Optimal control of a mathematical model for Japanese encephalitis transmission

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Optimal control of a mathematical model for Japanese encephalitis transmission

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Abstract. Japanese encephalitis (JE) is a vector-borne disease that causes encephalitis mostly children in Asia and livestock. A mathematical model can be used to predict JE spread in the future. In this paper, we analysed a mathematical model of JE transmission. We also applied several optimal control variables such as vaccination and treatment to the human population, insecticide to mosquito population, and vaccination to pig population. Based on the analysis results, we obtained two equilibriums, namely disease-free equilibrium and endemic equilibrium. The existence and stability of the equilibriums depended on R_0 (basic reproduction ratio). The disease-free equilibrium is locally asymptotically stable if $R_0 < 1$, while the endemic equilibrium is locally asymptotically stable if $R_0 > 1$. Furthermore, we determined the existence of the optimal control variables by Pontryagin Maximum Principle. Numerical simulation showed that the control strategies are effective to minimize the number of active JE in human, mosquito and pig population.

1. Introduction

Japanese encephalitis (JE) is an infectious disease that causes encephalitis mostly in children (under 15 years old) and livestock [1]. The disease is maintained in mosquitoes and vertebrate hosts life cycle. Culex tritaeniorrhynchus is the most particular disseminator that generally lives in rice cultivation and pig farming. Pig and wading birds serve as virus reservoirs. Humans are dead-end hosts of JE disease. Furthermore, humans do not acquire high concentrations of JE virus in their bloodstreams to infect feeding mosquitoes. JE disease may begin when the infected pig is bitted by Culex tritaeniorrhynchus, then the mosquitoes can transmit JE virus to human or livestock [2]. The presence of JE is recognized as a public health issue in the world, due to the number of cases that significantly increase. It is estimated that among 68,000 JE cases every year, there are approximately 13,600 to 20,400 death cases caused by JE infection. JE is difficult to diagnose due to most JE infections are mild or without obvious symptoms. The common symptoms are fever and headache. The case-fatality rate can be as high as 30% among those with disease symptoms. For those who survive, JE disease can leave suffer permanent intellectual, behavior or neurological problems such as paralyses, recurrent seizures or the inability to speak [3].

JE is a mosquito-borne flavivirus and belongs to the same genus as dengue, yellow fever, and West Nile viruses. It was firstly reported in Japan in 1871. Now, JE was being endemic in 24 countries in South-East Asia and Western Pacific. It is estimated that more than 3 billion people risk of infection

[3]. In Indonesia, the highest case was found in Bali in 2016 that approximately reached 226 from 326 cases. It was related with a number of wet rice field and pig farm around living place, especially in wet season. Based on the most cases, JE primarily affects children. Nearly 85% of cases of JE in 2016 were reported to the children under 15-year-old [4]. Mostly adults in endemic areas have a natural immunity that not infected again. This disease may affect individuals of any age, especially when the virus enters a new area [3].

Until now, there is no cure for JE patients. However, supportive treatment can relieve symptoms and stabilize the patient. The prime intervention of JE is vaccination, besides vector and environment control. Although the number of JE-confirmed cases is low, vaccination could be considered as a strategy to prevent the JE disease. All visitors to JE-endemic areas should take the vaccination to prevent a risk of JE [4].

A mathematical modeling is a powerful tool to understand the dynamics of epidemic infection. In recent years, there has been an increasing interest in JE transmission model. The authors in [5] have developed a mathematical model for JE transmission in two populations, both human and vertebrate reservoir. Then, they extend a model of JE in three populations include human, vertebrate reservoir and vector [6]. The authors in [7] incorporate the environment factor to JE transmission model. Recently, De et al [8] developed a JE spread model with various control. In [8], the authors presented a JE model in nine compartments that arranged of human, mosquito and pig population. Furthermore, De et al [8] applied for a vaccination, insecticide, and medicine as fixed and variable controls.

In this paper, we proposed the dynamic model of JE transmission that previously developed by De et al in [8] with ignoring the vaccinated human and pigs compartment. We also incorporate several control variables such as vaccination and medicine to the human, insecticide to the mosquito, and vaccination to pig populations. The structure of the paper is arranged as follows. In section 2, we introduce the description of the model formulation. In section 3, we analyze the stability of the equilibriums of the model. In section 4, we carry out the solution of the optimal control problem. In section 5, we show some numerical insight of the dynamic model with and without optimal control variables. In the last section, we give a conclusion.

