} &= \varepsilon S_{hn} - (\mu_h + \alpha) S_{hr} \\
\frac{dI_{hn}}{dr} &= \frac{b \beta_h I_{hn} S_{hn}}{N_h} + \alpha I_{hr} - (\mu_h + \gamma_h + \varepsilon) I_{hn} \\
\frac{dI_{hr}}{dr} &= \varepsilon I_{hn} - (\mu_h + \gamma_h + \alpha) I_{hr} \\
\frac{dR_{hn}}{dr} &= p \mu_h + (I_{hn} + I_{hr}) \gamma_h + \alpha R_{hr} - (\mu_h + \varepsilon) R_{hn} \\
\frac{dR_{hr}}{dr} &= \varepsilon R_{hn} - (\mu_h + \alpha) R_{hr} \\
\frac{dS_s}{dr} &= \mu_s N_s - \left( \mu_s + \frac{b \beta_s I_{hn}}{N_h} \right) S_s \\
\frac{dI_s}{dr} &= \mu_s N_s S_s - \mu_s I_s \\
\end{aligned}
\]
3.1.1. Disease-Free Equilibrium Point  The disease-free equilibrium point stated that the balance situation means no infection when \( i_m(t) = 0 \). For example, the disease-free equilibrium point is

\[
P_0 = \left( s_{hm}^*, s_{hr}^*, i_{hm}^*, i_{hr}^*, r_{hm}^*, r_{hr}^*, s_v^*, i_v^* \right),
\]

then it is obtained

\[
P_0 = \left( \frac{\mu_h + \alpha}{\alpha + \varepsilon + \mu_h}, \frac{\varepsilon}{\alpha + \varepsilon + \mu_h}, 0, 0, 0, 0, 1, 0 \right).
\]

3.1.2. Endemic Equilibrium Point  Endemic equilibrium point stated that the balance situation is when the disease spreads to an area when \( i_m(t) > 0 \). For example, the endemic equilibrium point is \( P_0 = \left( s_{hm}^*, s_{hr}^*, i_{hm}^*, i_{hr}^*, r_{hm}^*, r_{hr}^*, s_v^*, i_v^* \right) \) so it is obtained

\[
\begin{align*}
    s_{hm}^* &= \left( \mu_h + \alpha \right) \left( \gamma_h + \alpha + \varepsilon + \mu_h \right) \mu_h + b\beta, \mu_h \left( \mu_h + \gamma_h + \alpha \right) \\
    &\quad \left( \mu_h + \gamma_h + \alpha \right) \beta_t \left( \mu_h^2 + \left( b\rho\beta_h + \alpha + \varepsilon \right) \mu_h + \alpha b\rho\beta_h \right) b \\
    s_{hr}^* &= \frac{\varepsilon \left( \mu_h + \gamma_h \right) \left( \gamma_h + \alpha + \varepsilon + \mu_h \right) \mu_h + b\beta}{\left( \mu_h + \gamma_h + \alpha \right) \beta_t \left( \mu_h^2 + \left( b\rho\beta_h + \alpha + \varepsilon \right) \mu_h + \alpha b\rho\beta_h \right) b} \\
    i_{hm}^* &= \frac{\beta_t \left( \mu_h + \gamma_h \right) \left( \gamma_h + \alpha + \varepsilon + \mu_h \right) \mu_h + b\beta}{\left( \mu_h + \gamma_h + \alpha \right) \beta_t \left( \mu_h^2 + \left( b\rho\beta_h + \alpha + \varepsilon \right) \mu_h + \alpha b\rho\beta_h \right) b} \\
    i_{hr}^* &= \frac{\varepsilon \gamma_h \left( \mu_h + \gamma_h \right) \beta_t \left( \mu_h^2 + \left( b\rho\beta_h + \alpha + \varepsilon \right) \mu_h + \alpha b\rho\beta_h \right) b}{\left( \mu_h + \gamma_h + \alpha \right) \beta_t \left( \mu_h^2 + \left( b\rho\beta_h + \alpha + \varepsilon \right) \mu_h + \alpha b\rho\beta_h \right) b} \\
    r_{hm}^* &= \frac{\mu_t \left( \mu_h + \gamma_h \right) \left( \gamma_h + \alpha + \varepsilon + \mu_h \right) \mu_h + b\beta}{\left( \mu_h + \gamma_h + \alpha \right) \beta_t \left( \mu_h^2 + \left( b\rho\beta_h + \alpha + \varepsilon \right) \mu_h + \alpha b\rho\beta_h \right) b} \\
    r_{hr}^* &= \frac{\mu_t \left( \mu_h + \gamma_h \right) \left( \gamma_h + \alpha + \varepsilon + \mu_h \right) \mu_h + b\beta}{\left( \mu_h + \gamma_h + \alpha \right) \beta_t \left( \mu_h^2 + \left( b\rho\beta_h + \alpha + \varepsilon \right) \mu_h + \alpha b\rho\beta_h \right) b} \\
    s_v^* &= \frac{\beta_t \left( \mu_h + \alpha \right) \left( \gamma_h + \alpha + \varepsilon + \mu_h \right) \mu_h + b\beta}{\left( \mu_h + \gamma_h + \alpha \right) \beta_t \left( \mu_h^2 + \left( b\rho\beta_h + \alpha + \varepsilon \right) \mu_h + \alpha b\rho\beta_h \right) b} \\
    i_v^* &= \frac{\beta_t \left( \mu_h + \alpha \right) \left( \gamma_h + \alpha + \varepsilon + \mu_h \right) \mu_h + b\beta}{\left( \mu_h + \gamma_h + \alpha \right) \beta_t \left( \mu_h^2 + \left( b\rho\beta_h + \alpha + \varepsilon \right) \mu_h + \alpha b\rho\beta_h \right) b}
\end{align*}
\]

