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Optimal control of Zika virus infection by vector elimination, vector-to-human and human-to-human contact reduction

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Abstract

The recent outbreak of mosquito-borne Zika virus (ZIKV) in Brazil, with estimated cases surpassing 1.5 million, has gained attention due to its rapid spread and neurological complications associated with the infection such as microcephaly and Guillain-Barré syndrome. Beside vector transmission, primarily via *Aedes* mosquitoes, sexual transmission also contributes to the virus outbreak. The epidemiological patterns of these viruses suggest that Zika virus could cause other outbreaks, particularly in tropical regions with high vector concentration. To plan and prepare for a counter-control measure, it is important to study the previous cases. Hence, the control model is proposed from the deterministic model of Zika virus infection. Regarding control measures, the control functions for these strategies; vector elimination, vector-to-human contact reduction, and human-to-human contact reduction are introduced into the system. The necessary conditions for the optimal controls are determined using Pontryagin's maximum principle and the optimality system is solved using Rung-Kutta fourth order scheme. Consequently, numerical results of the system with control and the system without control are shown and discussed.

Keywords: Zika virus; epidemic model; Pontryagin's maximum principle; optimal control; mosquito; sexual transmission

1 Introduction

Zika virus (ZIKV) is a mosquito-borne virus first discovered in Africa, named after the Zika forest, located in Uganda. This virus infects human primarily via Aeges mosquitoes as the transmission vector. These mosquitoes are widely populated in tropical regions and also transmit other arboviruses such as dengue and chikungunya. The virus infection is typically accompanied by mild illness such as fever, skin rash, malaise, headache, muscle pain, and joint pain [1]. Despite being discovered since 1947, only 14 cases of human infection were reported before 2007. This arbovirus started gaining attention since the outbreak in Yap Island and French Polynesia, particularly the latter outbreak with more than 30,000 estimated cases attending the health care facilities. Moreover, there are reports on the connection between the increasing number of some neurological complications, microcephaly and Guillain-Barré Syndrome (GBS) for instance, and ZIKV infections in French Polynesia [2].

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The recent ZIKV outbreak in Brazil with over 1.5 million estimated cases from 2015 to 2016 received significant attention globally. The main reasons are its large number of infections, rapid transmission, and the increasing in the number of reported microcephaly coincided with the infection. The incidence became public health emergency and followed by the warning announcement from the World Health Organization(WHO).

Apart from the vector-mediated transmission, a human can also be infected by the Zika virus through sexual transmission. The virus has been detected in blood and semen [3]. There is a report of virus persisting in urine and semen after it disappeared from serum [4]. There are reported cases of ZIKV transmitted through sexual intercourse, and the virus transmitted from a man even before the onset of symptoms in one case [5]. An article studied on the Zika incidence of both genders in Rio [6] also suggests that sexual transmission could affect the overall outbreak. Consequently, mainly focusing on reducing mosquito population or the contacts between human and mosquitoes might not be sufficient. Hence, the measure against sexual transmission of the virus should be considered.

There is a possibility that ZIKV outbreak may emerge again in the future, especially in high vector concentration areas. To understand the dynamics and predict the situation in advance, mathematical models of Zika virus infection [2] that have previously been published should be studied. Beside vector transmission, the model proposed by Gao *et al.* [7] considers the direct transmission from exposed, symptomatically infected, and convalescent human to susceptible human via sexual contacts. Optimal control is also an important mathematical method deciding a strategy regarding epidemic control with provided scenarios [8–10]. There are some studies of the optimal control of several diseases such as dengue [11], chikungunya [12], and HIV [13]. The results show that optimal control helps in reducing the number of infected individuals and the spread of the virus. Hence, the optimal control problem will be derived, with an attempt to minimize the number of infected individuals as well as the cost of implementing the control strategy. There were suggestions of mosquito elimination, such as using insecticides, and human-to-mosquito contact reduction, such as using insect repellents or mosquito nets, as the control measures for Dengue epidemic [11, 14, 15]. Lastly, there is a suggestion of abstaining from sexual activity or consistently using protection during sexual intercourse [16]. This could be referred as human-to-human contact reduction.

Hence, the main goal of this work is to study a Zika virus infection model and propose an optimal control problem as previously stated. The control parameters introduced here are vector elimination, vector-to-human contact reduction, and human-to-human contact reduction. The mathematical model, consisting of vector transmission and sexual transmission, is from the study proposed by Gao *et al.* [7]. The control model is constructed by including control parameters into the model system, then analyzing the model using optimal control theory. The necessary conditions that an optimal control and corresponding state must satisfy will be determined using Pontryagin's maximum principle. After that, the optimality system of the optimal control problem will be shown. Lastly, the numerical results shall be shown and discussed sequentially.

