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# Mathematical Modeling for Control Zika Transmission

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**Abstract.** After 70 years since the zika was identified in Uganda, zika is now documented in 62 countries. In general, people infected with this disease do not experience severe conditions, but for pregnant women can cause serious problems because the zika can spread to the fetus. One result, zika can cause abnormalities in the fetal brain called microcephaly. Control and prevention are very important to reduce the spread of this disease. Here, we discussed the problem of optimal control in the model of zika transmission associated with the use of insecticide-treated nets (ITN) and indoor residual spraying (IRS). Using the approach of optimal control theory, we completed the objective function so that the infected population and its control cost are minimum. Numerically using the Forward-Backward Sweep Method, we obtained the control design of ITN and IRS as a function of time. The results show that the use of both simultaneously is more effective in reducing the population of infection than the use of ITN alone or the IRS alone.

## INTRODUCTION

Currently, zika is a serious problem that become global health threat for the world community because of the increasing number of cases and the rapidly expanding geographic range [1]. The disease is transmitted through the bite of A. aegypti mosquito. In addition, sexual contact can transmit zika between humans directly as reported in Argentina, Canada, Chile, France, Italy, New Zealand, Peru, Portugal and the USA [2, 3]. Usually this disease does not pose a threat of life, but if pregnant women are infected with this disease may increase the risk of abnormalities in the fetal brain such as microcephaly [4, 5]. Unfortunately, no vaccine, specific treatment, or fast diagnostic test is available to treat, prevent, or diagnose zika virus infection at this time.

Mathematical models have been used by several researchers to study the transmission dynamics [6, 7] and control of vector-borne diseases [2, 8]. These models simulate the effect of different control strategies including mosquito control, reduction of contact with mosquitoes, avoidance of sexual contact (for zika), sound environmental management practices and community education. This type of model is used to understand not only the dynamics of the spread of vector-borne diseases but also to conduct experiments to evaluate the effectiveness of interventions / control measures aimed at improving their impact on the population level, or to a higher level [6, 9]. In recent study, Padmanabhan et. al. in [10] developed zika transmission with considering sexual contact can transmit the disease in the frame work *SEIR-SEI*. They also investigate the effect of Insecticide-Treated Mosquito Nets (ITN) and Indoor Residual Spraying (IRS) to infection population without using optimization technique. In this model, they set the values of parameter ITN and IRS are constant.

Over the last two decades, two prominent approaches for controlling vector populations, recommended by WHO and CDC, involve the use of ITN and IRS. Using ITN can help reduce contacts between mosquitoes and humans at home. Further, mosquitoes that remain within the boundaries of sprayed homes after their meals can die as a result of IRS [10]. In this work, we design control as intervention of ITN and IRS in [10] as function time such that the infection population and cost of the interventions will be minimum.

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## MATHEMATICAL MODEL

We adapt an model in previous work in [10] that consider zika are not only spread through the bite of A. Aegyti mosquitoes but also through sexual. The human population is divided into five compartments, i.e. susceptible ($x_1$), exposed ($x_2$), symptomatic infected($x_3$), asymptomatic infected ($x_4$) and recovery ($x_5$). The mosquito population is divided into three compartments, i.e. susceptible ($x_6$), exposed ($x_7$) and infected($x_8$). Human population size is denoted by $x_h$ and mosquito population size is denoted by $x_m$. Zika transmitted through interaction human and mosquito with contact rate $\beta_1 = \frac{bp_1}{x_h}$ and $\beta_2 = \frac{bp_2}{x_h}$, and sexual with contact rate $\beta_3 = \frac{a_h}{x_h}$. This model is controlled by input parameter of $u_1$ and $u_2$ that represent ITN and IRS, respectively. The change rate of individual in each compartment is stated by the following differential equation system

$$\dot{x}_1 = -\beta_1 (1-u_1) x_1 x_8 - \beta_3 (x_3 + x_4) x_1 \quad (1)$$

$$\dot{x}_2 = \beta_1 (1-u_1) x_1 x_8 + \beta_3 (x_3 + x_4) x_1 - \alpha_1 x_2 \quad (2)$$

