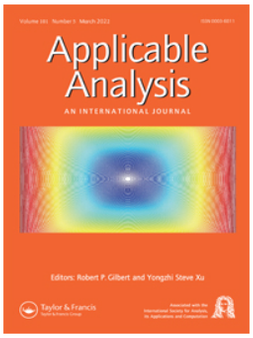

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Malaria modeling and optimal control using sterile insect technique and insecticide-treated net

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ABSTRACT

We investigate a malaria transmission model with SEIR (susceptible-exposed-infected-recovered) classes for the human population, SEI (susceptible-exposed-infected) classes for the wild mosquitoes and an additional class for the sterile mosquitoes. The basic reproduction number of the disease transmission is obtained, and a release threshold of the sterile mosquitoes is provided. We formulate an optimal control problem in which the goal is to minimize both the infected human populations and the cost to implement two control strategies: the release of sterile mosquitoes and the usage of insecticide-treated nets to reduce the malaria transmission. Adjoint equations are derived, and the characterization of the optimal controls is established. Finally, we quantify the effectiveness of the two interventions aimed at limiting the spread of malaria transmission. A combination of both strategies leads to more rapid elimination of the wild mosquito population that can suppress malaria transmission. Numerical simulations are provided to illustrate the results.

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1. Introduction

Malaria is a mosquito-borne disease. It is still a leading cause of death and disease in many developing countries [1–5]. In 2019, an estimated 229 million cases of malaria occurred worldwide and 409,000 people died, mostly infection occurring in the African Region [5]. To prevent malaria transmission and infection, various control approaches have been explored. Malaria infection has been somewhat lessened in many regions through vector-targeted intervention such as insecticide-treated bed nets (ITNs) and indoor residual sprays (IRS). Since massive and long-time spraying of insecticide has commonly been chemically based, the effectiveness of these measures has been hampered by the appearance of insecticide-resistant vector strains [6–8]. The recently released World Malaria Report [5] on insecticide resistance in malaria vectors for 2010–2019 showed that resistance to the commonly used insecticide classes pyretganochlorines, carbamates and organophosphates is widespread in all major malaria vectors across the WHO regions of Africa, the Americas, South-East Asia, the Eastern Mediterranean and the Western pacific. In 2019, the first malaria vaccine was rolled out in Africa, but it only reduced malaria cases in young children with limited efficacy.

Currently, biological control methods of mosquito populations, including the genetic approaches [9–11], sterile insect technique (SIT) [12] and the Wolbachia control techniques [13–15], have been applied in the laboratories or fields. To explore the impact and effectiveness of these biological control measures, many novel mathematical models have been formulated and analyzed. Modeling of the

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genetically altered or transgenic mosquitoes has provided a potentially weapon to fight the mosquito-borne diseases [16–18]. Modeling of the releasing of Wolbachia-infected mosquitoes and studying the mosquitoes suppression effects have provided applicable guidance [19–21]. SIT [12] is an environmentally friendly alternative strategy, which has been gaining renewed interest for the control of mosquito populations. The technique involves the massive release of male mosquitoes (sterilized through radiological or chemical means) into the environment to mate with wild mosquitoes in the environment. Female mosquitoes mating successfully with a sterile male will either not reproduce, or produce eggs that will not hatch. Recently, mathematical models show that it is useful and effective to reduce or suppress a wild mosquito population [11,22–30]. By applying different releasing strategies of sterile mosquitoes, including constant releases, proportional releases, periodic and impulsive releases, mathematical modeling analysis further shows the complex and interesting dynamics of the interactive mosquito populations [27,31–35].

There is still much work to be completed in the search for biological control of mosquitoes and preventing malaria infection. For example, how to model the malaria transmission coupling with the releases of sterile mosquitoes is not fully understood [18,36]. Using multiple strategies simultaneously has proved remarkably effective at reducing malaria burden [37], and part of the recent reduction in malaria burden worldwide can be attributed to the integrated use of treatment and vector control strategies [38,39]. Optimal control theory has been applied to explore malaria control strategies with releasing SIT [26,29,40–43]. For example, Khamis et al. [41] investigated the optimal control problem for malaria by using drug therapy and releasing modified mosquitoes. Their results show that it is the most effective method against malaria transmission by the combination of both vector control and drug therapies. Fister et al. [26] studied an optimal control problem for sterile type mosquito population with diffusion. They show that the release effect of the sterile mosquitoes is optimal by the combination of both strategies: control of the fecundity (using larvicide) and the release of the sterile mosquitoes. If larvicide is allowed, the control effect of wild mosquito populations can arrive at a maximal level. Multerer et al. [29] further investigated the optimal release problem on the impact of releasing sterile male mosquitoes to the wild mosquito population by using a spatial–temporal model on an island. The optimal solutions of the system for a single location are identified and the optimal releasing strategies of the sterile male mosquitoes are given. However, authors seldom investigate the optimal control strategies of malaria transmission by the combination of SIT and insecticide-treated bed nets (ITN).

In this paper, we formulate a malaria transmission model with SEIR (susceptible-exposed-infected-recovered) classes for human population, SEI (susceptible-exposed-infected) classes for the wild mosquitoes, coupling with the releasing of the sterile mosquito populations as our baseline model in Section 2. We derive the basic reproduction number R_0 for the baseline model and analyze the existence of the endemic equilibria as the reproductive number exceeds one. Based on the baseline malaria model, we then formulate an optimal control problem in which the goal is to minimize both the infected human populations and the cost to implement two control strategies: the release of sterile mosquitoes (SIT) and the usage of insecticide-treated nets (ITN) in Section 3. Adjoint equations are derived and the characterization of the optimal controls are established. Finally, we quantify the effectiveness of the two interventions aimed at limiting the spread of malaria. Numerical simulations are provided to illustrate the results. We simulated human, wild and sterile mosquitoes population dynamics using two controls (both SIT and ITN), and using a single control (either SIT or ITN). We found the optimal control strategies under each circumstance. It turns out the combination of both strategies leads to more rapid elimination of the wild mosquito population, which can suppress the malaria transmission in a cost-effective way.

2. Malaria transmission model

We consider human and mosquito populations in a closed, homogeneous environment using a system of differential equations. The human population of size $N_h(t)$ is divided into four compartments:

susceptible $S_h(t)$, exposed $E_h(t)$, infected $I_h(t)$, and recovered from clinical malaria $R_h(t)$, where $N_h(t) = S_h(t) + E_h(t) + I_h(t) + R_h(t)$. Due to the facts that only female mosquitoes bite people and transmit malaria, the total female mosquitoes population $N_v(t)$ is split into susceptible $S_v(t)$, latent $E_v(t)$ and infected mosquitoes $I_v(t)$. Let $N_v(t) = S_v(t) + E_v(t) + I_v(t)$, and $S_g(t)$ be the number of sterile mosquitoes at time t. Note the mosquito lifespan is usually shorter than their infection period, no recovered mosquitoes are included. The system of ordinary differential equations in system (1) describes the disease dynamics in humans, wild mosquitoes and the releasing sterile mosquitoes. As in [44,45], we assume that $f_h(N_h) = \mu_{1h} + \mu_{2h}N_h$ stands for the per capita density-dependent death and emigration rate of humans, $f_v(N_v + S_g) = \mu_{1v} + \mu_{2v}(N_v + S_g)$, $f_g(N_v + S_g) = \mu_{1g} + \mu_{2g}(N_v + S_g)$, are, the per capita density-dependent death rate for wild and sterile mosquitoes, respectively, with μ_{1j}, μ_{2j}, $(j = h, v, g)$ denoting, respectively, the density-independent and density dependent death rate for humans. As in [12,23], we assume that wild-type female mosquitoes are assumed to mate proportionately to their relative abundance, where the number of the male mosquitoes is equal to the number of females at any moment. The intrinsic growth rate of the wild mosquito population given by

$$\psi_v \frac{N_v}{N_v + S_g} N_v.$$

As in [44], we define the force of infection from mosquitoes to humans, $\lambda_h(t)$, as the product of the number of mosquito bites that one human has per unit time $b_h(N_h, N_v)$, the probability of disease transmission from the mosquito to the human β_{hv}, and the probability that the mosquito is infectious, I_v/N_v. Immunity is one of the important inter-related factors for transmission of malaria in a population. The neglect of immunity led to unrealistic predictions [46]. Dietz et al. [47] first considered seven compartments of human incorporation of immunity in the malaria model. Their model has shown a good fit to the data obtained from northern Nigeria [47]. In a similar theme, the importance of incorporation of immunity in malaria models is aptly emphasized and applied by some authors [44,45,48]. Chitnis et al. [44,45] have addressed that 'the recovered humans have some immunity to malaria and do not get clinically ill, but they still harbor low levels of parasite in their blood streams and can pass the infection to mosquitoes'. Applying the similar ideas in [44,45], we define the force of infection from humans to mosquitoes, $\lambda_v(t)$, as the sum of the force of infection from infectious humans and from recovered humans. These are defined as the number of human bites one mosquito has per unit time $b_v(N_h, N_v)$, the probability of disease transmission from the human to the mosquito β_{vh}, and $\tilde{\beta}_{vh}$, and the probability that the human is infectious or recovered I_h/N_h and R_h/N_h. The total number of mosquito bites, and the infection rates are, respectively, defined as