2 Mathematical model

The Zika virus infection model with mosquito-borne and sexual transmission is proposed by Gao *et al.* [7]. In the human-mosquito model, the total human or host population at time t or $N_h(t)$, is partitioned into six classes: susceptible $S_h(t)$, exposed $E_h(t)$,

symptomatically infected $I_{h1}(t)$, convalescent $I_{h2}(t)$, asymptomatically infected $A_h(t)$, and recovered $R_h(t)$. The total mosquito or vector population $N_v(t)$ is partitioned into three classes: susceptible $S_v(t)$, exposed $E_v(t)$, and infectious $I_v(t)$. Thus, the total host population $N_h = S_h + E_h + I_{h1} + I_{h2} + A_h + R_h$ and the total vector population $N_v = S_v + E_v + I_v$, where both are assumed to be constant. Therefore, the Zika virus infection model is governed by a system of differential equations as follows:

$$
\begin{aligned}
\frac{dS_h}{dt} &= -ab\frac{I_v}{N_h}S_h - \beta\frac{KE_h + I_{h1} + \tau I_{h2}}{N_h}S_h, \\
\frac{dE_h}{dt} &= \theta\left(ab\frac{I_v}{N_h}S_h + \beta\frac{KE_h + I_{h1} + \tau I_{h2}}{N_h}S_h\right) - \alpha_h E_h, \\
\frac{dI_{h1}}{dt} &= \alpha_h E_h - \gamma_{h1} I_{h1}, \\
\frac{dI_{h2}}{dt} &= \gamma_{h1} I_{h1} - \gamma_{h2} I_{h2}, \\
\frac{dA_h}{dt} &= (1-\theta)\left(ab\frac{I_v}{N_h}S_h + \beta\frac{KE_h + I_{h1} + \tau I_{h2}}{N_h}S_h\right) - \gamma_h A_h, \\
\frac{dR_h}{dt} &= \gamma_{h2} I_{h2} + \gamma_h A_h, \\
\frac{dS_v}{dt} &= \mu_v N_v - ac\frac{\eta E_h + I_{h1}}{N_h}S_v - \mu_v S_v, \\
\frac{dE_v}{dt} &= ac\frac{\eta E_h + I_{h1}}{N_h}S_v - (\alpha_v + \mu_v)E_v, \\
\frac{dI_v}{dt} &= \alpha_v E_v - \mu_v I_v.
\end{aligned}
\tag{1}
$$

In the system, a susceptible human can be infected either through the bite of an infectious mosquito or sexual contacts with an exposed, symptomatically infected, and convalescent human. The exposed human becomes symptomatically infected after the virus incubation period. The exposed and symptomatically infected human can sexually transmit the disease to both susceptible human and mosquitoes, whereas the symptomatically infected class is more contagious due to the higher load of viremia and virusemenia [17]. After the end of viremia period, the symptomatically infected individual enters convalescent phase. In this phase, the virus still appears in semen but disappears from the serum. Hence a convalescent individual can pass the virus to a susceptible human but cannot transmit to mosquitoes. The end of the viremic period is assumed to coincide with the disappearance of symptoms in symptomatically infected individuals. The asymptomatically infected human is assumed to be noncontagious to both human and vector. Furthermore, the death and birth rate of human are ignored since the epidemiological period is much shorter than a human lifespan. All parameter descriptions are summarized in Table 1.

3 Optimal control problem

The control strategy for the outbreak is proposed considering campaigns and suggestions from WHO and health organizations regarding Zika virus infection. Considering the vector transmission and sexual transmission, three control parameters are introduced for constructing the control model. The control variable $u_1(t)$ is the use of preventive measures such as insect repellent or mosquito net to reduce the contacts between human and

Table 1 Model parameters

Parameters	Description	Value	Reference
a	Biting rate of mosquito (number of bites per mosquito per day)	0.5	[18]
b	Probability of transmission from an infectious mosquito to a susceptible human per bite (dimensionless)	0.4	[18]
c	Probability of transmission from a symptomatically infected human to a susceptible mosquito per bite (dimensionless)	0.5	[19]
β	Transmission rate from a symptomatically infected humans to susceptible humans (*per* day)	0.05	[7]
K	Relative human-to-human transmissibility of exposed to symptomatically infected humans (dimensionless)	0.6	[7]
τ	Relative human-to-human transmissibility of convalescent to symptomatically infected humans (dimensionless)	0.3	[7]
η	Relative human-to-mosquito transmission probability of exposed humans to symptomatically infected human (dimensionless)	0.1	[7]
θ (%)	Proportion of symptomatic infections (dimensionless)	18	[20]
$1/\alpha_h$	Intrinsic incubation period (days)	5	[21]
$1/\alpha_v$	Extrinsic incubation period (days)	10	[18]
$1/\gamma_{h1}$	Period of acute phase (days)	5	[21]
$1/\gamma_{h2}$	Period of convalescent phase (days)	20	[4]
$1/\gamma_h$	Period of asymptomatic infection (days)	7	[7]
$1/\mu_v$	Mosquito lifespan (days)	14	[18, 19]

