

Research Article

A Malaria Model with Two Delays

Hui Wan¹ and Jing-an Cui²

¹ Jiangsu Key Laboratory for NSLSCS, School of Mathematical Sciences, Nanjing Normal University, Nanjing 210046, China

² School of Sciences, Beijing University of Civil Engineering and Architecture, Beijing 100044, China

Correspondence should be addressed to Jing-an Cui; cuijingan@bucea.edu.cn

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A transmission model of malaria with two delays is formulated. We calculate the basic reproduction number R_0 for the model. It is shown that the basic reproduction number is a decreasing function of two time delays. The existence of the equilibria is studied. Our results suggest that the model undergoes a backward bifurcation, which implies that bringing the basic reproduction number below 1 is not enough to eradicate malaria.

1. Introduction

Malaria is a mosquito-borne disease which is due to the four species of the genus *Plasmodium*, namely, *Plasmodium falciparum*, *Plasmodium vivax*, *Plasmodium malariae*, and *Plasmodium ovale*. These parasites are transmitted to the human host through a bite by an infected female anopheles mosquito.

Sporozoites are injected into a human host, which are carried through the blood to the liver within 30 min [1]. They invade hepatocytes and undergo a process of asexual replication (exoerythrocytic schizogony) to give rise to 10–40 thousand merozoites per sporozoite. Up to this point, the infection is nonpathogenic and clinically silent. After about 7–9 days, the liver schizonts rupture to release the merozoites into the blood and clinical symptoms, such as fever, pain, chills, and sweats, may develop. Each merozoite invades an erythrocyte and divides to form an erythrocytic schizont containing about 16 daughter merozoites [2]. These merozoites either reinfect fresh erythrocytes, giving rise to cyclical blood-stage infection with a periodicity of 48–72 h, depending on the *Plasmodium* species, or differentiate into sexual transmission stages called gametocytes. When a second mosquito bites the infected human, the gametocytes are ingested, giving rise to extracellular gametes. In the mosquito midgut, the gametes fuse to form a motile zygote (ookinete), which penetrates the mid-gut wall and forms an oocyst, within which meiosis takes place and haploid sporozoites develop. These sporozoites

migrate to the salivary glands. The incubation period within the mosquito may last 8–22 days [3]. The variation in the length of time is due to the environmental temperature. For *P. falciparum*, the average time is 12 days [4, 5]. Malaria can also be transmitted through blood transfusion, organ transplantation and transplacental malaria (i.e., congenital malaria) can also be significant in populations which are partially immune to malaria.

The application of mathematics to study of infectious disease appear to have been initiated by Berniulli, 1760. Presently, a lot of mathematical models have been proposed to evaluate and compare control procedures and preventive strategies, and to investigate the relative effects of various sociological, biological, and environmental factors on the spread of diseases ([6–14], etc.). These models have played a very important role in the history and development of epidemiology.

The transmission process involves considerable time delay both in human and in mosquitoes due to the incubation periods of the several forms of the parasites [9]. Several works have been done to consider the effect of delay. Taking account of the incubation period in vector (mosquito), Takeuchi et al. [10] considered a differential-delay model for vector-borne diseases and get the global stability of the endemic equilibrium under appropriate conditions. While Wei et al. [15] proposed a similar model of vector-borne disease which has direct mode of transmission in addition to the vector-mediated transmission and proved that the introduction of

a time delay in the host-to-vector transmission term can destabilize the system and periodic solutions can arise through Hopf bifurcation. In [9], Ruan et al. proposed a delayed Ross-Macdonald model with delays both in human and in mosquitoes. The effect of time delays on the basic reproduction number and the dynamics of the transmission was studied.

Both the models in [10, 15] adopted mass action formulation, where the contact rate depends on the size of the total host population while the model in [9] adopted standard incidence formulation, where the contact rate is assumed to be constant (see [16] for detailed derivation of these incidence functions). The choice of one formulation over the other really depends on the disease being modeled and, in some cases, the need for mathematical (analytical) tractability [17]. A crucial question is which of the two incidence functions is more suitable for modeling infectious disease in general, and malaria in particular? As noted in [16], data ([4, 18]) strongly suggests that standard incidence is better for modeling human diseases than mass action incidence. Consequently, standard incidence rate is adopted in this paper.

2. Derivation of the Model

In order to study the impact of incubation periods in both human and mosquitoes on the basic reproduction number and the transmission dynamics of malaria over long periods, we propose a model based on SIRS in human population and SI for the mosquito vector population. Since the mosquito dynamics operates on a much faster time scale than the human dynamics and the turnover of the mosquito population is very high and the total size of vector population is largely exceeding the human total size, the mosquito population can be considered to be at an equilibrium with respect to changes in the human population. Hence, the total number of mosquito population is assumed to be constant.

We formulate an SIRS-SI model for the spread of malaria in the human and mosquito population with the total population size at time t is given by $N_h(t)$ and $N_v(t)$, correspondingly. For the human population, the three compartments represent individuals who are susceptible, infectious, and partially immune, with sizes at time t denoted by $S_h(t)$, $I_h(t)$, and $R_h(t)$, respectively. The incubation period in a human has duration $\tau_1 \geq 0$. A susceptible individual infected by a mosquito will not become infectious until τ_1 time units later and we assume that no one recovers during this incubation period. At the infectious stage a host may die from the disease, recover into the susceptible class, or may recover with acquired partial immunity. Infectious human hosts are those with infectious gametocytes in the blood stream. Partially immune hosts still have protective antibodies and other immune effectors at low levels. $\Lambda_h > 0$ is the human input (birth) rate. $\mu_h > 0$ and $\alpha_h \geq 0$ are the natural and disease-induced death rates, respectively. $\gamma_h > 0$ is the rate at which human hosts acquire immunity. $\theta \geq 0$ is the per capita rate of recovery into the susceptible class from being infectious. $\rho \geq 0$ is the per capita rate of loss of immunity in human hosts. $\beta_h > 0$ is the proportion of bites on man that produce

