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A reaction–diffusion malaria model with incubation period in the vector population

Yijun Lou · Xiao-Qiang Zhao

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Abstract Malaria is one of the most important parasitic infections in humans and more than two billion people are at risk every year. To understand how the spatial heterogeneity and extrinsic incubation period (EIP) of the parasite within the mosquito affect the dynamics of malaria epidemiology, we propose a nonlocal and time-delayed reaction–diffusion model. We then define the basic reproduction ratio $\mathcal{R}_0$ and show that $\mathcal{R}_0$ serves as a threshold parameter that predicts whether malaria will spread. Furthermore, a sufficient condition is obtained to guarantee that the disease will stabilize at a positive steady state eventually in the case where all the parameters are spatially independent. Numerically, we show that the use of the spatially averaged system may highly underestimate the malaria risk. The spatially heterogeneous framework in this paper can be used to design the spatial allocation of control resources.

Keywords Malaria transmission · Spatial heterogeneity · Incubation period · Basic reproduction ratio · Threshold dynamics · Global attractivity

Mathematics Subject Classification (2000) 35K57 · 37N25 · 92D30

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Y. Lou (✉) · X.-Q. Zhao
Department of Mathematics and Statistics, Memorial University of Newfoundland, St. John's, NL A1C 5S7, Canada
e-mail: yijunlou@hotmail.com; ylou@mun.ca

X.-Q. Zhao
e-mail: zhao@mun.ca

1 Introduction

Each year, approximately 2.2 billion people are affected by *Plasmodium falciparum* malaria worldwide, claiming about 515 million endemic cases (Snow et al. 2005). Hence, there is an essential need for more information on the spatial and temporal patterns of disease burden, distribution and control strategies. Human malaria is caused by parasites belonging to the genus *Plasmodium*, which can be transmitted by several species of female *anopheles* mosquitoes. Since the pioneering work of Ronald Ross (Ross 1911), who proved that mosquitoes transmit malaria and presented the first mathematical model for the disease, modeling of malaria has flourished (see, e.g., Macdonald 1957; Aron and May 1982; Koella 1991; Lou and Zhao 2009; Ruan et al. 2008 and references therein). However, only a few studies with malaria consider the spatial heterogeneity and extrinsic incubation period (EIP) of the parasite within the mosquito simultaneously (see, e.g., Smith et al. 2004).

According to etiological literature, mosquitoes may spend a period of time during which they can not transmit the disease to humans after taking an infected blood meal, which is the extrinsic incubation period (EIP). This incubation period varies from 10 to 14 days (Charlwood et al. 1997; Killeen et al. 2000), which is long compared with the longevity of the adult mosquito (within 12 days (Charlwood et al. 1997)). These infected mosquitoes that survive the incubation period will remain infectious for the rest of their lives. Thus, EIP may greatly influence the number of infected mosquitoes that live long enough to become infectious. On the other hand, spatial heterogeneity, spatial movement of human and vector populations may be important for the malaria dynamics (Cosner et al. 2009; Lou and Zhao 2009; Tatem et al. 2006). It is therefore necessary to study the impacts of the EIP and the spatial heterogeneity on the transmission of the malaria parasite (Smith et al. 2004).

In this paper, we modify the standard Ross's malaria model (Ross 1911) to incorporate the extrinsic incubation period and human and vector movements in spatially heterogeneous environments. However, the modeling process is not trivial since mosquitoes may not stay at the same location in space during the incubation period, which involves a delay term with spatial averaging on the whole spatial domain (Britton 1990; Gourley and Wu 2006). Our analysis suggests that the model admits a basic reproduction ratio $\mathcal{R}_0$ and it serves as a threshold parameter for disease persistence. Moreover, we show that the risk based on the model with spatially averaged parameters may significantly underestimate the transmission intensity.

The rest of this paper is organized as follows. The next section presents the model, which turns out to be a nonlocal and time-delayed reaction–diffusion system. The basic reproduction ratio and mathematical analysis are established in Sect. 3. Section 4 is devoted to the study of the model with spatially independent parameters. Some carefully designed numerical simulations and a discussion section complete the paper.

2 Model formulation

The model is based on monitoring the temporal and spatial dynamics of host (the human) and vector (the adult female mosquito) densities. We develop a spatial model

for malaria infection by ignoring superinfection, immunity and clinical death (see, e.g., Aron and May 1982; Smith et al. 2004). The human population is divided into two epidemiological classes: susceptible (S_h) and infectious classes (I_h). Assume that the density of total human population $N_h(t,x) = S_h(t,x) + I_h(t,x)$ is described by a logistic population growth law, and that all populations perform an unbiased random walk. Thus, we have the following reaction–diffusion equation,

$$\frac{\partial N_h(t,x)}{\partial t} = D_h \Delta N_h(t,x) + b_h N_h(t,x)\left[1 - \frac{N_h(t,x)}{K(x)}\right],$$

where Δ is the usual Laplacian operator. The diffusion coefficient D_h and the natural growth rate b_h for humans are supposed to be positive constants while the carrying capacity $K(x)$ is a positive function of location x, allowing for the diversity in habitats. Let Ω be a spatial habitat with smooth boundary $\partial\Omega$. We assume that all populations remain confined to the region Ω for all time, and supplement the Neumann boundary condition to the above equation

$$\frac{\partial N_h}{\partial n} = 0, \quad \forall t > 0, \quad x \in \partial\Omega,$$

where $\frac{\partial}{\partial n}$ denotes the differentiation along the outward normal n to $\partial\Omega$. It easily follows that the above reaction–diffusion equation admits a unique positive steady state $H(x)$ such that $\lim_{t\to\infty} N_h(t,x) = H(x)$ for all solutions with nonnegative and nonzero initial data (see, e.g., Zhao 2003, Theorem 3.1.5 and the proof of Theorem 3.1.6). Biologically, we may suppose that the total human density at location point x stabilizes at $H(x)$, that is, $N_h(t,x) = H(x)$, $\forall t \geq 0$.

Human acquire malaria through effective contact with infectious mosquitoes. For the disease transmission term, we take into account the conservation of bites, that is, the total number of bites made by mosquitoes equals to the number of bites received by host at a fixed habitat x (see, e.g., Bowman et al. 2005). Thus, we suppose the force of infection at location x and time t is given by

$$c\beta(x)\frac{S_h(t,x)}{H(x)} I_m(t,x) = c\beta(x)\frac{H(x) - I_h(t,x)}{H(x)} I_m(t,x),$$

where c is the transmission probability per bite from infectious mosquitoes to susceptible humans, $\beta(x)$ is the habitat dependent biting rate of female mosquitoes, and I_m is the density of female mosquitoes. This cross-infection between hosts and vectors is modeled as mass-action mechanism normalized by host-density, see, e.g., Bowman et al. (2005) and Wonham et al. (2006). It then follows that the density of infectious human population can be described by

$$\frac{\partial I_h(t,x)}{\partial t} = D_h \Delta I_h(t,x) + \frac{c\beta(x)}{H(x)}(H(x) - I_h(t,x))I_m(t,x) - (d_h + \rho)I_h(t,x), \tag{1}$$

where d_h is the human natural death rate, and ρ is the recovery rate, i.e., $1/\rho$ is the human infectious period.

The susceptible adult mosquito population is increased via the recruitment of aquatic mosquitoes, and diminished by infection and by natural death at a rate d_m. Suppose that $\mu(x)$ denotes the habitat dependent recruitment rate at which adult female mosquitoes emerge from larval. As in Hancock et al. (2009) and Smith et al. (2004), here we assume that the emergence of adults is not explicitly linked to the density of adult mosquitoes. Moreover, the force of infection for mosquito population is

$$\frac{b\beta(x)}{H(x)} S_m(t,x) I_h(t,x),$$

where b is the transmission probability per bite from infectious humans to susceptible mosquitoes. Thus, the dynamics of susceptible adult mosquitoes can be described by

$$\frac{\partial S_m(t,x)}{\partial t} = D_m \Delta S_m(t,x) + \mu(x) - \frac{b\beta(x)}{H(x)} S_m(t,x) I_h(t,x) - d_m S_m(t,x). \tag{2}$$

To incorporate an extrinsic incubation period (EIP) into Ross's model (Ross 1911), the infected mosquito population is divided into two epidemiological categories: latent (E_m) and infectious (I_m) classes. Since these latent mosquitoes can fly around during the incubation period, we should carefully formulate this process. To achieve this, we introduce an infection age variable a and let $y(t,a,x)$ be the density of the mosquito population with infection age a at time t and habitat x. Using the standard method on describing age structured population with spatial diffusion (see, e.g., Gourley and Wu 2006 and references therein), we get

$$\frac{\partial y(t,a,x)}{\partial t} + \frac{\partial y(t,a,x)}{\partial a} = D_m \Delta y(t,a,x) - d_m y(t,a,x), \tag{3}$$

where D_m is the mosquito diffusion coefficient and d_m is the mosquito death rate. Suppose that τ is the average incubation period, we then have

$$E_m(t,x) = \int_0^\tau y(t,a,x) da,$$

and

$$I_m(t,x) = \int_\tau^\infty y(t,a,x) da.$$

Integrating both sides of Eq. (3) from 0 to τ, and from τ to ∞, we obtain

$$\frac{\partial E_m(t,x)}{\partial t} = D_m \Delta E_m(t,x) - d_m E_m(t,x) - y(t,\tau,x) + y(t,0,x),$$

and

$$\frac{\partial I_m(t,x)}{\partial t} = D_m \Delta I_m(t,x) - d_m I_m(t,x) - y(t,\infty,x) + y(t,\tau,x),$$

respectively. Biologically, we assume that $y(t,\infty,x) = 0$. Since the recruitment of newly infected mosquitoes ($y(t,0,x)$) is due to the contact of susceptible mosquitoes and infectious humans, it follows that

$$y(t,0,x) = \frac{b\beta(x)}{H(x)} S_m(t,x) I_h(t,x).$$

It is then necessary to determine $y(t,\tau,x)$, which can be done by the integration along characteristics. Let $v(r,a,x) = y(a+r,a,x)$, with $r \geq 0$. Then we have

$$\begin{cases} \frac{\partial v(r,a,x)}{\partial a} &= \left[\frac{\partial y(t,a,x)}{\partial t} + \frac{\partial y(t,a,x)}{\partial a}\right]_{t=a+r} \\ &= D_m \Delta y(a+r,a,x) - d_m y(a+r,a,x) \\ &= D_m \Delta v(r,a,x) - d_m v(r,a,x), \\ v(r,0,x) &= \frac{b\beta(x)}{H(x)} S_m(r,x) I_h(r,x). \end{cases}$$