2. Model formulation

In this section, we propose a mathematical model of JE transmission. In this model, the population is classified into three classes, namely the population of human, mosquito, and pig. Furthermore, the human population is divided into three classes, namely susceptible human class (S_h), infected human class (I_h) and recovered human class (R_h). The mosquito population is also classified into two classes, namely susceptible mosquito class (S_m) and infected mosquito class (I_m). Similarly, the pig population is also partitioned into two class, namely susceptible pig class (S_p) and infected pig class (I_p). Therefore, total of each population are $N_h = S_h + I_h + R_h$, $N_m = S_m + I_m$ and $N_p = S_p + I_p$.

It is assumed that recruitment rate into susceptible humans (Λ), the total population of mosquito (N_m) and the total population of pig (N_p) are constant. The transmission of JE disease occurs because of the interaction among mosquitoes, humans, and pigs. The mosquitoes and pigs can transmit to each other. While JE spread to human due to the susceptible human is bitten by the infected mosquitoes. Recovery humans have temporary immunity so that they can return to being susceptible to JE.

We derive our model on transmission diagram as in Figure 1.

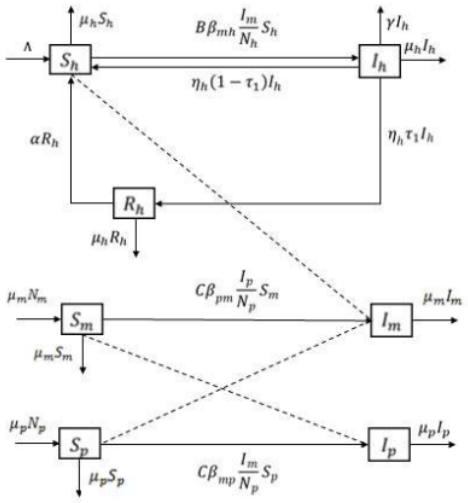

Figure 1. Japanese encephalitis transmission diagram.

The model is as follows:

$$\begin{aligned}
\frac{dS_h}{dt} &= \Lambda - B\beta_{mh}\frac{I_m}{N_h}S_h - \mu_h S_h + \eta_h(1-\tau_1)I_h + \alpha R_h \\
\frac{dI_h}{dt} &= B\beta_{mh}\frac{I_m}{N_h}S_h - \eta_h I_h - \mu_h I_h - \gamma I_h \\
\frac{dR_h}{dt} &= -\mu_h R_h - \alpha R_h + \eta_h\tau_1 I_h \\
\frac{dS_m}{dt} &= \mu_m N_m - \mu_m S_m - C\beta_{pm}\frac{I_p}{N_p}S_m \\
\frac{dI_m}{dt} &= C\beta_{pm}\frac{I_p}{N_p}S_m - \mu_m I_m \\
\frac{dS_p}{dt} &= \mu_p N_p - C\beta_{mp}\frac{I_m}{N_p}S_p - \mu_p S_p \\
\frac{dI_p}{dt} &= C\beta_{mp}\frac{I_m}{N_p}S_p - \mu_p I_p
\end{aligned} \tag{1}$$

which $S_h, I_h, R_h, S_m, I_m, S_p, I_p \geq 0$. All parameters in the model (1) are also assumed non-negative. The description of parameters used in model (1) could be seen in Table 1.

3. Analysis of the model

In this section, we discuss the stability of the equilibriums of the model (1). The equilibriums are obtained by equating all equations of the model (1) to zero. Model (1) has the disease-free equilibrium $E_0 = (S_h, I_h, R_h, S_m, I_m, S_p, I_p) = \left(\frac{\Lambda}{\mu_h}, 0, 0, N_m, 0, N_p, 0\right)$. It is noted that if the mortality rate due to disease (γ) is zero, then we have $\lim_{t\to\infty} N_h(t) = \frac{\Lambda}{\mu_h}$.