an infection. For the mosquito population, the two compartments represent susceptible and infectious mosquitoes, with sizes at time t denoted by $S_v(t)$ and $I_v(t)$, respectively. The vector component of the model does not include immune class as mosquitoes never recover from infection that is, their infective period ends with their death due to their relatively short life cycle. Thus the immune class in the mosquito population is negligible and death occurs equally in all groups. Our model also excludes the immature mosquitoes since they do not participate in the infection cycle and are, thus, in the waiting period, which limits the vector population growth. We assume that the mosquito population is constant and equal to N_v , with birth and death rate constants equal to μ_v . β_v is the probability that a mosquito becomes infectious when it bites an infectious human. The biting rate b of mosquitoes is the average number of bites per mosquito per day. This rate depends on a number of factors, in particular, climatic ones, but for simplicity in this paper, we assume b constant. The incubation interval in the mosquito has duration $\tau_2 \geq 0$.

Considering the assumption made above, the interaction between human hosts and the mosquito vector population with standard incidence rate is described as shown below:

$$\begin{aligned}
 \frac{dS_h}{dt} &= \Lambda_h - \frac{b\beta_h}{N_h(t-\tau_1)} I_v(t-\tau_1) S_h(t-\tau_1) e^{-\mu_h \tau_1} - \mu_h S_h \\
 &\quad + \theta I_h + \rho R_h, \\
 \frac{dI_h}{dt} &= \frac{b\beta_h}{N_h(t-\tau_1)} I_v(t-\tau_1) S_h(t-\tau_1) e^{-\mu_h \tau_1} \\
 &\quad - (\gamma_h + \mu_h + \alpha_h + \theta) I_h, \\
 \frac{dR_h}{dt} &= \gamma_h I_h - \mu_h R_h - \rho R_h, \\
 \frac{dS_v}{dt} &= \mu_v S_v + \mu_v I_v \\
 &\quad - \frac{b\beta_v}{N_h(t-\tau_2)} I_h(t-\tau_2) S_v(t-\tau_2) e^{-\mu_v \tau_2} - \mu_v S_v, \\
 \frac{dI_v}{dt} &= \frac{b\beta_v}{N_h(t-\tau_2)} I_h(t-\tau_2) S_v(t-\tau_2) e^{-\mu_v \tau_2} - \mu_v I_v, \\
 \frac{dN_h}{dt} &= \Lambda_h - \mu_h N_h - \alpha_h I_h,
 \end{aligned} \tag{1}$$

where $S_h(t)$, $I_h(t)$, and $R_h(t)$ denote the number of susceptible, infective, and recovered in the human population, and $S_v(t)$, $I_v(t)$ denote the number of susceptible and infective in the mosquito vector population. In addition, $S_h + I_h + R_h = N_h$ and $S_v + I_v = N_v$.

System (1) satisfies the initial conditions: $S_h(\theta) = S_{h0}(\theta)$, $I_h(\theta) = I_{h0}(\theta)$, $R_h(\theta) = R_{h0}(\theta)$, $S_v(\theta) = S_{v0}(\theta)$, $I_v(\theta) = I_{v0}(\theta)$, $\theta \in [-\tau, 0]$, where $\tau = \max\{\tau_1, \tau_2\}$. The nonnegative cone of R^6 space $S_h I_h R_h S_v I_v N_h$ is positively invariant for system (1) since the vector field on the boundary does not point to the exterior. What is more, since $dN_h/dt < 0$ for $N_h > \Lambda_h/\mu_h$

and N_v is constant, all trajectories in the first quadrant enter or stay inside the region

$$Z_+ = \left\{ S_h + I_h + R_h = N_h \leq \frac{\Lambda_h}{\mu_h}, S_v + I_v = N_v \right\}. \quad (2)$$

The continuity of the right-hand side of (1) implies that unique solutions exist on a maximal interval. Since solutions approach, enter or stay in D_+ , they are eventually bounded and hence exist for $t > 0$. Therefore, the initial value problem for system (1) is mathematically well posed and biologically reasonable since all variables remain nonnegative.

In order to reduce the number of parameters and simplify system (1), we normalize the human and mosquito vector population $s_h = S_h/(\Lambda_h/\mu_h)$, $i_h = I_h/(\Lambda_h/\mu_h)$, $r_h = R_h/(\Lambda_h/\mu_h)$, $n_h = N_h/(\Lambda_h/\mu_h)$, $s_v = S_v/N_v$, $i_v = I_v/N_v$, and $m = N_v/(\Lambda_h/\mu_h)$.

Since $r_h = n_h - s_h - i_h$ and $s_v = 1 - i_v$, the dynamics of system (1) is qualitatively equivalent to the dynamics of system given by

$$\begin{aligned} \frac{ds_h}{dt} &= \mu_h - \frac{b\beta_h m}{n_h(t-\tau_1)} i_v(t-\tau_1) s_h(t-\tau_1) e^{-\mu_h \tau_1} \\ &\quad - \mu_h s_h + \theta i_h + \rho(n_h - s_h - i_h), \\ \frac{di_h}{dt} &= \frac{b\beta_h m}{n_h(t-\tau_1)} i_v(t-\tau_1) s_h(t-\tau_1) e^{-\mu_h \tau_1} \\ &\quad - (\gamma_h + \mu_h + \alpha_h + \theta) i_h, \\ \frac{di_v}{dt} &= \frac{b\beta_v}{n_h(t-\tau_2)} i_h(t-\tau_2) (1 - i_v(t-\tau_2)) e^{-\mu_v \tau_2} - \mu_v i_v, \\ \frac{dn_h}{dt} &= \mu_h - \mu_h n_h - \alpha_h i_h, \end{aligned} \quad (3)$$

and all trajectories in the nonnegative cone R_+^4 enter or stay inside the region $D = \{0 \leq s_h, 0 \leq i_h, s_h + i_h \leq n_h \leq 1, 0 \leq i_v \leq 1\}$.

