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Conference Paper

An Optimal Control Approach to Malaria Prevention via Insecticide-Treated Nets

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Malaria is a life threatening disease, entirely preventable and treatable, provided that the currently recommended interventions are properly implemented. These interventions include vector control through the use of insecticide-treated nets (ITNs). However, ITN possession is not necessarily translated into use. Human behavior change interventions, including information, education, communication (IEC) campaigns and postdistribution hang-up campaigns, are strongly recommended. In this paper, we consider a recent mathematical model for the effects of ITNs on the transmission dynamics of malaria infection, which takes into account the human behavior. We introduce in this model a *supervision* control, representing IEC campaigns for improving the ITN usage. We propose and solve an optimal control problem where the aim is to minimize the number of infected humans while keeping the cost as low as possible. Numerical results are provided, which show the effectiveness of the optimal control interventions.

1. Introduction

Malaria is a life threatening disease caused by *Plasmodium* parasites and transmitted from one individual to another by the bite of infected female anopheline mosquitoes [1, 2]. In the human body, the parasites multiply in the liver and then infect red blood cells. Following World Health Organization (WHO) 2012 report, an estimated 3.3 billion people were at risk of malaria in 2011, with populations living in Sub-Saharan Africa having the highest risk of acquiring malaria [3]. Malaria is an entirely preventable and treatable disease, provided the currently recommended interventions are properly implemented. Following WHO, these interventions include (i) vector control through the use of insecticide-treated nets (ITNs), indoor residual spraying and, in some specific settings, larval control, (ii) chemoprevention for the most vulnerable populations, particularly pregnant women and infants, (iii) confirmation of malaria diagnosis through microscopy or rapid diagnostic tests for every suspected case, and (iv) timely treatment with appropriate antimalarial medicines [3]. An ITN is a mosquito net that repels, disables, and/or kills mosquitoes coming into contact with insecticide on the netting material. ITNs are considered one of the most effective interventions against malaria [4]. In 2007, WHO recommended full ITN coverage of all people at risk of malaria, even in high-transmission settings [5]. By 2011, 32 countries in the African region and 78 other countries worldwide, had adopted the WHO recommendation. A total of 89 countries, including 39 in Africa, distribute ITNs free of charge. Between 2004 and 2010, the numbers of ITNs delivered annually by manufacturers to malaria-endemic countries in Sub-Saharan Africa increased from 6 million to 145 million. However, the numbers delivered in 2011 and 2012 are below the number of ITNs required to protect all population at risk. There is an urgent need to identify new funding sources to maintain and expand coverage levels of interventions so that outbreaks of disease can be avoided and international targets for reducing malaria cases and deaths can be attained [3].

A number of studies reported that ITN possession is not necessarily translated into use. Human behavior change interventions, including information, education, and

communication (IEC) campaigns and postdistribution hang-up campaigns, are strongly recommended, especially where there is evidence of their effectiveness in improving ITN usage [3, 6, 7]. In this paper, we consider the model from [8] for the effects of ITNs on the transmission dynamics of malaria infection. Other articles considered the impact of intervention strategies using ITN (see, e.g., [9, 10]). However, only in [8], the human behavior is incorporated into the model. We introduce in the model of [8] a *supervision* control, u, which represents IEC campaigns for improving the ITN usage. The reader interested in the use of optimal control to infectious diseases is referred to [11, 12] and the references cited therein. For the state of the art in malaria research see [2].

The text is organized as follows. In Section 2, we present the mathematical model for malaria transmission with one control function u. In Section 3, we propose an optimal control problem for the minimization of the number of infected humans while controlling the cost of control interventions. Finally, in Section 4 some numerical results are analyzed and interpreted from the epidemiological point of view.

2. Controlled Model

We consider a mathematical model presented in [8] for the effects of ITN on the transmission of malaria infection and introduce a time-dependent *supervision* control u. The model considers transmission of malaria infection of mosquito (also referred as vector) and human (also referred as host) population. The host population is divided into two compartments, susceptible (S_h) and infected (I_h), with a total population (N_h) given by $N_h = S_h + I_h$. Analogously, the vector population is divided into two compartments, susceptible (S_v) and infected (I_v), with a total population (N_v) given by $N_v = S_v + I_v$. The model is constructed under the following assumptions: all newborns individuals are assumed to be susceptible and no infected individuals are assumed to come from outside the community. The human and mosquito recruitment rates are denoted by Λ_h and Λ_v, respectively. The disease is fast progressing, and thus the exposed stage is minimal and is not considered. Infected individuals can die from the disease or become susceptible after recovery while the mosquito population does not recover from infection. ITNs contribute for the mortality of mosquitoes. The average number of bites per mosquito, per unit of time (mosquito-human contact rate), is given by

