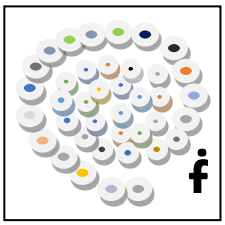

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Optimal recruitment of Wolbachia-infected mosquitoes to control Zika virus disease

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Abstract

This paper presents optimal control of zika virus disease when wolbachia-infected Aedes aegypti mosquito is used as bio-control. In using wolbachia-infected mosquitoes to fight the spread of zika virus disease, the natural mosquitoes are infected with wolbachia in a laboratory and released in the wild at different times to mate with the uninfected ones. In this paper therefore, we model this control procedure using a system of non-linear ordinary differential equations. The Pontryagin maximum principle is then applied to determine the levels of recruitment or release of the wolbachia-infected mosquitoes that would optimally reduce the population of susceptible wolbachia-free mosquitoes. With the help of forward-backward sweep numerical method, the resulting optimal control model is solved. The graphical solution shows that the population of wolbachia-free mosquitoes are reduced when the recruitment level of the wolbachia-free mosquitoes is optimal compared to when no control is applied.

Keywords: zika; aedes aegypti; wolbachia; optimal control; maximum principle

1 Introduction

The use of wolbachia-infected mosquitoes in tackling the spread of mosquito-born diseases has long been proposed and used in some countries where dengue and zika virus diseases are endemic [12]. This mosquito technology involves infecting mosquitoes' offspring with wolbachia in a laboratory, reared until they mature to adult mosquitoes, and then released to mate with wolbachia-free mosquitoes present in the wild [5]. Wolbachia is a symbiotic bacteria that live naturally in most arthropods, except in aedes aegypti mosquitoes. Scientists have proved that when wolbachia is present in mosquitoes that are infected with disease-causing viruses, it increases the incubation period(or reduces the incubation rate) of the virus in the mosquitoes, thereby increasing the time it takes the mosquito carrying the virus to become infectious. Since the adult life of the mosquito is short, most of the mosquitoes carrying the virus die before they become infectious. In this way, the infected wolbachia-carrier mosquitoes may not transmit the virus to humans through their bites before they die. It is also known that Wolbachia induces cytoplasmic incompatibility(CI), a complex biochemical reaction which prevents development of embryos, when wolbachia-carrier male mosquitoes mate with wolbachia-free female mosquitoes or mate with female mosquitoes that carry a different wolbachia strain [9]. In this way, CI helps its host mosquito to invade and replace the wolbachia-free aedes aegypti mosquitoes population in the wild [7].

In this paper, we model the use of this technique as biological control for zika, a flavivirus disease which spreads through bites of female adult Aedes aegypti mosquitoes. Since the wolbachia-infected mosquitoes are to be released at different intervals from the laboratory, our aim is to determine the appropriate number of wolbachia-infected mosquitoes that should be recruited at different times in order to achieve optimal control of zika virus disease. Invariably, we seek to determine the level of recruitment of wolbachia-infected mosquitoes that would optimally reduce the population of susceptible wolbachia-free mosquitoes. This is achieved through the application of the Pontryagin Maximum Principle.

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2 The model assumptions and formulation

In this model, we assume that humans get infected with zika virus, only when bitten by infectious female Aedes *aegypti* mosquito. On the other hand, transmission of zika virus from human to mosquito occurs when an adult, uninfected female Aedes *aegypti* mosquito bites infected humans to suck blood. Therefore, this model involves three populations: humans, adult female wolbachia-free aedes *aegypti* and adult female wolbachia-carrier aedes *aegypti*, used for control.