$$\begin{aligned}
b(N_h, N_v) &= \frac{\sigma_v \sigma_h N_v N_h}{\sigma_v N_v + \sigma_h N_h}, \quad b_h(N_h, N_v) = \frac{b(N_h, N_v)}{N_h}, \quad b_v(N_h, N_v) = \frac{b(N_h, N_v)}{N_v}, \\
\lambda_h(t) &= b_h(N_h, N_v)\beta_{hv}\frac{I_v}{N_v} = \frac{\beta_{hv}\sigma_v\sigma_h}{\sigma_v N_v + \sigma_h N_h} I_v, \\
\lambda_v(t) &= b_v(N_h, N_v)\left(\beta_{vh}\frac{I_h}{N_h} + \tilde{\beta}_{vh}\frac{R_h}{N_h}\right) = \frac{\sigma_v\sigma_h}{\sigma_v N_v + \sigma_h N_h}(\beta_{vh} I_h + \tilde{\beta}_{vh} R_h),
\end{aligned}$$

where σ_v is the rate at which a mosquito would like to bite a human, and σ_h is the maximum number of bites that a human can have per unit time. Then $\sigma_v N_v$ is the total number of bites that the mosquitoes would like to achieve in unit time and $\sigma_h N_h$ is the availability of humans. The total number of mosquito–human contacts is half the harmonic mean of $\sigma_v N_v$ and $\sigma_h N_h$. It is assumed that the rate of releases is a constant, denoted by b. All model state variables and parameters are summarized in Tables 1 and 2, respectively; the flowchart of malaria transmission dynamics is presented in Figure 1.

Table 1. Description of state variables.

State variables	Description
S_h	Susceptible, non-immune individuals
E_h	Infected, non-infectious, exposed individuals
I_h	Infectious, potentially clinically ill, non-immunes
R_h	Infectious asymptomatic non-immunes, partially protected
S_v	Proportion of the susceptible mosquitoes
E_v	Proportion of the infected mosquitoes
I_v	Proportion of infectious mosquitoes
S_g	Proportion of the released sterile mosquitoes

Table 2. Descriptions of the model parameters.

Parameter	Description
Λ_h	Immigrate rate of humans. Humans $\times$ Days^{-1}
ψ_h	Per capita birth rate of humans. Days^{-1}
ψ_v	Per capita birth rate of mosquitoes. Days^{-1}
σ_v	Number of times one mosquito would bite humans per unit time. Days^{-1}
σ_h	The maximum number of mosquito bites a human can have per unit time. Days^{-1}
β_{hv}	Transmission probability from an infectious mosquito to a susceptible human if contact (bite) occurs. dimensionless
β_{vh}	Transmission probability from an infectious human to a susceptible mosquito if contact (bite) occurs. dimensionless
$\tilde{\beta}_{vh}$	Transmission probability from a recovered human to a susceptible mosquito if contact (bite) occurs. dimensionless
ξ_h, ξ_v	Per capita rate of progression of human/mosquitoes from the exposed state to the infectious state. Days^{-1}
δ_h	Per capita disease-induced death rate for humans. Days^{-1}
μ_{1h}, μ_{2h}	Density-independent and density dependent death rate for humans, respectively. Days^{-1}, Humans $\times$ Days^{-1}
μ_{1v}, μ_{2v}	Density-independent and density dependent death rate for wild mosquitoes, respectively. Days^{-1}, Mosquitoes $\times$ Days^{-1}
μ_{1g}, μ_{2g}	Density-independent and density dependent death rate for sterile mosquitoes, respectively. Days^{-1}, Mosquitoes $\times$ Days^{-1}
ρ_h	Per capita rate of loss of immunity for human. Days^{-1}
γ_h	Per capita recovery rate for humans from the infectious state to the recovered state. Days^{-1}
b	The release rate of sterile mosquitoes. Days^{-1}

Using ideas from [23,44,45], based on the flowchart in Figure 1, the malaria transmission model is given by the following differential equations

$$\begin{aligned}
\frac{dS_h}{dt} &= \Lambda_h + \psi_h N_h + \rho_h R_h - \lambda_h(t) S_h - f_h(N_h) S_h,\\
\frac{dE_h}{dt} &= \lambda_h(t) S_h - \xi_h E_h - f_h(N_h) E_h,\\
\frac{dI_h}{dt} &= \xi_h E_h - \gamma_h I_h - f_h(N_h) I_h - \delta_h I_h,\\
\frac{dR_h}{dt} &= \gamma_h I_h - \rho_h R_h - f_h(N_h) R_h,\\
\frac{dS_v}{dt} &= \psi_v \frac{N_v}{N_v + S_g} N_v - \lambda_v(t) S_v - f_v(N_v + S_g) S_v,\\
\frac{dE_v}{dt} &= \lambda_v(t) S_v - \xi_v E_v - f_v(N_v + S_g) E_v,
\end{aligned}$$

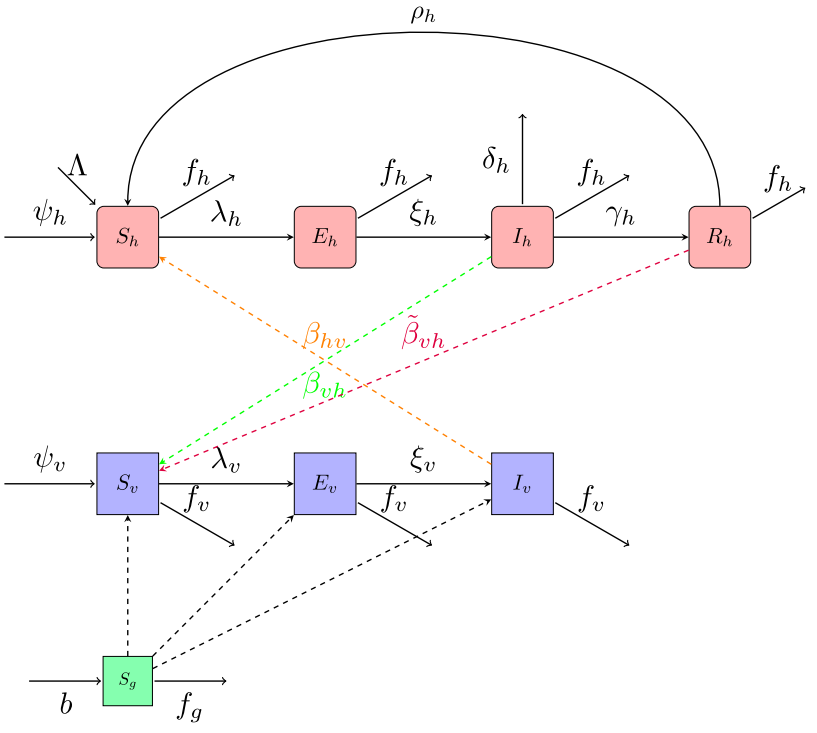

Figure 1. Flow diagram for model (1).

$$\begin{aligned}\frac{\mathrm{d}I_v}{\mathrm{d}t} &= \xi_v E_v - f_v(N_v + S_g)I_v,\\ \frac{\mathrm{d}S_g}{\mathrm{d}t} &= b - f_g(N_v + S_g)S_g.\end{aligned} \tag{1}$$

The initial conditions of system (1) satisfy

$$\begin{aligned}&S_h(0) = S_{h0}, \quad E_h(0) = E_{h0}, \quad I_h(0) = I_{h0}, \quad R_h(0) = R_{h0},\\ &S_v(0) = S_{v0}, \quad E_v(0) = E_{v0}, \quad I_v(0) = I_{v0}, \quad S_g(0) = S_{g0}.\end{aligned} \tag{2}$$

2.1. Preliminary analysis of system (1)

In this section, we first analyze the positivity and boundedness of solutions of system (1). From system (1), directly calculating shows

$$\begin{aligned}\frac{\mathrm{d}N_h(t)}{\mathrm{d}t} &= \Lambda_h + \psi_h N_h - f_h(N_h)N_h,\\ \frac{\mathrm{d}N_v(t)}{\mathrm{d}t} &= \frac{\psi_v N_v}{N_v + S_g}N_v - f_v(N_h + S_g)N_v,\\ \frac{\mathrm{d}S_g(t)}{\mathrm{d}t} &= b - f_g(N_v + S_g)S_g.\end{aligned} \tag{3}$$

From the first equation of Equation (3) and using the expressions of $f_h(N_h)$, we have

$$\frac{\mathrm{d}N_h(t)}{\mathrm{d}t} = \Lambda_h + \frac{(\psi_h - \mu_{1h})^2}{4\mu_{2h}} - \mu_{2h}\left(N_h - \frac{\psi_h - \mu_{1h}}{2\mu_{2h}}\right)^2.$$

Let

$$K_0 = \Lambda_h + \frac{(\psi_h - \mu_{1h})^2}{4\mu_{2h}},$$

we obtain

$$0 \le N_h = S_h + E_h + I_h + R_h \le K_0.$$

Let $N_{vg} = N_v + S_g$. It follows from the second and third equation of (3) that

$$\frac{\mathrm{d}N_{vg}}{\mathrm{d}t} = \frac{aN_v^2}{N_{vg}} + b - \mu_{1v}N_v - \mu_{1g}S_g - \mu_{2v}N_{vg}N_v - \mu_{2g}N_{vg}S_g.$$