Regarding r as a parameter and integrating the last equation, we obtain

$$v(r,a,x) = e^{-d_m a} \int_\Omega \Gamma(D_m a, x, y) \frac{b\beta(y)}{H(y)} S_m(r,y) I_h(r,y) dy,$$

where Γ is the Green function associated with Δ and the Neumann boundary condition. Since $y(t,\tau,x) = v(t-\tau,\tau,x)$, $\forall t \geq \tau$, we can derive the formula for $y(t,\tau,x)$:

$$y(t,\tau,x) = e^{-d_m \tau} \int_\Omega \Gamma(D_m \tau, x, y) \frac{b\beta(y)}{H(y)} S_m(t-\tau,y) I_h(t-\tau,y) dy, \quad \forall t \geq \tau.$$

It then follows that

$$\begin{aligned} \frac{\partial E_m(t,x)}{\partial t} &= D_m \Delta E_m(t,x) - d_m E_m(t,x) + \frac{b\beta(x)}{H(x)} S_m(t,x) I_h(t,x) \\ &\quad - e^{-d_m \tau} \int_\Omega \Gamma(D_m \tau, x, y) \frac{b\beta(y)}{H(y)} S_m(t-\tau,y) I_h(t-\tau,y) dy, \quad t \geq \tau, \end{aligned} \tag{4}$$

and

$$\frac{\partial I_m(t,x)}{\partial t} = D_m \Delta I_m(t,x) - d_m I_m(t,x) + e^{-d_m\tau}\int_\Omega \Gamma(D_m\tau, x, y)\frac{b\beta(y)}{H(y)} S_m(t-\tau,y) I_h(t-\tau,y)dy, \quad t \geq \tau. \tag{5}$$

Consequently, we have a full model (1), (2), (4) and (5) subject to the Neumann boundary condition. Since system (1), (2), (4) and (5) is an autonomous system, we may assume that the starting time is 0 and the initial data is in $C([-\tau, 0], \mathbb{R}^4_+)$. Note that E_m can be determined if I_h, S_m, and I_m are known. It then suffices to study the following nonlocal and time-delayed reaction–diffusion system

$$\begin{aligned}
\frac{\partial u_1(t,x)}{\partial t} &= D_h \Delta u_1(t,x) + \frac{c\beta(x)}{H(x)}(H(x) - u_1(t,x))u_3(t,x) - (d_h + \rho)u_1(t,x),\\
\frac{\partial u_2(t,x)}{\partial t} &= D_m \Delta u_2(t,x) + \mu(x) - \frac{b\beta(x)}{H(x)} u_2(t,x)u_1(t,x) - d_m u_2(t,x),\\
\frac{\partial u_3(t,x)}{\partial t} &= D_m \Delta u_3(t,x) - d_m u_3(t,x)\\
&\quad + e^{-d_m\tau}\int_\Omega \Gamma(D_m\tau, x, y)\frac{b\beta(y)}{H(y)} u_2(t-\tau,y) u_1(t-\tau,y)dy,\\
\frac{\partial u_i}{\partial n} &= 0, \quad \forall x \in \partial\Omega, \ t > 0, \ i = 1, 2, 3,
\end{aligned} \tag{6}$$

where $u(t,x) = (u_1(t,x), u_2(t,x), u_3(t,x))^T = (I_h(t,x), S_m(t,x), I_m(t,x))^T$.

3 Threshold dynamics

In this section, we define the basic reproduction ratio $\mathcal{R}_0$ and show that $\mathcal{R}_0$ is a threshold index to determine the disease invasion. We start with some basic properties for system (6).

Let $\mathbb{X} := C(\bar{\Omega}, \mathbb{R}^3)$ be the Banach space with the supremum norm $\|\cdot\|_{\mathbb{X}}$. For $\tau \geq 0$, define $C = C([-\tau, 0], \mathbb{X})$ with the norm $\|\phi\| = \max_{\theta\in[-\tau,0]} \|\phi(\theta)\|_{\mathbb{X}}$. Then, C is a Banach space. Define $\mathbb{X}^+ := C(\bar{\Omega}, \mathbb{R}^3_+)$ and $C^+ := C([-\tau, 0], \mathbb{X}^+)$, then both $(\mathbb{X}, \mathbb{X}^+)$ and (C, C^+) are strongly ordered spaces. Given a function $u : [-\tau, \sigma) \to \mathbb{X}$ for $\sigma > 0$, define $u_t \in C$ by $u_t(\theta) = u(t + \theta)$, $\theta \in [-\tau, 0]$. Let $\mathbb{X}_H$ and C_H be the subsets in $\mathbb{X}$ and C defined by

$$\mathbb{X}_H := \left\{\phi = (\phi_1, \phi_2, \phi_3)^T \in \mathbb{X}^+ : 0 \leq \phi_1(x) \leq H(x), \forall x \in \bar{\Omega}\right\}$$

and

$$C_H := C\left([-\tau, 0], \mathbb{X}_H\right),$$

respectively.

Let $\mathbb{Y} := C(\bar{\Omega}, \mathbb{R})$ and $\mathbb{Y}^+ := C(\bar{\Omega}, \mathbb{R}_+)$. Suppose that $T_1(t)$, $T_2(t)$: $\mathbb{Y} \to \mathbb{Y}$, $t \geq 0$, are the strongly continuous semigroups associated with $D_h\Delta - (d_h + \rho)$ and $D_m\Delta - d_m$ subject to the Neumann boundary condition, respectively. It then follows that for each $t > 0$, $T_i(t) : \mathbb{Y} \to \mathbb{Y}$, $i = 1, 2$, is compact and strongly positive (see, e.g., Smith 1995, Section 7.1 and Corollary 7.2.3). Clearly, for any $\varphi \in \mathbb{Y}$, $t \geq 0$,

$$T_1(t)\varphi(x) = e^{-(d_h+\rho)t} \int_\Omega \Gamma(D_h t, x, y)\varphi(y)dy,$$

and

$$T_2(t)\varphi(x) = e^{-d_m t} \int_\Omega \Gamma(D_m t, x, y)\varphi(y)dy.$$

Moreover, $T(t) = (T_1(t), T_2(t), T_2(t))$: $\mathbb{X} \to \mathbb{X}$, $t \geq 0$, is a strongly continuous semigroup. Let $A_i : D(A_i) \to \mathbb{Y}$ be the generator of T_i, $i = 1, 2$. Then $T(t) : \mathbb{X} \to \mathbb{X}$ is a semigroup generated by the operator $A = (A_1, A_2, A_2)$ defined on $D(A) = D(A_1) \times D(A_2) \times D(A_2)$.

Define $F = (F_1, F_2, F_3) : C_H \to \mathbb{X}$ by

$$\begin{aligned} F_1(\phi)(x) &= \frac{c\beta(x)}{H(x)}(H(x) - \phi_1(0, x))\phi_3(0, x), \\ F_2(\phi)(x) &= \mu(x) - \frac{b\beta(x)}{H(x)}\phi_2(0, x)\phi_1(0, x), \\ F_3(\phi)(x) &= e^{-d_m\tau} \int_\Omega \Gamma(D_m\tau, x, y)\frac{b\beta(y)}{H(y)}\phi_2(-\tau, y)\phi_1(-\tau, y)dy, \end{aligned} \tag{7}$$

$\forall x \in \bar{\Omega}$, $\phi = (\phi_1, \phi_2, \phi_3)^T \in C_H$. Then system (6) can be rewritten as the following abstract functional differential equation:

$$\begin{cases} \frac{du}{dt} = Au + F(u_t), \quad t > 0, \\ u_0 = \phi \in C_H. \end{cases} \tag{8}$$

Let $\bar{\beta} = \max_{x\in\bar{\Omega}} \beta(x)$ and $\tilde{H} = \min_{x\in\bar{\Omega}} H(x)$. For any $\phi \in C_H$ and $k \geq 0$, we then have

$$\begin{aligned}
&\phi(0,x)+kF(\phi)(x)\\
&=\begin{pmatrix}
\phi_1(0,x)+k\frac{c\beta(x)}{H(x)}(H(x)-\phi_1(0,x))\phi_3(0,x)\\
\phi_2(0,x)+k(\mu-\frac{b\beta(x)}{H(x)}\phi_2(0,x)\phi_1(0,x))\\
\phi_3(0,x)+k(e^{-d_m\tau}\int_\Omega \Gamma(D_m\tau,x,y)\frac{b\beta(y)}{H(y)}\phi_2(-\tau,y)\phi_1(-\tau,y)dy)
\end{pmatrix}\\
&\geq\begin{pmatrix}
\phi_1(0,x)[1-k\frac{c\bar\beta}{\tilde H}\phi_3(0,x)]\\
\phi_2(0,x)[1-k\frac{b\bar\beta}{\tilde H}\phi_1(0,x)]\\
\phi_3(0,x)
\end{pmatrix},
\end{aligned}$$

and

$$H(x)-(\phi_1(0,x)+kF_1(\phi)(x))=(H(x)-\phi_1(0,x))\left[1-k\frac{c\beta(x)}{H(x)}\phi_3(0,x)\right].$$

This implies that

$$\lim_{k\to 0^+}\frac{1}{k}dist(\phi(0)+kF(\phi),\mathbb{X}_H)=0,\ \forall\phi\in C_H.$$

It then follows from Martin and Smith (1990, Corollary 4) (see also Wu 1996, Corollary 8.1.3) that for each $\phi\in C_H$, there exists a unique non-continuable mild solution $u(t,\phi)$ on $(0,\sigma_\phi)$ with $u_0=\phi$. Moreover, $u(t,\phi)\in\mathbb{X}_H$ for all $t\in(0,\sigma_\phi)$ and $u(t,\phi)$ is a classical solution of (6) for $t>\tau$.