There are 4 classes in the human population: Susceptible(S_1), Exposed(E_1), Infectious(I_1), and Recovered(R). In the mosquito population, we have 3 classes namely; Susceptible(S_i), Exposed(E_i), Infectious($I_i), i = 2, 3$, where 2 and 3 represents wolbachia-free and wolbachia-carrier mosquitoes, respectively. Therefore, the total population of human, wolbachia-free mosquitoes and wolbachia-carrier mosquitoes can be represented as $N_1 = S_1+E_1+I_1+R, N_2 = S_2+E_2+I_2$ and $N_3 = S_3+E_3+I_3$, respectively. The rates at which the susceptible classes S_1, S_2 and S_3 increases are $\Lambda_1, \Lambda_2+q\kappa\mu_1 N_2$, and $\Lambda_2 + q\kappa\mu_1 N_2$, respectively, where Λ_1, Λ_2 and Λ_3 are the rates of recruitments of humans,female adult wolbachia-free mosquitoes and female adult wolbachia-infected mosquitoes, into S_1, S_2 and S_3, respectively. The parameters μ_1 and μ_2 are the rates at which N_2 and N_3 lay eggs, respectively, κ is the proportion of the eggs that give rise to female mosquitoes, and $q \in (0, 1)$ is used to represent the effect of cytoplasmic incompatibility in the population of wolbachia-free mosquitoes. Susceptible humans contract zika virus through bites of wolbachia-free and wolbachia-carrier mosquitoes, with probabilities of infection α_1 and α_2, respectively, with the understanding that $\alpha_2 \ll \alpha_1$. Therefore, the force of infection in human population is $\frac{b_1\alpha_1 I_2}{N_2} + \frac{b_2\alpha_2 I_3}{N_3}$, while, $\frac{b_1\alpha_3 I_1}{N_1}$ and $\frac{b_2\alpha_4 I_1}{N_1}$, respectively, are the rates at which infectious humans infect susceptible wolbachia-free and wolbachia-carrier mosquitoes. After contracting zika virus, humans become infectious at the incubation rate, β_1, while the exposed mosquitoes E_2 and E_3 become infectious at the rates β_2 and β_3, respectively. The mosquitoes do not recover from the infection, while humans recover at the rate γ. The natural death for humans and mosquitoes are σ_1 and σ_2, respectively, while σ_1' is the negligible rate at which infected humans die due to zika virus disease infection. The above assumptions on the dynamics of zika virus disease in human and mosquitoes populations give rise to the following system of nonlinear ordinary differential equation:

$$
\begin{aligned}
\frac{dS_1(t)}{dt} &= \Lambda_1 - \left(\frac{b_1\alpha_1 I_2(t)}{N_2(t)} + \frac{b_2\alpha_2 I_3(t)}{N_3(t)}\right) S_1(t) - \sigma_1 S_1(t),\\
\frac{dE_1(t)}{dt} &= \left(\frac{b_1\alpha_1 I_2(t)}{N_2(t)} + \frac{b_2\alpha_2 I_3(t)}{N_3(t)}\right) S_1(t) - (\beta_1 + \sigma_1)E_1(t),\\
\frac{dI_1(t)}{dt} &= \beta_1 E_1(t) - (\gamma + \sigma_1 + \sigma_1')I_1(t),\\
\frac{dR(t)}{dt} &= \gamma I_1(t) - \sigma_1 R(t),\\
\frac{dS_2(t)}{dt} &= \Lambda_2 + q\kappa\mu_1 N_2(t) - \frac{b_1\alpha_3 I_1(t)}{N_1(t)} S_2(t) - \sigma_2 S_2(t),\\
\frac{dE_2(t)}{dt} &= \frac{b_1\alpha_3 I_1(t)}{N_1(t)} S_2(t) - (\beta_2 + \sigma_2)E_2(t),\\
\frac{dI_2(t)}{dt} &= \beta_2 E_2(t) - \sigma_2 I_2(t),\\
\frac{dS_3(t)}{dt} &= \Lambda_3 + \kappa\mu_2 N_3(t) - \frac{b_2\alpha_4 I_1(t)}{N_1(t)} S_3(t) - \sigma_2 S_3(t),\\
\frac{dE_3(t)}{dt} &= \frac{b_2\alpha_4 I_1(t)}{N_1(t)} S_3(t) - (\beta_3 + \sigma_2)E_3(t),\\
\frac{dI_3(t)}{dt} &= \beta_3 E_3(t) - \sigma_2 I_3(t),
\end{aligned}
\tag{1}
$$

The initial conditions are $S_1(0) = S_1^0, E_1(0) = E_1^0, I_1(0) = I_1^0, R(0) = R^0, S_2(0) = S_2^0, E_2(0) = E_2^0, I_2(0) = I_2^0, S_3(0) = S_3^0, E_3(0) = E_3^0, I_3(0) = I_3^0$, which we assume to be nonnegative quantities.

The domain of existence of the solution to this system can be described as $\mathcal{D} = D_1 \cup D_2 \cup D_3$, where $D_1 = \{S_1, E_1, I_1, R) \in \mathbb{R}_+^4 | S_1 + E_1 + I_1 + R \leq N_1\}, D_2 = \{(S_2, E_2, I_2) \in \mathbb{R}_+^3 | S_2 + E_2 + I_2 \leq N_2\}$, and $D_3 = \{(S_3, E_3, I_3) \in \mathbb{R}_+^3 | S_3 + E_3 + I_3 \leq N_3\}$.