From the above expression, it is easy to obtain that

$$\begin{aligned}\frac{\mathrm{d}N_{vg}}{\mathrm{d}t} &\le aN_{vg} + b - (\tilde{\mu}_1 + \tilde{\mu}_2 N_{vg})N_{vg} \\ &= (b - \tilde{\mu}_1 N_{vg}) + (a - \tilde{\mu}_2 N_{vg})N_{vg} < 0, \quad \forall\, N_{vg} > \max\{b/\tilde{\mu}_1, a/\tilde{\mu}_2\},\end{aligned}$$

where $\tilde{\mu}_1 = \min\{\mu_{1v},\ \mu_{1g}\}$ and $\tilde{\mu}_2 = \min\{\mu_{2v},\ \mu_{2g}\}$. For any fixed constant K_1 such that $K_1 > \max\{b/\tilde{\mu}_1, \psi_v/\tilde{\mu}_2\}$, it is easy to verify that the set

$$\Omega_0 := \{(N_h, N_v, S_g) :\ 0 \le N_h \le K_0,\ 0 < N_v + S_g < K_1\}$$

is a positively invariant and attracting set for the flows of system (1) in the positive quadrant.

In fact, the right-hand side of system (1) is continuous with continuous partial derivatives in Ω_0, so system (1) has a unique solution. It is clear that $\frac{\mathrm{d}N_h(t)}{\mathrm{d}t} \ge 0$, $\frac{\mathrm{d}N_v(t)}{\mathrm{d}t} \ge 0$, $\frac{\mathrm{d}S_g(t)}{\mathrm{d}t} \ge 0$, for $t \ge 0$ when the right-hand state variable function are zero, respectively, in system (1). Thus, the human and mosquito populations N_h, N_v and S_g are positive. From the discussion, we have the region Ω is a positively invariant and attracting set. All solutions of system (1) in R_+^8 eventually enter Ω_0.

Now, we shall investigate the existence of the disease-free equilibrium and the reproduction number of system (1). In system (1), let

$$E_h = 0, \quad I_h = 0, \quad R_h = 0, \quad E_v = 0, \quad I_v = 0.$$

The disease-free equilibrium of system (1) satisfies the following equations:

$$\begin{aligned}&\Lambda_h + \psi_h S_h - (\mu_{1h} + \mu_{2h}S_h)S_h = 0,\\ &\frac{\psi_v S_v}{S_v + S_g} S_v - (\mu_{1v} + \mu_{2v}(S_v + S_g))S_v = 0,\\ &b - (\mu_{1g} + \mu_{2g}(S_v + S_g))S_g = 0.\end{aligned} \tag{4}$$

From the first equation of (4), there always exists a positive root:

$$S_{h0} := \frac{(\psi_h - \mu_{1h}) + \sqrt{(\psi_h - \mu_{1h})^2 + 4\mu_{2h}\Lambda_h}}{2\mu_{2h}}. \tag{5}$$

From the second and third equation of (4), its positive components satisfy

$$\begin{aligned}\frac{\psi_v S_v}{S_v + S_g} &= (\mu_{1v} + \mu_{2v}(S_v + S_g))S_v,\\ b &= (\mu_{1g} + \mu_{2g}(S_v + S_g))S_g.\end{aligned}$$

Let $N_{vg} = S_v + S_g$. We have

$$\psi_v S_v = N_{vg}(\mu_{1v} + \mu_{2v})N_{vg}, \quad \psi_v S_g = \frac{\psi_v b}{\mu_{1g} + \mu_{2g}N_{vg}}.$$

Adding the above two equations, we have

$$\psi_v N_{vg} = N_{vg}(\mu_{1v} + \mu_{2v}N_{vg}) + \frac{\psi_v b}{\mu_{1g} + \mu_{2g}N_{vg}}.$$

Define

$$\begin{aligned} P(N_{vg}) :&= \mu_{2v}\mu_{2g}N_{vg}^3 - \big(\mu_{2g}(\psi_v - \mu_{1v}) - \mu_{2v}\mu_{1g}\big)N_{vg}^2 \\ &\quad - (\psi_v - \mu_{1v})\mu_{1g}N_{vg} + \psi_v b = 0. \end{aligned} \tag{6}$$

It follows from Equation (6)

$$P'(N_{vg}) = 3\mu_{2v}\mu_{2g}N_{vg}^2 - 2\big(\mu_{2g}(\psi_v - \mu_{1v}) - \mu_{2v}\mu_{1g}\big)N_{vg} - (\psi_v - \mu_{1v})\mu_{1g},$$

that if $\bar{N}_{vg} > 0$ is a critical point of $P(N_{vg})$ with $P'(\bar{N}_{vg}) = 0$, then

$$\begin{aligned} \bar{N}_{vg} = \frac{1}{3\mu_{2v}\mu_{2g}}\Bigg(&\sqrt{\big(\mu_{2g}(\psi_v - \mu_{1v}) - \mu_{2v}\mu_{1g}\big)^2 + 3\mu_{2v}\mu_{2g}(\psi_v - \mu_{1v})\mu_{1g}} \\ &+ \mu_{2g}(\psi_v - \mu_{1v}) - \mu_{2v}\mu_{1g}\Bigg). \end{aligned}$$

Note that

$$2P(\bar{N}_{vg}) = 2P(\bar{N}_{vg}) - P'(\bar{N}_{vg})\bar{N}_{vg} = -\mu_{1v}\mu_{2g}\bar{N}_{vg}^3 - (\psi_v - \mu_{1v})\mu_{1g}\bar{N}_{vg} + 2\psi_v b.$$

Hence, if we define the release threshold of sterile mosquitoes as

$$b_0 := \frac{1}{2\psi_v}(\mu_{2v}\mu_{2g}\bar{N}_{vg}^2 + (\psi_v - \mu_{1v})\mu_{1g})\bar{N}_{vg},$$

then $P(\bar{N}_{vg}) < 0$ if and only if $b < b_0$, and thus, it follows from $P(0) = \psi_v b > 0$ and $\lim_{N\to\infty} P(N_{vg}) = \infty$ that there exists a unique positive solution, $N_{vg}^* = \bar{N}_{vg}$, of (6) if and only if $b = b_0$. In this case, Equation (4) has a unique positive solution, denoted by $(\bar{S}_{h0}, \bar{S}_v, \bar{S}_g)$, where $\bar{S}_{h0} = S_{h0}$, and $\bar{S}_v, \bar{S}_g$ given by

$$\bar{S}_v = \frac{(\mu_{1v} + \mu_{2v}\bar{N}_{vg})\bar{N}_{vg}}{\psi_v}, \quad \bar{S}_g = \frac{b}{\mu_{1g} + \mu_{2g}\bar{N}_{vg}}. \tag{7}$$

If $b < b_0$, Equation (6) have two positive solutions, denoted by N_{1vg}^* and N_{2vg}^* with $N_{1vg}^* < \bar{N}_{vg} < N_{2vg}^*$. In this case, the two positive solutions of Equation (4) are, respectively, denoted as $(S_{h0}, S_{v1}^*, S_{1g}^*)$,

and $(S_{h0}, S^*_{v2}, S^*_{2g})$, given by

$$\begin{aligned} S^*_{v1} &= \frac{(\mu_{1v} + \mu_{2v}N^*_{1vg})N^*_{1vg}}{\psi_v} < S^*_{v2} = \frac{(\mu_{1v} + \mu_{2v}N^*_{2vg})N^*_{2vg}}{\psi_v}, \\ S^*_{2g} &= \frac{b}{\mu_{1g} + \mu_{2g}N^*_{2vg}} < S^*_{1g} = \frac{b}{\mu_{1g} + \mu_{2g}N^*_{1vg}}. \end{aligned} \tag{8}$$

Obviously, if $b > b_0$, then $(S_{h0}, 0, S^0_g)$ is a unique solution of Equation (4), where

$$S^0_g = \frac{\sqrt{\mu^2_{1g} + 4b\mu_{2g}}}{2\mu_{2g}}. \tag{9}$$

From the above discussion, we summarize the existence results for the disease-free equilibrium of system (1).

