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Transmission Dynamics of Some Epidemiological Patch Models

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TRANSMISSION DYNAMICS OF SOME EPIDEMIOLOGICAL PATCH MODELS

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As we known, infectious diseases can be transmitted from one region to another due to extensive travel and migration. Meanwhile, different regions have different demographic and epidemiological characteristics. To capture these features, multi-patch epidemic models have been developed to study disease transmission in heterogeneous environments. These models are usually described by a system of differential equations with the dynamics of each patch coupled to that of other patches by population dispersal. Typically, a patch may represent a city, a village, or a biological habitat. A full understanding the effect of travel on the spatial spread of disease between patches can definitely improve disease control and prevention measures. In this thesis, we propose several epidemic models in a patchy environment to investigate some specific epidemiological problems.

In the first chapter , a susceptible-infectious-susceptible patch model with nonconstant transmission coefficients is formulated to investigate the effect of media coverage and human movement on the spread of infectious diseases among patches. The basic reproduction number $\mathcal{R}_0$ is determined. It is shown that the disease-free equilibrium is globally asymptotically stable if $\mathcal{R}_0 \leq 1$, and the disease is uniformly persistent and there exists at least one endemic equilibrium if $\mathcal{R}_0 > 1$. In particular, when the disease is nonfatal and the travel rates of susceptible and infectious individuals in each

patch are the same, the endemic equilibrium is unique and is globally asymptotically stable as $\mathcal{R}_0 > 1$. Numerical calculations are performed to illustrate some results for the case with two patches.

In chapter 2, we propose a multi-patch 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.

In Chapter 3, based on the classical Ross-Macdonald model, we propose a periodic malaria model to incorporate the effects of temporal and spatial heterogeneity in disease transmission. We define the basic reproduction number $\mathcal{R}_0$ and show that either the disease-free periodic solution or the positive periodic solution is globally asymptotically stable. Numerical simulations are conducted to confirm the analytical results.

Chapter 4 is devoted to studying the spatial spread of Rift Valley fever in Egypt. We propose a three-patch model for the process that animals enter Egypt from Sudan are moved up the Nile, and then consumed at the feast. The basic reproduction number for each patch is introduced and then the threshold dynamics of the model is established. We simulate an interesting scenario showing possible explanation to the

observed phenomenon in Egypt.

Finally, we summarize the main results of this thesis and list some possible future research directions in Chapter 5.

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Chapter 1

An SIS Patch Model with Variable Transmission Coefficients

1.1 Background

It has been observed that media coverage can affect the spread and control of infectious diseases (see Liu et al. [50] and the references cited therein). During outbreaks of serious infectious diseases such as the SARS outbreak in 2003 and the H1N1 influenza pandemic in 2009, public media has massive reports on the number of infections and deaths per day, the locations where these happen, the symptoms of the disease, the proper protections to decrease the possibility of being infected, etc. People follow the reports and thus choose to protect themselves by reducing their social activities and direct contact with others, especially with those high-risk groups, which could therefore lead to a reduction of effective contacts between susceptible individuals and infectious individuals. In a recent paper [20], Cui et al. proposed an SIS (susceptible-infectious-susceptible) epidemiological model incorporating media coverage

$$\begin{aligned} \frac{dS}{dt} &= A - dS - \beta(I)\frac{SI}{S+I} + \gamma I, \\ \frac{dI}{dt} &= \beta(I)\frac{SI}{S+I} - (d+\nu+\gamma)I, \end{aligned} \tag{1.1.1}$$

where the transmission coefficient $\beta(I)$ is a nonincreasing function of the number of the infectious individuals. They defined a threshold for (1.1.1) below which all orbits converge to the disease-free equilibrium and above which all orbits with $I(0) > 0$ converge to a unique endemic equilibrium.

In this chapter, we shall study an SIS patch model for the transmission of an infectious disease with population dispersal among p patches. Within a single patch, our model is based on that of Cui et al. [20]. Let $S_i(t)$ and $I_i(t)$ denote, respectively, the number of susceptible and infectious individuals in patch i at time t. The population dynamics are described by the following system of ordinary differential equations with nonnegative initial conditions:

$$\begin{aligned} \frac{dS_i}{dt} &= A_i - d_i S_i - \beta_i(I_i)\frac{S_i I_i}{S_i + I_i} + \gamma_i I_i + \sum_{j=1}^{p} m_{ij} S_j,\ 1 \le i \le p, \\ \frac{dI_i}{dt} &= \beta_i(I_i)\frac{S_i I_i}{S_i + I_i} - (d_i + \nu_i + \gamma_i) I_i + \sum_{j=1}^{p} n_{ij} I_j,\ 1 \le i \le p. \end{aligned} \tag{1.1.2}$$

In patch i, $A_i > 0$ is the recruitment rate, $d_i > 0$ is the natural death rate, $\gamma_i > 0$ is the recovery rate and $\nu_i \ge 0$ is the disease-induced death rate. The transmission coefficient in patch i is $\beta_i(I_i) = a_i - b_i f_i(I_i)$, where a_i is the usual transmission coefficient without considering the impact of media reported number of infective individuals, b_i is the maximum reduced transmission coefficient due to the media effect and $f_i(I_i)$ is a saturation function to measure the impact of the reported number of infected individuals. Similar to Cui et al [20], we assume that

$$a_i > b_i \ge 0,\ f_i(0) = 0,\ f_i(I_i) \in C^1([0,\infty)) \text{ with } f_i'(I_i) \ge 0,\ \lim_{I_i \to \infty} f_i(I_i) = 1$$

for $i = 1, \ldots, p$. Typical examples of $f_i(I_i)$ with such properties are $1 - k_i/(k_i + I_i^{n_i})$ with $k_i > 0$ and $n_i > 0$, and $1 - e^{-k_i I_i}$ with $k_i > 0$. When $b_i = 0$ for $i = 1, 2, \ldots, p$, i.e., the media impact is ignored, model (1.1.2) with two patches was studied in Salmani and van den Driessche [76]. The immigration rates from patch j to patch i for $i \neq j$ of susceptible and infectious humans are denoted, respectively, by $m_{ij} \geq 0$ and $n_{ij} \geq 0$, while the emigration rates of susceptible and infectious humans in patch i are denoted, respectively, by $-m_{ii} \geq 0$ and $-n_{ii} \geq 0$. For simplicity, deaths and births during travel are neglected. Thus, we have

$$\sum_{j=1}^{p} m_{ji} = 0 \text{ and } \sum_{j=1}^{p} n_{ji} = 0 \text{ for } i = 1, 2, \ldots, p.$$

Unless otherwise indicated, the travel rate matrices $(m_{ij})_{p\times p}$ and $(n_{ij})_{p\times p}$ are assumed to be irreducible.

The organization of this chapter is as follows. In Section 2, the basic reproduction number $\mathcal{R}_0$ is defined and it is shown to be a threshold of the disease dynamics. Namely, the disease can be eradicated if $\mathcal{R}_0 \leq 1$ and will be endemic if $\mathcal{R}_0 > 1$. In Section 3, we consider the special case when susceptible and infectious individuals have identical travel rates and there is no disease-induced death, and present a global qualitative analysis. In the final section, we conclude with some numerical examples and a brief discussion.

1.2 Threshold Dynamics

We first introduce some notations which will be used throughout this chapter. Let $\mathbb{R}^p_+ = \{x \in \mathbb{R}^p : x_i \geq 0 \text{ for } 1 \leq i \leq p\}$ be the positive orthant in $\mathbb{R}^p$ and $\text{Int}\mathbb{R}^p_+ = \{x \in$

$\mathbb{R}^p : x_i > 0 \text{ for } 1 \le i \le p\}$ be the interior of $\mathbb{R}^p_+$. We write $x \le y$ and $y \ge x$ whenever $y - x \in \mathbb{R}^p_+$, $x < y$ and $y > x$ whenever $y - x \in \mathbb{R}^p_+$ and $x \ne y$, and $x \ll y$ and $y \gg x$ whenever $y - x \in \text{Int}\mathbb{R}^p_+$. If $x, y \in \mathbb{R}^p_+$ and $x \le y$, we let $[x, y] = \{z \in \mathbb{R}^p_+ : x \le z \le y\}$.