We determine the basic reproduction ratio (R_0) using the next-generation matrix method [9]. This ratio describes the number of secondary case of a primary case during the infectious period due to the infection [10]. For the next-generation matrix method [9], we have the infected compartments (I_h, I_m, I_p). The Jacobian matrices $\mathbb{F}$ (of the new infection terms) and $\mathbb{V}$ (of the transmission term) evaluated at E_0, are given, respectively, by;

$$\mathbb{F} = \begin{pmatrix} 0 & B\beta_{mh} & 0 \\ 0 & 0 & \frac{C\beta_{pm}N_m}{N_p} \\ 0 & C\beta_{mp} & 0 \end{pmatrix} \text{ and } \mathbb{V} = \begin{pmatrix} \eta_h + \mu_h + \gamma & 0 & 0 \\ 0 & \mu_m & 0 \\ 0 & 0 & \mu_p \end{pmatrix}.$$

Table 1. Description of parameters of model (1)

Parameter	Description
$\boldsymbol{\Lambda}$	Recruitment rate of human population
$\boldsymbol{\mu_h}$	Natural death rate of human population
$\boldsymbol{\mu_m}$	Natural and death rate of mosquito population
$\boldsymbol{\mu_p}$	Natural and death rate of pig population
$\boldsymbol{\beta_{mp}}$	Disease transmission rate from I_m to S_p
$\boldsymbol{\beta_{pm}}$	Disease transmission rate from I_p to S_m
$\boldsymbol{\tau_1}$	Natural recovered rate of human population
$\boldsymbol{\gamma}$	Mortality rate due to disease
$\boldsymbol{B}$	Average number of bites on human by mosquito population per day
$\boldsymbol{\beta_{mh}}$	Disease transmission rate from I_m to S_h
$\boldsymbol{\eta_h}$	Recovery rate of human population
$\boldsymbol{\alpha}$	Immunity lose rate of human population
$\boldsymbol{C}$	Average number of bites on pig by mosquito population per day

The basic reproduction ratio of model (1) is the spectral radius of the matrix $\mathbb{F}\mathbb{V}^{-1}$. Hence, we have the basic reproduction ratio as

$$R_0 = \sqrt{\frac{C^2 N_m \beta_{mp} \beta_{pm}}{\mu_m \mu_p N_p}}.$$

The following theorem gives the stability of the disease-free equilibrium.

Theorem 1 *The disease-free equilibrium* E_0 *is locally asymptotically stable if* $R_0 < 1$ *and it is unstable if* $R_0 > 1$.

Proof. By linearizing model (1) at the disease-free equilibrium E_0, we find the following eigenvalues: $\lambda_1 = -\mu_h, \lambda_2 = -(\mu_h + \alpha)$, $\lambda_3 = -(\eta_h + \mu_h + \gamma)$, $\lambda_4 = -\mu_m$, $\lambda_5 = -\mu_p$ and the roots of quadratic equation $\left(\lambda^2 + (\mu_m + \mu_p)\lambda + \mu_m\mu_p(1 - T_0)\right) = 0$, where $T_0 = {R_0}^2$. By applying Routh-Hurwitz criteria, the quadratic equation will has negative roots or complex root with negative real part if $T_0 < 1$ or equivalently $R_0 < 1$. It is obvious that all eigenvalues are negative or or complex eigenvalues with negative real part if $R_0 < 1$. Therefore the disease-free equilibrium E_0 is locally asymptotically stable if $R_0 < 1$. Otherwise, it is unstable.

The model (1) also has the endemic equilibrium $E_1 = (S_h^*, I_h^*, R_h^*, S_m^*, I_m^*, S_P^*, I_p^*)$. All of the components of E_1 are non-zero and depend on equilibrium state I_m^*. The equilibrium state I_m^* is the only positive root of quadratic equation $aI_m^2 + bI_m + c = 0$ if $R_0 > 1$. The coefficient a is always positive, while the coefficient c is equal to $-\mu_m^2\mu_p^4N_p^6(T_0 - 1)$ where ${T_0 = R_0}^2$. Hence, the coefficient c has a negative value if $R_0 > 1$. Therefore, model (1) has an endemic equilibrium if $R_0 > 1$. It is not easy to prove analytically the stability of the equilibrium E_1. Numerical simulation of the model (1), depicted in Figure 2, show that the equilibrium E_1 is locally asymptotically stable if $R_0 > 1$. The parameter values of the simulation are given in Table 2. In this case, the value of the basic reproduction ratio is $R_0 = 2.0125 > 1$. We use three different initial values for the simulation. Those orbits converge to the same point as time evolves.