For the scalar reaction–diffusion equation

$$\begin{aligned}
\frac{\partial w(t,x)}{\partial t}&=D\Delta w(t,x)+g(x)-dw(t,x),\quad t>0,\ x\in\Omega,\\
\frac{\partial w}{\partial n}&=0,\quad x\in\partial\Omega,
\end{aligned}\tag{9}$$

where $D>0$, $d>0$, and $g(x)$ is a continuous and positive function on $\bar\Omega$, we have the following observation.

Lemma 1 *Equation (9) admits a unique positive steady state w^* which is globally attractive in $\mathbb{Y}$. Moreover, if $g(x)\equiv g$, $\forall x\in\bar\Omega$, then $w^*=\frac{g}{d}$.*

Proof Denote $\tilde g=\min_{x\in\bar\Omega}g(x)$ and $\bar g=\max_{x\in\bar\Omega}g(x)$. It is easy to see that for any $\psi\in C(\bar\Omega,\mathbb{R}_+)$, (9) has a unique solution $w(t,\psi)$ on $[0,\infty)$ with $w(0,\psi)=\psi$. Let $P(t)$ be the solution semiflow associated with (9), that is, $P(t)\psi=w(t,\psi)$. By the standard comparison arguments, it then follows that for any $\psi\in\mathbb{Y}$, the omega limit set $\omega(\psi)$ satisfies

$$\omega(\psi)\subset\left\{\varphi:\frac{\tilde g}{d}\leq\varphi\leq\frac{\bar g}{d}\right\}.$$

Again, by the comparison principle, we have $P(t)\varphi \gg P(t)\psi$, $\forall t > 0$, whenever $\varphi > \psi$. Note that $f(x, w) := g(x) - dw$ is strictly subhomogeneous in the sense that $f(x, \alpha w) > \alpha f(x, w)$ for any $\alpha \in (0, 1)$ and $w \gg 0$. By a similar argument as in (Freedman and Zhao, 1997, Theorem 2.2), we see that $P(t)\psi$ is strictly subhomogeneous, i.e., $P(t)\alpha\psi > \alpha P(t)\psi$ for any $\alpha \in (0, 1)$ and $\psi \gg 0$. It then follows from (Zhao, 2003, Theorem 2.3.1) that $P(t)$ has a positive equilibrium $w^*(x)$ such that $\omega(\psi) = w^* \in \mathbb{Y}, \forall \psi \in \mathbb{Y}$. In particular, if $g(x) \equiv g, \forall x \in \bar{\Omega}$, then $w^* = \frac{g}{d}$.

The following result shows that solutions of system (6) exist globally on $[0, \infty)$ and converge to a compact attractor in C_H.

Theorem 1 *For any $\phi \in C_H$, system (6) has a unique solution $u(t, \phi)$ on $[0, \infty)$, and the solution semiflow $\Phi(t) = u_t(\cdot) : C_H \to C_H$, $t \geq 0$, has a global compact attractor.*

Proof Let $\bar{\mu} = \max_{x\in\bar{\Omega}} \mu(x)$. By Lemma 1, $\frac{\bar{\mu}}{d_m}$ is globally attractive in $\mathbb{Y}$ for the scalar parabolic equation

$$\begin{aligned} \frac{\partial w(t, x)}{\partial t} &= D_m \Delta w(t, x) + \bar{\mu} - d_m w(t, x), \quad x \in \Omega, \ t > 0, \\ \frac{\partial w}{\partial n} &= 0, \quad x \in \partial\Omega, \ t > 0. \end{aligned} \tag{10}$$

Since the second equation of system (6) is dominated by Eq. (10), the standard parabolic comparison theorem (see, e.g., Smith 1995, Theorem 7.3.4) implies that $u_2(t, \phi)$ is bounded on $[0, \sigma_\phi)$. Thus, there exists a positive number Q such that the third equation of system (6) is dominated by the equation

$$\begin{aligned} \frac{\partial w(t, x)}{\partial t} &= D_m \Delta w(t, x) - d_m w(t, x) + Q, \quad x \in \Omega, \ t > 0, \\ \frac{\partial w}{\partial n} &= 0, \quad x \in \partial\Omega, \ t > 0. \end{aligned} \tag{11}$$

Again, from Lemma 1 and the comparison principle, $u_3(t, \phi)$ is bounded on $[0, \sigma_\phi)$. It then follows that $u(t, \phi) = (u_1(t, \phi), u_2(t, \phi), u_3(t, \phi))^T$ is bounded on $[0, \sigma_\phi)$, and hence $\sigma_\phi = +\infty$ for each $\phi \in C_H$. Therefore, system (6) defines a semiflow $\Phi(t)$: $C_H \to C_H$ by

$$(\Phi(t)\phi)(\theta, x) = u(t + \theta, x, \phi), \quad \forall \theta \in [-\tau, 0], \ x \in \bar{\Omega}.$$

For any fixed $\phi \in C_H$, we have some $t_1(\phi)$ such that $u_2(t, \phi) \leq 2\frac{\bar{\mu}}{d_m}$ when $t > t_1$, and

$$\begin{aligned} \frac{\partial u_3(t, x)}{\partial t} &\leq D_m \Delta w(t, x) - d_m w(t, x) + 2e^{-d_m\tau} \frac{\bar{\mu}}{d_m} b\bar{\beta}, \quad x \in \Omega, \ t > t_1, \\ \frac{\partial u_3}{\partial n} &= 0, \quad x \in \partial\Omega, \ t > t_1. \end{aligned}$$

It then follows from Lemma 1 that there is a $t_2(\phi) > t_1$ such that $u_3(t,\phi) \le 4e^{-d_m\tau}\frac{\tilde{\mu}}{d_m^2}b\bar{\beta}$, $\forall t > t_2$. Therefore, the solution semiflow $\Phi(t)\colon C_H \to C_H$ is point dissipative. Moreover, $\Phi(t)\colon C_H \to C_H$ is compact for each $t > \tau$ by Wu (1996, Theorem 2.1.8). Thus, Hale (1988, Theorem 3.4.8) implies that $\Phi(t)\colon C_H \to C_H$, $t \ge 0$, has a global compact attractor.

The following result is a consequence of the comparison principle for scalar parabolic equations.

Lemma 2 *Let $u(t,x,\phi)$ be the solution of system (6) with $u_0 = \phi \in C_H$. If there exists some $t_0 \ge 0$ such that $u_i(t_0,\cdot,\phi) \not\equiv 0$, for some $i \in \{1,3\}$, then $u_i(t,x,\phi) > 0$, $\forall t > t_0$, $x \in \bar{\Omega}$. Moreover, for any $\phi \in C_H$, we have $u_2(t,x,\phi) > 0$, $\forall t > 0$, $x \in \bar{\Omega}$ and $\liminf_{t\to\infty} u_2(t,x) \ge \frac{\tilde{\mu}}{d_m + b\bar{\beta}}$ uniformly for $x \in \bar{\Omega}$, where $\bar{\beta} = \max_{x\in\bar{\Omega}}\beta(x)$ and $\tilde{\mu} = \min_{x\in\bar{\Omega}}\mu(x)$.*

Proof It is easy to see that $u_1(t,x,\phi)$ and $u_3(t,x,\phi)$ satisfy

$$\begin{aligned}
\frac{\partial u_1(t,x)}{\partial t} &\ge D_m\Delta u_1(t,x) - (d_h+\rho)u_1(t,x),\\
\frac{\partial u_3(t,x)}{\partial t} &\ge D_m\Delta u_3(t,x) - d_m u_3(t,x),\\
\frac{\partial u_1}{\partial n} &= \frac{\partial u_3}{\partial n} = 0, \quad x \in \partial\Omega.
\end{aligned}$$

If $u_i(t_0,\cdot,\phi) \not\equiv 0$ for some $t_0 \ge 0$, $i \in \{1,3\}$, it then follows from the comparison principle that $u_i(t,x,\phi) > 0$ for all $t > t_0$, $x \in \bar{\Omega}$.

Let $v(t,x,\phi)$ be the solution of

$$\begin{aligned}
\frac{\partial v(t,x)}{\partial t} &= D_m\Delta v(t,x) + \tilde{\mu} - (b\bar{\beta}+d_m)v(t,x),\\
\frac{\partial v}{\partial n} &= 0, \quad x \in \partial\Omega,\\
v(0,x) &= \phi(0,x).
\end{aligned}$$

Then we have $u_2(t,x,\phi) \ge v(t,x,\phi) > 0, \forall t > 0, x \in \bar{\Omega}$. Furthermore, by Lemma 1 and the comparison principle, $\liminf_{t\to\infty} u_2(t,x,\phi) \ge \frac{\tilde{\mu}}{b\bar{\beta}+d_m}$ uniformly for $x \in \bar{\Omega}$.