Define the basic reproduction number by

$$R_0 = \frac{mb^2 \beta_h \beta_v e^{-\mu_h \tau_1} e^{-\mu_v \tau_2}}{\mu_v (\gamma_h + \mu_h + \alpha_h + \theta)}. \quad (4)$$

It represents the expected number of secondary cases caused by a single infected individual introduced into an otherwise susceptible population of hosts and vectors. Take a primary case of host with a natural death rate of μ_h , the average time spent in an infectious state is $1/(\gamma_h + \mu_h + \alpha_h + \theta)$. Since the incubation period in mosquitoes has duration τ_2 , during which period some mosquitoes may die, the average number of mosquito bites received from m susceptible mosquitoes each with a biting rate b gives a total of $b\beta_v m e^{-\mu_v \tau_2}/(\gamma_h + \mu_h + \alpha_h + \theta)$ mosquitoes successfully infected by the primary human case. Each of these mosquitoes survives for an average time $1/\mu_v$. Because of another incubation period τ_1 in human, during which period some individuals may die, totally $b\beta_h e^{-\mu_h \tau_1}/\mu_v$ hosts will be infected by a single mosquito.

Therefore, the total number of secondary cases is thus $mb^2 \beta_h \beta_v e^{-\mu_h \tau_1} e^{-\mu_v \tau_2} / \mu_v (\gamma_h + \mu_h + \alpha_h + \theta)$, which is the basic reproduction number R_0 .

3. Existence of Equilibria

Equating the derivatives on the left-hand side to zero and solving the resulting algebraic equations. The points of equilibrium $\widehat{P}(\widehat{s}_h, \widehat{i}_h, \widehat{i}_v, \widehat{n}_h)$ satisfy the following relations:

$$\begin{aligned} \widehat{s}_h &= \frac{\mu_h + \rho - H \widehat{i}_h}{\mu_h + \rho}, \\ \widehat{n}_h &= \frac{\mu_h - \alpha_h \widehat{i}_h}{\mu_h}, \\ \widehat{i}_v &= \frac{b\beta_v \mu_h \widehat{i}_h e^{-\mu_v \tau_2}}{(b\beta_v \mu_h e^{-\mu_v \tau_2} - \alpha_h \mu_v) \widehat{i}_h + \mu_v \mu_h}, \end{aligned} \quad (5)$$

where $H = \gamma_h + \mu_h + \alpha_h + \rho + \rho(\alpha_h/\mu_h)$. Substituting (5) in the corresponding second equilibrium equation of (3), we obtain that the solutions are $\widehat{i}_h = 0$, and the zero points of the quadratic polynomial

$$r(i_h) = a_1 i_h^2 + a_2 i_h + a_3, \quad (6)$$

where

$$\begin{aligned} a_1 &= (b\beta_v \mu_h e^{-\mu_v \tau_2} - \alpha_h \mu_v) \frac{\alpha_h}{\mu_h}, \\ a_2 &= 2\alpha_h \mu_v - b\beta_v \mu_h e^{-\mu_v \tau_2} \\ &\quad - \frac{mb^2 \beta_h \beta_v \mu_h H}{(\mu_h + \rho)(\gamma_h + \mu_h + \alpha_h + \theta)} e^{-\mu_h \tau_1} e^{-\mu_v \tau_2}, \\ a_3 &= \mu_h \mu_v (R_0 - 1), \end{aligned} \quad (7)$$

$$R_0 = \frac{mb^2 \beta_h \beta_v e^{-\mu_h \tau_1} e^{-\mu_v \tau_2}}{\mu_v (\gamma_h + \mu_h + \alpha_h + \theta)}.$$

The solution $\widehat{i}_h = 0$ gives the disease-free equilibrium point $P_0(1, 0, 0, 1)$. We are looking for nontrivial equilibrium solutions in the interior of Ω . From (5), in order to keep \widehat{s}_h and \widehat{n}_h positive, $\widehat{i}_h \in (0, (\mu_h + \rho)/H)$ must be satisfied. Evaluating $r(i_h)$ at the end points of the interval, we obtain

$$\begin{aligned} r(0) &= \mu_h \mu_v (R_0 - 1), \\ r\left(\frac{\mu_h + \rho}{H}\right) &< 0. \end{aligned} \quad (8)$$

When $R_0 > 1$, then $r(0) > 0$; therefore, there exists a unique root in the interval $(0, (\mu_h + \rho)/H)$, which implies the existence of a unique equilibrium point $P^*(\widehat{s}_h^*, \widehat{i}_h^*, \widehat{i}_v^*, \widehat{n}_h^*)$, where \widehat{i}_h^* satisfies: if $a_1 = 0$,

$$\widehat{i}_h^* = \frac{-a_3}{a_2}. \quad (9)$$

If $a_1 \neq 0$,

$$\hat{i}_h^* = \frac{-a_2 - \sqrt{\Delta}}{2a_1}, \quad (10)$$

where $\Delta = a_2^2 - 4a_1a_3$.

When $R_0 = 1$, the roots of (6) are 0 and $-a_2/a_1$. It is easy to see that there exists a unique root in the interval $(0, (\mu_h + \rho)/H)$ if and only if $a_2 > 0$, which implies the existence of a unique equilibrium point P^* .