From (1), we see that the total populations of human, wolbachia-free and wolbachia-carrier mosquitoes, respectively, satisfy the equations

$$
\begin{aligned}
\frac{dN_1}{dt} &= \Lambda_1 - \sigma_1 N_1 - \sigma_1' I_H,\\
\frac{dN_2}{dt} &= \Lambda_2 + (q\kappa\mu_1 - \sigma_2)\, N_2,\\
\frac{dN_3}{dt} &= \Lambda_3 + (\kappa\mu_2 - \sigma_2)\, N_3.
\end{aligned}
\tag{2}
$$

respectively. Let $f(X(t))$ represent the right-hand side of (1), where
$X(t) = (S_1, E_2, I_1, R, S_2, E_2, I_2, S_3, E_3, I_3)$. Since the total human and mosquito populations cannot be zero, we see that $f(X(t))$ is continuous, and has continuous partial derivatives with respect to each of the state variables. Hence, there exists a unique solution $X(t)$, to the system, (1) that passes through the initial solution.

2.0.1 Positivity of the Solution

Since the model describes the dynamics of zika virus disease in human and mosquito populations, it will be epidemiologically and mathematically meaningful if all the state variables(all human and mosquitoes subpopulations) are nonnegative $\forall t \geq 0$. Moreover, given that the initial conditions are nonnegative in the octant $\mathcal{D}$, we need to establish that the solution remains positive in the set. Using differential

inequality on the model system, we have that

$$\begin{aligned}
S_1(t) &> S_1(0)e^{-\int^t(\nu(s)+\sigma_1)ds} \\
E_1(t) &> E_1(0)e^{-(\beta_1+\sigma_1)t} \\
I_1(t) &> I_1(0)e^{-(\gamma+\sigma_1+\sigma_1')t} \\
R(t) &> R(0)e^{-\sigma_1 t} \\
S_2(t) &> S_2(0)e^{-\int^t\left(\frac{b_1\alpha_3 I_1(s)}{N_1(s)}+\sigma_2\right)ds} \\
E_2(t) &> E_2(0)e^{-(\beta_2+\sigma_2)t} \\
I_2(t) &> I_2(0)e^{-\sigma_2 t} \\
S_3(t) &> S_3(0)e^{-\int^t\left(\frac{b_2\alpha_4 I_1(s)}{N_1(s)}+\sigma_2\right)ds} \\
E_3(t) &> E_3(0)e^{-(\beta_3+\sigma_2)t} \\
I_3(t) &> I_3(0)e^{-\sigma_2 t}
\end{aligned}$$

where $\nu(s) = \frac{b_1\alpha_1 I_2(s)}{N_2(s)} + \frac{b_2\alpha_2 I_3(s)}{N_3(s)}$. Since the individual initial solutions are all positive, we have that the solution remains positive in $\mathcal{D}$ $\forall t > 0$.

2.0.2 Positive Invariant Region

To show that $\mathcal{D}$ is positive invariant with respect to the flow of the model system, we use the total populations in (2). It is easy to show from (2) that

$$\begin{aligned}
N_1(t) &\leq \frac{\Lambda_1}{\sigma_1} - \left(\frac{\Lambda_1}{\sigma_1} - N_1(0)\right)e^{-\sigma_1 t} \\
N_2(t) &\leq \frac{\Lambda_2}{\sigma_2-\mu_1} + \left(N_2(0) - \frac{\Lambda_2}{\sigma_2-\mu_1}\right)e^{-(\sigma_2-qk\mu_1)t} \\
N_3(t) &\leq \frac{\Lambda_3}{\sigma_2-\mu_2} + \left(N_3(0) - \frac{\Lambda_3}{\sigma_2-\mu_2}\right)e^{-(\sigma_2-k\mu_2)t}
\end{aligned}$$

Hence, we have that as $t \to \infty, N_1 \leq \frac{\Lambda_1}{\sigma_1}, N_2 \leq \frac{\Lambda_2}{\sigma_2-qk\mu_1}, N_3 \leq \frac{\Lambda_3}{\sigma_2-k\mu_2}$ Since the total human and mosquito populations are bounded above, it implies that all the solutions enter and remain in the domain $\mathcal{D}$ $\forall t \geq 0$. This shows that $\mathcal{D}$ is positive invariant.

3 Optimal Control Analysis of the Model

Recall that the aim of recruiting the wolbachia-infected mosquitoes is to reduce the population of the susceptible wolbachia-free mosquitoes in the zika-endemic area. This will subsequently reduce the populations of exposed and infectious wolbachia-free mosquitoes. The level of recruitment, Λ_3, of wolbachia-infected mosquitoes, is therefore considered as the control parameter in using this method to fight zika virus disease. In this case, we assume that the level of recruitment is not constant but a function of time; $\Lambda_3 = \Lambda_3(t)$. Therefore, we consider an optimal control problem with objective function given by

$$J(x;\Lambda_3) = \int_0^T A_1 S_2(t) + A_2 E_2(t) + A_3 I_2(t) + \frac{B}{2}\Lambda_3^2(t)dt \tag{3}$$