with \( w_1 = b^2 \rho b\beta_h \beta \left( \mu_h + \alpha \right) \left( \mu_h + \gamma_h + \alpha \right) \) and \( w_2 = \left( \mu_h + \gamma_h \right) \left( \alpha + \varepsilon + \mu_h \right) \left( \gamma_h + \alpha + \varepsilon + \mu_h \right) \mu_v \).

So, the endemic equilibrium point is said to be exist when \( w_1 > w_2 \).

3.1.3. Basic Reproduction Ratio and Stable Point Analysis  Basic reproduction numbers are numbers that represent many vulnerable individuals who can suffer from illness due to infected individuals. Basic reproduction numbers are denoted by \( R_0 \). Basic reproduction numbers can be determined by Next Generation Matrix (NGM). This matrix is constructed from compartments which are spreading infection in the population. Furthermore, the calculation of basic reproduction numbers is based on the linearization of disease-free equilibrium points and NGM is obtained as follows.

\[
NGM = \begin{bmatrix}
0 & \rho b\beta_h \left( \mu_h + \alpha \right) \\
\beta_t & \frac{\mu_h^2 + \left( b\rho\beta_h + \alpha + \varepsilon \right) \mu_h + \alpha b\rho\beta_h}{\mu_h + \gamma_h + \alpha} \\
\mu_h + \gamma_h + \varepsilon & 0
\end{bmatrix}
\]

Then we can obtain \( R_0 \) as follows.
\[ R_0 = \frac{N_b^2 \beta_h \beta_v}{N_h \mu_h \gamma_h + \mu_h} \]  

(5)

If \( R_0 < 1 \), so the disease free equilibrium point is asymptotically stable and the disease does not spread in the population, but if \( R_0 > 1 \) then the disease-free equilibrium point is unstable and the disease can spread in the population.

4. Optimal Control

Optimal control of vaccination and repellent for humans will be applied to the equation system (2) and aims to minimize the number of infected individuals.

To minimize the number of infected individuals control action is given by controlling action is as follows.

\[
\begin{align*}
\frac{ds_{hn}}{dt} &= (1-u_1)\mu_h + \alpha u_2 s_{hr} - (\mu_h + \phi b \beta_h + \varepsilon) s_{hn} \\
\frac{ds_{hr}}{dt} &= \varepsilon s_{hn} - (\mu_h + \alpha u_2) s_{hr} \\
\frac{di_{hr}}{dt} &= \phi b \beta_h s_{hn} + \alpha u_2 i_{hr} - (\mu_h + \gamma_h + \varepsilon) i_{hr} \\
\frac{di_{hn}}{dt} &= \varepsilon i_{hn} - (\mu_h + \mu + \gamma_h + \varepsilon) i_{hn} \\
\frac{dr_{hr}}{dt} &= u_1 \mu_h + (i_{hn} + i_{hr}) \gamma_h + \alpha u_2 r_{hr} - (\mu_h + \varepsilon) r_{hn} \\
\frac{dr_{hn}}{dt} &= \varepsilon r_{hn} - (\mu_h + \varepsilon) r_{hn} \\
\frac{dv}{dt} &= \mu_v - (\mu_v + b \beta_v) i_v \\
\frac{di_v}{dt} &= b \beta_v i_{hr} s_v - \mu_i i_v
\end{align*}
\]