When $R_0 < 1$, then $r(0) < 0$. The conditions to have at least one root in the mentioned interval are $a_1 < 0$, $0 < -a_2/2a_1 < (\mu_h + \rho)/H$ and $\Delta = a_2^2 - 4a_1a_3 \geq 0$. If $\Delta > 0$, there exist two roots in the interval mentioned above, which implies the existence of two equilibria $P_1(\hat{s}_{h1}, \hat{i}_{h1}, \hat{i}_{v1}, \hat{n}_{h1})$ and $P_2(\hat{s}_{h2}, \hat{i}_{h2}, \hat{i}_{v2}, \hat{n}_{h2})$, where

$$\begin{aligned} \hat{i}_{h1} &= \frac{-a_2 + \sqrt{\Delta}}{2a_1}, \\ \hat{i}_{h2} &= \frac{-a_2 - \sqrt{\Delta}}{2a_1}. \end{aligned} \quad (11)$$

If $\Delta = 0$, there is a unique root in the interval mentioned above, which implies the existence of unique equilibrium.

Then, we can conclude the above results in the following theorem.

Theorem 1. (1) *The disease-free equilibrium $P_0(1, 0, 0, 1)$ always exists.*

(2) *If $R_0 > 1$, there exists a unique positive equilibrium $P^*(\hat{s}_h^*, \hat{i}_h^*, \hat{i}_v^*, \hat{n}_h^*)$.*

(3) *If $R_0 = 1$, then there is a positive equilibrium $P^*(\hat{s}_h^*, \hat{i}_h^*, \hat{i}_v^*, \hat{n}_h^*)$ when $a_2 > 0$; otherwise, there is no positive equilibrium.*

(4) *If $R_0 < 1$, then (a) if $a_1 \geq 0$, there is no positive equilibrium; (b) if $a_1 < 0$, the system (3) has two positive equilibria $P_1(\hat{s}_{h1}, \hat{i}_{h1}, \hat{i}_{v1}, \hat{n}_{h1})$ and $P_2(\hat{s}_{h2}, \hat{i}_{h2}, \hat{i}_{v2}, \hat{n}_{h2})$ if and only if $\Delta > 0$ and $0 < -a_2/2a_1 < (\mu_h + \rho)/H$, and these two equilibria merge with each other if and only if $0 < -a_2/2a_1 < (\mu_h + \rho)/H$ and $\Delta = 0$; otherwise, there is no positive equilibrium.*

4. Disease-Free Equilibrium

It is easy to see the disease-free equilibrium $P_0(1, 0, 0, 1)$ always exists. In this section, we study the stability of the disease-free equilibrium P_0 .

Theorem 2. P_0 is locally stable if $R_0 < 1$. P_0 is a degenerate equilibrium of codimension one and is stable except in one direction if $R_0 = 1$. P_0 is unstable if $R_0 > 1$.

Proof. Linearizing the system (3) at P_0 . The eigenvalues of the Jacobian matrix $J(P_0)$ are $-\mu_h - \rho$, $-\mu_h$ and the solutions of the following transcendental equation:

$$\begin{aligned} (\lambda + \mu_v)(\gamma_h + \mu_h + \alpha_h + \theta) \\ - mb^2 \beta_h \beta_v e^{-\mu_h \tau_1 - \mu_v \tau_2} e^{-(\tau_1 + \tau_2)\lambda} = 0. \end{aligned} \quad (12)$$

Let

$$\begin{aligned} F(\lambda, \tau_1, \tau_2) &= (\lambda + \mu_v)(\gamma_h + \mu_h + \alpha_h + \theta) \\ &\quad - mb^2 \beta_h \beta_v e^{-\mu_h \tau_1 - \mu_v \tau_2} e^{-(\tau_1 + \tau_2)\lambda}. \end{aligned} \quad (13)$$

Clearly, $F(\lambda, \tau_1, \tau_2)$ is an analytic function. $F(0, \tau_1, \tau_2) = \mu_v(\gamma_h + \mu_h + \alpha_h + \theta)(1 - R_0)$, and $F(\lambda, 0, 0) = (\lambda + \mu_v)(\gamma_h + \mu_h + \alpha_h + \theta) - mb^2 \beta_h \beta_v$. In the following, we discuss the distribution of the solutions of (12) in three cases.

(i) $R_0 < 1$, then $F(0, \tau_1, \tau_2) > 0$. Since $F'_\lambda(\lambda, \tau_1, \tau_2) > 0$ for $\lambda \geq 0$, $\tau_1 > 0$ and $\tau_2 > 0$, (12) has no zero root and positive real roots for all positive τ_1 and τ_2 . Now we claim that (12) does not have any purely imaginary roots. Suppose that (12) has a pair of purely imaginary roots ωi , $\omega > 0$ for some τ_1 and τ_2 . Then, by calculation, ω must be a positive real root of

$$\begin{aligned} \omega^4 + [(\gamma_h + \mu_h + \alpha_h + \theta)^2 + \mu_v^2] \omega^2 + (\gamma_h + \mu_h + \alpha_h + \theta)^2 \mu_v^2 \\ - (mb^2 \beta_h \beta_v e^{-\mu_h \tau_1 - \mu_v \tau_2})^2 = 0. \end{aligned} \quad (14)$$

However, it is easy to see that (14) does not have nonnegative real roots when $R_0 < 1$. Hence, (12) does not have any purely imaginary roots.

On the other hand, one can easily get that the roots of $F(\lambda, 0, 0) = 0$ all have negative real parts when $R_0 < 1$. By the implicit function theorem and the continuity of $F(\lambda, \tau_1, \tau_2)$, we know that all roots of (12) have negative real parts for positive τ_1 and τ_2 , which implies that P_0 is stable.

(ii) $R_0 = 1$, then $F(0, \tau_1, \tau_2) = 0$. Since $F'_\lambda(\lambda, \tau_1, \tau_2) > 0$ for $\lambda \geq 0$, $\tau_1 > 0$ and $\tau_2 > 0$, (12) has a simple zero root and no positive root for all positive τ_1 and τ_2 . Using a similar argument as in (i), we can obtain that except a zero root, all roots of (12) have negative real parts for positive τ_1 and τ_2 . Thus, P_0 is a degenerate equilibrium of codimension one and is stable except in one direction.