mosquito. The control variable $u_2(t)$ is the measure of abstaining from sexual activity or consistent use of protections in sexual activity. The control variable $u_3(t)$ is the use of pesticides or chemicals at mosquito breeding sites to eliminate or reduce the total number of mosquitoes. Consequently, from control strategy, the forces of infection in the human population are reduced by the factors of $(1 - u_1(t))$ and $(1 - u_2(t))$. Similarly, the force of infection in the mosquito population is reduced by a factor of $(1 - u_1(t))$. Moreover, the mosquito birth rate is reduced by a factor of $(1 - u_3(t))$. It is also assumed that the mosquito death rate increases by $r_0 u_3(t)$, where $r_0 > 0$. Therefore, the dynamics of the system (1) with control components is governed by the system of differential equations as follows:

$$\frac{dS_h}{dt} = -ab\frac{I_v}{N_h}S_h(1 - u_1) - \beta\frac{KE_h + I_{h1} + \tau I_{h2}}{N_h}S_h(1 - u_2),$$

$$\frac{dE_h}{dt} = \theta\left(ab\frac{I_v}{N_h}S_h(1 - u_1) + \beta\frac{KE_h + I_{h1} + \tau I_{h2}}{N_h}S_h(1 - u_2)\right) - \alpha_h E_h,$$

$$\frac{dI_{h1}}{dt} = \alpha_h E_h - \gamma_{h1}I_{h1},$$

$$\frac{dI_{h2}}{dt} = \gamma_{h1}I_{h1} - \gamma_{h2}I_{h2},$$

$$\frac{dA_h}{dt} = (1 - \theta)\left(ab\frac{I_v}{N_h}S_h(1 - u_1) + \beta\frac{KE_h + I_{h1} + \tau I_{h2}}{N_h}S_h(1 - u_2)\right) - \gamma_h A_h, \qquad (2)$$

$$\frac{dR_h}{dt} = \gamma_{h2}I_{h2} + \gamma_h A_h,$$

$$\frac{dS_v}{dt} = \mu_v N_v(1 - u_3) - ac\frac{\eta E_h + I_{h1}}{N_h}S_v(1 - u_1) - (\mu_v + r_0 u_3)S_v,$$

$$\frac{dE_v}{dt} = ac\frac{\eta E_h + I_{h1}}{N_h}S_v(1 - u_1) - (\alpha_v + \mu_v + r_0 u_3)E_v,$$

$$\frac{dI_v}{dt} = \alpha_v E_v - (\mu_v + r_0 u_3)I_v.$$

Next, we define our objective function:

$$J(u_1, u_2, u_3) = \int_0^T \left(A_1 E_h + A_2 I_h + A_3 N_v + \frac{1}{2}\left(B_1 u_1^2 + B_2 u_2^2 + B_3 u_3^2\right) \right) dt, \tag{3}$$

subject to the state system of (2).

Next, we will find the optimal controls, namely the controls that optimize our objective function. Regarding this work, we will find a set of controls that minimizes the number of exposed human, symptomatically infected human, and the total number of mosquitoes as well as the costs associated with implementing the control strategy. The constants A_1, A_2, and A_3, are the weighted constants associated with exposed human, symptomatically infected human, and the total number of mosquito, respectively. The constants B_1, B_2, and B_3 are the weighted constants of the control variables u_1, u_2 and u_3, respectively. The terms $\frac{1}{2}B_1 u_1^2$, $\frac{1}{2}B_2 u_2^2$, and $\frac{1}{2}B_3 u_3^2$ are the costs associated with implementing each of the three controls. The cost related to the first control might be the expenses of using insect repellent, mosquito net, and herbal spray for instance. The cost related to second control might be the expenses of providing protections or warning leaflets about the safe sexual activity. The cost related to the last control could come from the expenses of using mosquito pesticides and the process implementation.

Let u_1^*, u_2^*, and u_3^* be the optimal controls, we will find a set of control functions such that

$$J\left(u_1^*, u_2^*, u_3^*\right) = \min J(u_1, u_2, u_3), \quad (u_1, u_2, u_3) \in U \tag{4}$$

subject to the state system (2), where the control set U is

$$U = \left\{ (u_1, u_2, u_3) | u_i(t) \text{ is Lebesgue measurable on } [0,1], 0 \le u_i(t) \le 1, i = 1, 2, 3 \right\}.$$

