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A MULTIPATCH MALARIA MODEL WITH LOGISTIC GROWTH POPULATIONS*

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Abstract. In this paper, we propose a multipatch model to study the effects of population dispersal on the spatial spread of malaria between patches. The basic reproduction number $\mathcal{R}_0$ is derived, and it is shown that the disease-free equilibrium is locally asymptotically stable if $\mathcal{R}_0 < 1$ and unstable if $\mathcal{R}_0 > 1$. Bounds on the disease-free equilibrium and $\mathcal{R}_0$ are given. A sufficient condition for the existence of an endemic equilibrium when $\mathcal{R}_0 > 1$ is obtained. For the two-patch submodel, the dependence of $\mathcal{R}_0$ on the movement of exposed, infectious, and recovered humans between the two patches is investigated. Numerical simulations indicate that travel can help the disease to become endemic in both patches, even though the disease dies out in each isolated patch. However, if travel rates are continuously increased, the disease may die out again in both patches.

Key words. basic reproduction number, malaria, patch model, human movement, travel rate, disease-free equilibrium, monotonicity

AMS subject classifications. 92D30, 34D20

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1. Introduction.

Malaria is a parasitic vector-borne disease caused by the *Plasmodium*, which is transmitted to people via the bites of infected female mosquitoes of the genus *Anopheles*. People with malaria often experience fever, chills, and flu-like illness. If not treated promptly or effectively, an infected individual may develop severe complications and die. Vaccines for malaria are under development, with no approved vaccine yet available. About half of the world's population is at risk of malaria. This leads to an estimated 225 million malaria cases and nearly 781,000 deaths worldwide in 2008, the vast majority are children under five in Africa region (WHO [48]).

Following the pioneering work of Ross [35] and Macdonald [24, 25, 26], mathematical modeling of malaria transmission has been developed rapidly. Among these, we would like to mention Dietz, Molineaux, and Thomas [12], Aron and May [4], Nedelman [30], Koella [22], Gupta, Swinton, and Anderson [16], Ngwa and Shu [33], Ngwa [32], Chitnis, Cushing, and Hyman [7], Chitnis, Hyman, and Cushing [8], Ruan, Xiao, and Beier [36], Lou and Zhao [23], and the references cited therein.

In [33] (also Ngwa [32]), Ngwa and Shu introduced a compartmental model described by ordinary differential equations (ODEs) for the spread of malaria involving variable human and mosquito populations, in which the human population is classified as susceptible, exposed, infectious, and recovered, and the mosquito population is divided into classes containing susceptible, exposed, and infectious individuals. They established a threshold below which the disease-free equilibrium is stable and above which the disease can persist. Chitnis, Cushing, and Hyman [7] and Chitnis, Hyman, and Cushing [8] extended the model in Ngwa and Shu [33] and Ngwa [32] to generalize the mosquito biting rate, include human immigration, and exclude direct infectious-

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to-susceptible human recovery. They presented a bifurcation analysis in [7], defined a reproductive number, and showed the existence and stability of the disease-free and endemic equilibria. To determine the relative importance of model parameters in disease transmission and prevalence, sensitivity indices of the reproductive number and the endemic equilibrium were computed in [8].

Malaria varies greatly among different regions in the vectors that transmit it, in the species causing the disease, and in the level of intensity. It can be easily transmitted from one region to another due to extensive travel and migration (Martens and Hall [27], Tatem, Hay, and Rogers [41]). This leads to new outbreaks in some former malaria-free or lower transmission areas. For instance, even though malaria has been eliminated in the United States since the 1950's, about 1,500 malaria cases are diagnosed every year in this country, of which approximately 60% are among U.S. travelers (Newman et al. [31]). Thus it is necessary to distinguish the regions and understand the influence of population dispersal on the propagation of the disease between regions, which may improve malaria control programs.

Multipatch models have been developed to study the spatial spread of infectious diseases by many researchers over the past three decades. In particular, models of malaria in this direction include Dye and Hasibeder [13], Hasibeder and Dye [17], Torres-Sorando and Rodriguez [44], Rodriguez and Torres-Sorando [34], Smith, Dushoff, and McKenzie [38], Auger et al. [5], Cosner et al. [9], Arino, Ducrot, and Zongo [3], etc. For references on general epidemic models in a patchy environment, we refer the reader to two review articles by Wang [46] and Arino [2]. Most of these studies focus on evaluating the basic reproduction number R_0 and establishing the existence and stability of the disease-free and endemic equilibria. One of the goals in considering multipatch epidemic models is to study how the dispersal of individuals, in particular of exposed and infectious individuals, contributes to the spread of diseases from region to region. Mathematically, one way to investigate this problem is to determine how R_0 depends on model parameters, especially those describing the movement of exposed and infectious individuals. This indeed is a very interesting and challenging problem and there are very few results on this aspect (see Theorem 4.2 in Hsieh, van den Driessche, and Wang [20] and Lemma 3.4 in Allen et al. [1]). The reason is that for a multipatch model R_0 usually cannot be expressed analytically in terms of model parameters and the monotone dependence of R_0 on model parameters is very complicated.

In this paper, based on the model of Ngwa and Shu [33] (also Ngwa [32], Chitnis, Cushing, and Hyman [7], and Chitnis, Hyman, and Cushing [8]), we propose a multipatch model to examine how population dispersal affects malaria spread between patches. This paper is organized as follows. In next section, we describe our model in detail. The basic reproduction number $\mathcal{R}_0$ is derived and shown to be a threshold in section 3. In section 4, we analyze the dependence of $\mathcal{R}_0$ on the model parameters, in particular on the travel rates of exposed, infectious, and recovered humans, for the two-patch submodel using the matrix theory. In section 5, numerical simulations are performed to investigate the effects of human movement on disease dynamics. Section 6 gives a brief discussion of main results and future work.

2. Model formulation. We model the transmission dynamics of malaria between humans and mosquitoes within a patch and the spatial dispersal between n patches. Within a single patch, our model is based on that of Ngwa and Shu [33] (also Ngwa [32], Chitnis, Cushing, and Hyman [7], and Chitnis, Hyman, and Cushing [8]) with a susceptible-exposed-infectious-recovered (SEIR) structure for humans

and a susceptible-exposed-infectious (SEI) structure for mosquitoes. Hereafter, the subscript i refers to patch i and the superscript h/v refers to humans/mosquitoes. Let $S_i^h(t)$, $E_i^h(t)$, $I_i^h(t)$, and $R_i^h(t)$ denote, respectively, the number of susceptible, exposed, infectious, and recovered humans in patch i at time t. The total human population in patch i at time t is $N_i^h(t) = S_i^h(t) + E_i^h(t) + I_i^h(t) + R_i^h(t)$. Similarly, let $S_i^v(t)$, $E_i^v(t)$, and $I_i^v(t)$ denote, respectively, the number of susceptible, exposed, and infectious mosquitoes in patch i at time t. The total mosquito population in patch i at time t is $N_i^v(t) = S_i^v(t) + E_i^v(t) + I_i^v(t)$. The mosquito population has no recovered class since we assume that the mosquito's infective period ends with its death.

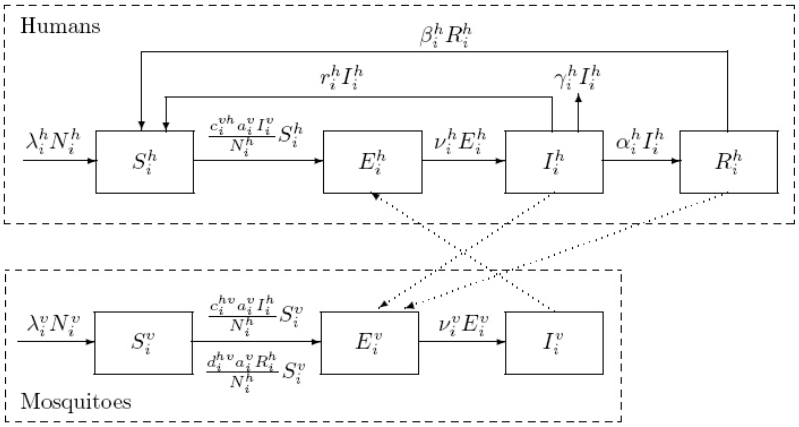

FIG. 1. *Flow diagram of the mosquito-borne model in patch i.*

For patch i, all newborns in both populations are assumed to fall into the susceptible class (no vertical transmission). Susceptible humans, S_i^h, may become exposed when they are bitten by infectious mosquitoes. The exposed humans, E_i^h, become infectious as the incubation period ends. Infectious humans, I_i^h, either reenter the susceptible class or recover in the immune compartment, R_i^h, where they remain for the period of their immunity before returning to the susceptible class. Susceptible mosquitoes, S_i^v, can be infected when they bite infectious or recovered humans and once infected they progress through the exposed, E_i^v, and infectious, I_i^v, classes. Both human and mosquito populations follow a logistic growth and migrate between patches, with humans having additional disease-induced death. The flowchart of malaria transmission for patch i omitting density-dependent death and travel is illustrated in Figure 1. Solid arrows denote within-species progression while dotted arrows denote interspecies transmission.

The interactions between humans and mosquitoes in patch i (with $i = 1, 2, \ldots, n$) based on the above assumptions are then described by the following differential equations with nonnegative initial conditions satisfying $N_i^h(0) > 0$:

$$\frac{dS_i^h}{dt} = \lambda_i^h N_i^h + \beta_i^h R_i^h + r_i^h I_i^h - \frac{c_i^{vh} a_i^v I_i^v}{N_i^h} S_i^h - f_i^h(N_i^h) S_i^h + \sum_{j=1}^{n} \varphi_{ij}^S S_j^h,$$

$$\frac{dE_i^h}{dt} = \frac{c_i^{vh} a_i^v I_i^v}{N_i^h} S_i^h - (\nu_i^h + f_i^h(N_i^h)) E_i^h + \sum_{j=1}^{n} \varphi_{ij}^E E_j^h,$$

$$
\begin{aligned}
\frac{dI_i^h}{dt} &= \nu_i^h E_i^h - (r_i^h + \alpha_i^h + \gamma_i^h + f_i^h(N_i^h))I_i^h + \sum_{j=1}^{n} \varphi_{ij}^I I_j^h,\\
\frac{dR_i^h}{dt} &= \alpha_i^h I_i^h - (\beta_i^h + f_i^h(N_i^h))R_i^h + \sum_{j=1}^{n} \varphi_{ij}^R R_j^h,\\
\frac{dS_i^v}{dt} &= \lambda_i^v N_i^v - \frac{c_i^{hv} a_i^v I_i^h}{N_i^h} S_i^v - \frac{d_i^{hv} a_i^v R_i^h}{N_i^h} S_i^v - f_i^v(N_i^v) S_i^v + \sum_{j=1}^{n} \psi_{ij}^S S_j^v,\\
\frac{dE_i^v}{dt} &= \frac{c_i^{hv} a_i^v I_i^h}{N_i^h} S_i^v + \frac{d_i^{hv} a_i^v R_i^h}{N_i^h} S_i^v - (\nu_i^v + f_i^v(N_i^v))E_i^v + \sum_{j=1}^{n} \psi_{ij}^E E_j^v,\\
\frac{dI_i^v}{dt} &= \nu_i^v E_i^v - f_i^v(N_i^v) I_i^v + \sum_{j=1}^{n} \psi_{ij}^I I_j^v,
\end{aligned} \tag{2.1}
$$

where

$f_i^h(N_i^h)$ $= \mu_i^h + \rho_i^h N_i^h$ is the density-dependent death rate for humans;
$f_i^v(N_i^v)$ $= \mu_i^v + \rho_i^v N_i^v$ is the density-dependent death rate for mosquitoes;
λ_i^h is the birth rate of humans;
λ_i^v is the birth rate of mosquitoes;
a_i^v is the mosquito biting rate;
c_i^{vh} is the probability that a bite by an infectious mosquito on a susceptible human will transfer the infection to the human;
c_i^{hv} is the probability that a bite by a susceptible mosquito on an infectious human will transfer the infection to the mosquito;
d_i^{hv} is the probability that a bite by a susceptible mosquito on a recovered human will transfer the infection to the mosquito;
ν_i^h is the progression rate that exposed humans become infectious;
ν_i^v is the progression rate that exposed mosquitoes become infectious;
r_i^h is the recovery rate that infectious humans become susceptible;
α_i^h is the recovery rate that infectious humans become recovered;
γ_i^h is the disease-induced death rate for humans;
β_i^h is the rate of loss of immunity for humans;
$\varphi_{ij}^K \geq 0$ for $K = S, E, I, R$ is the immigration rate from patch j to patch i for $i \neq j$ of susceptible, exposed, infectious, and recovered humans, respectively;
$\psi_{ij}^L \geq 0$ for $L = S, E, I$ is the immigration rate from patch j to patch i for $i \neq j$ of susceptible, exposed, and infectious mosquitoes, respectively;
$-\varphi_{ii}^K \geq 0$ for $K = S, E, I, R$ is the emigration rate of susceptible, exposed, infectious, and recovered humans in patch i, respectively;
$-\psi_{ii}^L \geq 0$ for $L = S, E, I$, is the emigration rate of susceptible, exposed, and infectious mosquitoes in patch i, respectively.