Let $N_i(t) = S_i(t) + I_i(t)$ be the total population in patch i at time t, and let the new infection term in patch i equal zero whenever $N_i = 0$ (Greenhalgh [29]). The following result indicates that model (1.1.2) is mathematically and biologically well posed.

Theorem 1.1. *Consider system* (1.1.2) *with non-negative initial conditions. Then the system has a unique solution defined for all time* $t \ge 0$*, and all disease state variables remain non-negative. Moreover, the total population* $N(t) = \sum_{i=1}^{p} N_i(t)$ *is bounded.*

Proof. The vector field defined by (1.1.2) is Lipschitzian in each compact set in $\mathbb{R}^{2p}_+$, so the initial value problem has a unique solution which exists for all $t \ge 0$ (Zhang et al. [102]). The non-negative property of state variables can be immediately verified.

Let $\mathcal{A} = \sum_{i=1}^{p} A_i$ and $\mathcal{D} = \min_{1 \le i \le p} d_i$. Since

$$\frac{dN}{dt} = \sum_{i=1}^{p} (A_i - d_i N_i - \nu_i I_i) \le \sum_{i=1}^{p} (A_i - d_i N_i) \le \mathcal{A} - \mathcal{D}N,$$

by a comparison theorem, $N(t)$ is bounded above by $\max\{\mathcal{A}/\mathcal{D}, N(0)\}$. □

1.2.1 Basic Reproduction Number

Let the right hand side of (1.1.2) be zero, one can verify that model (1.1.2) always admits a disease-free equilibrium (DFE), denoted by $E_0 = (S_1^0, S_2^0, \ldots, S_p^0, 0, 0, \ldots, 0)$. Indeed, there is a DFE if and only if $S^0 = (S_1^0, S_2^0, \ldots, S_p^0)$ satisfies $B(S^0)^T = \mathbf{A}$, where

$B = (\delta_{ij}d_i - m_{ij})_{p\times p}$ and $\mathbf{A} = (A_1, A_2, \ldots, A_p)^T$. Here δ_{ij} denotes the Kronecker delta (i.e. 1 when $i = j$ and 0 otherwise). It follows from Corollary 4.3.2 in Smith [80] that B^{-1} is a positive matrix. Hence $S^0 = (B^{-1}\mathbf{A})^T \gg 0$ guarantees the existence and uniqueness of the disease-free equilibrium.

Now, we calculate the basic reproduction number of (1.1.2). Using the recipe of van den Driessche and Watmough [90], we have

$$F = (\delta_{ij}a_i)_{p\times p} \quad \text{and} \quad V = (\delta_{ij}(d_i + \nu_i + \gamma_i) - n_{ij})_{p\times p}.$$

Therefore, the basic reproduction number is $\mathcal{R}_0 = \rho(FV^{-1})$, where ρ denotes the spectral radius and it is the same as that of the classical model with fixed transmission coefficients.

Observe that $\mathcal{R}_0$ is independent of the parameters A_i, b_i for $i = 1, 2, \ldots, p$, and the travel rates of susceptible individuals. It is easy to see that $\mathcal{R}_0$ is increasing in a_i while it is decreasing with respect to d_i, ν_i and γ_i. The following estimation on the basic reproduction number was already showed by Wang and Mulone [93] and Salmani and van den Driessche [76] for $p = 2$, so here is an interesting generalization for general p.

Proposition 1.2. *Let $\mathcal{R}_0^{(i)} = a_i/(d_i + \nu_i + \gamma_i)$ be the basic reproduction number for patch i in isolation and write $\tilde{\mathcal{R}}_0^{(i)} = a_i/(d_i + \nu_i + \gamma_i - n_{ii})$ as a modified reproduction number that contains travel of infectives out of patch i. Then*

$$\max\{\max_{1\le i\le p} \tilde{\mathcal{R}}_0^{(i)}, \min_{1\le i\le p} \mathcal{R}_0^{(i)}\} \le \mathcal{R}_0 \le \max_{1\le i\le p} \mathcal{R}_0^{(i)}.$$

Proof. The inequality $\max\limits_{1\leq i\leq p}\tilde{\mathcal{R}}_0^{(i)} \leq \mathcal{R}_0 \leq \max\limits_{1\leq i\leq p}\mathcal{R}_0^{(i)}$ follows a similar analysis used in the proof of Theorem 3.4 in Gao and Ruan [28]. It then suffices to prove that $\min\limits_{1\leq i\leq p}\mathcal{R}_0^{(i)} \leq \mathcal{R}_0$.

Let $c_i = d_i + \nu_i + \gamma_i$ for $i = 1, 2, \ldots, p$ and $s(\cdot)$ denote the spectral bound of a matrix. Since V has a positive inverse, FV^{-1} is a positive matrix. Using the Perron-Frobenius theorem, $\mathcal{R}_0 = s(FV^{-1})$ is a simple eigenvalue of FV^{-1} associated to a positive eigenvector $\mathbf{v}$ and any eigenvector $\mathbf{w} > 0$ of FV^{-1} is a positive multiple of $\mathbf{v}$ (see Smith [80]). Hence, $FV^{-1}\mathbf{v} = \mathcal{R}_0\mathbf{v}$, which is equivalent to $-VF^{-1}\mathbf{v} = -\frac{1}{\mathcal{R}_0}\mathbf{v}$, where

$$-VF^{-1} = (n_{ij})_{p\times p}F^{-1} - diag\{1/\mathcal{R}_0^{(1)}, 1/\mathcal{R}_0^{(2)}, \ldots, 1/\mathcal{R}_0^{(p)}\}.$$

Since $-VF^{-1}$ is a quasi-positive and irreducible matrix and $\mathbf{v}$ is positive, we conclude that $s(-VF^{-1}) = -1/\mathcal{R}_0$. The facts $M_L \leq -VF^{-1} \leq M_U$ and $s((n_{ij})_{p\times p}F^{-1}) = 0$ imply that

$$s(M_L) = -\max_{1\leq i\leq p}\frac{1}{\mathcal{R}_0^{(i)}} \leq s(-VF^{-1}) = -1/\mathcal{R}_0 \leq s(M_U) = -\min_{1\leq i\leq p}\frac{1}{\mathcal{R}_0^{(i)}},$$

where

$$M_L = (n_{ij})_{p\times p}F^{-1} - \max_{1\leq i\leq p}\frac{1}{\mathcal{R}_0^{(i)}}\cdot diag\{1, 1, \ldots, 1\},$$
$$M_U = (n_{ij})_{p\times p}F^{-1} - \min_{1\leq i\leq p}\frac{1}{\mathcal{R}_0^{(i)}}\cdot diag\{1, 1, \ldots, 1\}.$$

A direct simplification completes the proof of the proposition. □

Remark 1.3. By the results in Hadeler and Thieme [32], $s(-VF^{-1})$ depends in a monotone way on the travel rate of infectious humans n_{ij} for $i, j = 1, 2, \ldots, p$ and

$i \neq j$. More precisely, it is always strictly decreasing or strictly increasing or it is constant. So is $\mathcal{R}_0 = -1/s(-VF^{-1})$.

Like in the single patch model (1.1.2) or many other epidemic models, we have the global stability of the DFE for system (1.1.2) as $\mathcal{R}_0 < 1$.

Theorem 1.4. *The DFE of system* (1.1.2) *is globally asymptotically stable (GAS) if* $\mathcal{R}_0 \leq 1$ *and unstable if* $\mathcal{R}_0 > 1$.

Proof. From Theorem 2 in van den Driessche and Watmough [90], E_0 is locally asymptotically stable if $\mathcal{R}_0 < 1$, but unstable if $\mathcal{R}_0 > 1$. Now it suffices to prove that all solutions converge to the DFE when $\mathcal{R}_0 \leq 1$. The inequalities $S_i/N_i \leq 1$ and $\beta_i(I_i) \leq a_i$ yield

$$\frac{dI_i}{dt} \leq a_i I_i - (d_i + \nu_i + \gamma_i)I_i + \sum_{j=1}^{p} n_{ij} I_j, \ 1 \leq i \leq p.$$

By applying the algorithm in Kamgang and Sallet [44], we know that the DFE is GAS whenever $\mathcal{R}_0 \leq 1$ (or like in Sun et al. [85], by a standard comparison theorem). □

1.2.2 Uniform Persistence

Using the techniques of persistence theory (Zhao [104]), we can show the uniform persistence of the disease and the existence of at least one endemic equilibrium when $\mathcal{R}_0 > 1$. Thus, the basic reproduction number $\mathcal{R}_0$ is a threshold parameter of the disease dynamics. The proof below is analogous to those of Theorem 2.3 in Wang and Zhao [94] and Theorem 4.1 in Gao and Ruan [28].