Theorem 2.1: *If $b > b_0$, system* (1) *has no wild mosquito populations $E_0(S_{h0}, 0, 0, 0, 0, 0, 0, S^0_g)$, with S_{h0}, S^0_g given in* (5), (9), *respectively. If $b = b_0$, system* (1) *has a unique disease-free equilibria $\bar{E}(S_{h0}, 0, 0, 0, \bar{S}_v, 0, 0, \bar{S}_g)$, with $\bar{S}_v, \bar{S}_g$ given in* (7). *If $b < b_0$, system* (1) *have two disease-free equilibria $E^*_1(S_{h0}, 0, 0, 0, S^*_{v1}, 0, 0, S^*_{1g})$, and $E^*_2(S_{h0}, 0, 0, 0, S^*_{v2}, 0, 0, S^*_{2g})$, with $S_{h0}, S^*_{v1}, S^*_{1g}, S^*_{v2}, S^*_{2g}$ are given in* (5), (8), *respectively.*

Remark 2.1: By applying similar analysis as in [23], it is easy to show that the boundary equilibrium $E_0(S_{h0}, 0, 0, 0, 0, 0, 0, S^0_g)$ is always locally asymptotically stable. In this case, since there is no wild mosquitoes at this boundary equilibrium, it is unrealistic in practice. If $b < b_0$, then there exist two equilibria $E^*_1(S_{h0}, 0, 0, 0, S^*_{v1}, 0, 0, S^*_{1g})$, and $E^*_2(S_{h0}, 0, 0, 0, S^*_{v2}, 0, 0, S^*_{2g})$, where E^*_1 is stable and E^*_2 is a saddle-node point. As the release rate b increases, the two equilibria are getting closer. They collide at $b = b_0$, and become a unique saddle-node point.

Remark 2.2: We established a release threshold b_0 of sterile mosquitoes in system (1). It is important to determine a threshold release value in eliminating malaria transmission. These obtained results are similar to those in recent papers [23,31,49], whereas the release number of sterile mosquitoes exceeds the threshold value, the boundary equilibrium is asymptotically stable, which means all wild mosquitoes go extinct eventually. On the other hand, if the release rate is less than the threshold, the model has two disease-free equilibria, one of which is always a saddle point, and the other is locally asymptotically stable.

2.2. The reproduction number

Now, we derive the basic reproduction number of system (1), The basic reproduction number is calculated by using the next generation matrix method as described by Van den Driessche and Watmough [50]. We denote $\mathcal{F}$ as the matrix of the rates of secondary infections, and $\mathcal{V}$ as the matrix of the rate of disease progression. Thus, we have

$$\mathbf{F} = \begin{pmatrix} \dfrac{\sigma_v\sigma_h}{\sigma_v N_v + \sigma_h N_h}(\beta_{vh}I_h + \tilde{\beta}_{vh}R_h)S_v \\ 0 \\ \dfrac{\beta_{hv}\sigma_v\sigma_h}{\sigma_v N_v + \sigma_h N_h} I_v S_h \\ 0 \\ 0 \end{pmatrix}$$

and

$$\mathbf{V}=\begin{pmatrix}\xi_v E_v+(\mu_{1v}+\mu_{2v}(N_v+S_g))E_v\\ -\xi_v E_v+(\mu_{1v}+\mu_{2v}(N_v+S_g))I_v\\ \xi_h E_h+(\mu_{1h}+\mu_{2h}N_h)E_h\\ -\xi_h E_h+\gamma_h I_h+(\mu_{1h}+\mu_{2h}N_h)I_h+\delta_h I_h\\ -\gamma_h I_h+\rho_h R_h+(\mu_{1h}+\mu_{2h}N_h)R_h\end{pmatrix}.$$

According to Theorem 2.1, in system (1), we evaluate the derivatives of $\mathcal{F}$ and $\mathcal{V}$ at the infection-free equilibrium $E_1^*(S_{h0},0,0,0,S_{v1}^*,0,0,S_{1g}^*)$ due to the other equilibria may be saddle-point, which they are not suitable.

Let $k_1=\xi_v+\mu_{1v}+\mu_{2v}(S_{v1}^*+S_{1g}^*)$, $k_2=\mu_{1v}+\mu_{2v}(S_{v1}^*+S_{1g}^*)$, $k_3=\xi_h+\mu_{1h}+\mu_{2h}S_{ho}$, $k_4=\gamma_h+\mu_{1h}+\mu_{2h}S_{ho}+\delta_h$, $k_5=\rho_h+\mu_{1h}+\mu_{2h}S_{ho}$. We have

$$\mathbf{F}=\begin{pmatrix}0&0&0&\dfrac{\beta_{vh}\sigma_h\sigma_v S_{v1}^*}{\sigma_h S_{ho}+\sigma_v S_{v1}^*}&\dfrac{\tilde{\beta}_{vh}\sigma_h\sigma_v S_{v1}^*}{\sigma_h S_{ho}+\sigma_v S_{v1}^*}\\ 0&0&0&0&0\\ 0&\dfrac{\beta_{hv}\sigma_h\sigma_v S_{ho}}{\sigma_h S_{ho}+\sigma_v S_{v1}^*}&0&0&0\\ 0&0&0&0&0\\ 0&0&0&0&0\end{pmatrix}$$

and

$$\mathbf{V}=\begin{pmatrix}k_1&0&0&0&0\\ -\xi_v&k_2&0&0&0\\ 0&0&k_3&0&0\\ 0&0&-\xi_h&k_4&0\\ 0&0&0&-\gamma_h&k_5\end{pmatrix}.$$

By direct calculation, we have

$$\mathbf{V^{-1}}=\begin{pmatrix}\dfrac{1}{k_1}&0&0&0&0\\ \dfrac{\xi_v}{k_1k_2}&\dfrac{1}{k_2}&0&0&0\\ 0&0&\dfrac{1}{k_3}&0&0\\ 0&0&\dfrac{\xi_h}{k_3k_4}&\dfrac{1}{k_4}&0\\ 0&0&\dfrac{\gamma_h\xi_h}{k_3k_4k_5}&\dfrac{\gamma_h}{k_4k_5}&\dfrac{1}{k_5}\end{pmatrix}$$

Thus, the next generation matrix is

$$\mathbf{K}=\mathbf{FV^{-1}}$$
$$=\begin{pmatrix}0&0&\dfrac{\xi_h\sigma_h\sigma_v(k_5\beta_{vh}+\gamma_h\tilde{\beta}_{vh})S_{v1}^*}{k_3k_4k_5(\sigma_h S_{ho}+\sigma_v S_{v1}^*)}\\ 0&0&0\\ \dfrac{\beta_{hv}\xi_v\sigma_h\sigma_v S_{ho}}{k_1k_2(\sigma_h S_{ho}+\sigma_v S_{v1}^*)}&\dfrac{\beta_{hv}\sigma_h\sigma_v S_{ho}}{k_2(\sigma_h S_{ho}+\sigma_v S_{v1}^*)}&0\\ 0&0&0\\ 0&0&0\end{pmatrix}$$

$$\begin{pmatrix} \frac{\sigma_h\sigma_v(k_5\beta_{vh}+\gamma_h\tilde{\beta}_{vh})S^*_{v1}}{k_4k_5(\sigma_hS_{ho}+\sigma_vS^*_{v1})} & \frac{\tilde{\beta}_{vh}\sigma_h\sigma_vS^*_{v1}}{k_5(\sigma_hS_{h0}+\sigma_vS^*_{v1})} \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \end{pmatrix}.$$

By calculating the eigenvalues of the next generation matrix **K**, we obtain the threshold

$$\mathcal{R}_0 = \sqrt{\frac{\beta_{hv}\xi_v\sigma_v\sigma_hS_{ho}}{k_1k_2(\sigma_vS^*_{v1}+\sigma_hS_{ho})}\left(\frac{\beta_{vh}\xi_h\sigma_v\sigma_hS_{vo}}{k_3k_4(\sigma_vS^*_{v1}+\sigma_hS_{ho})}+\frac{\tilde{\beta}_{vh}\xi_h\gamma_h\sigma_v\sigma_hS^*_{v1}}{k_3k_4k_5(\sigma_vS^*_{v1}+\sigma_hS_{ho})}\right)}. \tag{10}$$

Let

$$A_{hv} = \frac{\xi_v}{\xi_v+\mu_{1v}+\mu_{2v}(S^*_{v1}+S^*_{1g})}\cdot\frac{\sigma_vS^*_{v1}\sigma_hS_{ho}}{(\sigma_v(S^*_{v1}+\sigma_hS^*_{1g}))S^*_{v1}}\cdot\beta_{vh}\cdot\frac{1}{\mu_{1v}+\mu_{2v}(S^*_{v1}+S^*_{1g})},$$

$$B_{vh} = \frac{\xi_h}{\xi_h+\mu_{1h}+\mu_{2h}S_{ho}}\cdot\tilde{\beta}_{vh}\cdot\frac{1}{\gamma_h+\mu_{1h}+\mu_{2h}S_{ho}+\delta_h}+\frac{\xi_h}{\xi_h+\mu_{1h}+\mu_{2h}S_{ho}}$$
$$\cdot\frac{\gamma_h}{\gamma_h+\mu_{1h}+\mu_{2h}S_{ho}+\delta_h}\cdot\frac{\sigma_hS_{ho}\sigma_vS^*_{v1}}{(\sigma_vS^*_{v1}+\sigma_hS_{ho})S_{ho}}\cdot\frac{1}{\rho_h+\mu_{1h}+\mu_{2h}S_{ho}}.$$

Notice $\xi_v/(\xi_v+\mu_{1v}+\mu_{2v}(S^*_{v1}+S^*_{1g}))$ is the probability that a mosquito will survive the exposed state to become infectious; $1/(\mu_{1v}+\mu_{2v}(S^*_{v1}+S^*_{1g}))$ is the average duration of the infectious lifetime of the mosquito, $(\sigma_vS^*_{v1}\sigma_hS_{ho})/(\sigma_vS^*_{v1}+\sigma_hS_{ho})S^*_{v1}$ is the number of bites per mosquito per unit time; $\xi_h/(\xi_h+\mu_{1h}+\mu_{2h}S_{ho})$ is the probability that a human will survive the exposed state to become infectious; $1/(\gamma_h+\mu_{1h}+\mu_{2h}S_{ho}+\delta_h)$ is the average duration of the infectious lifetime of a human. $\sigma_hS_{ho}\sigma_vS^*_{v1}/(\sigma_vS^*_{v1}+\sigma_hS_{ho})S_{ho}$ is the number of bites per human per unit time; and $1/(\rho_h+\mu_{1h}+\mu_{2h}S_{ho})$ is the average duration of the recovered period of a human.