$$\beta = \beta_{\max}(1 - b), \tag{1}$$

where $\beta_{\max}$ denotes the maximum transmission rate and b the proportion of ITN usage. It is assumed that the minimum transmission rate is zero. The value of β is the same for human and mosquito population, so the average number of bites per human per unit of time is $\beta N_v/N_h$ (see [8] and the references cited therein). Thus, the force of infection for susceptible humans (λ_h) and susceptible vectors (λ_v) are given by

$$\lambda_h = \frac{p_1 \beta I_v}{N_h}, \qquad \lambda_v = \frac{p_2 \beta I_h}{N_h}, \tag{2}$$

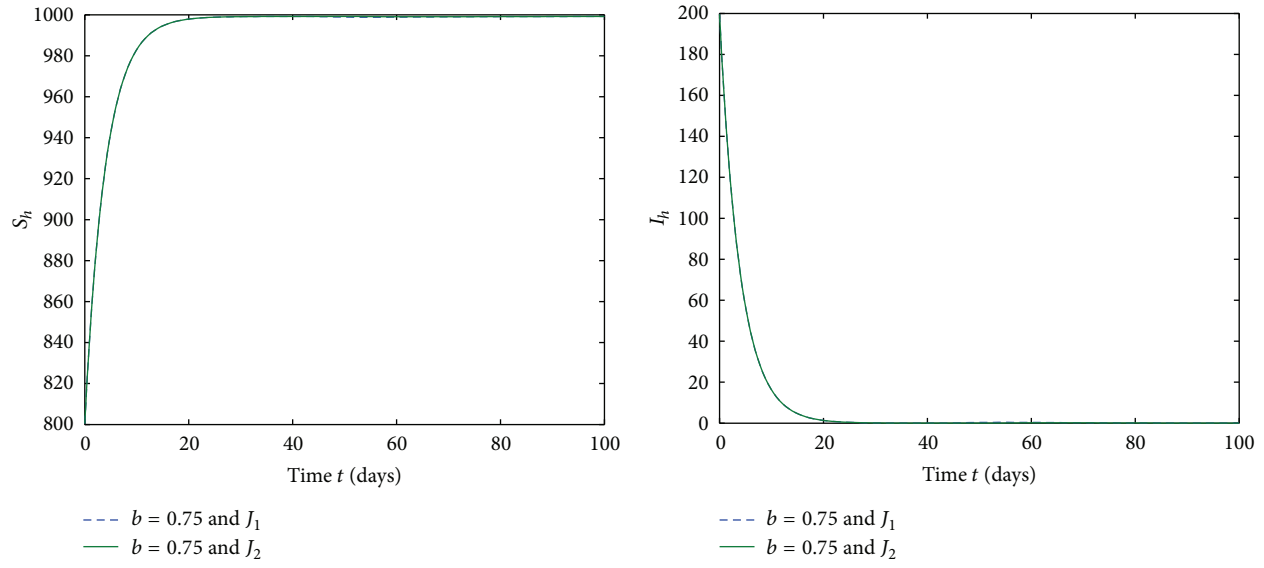
Table 1: Parameter values.

Symbol	Description	Value
Λ_h	Recruitment rate in humans	$10^3/(70 \times 365)$
Λ_v	Recruitment rate in mosquitoes	$10^4/21$
μ_h	Natural mortality rate in humans	$1/(70 \times 365)$
δ_h	Disease induced mortality rate in humans	10^{-3}
b	Proportion of treated net usage	0.25; 0.3; 0.4; 0.5; 0.6; 0.7; 0.75
γ_h	Recovery rate of infected humans to be susceptible	1/4
μ_{v_1}	Natural mortality rate of mosquitoes	1/21
$\mu_{\max} b$	Mortality rate of mosquitoes due to treated net	1/21
$\beta_{\max}$	Maximum mosquito-human contact rate	0.1
p_1	Probability of disease transmission from mosquito	1
p_2	Probability of disease transmission from human to mosquito	1
A_1	Weight constant on infected humans	25
C	Weight constant on control	50
$S_h(0)$	Susceptible individuals initial value	800
$I_h(0)$	Infected individuals initial value	200
$S_v(0)$	Susceptible vectors initial value	4000
$I_v(0)$	Infectious vectors initial value	900