Theorem 1.5. *For model* (1.1.2)*, if* $\mathcal{R}_0 > 1$*, then the disease is uniformly persistent, i.e., there exists a constant* $\kappa > 0$ *such that every solution* $\phi_t(\mathbf{x}_0) \equiv (S_1(t), \ldots, S_p(t), I_1(t), \ldots, I_p(t))$ *of system* (1.1.2) *with* $\mathbf{x}_0 \equiv (S_1(0), \ldots, S_p(0), I_1(0), \ldots, I_p(0)) \in \mathbb{R}^p_+ \times \mathbb{R}^p_+ \backslash \{0\}$ *satisfies*

$$\liminf_{t\to\infty} I_i(t) > \kappa \text{ for } i = 1, 2, \ldots, p,$$

and (1.1.2) *admits at least one endemic equilibrium.*

Proof. Let

$$\begin{aligned} X &= \{(S_1, \ldots, S_p, I_1, \ldots, I_p) : S_i \geq 0, I_i \geq 0, i = 1, 2, \ldots, p\}, \\ X_0 &= \{(S_1, \ldots, S_p, I_1, \ldots, I_p) \in X : I_i > 0, i = 1, 2, \ldots, p\}, \\ \partial X_0 &= X \backslash X_0 = \{(S_1, \ldots, S_p, I_1, \ldots, I_p) \in X : I_i = 0 \text{ for some } i \in \{1, 2, \ldots, p\}\}. \end{aligned}$$

It suffices to prove that ∂X_0 repels uniformly the solutions of system (1.1.2) in X_0. Clearly, ∂X_0 is relatively closed in X. It is immediate that X and X_0 are positively invariant. Theorem 1.1 implies that system (1.1.2) is point dissipative.

Denote $M_\partial = \{\mathbf{x}_0 \in \partial X_0 : \phi_t(\mathbf{x}_0) \in \partial X_0 \text{ for } t \geq 0\}$ and $D = \{\mathbf{x}_0 \in X : I_i = 0, i = 1, 2, \ldots, p\}$. Obviously, $D \subset M_\partial$. On the other hand, we have $I_1(0) + \cdots + I_p(0) > 0$ for any $\mathbf{x}_0 \in \partial X_0 \backslash D$. By the irreducibility of the travel rate matrix $(n_{ij})_{p\times p}$, we know that $\phi_t(\mathbf{x}_0) \in X_0$ for all $t > 0$. Therefore, $\mathbf{x}_0 \notin M_\partial$ and $M_\partial \subset D$, which implies that $M_\partial = D$.

The disease-free equilibrium E_0 is the unique equilibrium in M_∂. Let $W^s(E_0)$ be

the stable manifold of E_0. We now show that $W^s(E_0) \cap X_0 = \emptyset$ when $\mathcal{R}_0 > 1$. Let

$$M_\epsilon = F - V - diag\{a_1\epsilon + b_1\epsilon - b_1\epsilon^2, \ldots, a_p\epsilon + b_p\epsilon - b_p\epsilon^2\}.$$

Since $s(F - V) > 0$ if and only if $\mathcal{R}_0 > 1$, there is an $\epsilon_1 > 0$ such that $s(M_\epsilon) > 0$ for $\epsilon \in [0, \epsilon_1]$. Choose η small enough such that

$$S_i(0)/N_i(0) \geq 1 - \epsilon_1 \text{ and } f_i(I_i(0)) \leq \epsilon_1 \text{ for } i = 1, \ldots, p, \ \|\mathbf{x}_0 - E_0\| \leq \eta.$$

We claim that $\limsup_{t\to\infty} \|\phi_t(\mathbf{x}_0) - E_0\| > \eta$ for $\mathbf{x}_0 \in X_0$, where $\|\cdot\|$ is the usual Euclidean norm. Suppose not, after translation, we have $\|\phi_t(\mathbf{x}_0) - E_0\| \leq \eta$ for all $t \geq 0$ and hence

$$\frac{dI_i}{dt} \geq (a_i - b_i\epsilon_1)(1 - \epsilon_1)I_i - (d_i + \nu_i + \gamma_i)I_i + \sum_{j=1}^{p} n_{ij}I_j, \ 1 \leq i \leq p.$$

Notice that M_{ϵ_1} has a positive eigenvalue $s(M_{\epsilon_1})$ associated to a positive eigenvector. It follows from a comparison theorem that $I_i(t) \to \infty$ as $t \to \infty$ for $i = 1, 2, \ldots, p$, a contradiction.

Since E_0 is globally stable in M_∂, it follows that $\{E_0\}$ is an isolated invariant set and acyclic. By Theorem 4.6 in Thieme [88], system (1.1.2) is uniformly persistent with respect to $(X_0, \partial X_0)$. Furthermore, by Theorem 2.4 in Zhao [103], we know that system (1.1.2) has an equilibrium $\bar{E} = (\bar{S}_1, \ldots, \bar{S}_p, \bar{I}_1, \ldots, \bar{I}_p) \in X_0$. The first equation of (1.1.2) ensures that $\bar{S}_i > 0$ for $i = 1, \ldots, p$. This means that $\bar{E}$ is an endemic equilibrium of system (1.1.2). □

Remark 1.6. Neither the travel of susceptible individuals nor the media coverage affects the persistence and extinction of the disease. By Proposition 1.2, if $\mathcal{R}_0^{(i)} > 1$ (or ≤ 1) for $i = 1, 2, \ldots, p$, then $\mathcal{R}_0 > 1$ (or ≤ 1). Biologically, this means that the disease persists or dies out in each isolated patch then remains persistent or extinct, respectively, when human movement occurs.

1.3 Model with Restrictions

In the case where there is no disease-induced death (i.e., $\nu_i = 0$ for $i = 1, 2, \ldots, p$) and susceptible and infectious individuals have identical travel rates (i.e., $m_{ij} = n_{ij}$ for $i, j = 1, 2, \ldots, p$), the dynamics of the individuals are governed by the following model:

$$\begin{aligned} \frac{dS_i}{dt} &= A_i - d_i S_i - \beta_i(I_i)\frac{S_i I_i}{S_i + I_i} + \gamma_i I_i + \sum_{j=1}^{p} m_{ij} S_j, \ 1 \leq i \leq p, \\ \frac{dI_i}{dt} &= \beta_i(I_i)\frac{S_i I_i}{S_i + I_i} - (d_i + \gamma_i) I_i + \sum_{j=1}^{p} m_{ij} I_j, \ 1 \leq i \leq p. \end{aligned} \tag{1.3.1}$$

Sun et al. [85] presented a global qualitative analysis for system (1.3.1) with two-patch when $\mathcal{R}_0 > 1$. Here we study the model with an arbitrary number of patches by using the theory of monotone dynamical systems (Smith [80]).