$$\dot{x}_3 = (1-q)\alpha_1 x_2 - \gamma_1 x_3 \quad (3)$$

$$\dot{x}_4 = q\alpha_1 x_2 - \gamma_2 x_4 \quad (4)$$

$$\dot{x}_5 = \gamma_1 x_3 + \gamma_2 x_4 \quad (5)$$

$$\dot{x}_6 = \mu x_m - \mu x_6 - \beta_2 (1-u_1)(x_3 + x_4) x_6 - (hu_1 + ju_2) x_6 \quad (6)$$

$$\dot{x}_7 = -\alpha_2 x_7 - \mu x_7 + \beta_2 (1-u_1)(x_3 + x_4) x_6 - (hu_1 + ju_2) x_7 \quad (7)$$

$$\dot{x}_8 = \alpha_2 x_7 - \mu x_8 - (hu_1 + ju_2) x_8 \quad (8)$$

with region of biological interest
$\Omega = \{x_1, x_2, x_3, x_4, x_5, x_6, x_7, x_8 \in \mathbb{R}^8_+ | x_1 + x_2 + x_3 + x_4 + x_5 + x_6 + x_7 + x_8 = x_h, x_6 + x_7 + x_8 = x_m\}$
The description of all parameters and their values are provided in the following table.

**TABLE 1.** Parameters Description

| Parameters | Description | Value | Unit | References |
|---|---|---|---|---|
| $b$ | Biting rate of vector | 0.5 | day$^{-1}$ | [11] |
| $a_h$ | Sexual transmission rate of zika | 0.2 | day$^{-1}$ | [2] |
| $p_1$ | Probability zika transmission from vector to human | 0.4 | day$^{-1}$ | [11] |
| $p_2$ | Probability zika transmission from human to vector | 0.5 | day$^{-1}$ | [12] |
| $\alpha_1$ | Human incubation rate | 0.2 | day$^{-1}$ | [13] |
| $\alpha_2$ | Vector incubation rate | 0.1 | day$^{-1}$ | [11, 14] |
| $\gamma_1$ | Symptomatic human recovery rate | 0.25 | day$^{-1}$ | [2] |
| $\gamma_2$ | Asymptomatic human recovery rate | 0.14 | day$^{-1}$ | [2] |
| $\mu$ | Natural death of vector | 0.04 | day$^{-1}$ | [15] |
| $q$ | Proportion of asymptomatic infection | [0,1] | dimensionless | Assumed |
| $h$ | Parameter for ITN rate | [0,1] | day$^{-1}$ | Assumed |
| $j$ | Parameter for IRS rate | [0,1] | day$^{-1}$ | Assumed |
| $u_1$ | Control variable of ITN | [0,1] | day$^{-1}$ | [10] |
| $u_2$ | Control variable of IRS | [0,1] | day$^{-1}$ | [10] |

The model has basic reproduction number as follows

$$R_0 = \frac{a_h}{2}\left(\frac{1-q}{\gamma_1} + \frac{q}{\gamma_2}\right) + \frac{1}{2}\sqrt{a_h^2\left(\frac{1-q}{\gamma_1} + \frac{q}{\gamma_2}\right)^2 + R_{0,a}^2 + R_{0,s}^2} \quad (9)$$

where

$$R_{0,a}^2 = \frac{b^2\beta_1\beta_1\alpha_2(1-q)(1-u_1)^2}{\gamma_1 x_h(\mu + \alpha_2 + hu_1 + ju_2)(\mu + hu_1 + ju_2)}$$

$$R_{0,s}^2 = \frac{b^2\beta_1\beta_2\alpha_2 q(1-u_1)^2}{\gamma_2 x_h(\mu + \alpha_2 + hu_1 + ju_2)(\mu + hu_1 + ju_2)}$$

In epidemiology, $R_0$ is an important parameter that indicates whether a disease will continue to grow or cause death. If $R_0 < 1$ then the disease will go to the disease free point, but if $R_0 > 1$, then the endemic point will arise where the illness will remain for a long time.