3.1 Characterization of the control problem

We will use Pontryagin's maximum principle [22] to find the optimal controls that satisfy the necessary conditions [23]. Firstly, the Lagrangian for the optimal control problem is defined by

$$L = A_1 E_h + A_2 I_h + A_3 N_v + 1/2\left(B_1 u_1^2 B_2 u_2^2 B_3 u_3^2\right) \tag{5}$$

and the Hamiltonian H

$$
\begin{aligned}
H = {} & L(E_h, I_h, N_v, u_1, u_2, u_3) + \lambda_1 \frac{dS_h}{dt} + \lambda_2 \frac{dE_h}{dt} + \lambda_3 \frac{dI_{h1}}{dt} + \lambda_4 \frac{dI_{h2}}{dt} \\
& + \lambda_5 \frac{dA_h}{dt} + \lambda_6 \frac{dS_v}{dt} + \lambda_7 \frac{dE_v}{dt} + \lambda_8 \frac{dI_v}{dt} \\
= {} & A_1 E_h + A_2 I_{h1} + A_3 N_v + \frac{1}{2}\left(B_1 u_1^2 + B_2 u_2^2 + B_3 u_3^2\right) \\
& + \lambda_1 \left\{ -ab\frac{I_v}{N_h} S_h(1 - u_1) - \beta \frac{KE_h + I_{h1} + \tau I_{h2}}{N_h} S_h(1 - u_2) \right\} \\
& + \lambda_2 \left\{ \theta \left(ab\frac{I_v}{N_h} S_h(1 - u_1) + \beta \frac{KE_h + I_{h1} + \tau I_{h2}}{N_h} S_h(1 - u_2) \right) - \alpha_h E_h \right\}
\end{aligned}
$$

$$+ \lambda_3\{\alpha_h E_h - \gamma_{h1} I_{h1}\} + \lambda_4\{\gamma_{h1} I_{h1} - \gamma_{h2} I_{h2}\}$$

$$+ \lambda_5\left\{(1-\theta)\left(ab\frac{I_v}{N_h}S_h(1-u_1) + \beta\frac{KE_h + I_{h1} + \tau I_{h2}}{N_h}S_h(1-u_2)\right) - \gamma_h A_h\right\}$$

$$+ \lambda_6\left\{\mu_v N_v(1-u_3) - ac\frac{\eta E_h + I_{h1}}{N_h}S_v(1-u_1) - (\mu_v + r_0 u_3)S_v\right\}$$

$$+ \lambda_7\left\{ac\frac{\eta E_h + I_{h1}}{N_h}S_v(1-u_1) - (\alpha_v + \mu_v + r_0 u_3)E_v\right\}$$

$$+ \lambda_8\{\alpha_v E_v - (\mu_v + r_0 u_3)I_v\}, \tag{6}$$

where λ_1, λ_2, λ_3, λ_4, λ_5, λ_6, λ_7, and λ_8 are the adjoint variables satisfying the following adjoint system:

$$\lambda_1' = -\frac{\partial H}{\partial S_h} = \frac{1}{N_h}\big(\lambda_1 - \lambda_2\theta - \lambda_5(1-\theta)\big)\big(abI_v(1-u_1) + \beta(KE_h + I_{h1} + \tau I_{h2})(1-u_2)\big),$$

$$\lambda_2' = -\frac{\partial H}{\partial E_h} = -A_1 + \frac{K\beta}{N_h}S_h(1-u_2)\big(\lambda_1 - \lambda_2\theta - \lambda_5(1-\theta)\big)$$

$$+ (\lambda_2 - \lambda_3)\alpha_h + \frac{ac}{N_h}S_v\eta(1-u_1)(\lambda_6 - \lambda_7),$$

$$\lambda_3' = -\frac{\partial H}{\partial I_{h1}} = -A_2 + \frac{\beta}{N_h}S_h(1-u_2)\big(\lambda_1 - \lambda_2\theta - \lambda_5(1-\theta)\big)$$

$$+ (\lambda_3 - \lambda_4)\gamma_{h1} + \frac{ac}{N_h}S_v(1-u_1)(\lambda_6 - \lambda_7),$$

$$\lambda_4' = -\frac{\partial H}{\partial I_{h2}} = \frac{\beta\tau}{N_h}S_h(1-u_2)\big(\lambda_1 - \lambda_2\theta - \lambda_5(1-\theta)\big) + \lambda_4\gamma_{h2}, \tag{7}$$

$$\lambda_5' = -\frac{\partial H}{\partial A_h} = \lambda_5\gamma_h,$$

$$\lambda_6' = -\frac{\partial H}{\partial S_v} = -A_3 + \frac{ac}{N_h}(\eta E_h + I_h)(1-u_1)(\lambda_6 - \lambda_7) + (\mu_v + r_0)u_3\lambda_6,$$

$$\lambda_7' = -\frac{\partial H}{\partial E_v} = -A_3 - \lambda_6\mu_v(1-u_3) + \lambda_7(\alpha_v + \mu_v + r_0 u_3) - \lambda_8\alpha_v,$$

$$\lambda_8' = -\frac{\partial H}{\partial I_v} = -A_3 + \frac{ab}{N_h}S_h(1-u_1)\big(\lambda_1 - \lambda_2\theta - \lambda_5(1-\theta)\big)$$

$$- \lambda_6\mu_v(1-u_3) - \lambda_8(\mu_v + r_0 u_3).$$

The transversality conditions (or boundary conditions) are

$$\lambda_i(T) = 0, \quad i = 1, 2, \ldots, 8, \text{where } T \text{ is the end of the time period.} \tag{8}$$