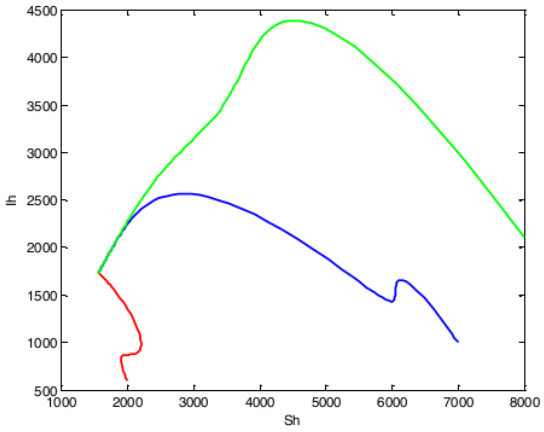

Figure 2. Phase portrait of model (1) in $S_h - I_h$ plane.

Table 2. Parameters value for simulations

Parameter	Value	Ref.
$\boldsymbol{\Lambda}$	150	[7]
$\boldsymbol{\mu_h}$	1/65	[7]
$\boldsymbol{\mu_m}$	0.3	[7]
$\boldsymbol{\mu_p}$	0.1	[7]
$\boldsymbol{B}$	3.2	Assumed
$\boldsymbol{\beta_{mh}}$	0.5	Assumed
$\boldsymbol{\eta_h}$	0.2	Assumed
$\boldsymbol{\alpha}$	0.2	Assumed
C	0.9	[8]
$\boldsymbol{\beta_{mp}}$	0.3	[8]
$\boldsymbol{\beta_{pm}}$	0.3	[8]
$\boldsymbol{N_m}$	5000	Assumed
$\boldsymbol{N_p}$	3000	Assumed
$\boldsymbol{\tau_1}$	0.5	[8]
$\boldsymbol{\gamma}$	0.05	Assumed

4. Analysis of optimal control problem

In this section, we analyze the optimal control of the JE transmission model. The control variables to be applied in this study are vaccination (u_1) and treatment (u_2) to the human population, insecticide to mosquito population (u_3) and vaccination to pig population (u_4). The JE transmission model with control variables are as following:

$$\begin{aligned}
\frac{dS_h}{dt} &= \Lambda - (1-u_1)\mu_h B\beta_{mh}\frac{I_m}{\Lambda}S_h - \mu_h S_h + \eta_h(1-\tau_1)I_h + \delta u_2(1-\tau_2)I_h + \alpha R_h \\
\frac{dI_h}{dt} &= (1-u_1)\mu_h B\beta_{mh}\frac{I_m}{\Lambda}S_h - \eta_h I_h - \mu_h I_h - \gamma I_h - \delta u_2 I_h \\
\frac{dR_h}{dt} &= -\mu_h R_h - \alpha R_h + \eta_h\tau_1 I_h + \delta u_2\tau_2 I_h \\
\frac{dS_m}{dt} &= \mu_m N_m - \mu_m S_m - C\beta_{pm}\frac{I_p}{N_p}S_m - \theta u_3 S_m \\
\frac{dI_m}{dt} &= C\beta_{pm}\frac{I_p}{N_p}S_m - \mu_m I_m - \theta u_3 I_m \\
\frac{dS_p}{dt} &= \mu_p N_p - (1-u_4)C\beta_{mp}\frac{I_m}{N_p}S_p - \mu_p S_p \\
\frac{dI_p}{dt} &= (1-u_4)C\beta_{mp}\frac{I_m}{N_p}S_p - \mu_p I_p
\end{aligned} \tag{2}$$

The parameter δ means the effectiveness of treatment, τ_2 represents the recovery rate of the infected human due to the treatment, while θ denotes rate in which mosquito die by insecticide. Furthermore, the objective cost function of JE transmission model with optimal control applies followed as:

$$min\, J = \int_0^{t_f}\left[I_h(t) + I_m(t) + I_p(t) + 0.5(B_1{u_1}^2 + B_2{u_2}^2 + B_3{u_3}^2 + B_4{u_4}^2)\right]\, dt \tag{3}$$

where $0 \le u_i(t) \le 1$ for $t \in [0, t_f]$, $i = 1,2,3,4$, while B_1, B_2, B_3, B_4 are positive constants for vaccination effort of human, treatment of human, insecticide, and vaccination effort of pig, respectively. The quadratic forms of the control cost are taken, stated in [11, 12]. The term ${B_1u_1}^2, {B_2u_2}^2, {B_3u_3}^2$, and ${B_4u_4}^2$ describe the cost associated with the vaccination for human, treatment for human, insecticide, and vaccination for pig, respectively.