For simplicity, death rates and birth rates of the individuals during travel are ignored. Thus, we have

$$
\varphi_{ii}^K = -\sum_{\substack{j=1\\ j\neq i}}^{n} \varphi_{ji}^K,\ K = S, E, I, R \quad \text{and} \quad \psi_{ii}^L = -\sum_{\substack{j=1\\ j\neq i}}^{n} \psi_{ji}^L,\ L = S, E, I,\ 1 \leq i \leq n.
$$

Unless otherwise indicated, the travel rate matrices $(\varphi_{ij}^K)_{n\times n}$ for $K = S, E, I, R$ and $(\psi_{ij}^L)_{n\times n}$ for $L = S, E, I$ are assumed to be irreducible. Here the movement of humans

and mosquitoes between patches is governed by the Eulerian approach (Cosner et al. [9]), that is, humans and mosquitoes change their residences when they move from one patch to another. It is worth noting that they may have different spatial scales because humans can travel much longer distances than mosquitoes.

In the absence of disease and dispersal, both human and mosquito populations in each patch are modeled by logistic growth. For the persistence of the dispersal system, we assume that

$$s(((\lambda_i^h - \mu_i^h)\delta_{ij} + \varphi_{ij}^S)_{n\times n}) > 0 \quad \text{and} \quad s(((\lambda_i^v - \mu_i^v)\delta_{ij} + \psi_{ij}^S)_{n\times n}) > 0,$$

where s denotes the spectral bound of a matrix, which is the largest real part of any eigenvalue of the matrix, and δ_{ij} denotes the Kronecker delta (i.e., 1 when $i = j$ and 0 otherwise), or else they will die out in all patches. This implies that $\lambda_i^h > \mu_i^h$ and $\lambda_j^v > \mu_j^v$ for some i and j.

Furthermore, it is assumed that all parameters in the model are strictly positive with the exception of the travel rates.

Let $N^h(t) = \sum_{i=1}^n N_i^h(t)$ and $N^v(t) = \sum_{i=1}^n N_i^v(t)$. The following theorem demonstrates that model (2.1) is mathematically well posed and epidemiologically reasonable.

THEOREM 2.1. *Consider model* (2.1) *with nonnegative initial conditions satisfying* $N_i^h(0) > 0$ *for* $i = 1, \ldots, n$. *Then the system has a unique solution and all disease state variables remain nonnegative for all time* $t \geq 0$. *Moreover, both the total human population* $N^h(t)$ *and the total mosquito population* $N^v(t)$ *are bounded.*

Proof. The vector field defined by (2.1) is continuously differentiable, so the initial value problem has a unique solution which exists for all $t \geq 0$. The nonnegative property of state variables can be easily verified.

Denote $\chi^v = \max_{1\leq i\leq n}(\lambda_i^v - \mu_i^v) > 0$ and $\rho^v = \min_{1\leq i\leq n} \rho_i^v$. Then

$$\begin{aligned}\frac{dN^v}{dt} &= \sum_{i=1}^n (\lambda_i^v N_i^v - f_i^v(N_i^v)N_i^v) = \sum_{i=1}^n ((\lambda_i^v - \mu_i^v)N_i^v - \rho_i^v(N_i^v)^2) \\ &\leq \chi^v \sum_{i=1}^n N_i^v - \rho^v \sum_{i=1}^n (N_i^v)^2 \leq \chi^v \sum_{i=1}^n N_i^v - \rho^v \left(\sum_{i=1}^n N_i^v\right)^2 /n \\ &= \chi^v N^v - \rho^v (N^v)^2/n = (\chi^v - \rho^v N^v/n)N^v.\end{aligned}$$

Hence, by a comparison theorem, $N^v(t)$ is bounded from above by $\max\{n\chi^v/\rho^v, N^v(0)\}$. Similarly, we can find an upper bound for $N^h(t)$. The proof is complete. ∎

3. Threshold dynamics. We first show the existence of a disease-free equilibrium (DFE) for (2.1), then calculate the basic reproduction number $\mathcal{R}_0$ and give an estimate of it. Uniform persistence of the disease and the existence of an endemic equilibrium are discussed at the end of this section.

3.1. Disease-free equilibrium. A disease-free equilibrium is a steady state solution of system (2.1) where there is no disease, namely, $S_i^h = S_i^{h*} > 0, S_i^v = S_i^{v*} > 0$, and all other variables $E_i^h, E_i^v, I_i^h, I_i^v, R_i^h = 0$ for $i = 1, 2, \ldots, n$. The partially immune human, R_i^h, is regarded as infected because individuals in this status are still infective to susceptible mosquitoes. Mathematically, if $E_i^h = E_i^v = I_i^h = I_i^v = 0$ for all i at a steady state, then by summing the fourth equation of (2.1) up from 1 to n,

we have

$$-\sum_{i=1}^{n}(\beta_i^h + f_i^h(N_i^h))R_i^h + \sum_{i=1}^{n}\sum_{j=1}^{n}\varphi_{ij}^R R_j^h = -\sum_{i=1}^{n}(\beta_i^h + f_i^h(N_i^h))R_i^h + \sum_{i=1}^{n}\sum_{j=1}^{n}\varphi_{ji}^R R_i^h = 0.$$

Hence, $-\sum_{i=1}^{n}(\beta_i^h + f_i^h(N_i^h))R_i^h = 0$. This implies $R_i^h = 0$ for $i = 1, 2, \ldots, n$.

Let $S^{h*} = (S_1^{h*}, S_2^{h*}, \ldots, S_n^{h*})$ and let $S^{v*} = (S_1^{v*}, S_2^{v*}, \ldots, S_n^{v*})$. Thus there is a DFE for (2.1) if and only if S^{h*} and S^{v*} are positive equilibria to the subsystems

$$\frac{dS_i^h}{dt} = \lambda_i^h S_i^h - f_i^h(S_i^h)S_i^h + \sum_{j=1}^{n}\varphi_{ij}^S S_j^h, 1 \le i \le n \tag{3.1}$$

and

$$\frac{dS_i^v}{dt} = \lambda_i^v S_i^v - f_i^v(S_i^v)S_i^v + \sum_{j=1}^{n}\psi_{ij}^S S_j^v, 1 \le i \le n, \tag{3.2}$$

respectively. They are guaranteed by the following lemma.

LEMMA 3.1. *Let* $\mathrm{Int}\mathbb{R}_+^n$ *be the interior of* $\mathbb{R}_+^n$. *For system* (3.1), *there is a unique nonzero equilibrium* $S^{h*} \in \mathrm{Int}\mathbb{R}_+^n$ *which is globally asymptotically stable with respect to* $\mathbb{R}_+^n \backslash \{0\}$. *Moreover, if* $\lambda_i^h > \mu_i^h$ *for* $1 \le i \le n$, *we have*

$$P^h \equiv \min_{1\le i\le n}\frac{K_i^h}{L_i^h}\cdot L^h \le S^{h*} \le Q^h \equiv \max_{1\le i\le n}\frac{K_i^h}{L_i^h}\cdot L^h,$$

where $K_i^h = \frac{\lambda_i^h - \mu_i^h}{\rho_i^h}$ *for* $1 \le i \le n$, *and* $L^h = (L_1^h, \ldots, L_{n-1}^h, L_n^h)$ *is the unique solution to*

$$\sum_{j=1}^{n}\varphi_{ij}^S S_j^h = 0, i = 1, \ldots, n, \text{ and } S_n^h = 1$$

with $L_i^h > 0$ *for* $1 \le i \le n-1$ *and* $L_n^h = 1$. *A similar result holds for system* (3.2).

Proof. It is easy to see that system (3.1) is cooperative and irreducible. The existence, uniqueness, and global asymptotic stability of S^{h*} can be proved by applying Theorem 6.1 in Hirsch [18] or Corollary 3.2 in Zhao and Jing [50].

Let $L^h = (L_1^h, \ldots, L_{n-1}^h, L_n^h)$ be the right eigenvector of the irreducible matrix $(\varphi_{ij}^S)_{n\times n}$ corresponding to the principal eigenvalue 0 normalized so that its last entry equals 1. The existence, uniqueness, and positivity of L^h is proved in Lemma 1 of Cosner et al. [9] or Lemma 2.1 of Guo, Li, and Shuai [15]. We denote by f^h the vector field defined by (3.1) and let ϕ_t^h denote the corresponding flow. Then the ith component of f^h evaluated at mL^h satisfies

$$\lambda_i^h(mL_i^h) - f_i^h(mL_i^h)\cdot mL_i^h + \sum_{j=1}^{n}\varphi_{ij}^S mL_j^h = \lambda_i^h(mL_i^h) - f_i^h(mL_i^h)\cdot mL_i^h$$

$$= m((\lambda_i^h - \mu_i^h) - \rho_i^h mL_i^h)L_i^h = m\rho_i^h L_i^h\left(\frac{\lambda_i^h - \mu_i^h}{\rho_i^h L_i^h} - m\right)L_i^h = m\rho_i^h L_i^h\left(\frac{K_i^h}{L_i^h} - m\right)L_i^h$$

for $m > 0$ and $i = 1, \ldots, n$. Thus $f^h(mL^h) \ge 0$ for $m \le \min_{1\le i\le n}\frac{K_i^h}{L_i^h}$ and $f^h(mL^h) \le 0$ for $m \ge \max_{1\le i\le n}\frac{K_i^h}{L_i^h}$. In particular, $f^h(P^h) \ge 0$ and $f^h(Q^h) \le 0$. It follows from the theory of monotone dynamical systems (Smith [39]) that $\phi_t^h(P^h)$ is nondecreasing and $\phi_t^h(Q^h)$ is nonincreasing for $t \ge 0$. Since both $\phi_t^h(P^h)$ and $\phi_t^h(Q^h)$ converge to S^{h*}, we have $P^h \le S^{h*} \le Q^h$. ∎