## CONTROL PROBLEM

Since we want to design $u = (u_1, u_2)$ that infected human and cost of ITN and IRS interventions are minimum, then we consider the following objective function

$$\min_{\Gamma} J(u_1, u_2) = \int_0^{t_f} \left[ A_1 x_2^2 + A_2 x_3^2 + A_3 x_4^2 + \frac{1}{2} A_4 u_1(t)^2 + \frac{1}{2} A_5 u_2(t)^2 \right] dt \tag{10}$$

subject to system (1)-(8)

where $A_i, i = 1, 2, 3, 4, 5$ are weighting parameters used for state variables $x_2, x_3, x_4$ and control variables $u_1$ and $u_2$ and $\Gamma = \{ (u_1, u_2) \mid 0 \le u_i \le 1, i = 1, 2\}$.
Lagrange equation of the control problem is

$$L = A_1 x_2^2 + A_2 x_3^2 + A_3 x_4^2 + \frac{1}{2} A_4 u_1(t)^2 + \frac{1}{2} A_5 u_2(t)^2$$

Hamiltonian equation is

$$\begin{aligned} H &= L + \sum_{i=1}^{8} \lambda_i g_i(t, x, u) \\ &= A_1 x_2^2 + A_2 x_3^2 + A_3 x_4^2 + \frac{1}{2} A_4 u_1(t)^2 + \frac{1}{2} A_5 u_2(t)^2 + \lambda_1 \dot{x}_1 + \lambda_2 \dot{x}_2 + \lambda_3 \dot{x}_3 + \lambda_4 \dot{x}_4 + \lambda_5 \dot{x}_5 + \lambda_6 \dot{x}_6 + \lambda_7 \dot{x}_7 + \lambda_8 \dot{x}_8 \end{aligned}$$

where $\lambda_i(t), i = 1, 2, ..., 13$ is called adjoint function. We will use Pontryagin Maximum Principle (PMP) [16] to determine necessary condition for the optimal condition. Let $x^*(t)$ and $u^*(t)$ is solution for the problem, then there are non trivial vector function $\lambda(t) = (\lambda_1(t), \lambda_2(t), ..., \lambda_{10}(t))$ that satisfy the following equation

$$x'(t) = \frac{\partial H(t, x^*, u^*, \lambda)}{\partial \lambda}, \quad \lambda'(t) = -\frac{\partial H(t, x^*, u^*, \lambda)}{\partial x}, \quad \frac{\partial H(t, x^*, u^*, \lambda)}{\partial u} = 0 \tag{11}$$

**Theorem 1** *Given the optimal controls $u_1^*, u_2^*$ and solution $x_1*, x_2*, x_3*, x_4*, x_5*, x_6*, x_7*, x_8*$ of the corresponding state system (1)-(8), there exist adjoint variables $\lambda_1, \lambda_2, \lambda_3, \lambda_4, \lambda_5, \lambda_6, \lambda_7, \lambda_8$ satisfy the following adjoint equations*

$$\dot{\lambda}_1 = (\beta_1 (1 - u_1) x_8 + \beta_3 (x_3 + x_4)) (\lambda_1 - \lambda_2) \tag{12}$$

$$\dot{\lambda}_2 = -2A_1 x_2 + \alpha_1 (\lambda_2 - (1 - q)\lambda_3 - q\lambda_4) \tag{13}$$

$$\dot{\lambda}_3 = -2A_1 x_3 + \gamma_1 (\lambda_3 - \lambda_5) + \beta_2 x_6 (1 - u_1) (\lambda_6 - \lambda_7) + \beta_3 x_1 (\lambda_1 - \lambda_2) \tag{14}$$

$$\dot{\lambda}_4 = -2A_2 x_4 + \gamma_2 (\lambda_4 - \lambda_5) + \beta_2 x_6 (1 - u_1) (\lambda_6 - \lambda_7) + b_h x_1 (\lambda_1 - \lambda_2) \tag{15}$$

$$\dot{\lambda}_5 = 0 \tag{16}$$

$$\dot{\lambda}_6 = (\mu + hu_1 + ju_2) \lambda_6 + \beta_2 (1 - u_1) (x_3 + x_4) (\lambda_6 - \lambda_7) \tag{17}$$

$$\dot{\lambda}_7 = \alpha_2 (\lambda_7 - \lambda_8) + (\mu + hu_1 + ju_2) \lambda_7 \tag{18}$$

$$\dot{\lambda}_8 = (\mu + hu_1 + ju_2) \lambda_8 + \beta_1 x_1 (1 - u_1) (\lambda_1 - \lambda_2) \tag{19}$$