where p_1 and p_2 are the transmission probability per bite from infectious mosquitoes to humans and from infected humans to mosquitoes, respectively. The death rate of the mosquitoes is modeled by $\mu_{vb} = \mu_{v1} + \mu_{\max} b$, where μ_{v1} is the natural death rate and $\mu_{\max} b$ is the death rate due to pesticide on ITNs. The coefficient $1 - u$ represents the effort of susceptible humans that become infected by infectious mosquitoes bites, such as educational programs/campaigns for the correct use of ITNs, supervision teams that visit every house in a certain region and assure that every person has access to an ITN, know how to use it correctly, and recognize its importance on the reduction of malaria disease transmission. The values of the parameters Λ_h, Λ_v, μ_h, δ_h, γ_h, μ_{v1}, $\mu_{\max} b$, $\beta_{\max}$, p_1, and p_2 are taken from [8] (see Table 1).

The state system of the controlled malaria model is given by

$$\begin{aligned}
\dot{S}_h(t) &= \Lambda_h - (1 - u(t))\lambda_h S_h(t) \\
&\quad + \gamma_h I_h(t) - \mu_h S_h(t), \\
\dot{I}_h(t) &= (1 - u(t))\lambda_h S_h(t) \\
&\quad - (\mu_h + \gamma_h + \delta_h) I_h(t), \\
\dot{S}_v(t) &= \Lambda_v - \lambda_v S_v(t) - \mu_{vb} S_v(t), \\
\dot{I}_v(t) &= p_2 \lambda_v S_v(t) - \mu_{vb} I_v(t).
\end{aligned} \tag{3}$$



(a) Susceptible humans for J_1 and J_2

(b) Infected humans for J_1 and J_2

FIGURE 1: Susceptible and infected individuals for different cost functionals J_1 and J_2 (parameter/constant values from Table 1 and $b = 0.75$).

The rate of change of the total human and mosquito populations is given by

$$\begin{aligned} \dot{N}_h(t) &= \Lambda_h - \mu_h N_h(t) - \delta_h I_h(t), \\ \dot{N}_v(t) &= \Lambda_v - \mu_{vb} N_v(t). \end{aligned} \tag{4}$$

3. Optimal Control Problem

We formulate an optimal control problem that describes the goal and restrictions of the epidemic. In [8] it is found that the ITN usage must attain 75% ($b = 0.75$) of the host population in order to extinct malaria. Therefore, educational campaigns must continue encouraging the population to use ITNs. Moreover, it is very important to assure that ITNs are in good conditions and each individual knows how to use them properly. Having this in mind, we introduce a *supervision* control function, u, where the coefficient $1 - u$ represents the effort to reduce the number of susceptible humans that become infected by infectious mosquitoes bites, assuring that ITNs are correctly used by the fraction b of the host population.

We consider the state system (3) of ordinary differential equations in $\mathbb{R}^4$ with the set of admissible control functions given by

$$\Omega = \left\{ u(\cdot) \in L^{\infty}\left(0, t_f\right) \mid 0 \leqslant u(t) \leqslant 1, \forall t \in \left[0, t_f\right] \right\}. \tag{5}$$

The objective functional is given by

$$J_1(u) = \int_0^{t_f} A_1 I_h(t) + \frac{C}{2} u^2(t)\, dt, \tag{6}$$

where the weight coefficient, C, is a measure of the relative cost of the interventions associated to the control u and A_1 is the weight coefficient for the class I_h. The aim is to minimize the infected humans while keeping the cost low. More precisely, we propose the optimal control problem of determining $(S_h^*, I_h^*, S_v^*, I_v^*)$ associated to an admissible control $u^*(\cdot) \in \Omega$ on the time interval $[0, t_f]$, satisfying (3), the initial conditions $S_h(0)$, $I_h(0)$, $S_v(0)$, and $I_v(0)$ (see Table 1) and minimizing the cost functional (6), that is,