By the optimality condition, we have

$$\frac{\partial H}{\partial u_i} = 0, \quad i = 1, 2, 3, \text{at } u_i \Rightarrow u_i^*.$$

Thus,

$$\frac{\partial H}{\partial u_1} = B_1 u_1 + \frac{a}{N_h}\big(bS_h I_v\big(\lambda_1 - \lambda_2\theta - \lambda_5(1-\theta)\big) + cS_v(\eta E_h + I_{h1})(\lambda_6 - \lambda_7)\big) = 0,$$

$$\frac{\partial H}{\partial u_2} = B_2 u_2 + \frac{\beta S_h}{N_h}(KE_h + I_{h1} + \tau I_{h2})\big(\lambda_1 - \lambda_2\theta - \lambda_5(1-\theta)\big) = 0,$$

$$\frac{\partial H}{\partial u_3} = B_3 u_3 - \big(\lambda_6(\mu_v N_v + r_0 S_v) - r_0\lambda_7 E_v - r_0\lambda_8 I_v\big) = 0.$$
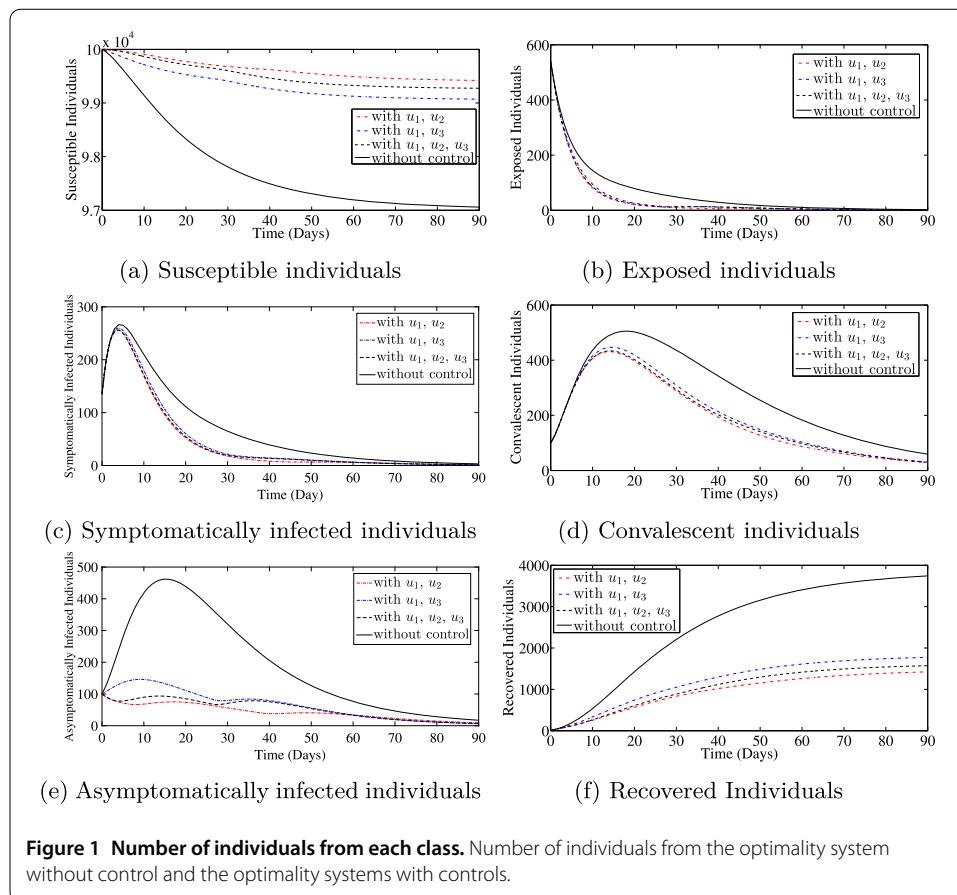
We obtain

$$u_1^* = \max\left\{\min\left\{\frac{a}{B_1 N_h}\big(bS_h I_v\big(-\lambda_1 + \lambda_2\theta + \lambda_5(1-\theta)\big) + cS_v(\eta E_h + I_{h1})(\lambda_7 - \lambda_6)\big), 1\right\}, 0\right\},$$

$$u_2^* = \max\left\{\min\left\{\frac{\beta S_h}{B_2 N_h}(KE_h + I_{h1} + \tau I_{h2})\big(-\lambda_1 + \lambda_2\theta + \lambda_5(1-\theta)\big), 1\right\}, 0\right\}, \qquad (9)$$

$$u_3^* = \max\left\{\min\left\{\frac{1}{B_3}\big(\lambda_6(\mu_v N_v + r_0 S_v) + r_0\lambda_7 E_v + r_0\lambda_8 I_v\big), 1\right\}, 0\right\}.$$