In order to define the basic reproduction ratio, we should first find the disease-free equilibrium (infection-free steady state). By letting the densities of the diseased compartments (u_1 and u_3) be zero, we get the following equation for the density of susceptible mosquitoes,

$$\begin{aligned}
\frac{\partial w(t,x)}{\partial t} &= D_m\Delta w(t,x) + \mu(x) - d_m w(t,x), \quad t > 0, \quad x \in \Omega,\\
\frac{\partial w}{\partial n} &= 0, \quad x \in \partial\Omega.
\end{aligned} \tag{12}$$

By Lemma 1, it is easy to see that Eq. (12) has a positive steady state m^*, which is globally asymptotically stable. Linearizing system (6) at the disease-free equilibrium $(0, m^*, 0)^T$, we get the following time-delayed nonlocal and cooperative system for the infectious compartments:

$$\begin{aligned}
\frac{\partial w_1}{\partial t} &= D_h \Delta w_1(t,x) + c\frac{\beta(x)}{H(x)} h(x) w_2(t,x) - (d_h+\rho) w_1(t,x),\\
\frac{\partial w_2}{\partial t} &= D_m \Delta w_2(t,x) - d_m w_2(t,x)\\
&\quad + e^{-d_m \tau} \int_\Omega \Gamma(D_m \tau, x, y) \frac{b\beta(y)}{H(y)} m(y) w_1(t-\tau, y) dy,\\
\frac{\partial w_1}{\partial n} &= \frac{\partial w_2}{\partial n} = 0, \quad \forall x \in \partial\Omega,
\end{aligned} \tag{13}$$

with $h(x) = H(x)$ and $m(x) = m^*(x)$.

Before defining the basic reproduction ratio, we need to study the following linear nonlocal and cooperative system

$$\begin{aligned}
\frac{\partial w_1}{\partial t} &= D_h \Delta w_1(t,x) + \frac{c\beta(x)}{H(x)} h(x) w_2(t,x) - (d_h+\rho) w_1(t,x),\\
\frac{\partial w_2}{\partial t} &= D_m \Delta w_2(t,x) - d_m w_2(t,x)\\
&\quad + e^{-d_m \tau} \int_\Omega \Gamma(D_m \tau, x, y) \frac{b\beta(y)}{H(y)} m(y) w_1(t, y) dy,\\
\frac{\partial w_1}{\partial n} &= \frac{\partial w_2}{\partial n} = 0, \quad \forall x \in \partial\Omega,
\end{aligned} \tag{14}$$

with $h(x) > 0, m(x) > 0, \forall x \in \bar{\Omega}$.

Substituting $w_1(t,x) = e^{\lambda t}\psi_1(x)$ and $w_2(t,x) = e^{\lambda t}\psi_2(x)$ into (14), we obtain the following nonlocal eigenvalue problem

$$\begin{aligned}
\lambda\psi_1(x) &= D_h \Delta \psi_1(x) + \frac{c\beta(x)}{H(x)} h(x) \psi_2(x) - (d_h+\rho)\psi_1(x), \quad x \in \Omega,\\
\lambda\psi_2(x) &= D_m \Delta \psi_2(x) - d_m \psi_2(x)\\
&\quad + e^{-d_m \tau} \int_\Omega \Gamma(D_m \tau, x, y) \frac{b\beta(y)}{H(y)} m(y) \psi_1(y) dy, \quad x \in \Omega,\\
\frac{\partial \psi_1}{\partial n} &= \frac{\partial \psi_2}{\partial n} = 0, \quad x \in \partial\Omega.
\end{aligned} \tag{15}$$

By a similar argument as in Smith (1995, Theorem 7.6.1), it follows that (15) has a principal eigenvalue $\lambda(h, m)$ with a positive eigenfunction.

Define $\mathbb{E} := C([-\tau, 0], \mathbb{Y}) \times \mathbb{Y}$ and $\mathbb{E}^+ := C([-\tau, 0], \mathbb{Y}^+) \times \mathbb{Y}^+$. For any $\psi \in \mathbb{E}^+ \backslash \{0\}$, let $w(t, \psi)$, $t \geq 0$, be the solution of the system (13). We claim

that $w_i(t,\psi)(x) > 0$ for all $x \in \bar{\Omega}$ and $t > \tau$, $i = 1, 2$. Indeed, if $\psi_1(0,\cdot) \not\equiv 0$ or $\psi_2 \not\equiv 0$, then the parabolic maximum principle implies that $w_1(t,\psi)(x) > 0$ and $w_2(t,\psi)(x) > 0$ for all $x \in \partial\bar{\Omega}$, $t > \tau$. If there is a $\theta_0 \in (0,\tau)$ such that $\psi_1(-\theta_0,\cdot) \not\equiv 0$, then we can show that $w_2(\tau-\theta_0,\psi) \not\equiv 0$ as follows. Suppose, by contradiction, that $w_2(\tau-\theta_0,\psi) \equiv 0$, then

$$\frac{\partial w_2(\tau-\theta_0,x)}{\partial t} = e^{-d_m\tau}\int_\Omega \Gamma(D_m\tau,x,y)\frac{b\beta(y)}{H(y)}m(y)\psi_1(-\theta_0,y)dy > 0, \quad \forall x \in \Omega.$$

Since $w_2(t,\psi) \geq 0, t \geq 0$, and $w_2(\tau-\theta_0,\psi)(x) = 0, \forall x \in \bar{\Omega}$, then $\frac{\partial w_2(\tau-\theta_0,x)}{\partial t} \leq 0$, which is a contradiction. Thus, we have $w_2(t,\psi)(x) > 0, \forall t > \tau-\theta_0, x \in \bar{\Omega}$. It then follows that $w_1(t,\psi)(x) > 0, \forall t > \tau-\theta_0, x \in \bar{\Omega}$.

By similar arguments as in Thieme and Zhao (2001, Theorem 2.2), we have the following result on the nonlocal eigenvalue problem corresponding to (13):

$$\begin{aligned}
\lambda\psi_1(x) &= D_h\Delta\psi_1(x) + \frac{c\beta(x)}{H(x)}h(x)\psi_2(x) - (d_h+\rho)\psi_1(x), \quad x \in \Omega,\\
\lambda\psi_2(x) &= D_m\Delta\psi_2(x) - d_m\psi_2(x)\\
&\quad + e^{-d_m\tau}e^{-\lambda\tau}\int_\Omega \Gamma(D_m\tau,x,y)\frac{b\beta(y)}{H(y)}m(y)\psi_1(y)dy, \quad x \in \Omega,\\
\frac{\partial\psi_1}{\partial n} &= \frac{\partial\psi_2}{\partial n} = 0, \quad x \in \partial\Omega.
\end{aligned} \tag{16}$$

Lemma 3 *There exists a principal eigenvalue $\bar{\lambda}(h,m,\tau)$ of (16) associated with a strongly positive eigenvector, and for any $\tau \geq 0$, $\bar{\lambda}(h,m,\tau)$ has the same sign as $\lambda(h,m)$.*

Next, we use the same idea as in Wang and Zhao (2009) to define the basic reproduction ratio for system (6). Assume that both human and mosquito populations are near the disease free equilibrium $(0,m^*,0)^T$. Let $(\psi_1(x),\psi_2(x))^T$ be the spatial distribution of initial infective humans and mosquitoes, and assume that the temporal distribution of this initial data is homogeneous. From system (14), with $h(x) = H(x)$, $m(x) = m^*(x)$, we then see that $S(t)\psi := (T_1(t)\psi_1, T_2(t)\psi_2)^T$ represents the remaining distribution of infective humans and mosquitoes at time $t > 0$. Let V be the positive linear operator on $\mathbb{Y}\times\mathbb{Y}$ defined by

$$V(\psi)(x) = (V_1(\psi)(x), V_2(\psi)(x)), \quad \forall\psi \in \mathbb{Y}\times\mathbb{Y}, \quad x \in \bar{\Omega},$$

where

$$V_1(\psi)(x) = c\beta(x)\psi_2(x),$$

and

$$V_2(\psi)(x) = e^{-d_m\tau}\int_\Omega \Gamma(D_m\tau, x, y)m^*(y)\frac{b\beta(y)}{H(y)}\psi_1(y)dy.$$

Then, $V(S(t)\psi)$ is the distribution of newly infected humans and mosquitoes at time t. It follows that

$$L(\psi) := \int_0^\infty V(S(t)\psi)dt = V\left(\int_0^\infty S(t)\psi dt\right)$$

represents the distribution of the total infective humans and mosquitoes produced during the infection period, and hence, L is the next infection operator. We define the spectral radius of L as the basic reproduction ratio, that is,

$$\mathcal{R}_0 := r(L)$$

for model (6).

By the general results in Thieme (2009) and the same arguments as in Wang and Zhao (2009, Lemma 2.2), we have the following observation.

Lemma 4 *$\mathcal{R}_0 - 1$ has the same sign as $\lambda(H, m^*)$.*

By this lemma, combined with Lemma 3, we see that $\mathcal{R}_0$ is a threshold parameter for the stability of the the zero solution for system (13) with $h(x) = H(x)$ and $m(x) = m^*(x)$.

Now we are in position to prove the main result of this section, which indicates that $\mathcal{R}_0$ is also a threshold index for disease persistence.

Theorem 2 *Let $u(t, x, \phi)$ be the solution of (6) with $u_0 = \phi \in C_H$. Then the following two statements are valid*:

(i) *If $\mathcal{R}_0 < 1$, then the disease free equilibrium $(0, m^*, 0)^T$ is globally attractive.*
(ii) *If $\mathcal{R}_0 > 1$, then system (6) admits at least one positive steady state $u^*(x)$, and there exists an $\eta > 0$ such that for any $\phi \in C_H$ with $\phi_i(0, \cdot) \not\equiv 0$ for $i = 1, 3$, we have*

$$\liminf_{t\to\infty} u_i(t, x) \geq \eta, \quad \forall i = 1, 2, 3,$$

uniformly for all $x \in \bar{\Omega}$.