Theorem 1.7. *If $\mathcal{R}_0 > 1$, then system* (1.3.1) *has a unique endemic equilibrium which is globally asymptotically stable relative to $\mathbb{R}_+^p \times \mathbb{R}_+^p \backslash \{0\}$.*

Proof. Adding the two equations in system (1.3.1) leads to

$$\frac{dN_i}{dt} = A_i - d_i N_i + \sum_{j=1}^{p} m_{ij} N_j, \ 1 \leq i \leq p. \tag{1.3.2}$$

Obviously, system (1.3.2) has a unique equilibrium, labeled by $N^* = (N_1^*, N_2^*, \ldots, N_n^*)$, which is equal to $S^0 = (S_1^0, S_2^0, \ldots, S_p^0)$ and is globally asymptotically stable for (1.3.2). System (1.3.1) is then equivalent to the following system

$$\begin{aligned} \frac{dN_i}{dt} &= A_i - d_i N_i + \sum_{j=1}^{p} m_{ij} N_j,\ 1 \le i \le p, \\ \frac{dI_i}{dt} &= \beta_i(I_i)\frac{N_i - I_i}{N_i} I_i - (d_i + \gamma_i) I_i + \sum_{j=1}^{p} m_{ij} I_j,\ 1 \le i \le p. \end{aligned} \tag{1.3.3}$$

Since $N_i(t) \to N_i^*, i = 1, 2, \ldots, p$, as $t \to \infty$, (1.3.3) gives the following limit system

$$\frac{dI_i}{dt} = h_i(I_1, \ldots, I_p) = \beta_i(I_i)\frac{N_i^* - I_i}{N_i^*} I_i - (d_i + \gamma_i) I_i + \sum_{j=1}^{p} m_{ij} I_j,\ i = 1, 2, \ldots, p. \tag{1.3.4}$$

Let $h : \mathbb{R}_+^p \to \mathbb{R}^p$ denote the vector field described by (1.3.4) and ψ_t denote the corresponding flow. For any $\alpha \in (0, 1)$ and any $(I_1, \ldots, I_p) \in \mathrm{Int}\mathbb{R}_+^p \cap \mathbb{D}$ with $\mathbb{D} = [0, N^*]$, there hold

$$\begin{aligned} &\beta_i(\alpha I_i)\frac{N_i^* - \alpha I_i}{N_i^*}\alpha I_i - (d_i + \gamma_i)\alpha I_i + \sum_{j=1}^{p} m_{ij}\alpha I_j \\ >&\alpha\left(\beta_i(I_i)\frac{N_i^* - I_i}{N_i^*} I_i - (d_i + \gamma_i) I_i + \sum_{j=1}^{p} m_{ij} I_j\right),\ i = 1, 2, \ldots, p, \end{aligned}$$

that is, $h(\alpha(I_1, \ldots, I_p)) \gg \alpha h(I_1, \ldots, I_p)$. Thus h is strongly sublinear on $\mathbb{D}$. In addition, $\mathbb{D}$ is positively invariant for (1.3.4) since

$$h_i(N^*) = -(d_i + \gamma_i)N_i^* + \sum_{j=1}^{p} m_{ij} N_j^* = -A_i - \gamma_i N_i^* < 0, i = 1, 2, \ldots, p.$$

Note that the Jacobian matrix of system (1.3.4) at the origin, $Dh(0)$, satisfies $s(Dh(0)) = s(F - V) > 0$. It is easy to see that Corollary 3.2 in Zhao and Jing [105] also holds if $\mathbb{R}^p_+$ is replaced by a positively invariant order interval in $\mathbb{R}^p_+$. Therefore, system (1.3.4) has a positive equilibrium $I^* = (I^*_1, I^*_2, \ldots, I^*_p) \in \mathbb{D}$, which is globally asymptotically stable in $\mathbb{D}\backslash\{0\}$. It is clear from the first equation of (1.3.1) that $S^*_i = N^*_i - I^*_i > 0$ for $i = 1, 2, \ldots, p$. Hence (1.3.1) admits a unique positive equilibrium $E^* = (S^*_1, S^*_2, \ldots, S^*_p, I^*_1, I^*_2, \ldots, I^*_p)$.

Next, we prove that every nontrivial solution to (1.3.4) in $\mathbb{R}^p_+$ converges to I^*. We claim that (1.3.4) has no equilibrium in $\mathbb{R}^p_+\backslash\mathbb{D}$. Assume, by contrary, that $I^{**} = (I^{**}_1, \ldots, I^{**}_p)$ is an equilibrium of (1.3.4) in $\mathbb{R}^p_+\backslash\mathbb{D}$. It follows from the strong monotonicity of the flow ψ_t that $I^* \ll I^{**}$. From (1.3.4), we have $M^*(I^*)^T = 0$ and $M^{**}(I^{**})^T = 0$, where $M^* = ((\beta_i(I^*_i)(N^*_i - I^*_i)/N^*_i - (d_i + \gamma_i))\delta_{ij} + m_{ij})_{p\times p}$ and $M^{**} = ((\beta_i(I^{**}_i)(N^*_i - I^{**}_i)/N^*_i - (d_i + \gamma_i))\delta_{ij} + m_{ij})_{p\times p}$. Then $s(M^*) = s(M^{**}) = 0$, which is in contradiction to

$$M^* - M^{**} = ((\beta_i(I^*_i)(N^*_i - I^*_i)/N^*_i - \beta_i(I^{**}_i)(N^*_i - I^{**}_i)/N^*_i)\delta_{ij})_{p\times p} > 0.$$

So, I^* is the unique nontrivial equilibrium of (1.3.4) in $\mathbb{R}^p_+$. For any $\mathbf{y}_0 \in \mathbb{R}^p_+\backslash\mathbb{D}$, we have $\mathbf{y}_0 \ll lN^*$ for sufficiently large $l > 1$ and therefore $\psi_t(\mathbf{y}_0) \ll \psi_t(lN^*)$ for $t \geq 0$. Note that $h(lN^*) \ll 0$ for $l \geq 1$, so $\psi_t(lN^*) \to I^*$ as $t \to \infty$. This means that $\psi_t(\mathbf{y}_0)$ enters into $\mathbb{D}$ for large t and thus $\psi_t(\mathbf{y}_0)$ approaches I^* as $t \to \infty$.

Since both systems (1.3.2) and (1.3.4) are locally (globally) asymptotically stable, system (1.3.3) has $\mathcal{E}^* = (N^*_1, N^*_2, \ldots, N^*_p, I^*_1, I^*_2, \ldots, I^*_p)$ as a locally asymptotically stable state (Vidyasagar [91]). A comparison theorem implies that all orbits of (1.3.3) are forward bounded, while the proof of Theorem 1.5 indicates that no orbit of system

(1.3.3) starting at a point in $\mathbb{R}^p_+ \times \mathbb{R}^p_+ \backslash \{0\}$ tends to $(N_1^*, \ldots, N_p^*, 0, \ldots, 0)$ if $\mathcal{R}_0 > 1$. It then follows a similar argument used in the proof of Theorem 4.2 in Seibert and Suarez [77] that $\mathcal{E}^*$ is globally asymptotically stable for system (1.3.3) relative to $\mathbb{R}^p_+ \times \mathbb{R}^p_+ \backslash \{0\}$. So is E^* for system (1.3.1). □

Remark 1.8. The above approach works for a class of SIS patch models where there is no disease-induced death and susceptible and infectious individuals travel at the same rates. As far as we know, most of the existing global results on these models are only for two-patch case. With our approach, for example, one can generalize Theorem 2.7 in Wang and Mulone [93] and Theorem 3.3 in Jin and Wang [42] to arbitrary number of patches where the respective limit system is strongly sublinear in the positive orthant and hence Corollary 3.2 in Zhao and Jing [105] can be applied directly.

Remark 1.9. The existence and global asymptotic stability of the positive equilibrium of system (1.3.4) can also be proved in a manner similar to the proof for Theorem 2 in Cosner et al. [16]. Clearly, our result is a generalization of Theorem 3.1 in Salmani and van den Driessche [76] where two patches are concerned and there is no impact of media coverage ($b_i = 0$ for $i = 1, 2$).

Remark 1.10. The endemic equilibrium E^* for (1.3.1) is also linearly stable. To prove this, it is equivalent to consider the stability of the Jacobian matrix of system (1.3.3) at $\mathcal{E}^*$, i.e.,

$$J(\mathcal{E}^*) = \begin{pmatrix} ((-d_i)\delta_{ij} + m_{ij})_{p\times p} & 0_{p\times p} \\ (\beta_i(I_i^*)(I_i^*/N_i^*)^2\delta_{ij})_{p\times p} & M' \end{pmatrix},$$

where $M' = ((\beta_i'(I_i^*)\frac{N_i^*-I_i^*}{N_i^*}I_i^* + \beta_i(I_i^*)\frac{N_i^*-2I_i^*}{N_i^*} - (d_i+\gamma_i))\delta_{ij} + m_{ij})_{p\times p}$. Obviously,

$s(((-d_i)\delta_{ij} + m_{ij})_{p\times p}) < 0$. Meanwhile, $s(M') < 0$ is proved by observing that $s(M^*) = 0$ and

$$M' - M^* = ((\beta_i'(I_i^*)\frac{N_i^* - I_i^*}{N_i^*}I_i^* - \beta_i(I_i^*)\frac{I_i^*}{N_i^*})\delta_{ij})_{p\times p} < 0.$$

Consequently, all eigenvalues of $J(\mathcal{E}^*)$ have negative real parts.