(iii) $R_0 > 1$, then $F(0, \tau_1, \tau_2) < 0$. Since $\lim_{\lambda \rightarrow \infty} F(\lambda, \tau_1, \tau_2) = \infty$ and $F'_\lambda(\lambda, \tau_1, \tau_2) > 0$ for $\lambda \geq 0$, $\tau_1 > 0$ and $\tau_2 > 0$, (12) has a unique positive real root for all positive τ_1 and τ_2 and P_0 is unstable. □

Theorem 3. *If $R_0 \leq 1$, the disease-free equilibrium P_0 is globally asymptotically stable when $\alpha = 0$.*

Proof. We denote by x_t the translation of the solution of the system (3), that is, $x_t = (s_h(t + \theta), i_h(t + \theta), i_v(t + \theta), n_h(t + \theta))$ where $\theta \in [-\tau, 0]$, $\tau = \max\{\tau_1, \tau_2\}$. In order to prove

the globally stability of P_0 , we define a Lyapunov function:

$$L(x_t) = e^{\mu_h \tau_1} i_h + \frac{mb\beta_h}{\mu_v} e^{\mu_v \tau_2} i_v(t) + mb\beta_h \int_{t-\tau_1}^t i_v(t) \frac{s_h(t)}{n_h(t)} dt + \frac{mb^2\beta_h\beta_v}{\mu_v} \int_{t-\tau_2}^t i_h(t) \frac{1-i_v(t)}{n_h(t)} dt. \tag{15}$$

The derivative of L along the solutions of (3) is given by

$$\frac{dL(x_t)}{dt} = -(\mu_h + \gamma_h + \theta) e^{\mu_h \tau_1} i_h(t) \left(1 - R_0 e^{-\mu_h \tau_1} \frac{1-i_v(t)}{n_h(t)}\right) - mb\beta_h e^{\mu_v \tau_2} i_v(t) \left(1 - \frac{s_h(t)}{n_h(t)} e^{-\mu_v \tau_2}\right). \tag{16}$$

Since $\lim_{t \rightarrow \infty} n_h = 1$ and $R_0 \leq 1$, we can easily get that $dL/dt \leq 0$ and the set $\{P_0\}$ is the largest invariant set within the set where $dL(x_t)/dt = 0$. By LaSalle-Lyapunov Theorem, all trajectories approach P_0 as $t \rightarrow \infty$. \square

Usually, the disease can be controlled if the basic reproduction number is smaller than one. Nevertheless, Theorem 1 indicates the possibility of backward bifurcation (where the locally asymptotically stable DFE coexists with endemic equilibrium when $R_0 < 1$) when $a_1 < 0$ for the model (3) and it becomes impossible to control the disease by just reducing the basic reproduction number below one. Therefore a further threshold condition beyond the basic reproduction is essential for the control of the spread of malaria.

To check for this, the discriminant Δ is set to zero and solved for the critical value of R_0 , denoted by \widehat{R}_0 , given by

$$\widehat{R}_0 = 1 + \frac{a_2^2}{4a_1\mu_h\mu_v}. \tag{17}$$

Thus, backward bifurcation would occur for values of R_0 such that $\widehat{R}_0 < R_0 < 1$. This is illustrated by simulating the model with the following set of parameter values (it should be stated that these parameters are chosen for illustrative purpose only, and may not necessarily be realistic epidemiologically).

Let $\mu_h = 1/22000$, $\mu_v = 1/14$, $\beta_h = 0.3$, $\beta_v = 0.95$, $m = 0.5$, $\alpha_h = 0.05$, $\gamma_h = 0.26$, $b = 0.5$, $\rho = 0.01$, $\theta = 0.08$, $\tau_1 = 15$. With this set of parameters, $\widehat{R}_0 = 0.093970 < 1$. When $\tau_2 = 10$, $R_0 = 0.62555 < 1$, so that $\widehat{R}_0 < R_0 < 1$. There are two positive roots for (6), which are $\widehat{i}_{h1} = .3501527770e - 3$ and $\widehat{i}_{h2} = .8864197396e - 3$.

Thus, the following result is established.

Lemma 4. *The model (3) undergoes backward bifurcation when $a_1 < 0$ and $0 < -a_2/2a_1 < (\mu_h + \rho)/H$ holds and $\widehat{R}_0 < R_0 < 1$.*

Epidemiologically, because of the existence of backward bifurcation, whether malaria will prevail or not depends on

the initial states. $R_0 < 1$ is no longer sufficient for disease elimination. In order to eradicate the disease, we have a sub-threshold number \widehat{R}_0 and it is now necessary to reduce R_0 to a value less than \widehat{R}_0 .

The existence of the subthreshold condition \widehat{R}_0 also has some implications. In some areas where malaria dies out ($R_0 < \widehat{R}_0$), it is possible for the disease to reestablish itself in the population because of a small change in environmental or control variables which increase the basic reproduction number above. On the other hand, in some areas with endemic malaria, it may be possible to eradicate the disease with small increasing in control programs such that the basic reproduction number less than \widehat{R}_0 .

From the expression of R_0 , we can see that the basic reproduction number is a decreasing function of both time delays. The time delays have important effect on the basic reproduction number. Especially, since global warming decreases the duration of incubation period and R_0 increases with the decreasing of τ_1 or τ_2 , global warming will affect the transmission of malaria a lot.

From Theorem 3, if there is no disease-induced death, backward bifurcation will not occur and there is a unique endemic equilibrium when $R_0 > 1$. Therefore, the disease-induced death is the cause of the backward bifurcation phenomenon in the model (3).

5. Endemic Equilibria

To obtain precise results, we first assume that malaria does not produce significant mortality ($\alpha = 0$). The assumption is not justifiable in all regions where malaria is endemic but it is a useful first approximation. In this part, we will determine the stability of the unique endemic equilibria P^* when $R_0 > 1$.