Therefore, we obtain the optimality system which helps describe the behavior of the system with the optimal controls. The optimality system consists of the state system (2), initial conditions of the state variables, the adjoint system (7), the transversality conditions (8), and the characterization of the optimal control.

4 Numerical results and discussion

The main purpose of this research is to study the effect of the control strategy on the dynamics of the ZIKV outbreak. First, the optimality system is numerically solved using the iterative method with the Runge-Kutta fourth order scheme. The state system (2) is solved by the forward Runge-Kutta method with an initial guess, and the adjoint system (7) is solved by the backward Runge-Kutta method with the transversality condition [23]. For all simulations, some of the parameter values are from publications which are defined in Table 1. Other parameters are arbitrarily chosen with $r_0 = 0.01$, and $T = 90$ days. For illustration purpose, the initial values of the state variables for solving system (1) are given by the authors. For the human group, the initial number of susceptible, exposed, symptomatically infected, convalescent, asymptomatically infected, and recovered individuals $(S_h(0), E_h(0), I_{h1}(0), I_{h2}(0), A_h(0), R_h(0))$ is set by $(100{,}000, 540, 135, 100, 100, 12)$. For the mosquito group, the initial number of susceptible, exposed, and infected vectors $(S_v(0), E_v(0), I_v(0))$ is set by $(10{,}000, 1{,}000, 100)$. The weight constants are given as $A_1 = 0.05$, $A_2 = 0.05$, $A_3 = 0.05$, $B_1 = 10$, $B_2 = 10$, and $B_3 = 30$. For B_1, B_2, and B_3, which is based on the assumption that vector elimination or mosquito elimination is more expensive in terms of implementation costs than the other two controls. There are costs of pesticides and costs of operating the control, which might be time-consuming and labor-intensive. On the contrary, providing insect repellent or other types of protections against mosquito's biting is easier and probably cheaper. Similarly, for sexual transmission, providing protection such as condoms or promoting the priority of protected sexual activity requires less money and resources. T is chosen to be 90 days or about three months which is the average period of one season.