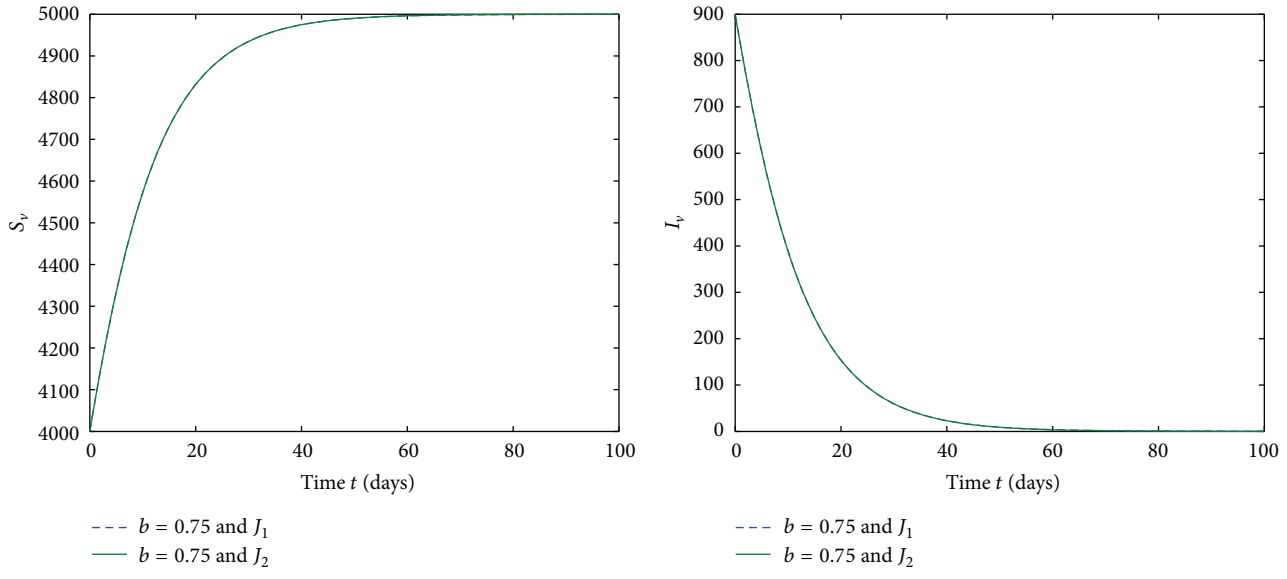
$$J_1\left(u^*(\cdot)\right) = \min_{\Omega} J_1(u(\cdot)). \tag{7}$$

The existence of an optimal control $u^*(\cdot)$ comes from the convexity of the Lagrangian of (6) with respect to the control and the regularity of the system (3) (see, e.g., [13, 14] for existence results of optimal solutions). Applying the Pontryagin maximum principle [15], we derive the optimal solution $(u^*, S_h^*, I_h^*, S_v^*, I_v^*)$ of the proposed optimal control problem (see the Appendix).

More generally, one could take the following cost functional:

$$J_2(u) = \int_0^{t_f} A_1 I_h(t) + A_2 I_v(t) + \frac{C}{2} u^2(t)\, dt, \tag{8}$$

where A_2 is the weight constant on infectious mosquitoes (for numerical simulations we considered $A_2 = 25$). It turns out that when we include in the objective functional the number of infectious mosquitoes, the distribution of the total host population N_h, and vector population N_v by the categories S_h, I_h, and S_v, I_v, respectively, is the same for both cost functionals J_1 and J_2 (see Figures 1 and 2). On the other hand, the effort on the control is higher for the cost functional J_2 (see Figure 3). Therefore, we choose to use the cost functional J_1 in our numerical simulations (Section 4).



(a) Susceptible mosquitoes for J_1 and J_2

(b) Infectious mosquitoes for J_1 and J_2

FIGURE 2: Susceptible and infectious mosquitoes for different cost functions J_1 and J_2 (parameter/constant values from Table 1 and $b = 0.75$).

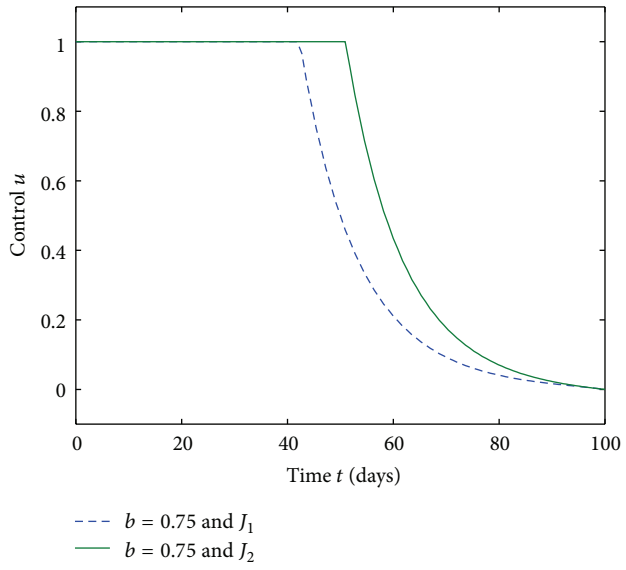


FIGURE 3: Optimal control u for different cost functionals J_1 and J_2 (parameter/constant values from Table 1 and $b = 0.75$).