We define $\mathcal{R}_0^2$ as the spectral radius of the next generation matrix, i.e. $\mathcal{R}_0^2 = A_{hv}B_{vh}$. $\mathcal{R}_0^2$ is the basic reproduction number of system (1). It can express as the mean number of secondary infections in both mosquito and human individuals produced by one infective individual (either mosquito or human) during their infectious period, assuming that previously all other humans and mosquitoes were susceptible [44,51,52]. Thus, we can establish the following result.

Theorem 2.2: *The disease-free equilibrium* $E^*_1(S_{h0},0,0,0,S^*_{v1},0,0,S^*_{1g})$ *of system* (1) *is locally asymptotically stable when* $\mathcal{R}_0^2<1$, *and unstable when* $\mathcal{R}_0^2>1$.

3. Optimal control of malaria model

In the malaria regions, many at-risk populations live in extremely destitute, remote areas. Poor, rural families are the least likely to have access to the preventative fundamental measures of malaria control. The economic burden of the disease is vast. It is estimated that malaria costs African countries more than $12 billion every year in direct losses [2]. In addition, SIT relies on the sterilization by irradiation of large numbers of male mosquitoes. This has unavoidable costs in terms of the fitness of the irradiated mosquitoes. The financial requirements of constructing and operating the radiation facility are high. So, limited resources and cost for malaria control must be considered. In this section, we used optimal control theory for system (1) to include two control variables. Let $u_1(t)$ denote the insecticide-treated bed net coverage, and $u_2(t)$ the release rate of sterile mosquitoes. These control variables are proportions, varying between zero and one.

In this formulation of the model, $\lambda_h(t)$ is replaced by $(1-u_1(t))\lambda_h(t)$, and b is replaced by $bu_2(t)$. When $u_1(t)=0$, there is no reduction in the transmission rates resulting from bednet efforts, while $u_1(t)=1$ represents perfect protection from bednet use. Although several species of mosquito blood feed primarily at night, 100% bednet coverage will not eliminate malaria transmissions. Similarly, when $u_2(t)=0$, no releasing of sterile mosquitoes, and when $u_2(t)=1$, the releasing of sterile mosquitoes occurs at the maximum possible rate. In real life, since the bednets may not be 100% effective, there is some effort required to maintain or replace bednets over time. The releasing of sterile mosquitoes is also similar.

The reformulated model with two controls is given by the following the differential equations:

$$\begin{aligned}
\frac{dS_h}{dt} &= \Lambda_h + \psi_h N_h + \rho_h R_h - (1-u_1(t))\lambda_h(t)S_h - f_h(N_h)S_h,\\
\frac{dE_h}{dt} &= (1-u_1(t))\lambda_h(t)S_h - \xi_h E_h - f_h(N_h)E_h,\\
\frac{dI_h}{dt} &= \xi_h E_h - \gamma_h I_h - f_h(N_h)I_h - \delta_h I_h,\\
\frac{dR_h}{dt} &= \gamma_h I_h - \rho_h R_h - f_h(N_h)R_h,\\
\frac{dS_v}{dt} &= \frac{\psi_v N_v^2}{N_v+S_g} - (1-u_1(t))\lambda_v(t)S_v - f_v(N_v+S_g)S_v,\\
\frac{dE_v}{dt} &= (1-u_1(t))\lambda_v(t)S_v - \xi_v E_v - f_v(N_v+S_g)E_v,\\
\frac{dI_v}{dt} &= \xi_v E_v - f_v(N_v+S_g)I_v,\\
\frac{dS_g}{dt} &= bu_2(t) - f_g(N_v+S_g)S_g.
\end{aligned} \tag{11}$$

The initial conditions of system (11) are

$$\begin{aligned}
&S_h(0)=S_{h0}, \quad E_h(0)=E_{h0}, \quad I_h(0)=I_{h0}, \quad R_h(0)=R_{h0},\\
&S_v(0)=S_{v0}, \quad E_v(0)=E_{v0}, \quad I_v(0)=I_{v0}, \quad S_g(0)=S_{g0}.
\end{aligned} \tag{12}$$

As previously mentioned, implementing control measures incurs a cost. Our goal in applying optimal control theory to the malaria model was to determine a control strategy (using the combination of releasing sterile mosquitoes and the bed net coverage) that minimizes the number of human infections and the cost of the program. Mathematically, the goal was to determine an optimal control pair $(u_1^*(t), u_2^*(t))$ that minimizes the objective functional:

$$J(u_1,u_2) = \int_0^T w_1 I_h(t) + \frac{1}{2}(w_2 u_1^2(t) + w_3 u_2^2(t))\,dt, \tag{13}$$

where the interval $[0,T]$ represents the time interval over which the control program is conducted, and the $w_i (i=1,2,3)$ are weights representing the relative costs of I_h and the control measures. The term $w_2u_1^2 + w_3u_2^2$ in the objective functional J incorporated the nonlinear costs of the controls.

This state system with Lebesque measurable coefficients has a unique non-negative bounded solution on the finite time interval $[0,T]$ [53]. Note for this system, the control set and the objective functional have the appropriate compactness and convexity assumptions to guarantee the existence of an optimal control pair and the corresponding states [54,55]. Having the existence of an optimal control, we can now apply Pontryagin's Maximum Principle [55,56], we reformulate the problem of

finding time-dependent control variables $u_1^*(t)$, and $u_2^*(t)$ that minimize J into the equivalent problem of minimizing the Hamiltonian

$$\begin{aligned}
H = {} & w_1 I_h + \frac{1}{2}(w_2 u_1^2 + w_3 u_2^2) \\
& + \lambda_1 \left(\Lambda_h + \psi_h N_h + \rho_h R_h - (1-u_1(t)) \frac{\beta_{hv}\sigma_v\sigma_h}{\sigma_v N_v + \sigma_h N_h} I_v S_h - (\mu_{1h} + \mu_{2h} N_h) S_h \right) \\
& + \lambda_2 \left((1-u_1(t)) \frac{\beta_{hv}\sigma_v\sigma_h}{\sigma_v N_v + \sigma_h N_h} I_v S_h - \xi_h E_h - (\mu_{1h} + \mu_{2h} N_h) E_h \right) \\
& + \lambda_3 (\xi_h E_h - \gamma_h I_h - (\mu_{1h} + \mu_{2h} N_h) I_h - \delta_h I_h) \\
& + \lambda_4 (\gamma_h I_h - \rho_h R_h - (\mu_{1h} + \mu_{2h} N_h) R_h) \\
& + \lambda_5 \left(\psi_v \frac{N_v}{N_v + S_g} N_v - (1-u_1(t)) \frac{\sigma_v\sigma_h}{\sigma_v N_v + \sigma_h N_h} (\beta_{vh} I_h + \tilde{\beta}_{vh} R_h) S_v \right. \\
& \left. - (\mu_{1v} + \mu_{2v}(N_v + S_g)) S_v \right) \\
& + \lambda_6 \left((1-u_1(t)) \frac{\sigma_v\sigma_h}{\sigma_v N_v + \sigma_h N_h} (\beta_{vh} I_h + \tilde{\beta}_{vh} R_h) S_v - \xi_v E_v - (\mu_{1v} + \mu_{2v}(N_v + S_g)) E_v \right) \\
& + \lambda_7 (\xi_v E_v - (\mu_{1v} + \mu_{2v}(N_v + S_g)) I_v) \\
& + \lambda_8 (b \cdot u_2(t) - (\mu_{1g} + \mu_{2g}(N_v + S_g)) S_g). \qquad (14)
\end{aligned}$$