*with transversality condition $\lambda_i(t_f) = 0, i = 1, 2, ..., 8$. Furthermore $u_1^*, u_2^*$ are represented by*

$$u_1^* = \max \left\{ 0, \min \left( 0.5, \frac{\beta_1 x_1^* x_8^* (\lambda_2 - \lambda_1) + \beta_2 x_6^* (x_3^* + x_4^*)(\lambda_7 - \lambda_6) + h \left( x_6^* \lambda_6 + x_7^* \lambda_7 + x_8^* \lambda_8 \right)}{A_4} \right) \right\} \tag{20}$$

$$u_2^* = \max \left\{ 0, \min \left( 1, \frac{j \left( x_6^* \lambda_6 + x_7^* \lambda_7 + x_8^* \lambda_8 \right)}{A_5} \right) \right\} \tag{21}$$

*Proof*. From necessary condition above (11), we have $\dot{\lambda} = -\frac{\partial H(t,x^*,u^*,\lambda)}{\partial x}$, it follows

$$\begin{aligned}
\dot{\lambda}_1 &= -\frac{\partial H(t,x^*,u_1^*,u_2^*,\lambda)}{\partial x_1} = (\beta_1(1-u_1)x_8 + \beta_3(x_3+x_4))(\lambda_1-\lambda_2)\\
\dot{\lambda}_2 &= -\frac{\partial H(t,x^*,u_1^*,u_2^*,\lambda)}{\partial x_2} = -2A_1x_2 + \alpha_1(\lambda_2 - (1-q)\lambda_3 - q\lambda_4)\\
\dot{\lambda}_3 &= -\frac{\partial H(t,x^*,u_1^*,u_2^*,\lambda)}{\partial x_3} = -2A_1x_3 + \gamma_1(\lambda_3-\lambda_5) + \beta_2x_6(1-u_1)(\lambda_6-\lambda_7) + \beta_3x_1(\lambda_1-\lambda_2)\\
\dot{\lambda}_4 &= -\frac{\partial H(t,x^*,u_1^*,u_2^*,\lambda)}{\partial x_4} = -2A_2x_4 + \gamma_2(\lambda_4-\lambda_5) + \beta_2x_6(1-u_1)(\lambda_6-\lambda_7) + b_hx_1(\lambda_1-\lambda_2)\\
\dot{\lambda}_5 &= -\frac{\partial H(t,x^*,u_1^*,u_2^*,\lambda)}{\partial x_5} = 0\\
\dot{\lambda}_6 &= -\frac{\partial H(t,x^*,u_1^*,u_2^*\lambda)}{\partial x_6} = (\mu + hu_1 + ju_2)\lambda_6 + \beta_2(1-u_1)(x_3+x_4)(\lambda_6-\lambda_7)\\
\dot{\lambda}_7 &= -\frac{\partial H(t,x^*,u_1^*,u_2^*\lambda)}{\partial x_7} = \alpha_2(\lambda_7-\lambda_8) + (\mu + hu_1 + ju_2)\lambda_7\\
\dot{\lambda}_8 &= -\frac{\partial H(t,x^*,u_1^*,u_2^*\lambda)}{\partial x_8} = (\mu + hu_1 + ju_2)\lambda_8 + \beta_1x_1(1-u_1)(\lambda_1-\lambda_2)
\end{aligned}$$

with transversality condition $\lambda_i(t_f) = 0, i = 1,2,...,8$. Let $x_1 = x_1^*, x_2 = x_2^*, x_3 = x_3^*, x_4 = x_4^*, x_4 = x_5^*, x_6 = x_6^*, x_7 = x_7^*, x_8 = x_8^*$ and necessary condition $\frac{\partial H(t,x^*,u^*,\lambda)}{\partial u} = 0$, yields