A combination of Theorem 1.4 and Theorem 1.7 yields a complete description of the dynamics of system (1.3.1) as follows.

Corollary 1.11. *For model* (1.3.1)*, the disease-free equilibrium E_0 is globally asymptotically stable if $\mathcal{R}_0 \leq 1$, and the endemic equilibrium E^* exists and is globally asymptotically stable on the non-negative orthant minus the disease-free state if $\mathcal{R}_0 > 1$.*

Remark 1.12. The media coverage has no influence on the dynamics of disease transmission of system (1.3.1). However, the final infected size in each patch can be strictly reduced with more media coverage when the disease persists (i.e., $\mathcal{R}_0 > 1$). Such media-induced reduction was demonstrated in Sun et al. [85] by numerical simulations. In fact, this is equivalent to say that $\partial I_i^*/\partial b_j < 0$ for $i, j = 1, 2, \ldots, p$. Since $(I_1^*, I_2^*, \ldots, I_p^*)$ is the unique positive solution of the following equations

$$\beta_i(I_i)\frac{N_i^* - I_i}{N_i^*}I_i - (d_i + \gamma_i)I_i + \sum_{j=1}^{p} m_{ij}I_j = 0,\ i = 1, 2, \ldots, p, \tag{1.3.5}$$

it follows from the implicit function theorem that $\partial I_i^*/\partial b_j$ exists. We consider without loss of generality the sign of $\partial I_i^*/\partial b_1$. Taking partial derivatives of (1.3.5) with respect

to b_1 gives

$$M'\left(\frac{\partial I_1^*}{\partial b_1}, \frac{\partial I_2^*}{\partial b_1}, \ldots, \frac{\partial I_p^*}{\partial b_1}\right)^T = \left(f_1(I_1^*)\frac{N_1^* - I_1^*}{N_1^*} I_1^*, 0, \ldots, 0\right)^T,$$

where M' is defined in Remark 1.10. Note that M' has a negative inverse, thus $\partial I_i^*/\partial b_1 < 0$ for $i = 1, 2, \ldots, p$.

When $\mathcal{R}_0 > 1$ for system (1.1.2), the following result shows that the existence, uniqueness and global attractivity of the endemic equilibrium still hold if the disease has mild effect on the travel of infectious humans (i.e., $n_{ij} \approx m_{ij}$ for $i, j = 1, 2, \ldots, p$) and the disease-induced death is seldom (i.e., $\nu_i \approx 0$ for $i = 1, 2, \ldots, p$). We omit the proof which is similar to that of Theorem 3.4 in Jin and Wang [42] by applying Theorem 4.3 and Remark 4.2 in Smith and Zhao [84] and Corollary 2.3 in Smith and Waltman [83].

Theorem 1.13. *Let $P = (m_{ij})_{p\times p}$ and $Q = (n_{ij})_{p\times p}$ be the travel rate matrices for the susceptible and infectious classes, respectively, and $\vec{\nu} = (\nu_1, \nu_2, \ldots, \nu_p)$ be the vector formed by the disease-induced death rates. Assume that all parameters in* (1.1.2) *are fixed except n_{ij} for $i, j = 1, 2, \ldots, p$ and ν_i for $i = 1, 2, \ldots, p$, and $\mathcal{R}_0 > 1$ when $Q = P$ and $\vec{\nu} = 0_{1\times p}$. Then there is a $\tau > 0$ such that for any Q and $\vec{\nu}$ with $\|Q - P\| < \tau$ and $\|\vec{\nu}\| < \tau$,* (1.1.2) *has a unique endemic equilibrium $E^*(Q, \vec{\nu})$, which is globally attractive with respect to $\mathbb{R}_+^p \times \mathbb{R}_+^p \backslash \{0\}$. Here $\|\cdot\|$ is the Frobenius norm if '$\cdot$' is a matrix and the Euclidean norm if '$\cdot$' is a vector.*

We end this section with a result on the number of endemic equilibria for a special

case of the two-patch model:

$$\begin{aligned}\frac{dN_i}{dt} &= A_i - d_iN_i - \nu_iI_i - m_{ji}(N_i - I_i) + m_{ij}(N_j - I_j),\ i,j = 1,2, i \neq j,\\ \frac{dI_i}{dt} &= \beta_i(I_i)\frac{N_i - I_i}{N_i}I_i - (d_i + \nu_i + \gamma_i)I_i,\ i,j = 1,2, i \neq j.\end{aligned} \tag{1.3.6}$$

Namely, when the infectious individuals in each patch do not travel to the other patch, we cannot obtain multiple endemic equilibria by choosing suitable saturation functions and parameter values, which is different from the two-patch model in Jin and Wang [42].

Theorem 1.14. *System* (1.3.6) *has at most one endemic equilibrium if* $m_{12} \geq 0$ *and* $m_{21} \geq 0$.

Proof. Assume that $E^* = (N_1^*, N_2^*, I_1^*, I_2^*)$ and $\hat{E} = (\hat{N}_1, \hat{N}_2, \hat{I}_1, \hat{I}_2)$ are two distinct positive equilibria of (1.3.6). Then they must satisfy the following four equations

$$\begin{aligned}&A_i - d_iN_i - \nu_iI_i - m_{ji}(N_i - I_i) + m_{ij}(N_j - I_j) = 0,\ i,j = 1,2, i \neq j,\\ &\beta_i(I_i)\frac{N_i - I_i}{N_i} - (d_i + \nu_i + \gamma_i) = 0,\ i,j = 1,2, i \neq j.\end{aligned}$$

Solving N_1, N_2 in terms of I_1, I_2 from the first two and the last two equations gives

$$N_i = ((d_j + m_{ij})(A_i - (\nu_i - m_{ji})I_i - m_{ij}I_j) + m_{ij}(A_j - m_{ji}I_i - (\nu_j - m_{ij})I_j))/\Delta \tag{1.3.7}$$

and

$$N_i = I_i/(1 - \Lambda_i/\beta_i(I_i)), \tag{1.3.8}$$

respectively, where $\Lambda_i = d_i + \nu_i + \gamma_i$, $i,j = 1,2$, $i \neq j$ and $\Delta = (d_1 + m_{21})(d_2 + m_{12}) -$

$m_{12}m_{21} > 0$. Thus, I_j can be solved in terms of I_i from (1.3.7) and (1.3.8) as follows:

$$(d_j+\nu_j)m_{ij}I_j =(d_j+m_{ij})A_i + m_{ij}A_j - ((d_j+m_{ij})\nu_i - d_jm_{ji})I_i - \frac{I_i\Delta}{1-\Lambda_i/\beta_i(I_i)} \tag{1.3.9}$$

for $i, j = 1, 2$ and $i \neq j$, or

$$I_j = \frac{(d_j+m_{ij})A_i + m_{ij}A_j - ((d_j+m_{ij})\nu_i - d_jm_{ji})I_i - I_i\Delta/(1-\Lambda_i/\beta_i(I_i))}{(d_j+\nu_j)m_{ij}} \tag{1.3.10}$$

if $m_{ij} \neq 0$. Next the proof is naturally divided into three cases.