3.2. The basic reproduction number. To derive the basic reproduction number $\mathcal{R}_0$ for (2.1), we order the infected variables first by disease state, then by patch, i.e.,

$$E_1^h, E_2^h, \dots, E_n^h, E_1^v, E_2^v, \dots, E_n^v, I_1^h, I_2^h, \dots, I_n^h, I_1^v, I_2^v, \dots, I_n^v, R_1^h, R_2^h, \dots, R_n^h,$$

and follow the recipe from van den Driessche and Watmough [45] to obtain

$$F = \begin{bmatrix} 0 & 0 & 0 & A_{64} & 0 \\ 0 & 0 & A_{73} & 0 & A_{75} \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{bmatrix} \text{ and } V = \begin{bmatrix} A_{11} & & & & \\ 0 & A_{22} & & & \\ -A_{31} & 0 & A_{33} & & \\ 0 & -A_{42} & 0 & A_{44} & \\ 0 & 0 & -A_{53} & 0 & A_{55} \end{bmatrix},$$

where

$$\begin{aligned}
A_{11} &= (\delta_{ij}(\nu_i^h + f_i^h(S_i^{h*})) - \varphi_{ij}^E)_{n\times n} = (\delta_{ij}(\nu_i^h + \mu_i^h + \rho_i^h S_i^{h*}) - \varphi_{ij}^E)_{n\times n},\\
A_{22} &= (\delta_{ij}(\nu_i^v + f_i^v(S_i^{v*})) - \psi_{ij}^E)_{n\times n} = (\delta_{ij}(\nu_i^v + \mu_i^v + \rho_i^v S_i^{v*}) - \psi_{ij}^E)_{n\times n},\\
A_{31} &= (\delta_{ij}\nu_i^h)_{n\times n} = \operatorname{diag}\{\nu_1^h, \nu_2^h, \dots, \nu_n^h\},\\
A_{33} &= (\delta_{ij}(r_i^h + \alpha_i^h + \gamma_i^h + f_i^h(S_i^{h*})) - \varphi_{ij}^I)_{n\times n}\\
&= (\delta_{ij}(r_i^h + \alpha_i^h + \gamma_i^h + \mu_i^h + \rho_i^h S_i^{h*}) - \varphi_{ij}^I)_{n\times n},\\
A_{42} &= (\delta_{ij}\nu_i^v)_{n\times n} = \operatorname{diag}\{\nu_1^v, \nu_2^v, \dots, \nu_n^v\},\\
A_{44} &= (\delta_{ij} f_i^v(S_i^{v*}) - \psi_{ij}^I)_{n\times n} = (\delta_{ij}(\mu_i^v + \rho_i^v S_i^{v*}) - \psi_{ij}^I)_{n\times n},\\
A_{53} &= (\delta_{ij}\alpha_i^h)_{n\times n} = \operatorname{diag}\{\alpha_1^h, \alpha_2^h, \dots, \alpha_n^h\},\\
A_{55} &= (\delta_{ij}(\beta_i^h + f_i^h(S_i^{h*})) - \varphi_{ij}^R)_{n\times n} = (\delta_{ij}(\beta_i^h + \mu_i^h + \rho_i^h S_i^{h*}) - \varphi_{ij}^R)_{n\times n},\\
A_{64} &= (\delta_{ij} c_i^{vh} a_i^v)_{n\times n} = \operatorname{diag}\{c_1^{vh}a_1^v, c_2^{vh}a_2^v, \dots, c_n^{vh}a_n^v\},\\
A_{73} &= (\delta_{ij} c_i^{hv} a_i^v S_i^{v*}/S_i^{h*})_{n\times n},\\
A_{75} &= (\delta_{ij} d_i^{hv} a_i^v S_i^{v*}/S_i^{h*})_{n\times n}.
\end{aligned}$$

The terms A_{64}, A_{73}, and A_{75} are named after the partial derivatives of the vector fields of susceptible humans to infectious mosquitoes, susceptible mosquitoes to infectious humans, and susceptible mosquitoes to recovered humans, respectively.

Since A_{ii} for $i = 1, \dots, 5$, is a strictly diagonally dominant matrix, by the Gershgorin circle theorem, the real parts of its eigenvalues are positive and therefore A_{ii}^{-1} exists. So the inverse of V exists and equals

$$V^{-1} = \begin{bmatrix} A_{11}^{-1} & & & & \\ 0 & A_{22}^{-1} & & & \\ A_{33}^{-1}A_{31}A_{11}^{-1} & 0 & A_{33}^{-1} & & \\ 0 & A_{44}^{-1}A_{42}A_{22}^{-1} & 0 & A_{44}^{-1} & \\ A_{55}^{-1}A_{53}A_{33}^{-1}A_{31}A_{11}^{-1} & 0 & A_{55}^{-1}A_{53}A_{33}^{-1} & 0 & A_{55}^{-1} \end{bmatrix}.$$

Thus, the next generation matrix (see Diekmann, Heesterbeek, and Metz [11]) is

$$FV^{-1} = \begin{bmatrix} 0 & M^{vh} & 0 & A_{64}A_{44}^{-1} & 0 \\ M^{hv} & 0 & (A_{73} + A_{75}A_{55}^{-1}A_{53})A_{33}^{-1} & 0 & A_{75}A_{55}^{-1} \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{bmatrix},$$

where $M^{vh} = A_{64}A_{44}^{-1}A_{42}A_{22}^{-1}$ and $M^{hv} = (A_{73} + A_{75}A_{55}^{-1}A_{53})A_{33}^{-1}A_{31}A_{11}^{-1}$. Note that M^{vh} and M^{hv} account for new human infections due to each infectious mosquito and new mosquito infections due to each infectious or recovered human, respectively.

By calculating $(FV^{-1})^2$, we find the basic reproduction number

$$\mathcal{R}_0 = \sqrt{\rho(M)},$$

where ρ denotes the spectral radius and M is the product of M^{vh} and M^{hv}, i.e.,

$$\begin{aligned} M = M^{vh}M^{hv} &= A_{64}A_{44}^{-1}A_{42}A_{22}^{-1}(A_{73} + A_{75}A_{55}^{-1}A_{53})A_{33}^{-1}A_{31}A_{11}^{-1} \\ &= A_{64}A_{44}^{-1}A_{42}A_{22}^{-1}A_{73}A_{33}^{-1}A_{31}A_{11}^{-1} + A_{64}A_{44}^{-1}A_{42}A_{22}^{-1}A_{75}A_{55}^{-1}A_{53}A_{33}^{-1}A_{31}A_{11}^{-1}. \end{aligned}$$

The first term in M represents infections related to infectious humans, while the second describes infections related to recovered humans who survive the infectious class and acquire partial immunity.

THEOREM 3.2. *The disease-free equilibrium of* (2.1) *is locally asymptotically stable if* $\mathcal{R}_0 < 1$ *and unstable if* $\mathcal{R}_0 > 1$.

Proof. To prove the stability of DFE, we need to check the hypotheses (A1)–(A5) in van den Driessche and Watmough [45]. Hypotheses (A1)–(A4) are easily verified while (A5) is satisfied if all eigenvalues of the $7n \times 7n$ matrix

$$J = \begin{bmatrix} -V & 0 \\ J_3 & J_4 \end{bmatrix}$$

have negative real parts. Here J_3 is a $2n \times 5n$ matrix and $J_4 = \text{diag}\{Df^h(S^{h*}), Df^v(S^{v*})\}$ where f^v denotes the vector field defined by (3.2). By Lemma 3.1, $s(J_4) < 0$. So is $s(J)$. ∎

Remark 3.3. The basic reproduction number for the ith patch in isolation (i.e., there is no travel between patch i and other patches) is given by

$$\mathcal{R}_0^{(i)} = \sqrt{\frac{c_i^{vh}(a_i^v)^2\nu_i^v(c_i^{hv}(\beta_i^h + \lambda_i^h) + d_i^{hv}\alpha_i^h)\nu_i^h(\lambda_i^v - \mu_i^v)\rho_i^h}{\lambda_i^v(\nu_i^v + \lambda_i^v)(r_i^h + \alpha_i^h + \gamma_i^h + \lambda_i^h)(\beta_i^h + \lambda_i^h)(\nu_i^h + \lambda_i^h)(\lambda_i^h - \mu_i^h)\rho_i^v}}. \tag{3.3}$$

This is slightly different from Ngwa and Shu's [33], which is $(\mathcal{R}_0^{(i)})^2$.

It is easy to see that in calculating $\mathcal{R}_0$, the matrix M is a positive matrix (all entries are positive) and hence $\rho(M)$ is an eigenvalue of M and it is simple. In fact, it follows from Corollary 3.2 in Smith [39] that $A_{ii}^{-1}, i = 1, \ldots, 5$, is a positive matrix. Moreover, as a consequence of Theorem 2.5.4 in Horn and Johnson [19], we know the determinants of both A_{ii}^{-1} for $i = 1, \ldots, 5$ and $A_{73} + A_{75}A_{55}^{-1}A_{53}$ are positive. So is M. In particular, M has two distinct positive eigenvalues when $n = 2$. This fact will be used later.

Similar to Theorem 2.3 in Salmani and van den Driessche [37] and Theorem 3.2 in Hsieh, van den Driessche, and Wang [20], we have the following result which gives bounds on the basic reproduction number.

THEOREM 3.4. $\max_{1\le i\le n}(\tilde{\mathcal{R}}_0^{(i)})^2 \le \mathcal{R}_0^2 \le \max_{1\le i\le n}(\hat{\mathcal{R}}_{01}^{(i)})^2 + \max_{1\le i\le n}(\hat{\mathcal{R}}_{02}^{(i)})^2$, *where*

$$\begin{aligned} (\tilde{\mathcal{R}}_0^{(i)})^2 = {} & c_i^{vh}a_i^v(\mu_i^v + \rho_i^v S_i^{v*} - \psi_{ii}^I)^{-1}\nu_i^v(\nu_i^v + \mu_i^v + \rho_i^v S_i^{v*} - \psi_{ii}^E)^{-1} \\ & \cdot \left(\frac{c_i^{hv}a_i^v S_i^{v*}}{S_i^{h*}} + \frac{d_i^{hv}a_i^v S_i^{v*}}{S_i^{h*}}(\beta_i^h + \mu_i^h + \rho_i^h S_i^{h*} - \varphi_{ii}^R)^{-1}\alpha_i^h\right) \\ & \cdot (r_i^h + \alpha_i^h + \gamma_i^h + \mu_i^h + \rho_i^h S_i^{h*} - \varphi_{ii}^I)^{-1}\nu_i^h(\nu_i^h + \mu_i^h + \rho_i^h S_i^{h*} - \varphi_{ii}^E)^{-1} \end{aligned}$$

and

$$(\hat{\mathcal{R}}_{01}^{(i)})^2 = c_i^{vh} a_i^v (\mu_i^v + \rho_i^v S_i^{v*})^{-1} \nu_i^v (\nu_i^v + \mu_i^v + \rho_i^v S_i^{v*})^{-1} \frac{c_i^{hv} a_i^v S_i^{v*}}{S_i^{h*}}$$
$$\cdot (r_i^h + \alpha_i^h + \gamma_i^h + \mu_i^h + \rho_i^h S_i^{h*})^{-1} \nu_i^h (\nu_i^h + \mu_i^h + \rho_i^h S_i^{h*})^{-1},$$
$$(\hat{\mathcal{R}}_{02}^{(i)})^2 = c_i^{vh} a_i^v (\mu_i^v + \rho_i^v S_i^{v*})^{-1} \nu_i^v (\nu_i^v + \mu_i^v + \rho_i^v S_i^{v*})^{-1} \frac{d_i^{hv} a_i^v S_i^{v*}}{S_i^{h*}} (\beta_i^h + \mu_i^h + \rho_i^h S_i^{h*})^{-1}$$
$$\cdot \alpha_i^h (r_i^h + \alpha_i^h + \gamma_i^h + \mu_i^h + \rho_i^h S_i^{h*})^{-1} \nu_i^h (\nu_i^h + \mu_i^h + \rho_i^h S_i^{h*})^{-1}.$$

Proof. The lower bound can be proved by applying Fischer's inequality (see Theorem 2.5.4(e), Horn and Johnson [19]) to estimate the diagonal entries of matrix $A_{ii}^{-1}, i = 1, \ldots, 5$. In fact, for example, let $A_{11} = (a_{ij})_{n\times n}$ and $A_{11}^{-1} = (\alpha_{ij})_{n\times n}$; then $1/a_{ii} \le \alpha_{ii}$ for $i = 1, \ldots, n$ and therefore

$$0 \le \operatorname{diag}\{1/a_{11}, \ldots, 1/a_{nn}\} \le \operatorname{diag}\{\alpha_{11}, \ldots, \alpha_{nn}\} \le A_{11}^{-1}.$$