(6)

The optimal control problem in the equation system consists of minimizing the objective functions given as follows.

\[
J = \min_{u_1, u_2} \int_0^{t_f} \left( A_1 + B_1 u_1^2 + B_2 u_2^2 \right) dt
\]

with \( 0 \leq t \leq t_f, 0 \leq u_1 \leq 1, \) and \( 0 \leq u_2 \leq 1, \) \( t_f \) is the end of the time, \( A = i_{hn} \) is the number of infected individuals, \( B_1 \) is the cost of vaccinating, and \( B_2 \) is the cost of giving repellent to humans.

The Hamiltonian function is firstly defined as follows.

\[
H = A_1 + B_1 u_1^2 + B_2 u_2^2 + \lambda_1 \left[ (1-u_1) \mu_h + \alpha u_2 s_{hr} - (\mu_h + \phi b \beta_h + \varepsilon) s_{hn} \right] + \lambda_2 \left[ \varepsilon s_{hn} - (\mu_h + \alpha u_2) s_{hr} \right] + \lambda_3 \phi b \beta_h i_s h + \alpha u_2 i_{hr} - (\mu_h + \gamma_h + \varepsilon) i_{hn} + \lambda_4 \left[ \varepsilon i_{hn} - (\mu_h + \gamma_h + \varepsilon) i_{hn} \right] + \lambda_5 \left[ u_1 \mu_h + (i_{hn} + i_{hr}) \gamma_h + \alpha u_2 r_{hr} - (\mu_h + \varepsilon) r_{hn} \right] + \lambda_6 \left[ \varepsilon r_{hn} - (\mu_h + \varepsilon) r_{hn} \right] + \lambda_7 \left[ \mu_v - (\mu_v + b \beta_v) i_v \right] + \lambda_8 \left[ b \beta_v i_{hr} s_v - \mu_i i_v \right]
\]

To complete the system (6) and minimize \( J \)’s objective function, the minimum principle of Pontryagin will be used, and with \( 0 \leq t \leq t_f, 0 \leq u \leq 1 \) so that it is obtained.
\[ u_1^*(t) = \min \left\{ 1, \max \left\{ 0, \frac{\left( \lambda_i(t) - \lambda_2(t) \right) \mu_i}{2B_1} \right\} \right\} \]

\[ u_2^*(t) = \min \left\{ 1, \max \left\{ 0, \frac{\left( \lambda_2(t) - \lambda_3(t) \right) \alpha s_i r_i + \left( \lambda_3(t) - \lambda_4(t) \right) \alpha s_i r_i + \left( \lambda_4(t) - \lambda_5(t) \right) \alpha n_i r_i}{2B_2} \right\} \right\} \]

With transversal condition is \( \lambda_i(t_f) = 0, i = 1, \ldots, 8. \)

5. Numerical Simulation

This section illustrates the dynamics of an infected human compartment and scenarios for controlling of Dengue. Optimal control simulation can be done by using the backward-forward sweep algorithm. The steps of the backward-forward sweep algorithm are as follows.

1. Determines the initial value, with \( 0 \leq t \leq 20 \), and using parameter values are given in the table 1.
2. Made initial guesses \( u_1 \) and \( u_2 \).
3. Calculate the value \( s_{in}(i+1), s_{hr}(i+1), i_{in}(i+1), i_{hr}(i+1), r_{in}(i+1), r_{hr}(i+1), s_i(i+1), \)
and \( i_t(i+1) \).
4. with the initial value in step 1 using the 4 steps forward Runge Kutta.
5. Calculate the value \( \lambda_1(k-1), \lambda_2(k-1), \lambda_3(k-1), \lambda_4(k-1), \lambda_5(k-1), \lambda_6(k-1), \lambda_7(k-1), \lambda_8(k-1), \lambda_9(k-1), \lambda_10(k-1), \lambda_11(k-1), \lambda_12(k-1) \).
6. with transversal conditions use the 4 steps backward Runge Kutta method.
7. Check for convergence. If the value of the variables in the current and previous iterations is close enough, then the present value is the solution. If not, then go back to step 2.

In this case, 3 control strategies were applied for the dengue epidemic model with parameter values in the table as follows.