Case 1. $m_{12} > 0, m_{21} > 0$. Note that $I_i^* \neq \hat{I}_i$ for $i = 1, 2$, since otherwise it follows from (1.3.8) and (1.3.10) that $E^* = \hat{E}$. For $i = 1, 2$, $N_i^* > 0$ and $\hat{N}_i > 0$ imply that $\beta_i(I_i) > \Lambda_i$, $I_i \in [\min\{I_i^*, \hat{I}_i\}, \max\{I_i^*, \hat{I}_i\}]$. We differentiate the right hand side of (1.3.10), denoted by $g_i(I_i)$, with respect to $I_i \in [\min\{I_i^*, \hat{I}_i\}, \max\{I_i^*, \hat{I}_i\}]$ and obtain

$$\begin{aligned}\frac{dg_i(I_i)}{dI_i} &= \frac{d_jm_{ji} - (d_j+m_{ij})\nu_i}{(d_j+\nu_j)m_{ij}} - \frac{\Delta}{(d_j+\nu_j)m_{ij}}\left(\frac{\beta_i(I_i)}{\beta_i(I_i)-\Lambda_i} - \frac{I_i\beta_i'(I_i)\Lambda_i}{(\beta_i(I_i)-\Lambda_i)^2}\right)\\ &\leq \frac{d_jm_{ji} - (d_j+m_{ij})\nu_i - \Delta}{(d_j+\nu_j)m_{ij}} = \Theta_i < 0,\ i, j = 1, 2, \text{ and } i \neq j.\end{aligned}$$

Direct algebraic manipulations yield

$$\begin{aligned}&(d_1m_{12} - (d_1+m_{21})\nu_2 - \Delta)(d_2m_{21} - (d_2+m_{12})\nu_1 - \Delta) - (d_1+\nu_1)(d_2+\nu_2)m_{12}m_{21}\\ =&(d_1+\nu_1)(d_2+\nu_2)(d_1d_2 + d_1m_{12} + d_2m_{21}) = (d_1+\nu_1)(d_2+\nu_2)\Delta > 0,\end{aligned}$$

which is equivalent to $\Theta_1 \cdot \Theta_2 > 1$. Without loss of generality, let $I_1^* < \hat{I}_1$. Hence,

$$\frac{dg_1(I_1)}{dI_1}\frac{dg_2(I_2)}{dI_2} > 1 \Longrightarrow \frac{dg_1(I_1)}{dI_1} < \left(\frac{dg_2(I_2)}{dI_2}\right)^{-1} < 0, I_1 \in [I_1^*, \hat{I}_1].$$

This means that in the I_1I_2-plane, after the point (I_1^*, I_2^*), the curve of $I_2 = g_1(I_1)$ is below the curve of $I_1 = g_2(I_2)$. So the two curves cannot intersect again at $(\hat{I}_1, \hat{I}_2)$.

Case 2. $m_{12} > 0$ and $m_{21} = 0$, or $m_{12} = 0$ and $m_{21} > 0$. It suffices to prove the result under the first condition. The negativity of the derivative of the right side of (1.3.9) with respect to I_2 $(i = 2, j = 1)$ means that $I_2^* = \hat{I}_2$. Once again, the negativity of the derivative of the right side of (1.3.9) with respect to I_1 $(i = 1, j = 2)$ means that $I_1^* = \hat{I}_1$. It follows (1.3.8) that $E^* = \hat{E}$, which is a contradiction.

Case 3. $m_{12} = m_{21} = 0$. The negativity of the derivative of the right side of (1.3.9) with respect to I_i means that $I_i^* = \hat{I}_i$ for $i = 1, 2$. So $E^* = \hat{E}$, a contradiction. □

Remark 1.15. An elementary but lengthy argument shows that system (1.3.6) can have up to four biologically meaningful equilibria in $\mathbb{R}^4_+$ if $m_{12} \geq 0$ and $m_{21} \geq 0$, that is, the DFE E_0, two one-patch disease-free steady states, and the endemic equilibrium. This is the same as the classic endemic model with $b_i = 0, i = 1, 2$ (see [76], [19]).

1.4 Examples and Discussions

As mentioned earlier, the media effect alone cannot drive an endemic disease extinct, but it plays a significant role in reducing the number of infectives and its proportion to the total population. To investigate this, we carry out a numerical example for the two-patch model.

Consider the saturation functions $f_i(I_i) = 1 - k_i/(k_i + I_i)$ for $i = 1, 2$ with $k_1 = 30$ and $k_2 = 50$, and take parameters in system (1.1.2) as follows: $A_1 = 20, a_1 = 0.10, d_1 = 3.6 \times 10^{-5}, \nu_1 = 0.02, \gamma_1 = 0.09$, $A_2 = 15, a_2 = 0.22, d_2 = 4.0 \times 10^{-5}, \nu_2 = 0.05, \gamma_2 = 0.05$, $b_2 = 0.11$. For these parameter values, the respective basic repro-

duction numbers for both patches are $\mathcal{R}_0^{(1)} = 0.9088 < 1$ and $\mathcal{R}_0^{(2)} = 2.1991 > 1$. If the two patches are disconnected, the disease eventually dies out in patch 1 while it persists in patch 2.

We fix the travel rates by letting $m_{12} = 0.10, m_{21} = 0.08, n_{12} = 0.08, n_{21} = 0.06$, thus $\mathcal{R}_0 = 1.6208$. Therefore, the disease becomes endemic in both patches and there exists an endemic equilibria. If we let b_1 vary from 0 to 0.05, the curves of the final sized infectives I_1^* and I_2^* against b_1 are depicted in Figure 1(a). Here numerical calculations indicate that the endemic equilibrium is unique for each $b_1 \in [0, 0.05]$ and is locally stable. Both I_1^* and I_2^* are strictly decreasing with respect to b_1 which means stronger media coverage in patch 1 is beneficial to individuals in both patches.

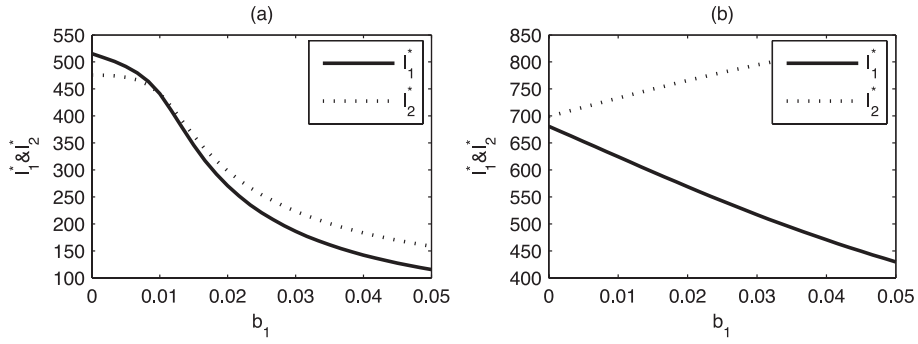

Figure 1.1: *The dependence of* I_1^* *and* I_2^* *on* b_1.

If we keep all parameter values unchanged except that $\nu_2 = 0.03, n_{12} = 0.04$ and $n_{21} = 0.02$, then Figure 1(b) shows how I_1^* and I_2^* vary with b_1 from 0 to 0.05. Here I_1^* is decreasing in b_1 but I_2^* is increasing in b_1. However, their proportions to the total population in each patch are strictly decreasing. Basically, appropriate media alert is helpful to disease control.

In this chapter, we proposed a multi-patch model to study the influence of media coverage and human movement on disease transmission. Our results show that the

basic reproduction number $\mathcal{R}_0$ is a threshold parameter of the disease dynamics. Particularly, either all positive solutions approach the disease-free equilibrium ($\mathcal{R}_0 \leq 1$) or a unique endemic equilibrium ($\mathcal{R}_0 > 1$) provided that the disease is nonfatal and susceptible and infectious individuals have the same travel rates. There are some unanswered questions with our model. For example, the nonexistence of multiple endemic equilibria is unclear even for $p = 2$. Can the model exhibit more complicated dynamical behaviors like Hopf bifurcation? Is there a possibility that media coverage has negative effect on controlling of infectious diseases?

We can generalize the current model in many aspects. A more realistic model should include the impact of media on the dispersal rates. Sometimes it is better to consider the transmission coefficient as a function of the ratio I_i/N_i in patch i. There is a difference between the time when data is collected and the time when audiences get to know it, so it may be reasonable to consider a system of delay differential equations. One can also incorporate media effect in other ways such as that in Mummert and Weiss [64].

Chapter 2

A Multi-patch Malaria Model with Logistic Growth Populations

2.1 Background

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 led to an estimated 225 million malaria cases and nearly $781,000$ deaths worldwide in 2008, the vast majority of which were children under five in Africa region (WHO [96]).