To establish the upper bound of $\mathcal{R}_0$, observe that, for example,

$$\vec{\mathbf{1}}(A_{44}B_{44}^{-1}) = \vec{\mathbf{1}} \Rightarrow \vec{\mathbf{1}}(B_{44}A_{44}^{-1}) = \vec{\mathbf{1}},$$

where $\vec{\mathbf{1}} = (1, 1, \ldots, 1)_{1\times n}$ and $B_{44} = A_{44} + (\psi_{ij}^I)_{n\times n} = \operatorname{diag}\{f_1^v(S_1^{v*}) \ldots, f_n^v(S_n^{v*})\}$. This implies that the spectral radius of $B_{44}A_{44}^{-1}$ is 1 and hence

$$\rho(A_{44}^{-1}) = \rho(B_{44}^{-1}B_{44}A_{44}^{-1}) \le \rho(B_{44}^{-1})\rho(B_{44}A_{44}^{-1}) = \rho(B_{44}^{-1}).$$

Finally, the proof is complete with the properties $\rho(M_1M_2) = \rho(M_2M_1)$ and $\rho(M_1 + M_2) \le \rho(M_1) + \rho(M_2)$ for any square matrices M_1, M_2 with the same order. □

Remark 3.5. The trick in finding an upper bound for the basic reproduction number seems very useful for general epidemic patch models. With such a trick, one can prove the upper bound in Theorem 2.3 of Salmani and van den Driessche [37] without any additional restriction on the parameters, which is a nice improvement. Also, the trick can be used to prove the upper bound in Theorem 3.2 of Hsieh, van den Driessche, and Wang [20] without assuming that $d_i = d$ for $i = 1, 2, \ldots, n$.

Remark 3.6. When $\lambda_i^h > \mu_i^h$ and $\lambda_i^v > \mu_i^v$ for $1 \le i \le n$, a combination of Lemma 3.1 and Theorem 3.4 yields an estimation of $\mathcal{R}_0$ which depends only on model parameters. However, this result might have little use, because we omitted some terms in the process of estimation.

3.3. Uniform persistence and the endemic equilibrium. Under certain conditions, we can use the techniques of persistence theory (Freedman, Ruan, and Tang [14], Thieme [43], Cantrell and Cosner [6], Smith and Thieme [40]) to show the uniform persistence of the disease and the existence of at least one endemic equilibrium when $\mathcal{R}_0 > 1$. The proof is similar to Theorem 2.3 in Wang and Zhao [47] and Theorem 3.2 in Lou and Zhao [23]. For convenience, we denote the vector $(S_1^h(t), \ldots, S_n^h(t))$ by $S^h(t)$ for $t \ge 0$. $E^h(t), I^h(t), R^h(t), S^v(t), E^v(t)$, and $I^v(t)$ can be introduced similarly.

THEOREM 3.7. *Let $\mathcal{E}_{11}$ denote the disease-free equilibrium of* (2.1)*, let $W^s(\mathcal{E}_{11})$ be the stable manifold of $\mathcal{E}_{11}$, and let X_0 be $\mathbb{R}_+^n \times \mathrm{Int}\mathbb{R}_+^{3n} \times \mathbb{R}_+^n \times \mathrm{Int}\mathbb{R}_+^{2n}$. Suppose that $\mathcal{R}_0 > 1$; then we have $W^s(\mathcal{E}_{11}) \cap X_0 = \emptyset$. If, in addition, assume that*

(i) $\lambda_i^h - \mu_i^h - \gamma_i^h > 0$ *for* $i = 1, 2, \ldots, n$;

(ii) $\varphi_{ij}^K > 0$ *for* $K = S, E, I, R$, $i, j = 1, 2, \ldots, n$, $i \ne j$;

(iii) $\lambda_i^v - \mu_i^v > 0$ *for* $i = 1, 2, \ldots, n$ *(or* $\psi_{ij}^S = \psi_{ij}^E = \psi_{ij}^I$ *for* $i, j = 1, 2, \ldots, n$*). Then the disease is uniformly persistent among patches, i.e., there is a constant* $\kappa > 0$ *such that each solution* $\Phi_t(\mathbf{x}_0) \equiv (S^h(t), E^h(t), I^h(t), R^h(t), S^v(t), E^v(t), I^v(t))$ *of system* (2.1) *with* $\mathbf{x}_0 \equiv (S^h(0), E^h(0), I^h(0), R^h(0), S^v(0), E^v(0), I^v(0)) \in X_0$ *satisfies*

$$\liminf_{t\to\infty}(E^h(t), I^h(t), R^h(t), E^v(t), I^v(t)) > (\kappa, \kappa, \ldots, \kappa)_{1\times 5n},$$

and (2.1) *admits at least one endemic equilibrium.*

Proof. We show first that $W^s(\mathcal{E}_{11}) \cap X_0 = \emptyset$ whenever $\mathcal{R}_0 > 1$. Define

$$\Delta = \begin{bmatrix} (\delta_{ij}\rho_i^h)_{n\times n} & 0 & 0 & (\delta_{ij}c_i^{vh}a_i^v)_{n\times n} & 0 \\ 0 & (\delta_{ij}\rho_i^v)_{n\times n} & (\delta_{ij}c_i^{hv}a_i^v)_{n\times n} & 0 & (\delta_{ij}d_i^{hv}a_i^v)_{n\times n} \\ 0 & 0 & (\delta_{ij}\rho_i^h)_{n\times n} & 0 & 0 \\ 0 & 0 & 0 & (\delta_{ij}\rho_i^v)_{n\times n} & 0 \\ 0 & 0 & 0 & 0 & (\delta_{ij}\rho_i^h)_{n\times n} \end{bmatrix}$$

and $M_\epsilon = F - V - \epsilon\Delta$. It follows from Theorem 2 in van den Driessche and Watmough [45] that $\mathcal{R}_0 > 1$ if and only if $s(F - V) > 0$. Thus, there exists an $\epsilon_1 > 0$ such that $s(M_\epsilon) > 0$ for $\epsilon \in [0, \epsilon_1]$. Let $|\cdot|$ be the Euclidean norm in $\mathbb{R}^{7n}$. Choose η small enough such that

$$\frac{S_i^v(0)}{N_i^h(0)} \geq \frac{S_i^{v*}}{S_i^{h*}} - \epsilon_1, \quad \frac{S_i^h(0)}{N_i^h(0)} \geq 1 - \epsilon_1, \quad N_i^h(0) \leq S_i^{h*} + \epsilon_1, \text{ and } N_i^v(0) \leq S_i^{v*} + \epsilon_1$$

for $i = 1, 2, \ldots, n$, $|\mathbf{x}_0 - \mathcal{E}_{11}| \leq \eta$. We now show that

$$\limsup_{t\to\infty} |\Phi_t(\mathbf{x}_0) - \mathcal{E}_{11}| > \eta \text{ for } \mathbf{x}_0 \in X_0.$$

Suppose, by contradiction, that there is a $T > 0$ such that $|\Phi_t(\mathbf{x}_0) - \mathcal{E}_{11}| \leq \eta$ for $t \geq T$. Pick $\Phi_T(\mathbf{x}_0) \in X_0$ as new $\mathbf{x}_0$; then $|\Phi_t(\mathbf{x}_0) - \mathcal{E}_{11}| \leq \eta$ for $t \geq 0$ and

$$\begin{aligned}
\frac{dE_i^h}{dt} &\geq c_i^{vh}a_i^v I_i^v(1-\epsilon_1) - (\nu_i^h + f_i^h(S_i^{h*} + \epsilon_1))E_i^h + \sum_{j=1}^n \varphi_{ij}^E E_j^h, \\
\frac{dE_i^v}{dt} &\geq c_i^{hv}a_i^v I_i^h\left(\frac{S_i^{v*}}{S_i^{h*}} - \epsilon_1\right) + d_i^{hv}a_i^v R_i^h\left(\frac{S_i^{v*}}{S_i^{h*}} - \epsilon_1\right) \\
&\quad -(\nu_i^v + f_i^v(S_i^{v*} + \epsilon_1))E_i^v + \sum_{j=1}^n \psi_{ij}^E E_j^v, \\
\frac{dI_i^h}{dt} &\geq \nu_i^h E_i^h - (r_i^h + \alpha_i^h + \gamma_i^h + f_i^h(S_i^{h*} + \epsilon_1))I_i^h + \sum_{j=1}^n \varphi_{ij}^I I_j^h, \\
\frac{dI_i^v}{dt} &\geq \nu_i^v E_i^v - f_i^v(S_i^{v*} + \epsilon_1)I_i^v + \sum_{j=1}^n \psi_{ij}^I I_j^v, \\
\frac{dR_i^h}{dt} &\geq \alpha_i^h I_i^h - (\beta_i^h + f_i^h(S_i^{h*} + \epsilon_1))R_i^h + \sum_{j=1}^n \varphi_{ij}^R R_j^h.
\end{aligned}$$

Consider an auxiliary system

$$\frac{d\omega(t)}{dt} = M_{\epsilon_1}\omega(t). \tag{3.4}$$

Note that M_{ϵ_1} is an irreducible, cooperative matrix for sufficiently small ϵ_1. Using the Perron–Frobenius theorem, $s(M_{\epsilon_1}) > 0$ is a simple eigenvalue associated to a positive eigenvector. It then follows that any solution of (3.4) with positive initial value goes to infinity as $t \to \infty$. By the comparison theorem, we have

$$\lim_{t\to\infty}(E_i^h(t), E_i^v(t), I_i^h(t), I_i^v(t), R_i^h(t)) = (\infty, \infty, \infty, \infty, \infty), \quad i = 1, 2, \ldots, n.$$

Suppose (i) and (ii) hold. Let $X = \{\mathbf{x}_0 \in \mathbb{R}_+^{7n} : N_i^h(0) > 0 \text{ for } i = 1, 2, \ldots, n\}$. We now claim that there exist $n + 1$ positive constants $\zeta_1, \zeta_2, \ldots, \zeta_n$ and Λ such that

$$\tilde{X} = \{\mathbf{x}_0 \in X : N_i^h(0) \geq \zeta_i \text{ for } i = 1, 2, \ldots, n \text{ and } N^h(0) \geq \Lambda\}$$

is closed positively invariant and each orbit of (2.1) starting in X eventually enters into $\tilde{X}$. The proof of this claim is straightforward, but tedious; we refer to Theorem 2 of Cui and Chen [10] for the approach.

Let $\tilde{X}_0 = \{\mathbf{x}_0 \in \tilde{X} : E_i^h(0), I_i^h(0), R_i^h(0), E_i^v(0), I_i^v(0) > 0 \text{ for } i = 1, 2, \ldots, n\}$ and $\partial\tilde{X}_0 = \tilde{X}\backslash\tilde{X}_0$. It is sufficient to prove that system (2.1) is uniformly persistent with respect to $(\tilde{X}_0, \partial\tilde{X}_0)$.