Noticing the integrand of the objective functional J, and λ_i $(i = 1, \ldots, 8)$ are the solution vector to the adjoint system of equations $\mathrm{d}\lambda_i/\mathrm{d}t = -\mathrm{d}H/\mathrm{d}t$ with the transversality condition $\lambda_i(T) = 0$, $i = 1, \ldots, 8$. By direct computation, we obtain the adjoint equations

$$\begin{aligned}
\lambda_1' = {} & \lambda_1 \left(-\psi_h + \mu_{1h} + \mu_{2h}(S_h + N_h) + \frac{(1-u_1)\beta_{hv}\sigma_h\sigma_v I_v(\sigma_h(E_h + I_h + R_h) + \sigma_v N_v)}{(\sigma_h N_h + \sigma_v N_v)^2} \right) \\
& + \lambda_2 \left(\mu_{2h} E_h - \frac{(1-u_1)\beta_{hv}\sigma_h\sigma_v I_v(\sigma_h(E_h + I_h + R_h) + \sigma_v N_v)}{(\sigma_h N_h + \sigma_v N_v)^2} \right) \\
& + \lambda_3 \mu_{2h} I_h + \lambda_4 \mu_{2h} R_h + (\lambda_6 - \lambda_5) \frac{(1-u_1)\sigma_h^2\sigma_v S_v(\beta_{vh} I_h + \tilde{\beta}_{vh} R_h)}{(\sigma_h N_h + \sigma_v N_v)^2}, \qquad (15) \\
\lambda_2' = {} & \lambda_1 \left(-\psi_h + \mu_{2h} S_h - \frac{(1-u_1)\beta_{hv}\sigma_h^2\sigma_v I_v S_h}{(\sigma_h N_h + \sigma_v N_v)^2} \right) \\
& + \lambda_2 \left(\mu_{1h} + \mu_{2h}(E_h + N_h) + \frac{(1-u_1)\beta_{hv}\sigma_h^2\sigma_v I_v S_h}{(\sigma_h N_h + \sigma_v N_v)^2} + \xi_h \right) \\
& + \lambda_3 (\mu_{2h} I_h - \xi_h) + \lambda_4 \mu_{2h} R_h + (\lambda_6 - \lambda_5) \frac{(1-u_1)\sigma_h^2\sigma_v S_v(\beta_{vh} I_h + \tilde{\beta}_{vh} R_h)}{(\sigma_h N_h + \sigma_v N_v)^2}, \qquad (16) \\
\lambda_3' = {} & \lambda_1 \left(-\psi_h + \mu_{2h} S_h - \frac{(1-u_1)\beta_{hv}\sigma_h^2\sigma_v I_v S_h}{(\sigma_h N_h + \sigma_v N_v)^2} \right) + \lambda_2 \left(\mu_{2h} E_h + \frac{(1-u_1)\beta_{hv}\sigma_h^2\sigma_v I_v S_h}{(\sigma_h N_h + \sigma_v N_v)^2} \right) \\
& + \lambda_3 (\gamma_h + \delta_h + \mu_{1h} + \mu_{2h}(I_h + N_h)) + \lambda_4 (\mu_{2h} R_h - \gamma_h) \\
& + (\lambda_5 - \lambda_6) \frac{(1-u_1)\sigma_v\sigma_h S_v}{(\sigma_h N_h + \sigma_v N_v)^2} (\beta_{vh}\sigma_h(E_h + R_h + S_h) - \tilde{\beta}_{vh}\sigma_h R_h + \beta_{vh}\sigma_v N_v) - w_1, \qquad (17)
\end{aligned}$$

$$\lambda_4' = \lambda_1\left(-\psi_h - \rho_h + \mu_{2h}S_h - \frac{(1-u_1)\beta_{hv}\sigma_h^2\sigma_v I_v S_h}{(\sigma_h N_h + \sigma_v N_v)^2}\right) + \lambda_2\left(\mu_{2h}E_h + \frac{(1-u_1)\beta_{hv}\sigma_h^2\sigma_v I_v S_h}{(\sigma_h N_h + \sigma_v N_v)^2}\right)$$
$$+ \lambda_3\mu_{2h}I_h + \lambda_4(\mu_{1h} + \mu_{2h}(R_h + N_h) + \rho_h)$$
$$+ (\lambda_5 - \lambda_6)\frac{(1-u_1)\sigma_h\sigma_v S_v}{(\sigma_h N_h + \sigma_v N_v)^2}(\tilde{\beta}_{vh}\sigma_h(E_h + I_h + S_h) - \beta_{vh}\sigma_h I_h + \tilde{\beta}_{vh}\sigma_v N_v), \tag{18}$$

$$\lambda_5' = (\lambda_2 - \lambda_1)\frac{(1-u_1)\beta_{hv}\sigma_h\sigma_v^2 I_v S_h}{(\sigma_h N_h + \sigma_v N_v)^2}$$
$$+ \lambda_5\left(\mu_{1v} + \mu_{2v}(N_v + S_v + S_g) - \frac{\psi_v N_v(N_v + 2S_g)}{(N_v + S_g)^2}\right.$$
$$\left.+\frac{(1-u_1)\sigma_h\sigma_v(\beta_{vh}I_h + \tilde{\beta}_{vh}R_h)}{(\sigma_h N_h + \sigma_v N_v)^2}(\sigma_v(E_v + I_v) + \sigma_h N_h)\right)$$
$$+ \lambda_6\left(\mu_{2v}E_v - \frac{(1-u_1)\sigma_h\sigma_v(\beta_{vh}I_h + \tilde{\beta}_{vh}R_h)}{(\sigma_h N_h + \sigma_v N_v)^2}(\sigma_v(E_v + I_v) + \sigma_h N_h)\right)$$
$$+ \lambda_7\mu_{2v}I_v + \lambda_8\mu_{2g}S_g, \tag{19}$$

$$\lambda_6' = (\lambda_2 - \lambda_1)\frac{(1-u_1)\beta_{hv}\sigma_h\sigma_v^2 I_v S_h}{(\sigma_h N_h + \sigma_v N_v)^2} + \lambda_5\left(\mu_{2v}S_v - \frac{\psi_v N_v(N_v + 2S_g)}{(N_v + S_g)^2}\right.$$
$$\left.-\frac{(1-u_1)\sigma_h\sigma_v^2 S_v(\beta_{vh}I_h + \tilde{\beta}_{vh}R_h)}{(\sigma_h N_h + \sigma_v N_v)^2}\right)$$
$$+ \lambda_6\left(\mu_{1v} + \mu_{2v}(E_v + N_v + S_g) + \xi_v + \frac{(1-u_1)\sigma_h\sigma_v^2 S_v(\beta_{vh}I_h + \tilde{\beta}_{vh}R_h)}{(\sigma_h N_h + \sigma_v N_v)^2}\right)$$
$$+ \lambda_7(\mu_{2v}I_v - \xi_v) + \lambda_8\mu_{2g}S_g, \tag{20}$$

$$\lambda_7' = (\lambda_1 - \lambda_2)\frac{(1-u_1)\beta_{hv}\sigma_h\sigma_v S_h}{(\sigma_h N_h + \sigma_v N_v)^2}(\sigma_h N_h + \sigma_v(E_v + S_v))$$
$$+ \lambda_5(\mu_{2v}S_v - \frac{\psi_v N_v(N_v + 2S_g)}{(N_v + S_g)^2} - \frac{(1-u_1)\sigma_h\sigma_v^2 S_v(\beta_{vh}I_h + \tilde{\beta}_{vh}R_h)}{(\sigma_h N_h + \sigma_v N_v)^2})$$
$$+ \lambda_6\left(\mu_{2v}E_v + \frac{(1-u_1)\sigma_h\sigma_v^2 S_v(\beta_{vh}I_h + \tilde{\beta}_{vh}R_h)}{(\sigma_h N_h + \sigma_v N_v)^2}\right)$$
$$+ \lambda_7(\mu_{1v} + \mu_{2v}(I_v + N_v + S_g)) + \lambda_8\mu_{2g}S_g, \tag{21}$$

$$\lambda_8' = \lambda_5\left(\frac{\psi_v N_v^2}{(N_v + S_g)^2} + \mu_{2v}S_v\right) + \lambda_6\mu_{2v}E_v + \lambda_7\mu_{2v}I_v + \lambda_8(\mu_{1g} + \mu_{2g}(N_v + 2S_g)). \tag{22}$$

The transversality conditions are

$$\lambda_i(T) = 0, \quad i = 1, \ldots, 8. \tag{23}$$

Taking the partial derivative of the Hamiltonian with respect to the control variable u_1, we have

$$\frac{\partial H}{\partial u_1} = u_1 w_2 + (\lambda_1 - \lambda_2)\frac{\beta_{hv}\sigma_h\sigma_v I_v S_h}{\sigma_h N_h + \sigma_v N_v} + (\lambda_5 - \lambda_6)\frac{\sigma_h\sigma_v(\beta_{vh}I_h + \tilde{\beta}_{vh}R_h)}{\sigma_h N_h + \sigma_v N_v}.$$

Solving $\frac{\partial H}{\partial u_1} = 0$, we have

$$u_1 = -\left((\lambda_1 - \lambda_2)\frac{\beta_{hv}\sigma_h\sigma_v I_v S_h}{\sigma_h N_h + \sigma_v N_v} + (\lambda_5 - \lambda_6)\frac{\sigma_h\sigma_v(\beta_{vh}I_h + \tilde{\beta}_{vh}R_h)}{\sigma_h N_h + \sigma_v N_v}\right) \Big/ w_2.$$