Following the pioneering work of Ross [74] and Macdonald [54–56], mathematical modeling of malaria transmission has progressed rapidly. Among many contributions to the development of mathematical modeling of malaria transmission , we would like to mention Dietz et al. [22], Aron and May [6], Nedelman [65], Koella [45], Gupta et al. [31], Ngwa and Shu [68], Ngwa [67], Chitnis et al. [14, 15], Ruan et al. [75], Lou and Zhao [51], and the references cited therein.

In paper [68] (also Ngwa [67]), 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 et al. [14, 15] extended the model in Ngwa and Shu [68] and Ngwa [67] to generalize the mosquito biting rate, include human immigration and exclude direct infectious-to-susceptible human recovery. They presented a bifurcation analysis in [14], 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 [15].

Malaria varies greatly in 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 [58], Tatem et al. [86]). 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 1950's, about 1,500 malaria cases are diagnosed every year in this country, of which approximately 60% are among US travelers (Newman et al. [66]). 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.

Multi-patch 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 [23], Hasibeder and Dye [34], Torres-Sorando and Rodriguez [89], Rodriguez and Torres-Sorando [73], Smith et al. [78], Auger et al. [8], Cosner et al. [16], Arino et al. [5], etc. For references on general epidemic models in a patchy environment, we refer the reader to two review articles by Wang [92] and Arino [4]. 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 multi-patch epidemic models is to study how the dispersal of individuals, in particular of the 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 et al. [39] and Lemma 3.4 in Allen et al. [3]). The reason is that for a multi-patch 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 chapter, based on the model of Ngwa and Shu [68] (also Ngwa [67] and Chitnis et al. [14, 15]), we propose a multi-patch model to examine how population dispersal affects malaria spread between patches. This chapter is organized as follows. In the 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.

2.2 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 [68] (also Ngwa [67] and Chitnis et al. [14,15]) with an SEIRS structure for humans and an 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.

For patch i, all newborns in both populations are assumed to be 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 into 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

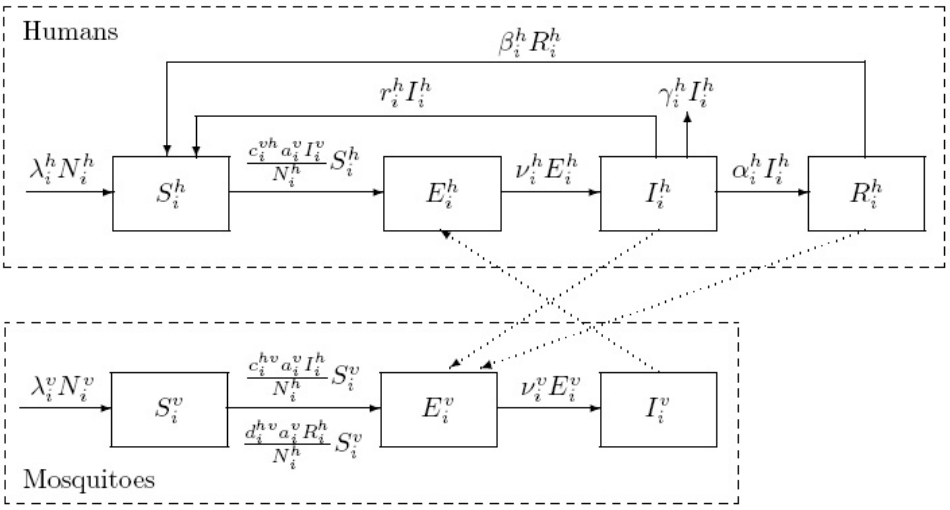

Figure 2.1: *Flow diagram of the mosquito-borne model in patch i.*

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 Fig 2.1. 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 non-negative initial conditions satisfying $N_i^h(0) > 0$:

$$
\begin{aligned}
\frac{dS_i^h}{dt} &= \lambda_i^h N_i^h + \beta_i^h R_i^h + r_i^h I_i^h - \frac{c_i^{vh} a_i^v I_i^v}{N_i^h} S_i^h - f_i^h(N_i^h) S_i^h + \sum_{j=1}^{n} \varphi_{ij}^S S_j^h, \\
\frac{dE_i^h}{dt} &= \frac{c_i^{vh} a_i^v I_i^v}{N_i^h} S_i^h - (\nu_i^h + f_i^h(N_i^h)) E_i^h + \sum_{j=1}^{n} \varphi_{ij}^E E_j^h, \\
\frac{dI_i^h}{dt} &= \nu_i^h E_i^h - (r_i^h + \alpha_i^h + \gamma_i^h + f_i^h(N_i^h)) I_i^h + \sum_{j=1}^{n} \varphi_{ij}^I I_j^h, \\
\frac{dR_i^h}{dt} &= \alpha_i^h I_i^h - (\beta_i^h + f_i^h(N_i^h)) R_i^h + \sum_{j=1}^{n} \varphi_{ij}^R R_j^h, \\
\frac{dS_i^v}{dt} &= \lambda_i^v N_i^v - \frac{c_i^{hv} a_i^v I_i^h}{N_i^h} S_i^v - \frac{d_i^{hv} a_i^v R_i^h}{N_i^h} S_i^v - f_i^v(N_i^v) S_i^v + \sum_{j=1}^{n} \psi_{ij}^S S_j^v, \\
\frac{dE_i^v}{dt} &= \frac{c_i^{hv} a_i^v I_i^h}{N_i^h} S_i^v + \frac{d_i^{hv} a_i^v R_i^h}{N_i^h} S_i^v - (\nu_i^v + f_i^v(N_i^v)) E_i^v + \sum_{j=1}^{n} \psi_{ij}^E E_j^v, \\
\frac{dI_i^v}{dt} &= \nu_i^v E_i^v - f_i^v(N_i^v) I_i^v + \sum_{j=1}^{n} \psi_{ij}^I I_j^v,
\end{aligned}
\tag{2.2.1}
$$

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

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

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. [16]), that is, humans and mosquitoes change their residences when they move

from one patch to another patch. 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 the 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 (2.2.1) is mathematically well-posed and epidemiologically reasonable.

Theorem 2.1. *Consider model* (2.2.1) *with non-negative 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 non-negative 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 (2.2.1) is continuously differentiable, so the initial value problem has a unique solution which exists for all $t \geq 0$. The non-negative 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. □

2.3 Threshold Dynamics

We first show the existence of a disease-free equilibrium (DFE) for (2.2.1), 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.

2.3.1 Disease-free Equilibrium

A disease-free equilibrium is a steady state solution of system (2.2.1) 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 (2.2.1) 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 $S^{v*} = (S_1^{v*}, S_2^{v*}, \ldots, S_n^{v*})$. Thus there is a DFE for (2.2.1) if and only if S^{h*} and S^{v*} are positive equilibria to the subsystems

$$\frac{dS_i^h}{dt} = \lambda_i^h S_i^h - f_i^h(S_i^h)S_i^h + \sum_{j=1}^{n}\varphi_{ij}^S S_j^h, 1 \le i \le n \tag{2.3.1}$$

and

$$\frac{dS_i^v}{dt} = \lambda_i^v S_i^v - f_i^v(S_i^v)S_i^v + \sum_{j=1}^{n}\psi_{ij}^S S_j^v, 1 \le i \le n, \tag{2.3.2}$$

respectively. They are guaranteed by the following lemma.

Lemma 2.2. *Let* $\mathrm{Int}\mathbb{R}_+^n$ *be the interior of* $\mathbb{R}_+^n$. *For system* (2.3.1), *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*

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

with $L_i^h > 0$ *for* $1 \le i \le n-1$ *and* $L_n^h = 1$. *A similar result holds for system* (2.3.2).

Proof. It is easy to see that system (2.3.1) is cooperative and irreducible. The existence, uniqueness and global asymptotic stability of S^{h*} can be proved by applying Theorem 6.1 in Hirsch [35] or Corollary 3.2 in Zhao and Jing [105].