Proof **(i)** In the case where $\mathcal{R}_0 < 1$, we have $\lambda(H, m^*) < 0$. Since

$$\lim_{\epsilon\to 0} \lambda(H, m^* + \epsilon) = \lambda(H, m^*) < 0,$$

there is an $\epsilon_0 > 0$ such that $\lambda(H, m^* + \epsilon_0) < 0$. For fixed $\epsilon_0 > 0$, by Lemma 1, there exists $t_0 = t_0(\phi)$ such that $u_2(t, x) \le m^*(x) + \epsilon_0$, $\forall t \ge t_0$, $x \in \bar{\Omega}$. Therefore, for all $t \ge t_0$, we have

$$\begin{cases} \frac{\partial u_1(t,x)}{\partial t} \le D_h \Delta u_1(t,x) + c\beta(x) u_3(t,x) - (d_h + \rho) u_1(t,x), \\ \frac{\partial u_3(t,x)}{\partial t} \le D_m \Delta u_3(t,x) - d_m u_3(t,x) \\ \qquad\qquad + e^{-d_m \tau} \int_\Omega \Gamma(D_m \tau, x, y) \frac{b\beta(y)}{H(y)} (m^*(y) + \epsilon_0) u_1(t-\tau, y) dy. \end{cases} \tag{17}$$

By Lemma 3, $\bar{\lambda}(H, m^* + \epsilon_0, \tau) < 0$ and there is a strongly positive eigenfunction ψ_0 corresponding to $\bar{\lambda}(H, m^* + \epsilon_0, \tau)$. It then follows that the linear system

$$\begin{aligned} \frac{\partial v_1(t,x)}{\partial t} &= D_h \Delta v_1 + c\beta(x) v_2 - (d_h + \rho) v_1, \quad t > 0, \ x \in \Omega, \\ \frac{\partial v_2(t,x)}{\partial t} &= D_m \Delta v_2 + e^{-d_m \tau} \int_\Omega \Gamma(D_m \tau, x, y) \frac{b\beta(y)}{H(y)} (m^*(y) + \epsilon_0) v_1(t-\tau, y) dy \\ &\quad - d_m v_2, \quad t > 0, \quad x \in \Omega, \\ \frac{\partial v_1}{\partial n} &= \frac{\partial v_2}{\partial n} = 0, \quad x \in \partial\Omega, \end{aligned}$$

admits a solution $v(t, x) = e^{\bar{\lambda}(H, m^* + \epsilon_0, \tau) t} \psi_0(x)$. Since for any given $\phi \in C_H$, there exists some $\alpha > 0$ such that $(u_1(t, \cdot, \phi), u_3(t, \cdot, \phi))^T \le \alpha v(t, \cdot)$, $\forall t \in [t_0 - \tau, t_0]$. By the comparison principle, it follows that

$$(u_1(t, x, \phi), u_3(t, x, \phi))^T \le \alpha e^{\bar{\lambda}(H, m^* + \epsilon_0, \tau) t} \psi_0(x), \quad \forall t \ge t_0.$$

Thus, $\lim_{t \to \infty} (u_1(t, x, \phi), u_3(t, x, \phi))^T = 0$ uniformly for $x \in \bar{\Omega}$. Then, the equation for u_2 is asymptotic to the following reaction–diffusion equation

$$\begin{cases} \frac{\partial w(t,x)}{\partial t} = D_m \Delta w(t,x) + \mu(x) - d_m w(t,x), \\ \frac{w(t,x)}{\partial n} = 0. \end{cases} \tag{18}$$

By the theory for asymptotically autonomous semiflows (see Thieme 1992, Corollary 4.3), we have

$$\lim_{t \to \infty} u_2(t, x, \phi) = m^*(x)$$

uniformly for $x \in \bar{\Omega}$.

(ii) In the case where $\mathcal{R}_0 > 1$, we have $\lambda(H, m^*) > 0$. It then follows from Lemma 3 that $\bar{\lambda}(H, m^*, \tau) > 0$. Let

$$\mathbb{W}_0 = \{\phi \in C_H : \phi_1(0, \cdot) \not\equiv 0 \text{ and } \phi_3(0, \cdot) \not\equiv 0\},$$

and

$$\partial \mathbb{W}_0 := C_H \backslash \mathbb{W}_0 = \{\phi \in C_H : \phi_1(0,\cdot) \equiv 0 \text{ or } \phi_3(0,\cdot) \equiv 0\}.$$

Note that for any $\phi \in \mathbb{W}_0$, Lemma 2 implies that $u_i(t,x,\phi) > 0$, $i = 1, 3$, $\forall x \in \bar{\Omega}$, $t > 0$, that is, $\Phi(t)\mathbb{W}_0 \subset \mathbb{W}_0$. Define

$$M_\partial := \{\phi \in \partial \mathbb{W}_0 : \Phi(t)\phi \in \partial \mathbb{W}_0,\ t \geq 0\}.$$

Let $\omega(\phi)$ be the omega limit set of the orbit $\gamma^+(\phi) := \{\Phi(t)\phi : \forall t \geq 0\}$, and set $M = (0, m^*, 0)^T$. For any given $\psi \in M_\partial$, we have $\Phi(t)\psi \in \partial \mathbb{W}_0$, $\forall t \geq 0$. It then follows that for each $t \geq 0$, either $u_1(t,\cdot,\psi) \equiv 0$ or $u_3(t,\cdot,\psi) \equiv 0$. In the case where $u_1(t,\cdot,\psi) \equiv 0$ for all $t \geq 0$, we see from Lemma 1 that $\lim_{t\to\infty} u_2(t,x,\psi) = m^*(x)$ uniformly for $x \in \bar{\Omega}$. In view of the u_3 equation in (6), we see that $\lim_{t\to\infty} u_3(t,x,\psi) = 0$ uniformly for $x \in \bar{\Omega}$. In the case where $u_1(t_0,\cdot,\psi) \not\equiv 0$ for some $t_0 \geq 0$, Lemma 2 implies that $u_1(t,x,\psi) > 0$, $\forall t > t_0$, $x \in \bar{\Omega}$. Thus, we have $u_3(t,\cdot,\psi) \equiv 0$, $\forall t \geq t_0$. In view of the u_1 equation in (6), we see that $\lim_{t\to\infty} u_1(t,x,\psi) = 0$ uniformly for $x \in \bar{\Omega}$. By the u_2 equation and the theory of asymptotically autonomous semiflows (see Thieme 1992, Corollary 4.3), it then follows that $\lim_{t\to\infty} u_2(t,x,\psi) = m^*(x)$ uniformly for $x \in \bar{\Omega}$. Thus, we have $\omega(\psi) = \{M\}$, $\forall \psi \in M_\partial$.

Since $\bar{\lambda}(H, m^*, \tau) > 0$, there exists a sufficiently small positive number δ_0 such that $\bar{\lambda}(H - \delta_0, m^* - \delta_0, \tau) > 0$. We now prove the following claim.

Claim M is a uniform weak repeller for $\mathbb{W}_0$ in the sense that

$$\limsup_{t\to\infty} \|\Phi(t)(\phi) - M\| \geq \delta_0 \quad \text{for all } \phi \in \mathbb{W}_0.$$

Suppose, by contradiction, that $\limsup_{t\to\infty} \|\Phi(t)(\phi_0) - M\| < \delta_0$ for some $\phi_0 \in \mathbb{W}_0$. Then, there exists $t_1 > 0$ such that $u_1(t,x,\phi_0) < \delta_0$ and $u_2(t,x,\phi_0) > m^*(x) - \delta_0$, $\forall t \geq t_1$, $x \in \bar{\Omega}$. Hence, $u(t,x,\phi_0)$ satisfies

$$\begin{aligned}
\frac{\partial u_1(t,x)}{\partial t} &\geq D_h \Delta u_1(t,x) + \frac{c\beta(x)}{H(x)}(H(x) - \delta_0)u_3(t,x) - (d_h + \rho)u_1(t,x),\\
\frac{\partial u_3(t,x)}{\partial t} &\geq D_m \Delta u_3(t,x) - d_m u_3(t,x)\\
&\quad + e^{-d_m\tau}\int_\Omega \Gamma(D_m\tau, x, y)\frac{b\beta(y)}{H(y)}(m^*(y) - \delta_0)u_1(t-\tau,y)dy,
\end{aligned} \tag{19}$$

for all $t > t_1$, $x \in \Omega$. Let φ_0 be the positive eigenfunction associated with $\bar{\lambda}(H - \delta_0, m^* - \delta_0, \tau)$. Then the linear system

$$\begin{aligned}
\frac{\partial v_1(t,x)}{\partial t} &= D_h \Delta v_1 + \frac{c\beta(x)}{H(x)}(H(x) - \delta_0)v_2 - (d_h + \rho)v_1,\\
\frac{\partial v_2(t,x)}{\partial t} &= D_m \Delta v_2 - d_m v_2\\
&\quad + e^{-d_m \tau} \int_\Omega \Gamma(D_m \tau, x, y) \frac{b\beta(y)}{H(y)}(m^*(y) - \delta_0)v_1(t - \tau, y)dy,\\
\frac{\partial v_1}{\partial n} &= \frac{\partial v_2}{\partial n} = 0, \quad x \in \partial\Omega.
\end{aligned}$$

admits a solution $v(t,x) = e^{\bar{\lambda}(H-\delta_0, m^*-\delta_0, \tau)t}\varphi_0(x)$. Since $u(t, x, \phi_0) \gg 0$ for all $t > 0$ and $x \in \bar{\Omega}$, there exists $\xi > 0$ such that $(u_1(t_1, x, \phi_0), u_3(t_1, x, \phi_0))^T \geq \xi v(t,x)$, $\forall t \in [t_1 - \tau, t_1]$, $x \in \bar{\Omega}$. According to (19) and the comparison principle, we have

$$(u_1(t,x,\phi_0), u_3(t,x,\phi_0))^T \geq \xi e^{\bar{\lambda}(H-\delta_0, m^*-\delta_0, \tau)t}\varphi_0(x), \quad \forall t > t_1, \quad x \in \bar{\Omega}.$$

Since $\bar{\lambda}(H - \delta_0, m^* - \delta_0, \tau) > 0$, it follows that $u(t, x, \phi_0)$ is unbounded, a contradiction. This proves the claim.