In this section, necessary conditions for determining the optimal control ${u_1}^*, {u_2}^*, {u_3}^*$ and ${u_4}^*$ that satisfy the condition (3) with constrain model (2) will be solved by the Pontryagin's Maximum Principle [13]. The principle converts (2) and (3) into a problem of minimizing a Hamiltonian H, with respect to (u_1, u_2, u_3, u_4) such that

$$H = I_h(t) + I_m(t) + I_p(t) + 0.5(B_1{u_1}^2 + B_2{u_2}^2 + B_3{u_3}^2 + B_4{u_4}^2) + \sum_{i=1}^{7}\phi_i f_i \tag{4}$$

where f_i is the right hand side of model (2) which is the i-th state variable equation. The variables $\phi_i, i = 1,2,\dots,7$ are called adjoint variables and they satisfy the following co-state equations:

$$\begin{aligned}
\dot{\phi_1} &= -\frac{\partial H}{\partial S_h} = (\phi_2 - \phi_1)(1-u_1)\mu_h B\beta_{mh}\frac{I_m}{\Lambda} - \phi_1\mu_h \\
\dot{\phi_2} &= -\frac{\partial H}{\partial I_h} = \phi_1(\eta_h(1-\tau_1) + \delta u_2(1-\tau_2)) - \phi_2(\eta_h + \mu_h + \gamma + \delta u_2) + \phi_3(\eta_h\tau_1 + \delta u_2\tau_2) \\
\dot{\phi_3} &= -\frac{\partial H}{\partial R_h} = \phi_1\alpha - \phi_3(\mu_h + \alpha) \\
\dot{\phi_4} &= -\frac{\partial H}{\partial S_m} = (\phi_5 - \phi_4)C\beta_{pm}\frac{I_p}{N_p} - \phi_4(\mu_m + \theta u_3) \\
\dot{\phi_5} &= -\frac{\partial H}{\partial I_m} = (\phi_2 - \phi_1)(1-u_1)\mu_h B\beta_{mh}\frac{S_h}{\Lambda} - \phi_5(\mu_m + \theta u_3) + (\phi_7 - \phi_6)(1-u_4)C\beta_{mp}\frac{S_p}{N_p} \\
\dot{\phi_6} &= -\frac{\partial H}{\partial S_p} = (\phi_7 - \phi_6)(1-u_4)C\beta_{mp}\frac{I_m}{N_p} - \phi_6\mu_p \\
\dot{\phi_7} &= -\frac{\partial H}{\partial I_p} = (\phi_5 - \phi_4)C\beta_{pm}\frac{S_m}{N_p} - \phi_7\mu_p
\end{aligned} \tag{5}$$

Steps to obtain the optimal controls $u = ({u_1}^*, {u_2}^*, {u_3}^*, {u_4}^*)$ are as following [14].

1. Minimize the Hamiltonian function H with respect to u that is $\frac{\partial H}{\partial u} = 0$ (stationary condition). Here we found that

$$u_1^* = \begin{cases} 0 & \text{If } \frac{(\phi_2-\phi_1)\mu_h B\beta_{mh} I_m S_h}{B_1\Lambda} \le 0 \\ \frac{(\phi_2-\phi_1)\mu_h B\beta_{mh} I_m S_h}{B_1\Lambda} & \text{if } 0 < \frac{(\phi_2-\phi_1)\mu_h B\beta_{mh} I_m S_h}{B_1\Lambda} < 1 \\ 1 & \text{if } \frac{(\phi_2-\phi_1)\mu_h B\beta_{mh} I_m S_h}{B_1\Lambda} \ge 1 \end{cases}$$