$$\begin{aligned}
u_1^* &= \frac{\beta_1x_1^*x_8^*(\lambda_2-\lambda_1) + \beta_2x_6^*(x_3^*+x_4^*)(\lambda_7-\lambda_6) + h\left(x_6^*\lambda_6 + x_7^*\lambda_7 + x_8^*\lambda_8\right)}{A_4}\\
u_2^* &= \frac{j\left(x_6^*\lambda_6 + x_7^*\lambda_7 + x_8^*\lambda_8\right)}{A_5}
\end{aligned}$$

since boundary condition of the controls, so we obtain

$$\begin{aligned}
u_1^* &= \max\left\{0, \min\left(0.5, \frac{\beta_1x_1^*x_8^*(\lambda_2-\lambda_1) + \beta_2x_6^*(x_3^*+x_4^*)(\lambda_7-\lambda_6) + h\left(x_6^*\lambda_6 + x_7^*\lambda_7 + x_8^*\lambda_8\right)}{A_4}\right)\right\}\\
u_2^* &= \max\left\{0, \min\left(1, \frac{j\left(x_6^*\lambda_6 + x_7^*\lambda_7 + x_8^*\lambda_8\right)}{A_5}\right)\right\}
\end{aligned}$$

## NUMERICAL SIMULATIONS

Now, we study the dynamics behaviour of human and mosquito population in the presence of ITN and IRS intervention by solving cost function 10 numerically by using Forward-Backward Sweep Method [17]. In this method, the system (1) - (8) is solved by the Fourth Runge Kutta Method with the forward time, while the adjoin system (12)-(19) is completed by the backward time and satisfies the transverse conditions. In the first iteration, the values of $u_1$ and $u_2$ are initialized and then updated according to equation (20) and (21). After the value of objective function is close enough to the previous value of objective function, iteration stops. To know the best way of controlling zika transmission, here we present simulations for three cases. Case I: ITN as control ($u_2 = 0$), case 2 : IRS as control ($u_1 = 0$) and case 3: ITN and IRS as controls ($u_1 \neq 0, u_2 \neq 0$) with initial condition $x_1(0) = 750, x_2(0) = 100, x_3(0) = 50, x_4(0) = 50, x_5(0) = 50, x_6(0) = 500, x_7(0) = 100, x_8 = 100$ and parameter values is provided at Table 1, but for best simulation we choose $b = 1$ and $\beta_3 = 0.25\beta_1$. The numerical result for all cases can be seen in Figure 1 and Figure 2. Figure 1 demonstrate impact the control $u_1$ and $u_2$ to infection population. From Figure 1 (a), Figure 1 (b) and Figure 1 (c), we know that all given intervention strategies have a significant effect on reducing the population of human infections and populations of mosquito infections. However, ITN and IRS interventions together provide a maximum reduction in the population of the infection. Figure 1 (d) shows the profile of basic reproduction number ($R_0$) vs time. This profile show that the values of $R_0$ increase when the values of $u_1$ and $u_2$ decrease, see Figure 1 (d) dan Figure (2).