Define a continuous function $p : C_H \to \mathbb{R}_+$ by

$$p(\phi) = \min\left\{\min_{x\in\bar{\Omega}} \phi_1(0,x), \min_{x\in\bar{\Omega}} \phi_3(0,x)\right\}, \quad \forall \phi \in C_H.$$

Clearly, $p^{-1}(0,\infty) \subset \mathbb{W}_0$. By Lemma 2, it then follows that p has the property that if $p(\phi) = 0$ and $\phi \in \mathbb{W}_0$ or $p(\phi) > 0$, then $p(\Phi(t)\phi) > 0$ for all $t > 0$. Thus, p is a generalized distance function for the semiflow $\Phi(t) : C_H \to C_H$ (see Smith and Zhao 2001). Note that any forward orbit of $\Phi(t)$ in M_∂ converges to M. Moreover, the claim above implies that M is isolated in C_H and $W^s(M) \cap \mathbb{W}_0 = \emptyset$, where $W^s(M)$ is the stable set of M. Further, there is no cycle in M_∂ from M to M. It then follows from Smith and Zhao (2001, Theorem 3) that there exists an $\eta > 0$ such that $\min\{p(\psi) : \psi \in \omega(\phi)\} > \eta$ for any $\phi \in \mathbb{W}_0$. Hence,

$$\liminf_{t\to\infty} u_i(t,x) \geq \eta, \quad i = 1, 3,$$

uniformly for all $x \in \bar{\Omega}$. Further, it follows from Lemma 2 that we can choose η small enough such that $\liminf_{t\to\infty} u_2(t,x) \geq \eta$ uniformly for all $x \in \bar{\Omega}$. Thus, the uniform persistence stated in the conclusion (ii) holds. By Magal and Zhao (2005, Theorem 3.7 and Remark 3.10), $\Phi(t) : \mathbb{W}_0 \to \mathbb{W}_0$ has a global attractor A_0. It then follows from Magal and Zhao (2005, Theorem 4.7) that $\Phi(t)$ has an equilibrium $u^* \in \mathbb{W}_0$. Clearly, Lemma 2 implies that $u^*(x)$ is a positive steady state of (6).

4 Global attractivity

In this section, we consider the reaction–diffusion system (6) in the case where $\beta(x)$, $H(x)$ and $\mu(x)$ are positive constants, that is,

$$\begin{aligned}
\frac{\partial u_1(t,x)}{\partial t} &= D_h \Delta u_1(t,x) + \frac{c\beta}{H}(H - u_1(t,x))u_3(t,x) - (d_h+\rho)u_1(t,x),\\
\frac{\partial u_2(t,x)}{\partial t} &= D_m \Delta u_2(t,x) + \mu - \frac{b\beta}{H}u_2(t,x)u_1(t,x) - d_m u_2(t,x),\\
\frac{\partial u_3(t,x)}{\partial t} &= D_m \Delta u_3(t,x) - d_m u_3(t,x)\\
&\quad + e^{-d_m\tau}\int_\Omega \Gamma(D_m\tau, x, y)\frac{b\beta}{H}u_2(t-\tau,y)u_1(t-\tau,y)dy,\\
\frac{\partial u_i}{\partial n} &= 0, \quad \forall t > 0, \quad x \in \partial\Omega, \quad i = 1,2,3.
\end{aligned} \tag{20}$$

By a similar argument as in Wang and Zhao (2009, Theorem 2.1), we can show that the basic reproduction ratio $\mathcal{R}_0$ equals the spectral radius of the following 2×2 matrix

$$M_0 = \begin{pmatrix} 0 & c\beta\frac{1}{d_m} \\ e^{-d_m\tau}\frac{\mu}{d_m}\frac{b\beta}{H}\frac{1}{(d_h+\rho)} & 0 \end{pmatrix},$$

and hence, we have the following formula for $\mathcal{R}_0$.

Lemma 5 *For system (20), the basic reproduction ratio*

$$\mathcal{R}_0 = \sqrt{c\beta\frac{1}{d_m}\times e^{-d_m\tau}\frac{\mu}{d_m}\frac{b\beta}{H}\frac{1}{(d_h+\rho)}}.$$

In addition to the threshold result in Theorem 2, we are able to prove the global attractivity of the positive steady state under some appropriate conditions.

Theorem 3 *Let $u(t,x,\phi)$ be the solution of (20) with $u_0 = \phi \in C_H$. Then the following three statements are valid*:

(i) *If $\mathcal{R}_0 < 1$, then the disease free equilibrium $(0, \frac{\mu}{d_m}, 0)^T$ is globally attractive.*

(ii) *If $\mathcal{R}_0 > 1$, then system (20) admits at least one positive steady state u^*, and there exists an $\eta > 0$ such that for any $\phi \in C_H$ with $\phi_i(0,\cdot) \not\equiv 0$ for $i = 1, 3$, we have $\liminf_{t\to\infty} u_i(t,x) \geq \eta$, $\forall i = 1,2,3$, uniformly for $x \in \bar{\Omega}$.*

(iii) *If $\mathcal{R}_0 > \max\{1, \sqrt{\frac{b\beta}{d_m}}\}$, then the system (20) has a unique constant steady state $u^* = (u_1^*, u_2^*, u_3^*)^T$ such that for any $\phi \in C_H$ with $\phi_1(0,\cdot) \not\equiv 0$ and $\phi_3(0,\cdot) \not\equiv 0$, $\lim_{t\to\infty} u(t,x,\phi) = u^*$ uniformly for $x \in \bar{\Omega}$.*

Proof It is easy to see from the proof of Theorem 1 that the set

$$A = \left\{ u \in C_H : u_2(\theta,x) \leq \frac{2\mu}{d_m},\ u_3(\theta,x) \leq 4e^{-d_m\tau}\frac{\mu}{d_m^2}b\beta,\ \forall\theta\in[-\tau,0],\ x\in\bar{\Omega}\right\}$$

is positively invariant for the solution semiflow $\Phi(t)$ and every forward orbit enters into A eventually. Therefore, we will study the dynamics of (20) on A. Conclusions (i) and (ii) follow directly from Theorem 2. To prove (iii), we use a fluctuation method, which was developed in Thieme and Zhao (2001) for a nonlocal, delayed and diffusive predator–prey model.

Since $\mathcal{R}_0 > 1$, there is a unique constant endemic equilibrium $u^* = (u_1^*, u_2^*, u_3^*)^T$ with

$$u_1^* = \frac{d_m^2(d_h+\rho)H^2(\mathcal{R}_0^2-1)}{b\beta(\mu c\beta e^{-d_m\tau}+(d_h+\rho)d_m H)}, \quad u_2^* = \frac{1}{b\beta+d_m}\left(\mu + \frac{H(d_h+\rho)d_m}{c\beta e^{-d_m\tau}}\right),$$
$$\text{and} \quad u_3^* = \frac{e^{-d_m\tau}}{d_m}\frac{b\beta}{H}u_1^*u_2^*.$$

For notational simplicity, we denote $\gamma = \frac{c\beta}{H}$ and $\gamma' = \frac{b\beta}{H}$. We choose a sufficiently large number $k > 0$ such that the function $ku_1 - (d_h+\rho)u_1 + \gamma(H-u_1)u_3$ is monotone increasing in u_1 for all $(u_1, u_3)^T \in [0, H] \times [0, 4e^{-d_m\tau}\frac{\mu}{d_m^2}b\beta]$. It then follows that

$$u_1(t,x) = e^{-kt}\int_\Omega \Gamma(D_h t, x, y)u_1(0,y)dy + \int_0^t e^{-ks}\int_\Omega \Gamma(D_h s, x, y)$$
$$[ku_1(t-s,y) - (d_h+\rho)u_1(t-s,y) + \gamma(H-u_1(t-s,y))u_3(t-s,y)]dyds.$$

Let

$$u_i^\infty(x) := \limsup_{t\to\infty} u_i(t,x), \quad u_{i\infty}(x) := \liminf_{t\to\infty} u_i(t,x), \quad i = 1,2,3.$$

By the uniform persistence of (20), there exists an $\eta > 0$ such that

$$u_i^\infty \geq u_{i\infty} \geq \eta, \quad \forall x \in \bar{\Omega}, \quad i = 1,2,3.$$

Using Fatou's lemma, we then get

$$u_1^\infty(x) \leq \int_0^\infty e^{-ks}\int_\Omega \Gamma(D_h s, x, y)[ku_1^\infty(y)$$
$$-(d_h+\rho)u_1^\infty(y) + \gamma(H-u_1^\infty(y))u_3^\infty(y)]dyds.$$

Let

$$\alpha_i^\infty := \sup_{x\in\bar{\Omega}} u_i^\infty(x) \quad \text{and} \quad \alpha_{i\infty} := \inf_{x\in\bar{\Omega}} u_{i\infty}(x).$$

Clearly, $\alpha_i^\infty \geq \alpha_{i\infty} \geq \eta$ and $\alpha_{1\infty} \leq \alpha_1^\infty \leq H$. Since $\int_\Omega \Gamma(D_h s, x, y)dy = 1$ for all $x \in \Omega$, $s > 0$, we have

$$\begin{aligned}\alpha_1^\infty &\leq \int_0^\infty e^{-ks}\left[k\alpha_1^\infty - (d_h+\rho)\alpha_1^\infty + \gamma(H-\alpha_1^\infty)\alpha_3^\infty\right]ds \\ &= \frac{1}{k}\left[k\alpha_1^\infty - (d_h+\rho)\alpha_1^\infty + \gamma(H-\alpha_1^\infty)\alpha_3^\infty\right],\end{aligned}$$

and hence,

$$0 \leq -(d_h+\rho)\alpha_1^\infty + \gamma(H-\alpha_1^\infty)\alpha_3^\infty. \tag{21}$$