Taking the partial derivative of the Hamiltonian with respect to the control variable u_2, we have

$$\frac{\partial H}{\partial u_2} = u_2 w_3 + b\lambda_8.$$

Solving $\frac{\partial H}{\partial u_2} = 0$, we have

$$u_2 = -\frac{b\lambda_8}{w_3}.$$

Taking into the account of the upper and lower bounds of the controls, we obtain the characterization of the optimal controls

$$\begin{aligned} u_1^* &= \min\left(\max\left(0, \left((\lambda_2 - \lambda_1)\frac{\beta_{hv}\sigma_h\sigma_v I_v S_h}{\sigma_h N_h + \sigma_v N_v} + (\lambda_6 - \lambda_5)\frac{\sigma_h\sigma_v(\beta_{vh}I_h + \tilde{\beta}_{vh}R_h)}{\sigma_h N_h + \sigma_v N_v}\right)/w_2\right), M_1\right) \\ u_2^* &= \min\left(\max\left(0, -\frac{b\lambda_8}{w_3}\right), M_2\right), \end{aligned} \tag{24}$$

where $M_i, i = 1, 2$ are the upper bounds for $u_i(t), i = 1, 2$, respectively. So we derived the following theorem:

Theorem 3.1: *Given optimal controls $u_1(t), u_2(t)$ and the corresponding state solutions $S_h(t), E_h(t), I_h(t), R_h(t), S_v(t), E_v(t), I_v(t), S_g(t)$ in the system* (11)*, there exist adjoint variables $\lambda_i(t), i = 1, \ldots, 8$, satisfying* (15)–(22) *with the transversality conditions $\lambda_i(T) = 0,\ i = 1, \ldots, 8$. Furthermore, the optimal controls $u_1(t), u_2(t)$ are given in* (24)*.*

The state system (11) and the adjoint Equations (15)–(22), together with the characterization of the optimal control (24) and the boundary conditions, are called the optimality system. We note the strict concavity of the objective functional J, as well as the Lipschitz continuity of the right-hand side of the state equations and the adjoint equations in the state and adjoint variables, yields the uniqueness of solutions of the optimality system for small-time [55].

4. Numerical simulations

In this section, we present the numerical results for various cases.

4.1. Optimal control strategies

We use Forward-Backward Sweep Method [55] to solve the optimal control problem. We solve the state system (11) forward in time with the initial conditions (12), the adjoint Equations (15)–(22) backward in time with the transversality conditions (23), then update the optimal control using the characterization (24) until the convergence criterion is met.

Parameters are taken from [23,45] with $\Lambda = 0.033$, $\psi_h = 0.00011$, $\psi_v = 0.13$, $\sigma_h = 19$, $\sigma_v = 0.5$, $\beta_{hv} = 0.022$, $\beta_{vh} = 0.48$, $\tilde{\beta}_{vh} = 0.048$, $\xi_h = 0.10$, $\xi_v = 0.091$, $\gamma_h = 0.0035$, $\delta_h = 0.00009$, $\rho_h = 0.00055$, $\mu_{1h} = 0.000016$, $\mu_{2h} = 0.0000003$, $\mu_{1v} = 0.033$, $\mu_{2v} = 0.00002$, $b = 100$, $\mu_{1g} = 0.012$, $\mu_{2g} = 0.00002$. The initial populations are $[S_h, E_h, I_h, R_h, S_v, E_v, I_v, S_g](0) = [500, 10, 30, 0, 4000, 100, 50, 0]$. We take the weights in the objective functional to be $w_1 = w_2 = w_3 = 1$, other choices of $w_i,\ i = 1, 2, 3$ have been explored, they illustrate similar patterns.

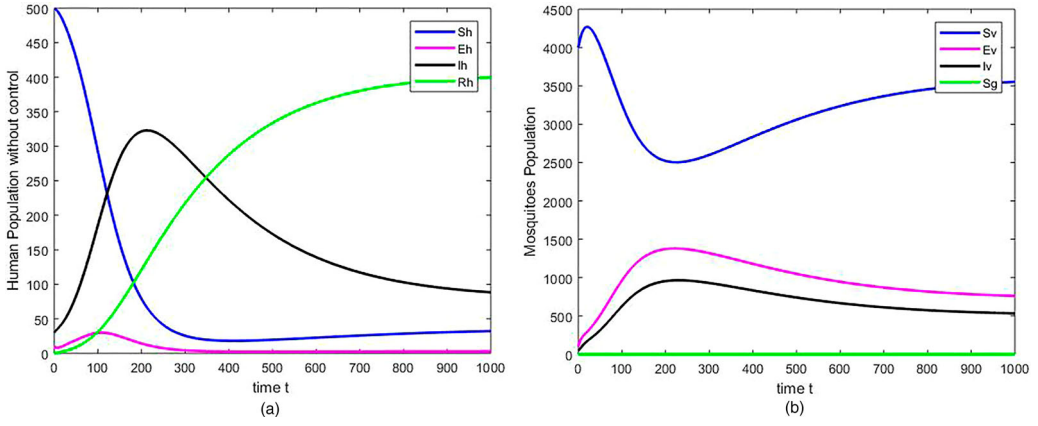

Figure 2. Human, $S_h(t)$, $E_h(t)$,$I_h(t)$, $R_h(t)$ and wild mosquitoes, $S_v(t)$, $E_v(t)$, $I_v(t)$, $S_g(t)$, without control. $N_h = 500$, $N_v = 4000$. (a) Human Population w/o Control. (b) Wild Mosquitoes Population w/o Control.

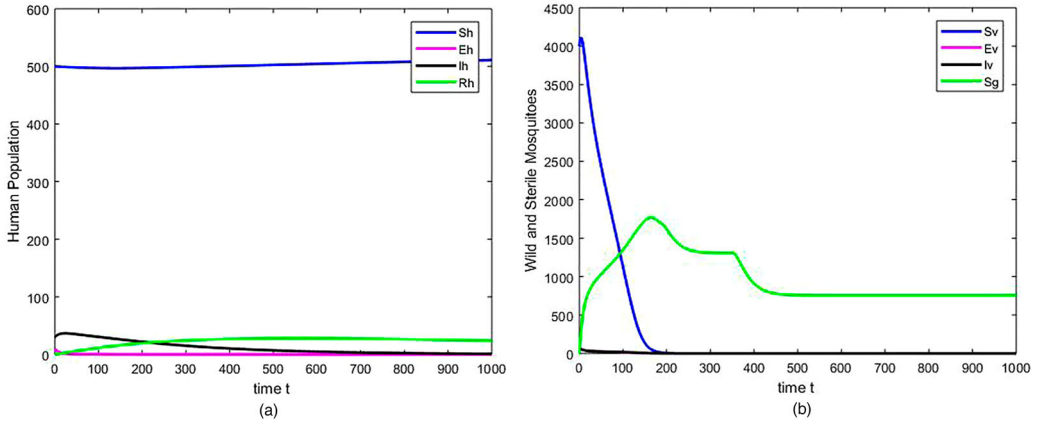

Figure 3. Human: $S_h(t)$, $E_h(t)$,$I_h(t)$, $R_h(t)$, wild mosquitoes: $S_v(t)$, $E_v(t)$, $I_v(t)$, and sterile mosquitoes $S_g(t)$ with 2 controls. $N_h = 500$, $N_v = 4000$. (a) Human Population with 2 controls. (b) Mosquito Population with 2 controls.

4.1.1. Two optimal controls

Figure 2 shows the susceptible, exposed, infected and recovered human population, with the susceptible, exposed and infected mosquitoes population, respectively, without any control strategies. Figure 3 illustrates the combination of usage of ITN and the releasing of sterile mosquitoes can dramatically reduce the amount of exposed and infected human population, susceptible, exposed, and infected mosquitoes populations, respectively, while maintaining a high level of susceptible humans. The corresponding two optimal controls are shown in Figure 4. Both control strategies show similar pattern: we apply the controls in a high level, gradually reducing the effort, and finally apply it at a low level.

4.1.2. One optimal control

The optimal control problem can be reformulated to find the optimal strategy of each control method when used alone.

We can turn off one of the two controls in Section 4.1.1 and see how it affects our system. Figure 5 gives the dynamics of susceptible, exposed, infected and recovered human population, susceptible, exposed, infected and sterile mosquitoes with only one control – SIT. Only releasing sterile

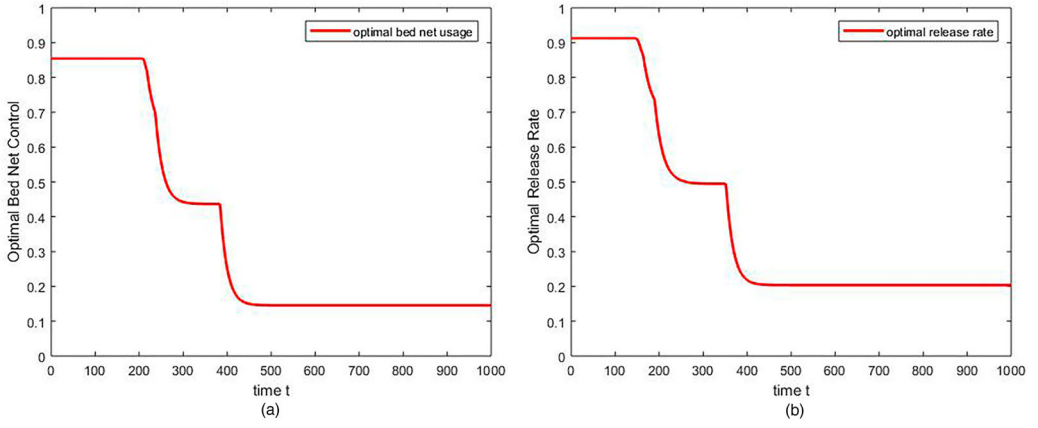

Figure 4. Humans: $S_h(t)$, $E_h(t)$, $I_h(t)$, $R_h(t)$ and Mosquitoes: $S_v(t)$, $E_v(t)$, $I_v(t)$, $S_g(t)$ with two controls. (a) Optimal bed net usage. (b) Optimal release rate of sterile mosquitoes.