Obviously, $\tilde{X}_0$ is relatively open in $\tilde{X}$. It is easy to check that $\tilde{X}_0$ is positively invariant. Theorem 2.1 implies that system (2.1) is point dissipative. Define

$$\begin{aligned}
M_\partial &= \{\mathbf{x}_0 \in \partial\tilde{X}_0 : \Phi_t(\mathbf{x}_0) \in \partial\tilde{X}_0 \forall t \geq 0\},\\
D_1 &= \{\mathbf{x}_0 \in \tilde{X} : E_i^h(0) = I_i^h(0) = R_i^h(0) = E_i^v(0) = I_i^v(0) = 0 \forall i \in \{1, 2, \ldots, n\}\},\\
D_2 &= \{\mathbf{x}_0 \in \tilde{X} : S_i^v(0) = E_i^v(0) = I_i^v(0) = 0 \forall i \in \{1, 2, \ldots, n\}\}.
\end{aligned}$$

We claim that $M_\partial = D_1 \cup D_2$. Clearly, $D_1 \cup D_2 \subset M_\partial$. It suffices to show that $M_\partial \subset D_1 \cup D_2$. For any $\mathbf{x}_0 \in \partial\tilde{X}_0\backslash(D_1 \cup D_2)$, we have $N_i^h(0) > 0$, $i = 1, 2, \ldots, n$, and

$$\sum_{i=1}^{n}(E_i^h(0) + I_i^h(0) + R_i^h(0) + E_i^v(0) + I_i^v(0)) > 0, \ \sum_{i=1}^{n}(S_i^v(0) + E_i^v(0) + I_i^v(0)) > 0.$$

By the form of (2.1) and the irreducibility of travel rate matrices, it follows that $\Phi_t(\mathbf{x}_0) \in \tilde{X}_0$ for $t > 0$. Hence $\mathbf{x}_0 \notin M_\partial$ and the claim is proved.

Let $\vec{\mathbf{0}} = (0, 0, \ldots, 0)_{1\times n}$. It is easy to verify that there are exactly two equilibria in M_∂, i.e., $\mathcal{E}_{10} = (S^{h*}, \vec{\mathbf{0}}, \vec{\mathbf{0}}, \vec{\mathbf{0}}, \vec{\mathbf{0}}, \vec{\mathbf{0}}, \vec{\mathbf{0}})$ and $\mathcal{E}_{11} = (S^{h*}, \vec{\mathbf{0}}, \vec{\mathbf{0}}, \vec{\mathbf{0}}, S^{v*}, \vec{\mathbf{0}}, \vec{\mathbf{0}})$. Clearly, the total mosquito population $N^v(t)$ is permanent with respect to X_0 provided that (iii) holds, and hence there is a $\delta > 0$ such that

$$\limsup_{t\to\infty} |\Phi_t(\mathbf{x}_0) - \mathcal{E}_{10}| \geq \delta \text{ for } \mathbf{x}_0 \in X_0.$$

Consequently, both $\{\mathcal{E}_{10}\}$ and $\{\mathcal{E}_{11}\}$ are isolated invariant sets in X, $W^s(\mathcal{E}_{10}) \cap X_0 = \emptyset$ and $W^s(\mathcal{E}_{11}) \cap X_0 = \emptyset$. Notice that every trajectory in M_∂ converges to either $\mathcal{E}_{10}$ or $\mathcal{E}_{11}$, and $\{\mathcal{E}_{10}\}$ and $\{\mathcal{E}_{11}\}$ are acyclic in M_∂. It follows from Theorem 4.6 in Thieme [43] that system (2.1) is uniformly persistent with respect to $(\tilde{X}_0, \partial\tilde{X}_0)$.

A well-known result in uniform persistence theory says that a bounded and uniformly persistent system has at least one interior equilibrium (see Hutson and Schmitt [21] or Theorem 2.4 in Zhao [49]). Since system (2.1) is bounded and uniformly persistent, we conclude that it has an equilibrium $\tilde{\mathcal{E}} \equiv (\tilde{S}^h, \tilde{E}^h, \tilde{I}^h, \tilde{R}^h, \tilde{S}^v, \tilde{E}^v, \tilde{I}^v) \in \tilde{X}_0$. By the first and fifth equations of (2.1), we find that $\tilde{S}^h \in \text{Int}\mathbb{R}_+^n$ and $\tilde{S}^v \in \text{Int}\mathbb{R}_+^n$, which indicates that $\tilde{\mathcal{E}}$ is an endemic equilibrium of (2.1). ∎

Remark 3.8. For $n = 1$, the theorem is an improvement of Proposition 3.3 of Ngwa and Shu [33]. By using the method in this proof, one can get similar or better results for some other epidemic metapopulation models such as those in Hsieh, van den Driessche, and Wang [20] and Salmani and van den Driessche [37].

4. The dependence of $\mathcal{R}_0$ on parameters. In an epidemic model, once the basic reproduction number is calculated and shown to be a threshold for the dynamics of the disease, a natural question about disease control is how the reproduction number depends on the model parameters. Is the dependence in a monotone way (Müller and Hadeler [29])? For a very special case of a two-patch epidemic model, Hsieh, van den Driessche, and Wang [20] showed (Theorem 4.2) that R_0 decreases when the travel rate of infected individuals increases. See also Allen et al. [1] (Lemma 3.4). In general there are very few results on this aspect. For model (2.1), it is easy to see that all parameters are directly or indirectly contained in $\mathcal{R}_0$. Obviously, $\mathcal{R}_0$ is increasing with respect to c_i^{vh}, c_i^{hv}, d_i^{hv}, or a_i^v. By Theorem 2.5.4 in Horn and Johnson [19], an increase in β_i^h, r_i^h, or γ_i^h will decrease $\mathcal{R}_0$. The dependence of $\mathcal{R}_0$ on other parameters is more complicated. For example, unlike in the single patch model, the following result indicates that in a multipatch model the parameters ν_i^h or ν_i^v can decrease or increase $\mathcal{R}_0$, and even more complicated dependence may exist. Recall that $\mathcal{R}_0^2 = \rho(M)$, where ρ denotes the spectral radius and $M = A_{64}A_{44}^{-1}A_{42}A_{22}^{-1}(A_{73} + A_{75}A_{55}^{-1}A_{53})A_{33}^{-1}A_{31}A_{11}^{-1}$. Only A_{31} and A_{11} contain ν_i^h, while only A_{42} and A_{22} contain ν_i^v. Then we have $\rho(M) = \rho(A^hA_{31}A_{11}^{-1}) = \rho(A^vA_{42}A_{22}^{-1})$, where $A^h = A_{64}A_{44}^{-1}A_{42}A_{22}^{-1}(A_{73} + A_{75}A_{55}^{-1}A_{53})A_{33}^{-1}$ and $A^v = (A_{73} + A_{75}A_{55}^{-1}A_{53})A_{33}^{-1}A_{31}A_{11}^{-1}A_{64}A_{44}^{-1}$ are positive matrices with positive determinants. For $n = 2$, that is, for the two-patch submodel, the question is reduced to a matrix problem.

PROPOSITION 4.1. *Let* $A = \left[\begin{smallmatrix} e & f \\ g & h \end{smallmatrix}\right]\left[\begin{smallmatrix} v_1 & \\ & v_2 \end{smallmatrix}\right]\left[\begin{smallmatrix} v_1+a_1+k_1 & -k_2 \\ -k_1 & v_2+a_2+k_2 \end{smallmatrix}\right]^{-1}$, *where all involving parameters are positive and satisfy* $eh > fg$. *Then* $\rho(A)$ *is decreasing in* v_1 *if*

$$\left(\left(1+\frac{a_2}{v_2}\right)(e+g) - f - h\right)k_1^2 + \left(e - h + 2g + \frac{a_2+k_2}{v_2}(e+g) + \frac{a_2}{v_2}g\right)a_1k_1 + \left(1+\frac{a_2+k_2}{v_2}\right)a_1^2 g < 0$$

and increasing otherwise.

Proof. The matrix A is the product of three matrices which correspond to A^h, A_{31}, and A_{11}^{-1} (or A^v, A_{42}, and A_{22}^{-1}) in M, respectively. So here v_i represents ν_i^h (or ν_i^v) and k_i represents φ_{ji}^E (or ψ_{ji}^E) for $i, j = 1, 2$ and $i \neq j$.

Note that A has two distinct positive eigenvalues and the inverses of the eigenvalues of A are the eigenvalues of A^{-1}. Thus it suffices to consider the monotonicity of the smaller eigenvalue $\lambda_1 = 1/\rho(A)$ of A^{-1} on v_1.

Let $\bar{a}_1 = a_1 + k_1$ and $\bar{a}_2 = a_2 + k_2$, and let $\left[\begin{smallmatrix} x & -y \\ -z & w \end{smallmatrix}\right] = \left[\begin{smallmatrix} e & f \\ g & h \end{smallmatrix}\right]^{-1}$; then $x, y, z, w > 0$ and $xw > yz$. The characteristic equation of matrix A^{-1} is $\lambda^2 - \mathcal{P}\lambda + \mathcal{Q} = 0$, where

$$\mathcal{P} = \operatorname{tr}(A^{-1}) = x(v_1 + \bar{a}_1)/v_1 + yk_1/v_1 + zk_2/v_2 + w(v_2 + \bar{a}_2)/v_2,$$
$$\mathcal{Q} = \det(A^{-1}) = (xw - yz)((v_1 + \bar{a}_1)(v_2 + \bar{a}_2) - k_1k_2)/(v_1v_2).$$

Thus, $\lambda_1 = (\mathcal{P} - \sqrt{\mathcal{P}^2 - 4\mathcal{Q}})/2$ and $\partial\lambda_1/\partial v_1 = (\dot{\mathcal{P}} - (\mathcal{P}\dot{\mathcal{P}} - 2\dot{\mathcal{Q}})/\sqrt{\mathcal{P}^2 - 4\mathcal{Q}})/2$, where $\dot{\mathcal{P}} = \partial\mathcal{P}/\partial v_1 = -(x\bar{a}_1 + yk_1)/v_1^2 < 0$ and $\dot{\mathcal{Q}} = \partial\mathcal{Q}/\partial v_1 = -(xw - yz)(\bar{a}_1(v_2 + \bar{a}_2) - k_1k_2)/(v_1^2v_2) < 0$. Then

$$\partial\lambda_1/\partial v_1 > 0 \Leftrightarrow \mathcal{P}\dot{\mathcal{P}} - 2\dot{\mathcal{Q}} < 0 \quad \text{and} \quad (\dot{\mathcal{P}})^2\mathcal{Q} + (\dot{\mathcal{Q}})^2 - \mathcal{P}\dot{\mathcal{P}}\dot{\mathcal{Q}} > 0.$$

The second inequality is equivalent to

$$(yv_2 + wk_2)k_1^2 + (xv_2 + zk_2)\bar{a}_1k_1 > (z\bar{a}_1 + wk_1)(v_2 + \bar{a}_2)\bar{a}_1. \tag{4.1}$$

Claim. Equation (4.1) implies $\mathcal{P}\dot{\mathcal{P}} - 2\dot{\mathcal{Q}} < 0$. In fact, we have

$$\begin{aligned}
-\mathcal{P}\dot{\mathcal{P}}v_1^2 &= (x(1 + \bar{a}_1/v_1) + yk_1/v_1 + zk_2/v_2 + w(1 + \bar{a}_2/v_2))(x\bar{a}_1 + yk_1)\\
&> (x + zk_2/v_2 + w(1 + \bar{a}_2/v_2))(x\bar{a}_1 + yk_1)\\
&= ((xv_2 + zk_2) + w(v_2 + \bar{a}_2))(\bar{a}_1k_1 + yk_1^2/x)x/(k_1v_2)\\
&> ((yv_2 + wk_2)k_1^2 + (xv_2 + zk_2)\bar{a}_1k_1 - wk_2k_1^2 + w(v_2 + \bar{a}_2)\bar{a}_1k_1)x/(k_1v_2)\\
&> ((z\bar{a}_1 + wk_1)(v_2 + \bar{a}_2)\bar{a}_1 - wk_2k_1^2 + w(v_2 + \bar{a}_2)\bar{a}_1k_1)x/(k_1v_2) \quad \text{by (4.1)}\\
&> (2w(v_2 + \bar{a}_2)\bar{a}_1k_1 - wk_2k_1^2)x/(k_1v_2) = (2xw\bar{a}_1(v_2 + \bar{a}_2) - xwk_1k_2)/v_2\\
&> 2(xw - yz)(\bar{a}_1(v_2 + \bar{a}_2) - k_1k_2)/v_2 = -2\dot{\mathcal{Q}}v_1^2.
\end{aligned}$$

The proof is complete by substituting $\bar{a}_1 = a_1 + k_1$ and $\bar{a}_2 = a_2 + k_2$ into (4.1). ∎

Remark 4.2. The biological interpretation of the inequality in Proposition 4.1 is not easy. However, if the emigration rate $k_1 = 0$, then the inequality is always failed and $\rho(A)$ is consistently increasing in v_1. So, the decreasing phenomenon is due to the emigration of the corresponding exposed class, and shortening the exposed period $(1/v_1)$ makes them migrate less to the other patch.