Similarly, we have the following inequality,

$$0 \geq -(d_h+\rho)\alpha_{1\infty} + \gamma(H-\alpha_{1\infty})\alpha_{3\infty}. \tag{22}$$

Using the second and third equations of (20), with arguments similar to those above, we further obtain

$$0 \leq \mu - \gamma'\alpha_{1\infty}\alpha_2^\infty - d_m\alpha_2^\infty, \tag{23}$$
$$0 \geq \mu - \gamma'\alpha_1^\infty\alpha_{2\infty} - d_m\alpha_{2\infty}, \tag{24}$$
$$0 \leq e^{-d_m\tau}\gamma'\alpha_1^\infty\alpha_2^\infty - d_m\alpha_3^\infty, \tag{25}$$
$$0 \geq e^{-d_m\tau}\gamma'\alpha_{1\infty}\alpha_{2\infty} - d_m\alpha_{3\infty}. \tag{26}$$

Inserting (25) into (21), we have

$$0 \leq -(d_h+\rho) + \gamma(H-\alpha_1^\infty)\frac{e^{-d_m\tau}}{d_m}\gamma'\alpha_2^\infty. \tag{27}$$

Similarly, combining (26) with (22), we obtain

$$0 \geq -(d_h+\rho) + \gamma(H-\alpha_{1\infty})\frac{e^{-d_m\tau}}{d_m}\gamma'\alpha_{2\infty}. \tag{28}$$

Inserting (23) and (24) into (27) and (28), respectively, we get

$$0 \leq -(d_h+\rho) + \gamma(H-\alpha_1^\infty)\frac{e^{-d_m\tau}}{d_m}\gamma'\frac{\mu}{\gamma'\alpha_{1\infty}+d_m}, \tag{29}$$

and

$$0 \geq -(d_h+\rho) + \gamma(H-\alpha_{1\infty})\frac{e^{-d_m\tau}}{d_m}\gamma'\frac{\mu}{\gamma'\alpha_1^\infty+d_m}. \tag{30}$$

It then follows that

$$(H-\alpha_1^\infty)\gamma\gamma' e^{-d_m\tau}\mu-(\gamma'\alpha_{1\infty}+d_m)(d_h+\rho)d_m\geq 0,$$

and

$$(H-\alpha_{1\infty})\gamma\gamma' e^{-d_m\tau}\mu-(\gamma'\alpha_1^\infty+d_m)(d_h+\rho)d_m\leq 0.$$

Thus, we have

$$\gamma\gamma' e^{-d_m\tau}\mu\alpha_1^\infty+\gamma'\alpha_{1\infty}(d_h+\rho)d_m\leq\gamma\gamma' e^{-d_m\tau}\mu\alpha_{1\infty}+\gamma'\alpha_1^\infty(d_h+\rho)d_m,$$

and hence,

$$(\gamma\gamma' e^{-d_m\tau}\mu-\gamma'(d_h+\rho)d_m)(\alpha_1^\infty-\alpha_{1\infty})\leq 0.$$

Since $\mathcal{R}_0>\sqrt{\frac{b\beta}{d_m}}$, that is, $\gamma\gamma' e^{-d_m\tau}\mu-\gamma'(d_h+\rho)d_m>0$, we must have $\alpha_1^\infty=\alpha_{1\infty}$. Moreover, we see from (23)–(26) that $\alpha_2^\infty=\alpha_{2\infty}$ and $\alpha_3^\infty=\alpha_{3\infty}$. It then follows that

$$\lim_{t\to\infty}u(t,x,\phi)=(\alpha_1^\infty,\alpha_2^\infty,\alpha_3^\infty)^T,\quad\forall x\in\bar{\Omega}. \tag{31}$$

Now we prove $\lim_{t\to\infty}u(t,x,\phi)=(\alpha_1^\infty,\alpha_2^\infty,\alpha_3^\infty)^T$ uniformly for all $x\in\bar{\Omega}$. For any $\psi\in\omega(\phi)$, there exists a sequence $t_n\to\infty$ such that $\Phi(t_n)\phi\to\psi$ in C_H as $n\to\infty$, and hence,

$$\lim_{t\to\infty}u(t_n+\theta,x,\phi)=\psi(\theta,x)$$

uniformly for $(\theta,x)\in[-\tau,0]\times\bar{\Omega}$. In view of (31), we have $\psi(\theta,x)=(\alpha_1^\infty,\alpha_2^\infty,\alpha_3^\infty)^T$, $\forall\theta\in[-\tau,0]$, $x\in\bar{\Omega}$. This implies that $\omega(\phi)=(\alpha_1^\infty,\alpha_2^\infty,\alpha_3^\infty)^T$. Since $\omega(\phi)$ is invariant for $\Phi(t)$, it follows that $(\alpha_1^\infty,\alpha_2^\infty,\alpha_3^\infty)^T$ is a positive constant equilibrium of system (20), and hence, $(\alpha_1^\infty,\alpha_2^\infty,\alpha_3^\infty)^T=u^*$.

To finish this section, we remark that every solution of the time-delayed differential system

$$\begin{aligned}\frac{du_1(t)}{dt}&=\frac{c\beta}{H}(H-u_1(t))u_3(t)-(d_h+\rho)u_1(t),\\ \frac{du_2(t)}{dt}&=\mu-\frac{b\beta}{H}u_2(t)u_1(t)-d_mu_2(t),\\ \frac{du_3(t)}{dt}&=-d_mu_3(t)+e^{-d_m\tau}\frac{b\beta}{H}u_2(t-\tau)u_1(t-\tau),\end{aligned} \tag{32}$$

is a spatially homogeneous solution of the time-delayed reaction–diffusion system (20). Thus, three statements in Theorem 3 are also valid for system (32).

5 Numerical simulations

In this section, we implement numerical simulations in order to show how to derive some epidemiological insights from our analytic results.

For the sake of convenience, we concentrate on one dimensional domain Ω, which can be taken, without loss of generality, to be $(0, \pi)$. Here, we adapt some parameter values from Smith et al. (2004) by choosing the transmission probabilities $b = c = 0.5$. Moreover, we suppose that the life expectancy of adult mosquitoes and the incubation period are 10 days. Then we have $d_m = 0.1\ \text{day}^{-1}$, and $\tau = 10$ days. Further, we set $\rho = 0.01\ \text{day}^{-1}$ by assuming the average human infectious period is 100 days. As pointed out in Smith et al. (2004), these values are roughly consistent with *Anopheles gambiae*. For illustration, we choose $d_h = \frac{1}{365\times 70}\ \text{day}^{-1}$, $D_m = 1.25 \times 10^{-2}\ \text{km}^2 \cdot \text{day}^{-1}$, $D_h = 1\ \text{km}^2 \cdot \text{day}^{-1}$ and allow other coefficients vary spatially. To describe the spatial heterogeneity on domain Ω, we suppose two ends are rural areas and the middle point of Ω is the urban area. Biologically, the human population density is higher in urban area while the *anopheline* species density and the likelihood of malaria transmission are lower in urban than rural areas with transmission lowest in central urban areas Robert et al. (2003). Hence, we choose the following location-dependent parameters $\beta(x) = 0.1(1.1 + \cos(2x))$, $H(x) = 100(1.1 - \cos(2x))$ and $\mu(x) = 20(1.1 + \cos(2x))\ \text{day}^{-1}$ as an example.

To compute the basic reproduction ratio $\mathcal{R}_0$, we use the orthogonal projection method in the computation of eigenvalues for compact linear operators (see, e.g., Chatelin 1981, Section 3.1). For this set of parameters, the basic reproduction ratio can be computed numerically and $\mathcal{R}_0 = 3.0611$. If we consider system (20) by setting $\tilde{\beta}(x) \equiv 0.3$, $\tilde{H}(x) \equiv 100$ and $\tilde{\mu}(x) \equiv 20$, then Lemma 5 implies $\tilde{\mathcal{R}}_0 = 1.4890$, which is significantly less than $\mathcal{R}_0$. This means that the spatially averaged system may be highly underestimating the disease burden.

In order to simulate the long-time behavior of system (6), we discretize it by the difference method on $(0, \pi)$. Our numerical scheme for the nonlocal and time-delayed reaction–diffusion model (6) was motivated by that given in Li and Zou (2009, Appendix). Figure 1 shows numerical plots of two diseased compartments, $u_1(t, x)$ and $u_3(t, x)$, with the initial data

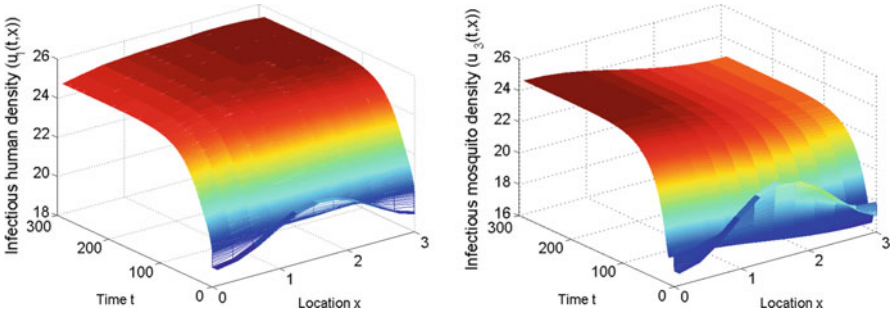

Fig. 1 Long term behavior of the diseased compartments

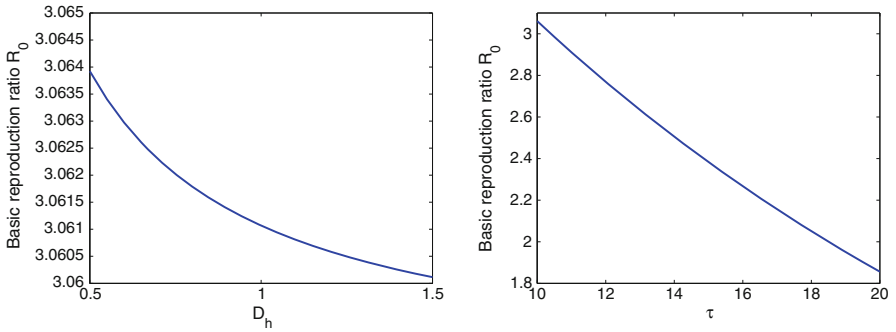

Fig. 2 $\mathcal{R}_0$ as functions of D_h and τ

$$u(\theta, x) = \begin{pmatrix} 20 - \cos 2x \\ 140 - 5\cos 2x \\ 19 - 2\cos 2x \end{pmatrix}, \quad \forall \theta \in [-\tau, 0], \quad x \in [0, \pi].$$

It indicates that the disease persists in host and vector populations in this case.