4. Numerical Results and Discussion

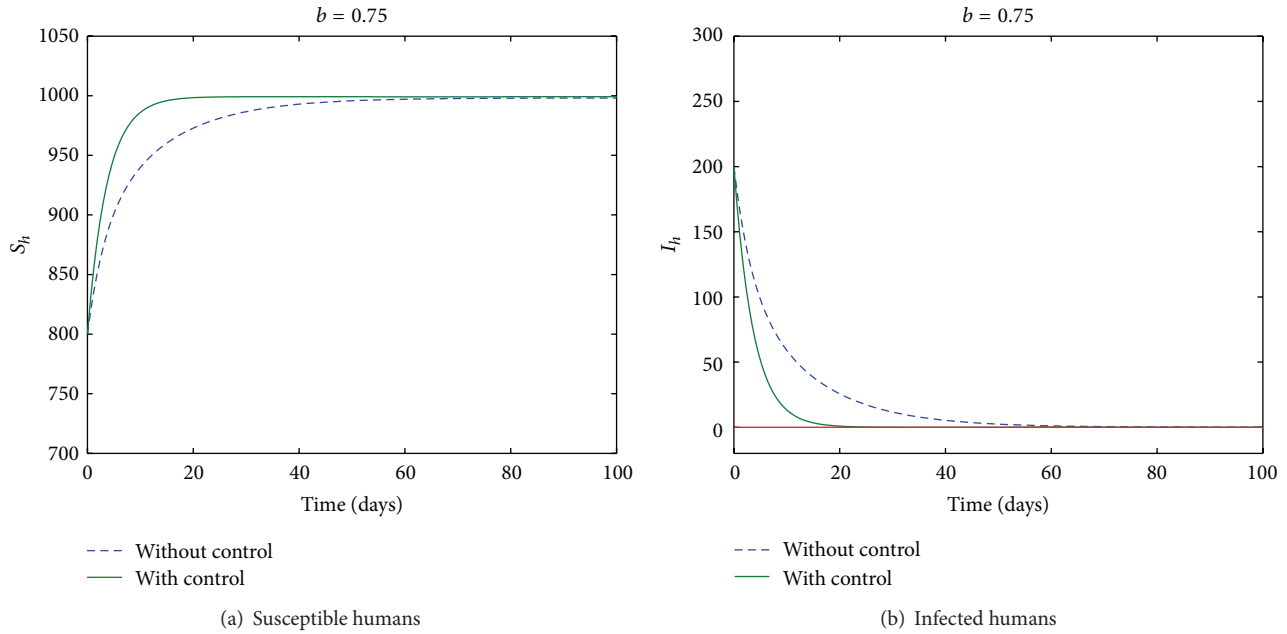
Our numerical results were obtained and confirmed following different approaches. The first approach consisted in using IPOPT [16] and the algebraic modeling language AMPL [17]. In a second approach, we used the PROPT MATLAB Optimal Control Software [18]. The results were coincident and are easily confirmed by the ones obtained using an iterative method that consists in solving the system of eight ODEs given by (3) and (A.6) in the Appendix. For that, one first solves system (3) with a guess for the control over the time interval $[0, t_f]$ using a forward fourth-order Runge-Kutta scheme and the transversality conditions (A.5) in Appendix. Then, system (A.6) is solved by a backward fourth-order Runge-Kutta scheme using the current iteration solution of (3). The control is updated by using a convex combination of the previous control and the value from (A.8) (see the Appendix). The iterative method ends when the values of the approximations at the previous iteration are close to the ones at the present iteration. For details, see [19, 20].

First of all, we consider $b = 0.75$ and show that when we apply the *supervision* control u, better results are obtained, that is, the number of infected humans vanishes faster when compared to the case where no control is used. If the control intervention u is applied, then the number of infected individuals vanishes after approximately 30 days. If no control is considered, then it takes approximately 70 days to assure that there are no infected humans (see Figure 4 for the fraction of susceptible and infected humans and Figure 5 for the optimal control).

For smaller proportions of ITN usage than $b = 0.75$, similar results on the reduction of infected humans are attained when we consider the optimal *supervision* control u (see Figures 6 and 7). We note that the control u does not contribute significantly for the decrease of I_v (see Figure 8).