Generally, in the absence of vaccination or treatment, it is recommended that one use pesticides or avoid being bitten by mosquitoes [24]. Hence, we first consider the setting where there are two controls u_1 and u_3. We also consider the scenario where there is no vector elimination, or control u_3 since it might be dangerous to use pesticides in some area such as hospitals or living habitats for a long time. This can be represented by the
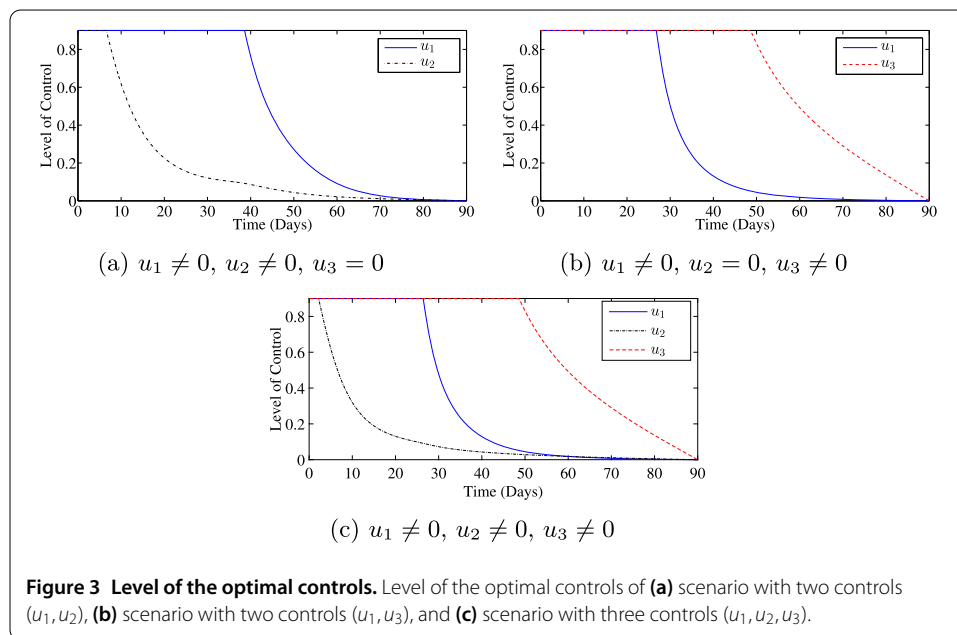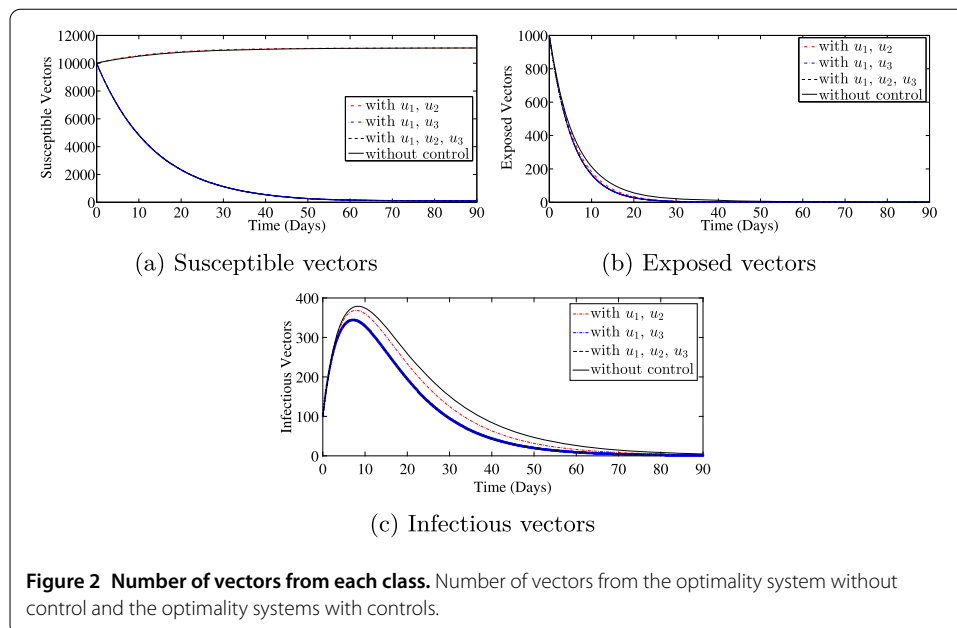
Figure 1 Number of individuals from each class. Number of individuals from the optimality system without control and the optimality systems with controls.

setting with only two controls, u_1 and u_2. Lastly, we consider the scenario where three controls are applied together. Therefore, the three scenarios are as follows: i) with controls u_1 and u_2, ii) with controls u_1 and u_3, and iii) with three controls u_1, u_2, and u_3. In practice, our strategy cannot be completely implemented, so the maximum value of each control is set to be 0.9 instead of 1. Consequently, we simulated three different scenarios to the optimality system with controls and the optimality system without control. The numerical results for each class of individuals and vectors are illustrated. In every graph, each of the individuals without control is represented by a solid line. The individuals with controls are represented as follows: a red dash-dot line for the system with controls u_1 and u_2, a blue dash-dot line for the system with controls u_1 and u_3, and a black dashed line for the system with all three controls.

Figure 1 shows the number of susceptible individuals, exposed individuals, symptomatically infected individuals, convalescent individuals, asymptomatically infected individuals, and recovered individuals from the optimality system without control and the optimality system with controls. Figure 2 shows the number of susceptible vectors, exposed vectors, and infectious vectors from the optimality system without control and optimality system with control. Figure 3 shows the level of optimal controls u_1, u_2, and u_3 at a time from different scenarios.
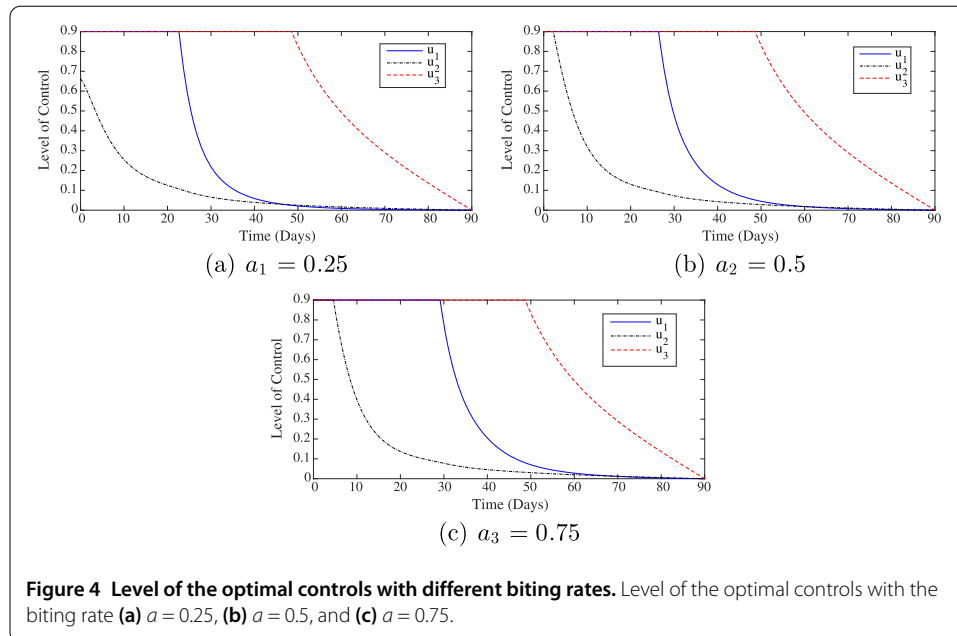
From Figure 1, it could be seen that the system with u_1 and u_2, and the system with three controls give the best result. The number of exposed, symptomatically infected, and convalescent of both mentioned systems are lowest, which means the disease will die out