$$u_2^* = \begin{cases} 0 & \text{if } \frac{(\phi_2-\phi_1)\delta I_h + (\phi_1-\phi_3)\delta\tau_2 I_h}{B_2} \le 0 \\ \frac{(\phi_2-\phi_1)\delta I_h + (\phi_1-\phi_3)\delta\tau_2 I_h}{B_2} & \text{if } 0 < \frac{(\phi_2-\phi_1)\delta I_h + (\phi_1-\phi_3)\delta\tau_2 I_h}{B_2} < 1 \\ 1 & \text{if } \frac{(\phi_2-\phi_1)\delta I_h + (\phi_1-\phi_3)\delta\tau_2 I_h}{B_2} \ge 1 \end{cases}$$

$$u_3^* = \begin{cases} 0 & \text{if } \frac{(\phi_4 S_m + \phi_5 I_m)\theta}{B_3} \le 0 \\ \frac{(\phi_4 S_m + \phi_5 I_m)\theta}{B_3} & \text{if } 0 < \frac{(\phi_4 S_m + \phi_5 I_m)\theta}{B_3} < 1 \\ 1 & \text{if } \frac{(\phi_4 S_m + \phi_5 I_m)\theta}{B_3} \ge 1 \end{cases}$$

$$u_4^* = \begin{cases} 0 & \text{if } \frac{(\phi_7-\phi_6)C\beta_{mp} I_m S_p}{B_4 N_p} \le 0 \\ \frac{(\phi_7-\phi_6)C\beta_{mp} I_m S_p}{B_4 N_p} & \text{if } 0 < \frac{(\phi_7-\phi_6)C\beta_{mp} I_m S_p}{B_4 N_p} < 1 \\ 1 & \text{if } \frac{(\phi_7-\phi_6)C\beta_{mp} I_m S_p}{B_4 N_p} \ge 1 \end{cases}$$

2. Solving the system $\dot{x} = \frac{\partial H}{\partial \phi}$, which is model (2), where $x = (S_h, I_h, R_h, S_m, I_m, S_p, I_p)^T$, $\phi = (\phi_1, \phi_2, \dots, \phi_7)$ and initial condition x_0.
3. Solving the co-state system $\dot{\phi} = -\frac{\partial H}{\partial x}$, which is system (5), with the end condition $\phi_i(t_f) = 0, i = 1,2,\dots,7$.

Based on the steps above, the optimal control characterization $(u_1^*, u_2^*, u_3^*, u_4^*)$ is given by

$$u_1^* = \min\left(1, \max\left(0, \frac{(\phi_2-\phi_1)\mu_h B\beta_{mh} I_m S_h}{B_1\Lambda}\right)\right),$$

$$u_2^* = \min\left(1, \max\left(0, \frac{(\phi_2-\phi_1)\delta I_h + (\phi_1-\phi_3)\delta\tau_2 I_h}{B_2}\right)\right),$$

$$u_3^* = \min\left(1, \max\left(0, \frac{(\phi_4 S_m + \phi_5 I_m)\theta}{B_3}\right)\right),$$

$$u_4^* = \min\left(1, \max\left(0, \frac{(\phi_7-\phi_6)C\beta_{mp} I_m S_p}{B_4 N_p}\right)\right).$$

where $\phi_i, i = 1,2,\dots,7$ are the solutions of co-state system (5).

By substituting optimal controls $(u_1^*, u_2^*, u_3^*, u_4^*)$, which is obtained from state system (2) and co-state system (5), we get the optimal system.

5. Numerical simulation

In this section, we give several numerical simulations of model (2) with and without control variables. We use an iterative scheme for solving the optimal system. The forward and backward Runge-Kutta methods of order 4 are adopted to solve the state and the co-state equations with the transversality conditions [15].

Using various combinations of the three controls at a time and four controls at a time, we investigate the following scenarios.

1. Combination of u_1, u_2 and u_3
2. Combination of u_1, u_2 and u_4
3. Combination of u_1, u_3 and u_4
4. Combination of u_2, u_3 and u_4
5. Combination of u_1, u_2, u_3 and u_4

Parameters used in these simulations could be seen in Table 2. We use the initial condition $S_h(0) = 7000$, $I_h(0) = 1000$, $R_h(0) = 600, S_m(0) = 2000$, $I_m(0) = 800$, $S_p(0) = 500$ and $I_p(0) = 250$, weighting constants $B_1 = 0.2$, $B_2 = 0.8, B_3 = 0.5$, and $B_4 = 0.1$ [8]. Here, we take 100 days for the time horizon.