Appendix

According to the Pontryagin maximum principle [15], if $u^*(\cdot) \in \Omega$ is optimal for the problem (3), (7) with the initial conditions given in Table 1 and fixed final time t_f, then there exists a nontrivial absolutely continuous mapping



(a) Susceptible humans

(b) Infected humans

Figure 4: Susceptible and infected humans for $b = 0.75$ with and without control.

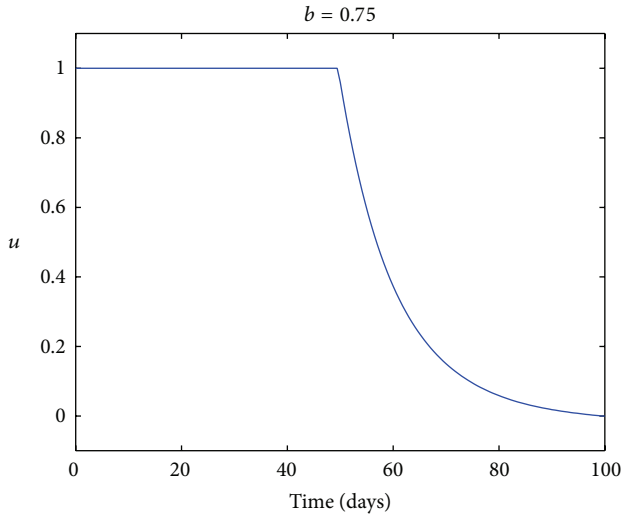


Figure 5: Optimal control u for $b = 0.75$.

$\lambda : [0, t_f] \to \mathbb{R}^4$, $\lambda(t) = (\lambda_1(t), \lambda_2(t), \lambda_3(t), \lambda_4(t))$, called *adjoint vector*, such that

$$\begin{aligned} \dot{S}_h &= \frac{\partial H}{\partial \lambda_1}, & \dot{I}_h &= \frac{\partial H}{\partial \lambda_2}, \\ \dot{S}_v &= \frac{\partial H}{\partial \lambda_3}, & \dot{I}_v &= \frac{\partial H}{\partial \lambda_4}, \end{aligned} \tag{A.1}$$

$$\begin{aligned} \dot{\lambda}_1 &= -\frac{\partial H}{\partial S_h}, & \dot{\lambda}_2 &= -\frac{\partial H}{\partial I_h}, \\ \dot{\lambda}_3 &= -\frac{\partial H}{\partial S_v}, & \dot{\lambda}_4 &= -\frac{\partial H}{\partial I_v}, \end{aligned} \tag{A.2}$$

where function H defined by

$$\begin{aligned} H &= H(S_h, I_h, S_v, I_v, \lambda, u) \\ &= A_1 I_h + \frac{C}{2} u^2 \\ &\quad + \lambda_1 \left(\Lambda_h - (1-u)\lambda_h S_h + \gamma_h I_h - \mu_h S_h\right) \\ &\quad + \lambda_2 \left((1-u)\lambda_h S_h - (\mu_h + \gamma_h + \delta_h) I_h\right) \\ &\quad + \lambda_3 \left(\Lambda_v - \lambda_v S_v - \mu_{vb} S_v\right) \\ &\quad + \lambda_4 \left(p_2 \lambda_v S_v - \mu_{vb} I_v\right) \end{aligned} \tag{A.3}$$