1. Strategy 1: the given control is only giving vaccinations to humans \( (u_1) \), with \( u_2 = 0 \).
2. Strategy 2: the given control is only giving repellent to humans \( (u_2) \), with \( u_1 = 0 \).
3. Strategy 3: the given controls are giving vaccinations and repellent to humans \( (u_1 \) and \( u_2) \).

The result of the simulation is as follows.

(a) Vaccination Control Graph
Figure 2. Strategy 1 on Vaccination Control Graph of Dengue Epidemic Model

In figure 2 the optimal control value is $u_1^*$ in strategy 1 decreases slowly until the time $t \in (0.20]$, and the control value at that time is $u_1^* = 0$. This means that initially the action of vaccination control was done fully and slowly decreases because the number of infected individuals slowly decreases, so the control value decreases gradually due to the decreasing value of the infected individuals.

Figure 3. Strategy 2 on Repellent Control Graph
In figure 3 the optimal control value is $u_2^*$ in strategy 2 decreases slowly until the time $t \in (0.20]$, and the control value at that time is $u_2^* = 0$. This means that initially the action of repellent control was done fully and slowly decreases because the number of infected individuals slowly decreases, so the control value decreases gradually due to the decreasing value of the infected individuals.

![Dengue Model with Vaccination and Repellent Control Simulation](image1.png)

(a) Vaccination and Repellent Control Graph

In figure 4 the optimal control value is $u_1^*, u_2^*$ in strategy 3 decreases slowly until the time $t \in (0.20]$, and the control value at that time is $u_1^*, u_2^* = 0$. This means that initially the action of vaccination and repellent control was done fully and slowly decreases because the number of infected individuals slowly decreases, so the control value decreases gradually due to the decreasing value of the infected individuals.

![Dengue Model Without Control Simulation](image2.png)

(b) $i_{hn}$ Graph of time $t$ (day)

![Dengue Model Without Control Simulation](image3.png)

(c) $i_{hr}$ Graph of time $t$ (day)

**Figure 4.** Strategy 3 on Vaccination and Repellent Control Graph

In figure 4 the optimal control value is $u_1^*, u_2^*$ in strategy 3 decreases slowly until the time $t \in (0.20]$, and the control value at that time is $u_1^*, u_2^* = 0$. This means that initially the action of vaccination and repellent control was done fully and slowly decreases because the number of infected individuals slowly decreases, so the control value decreases gradually due to the decreasing value of the infected individuals.

**Table 2. Comparison on The Number of Infected Individuals in The 20th day**

| Condition                  | Number of Infected Human (Non Repellent $i_{hn}$) | Number of Infected Human (With Repellent $i_{hr}$) |
|----------------------------|---------------------------------------------|---------------------------------------------|
| Without Control            | 0.0236                                      | 0.0007820                                   |
| Strategy 1: Vaccination Control | 0.0074                                      | 0.0002744                                   |
| Strategy 2: Repellent Control       | 0.0074                                      | 0.0002728                                   |
| Strategy 3: Vaccination and Repellent Control | 0.0070                                      | 0.0002708                                   |
Note that, at the end of the observation (day 20) the given control can reduce the number of infected people by using repellent or not. Vaccination control in strategy 1 was able to reduce the number of people who did not use repellent as much as 68.6% and reduce the number of infected people using repellent as much as 64.9%. The distribution of repellent control in strategy 2 was able to reduce the number of people who did not use repellent as much as 68.6% and reduce the number of infected people using repellent as much as 65%. The distribution of vaccination and repellent control in strategy 3 was able to reduce the number of people not using repellent as much as 70% and reduce the number of infected people using repellent as much as 65.3%. Based on the mean of the reduced number of infected people it can be concluded that strategy 3 is quite effective in minimizing the number of infected people.

Furthermore, the cost effectiveness of the three control strategies will be analyzed based on the objective function value (cost function).

| Table 3. Value on the Cost Function of 3 Control Strategies |
|-------------------------------------------------------------|
| Cost Function Value | Strategy 1 | Strategy 2 | Strategy 3 |
|---------------------|------------|------------|------------|
|                     | 0.173      | 0.1722     | 0.1720     |

Based on the cost function value obtained, giving vaccination control and repellent control provides a cost that is quite effective for the dengue epidemic model.

6. Conclusion

Based on the results of the discussion and numerical simulation described, it can be concluded that the dengue epidemic model can be created by adding vaccination control to vulnerable individuals and repellent control to each individual. If the two controllers are applied together, it will be effective enough to minimize the number of people who do not use repellent as much as 70% and 65.3%. Furthermore, based on the value of the objective function obtained, it can minimize the costs of vaccination and repellent.

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