where the constants $A_i, i = 1,2,3$ and B are positive weights which help to balance each term in the integrand. The quadratic term, $\frac{B}{2}\Lambda_3^2(t)$ represents the cost involved in recruiting the wolbachia-carrier mosquitoes and releasing them in the wild at any time t. In the above optimal control problem, we assume that the control parameter, $\Lambda_3^*(t)$ is Lebesgue measurable with $a < \Lambda_3^*(t) \leq b, \ \ \forall t \in [0, t_f]$. Therefore, we seek an optimal control, $\Lambda_3^*(t)$ such that

$$J(\Lambda_3^*(t)) = min\{J(\Lambda_3(t)) : \Lambda_3(t) \in \Omega\} \tag{4}$$

where the control set Ω is given by

$$\Omega = \{\Lambda_3(t) : \Lambda_3(t) \text{ is piecewise continuous on } [0,T], a \leq \Lambda_3(t) \leq b]\} \tag{5}$$

with a and b being nonnegative constants. As shown in Fleming and Rishel [3], the existence of the optimal control, $\Lambda_3^*(t)$ and the associated optimal solutions,$(S_1^*, E_1^*, I_1^*, R^*, S_2^*, E_2^*, I_2^*, S_3^*, E_3^*, I_3^*)$ is guaranteed since the state solutions are bounded as proved earlier, the state system satisfies the Lipschitz property with respect to the state variables, since the solutions exist and are unique. It remains to show the convexity of the integrand, $L(t, S_2, E_2, I_2, \Lambda_3) = A_1 S_2 + A_2 E_2 + A_3 I_2 + \frac{1}{2} B \Lambda_3^2$, with respect to the control parameter, Λ_3 in the set Ω. Therefore, we need to show that
$L(t, S_2, E_2, I_2, \lambda\Lambda_3 + (1-\lambda)\Lambda_3') \leq \lambda L(t, S_2, E_2, I_2, \Lambda_3) + (1-\lambda) L(t, S_2, E_2, I_2, \Lambda_3')$, for $\lambda \in (0,1)$. Note that

$$L(t, S_2, E_2, I_2, \lambda\Lambda_3 + (1-\lambda)\Lambda_3') = A_1 S_2 + A_2 E_2 + A_3 I_2 + \frac{1}{2} B(\lambda\Lambda_3 + (1-\lambda)\Lambda_3')^2, \tag{6}$$

and

$$\begin{aligned} \lambda L(t, S_2, E_2, I_2, \Lambda_3) + (1-\lambda) L(t, S_2, E_2, I_2, \Lambda_3') = A_1 S_2 + A_2 E_2 \\ + A_3 I_2 + \frac{1}{2} B\lambda\Lambda_3^2 + \frac{1}{2} B(1-\lambda)\Lambda_3'^2) \end{aligned} \tag{7}$$

This means that from (6) and (7), we must prove that $(\lambda\Lambda_3 + (1-\lambda)\Lambda_3')^2 \leq \lambda\Lambda_3^2 + (1-\lambda)\Lambda_3'^2$. Expanding $(\lambda\Lambda_3 + (1-\lambda)\Lambda_3')^2$ gives

$$\begin{aligned} (\lambda\Lambda_3 + (1-\lambda)\Lambda_3')^2 &= \lambda^2\Lambda_3^2 + 2\lambda(1-\lambda)\Lambda_3\Lambda_3' + (1-\lambda)^2\Lambda_3'^2 \\ &= \lambda(\lambda - 1 + 1)\Lambda_3^2 + 2\lambda(1-\lambda)\Lambda_3\Lambda_3' + (1-\lambda)(1-\lambda)\Lambda_3'^2 \\ &= \lambda\Lambda_3^2 + (1-\lambda)\Lambda_3'^2 - \lambda(1-\lambda)\left[\Lambda_3^2 - 2\Lambda_3\Lambda_3' + \Lambda_3'^2\right] \\ &= \lambda\Lambda_3^2 + (1-\lambda)\Lambda_3'^2 - \lambda(1-\lambda)\left[\Lambda_3 - \Lambda_3'\right]^2 \\ &\leq \lambda\Lambda_3^2 + (1-\lambda)\Lambda_3'^2. \end{aligned} \tag{8}$$

This proves the convexity of the integrand on the singleton, Ω.

3.1 The Pontryagin Maximum Principle

The Pontryagin maximum principle converts a constrained control problem to an unconstrained one by introducing additional variable called adjoint variable to the original problem. Generally, given a state x and a control u, the Pontryagin maximum principle stated below, provides the condition under which the pair (x^*, u^*) is optimal.