is called the *Hamiltonian*, and the minimization condition

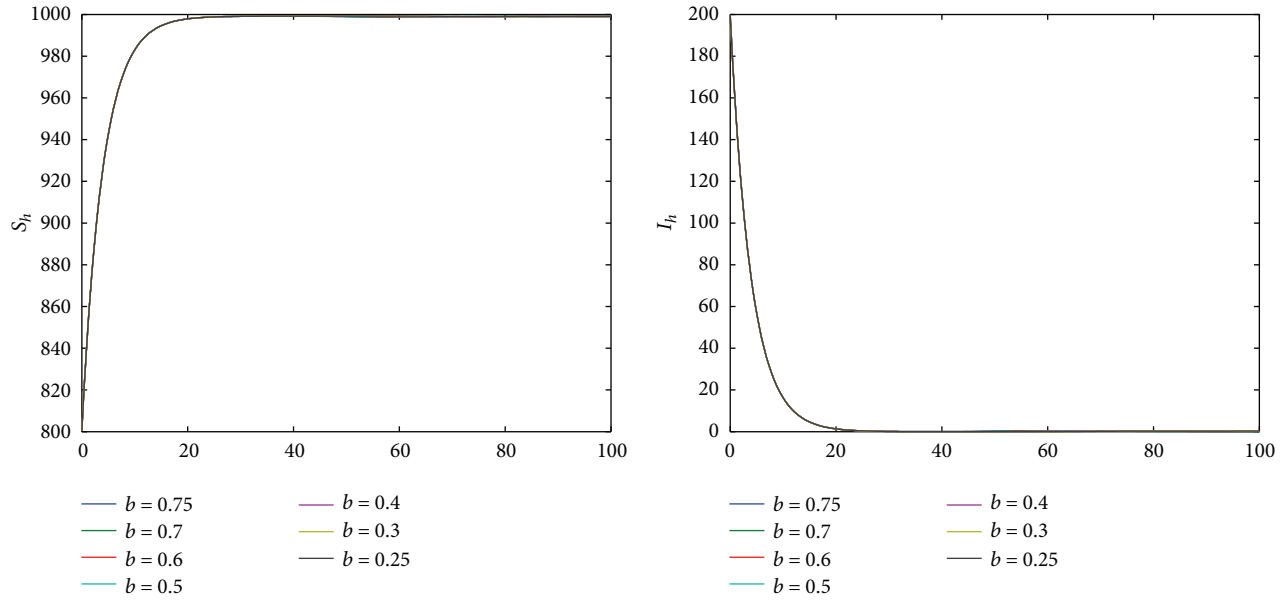
$$\begin{aligned} &H\left(S_h^*(t), I_h^*(t), S_v^*(t), I_v^*(t), \lambda^*(t), u^*(t)\right) \\ &\quad = \min_{0 \leqslant u \leqslant 1} H\left(S_h^*(t), I_h^*(t), S_v^*(t), I_v^*(t), \lambda^*(t), u\right) \end{aligned} \tag{A.4}$$

holds almost everywhere on $[0, t_f]$. Moreover, the transversality conditions

$$\lambda_i(t_f) = 0, \quad i = 1, \ldots, 4, \tag{A.5}$$

hold.

Theorem A.1. *Problem* (3), (7) *with fixed initial conditions* $S_h(0)$, $I_h(0)$, $S_v(0)$, *and* $I_v(0)$ *and fixed final time* t_f *admits a unique optimal solution* $(S_h^*(\cdot), I_h^*(\cdot), S_v^*(\cdot), I_v^*(\cdot))$ *associated*



(a) Susceptible humans

(b) Infected humans

FIGURE 6: Susceptible and infected humans for $b = 0.25; 0.3; 0.4; 0.5; 0.6; 0.7; 0.75$.

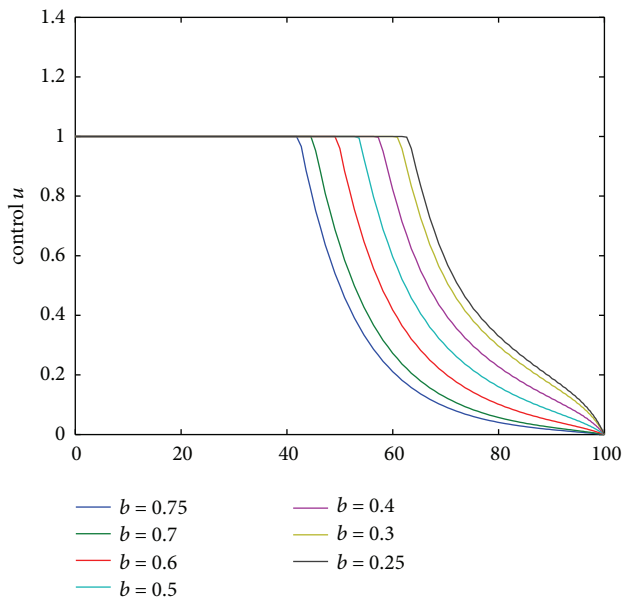


FIGURE 7: Optimal control u for $b = 0.25; 0.3; 0.4; 0.5; 0.6; 0.7; 0.75$.