Linearizing the system (3) at P^* . The eigenvalues of the Jacobian matrix $J(P^*)$ are $-\mu_h$ and the solutions of the following transcendental equation:

$$\lambda^3 + A_1\lambda^2 + A_2\lambda + A_3 = 0, \tag{18}$$

where

$$\begin{aligned} A_1 &= 2\mu_h + \gamma_h + \rho + \theta + \mu_v \\ &+ mb\beta_h\widehat{i}_v e^{-\mu_h\tau_1} e^{-\lambda\tau_1} + b\beta_v\widehat{i}_h e^{-\mu_v\tau_2} e^{-\lambda\tau_2}, \\ A_2 &= (\mu_h + \rho)(\gamma_h + \mu_h + \theta) + (\mu_h + \rho)\mu_v \\ &+ (\gamma_h + \mu_h + \theta)\mu_v \\ &+ (\mu_h + \rho + \gamma_h + \mu_h + \theta)b\beta_v\widehat{i}_h e^{-\mu_v\tau_2} e^{-\lambda\tau_2} \\ &- \mu_v(\gamma_h + \mu_h + \theta) e^{-(\tau_1+\tau_2)\lambda} \\ &+ (\gamma_h + \mu_h + \rho + \mu_v + b\beta_v\widehat{i}_h e^{-\mu_v\tau_2} e^{-\lambda\tau_2}) \\ &\times mb\beta_h\widehat{i}_v e^{-\mu_h\tau_1} e^{-\lambda\tau_1}, \end{aligned}$$

$$\begin{aligned}
A_3 &= (\mu_h + \rho)(\gamma_h + \mu_h + \theta)\mu_v \\
&+ (\mu_h + \rho)(\gamma_h + \mu_h + \theta)b\beta_v\widehat{i}_h e^{-\mu_v\tau_2} e^{-\lambda\tau_2} \\
&- (\mu_h + \rho)(\gamma_h + \mu_h + \theta)\mu_v e^{-(\tau_1 + \tau_2)\lambda} \\
&+ (\gamma_h + \mu_h + \rho)mb\beta_h\widehat{i}_v e^{-\mu_h\tau_1} e^{-\lambda\tau_1} \\
&\times (\mu_v + b\beta_v\widehat{i}_h e^{-\mu_v\tau_2} e^{-\lambda\tau_2}).
\end{aligned} \tag{19}$$

For any nonnegative τ_1 and τ_2 , we have the following proposition.

Proposition 5. For the endemic equilibrium $P^*(\widehat{s}_h^*, \widehat{i}_h^*, \widehat{i}_v^*, \widehat{n}_h^*)$ of the system with characteristic equation (18), one always has

$$A_1 > 0, \quad A_2 > 0, \quad A_3 > 0, \quad A_1 A_2 - A_3 > 0. \tag{20}$$

Proof. It is clear that $A_1 > 0$, $A_2 > 0$ and $A_3 > 0$. For $A_1 A_2 - A_3$, we have

$$\begin{aligned}
A_1 A_2 - A_3 &= (\gamma_h + \mu_h + \rho) \\
&\times \left\{ (\mu_h + \rho)(\gamma_h + \mu_h + \theta) \right. \\
&\quad + (\mu_h + \rho)\mu_v + (\gamma_h + \mu_h + \theta)\mu_v \\
&\quad + (\mu_h + \rho + \gamma_h + \mu_h + \theta)b\beta_v\widehat{i}_h e^{-\mu_v\tau_2} e^{-\lambda\tau_2} \\
&\quad - \mu_v(\gamma_h + \mu_h + \theta)e^{-(\tau_1 + \tau_2)\lambda} \\
&\quad \left. + (\gamma_h + \mu_h + \rho + \mu_v)mb\beta_h\widehat{i}_v e^{-\mu_h\tau_1} e^{-\lambda\tau_1} \right\} \\
&+ (mb\beta_h\widehat{i}_v e^{-\mu_h\tau_1} e^{-\lambda\tau_1} + \mu_h + \theta)A_2 \\
&+ (\mu_v + b\beta_v\widehat{i}_h e^{-\mu_v\tau_2} e^{-\lambda\tau_2}) \\
&\times \left\{ (\mu_h + \rho)\mu_v + (\gamma_h + \mu_h + \theta)\mu_v \right. \\
&\quad + (\mu_h + \rho + \gamma_h + \mu_h + \theta)b\beta_v\widehat{i}_h e^{-\mu_v\tau_2} e^{-\lambda\tau_2} \\
&\quad + (\gamma_h + \mu_h + \rho + \mu_v + b\beta_v\widehat{i}_h e^{-\mu_v\tau_2} e^{-\lambda\tau_2}) \\
&\quad \times mb\beta_h\widehat{i}_v e^{-\mu_h\tau_1} e^{-\lambda\tau_1} \\
&\quad \left. - \mu_v(\gamma_h + \mu_h + \theta)e^{-(\tau_1 + \tau_2)\lambda} \right\} \\
&+ (\mu_h + \rho)(\gamma_h + \mu_h + \theta)\mu_v e^{-(\tau_1 + \tau_2)\lambda} \\
&> 0.
\end{aligned} \tag{21}$$

□

Case 1. When $\tau_1 = \tau_2 = 0$, as a result of Proposition 5 and Hurwitz criterion, all roots of the characteristic equation (18) have negative real parts and the endemic equilibrium P^* of (3) is stable when $\tau_1 = \tau_2 = 0$.