In the rest of this section, we will study the dependence of $\mathcal{R}_0$ on the movement of exposed, infectious, and recovered humans for the two-patch case. As far as we know, there are very few results on this topic (Theorem 4.2 in Hsieh, van den Driessche, and Wang [20]; see also Allen et al. [1]). Note that only A_{11} contains φ_{ij}^E and only A_{33} contains φ_{ij}^I. We know $\rho(M) = \rho(A^EA_{11}^{-1}) = \rho(A^IA_{33}^{-1})$, where $A^E = A_{64}A_{44}^{-1}A_{42}A_{22}^{-1}(A_{73} + A_{75}A_{55}^{-1}A_{53})A_{33}^{-1}A_{31}$ and $A^I = A_{31}A_{11}^{-1}A_{64}A_{44}^{-1}A_{42}A_{22}^{-1}(A_{73} + A_{75}A_{55}^{-1}A_{53})$ are positive matrices with positive determinants. We first consider the case when the travel rates of exposed, infectious, and recovered humans from one patch to the other depend on both the residence and disease status. The question then becomes a matrix problem as follows.

PROPOSITION 4.3. *Let* $A = \left[\begin{smallmatrix} e & f \\ g & h \end{smallmatrix}\right]\left[\begin{smallmatrix} a_1+k_1 & -k_2 \\ -k_1 & a_2+k_2 \end{smallmatrix}\right]^{-1}$, *where all involving parameters are positive and satisfy* $eh > fg$. *Then* $\rho(A)$ *is decreasing in* k_1 *if* $(e + g)/a_1 > (f + h)/a_2$ *and increasing otherwise.*

Proof. The matrix A is the product of two matrices which correspond to A^E and A_{11}^{-1} (or A^I and A_{33}^{-1}) in M, respectively. Here k_i represents φ_{ji}^E (or φ_{ji}^I) for $i, j = 1, 2$ and $i \neq j$.

It suffices to consider the monotonicity of the smaller eigenvalue $\lambda_1 = 1/\rho(A)$ of A^{-1} on k_1.

Let $\left[\begin{smallmatrix} x & -y \\ -z & w \end{smallmatrix}\right] = \left[\begin{smallmatrix} e & f \\ g & h \end{smallmatrix}\right]^{-1}$. Then $x, y, z, w > 0$ and $xw > yz$. The characteristic equation of matrix A^{-1} is $\lambda^2 - \mathcal{P}\lambda + \mathcal{Q} = 0$, where

$$\begin{aligned}
\mathcal{P} &= \operatorname{tr}(A^{-1}) = x(a_1 + k_1) + yk_1 + zk_2 + w(a_2 + k_2),\\
\mathcal{Q} &= \det(A^{-1}) = (xw - yz)((a_1 + k_1)(a_2 + k_2) - k_1k_2).
\end{aligned}$$

Thus, $\lambda_1 = (\mathcal{P} - \sqrt{\mathcal{P}^2 - 4\mathcal{Q}})/2$. Direct calculation yields $\partial\lambda_1/\partial k_1 = (\dot{\mathcal{P}} - (\mathcal{P}\dot{\mathcal{P}} - 2\dot{\mathcal{Q}})/\sqrt{\mathcal{P}^2 - 4\mathcal{Q}})/2$, where $\dot{\mathcal{P}} = \partial\mathcal{P}/\partial k_1 = x + y$ and $\dot{\mathcal{Q}} = \partial\mathcal{Q}/\partial k_1 = (xw - yz)a_2$. Then

$$\partial\lambda_1/\partial k_1 > 0 \Leftrightarrow \mathcal{P}\dot{\mathcal{P}} - 2\dot{\mathcal{Q}} \leq 0 \quad \text{or} \quad (\dot{\mathcal{P}})^2\mathcal{Q} + (\dot{\mathcal{Q}})^2 - \mathcal{P}\dot{\mathcal{P}}\dot{\mathcal{Q}} < 0,$$

which is equivalent to

$$(x(a_1+k_1)+yk_1+zk_2+w(a_2+k_2))(x+y)-2(xw-yz)a_2\le 0 \tag{4.2}$$

or

$$(xk_2+y(a_2+k_2))((x+y)a_1-(z+w)a_2)(xw-yz)<0. \tag{4.3}$$

Since $xk_2+y(a_2+k_2)>0$ and $xw>yz$, (4.3) is reduced to $(x+y)a_1<(z+w)a_2$. It is easy to verify that (4.2) implies (4.3). Therefore, when $(x+y)a_1<(z+w)a_2$, i.e., $(f+h)/a_2<(e+g)/a_1$, $\rho(A)$ is decreasing in k_1. ∎

Remark 4.4. The conclusion in Proposition 4.3 still holds if $e,h,a_1,a_2>0$, $f,g,k_1,k_2\ge 0$, $eh>fg$, and $hk_2+f(a_2+k_2)>0$ (namely, $k_2>0$ or $f>0$, which implies that there is also infected (exposed, infectious, or recovered) human or infected mosquito migration from patch 2 to patch 1). In particular, when only the two classes associated to k_1 and k_2 travel between patches, $\rho(A)$ is decreasing in k_1 if $(g+e)/a_1=e/a_1=\mathcal{R}_0^{(1)}>(f+h)/a_2=h/a_2=\mathcal{R}_0^{(2)}$. Biologically, this means that the disease outbreak becomes less severe if more people migrate from the high transmission area to the low transmission area.

Remark 4.5. If $hk_2+f(a_2+k_2)=0$, namely $k_2=0$ and $f=0$, which means no infected (exposed, infectious, or recovered) human or infected mosquito migrates from patch 2 to patch 1, then

$$A=\begin{bmatrix} e & 0\\ g & h\end{bmatrix}\begin{bmatrix} a_1+k_1 & 0\\ -k_1 & a_2\end{bmatrix}^{-1}=\begin{bmatrix} e/(a_1+k_1) & 0\\ (ga_2+hk_1)/((a_1+k_1)a_2) & h/a_2\end{bmatrix}.$$

We have $\rho(A)=\max\{e/(a_1+k_1),h/a_2\}$, which is nonincreasing in k_1.

The following result assumes that the travel rates of exposed, infectious, and recovered humans depend on disease states but are independent of residences (i.e., the travel rate matrices $(\varphi_{ij}^E)_{n\times n}$ and $(\varphi_{ij}^I)_{n\times n}$ are symmetric).

PROPOSITION 4.6. *Let* $A=\left[\begin{smallmatrix} e & f\\ g & h\end{smallmatrix}\right]\left[\begin{smallmatrix} a_1+k & -k\\ -k & a_2+k\end{smallmatrix}\right]^{-1}$, *where all involving parameters are positive and satisfy* $eh>fg$. *Then* $\rho(A)$ *is decreasing in* k *if* $(e+f)/a_1>(g+h)/a_2$ *and* $(e+g)/a_1>(f+h)/a_2$, *or* $(e+f)/a_1<(g+h)/a_2$ *and* $(e+g)/a_1<(f+h)/a_2$, *and increasing otherwise.*

Proof. We use the same notation as in Proposition 4.3 and consider the monotonicity of the smaller eigenvalue $\lambda_1=1/\rho(A)$ of A^{-1} on k. The characteristic equation of matrix A^{-1} is $\lambda^2-\mathcal{P}\lambda+\mathcal{Q}=0$, where $\mathcal{P}=x(a_1+k)+yk+zk+w(a_2+k)$ and $\mathcal{Q}=(xw-yz)((a_1+k)(a_2+k)-k^2)$.

Obviously, $\dot{\mathcal{P}}=\partial\mathcal{P}/\partial k=x+y+z+w$ and $\dot{\mathcal{Q}}=\partial\mathcal{Q}/\partial k=(xw-yz)(a_1+a_2)$. Then

$$\partial\lambda_1/\partial k>0\Leftrightarrow \mathcal{P}\dot{\mathcal{P}}-2\dot{\mathcal{Q}}\le 0 \quad\text{or}\quad (\dot{\mathcal{P}})^2\mathcal{Q}+(\dot{\mathcal{Q}})^2-\mathcal{P}\dot{\mathcal{P}}\dot{\mathcal{Q}}<0,$$

which is equivalent to

$$(x(a_1+k)+yk+zk+w(a_2+k))(x+y+z+w)\le 2(xw-yz)(a_1+a_2) \tag{4.4}$$

or

$$-((x+z)a_1-(y+w)a_2)((x+y)a_1-(z+w)a_2)(xw-yz)<0. \tag{4.5}$$

Since $xw > yz$, the solutions to (4.5) satisfy $(x+z)a_1 < (y+w)a_2$ and $(x+y)a_1 < (z+w)a_2$, or $(x+z)a_1 > (y+w)a_2$ and $(x+y)a_1 > (z+w)a_2$. It is easy to verify that (4.4) implies (4.5). The proof is complete. □

Remark 4.7. The monotonicity of $\rho(A)$ is still true if $e, h, a_1, a_2 > 0$, $f, g, k \geq 0$, and $eh > fg$. Epidemiologically, this means that the disease trend depends on a double-side effect. If $f = g = 0$, $\rho(A)$ is always nonincreasing in k, which means that travel can reduce the disease severity when only the two classes associated to k migrate between patches.

So far all our analyses are carried out for all three classes of humans: exposed, infectious, and recovered. However, one would expect that the effect of the recovered human movement is different from that of the other two classes. In fact, the last two propositions do not work for the movement of recovered humans R_i^h, which is related to different matrices, i.e., $\left[\begin{smallmatrix} e & f \\ g & h \end{smallmatrix}\right]\left(\left[\begin{smallmatrix} d_1 & \\ & d_2 \end{smallmatrix}\right] + \left[\begin{smallmatrix} a_1+k_1 & -k_2 \\ -k_1 & a_2+k_2 \end{smallmatrix}\right]^{-1}\right)$ and $\left[\begin{smallmatrix} e & f \\ g & h \end{smallmatrix}\right]\left(\left[\begin{smallmatrix} d_1 & \\ & d_2 \end{smallmatrix}\right] + \left[\begin{smallmatrix} a_1+k & -k \\ -k & a_2+k \end{smallmatrix}\right]^{-1}\right)$, where all parameters are positive and $eh > fg$. A tentative analysis suggests that similar, but more complicated, results may hold for the recovered class.

Therefore, for the two-patch submodel, the basic reproduction number $\mathcal{R}_0$ varies monotonically with the travel rates of exposed, infectious, and recovered humans depending on their disease states. This demonstrates that if there is enough travel of humans between the two regions, malaria can be sustained in the region with lower or no transmission. Screening at borders usually can help to identify infected individuals with symptoms but not those individuals with subpatent parasitaemia or those with only liver stage infections (exposed). The analysis in this section shows that the travel of the infected individuals, with or without symptoms, can contribute to the spread of the disease from one patch to another. Thus, as far as malaria is concerned, screening at borders is not an effective control measure.

These results can be applied to general multipatch models when the impact of population dispersal on the spatial spread of an infectious disease is concerned. When the travel rate is independent of the disease state, but may or may not be independent of residence, the relationship between $\mathcal{R}_0$ and the travel rates of exposed, infectious, and recovered humans becomes even more complicated and nonmonotone dependence can occur. We will investigate these situations by presenting some examples in the next section.