Theorem 3.1. *(Pontryagin Maximum Principle): Suppose u^* and x^* are optimal for the control problem*

$$\min \int_{t_0}^{t_f} f(x(t), u(t))dt$$

subject to

$$\frac{dx(t)}{dt} = g(x(t), u(t)), \quad x(t_0) = x_0$$

then there exists a Piecewise differentiable function $\phi(t)$ called the adjoint variable or costate such that the Hamiltonian defined by

$$H(t, x, u, \phi) = f(t, x(t), u(t)) + \phi g(t, x(t), u(t)) \tag{9}$$

satisfies

$$
\begin{aligned}
H(t,x,u,\phi) &\leq H(t,x^*,u^*,\phi) && (10)\\
\frac{dH(t,x,u,\phi)}{du} &= 0 && (11)\\
\frac{d\phi(t)}{dt} &= -\frac{dH(t,x^*,u^*,\phi)}{dx} && (12)\\
\frac{dx(t)}{dt} &= \frac{dH(t,x^*,u^*,\phi)}{d\phi} && (13)
\end{aligned}
$$

for all controls u at each time t. The adjoint variable ϕ satisfies the transversality condition $\phi(t_f) = 0$

From (9), the Hamiltonian is given by

$$
\begin{aligned}
H = {} & A_1 S_2 + \frac{1}{2} B \Lambda_3^2(t) \\
& + \phi_1(t)\left(\Lambda_1 - \left(\frac{b_1\alpha_1 I_2}{N_2} + \frac{b_2\alpha_2 I_3}{N_3}\right) S_1 - \sigma_1 S_1\right) \\
& + \phi_2(t)\left(\left(\frac{b_1\alpha_1 I_2}{N_2} + \frac{b_2\alpha_2 I_3}{N_3}\right) S_1 - (\beta_1 + \sigma_1) E_1\right) \\
& + \phi_3(t)\left(\beta_1 E_1 - (\gamma + \sigma_1 + \sigma_1')I_1\right) \\
& + \phi_4(t)\left(\gamma I_1 - \sigma_1 R\right) + \phi_5(t)\left(\Lambda_2 + q\kappa\mu_1 N_2 - \frac{b_1\alpha_3 I_1}{N_1} S_2(t) - \sigma_2 S_2(t)\right) \\
& + \phi_6(t)\left(\frac{b_1\alpha_3 I_1}{N_1} S_2(t) - (\beta_2 + \sigma_2) E_2(t)\right) + \phi_7(t)\left(\beta_2 E_2(t) - \sigma_2 I_2(t)\right) \\
& + \phi_8(t)\left(\Lambda_3(t) + \kappa\mu_2 N_3 - \frac{b_2\alpha_4 I_1}{N_1} S_3(t) - \sigma_2 S_3(t)\right) \\
& + \phi_9(t)\left(\frac{b_2\alpha_4 I_1}{N_1} S_3(t) - (\beta_3 + \sigma_2) E_3(t)\right) + \phi_{10}(t)\left(\beta_3 E_3(t) - \sigma_2 I_3(t)\right).
\end{aligned} \tag{14}
$$

where the adjoint variables $\phi_i, i = 1, 2, \cdots 10$, satisfy the system of ordinary differential equations

$$
\begin{aligned}
\frac{d\phi_1}{dt} &= (\phi_1-\phi_2)\left(\frac{b_1\alpha_1 I_2}{N_2}+\frac{b_2\alpha_2 I_3}{N_3}\right)+\sigma_1\phi_1+(\phi_6-\phi_5)\frac{b_1\alpha_3 I_1}{N_1^2}S_2+(\phi_9-\phi_8)\frac{b_2\alpha_4 I_1}{N_1^2}S_3\\
\frac{d\phi_2}{dt} &= (\beta_1+\sigma_1)\phi_2-\beta_1\phi_3+(\phi_6-\phi_5)\frac{b_1\alpha_3 I_1}{N_1^2}S_2+(\phi_9-\phi_8)\frac{b_2\alpha_4 I_1}{N_1^2}S_3\\
\frac{d\phi_3}{dt} &= (\gamma+\sigma_1+\sigma_1')\phi_3-\gamma\phi_4+(\phi_5-\phi_6)\frac{(N_1-I_1)b_1\alpha_3}{N_1^2}S_2+(\phi_8-\phi_9)\frac{(N_1-I_1)b_2\alpha_4}{N_1^2}S_3\\
\frac{d\phi_4}{dt} &= \sigma_1\phi_4+(\phi_6-\phi_5)\frac{b_1\alpha_3 I_1}{N_1^2}S_2+(\phi_9-\phi_8)\frac{b_2\alpha_4 I_1}{N_1^2}S_3\\
\frac{d\phi_5}{dt} &= (\phi_2-\phi_1)\frac{\alpha_1 b_1 I_2}{N_2^2}S_1+(\phi_5-\phi_6)\frac{\alpha_3 b_1 I_1}{N_1}+(\sigma_2-q\kappa\mu_1)\phi_5-A_1\\
\frac{d\phi_6}{dt} &= (\phi_2-\phi_1)\frac{\alpha_1 b_1 I_2}{N_2^2}S_1+(\beta_2+\sigma_2)\phi_6-q\kappa\mu_1\phi_5-\beta_2\phi_7\\
\frac{d\phi_7}{dt} &= \sigma_2\phi_7+(\phi_1-\phi_2)\frac{(N_2-I_2)b_1\alpha_1}{N_2^2}S_1-q\kappa\mu_1\phi_5\\
\frac{d\phi_8}{dt} &= (\phi_2-\phi_1)\frac{\alpha_2 b_2 I_3}{N_3^2}S_1+(\phi_8-\phi_9)\frac{\alpha_4 b_2 I_1}{N_1}+(\sigma_2-\kappa\mu_2)\phi_8\\
\frac{d\phi_9}{dt} &= (\phi_2-\phi_1)\frac{\alpha_2 b_2 I_3}{N_3^2}S_1+(\beta_3+\sigma_2)\phi_9-\kappa\mu_2\phi_8-\beta_3\phi_{10}\\
\frac{d\phi_{10}}{dt} &= \sigma_2\phi_{10}+(\phi_1-\phi_2)\frac{(N_3-I_3)b_2\alpha_2}{N_3^2}S_1-\kappa\mu_2\phi_8
\end{aligned}
\tag{15}
$$