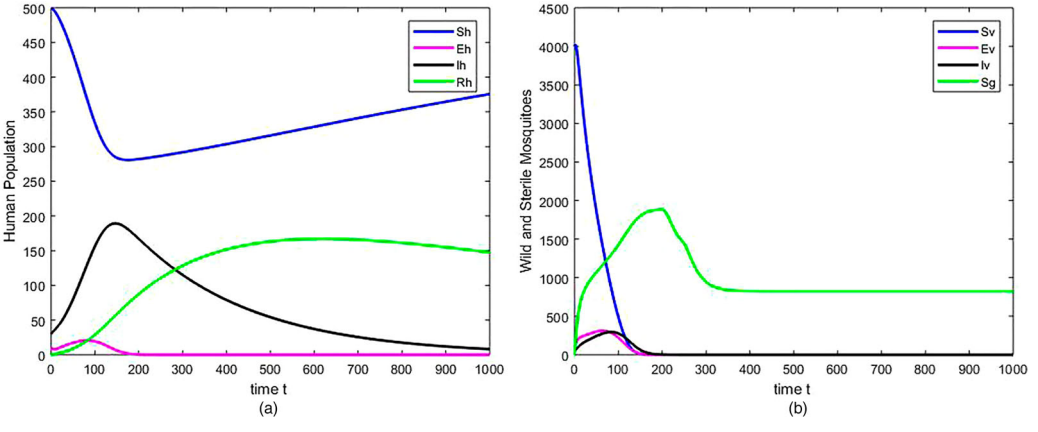

Figure 5. Human: $S_h(t)$, $E_h(t)$,$I_h(t)$, $R_h(t)$, wild mosquitoes: $S_v(t)$, $E_v(t)$, $I_v(t)$, and sterile mosquitoes $s_g(t)$ with 1 control (SIT). $N_h = 500$, $N_v = 4000$. (a) Human populations with 1 control (SIT). (b) Mosquitoes Populations with 1 control (SIT).

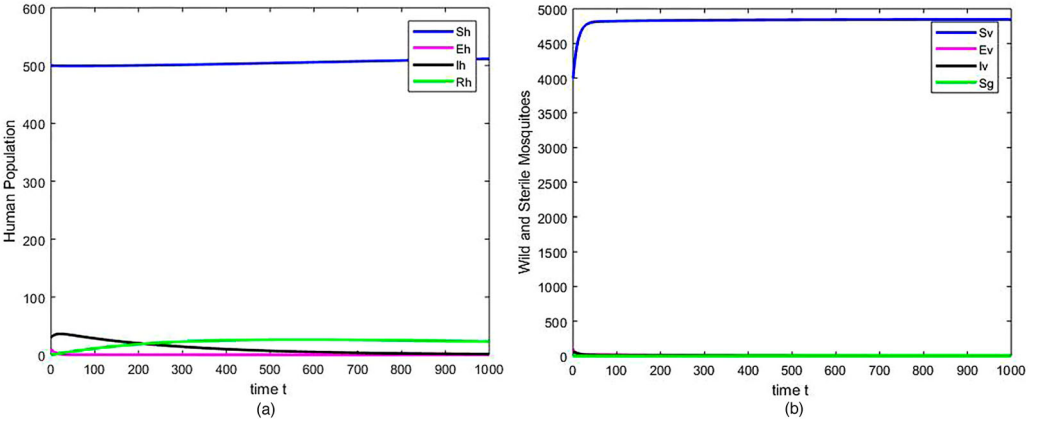

Figure 6. Human: $S_h(t)$, $E_h(t)$,$I_h(t)$, $R_h(t)$, wild mosquitoes: $S_v(t)$, $E_v(t)$, $I_v(t)$, and sterile mosquitoes $s_g(t)$ with 1 control (ITN). $N_h = 500$, $N_v = 4000$. (a) Human populations with 1 control (ITN). (b) Mosquitoes Populations with 1 control (ITN).

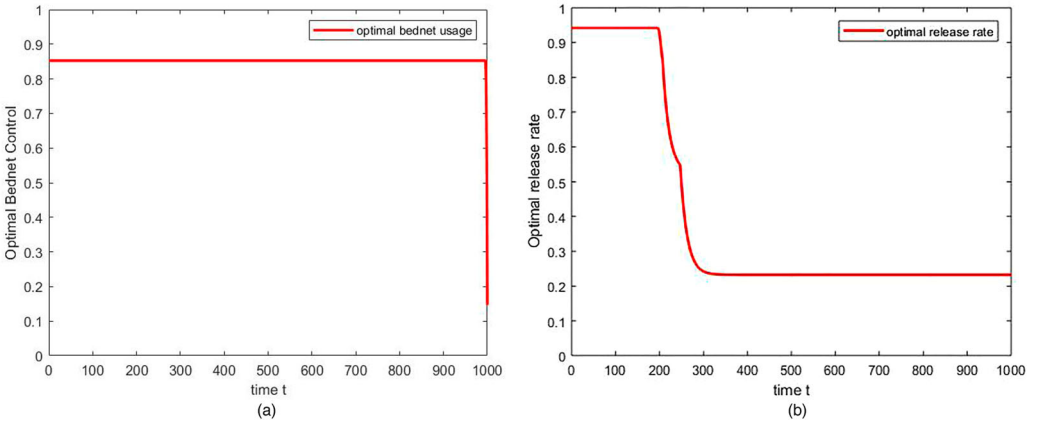

Figure 7. Optimal 1 control strategy: (a) ITN only; (b) SIT only.

mosquitoes can effectively reduce wild mosquitoes, but it cannot increase susceptible human population and decrease infected human population as efficiently as in Figure 3. Figure 6 illustrates the dynamical system with solely the other control – ITN. Only using bednet can significantly reduce infected human population while increasing susceptible human, but there will be much more susceptible wild mosquitoes as compared with Figure 3. We also observe more exposed and infected human, exposed and infected mosquitoes populations reduction using the ITN control when comparing Figures 5 and 6. Figure 7 gives each of the optimal control strategy without using the other control strategy. As we can see that only using ITN, it needs a constant high coverage for the bed net, while only using ITN, it needs to apply it for a short period of time of high level, then reducing to a low level.

5. Concluding remarks

In this paper, we have investigated a malaria transmission model with the release of sterile mosquitoes. Based on the next-generation matrix method [50], the basic reproduction number R_0 of the disease transmission is derived. To eradicate or suppress the wild mosquitoes, the releasing threshold b_0 of sterile mosquitoes is given in our Theorem 2.1.

Analysis of the basic reproduction number revealed that certain environments and control policies may, in fact, render the releasing of the sterile mosquitoes benefit to the goal of reducing the overall disease burden. In paper [44,45], the backward bifurcation phenomena are observed for malaria transmission without the releasing of the sterile mosquitoes. However, in system (1), from the expression of the basic reproduction number R_0, the releasing of the sterile mosquitoes is making a backward bifurcation less likely even if $R_0 < 1$. The suitable release of the sterile mosquitoes may help to avoid the potentially dangerous scenario of backward bifurcation. So we can guarantee that the disease-free equilibrium of system (1) is the only equilibrium, when control programs with sterile mosquitoes must strive to push R_0 less than one.

By choosing the parameters in paper [23,45], we investigate the optimal releasing of the sterile mosquitoes and the usage of ITN strategies and gain a qualitative understanding of how these two controls should be applied in dealing with malaria transmission, and how they should be used in different malaria-endemic settings. We quantify the effectiveness of the two interventions aimed at limiting the spread of malaria. We found the optimal control strategies and discovered the combination of both strategies leads to more rapid elimination of the wild mosquito population that can suppress malaria transmission.

Our analysis shows that SIT is an important method to control and eliminate the wild mosquito population. From the biological point of view, the wild mosquitoes will be eliminated if the release rate of sterile mosquitoes is large, which is unrealistic sometimes due to the cost. When the release rate of sterile mosquitoes lies in an intermediate level, whether the wild mosquito population is eliminated or not depends on the initial wild mosquitoes and sterile mosquitoes densities. In order to achieve the beneficial effect, the design of sterile-male release programs must account for the ecology, behavior and life history of mosquitoes [30]. Furthermore, maximizing the public health benefits of SIT-like system called RIDL (Release of Insects carrying a Dominant Lethal) technology involves optimizing all stages of the control program. The release strategy can profoundly affect the outcome of a control effort. For example, the strategies of releasing adult mosquitoes only, pupae only, or a combination of the two each have relative advantages in certain situations. Recommendations are also provided on effective approaches to achieve long-term suppression of a wild mosquitoes population using combined releases of adults and pupae. These items are not included in our present model. They will be scheduled to complete in the future.

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