In the first scenario, we used a combination of vaccination to human (u_1), treatment to human (u_2) and insecticide (u_3). Meanwhile, the vaccination to the pig (u_4) is not used. The profile of optimal controls of this scenario is plotted in Figure 3. It could be seen that in 100 days, both of the vaccination to human and insecticide control should be done intensively during the time observed, while the treatment to human should be done intensively for the first 25 days and then decreasing.

In the second scenario, we implemented a combination of vaccination to human (u_1), treatment to human (u_2) and vaccination to the pig (u_4). Meanwhile, the insecticide (u_3) is not applied. Profile of optimal controls of this scenario is plotted in Figure 4. It could be seen that in 100 days, both of the vaccination to human and vaccination to pig controls should be done intensively for the first 90 days and then decreasing, while the medicine to human takes 100% of the cost for the first 15 days and then decreasing.

In the third scenario, we employed a combination of vaccination to human (u_1), insecticide (u_3) and vaccination to the pig (u_4). Meanwhile, the medicine control (u_2) is not applied. Profile of optimal control of this scenario is plotted in Figure 5. It could be seen that in 100 days, the vaccination to human control should be done intensively for the first 85 days and then decreasing, while the insecticide just takes 100% of the cost for the first 35 days and then decreasing. The similar act to the vaccination to pig should be done intensively for 95 days at the first and then decreasing.

In the fourth scenario, a combination of medicine to human (u_2), insecticide (u_3) and vaccination to the pig (u_4) control are implemented. Meanwhile, the vaccination to human (u_2) is not used. The profile of optimal controls of this scenario is plotted in Figure 6. The treatment control to human should be done intensively for the first 45 days and then decreasing in 100 days, while the insecticide takes 100% of cost longer for the first 65 days and then decreasing. The similar act to the vaccination to pig should be done intensively for 95 days at the first and then decreasing.

In the last scenario, we used a combination of vaccination to human (u_1), treatment to human (u_2), insecticide (u_3) and vaccination to the pig (u_4) simultaneously. The profile of optimal control of this scenario is plotted in Figure 7. It could be seen that in 100 days, each of the vaccination and treatment to human should be done intensively for almost 85 and 15 days respectively and then decrease, while the insecticide should be done intensively for the first 45 days and then decreasing. Similarly to the vaccination to pig should be done 100% for 95 days and then decreasing.

The population dynamics of the infected human for different combinations of controls are shown in Figure 8, while the infected mosquito and pig population are given in Figure 9 and 10, respectively. From Figures 8-10, we observe that the various combinations of controls give a significant reduction of the infected human, mosquito, and pig population compared without controls. At the end of observation, all infected population tends to zero when the control strategies are applied to the system.

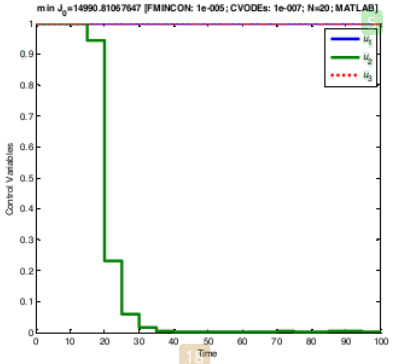

Figure 3. Profil of optimal controls u_1, u_2 and u_3.

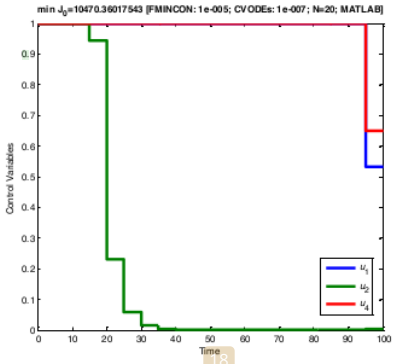

Figure 4. Profil of optimal controls u_1, u_2 and u_4.

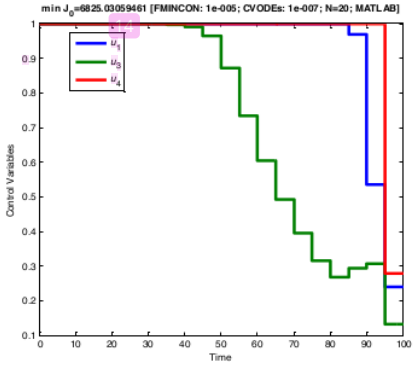

Figure 5. Profil of optimal controls u_1, u_3 and u_4.