with the transversality condition $\phi_i(T)=0, i=1,2,\cdots,10$. Using the optimality condition (11), we obtain that $\Lambda_3^*(t)=\frac{-\phi_8(t)}{B}$. Therefore, the optimal control parameter can be characterized as

$$\Lambda_3^*(t)=max\left(a,min\left(b,\frac{-\phi_8(t)}{B}\right)\right) \tag{16}$$

Hence, (16) gives the number of wolbachia-infected mosquitoes to be released at any time t for optimal control of zika virus disease.

Parameter	*Value*	*Source*	*Parameter*	*Value*	*Source*
Λ_1	250	assumed	σ_1'	0.00001	assumed
Λ_2	500	assumed	σ_1	0.0005	assumed
α_3	0.175	[4]	q	0.017	assumed
α_4	0.0005	assumed	μ_1	0.03	assumed
μ_2	0.03	assumed	σ_2	0.15	[11]
β_1	$\frac{1}{3}$	[8]	κ	0.5	[11]
b_1	0.0075	assumed	γ	0.5	assumed
b_2	0.7	assumed	α_2	0.001	assumed
β_2	$\frac{1}{9}$	[2]	α_1	0.0175	assumed
β_3	$\frac{1}{18}$	assumed			

Table 1: Parameter Values used in this model

4 Numerical Experiment And Discussion

Here, we conduct numerical experiment using the existing parameter values in Table 1 to visualize the effect of optimal use of wolbachia-carrier aedes aegypti for zika virus disease control. The forward-

backward sweep method for numerical solution of the optimal control is used to solve the optimal control model. This method involves solving the optimal state equation using forward Runge-Kutta order 4 method with the initial guesses for the optimal controls, followed by solving the adjoint system of equation with backward Runge-Kutta order 4 method with the transversality conditions $\phi_i(T) = 0$. The optimal controls are updated with the current state and adjoint solutions at the end of each iteration. The iteration is repeated until convergence is achieved. To present the result of the numerical experiment, we plot the graphs of susceptible wolbachia-free mosquitoes, exposed wolbachia-free mosquitoes and infectious wolbachia-free mosquitoes for the cases of when there is no control and when there is optimal control of the disease. The graph of the optimal control, $\Lambda_3(t)$ is also plotted. The initial solutions used are $S_1^0 = 1500, E_1^0 = 200, I_H^0 = 500, R^0 = 100, S_2^0 = 1500, E_2^0 = 300, I_2^0 = 400, S_3^0 = 2400, E_3^0 = 0, I_3 = 0$. We have also used $A_1 = 50, B = -0.000001, a = 0, b = 100000$. The results are presented in figure 1, figure 2, figure 3 and figure 4. In figure 1, we see that total population of wolbachia-free mosquitoes is higher when optimal control is applied than when when there is no control. Also, Figure 2 shows the population of susceptible wolbachia-free mosquitoes when there is no control, and when optimal control is applied. We see that in the absence of wolbachia-infected mosquitoes, the population of susceptible wolbachia-free mosquitoes is larger than when there is optimal control. This is because the wolbachia-infected mosquitoes have suppressed the wolbachia-free mosquitoes through cytoplasmic incompatibility. In figure 3, we have the populations of susceptible wolbachia-free and wolbachia-infected mosquitoes. The graph show that susceptible wolbachia-infected mosquitoes outgrows the susceptible wolbachia-free mosquitoes. This happens because wolbachia-infected mosquitoes have established themselves, and gradually eliminates wolbachia-free mosquitoes. Figure 4 presents the number of wolbachia-infected mosquitoes that need to be recruited at time, t for optimal control of zika virus disease. Initially, the number increases as more wolbachia-infected mosquitoes are needed to suppress the wolbachia-free ones, and later decreases gradually as time increases when the number of wolbachia-free mosquitoes decreases.