To investigate the sensitivity of $\mathcal{R}_0$ on model parameters, we have the following two graphs (Fig. 2) indicating the plots of $\mathcal{R}_0$ as functions of D_h and τ. It seems the disease cannot be contained solely by extending the incubation period with chemical measures.

To estimate the spatial heterogeneity effect on the disease risk $\mathcal{R}_0$, we take the variation of human distribution $H(x)$ for example. As more and more people leave villages and farms to live in cities, the distribution of whole human density will change, and urbanization may have impact on malaria risk. Set $H(x) = 100(1.1 - \delta\cos(2x))$, with $\delta \in [0, 1]$ being a parameter. Note that when $\delta = 0$, humans distribute evenly in space ($H(x) \equiv 110$, $\forall x \in \bar{\Omega}$), as δ changing from 0 to 1, more and more people leave the rural areas (near $x = 0$ or $x = \pi$) and accumulate at the urban area (around the middle point of Ω, i.e., $x = \frac{\pi}{2}$). However, the total human density on Ω remains unchanged since the spatial average of $H(x)$ does not change for all $\delta \in [0, 1]$. Thus, we can use $\delta \in [0, 1]$ to describe the urbanizing process. Figure 3 shows the relationship between $\mathcal{R}_0$ and δ. It indicates that urbanization may increase or decrease malaria risk depending on other model parameters. However, rapid urbanization may deteriorate the disease burden.

To simulate the efficiency of spatial control strategies, we take vaccination programs for example. Suppose that the unvaccinated population distribution for a vaccination program is $h(x)$, then the model with the vaccination program can be modified from our earlier model (6) as follows:

$$\frac{\partial u_1(t,x)}{\partial t} = D_h \Delta u_1(t,x) + \frac{c\beta(x)}{H(x)}(h(x) - u_1(t,x))u_3(t,x) - (d_h + \rho)u_1(t,x),$$
$$\frac{\partial u_2(t,x)}{\partial t} = D_m \Delta u_2(t,x) + \mu(x) - \frac{b\beta(x)}{H(x)}u_2(t,x)u_1(t,x) - d_m u_2(t,x),$$

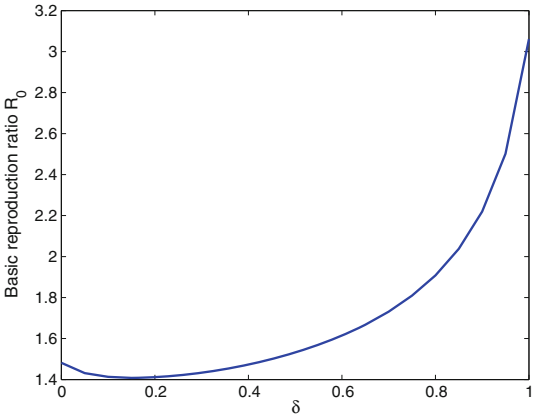

Fig. 3 Relationship between $\mathcal{R}_0$ and δ

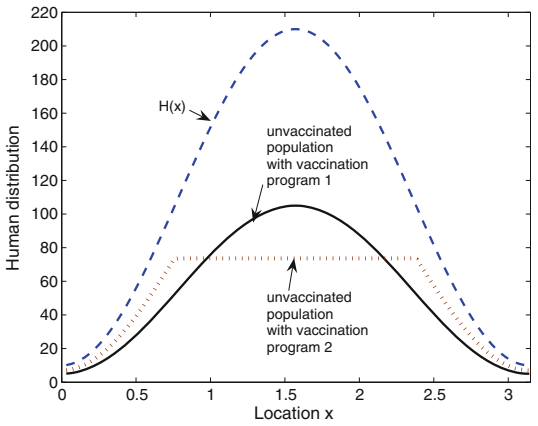

Fig. 4 Two vaccination programs

$$\begin{aligned}\frac{\partial u_3(t,x)}{\partial t} &= D_m \Delta u_3(t,x) - d_m u_3(t,x)\\ &\quad + e^{-d_m\tau}\int_\Omega \Gamma(D_m\tau, x, y)\frac{b\beta(y)}{H(y)}u_2(t-\tau,y)u_1(t-\tau,y)dy, \qquad (33)\\ \frac{\partial u_i}{\partial n} &= 0, \quad \forall x \in \partial\Omega, \ \ t > 0, \ \ i = 1,2,3.\end{aligned}$$

Using the same idea as in Sect. 3, we can define the basic reproduction ratio for system (33). Assume that we have two vaccination programs, program 1 and program 2, which are shown in Fig. 4.

The unvaccinated population distribution for program 1 is

$$h_1(x) = \frac{1}{2} \times 100 \times (1.1 - \cos 2x),$$

while that for program 2 is

$$h_2(x) = \begin{cases} 0.7036 \times 100, & \text{if } \frac{\pi}{4} \le x \le \frac{3\pi}{4}, \\ 0.7036 \times (100 - \cos 2x), & \text{if } x \ge \frac{3\pi}{4} \text{ or } x \le \frac{\pi}{4}. \end{cases}$$

In program 1, people living in the rural areas have the same opportunity to get vaccinated (half of the rural and urban populations is vaccinated). In program 2, people in urban area are easier to get access to the vaccination than those in rural areas. Note that the spatial average of $h_1(x)$ and $h_2(x)$ are same, being 55. This implies that the numbers of vaccinated population in these two vaccination programs are same. Numerical computation shows that the basic reproduction ratio corresponding to the first vaccination program is 2.1645 and that to the second program is 2.4979. Thus, the first spatial vaccination strategy seems to be more efficient.

6 Discussions

It is widely known in malariology that spatial heterogeneity and extrinsic incubation period (EIP) of the parasite in infected mosquitoes may affect the malaria transmission while the movement of human and mosquito populations leads to malaria spread. To understand the effects of these factors on malaria epidemic, we formulate and analyze a nonlocal and time-delayed reaction–diffusion model. For this mathematical model, we derive a biologically meaningful threshold index, the basic reproduction ratio $\mathcal{R}_0$. The basic reproduction ratio for this model is characterized as the spectral radius of the next generation operator and can be numerically calculated. Mathematically, we show that $\mathcal{R}_0 = 1$ defines a threshold. The disease will not invade if $\mathcal{R}_0 < 1$ and the disease becomes established in a previously uninfected populations if $\mathcal{R}_0 > 1$. For the model with spatially independent parameters, $\mathcal{R}_0$ can be explicitly calculated. Using a fluctuation method developed in Thieme and Zhao (2001), we get a set of sufficient conditions to guarantee that the disease will become established and stabilize at a unique spatially-homogeneous steady state. In particular, if $\mathcal{R}_0 > 1$ is large enough, the positive steady state is globally attractive.

As pointed out in Heffernan et al. (2005), the magnitude of $\mathcal{R}_0$ can be used to gauge the risk of an epidemic or pandemic in emerging infectious disease. Our result shows that this risk may be highly underestimated if we do just consider the model with spatially averaged parameters. By numerically calculating the basic reproduction ratio, our work suggests that spatial heterogeneity does strongly affect $\mathcal{R}_0$. As shown in Fig. 3, if δ, an index describing urbanization process, varies from 0 to 1, then the corresponding basic reproduction ratio changes from around 1.5 to 3.0, about two folds. It is worth for the field workers to determine those habitat-dependent parameters in the model.

With regard to application, the threshold result suggests that we should use chemical or physical strategies to reduce the value of $\mathcal{R}_0$ to be less than unity. As shown in the definition of the basic reproduction ratio, $\mathcal{R}_0$ also depends on spatial parameters in this model, which permits the assessment of spatial control strategies. Perhaps the most useful part of this framework would be to design an efficient spatial allocation

of financial resources for malaria control. For example, Fig. 4 shows two vaccination programs, and the numerical computation of $\mathcal{R}_0$ suggests that the first vaccination program is more efficient than the second one. In field work, with accurate spatial-dependent parameters, appropriate spatial vaccination strategies should be designed in the most efficient way. Analogously, we can study the effects of spatial insecticide treated nets (ITN) distribution and spatial indoor residual spraying (IRS) on the basic reproduction ratio.

Finally, we remark that there are quite a few spaces to improve and generalize our malaria model. For example, although it is shown in Theorem 2 that there exists a positive steady state for system (6) when $\mathcal{R}_0$ exceeds unity, its uniqueness and global attractivity still remain open. We expect to get some appropriate conditions as in Theorem 3 to guarantee the global attractivity of the positive steady state for system (6) when $\mathcal{R}_0 > 1$. Biologically, it is well-known that the weather fluctuation has impact on mosquito population dynamics and EIP, which has not been investigate here. It would be interesting to incorporate climate effects into the current model to depict the spatial–temporal transmission of malaria. We leave these problems for further investigation.

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