5. Numerical simulations. In the case when two patches are concerned, we study the effects of population dispersal on disease dynamics by performing numerical simulations. Some of the parameter values are chosen from the data in Chitnis, Hyman, and Cushing [8] and the references therein.

Example 5.1. To compare the importance of human movement of different exposed, infectious, and recovered classes in the geographical spread of the disease, we need to do sensitivity analysis of the basic reproduction number $\mathcal{R}_0$ on the dispersal rates $\varphi_{ij}^E, \varphi_{ij}^I$, and φ_{ij}^R, respectively.

Assume parameters in system (2.1) are as follows: $\lambda_i^h = 5.5 \times 10^{-5}$, $\mu_i^h = 8.8 \times 10^{-6}$, $\rho_i^h = 2.0 \times 10^{-7}$, $\lambda_i^v = 0.13$, $\mu_i^v = 0.033$, $\rho_i^v = 4.0 \times 10^{-5}$, $\nu_i^h = 0.1$, $\nu_i^v = 0.083$, $r_i^h = 2.2 \times 10^{-3}$, $\alpha_i^h = 4.8 \times 10^{-3}$, $\gamma_i^h = 2.0 \times 10^{-5}$, $\beta_i^h = 3.5 \times 10^{-3}$, $a_i^v = 0.14$ for $i = 1, 2$, and $c_1^{vh} = 0.11$, $c_1^{hv} = 0.08$, $d_1^{hv} = 0.02$, $c_2^{vh} = 0.02$, $c_2^{hv} = 0.337$, $d_2^{hv} = 0.06$. These parameters yield the respective basic reproduction numbers in isolation of $\mathcal{R}_0^{(1)} = 1.0127 > 1$ and $\mathcal{R}_0^{(2)} = 0.8535 < 1$. Thus, malaria is endemic in patch 1 and dies out in patch 2.

With migration between patches, we take the same travel rate for mosquitoes

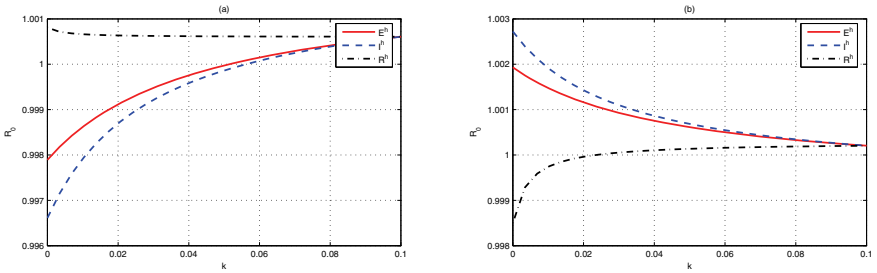

FIG. 2. *The basic reproduction number $\mathcal{R}_0$ in terms of k.* (a) $\mathcal{R}_0 = 1.0006$ *as* $k = 0.1$*; the optimal strategy for reducing $\mathcal{R}_0$ to be less than* 1 *is to restrict the travel of infectious humans.* (b) $\mathcal{R}_0 = 1.0002$ *as* $k = 0.1$*; the optimal strategy for reducing $\mathcal{R}_0$ to be less than* 1 *is to restrict the travel of recovered humans.*

from one patch to the other, namely, $\psi_{12}^S = \psi_{12}^E = \psi_{12}^I = \psi_{21}^S = \psi_{21}^E = \psi_{21}^I = 0.01$. For human movement, we assume that the travel rates are independent of residences and choose $\varphi_{12}^S = \varphi_{21}^S = 0.15$ for the susceptible. Now we keep two of the three travel rates, i.e., $\varphi_{12}^E = \varphi_{21}^E = k, \varphi_{12}^I = \varphi_{21}^I = 0.1k$, and $\varphi_{12}^R = \varphi_{21}^R = 0.4k$, fixed with $k = 0.1$ and let the remaining one decrease with k from 0.1 to 0. For example, if the first two travel rates are fixed with $k = 0.1$ and the remaining one decreases with k from 0.1 to 0, then $\varphi_{12}^E = \varphi_{21}^E = 0.1$ and $\varphi_{12}^I = \varphi_{21}^I = 0.01$, and $\varphi_{12}^R = \varphi_{21}^R = 0.4k, k \in [0, 0.1]$. The curves of $\mathcal{R}_0$ against k are illustrated in Figure 2(a). The monotonicity of the curves is predicted by Proposition 4.6. Since $\mathcal{R}_0 = 1.0006 > 1$ as $k = 0.1$, the disease is endemic in both patches by Theorem 3.7. To eradicate the disease, it is more efficient to restrict the travel of infectious humans in case we can only control the travel of one of the exposed, infectious, and recovered human classes.

However, the optimal control strategy is changed if the parameter values are varied. For example, taking the same parameters as above except that $c_2^{hv} = 0.23$ and $d_2^{hv} = 0.1365$, then $\mathcal{R}_0^{(1)} = 1.0127 > 1$, $\mathcal{R}_0^{(2)} = 0.8497 < 1$, and $\mathcal{R}_0 = 1.0002 > 1$ as $k = 0.1$. From Figure 2(b), the only choice is to strictly control the travel of the recovered humans, while travel restriction on the exposed and infectious humans has an adverse influence on disease control.

Example 5.2. For model (2.1), we present an example where the disease dies out or persists in each isolated patch but becomes endemic or extinct, respectively, when there is suitable migration between them. In fact, such a scenario may happen even for two identical patches from the aspect of ecology and epidemiology.

Case 1. $\mathcal{R}_0^{(1)} < 1$ *and* $\mathcal{R}_0^{(2)} < 1$*, but* $\mathcal{R}_0 > 1$. For $i = 1, 2$, suppose $\lambda_i^h = 5.5\times10^{-5}$, $\mu_i^h = 8.8 \times 10^{-6}$, $\rho_i^h = 2.0 \times 10^{-7}$, $\lambda_i^v = 0.13$, $\mu_i^v = 0.033$, $\rho_i^v = 4.0 \times 10^{-5}$, $\nu_i^h = 0.1$, $\nu_i^v = 0.083$, $r_i^h = 2.1 \times 10^{-3}$, $\alpha_i^h = 4.8 \times 10^{-3}$, $\gamma_i^h = 1.8 \times 10^{-5}$, $\beta_i^h = 2.7 \times 10^{-3}$, $a_i^v = 0.14$, $c_i^{vh} = 0.11$, $c_i^{hv} = 0.08$, $d_i^{hv} = 0.008$. We choose the travel rates as follows: $\varphi_{12}^S = k$, $\varphi_{12}^E = \varphi_{12}^I = \varphi_{12}^R = 0.2k$, $\varphi_{21}^S = 0.5k$, $\varphi_{21}^E = \varphi_{21}^I = \varphi_{21}^R = 0.3k$, and $\psi_{12}^S = \psi_{12}^E = \psi_{12}^I = \psi_{21}^S = \psi_{21}^E = \psi_{21}^I = 0$, where k increases from 0 to 0.10. Note that the travel rates of exposed, infectious, and recovered humans are independent of disease states but depend on their residences, and there is no mosquito migration between patches.

For the above parameter values, the dependence of $\mathcal{R}_0$ on k is shown in Figure 3. In particular, we have $\mathcal{R}_0^{(1)} = \mathcal{R}_0^{(2)} = 0.9557$, and the disease can die out in each isolated patch (see Figure 4(a)). When humans move between these two patches,

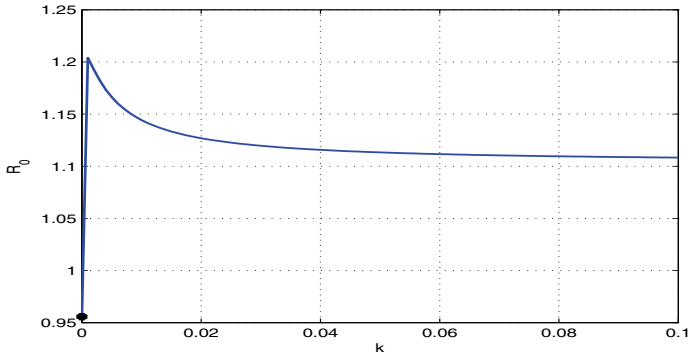

FIG. 3. $\mathcal{R}_0$ *as a function of* $k = \varphi_{12}^S$ *with* $\mathcal{R}_0^{(1)} = \mathcal{R}_0^{(2)} = 0.9557$. *The disease dies out in each isolated patch, but it becomes endemic in both patches even when there is small human movement.*

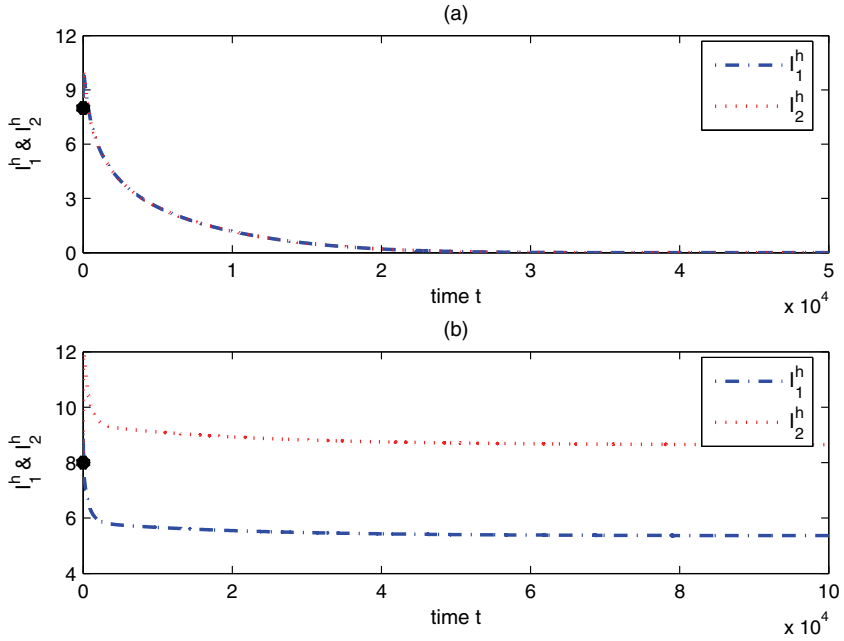

FIG. 4. *Numerical solutions of system* (2.1) *with* (a) $k = 0$ *(no human movement) and* (b) $k = 0.06$ *(the corresponding* $\mathcal{R}_0 = 1.1116$*), respectively. In both situations, the initial conditions are* $S_i^h(0) = 187, E_i^h(0) = 3, I_i^h(0) = 8, R_i^h(0) = 9, S_i^v(0) = 2310, E_i^v(0) = 10, I_i^v(0) = 4$ *for* $i = 1, 2$. *The solution in* (a) *approaches the disease-free equilibrium, while the solution in* (b) *approaches the endemic equilibrium. Note that the two trajectories in* (a) *coincide completely because they have the same initial values and the two patches have the same parameter values.*

even for a very small travel rate ($k > 10^{-5}$), $\mathcal{R}_0$ exceeds 1 and the disease becomes endemic in both patches (see Figure 4(b)), which is coincident with Theorem 3.7.

Case 2. $\mathcal{R}_0^{(1)} > 1$ *and* $\mathcal{R}_0^{(2)} > 1$, *but* $\mathcal{R}_0 < 1$. Use the same parameter values as in Case 1 except that $a_1^v = a_2^v = 0.15$ and the travel rates are different. We choose $\varphi_{12}^S = k$, $\varphi_{12}^E = \varphi_{12}^I = \varphi_{12}^R = 0.6k$, $\varphi_{21}^S = 0.5k$, $\varphi_{21}^E = \varphi_{21}^I = \varphi_{21}^R = 0.05k$, and $\psi_{12}^S = \psi_{12}^E = \psi_{12}^I = \psi_{21}^S = \psi_{21}^E = \psi_{21}^I = 0$, where k varies from 0 to 0.10. Thus,

$\mathcal{R}_0^{(1)} = \mathcal{R}_0^{(2)} = 1.0240$ and the dependence of $\mathcal{R}_0$ in k is shown in Figure 5. Suitable human movement may result in the extinction of the disease in both patches, even though the disease persists in each isolated patch (see Figure 6).