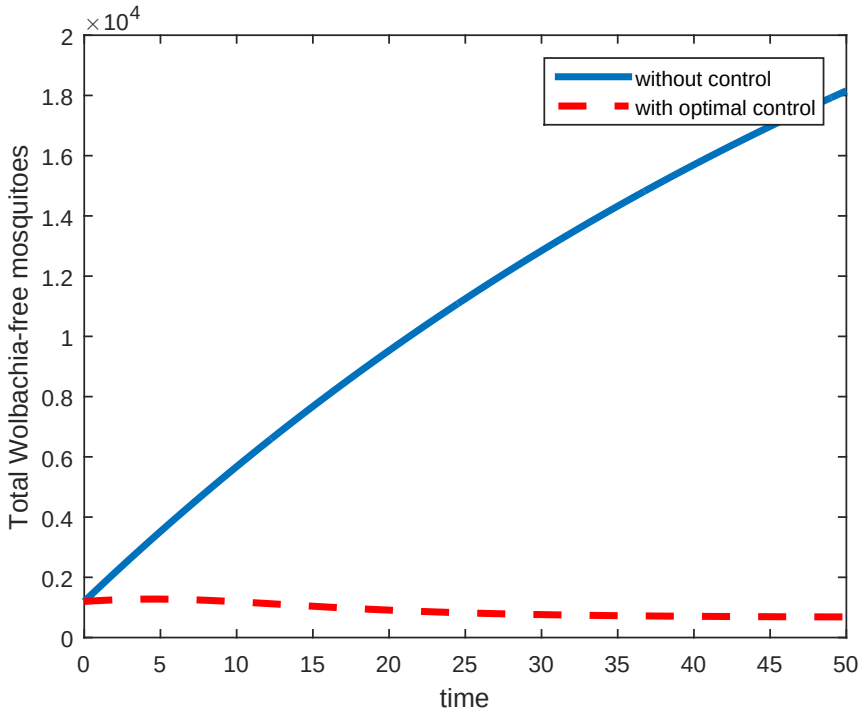

Figure 1: Graph of Total wolbachia-free Mosquitoes with and without control

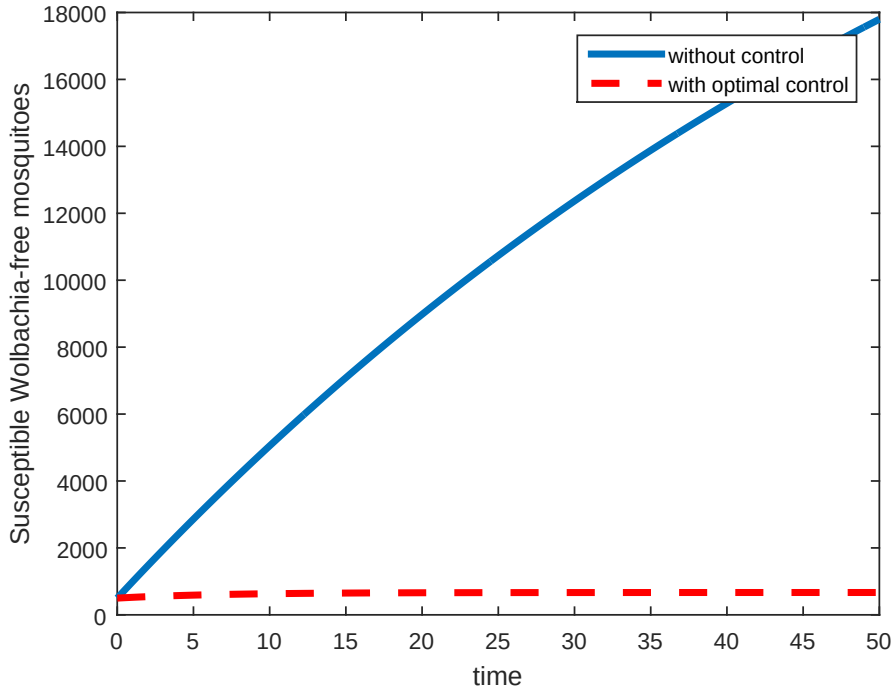

Figure 2: Graph of Susceptible wolbachia-free Mosquitoes with and without control