Case 2. When $\tau_1 > 0$, $\tau_2 = 0$, the characteristic equation (18) becomes

$$\lambda^3 + A_{11}\lambda^2 + A_{21}\lambda + A_{31} = e^{-\lambda\tau_1} (T_{11}\lambda^2 + T_{21}\lambda + T_{31}), \tag{22}$$

where

$$\begin{aligned}
A_{11} &= 2\mu_h + \gamma_h + \rho + \theta + \mu_v + b\beta_v\widehat{i}_h, \\
A_{21} &= (\mu_h + \rho)(\gamma_h + \mu_h + \theta) + (\mu_h + \rho)\mu_v \\
&\quad + (\gamma_h + \mu_h + \theta)\mu_v + (\mu_h + \rho + \gamma_h + \mu_h + \theta)b\beta_v\widehat{i}_h, \\
A_{31} &= (\mu_h + \rho)(\gamma_h + \mu_h + \theta)\mu_v \\
&\quad + (\mu_h + \rho)(\gamma_h + \mu_h + \theta)b\beta_v\widehat{i}_h, \\
T_{11} &= -mb\beta_h\widehat{i}_v e^{-\mu_h\tau_1}, \\
T_{21} &= (\gamma_h + \mu_h + \theta)\mu_v \\
&\quad - (\gamma_h + \mu_h + \rho + \mu_v + b\beta_v\widehat{i}_h)mb\beta_h\widehat{i}_v e^{-\mu_h\tau_1}, \\
T_{31} &= (\mu_h + \rho)(\gamma_h + \mu_h + \theta)\mu_v \\
&\quad - (\gamma_h + \mu_h + \rho)(\mu_v + b\beta_v\widehat{i}_h)mb\beta_h\widehat{i}_v e^{-\mu_h\tau_1}.
\end{aligned} \tag{23}$$

By the implicit function theorem and the continuity of the left-hand side function of (18), all roots of (22) have negative real parts for small τ_1 . Notice that the condition $R_0 > 1$ is equivalent to

$$\tau_1 < \tau_1^* = \frac{1}{\mu_h} \ln \frac{mb^2\beta_h\beta_v}{\mu_v(\gamma_h + \mu_h + \theta)}. \tag{24}$$

Furthermore, we claim that (22) does not have any nonnegative real roots for any $\tau_1 > 0$. Rewrite (22) by moving the positive terms from the right-hand side to the left-hand side. The rewritten (22) takes the form

$$\lambda^3 + A_{11}\lambda^2 + \widetilde{A}_{21}\lambda + \widetilde{A}_{31} = e^{-\lambda\tau_1} (T_{11}\lambda^2 + \widetilde{T}_{21}\lambda + \widetilde{T}_{31}), \tag{25}$$

where $\widetilde{A}_{21} = A_{21} - (\gamma_h + \mu_h + \theta)\mu_v e^{-\lambda\tau_1}$, $\widetilde{A}_{31} = A_{31} - (\mu_h + \rho)(\gamma_h + \mu_h + \theta)\mu_v e^{-\lambda\tau_1}$. It is easy to see $\widetilde{A}_{21} > 0$ and $\widetilde{A}_{31} > 0$ for all $\lambda \geq 0$ and $\tau_1 \in (0, \tau_1^*)$. Consequently, the left-hand side in (25) is positive for all $\lambda \geq 0$ while the right-hand side is negative for all $\lambda \geq 0$ and the two cannot be equal for any $\lambda \geq 0$. Therefore, (22) does not have any nonnegative real roots for any $\tau_1 \in (0, \tau_1^*)$. Now we want to show that all roots of (22) have negative real parts for all $\tau_1 \in (0, \tau_1^*)$. To do so, we show that (22) does not have any purely imaginary roots for all $\tau_1 \in (0, \tau_1^*)$.

We assume that $\lambda = i\omega$ with $\omega > 0$ being a root of (22). Then ω must satisfy the following system:

$$\begin{aligned}
A_{21}\omega - \omega^3 &= T_{21}\omega \cos(\omega\tau_1) - (T_{31} - T_{11}\omega^2) \sin(\omega\tau_1), \\
A_{31} - A_{11}\omega^2 &= (T_{31} - T_{11}\omega^2) \cos(\omega\tau_1) + T_{21}\omega \sin(\omega\tau_1).
\end{aligned} \tag{26}$$

Thus, ω must be a positive root of

$$\omega^6 + B_1\omega^4 + B_2\omega^2 + B_3 = 0, \tag{27}$$

where

$$\begin{aligned} B_1 &= A_{11}^2 - 2A_{21} - T_{11}^2, \\ B_2 &= A_{21} - 2A_{11}A_{31} + 2T_{11}T_{31} - T_{21}^2, \\ B_3 &= A_{31}^2 - T_{31}^2. \end{aligned} \quad (28)$$

Let $z = \omega^2$, then (27) becomes

$$z^3 + B_1z^2 + B_2z + B_3 = 0. \quad (29)$$

Clearly, If $B_1 \geq 0, B_2 \geq 0$ and $B_3 \geq 0$, then (29) has no positive real roots. Therefore, (22) does not have any purely imaginary roots for all $\tau_1 \in (0, \tau_1^*)$ so that all roots of the characteristic equation (22) have negative real parts and the endemic equilibrium P^* of (3) is stable.

Case 3. When $\tau_2 > 0, \tau_1 = 0$, the characteristic equation (18) becomes

$$\lambda^3 + A_{12}\lambda^2 + A_{22}\lambda + A_{32} = e^{-\lambda\tau_2} (T_{12}\lambda^2 + T_{22}\lambda + T_{32}), \quad (30)$$