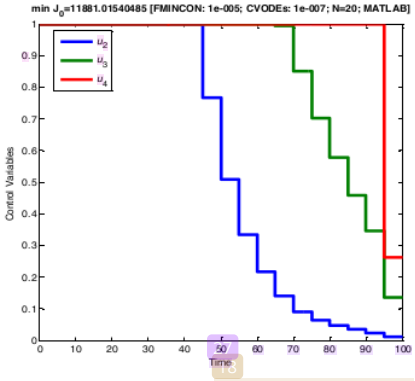

Figure 6. Profil of optimal controls u_2, u_3 and u_4.

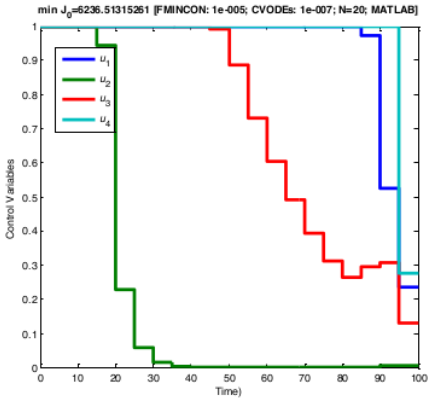

Figure 7. Profil of optimal controls u_1, u_2, u_3, and u_4

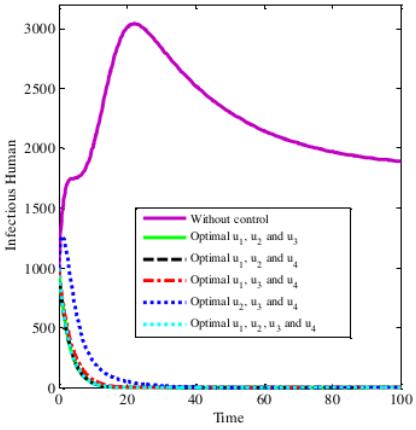

Figure 8. Dynamics of the infected human with and without controls.

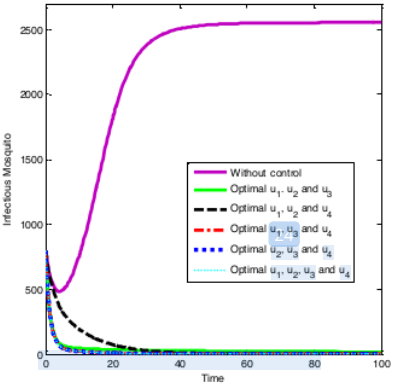

Figure 9. Dynamics of the infected mosquito with and without of controls.

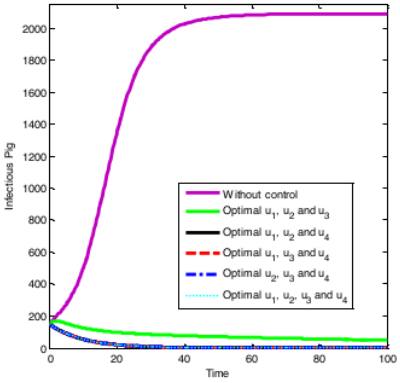

Figure 10. Dynamics of the infected pig with and without controls.

The optimal cost regarding the five scenarios could be seen in Table 3. The last scenario as the combination of all various controls gives the minimum cost.

Table 3. Optimal controls and their cost

Scenario	Optimal controls	Cost J
5	u_1, u_2, u_3 and u_4	6236.5132
3	u_1, u_3 and u_4	6852.0306
2	u_1, u_2 and u_4	10470.3602
4	u_2, u_3 and u_4	11881.0154
1	u_1, u_2 and u_3	14990.8107

6. Conclusion

In this paper, we have derived a mathematical model for Japanese encephalitis transmission. From the model, we found the basic reproduction ratios that determine the existence and stability of the equilibriums. We also found that the disease-free equilibrium is locally asymptotically stable if the ratio is less than one. It is contrast when the ratio is greater than one, then the disease will persist in the population. Then, the conditions for optimal control existence are analytically studied using the Pontryagin's Maximum Principle. In the numerical simulation, we used the combination of three controls at a time and the combination of four controls at a time to investigate and compare the effects of control applies on Japanese encephalitis elimination. It indicates that the best strategy is combination of the whole controls at one time.

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