Figure 2 Number of vectors from each class. Number of vectors from the optimality system without control and the optimality systems with controls.

Figure 3 Level of the optimal controls. Level of the optimal controls of **(a)** scenario with two controls (u_1, u_2), **(b)** scenario with two controls (u_1, u_3), and **(c)** scenario with three controls (u_1, u_2, u_3).

faster than the other systems. From Figures 2b-2c, it can be seen that the system with u_1 and u_3, and the system with three controls give the best result with the lowest number of exposed and infectious vectors. This could mean that both systems are the most effective in reducing the number of mosquitoes.

From Figure 3, the control variable u_1 stays at the maximum level about 40 days for the system with u_1, u_2, and lasts 30 days for the system with u_1, u_3 and the system with three controls. Note that E_h, I_{h1}, E_v, and I_v also become very low by that time. For the second control, u_2 is at maximum level for several days, then decreases sharply within about the first week, which corresponds to the peak of the number of I_{h1}. Lastly, the level of u_3 is at the maximum value until about day 50 before decreasing in every system setting. Note

Figure 4 Level of the optimal controls with different biting rates. Level of the optimal controls with the biting rate **(a)** $a = 0.25$, **(b)** $a = 0.5$, and **(c)** $a = 0.75$.

that u_3 starts decreasing when the total population of mosquitoes almost vanishes since the control u_3 contributes the most to reducing the total population of mosquitoes.

Over the last few decades, Zika virus infection occurred in many countries, and the behavior of the disease transmission might be different in each area. Considering the mosquito biting rate as one of the factors of the disease, we investigate the effect of the mosquito's biting rate on the control variables. Therefore, the numerical results of the level of controls by different setting of biting rate are illustrated in Figure 4, where biting rate (a) is varied as $a_1 = 0.25$, $a_2 = 0.5$, and $a_3 = 0.75$. From Figures 4a-4c, the level of u_1 stays at the maximum level about 23, 26, and 29 days for the setting a_1, a_2, and a_3, respectively. After that, the level of u_1 in each setting decreases sharply. The level of u_2 in the setting a_1 begins at 0.65 and gradually decreases as shown in the Figure 4a. From Figures 4b-4c, the level of u_2 for the setting a_2 and a_3 stays at the maximum level for two and five days, respectively, and decreases after that. The results indicate that the increasing of the value of biting rate leads to an extension of the period at the beginning where the control u_1 and u_2 are at the maximum level. On the contrary, the level of u_3 is the same in each setting.

5 Conclusions

In this paper, we derived a control model from the deterministic model of the Zika virus infection which consists of mosquito-borne transmission and sexual transmission by Gao *et al.* [7]. The optimal control problem is proposed with three selected controls; vector elimination, vector-to-human contact reduction, human-to-human contact reduction. The optimal control problem is developed to minimize the number of exposed humans, symptomatically infected humans, the total number of vectors as well as the costs associated with implementing the controls. We use Pontryagin's maximum principle to determine the necessary conditions, find the optimality system of the model and hence find the solution to the optimal control problem. Numerical simulations comparing the systems without control and the system with controls are presented. It is shown that an optimal control strategy is more effective in reducing the infected humans and vectors than without con-

trol strategy. From the numerical results, it is shown that time resource and human resource in implementing the strategy will be required mostly at the beginning of the period and then lessen over time. Additionally, the variation of the model parameter has an effect on the optimal controls. Our simulations imply that the areas with higher mosquito's biting rate require more efforts in controlling the disease. In conclusion, the behavior of the optimal controls should be changed according to the scenarios. This will help us to plan the strategy most efficiently. Furthermore, apart from mosquito elimination and protection against mosquito's biting which is the standard measures, the human-to-human contact reduction also contributes to the control of the outbreak. Besides using pesticides, using protection against mosquito contacts and sexual contacts could help in reducing the spread of Zika virus infection.

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