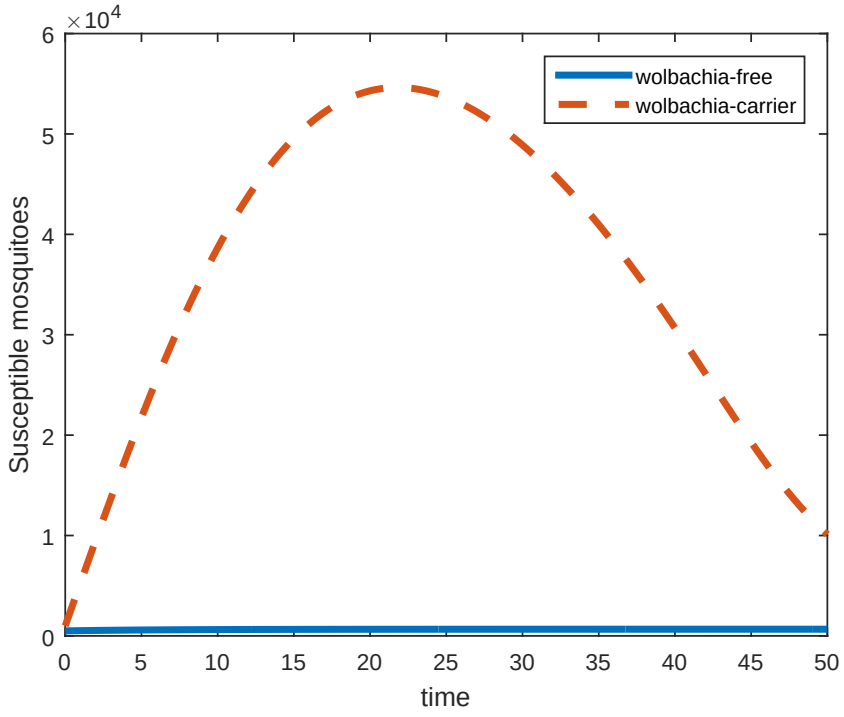

Figure 3: Graph of Susceptible Wolbachia-free and Wolbachia-carrier Mosquitoes

5 Conclusion

We have modeled in this paper, the use of wolbachia-infected aedes aegypti mosquitoes in stopping the spread of zika virus disease. The optimal control of the disease using this biocontrol method is investigated, and the level of recruitment of the wolbachia-infected mosquitoes required to achieve

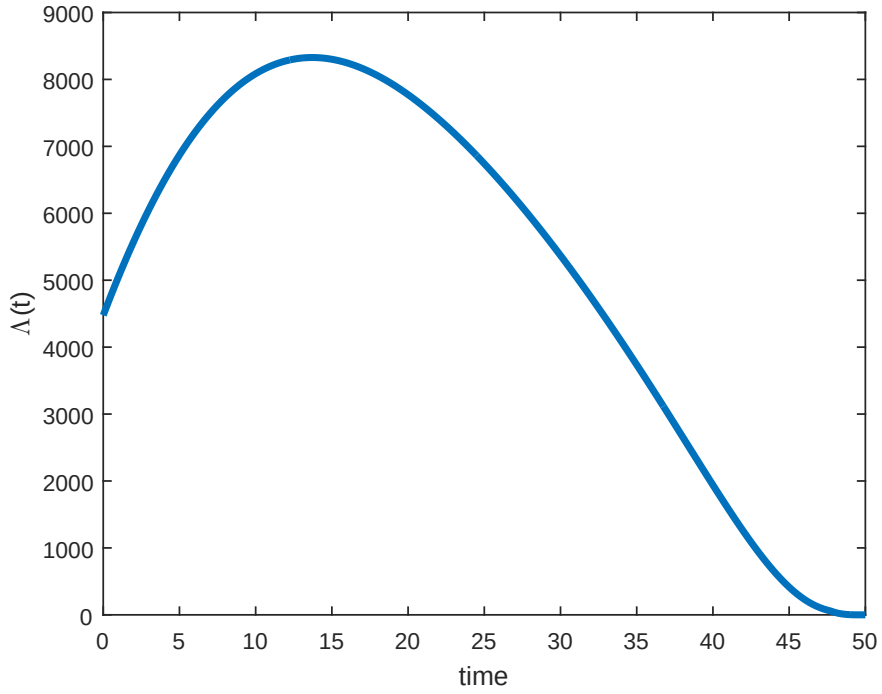

Figure 4: Graph of Optimal Recruitment Strategy for Wolbachia-carrier Mosquitoes

optimal control of the disease is obtained. We conclude that in order to achieve optimal control of zika virus disease using this control method, the obtained optimal recruitment level of wolbachia-infected aedes aegypti mosquitoes must be used.

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