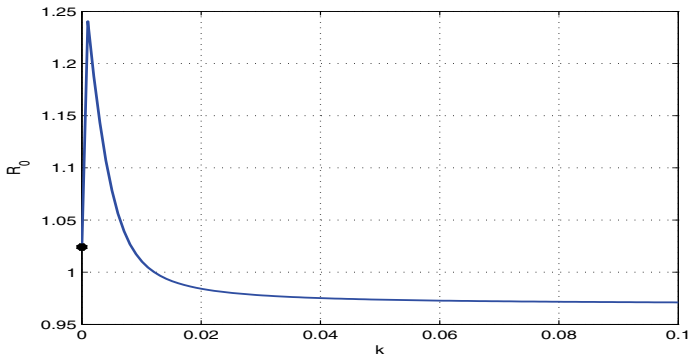

FIG. 5. *$\mathcal{R}_0$ in terms of $k = \varphi_{12}^S$ with $\mathcal{R}_0^{(1)} = \mathcal{R}_0^{(2)} = 1.0240$. The disease persists in each isolated patch, but it becomes extinct in both patches when there is suitable human movement.*

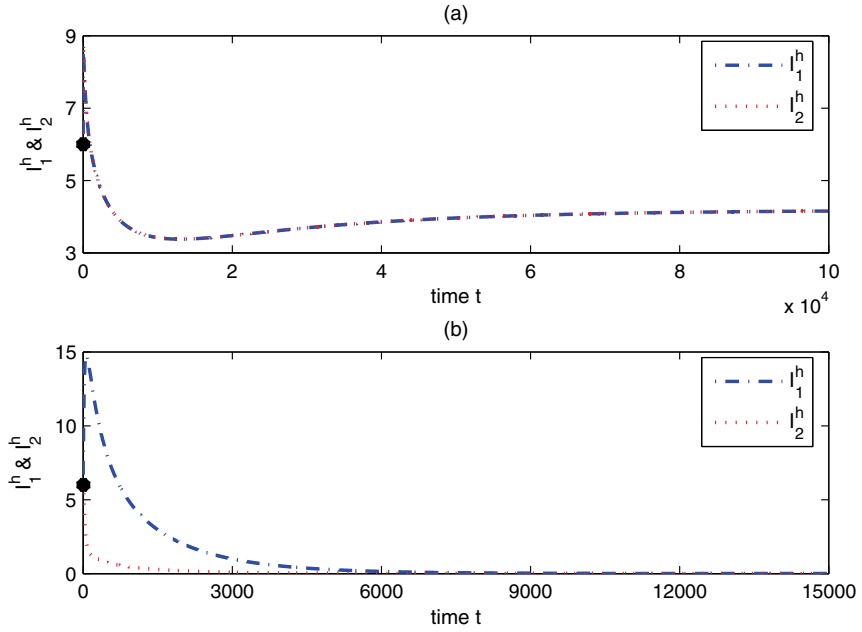

FIG. 6. *Numerical solutions of system* (2.1) *with* (a) $k = 0$ *(no human movement) and* (b) $k = 0.06$ *(the corresponding* $\mathcal{R}_0 = 0.9727$*), respectively. In both situations, the initial conditions are* $S_i^h(0) = 221, E_i^h(0) = 3, I_i^h(0) = 6, R_i^h(0) = 4, S_i^v(0) = 2150, E_i^v(0) = 8, I_i^v(0) = 7$ *for* $i = 1, 2$. *The solution in* (a) *approaches the endemic equilibrium, while the solution in* (b) *approaches the disease-free equilibrium. Note that the two trajectories in* (a) *coincide completely because the two patches have the same parameter values and the initial data are the same.*

In studying how travel affects the spatial spread of certain disease, Hsieh, van den Driessche, and Wang [20] considered two patches, a low prevalence patch with a

minor disease outbreak (basic reproduction number in isolation is less than 1) and a high prevalence patch with endemic disease (basic reproduction number in isolation is greater than 1). They numerically demonstrated the possibility that for the low prevalence patch, open travel with a high prevalence patch could lead to the endemic of the disease. However, for a high prevalence patch, open travel with a low prevalence patch could eradicate the disease. Our simulations in Example 5.2 present more interesting scenarios. Case 1 indicates that if both patches have low prevalence of the disease, travel of the exposed and infectious individuals from one patch to another would increase the chances of infecting the susceptible individuals in the second patch, and travel of susceptible individuals from one patch to another would give them more opportunities to be infected in the second patch, and vice versa. These travels would make the disease more likely to be endemic in both patches. Such a situation has also been observed in Cosner et al. [9] for a two-patch Ross–Macdonald malaria model. Case 2 is an ad hoc and probably less likely scenario which could occur when all exposed and infectious individuals from one patch moved to another while all the susceptible individuals in the second patch move to the first. This dilution of the overall prevalence could lessen the severity of the disease so that it becomes minor in both patches.

Example 5.3. Assume all parameters are as in Case 1 of Example 5.2 except that $c_1^{vh} = 0.118$, $c_1^{hv} = 0.08$, $d_1^{hv} = 0.008$, $c_2^{vh} = 0.012$, $c_2^{hv} = 0.50$, $d_2^{hv} = 0.176$, and the travel rates are different. This means that the two patches differ only in infectivity, namely, one with higher mosquito infectivity but lower human infectivity and the other with lower mosquito infectivity but higher human infectivity. Using formula (3.3), we obtain the respective basic reproduction numbers $\mathcal{R}_0^{(1)} = 0.9899 < 1$ and $\mathcal{R}_0^{(2)} = 0.9250 < 1$ for both patches in isolation. So the disease dies out in each isolated patch.

Next, when the patches are connected, we fix the travel rates of mosquitoes and susceptible humans by letting $\psi_{12}^S = \psi_{12}^E = \psi_{12}^I = \psi_{21}^S = \psi_{21}^E = \psi_{21}^I = 0.002$, $\varphi_{12}^S = \varphi_{21}^S = 0.15$, and want to see the effects of exposed, infectious, and recovered human movement on the disease dynamics. If the travel rates of exposed, infectious, and recovered humans are independent of residences and disease states, i.e., $\varphi_{12}^E = \varphi_{12}^I = \varphi_{12}^R = \varphi_{21}^E = \varphi_{21}^I = \varphi_{21}^R = k$, then $\mathcal{R}_0$ varies with k from 0 to 0.10 as shown in Figure 7.

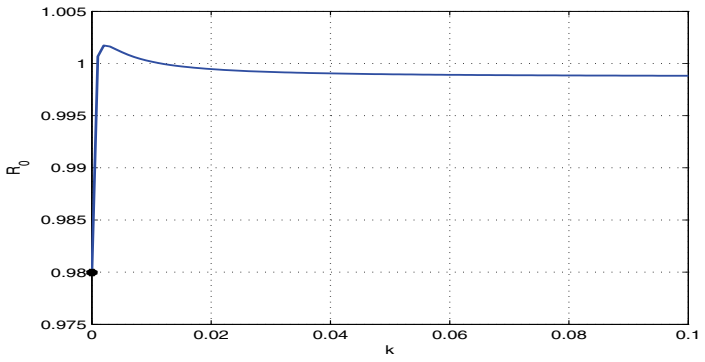

FIG. 7. *Relationship between* $\mathcal{R}_0$ *and* $k = \varphi_{12}^E = \varphi_{12}^I = \varphi_{12}^R = \varphi_{21}^E = \varphi_{21}^I = \varphi_{21}^R$. *The disease dies out when the exposed, infectious, and recovered human travel rate is small or large; it persists otherwise.*

The disease may die out if the exposed, infectious, and recovered human movement is weak. Stronger travel of exposed, infectious, and recovered humans between patches can lead the disease to become endemic in both patches. However, if the travel rate keeps increasing, the disease may again die out in both patches. This implies that inappropriate border control on exposed, infectious, and recovered humans could have negative results. Observe that it is also an example where $\mathcal{R}_0$ is not monotone in the exposed, infectious, and recovered human travel rate, which is independent of residence and disease state.

6. Discussion. Malaria is one of the world's most common infectious diseases and is a major cause of child death and poverty in Africa. This issue may become even more serious due to many factors such as the rapid expansion of modern transportation, urbanization in developing countries, deforestation, and so on. In this paper, taking the transmission heterogeneity into account, we proposed a multipatch model to study the impact of mobility of vector and host populations on malaria transmission. We have discussed the existence and stability of the disease-free equilibrium of the model and obtained a formula for the basic reproduction number $\mathcal{R}_0$. By applying some matrix inequalities, bounds on $\mathcal{R}_0$ were given. A sufficient condition was obtained to guarantee the existence of an endemic equilibrium. Then the dependence of $\mathcal{R}_0$ on the model parameters was analyzed. In particular, for a two-patch model, we studied the monotonicity of $\mathcal{R}_0$ in terms of the travel rates of exposed, infectious, and recovered humans. Our analysis indicates that $\mathcal{R}_0$ varies monotonously with the movement of exposed, infectious, and recovered humans, which depends on the disease state. We should mention that the monotonicity also holds for mosquito movement. Finally, three numerical examples were given to illustrate the impact of population dispersal on the disease spread. The first example explores the role of different exposed, infectious, and recovered classes in the disease propagation. The second shows that suitable human movement can both intensify and mitigate the disease spread even for two identical patches. In the last example, two patches which only differ in infectivity of humans and mosquitoes are concerned. Nonmonotonicity of $\mathcal{R}_0$ in the exposed, infectious, and recovered human travel rates, which are independent of the residence and disease state, is observed. These results suggest that human movement is a critical factor in the spatial spread of malaria around the world. Since the travel of exposed (latently infected) human individuals can also spread the disease geographically and screening at borders usually can only help to identify those infected with symptoms, inappropriate border control may make the disease transmission even worse, and to control or eliminate malaria we need global and regional strategies (Tatem and Smith [42]). Accordingly, a full understanding of its movement is important in designing effective antimalaria measures.

There is still much work to do with our model. First, we are interested in the global stability of the disease-free equilibrium when $\mathcal{R}_0 < 1$. Unfortunately, it is difficult to give an explicit formula for the disease-free equilibrium (even for $n = 2$), so is $\mathcal{R}_0$. Even if we obtained such a formula, it is too complicated to use it directly. Unlike models in Salmani and van den Driessche [37] and Hsieh, van den Driessche, and Wang [20], here we cannot use a comparison theorem for the vector-host model using their methods. Second, the existence, uniqueness, and stability of the endemic equilibrium is in general unclear. Third, the dependence of $\mathcal{R}_0$ on travel rates for three or more patches submodels would be extremely complicated since the interaction networks are more complex. However, at least we can do some numerical simulations. Furthermore, it is interesting to test our model with field data and carry out sensitivity

analysis to develop efficient intervention strategies.

We remark that there are many possibilities to generalize the ODEs model studied here to increase realism. For example, in the model it is assumed that all parameters are constant. In fact, the biological activity and geographic distribution of malaria parasite and its vector are greatly influenced by climatic factors such as rainfall, temperature, and humidity (Martens et al. [28], Smith, Dushoff, and McKenzie [38]). The impact of climate change can be investigated by assuming some parameters to be time or temperature dependent. It is also important to consider stochastic versions of these models. The basic modeling approach of dividing the population into subclasses according to their locations and then observing their moving behavior can be viewed as a Markov process with random coefficients (Langevin formulation) or with known transition probabilities between regions. We leave all these for future consideration.

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