with an optimal control $u^*(\cdot)$ on $[0, t_f]$. Moreover, there exist adjoint functions $\lambda_1^*(\cdot)$, $\lambda_2^*(\cdot)$, $\lambda_3^*(\cdot)$, and $\lambda_4^*(\cdot)$ such that

$$\begin{aligned}
\dot{\lambda}_1^*(t) &= \lambda_1^*(t)\left(\left(1-u^*(t)\right)\lambda_h + \mu_h\right) \\
&\quad - \lambda_2^*(t)\,\lambda_h\left(1-u^*(t)\right), \\
\dot{\lambda}_2^*(t) &= -A_1 - \lambda_1^*(t)\,\gamma_h + \lambda_2^*(t)\left(\mu_h + \gamma_h + \delta_h\right), \\
\dot{\lambda}_3^*(t) &= \lambda_3^*(t)\left(\lambda_v + \mu_{vb}\right) - \lambda_4^*(t)\,\lambda_v, \\
\dot{\lambda}_4^*(t) &= \lambda_4^*(t)\,\mu_{vb},
\end{aligned} \tag{A.6}$$

with transversality conditions

$$\lambda_i^*\left(t_f\right) = 0, \quad i = 1, \ldots, 4. \tag{A.7}$$

Furthermore,

$$u^*(t) = \min\left\{\max\left\{0, \frac{\lambda_h(b)\,S_h^*(t)}{C}\left(\lambda_2^*(t) - \lambda_1^*(t)\right)\right\}, 1\right\}. \tag{A.8}$$

Proof. Existence of an optimal solution $(S_h^*, I_h^*, S_v^*, I_v^*)$ associated with an optimal control u^* comes from the convexity of the integrand of the cost functional J with respect to the control u and the Lipschitz property of the state system with respect to state variables (S_h, I_h, S_v, I_v) (see, e.g., [13, 14]). System (A.6) is derived from the Pontryagin maximum principle (see (A.2), [15]) and the optimal control (A.8) comes from the minimization condition (A.4). The optimal control given by (A.8) is unique due to the boundedness of the state and adjoint functions and the Lipschitz property of systems (3) and (A.6) (see, e.g., [19] and the references cited therein). □

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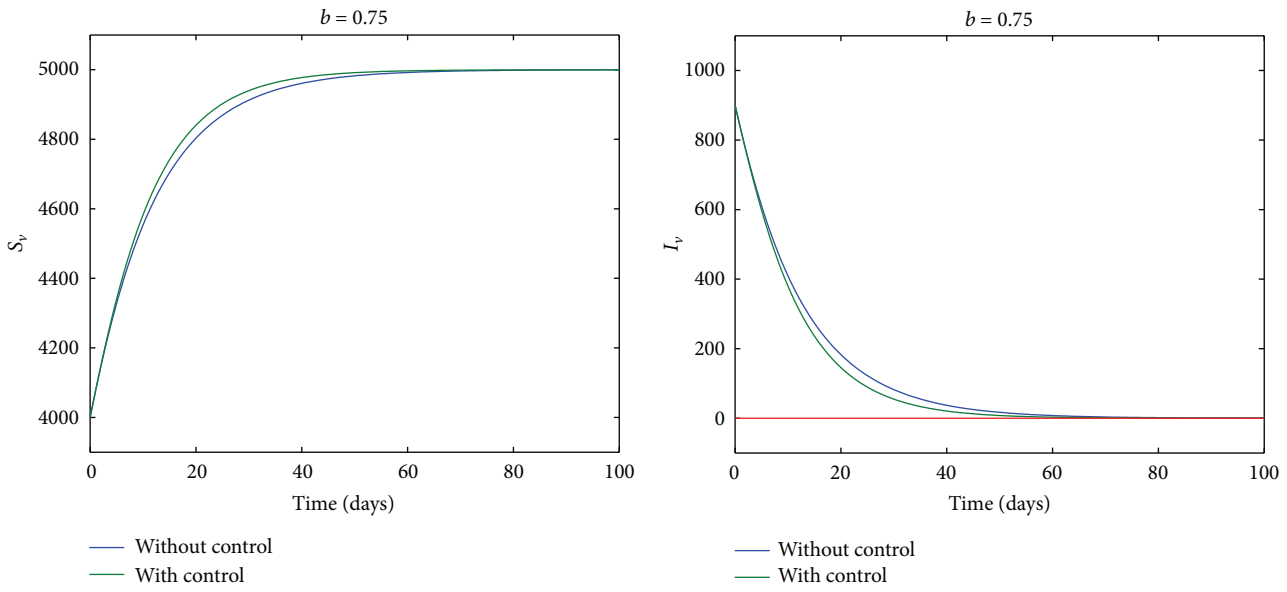

(a) Susceptible mosquitoes

(b) Infectious mosquitoes

FIGURE 8: Susceptible and infectious mosquitoes for $b = 0.75$ with and without control.

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