where

$$\begin{aligned} A_{12} &= 2\mu_h + \gamma_h + \rho + \theta + \mu_v + mb\beta_h\hat{i}_v, \\ A_{22} &= (\mu_h + \rho)(\gamma_h + \mu_h + \theta) + (\mu_h + \rho)\mu_v \\ &\quad + (\gamma_h + \mu_h + \theta)\mu_v + (\mu_h + \rho + \gamma_h + \mu_v)mb\beta_h\hat{i}_v, \\ A_{32} &= (\mu_h + \rho)(\gamma_h + \mu_h + \theta)\mu_v + \mu_v(\gamma_h + \mu_h + \rho)mb\beta_h\hat{i}_v, \\ T_{12} &= -b\beta_v\hat{i}_h e^{-\mu_v\tau_2}, \\ T_{22} &= (\gamma_h + \mu_h + \theta)\mu_v \\ &\quad - (2\mu_h + \gamma_h + \rho + \theta + mb\beta_h\hat{i}_v)b\beta_v\hat{i}_h e^{-\mu_v\tau_2}, \\ T_{32} &= (\mu_h + \rho)(\gamma_h + \mu_h + \theta)\mu_v \\ &\quad - (\gamma_h + \mu_h + \rho)mb^2\beta_h\beta_v\hat{i}_h\hat{i}_v e^{-\mu_v\tau_2} \\ &\quad - (\mu_h + \rho)(\gamma_h + \mu_h + \theta)b\beta_v\hat{i}_h e^{-\mu_v\tau_2}. \end{aligned} \quad (31)$$

The condition $R_0 > 1$ is equivalent to

$$\tau_2 < \tau_2^* = \frac{1}{\mu_v} \ln \frac{mb^2\beta_h\beta_v}{\mu_v(\gamma_h + \mu_h + \theta)}. \quad (32)$$

Using a similar argument as in Case 2, we know that all roots of (30) have negative real parts for $\tau_2 \in (0, \tau_2^*)$ when $C_1 \geq 0, C_2 \geq 0$, and $C_3 \geq 0$, where

$$\begin{aligned} C_1 &= A_{12}^2 - 2A_{22} - T_{12}^2, \\ C_2 &= A_{22} - 2A_{12}A_{32} + 2T_{12}T_{32} - T_{22}^2, \\ C_3 &= A_{32}^2 - T_{32}^2. \end{aligned} \quad (33)$$

Case 4. When $\tau_2 > 0, \tau_1 > 0$, the condition $R_0 > 1$ is equivalent to

$$\tau_2 < \tau_2^*(\tau_1) = \frac{1}{\mu_v} \ln \frac{mb^2\beta_h\beta_v e^{-\mu_h\tau_1}}{\mu_v(\gamma_h + \mu_h + \theta)}. \quad (34)$$

From Cases 1, and 2 the roots of (18) only have negative real parts for $\tau_1 \in [0, \tau_1^*)$ and $\tau_2 = 0$ under the condition of $B_i \geq 0, i = 1, 2, 3$. By the implicit function theorem and the continuity of the left-hand side function of (18), there is a $\bar{\tau}_2(\tau_1)$ satisfying $0 < \bar{\tau}_2(\tau_1) \leq \tau_2^*(\tau_1)$, such that all roots of (18) have negative real parts for $0 < \tau_2 < \bar{\tau}_2(\tau_1)$. We show that $\bar{\tau}_2(\tau_1) = \tau_2^*(\tau_1)$ when $B_i \geq 0$ and $C_i \geq 0, i = 1, 2, 3$. Suppose $\bar{\tau}_2(\tau_1) < \tau_2^*(\tau_1)$ for $\tau_1 \in [0, \tau_1^*)$, then there must be a $\tilde{\tau}_2(\tau_1), \bar{\tau}_2(\tau_1) < \tilde{\tau}_2(\tau_1) < \tau_2^*(\tau_1)$, such that one root of (18) has nonnegative real part for $\tau_2 = \tilde{\tau}_2(\tau_1)$. As a result of the continuity of τ_2 in τ_1 , we have $\tilde{\tau}_2(0) < \tau_2^*(0) = \tau_2^*$. However, from the argument in Case 3, we know that all the roots of (18) have negative real parts for $\tau_1 = 0$ and $\tau_2 \in (0, \tau_2^*)$. Contradict. Thus, $\bar{\tau}_2(\tau_1) = \tau_2^*(\tau_1)$ which implies that the endemic equilibrium P^* is stable when $\tau_1 \in [0, \tau_1^*), \tau_2 \in [0, \tau_2^*(\tau_1)), B_i \geq 0, i = 1, 2, 3$. The above analysis can be summarized into the following theorem.

Theorem 6. *If $R_0 > 1, B_i \geq 0$ and $C_i \geq 0, i = 1, 2, 3$, the unique endemic equilibrium P^* of system (3) is stable.*

6. Discussions

In this paper, in order to study the impact of the incubation periods in human and mosquitoes, we formulate a model with two delays for the transmission dynamics of malaria.

Existence of equilibria is obtained under different conditions and their stabilities are analyzed too. We have also identified the basic reproduction number R_0 , which gives the expected number of new infections (in mosquitoes or humans) from one infectious individual (human or mosquito) over the duration of the infectious period, given that all other members of the population are susceptible, in terms of the model parameters. Especially, we have proved mathematically backward bifurcation may occur for $R_0 < 1$ which implies that bringing the basic reproduction number below 1 is not enough to eradicate malaria.

The parameters τ_1 and τ_2 are the incubation periods in human and mosquitoes, which are temperature dependent. With the increasing of temperature in a range, they become shorter. Since the basic reproduction number is a monotone decreasing function of both time delays, global warming will then exacerbate the transmission of malaria.

The reason inducing backward bifurcation in [6] is the mosquito biting rate. While, the reasons inducing the backward bifurcation in our paper are the standard incidence rate and the disease-induced death rate which is big enough. By our results, the disease-free equilibrium is globally stable when $R_0 < 1$ if the disease-induced death is omitted. However, the result about backward bifurcation in this paper has important implications for malaria control, which implies

that bringing the basic reproduction number below 1 is not enough to eradicate malaria.

Malaria transmission can be affected by a lot of aspects. In this paper, we are trying to model the impact of temperature increasing on malaria transmission. In some extent, our results can provide a theoretical principle for allocating and using medical health resource reasonably, which can be applied in the practice of malaria prevention and control.

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