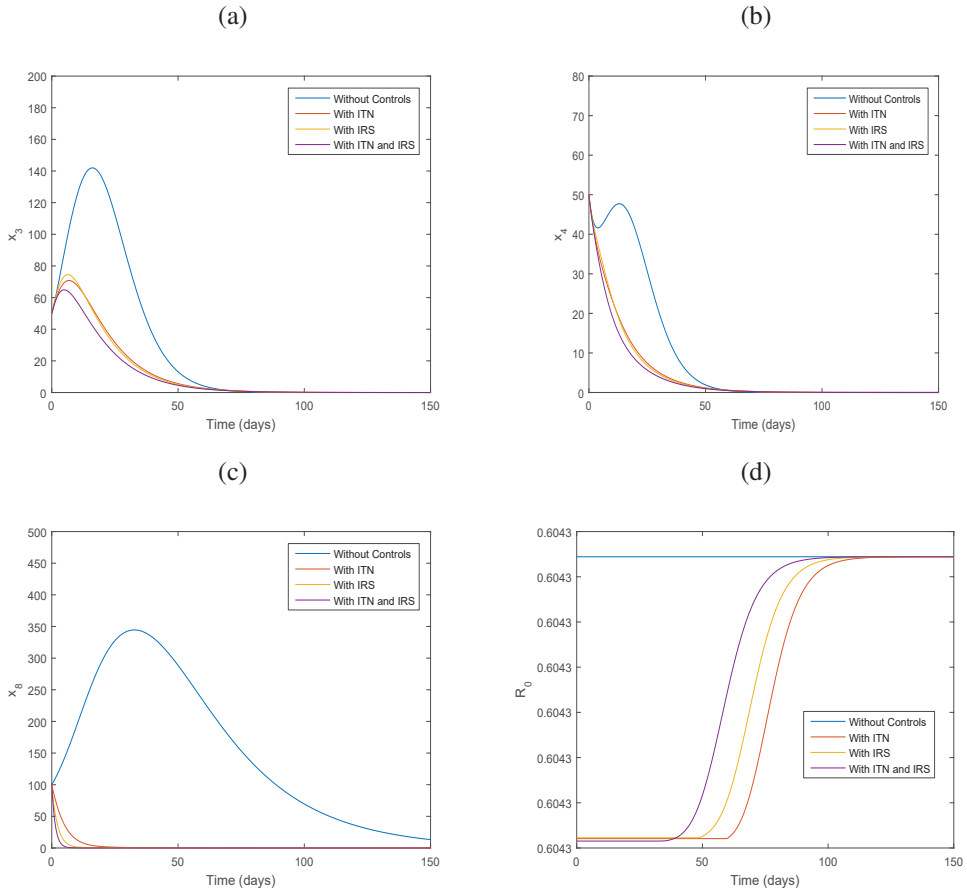


**FIGURE 1.** Dinamic population and basic reproduction number in the presence of control. (a) Dynamics of symptomatic infected human, (b) Dynamics of symptomatic infected human, (c) Dynamics of asymptomatic infected human, (d) Basic reproduction number as function of $t$

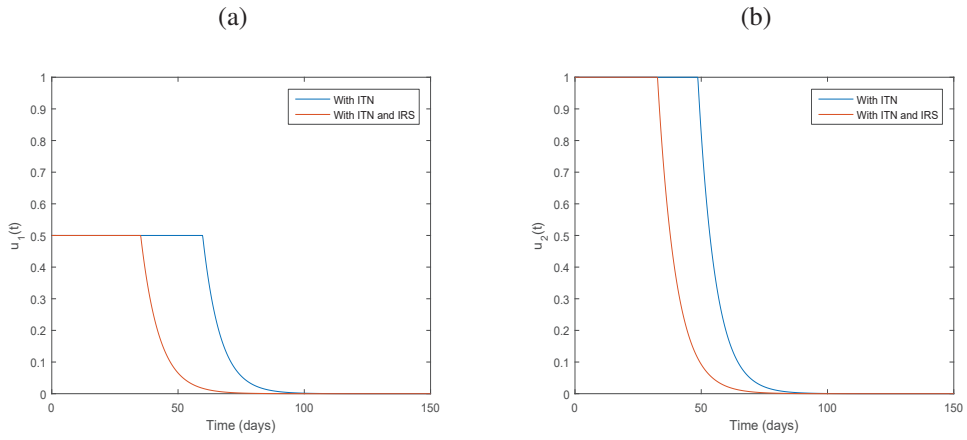


**FIGURE 2.** Control $u_1$ and $u_2$ as function of time ($t$)

## DISCUSSION AND CONCLUSION

In this work, we explore models in [10] taking into account that ITN and the IRS are not constant but time-dependent. We solved the objective function by using PMP and present simulations of design of $u_1$ and $u_2$ as well as infection dynamics using the Forward-Backward Sweep method. The results show that by using ITN, IRS or both, the infection population in humans and mosquitoes decreases faster and reaches zero compared to without intervention. Nevertheless, the use of both simultaneously produced the most significant impact on infectious populations compared with the use of them independently.

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