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. [16] or Lemma 2.1 of Guo et al. [30]. We denote by f^h the vector field defined by (2.3.1) and let ϕ_t^h denote the corresponding flow. Then the ith component of f^h evaluated at mL^h satisfies

$$\begin{aligned}
&\lambda_i^h(mL_i^h) - f_i^h(mL_i^h)\cdot mL_i^h + \sum_{j=1}^{n}\varphi_{ij}^S mL_j^h = \lambda_i^h(mL_i^h) - f_i^h(mL_i^h)\cdot mL_i^h \\
= \;& m((\lambda_i^h - \mu_i^h) - \rho_i^h mL_i^h)L_i^h = m\rho_i^h L_i^h\Big(\frac{\lambda_i^h - \mu_i^h}{\rho_i^h L_i^h} - m\Big)L_i^h = m\rho_i^h L_i^h\Big(\frac{K_i^h}{L_i^h} - m\Big)L_i^h
\end{aligned}$$

for $m > 0$ and $i = 1, \ldots, n$. Thus $f^h(mL^h) \geq 0$ for $m \leq \min\limits_{1\leq i\leq n}\frac{K_i^h}{L_i^h}$ and $f^h(mL^h) \leq 0$ for $m \geq \max\limits_{1\leq i\leq n}\frac{K_i^h}{L_i^h}$. In particular, $f^h(P^h) \geq 0$ and $f^h(Q^h) \leq 0$. It follows from the theory of monotone dynamical systems (Smith [80]) that $\phi_t^h(P^h)$ is non-decreasing and $\phi_t^h(Q^h)$ is non-increasing for $t \geq 0$. Since both $\phi_t^h(P^h)$ and $\phi_t^h(Q^h)$ converge to S^{h*}, we have $P^h \leq S^{h*} \leq Q^h$. □

2.3.2 The Basic Reproduction Number

To derive the basic reproduction number $\mathcal{R}_0$ for (2.2.1), we order the infected variables first by disease state, then by patch, i.e.,

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

and follow the recipe from van den Driessche and Watmough [90] 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

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

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 $i = 1, \ldots, 5$, 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 et al. [21]) 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 one describes infections related to recovered humans who survive the infectious class and acquire partial immunity.

Theorem 2.3. *The disease-free equilibrium of* (2.2.1) *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 [90]. (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 (2.3.2). By Lemma 2.2, $s(J_4) < 0$. So that of $s(J)$. □

Remark 2.4. 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

$$\mathcal{R}_0^{(i)} = \sqrt{\frac{c_i^{vh}(a_i^v)^2\nu_i^v(c_i^{hv}(\beta_i^h+\lambda_i^h)+d_i^{hv}\alpha_i^h)\nu_i^h(\lambda_i^v-\mu_i^v)\rho_i^h}{\lambda_i^v(\nu_i^v+\lambda_i^v)(r_i^h+\alpha_i^h+\gamma_i^h+\lambda_i^h)(\beta_i^h+\lambda_i^h)(\nu_i^h+\lambda_i^h)(\lambda_i^h-\mu_i^h)\rho_i^v}}. \quad (2.3.3)$$

This is slightly different from Ngwa and Shu's [68] 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 [80] 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 [38], 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 that of M. In particular, M has two distinct positive eigenvalues when $n = 2$. This fact will be used later.

Similarly to Theorem 2.3 in Salmani and van den Driessche [76] and Theorem 3.2 in Hsieh et al. [39], we have the following result which gives bounds on the basic reproduction number.

Theorem 2.5. $\max\limits_{1\le i\le n}(\tilde{\mathcal{R}}_0^{(i)})^2 \le \mathcal{R}_0^2 \le \max\limits_{1\le i\le n}(\hat{\mathcal{R}}_{01}^{(i)})^2 + \max\limits_{1\le i\le n}(\hat{\mathcal{R}}_{02}^{(i)})^2$, *where*

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

and

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

Proof. The lower bound can be proved by applying Fischer's inequality (see Theorem 2.5.4(e), Horn and Johnson [38]) 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 $1/a_{ii} \leq \alpha_{ii}$ for $i = 1, \ldots, n$ and therefore

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

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

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

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

Remark 2.6. 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 [76] 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 et al. [39] without assuming that $d_i = d$ for $i = 1, 2, \ldots, n$.

Remark 2.7. When $\lambda_i^h > \mu_i^h$ and $\lambda_i^v > \mu_i^v$ for $1 \leq i \leq n$, a combination of Lemma 2.2

and Theorem 2.5 yields an estimation of $\mathcal{R}_0$ which only depends on model parameters. However, this result might have little use, because we omitted some terms in the process of estimation.

2.3.3 Uniform Persistence and the Endemic Equilibrium

Under certain conditions, we can use the techniques of persistence theory (Freedman et al. [24], Thieme [88], Cantrell and Cosner [12], Smith and Thieme [81]) 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 [94] and Theorem 3.2 in Lou and Zhao [51]. For convenience, we denote the vector $(S_1^h(t), \ldots, S_n^h(t))$ by $S^h(t)$ for $t \geq 0$. $E^h(t), I^h(t), R^h(t), S^v(t), E^v(t)$ and $I^v(t)$ can be introduced similarly.

Theorem 2.8. *Let $\mathcal{E}_{11}$ denote the disease-free equilibrium of* (2.2.1)*, $W^s(\mathcal{E}_{11})$ be the stable manifold of $\mathcal{E}_{11}$, and 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* $K = S, E, I, R$, $i, j = 1, 2, \ldots, n$, $i \neq j$;

(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 (2.2.1) *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 (2.2.1) *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 [90] 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

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

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

$$\frac{dE_i^h}{dt} \geq c_i^{vh} a_i^v I_i^v (1-\epsilon_1) - (\nu_i^h + f_i^h(S_i^{h*} + \epsilon_1))E_i^h + \sum_{j=1}^{n} \varphi_{ij}^E E_j^h,$$

$$\frac{dE_i^v}{dt} \geq (c_i^{hv} a_i^v I_i^h + d_i^{hv} a_i^v R_i^h)\Big(\frac{S_i^{v*}}{S_i^{h*}} - \epsilon_1\Big) - (\nu_i^v + f_i^v(S_i^{v*} + \epsilon_1))E_i^v + \sum_{j=1}^{n} \psi_{ij}^E E_j^v,$$

$$\frac{dI_i^h}{dt} \geq \nu_i^h E_i^h - (r_i^h + \alpha_i^h + \gamma_i^h + f_i^h(S_i^{h*} + \epsilon_1))I_i^h + \sum_{j=1}^{n} \varphi_{ij}^I I_j^h,$$

$$\frac{dI_i^v}{dt} \geq \nu_i^v E_i^v - f_i^v(S_i^{v*} + \epsilon_1)I_i^v + \sum_{j=1}^{n} \psi_{ij}^I I_j^v,$$

$$\frac{dR_i^h}{dt} \geq \alpha_i^h I_i^h - (\beta_i^h + f_i^h(S_i^{h*} + \epsilon_1))R_i^h + \sum_{j=1}^{n} \varphi_{ij}^R R_j^h.$$

Consider an auxiliary system

$$\frac{d\omega(t)}{dt} = M_{\epsilon_1}\omega(t). \tag{2.3.4}$$

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 (2.3.4) with positive initial value goes to infinity as $t \to \infty$. By the comparison theorem, we have

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

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 (2.2.1) 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 [18] 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 (2.2.1) 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 (2.2.1) 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 (2.2.1) 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 [88] that system (2.2.1) 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 [40] or Theorem 2.4 in Zhao [103]). Since system (2.2.1) 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 (2.2.1), 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 (2.2.1). □

Remark 2.9. For $n = 1$, the theorem is an improvement of Proposition 3.3 of Ngwa and Shu [68]. 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 et al. [39] and Salmani and van den Driessche [76].

2.4 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. For example, is the dependence monotone is some sense (Müller and Hadeler [63])? For a very special

case of a two-patch epidemic model, Hsieh et al. [39] showed that (Theorem 4.2) R_0 decreases when the travel rate of infected individuals increases. See also Allen et al. [3] (Lemma 3.4). In general there are very few results in this direction. For model (2.2.1), 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 [38], 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 multi-patch 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 2.10. *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*

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

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

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

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

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

The second inequality is equivalent to

$$(yv_2 + wk_2)k_1^2 + (xv_2 + zk_2)\bar{a}_1k_1 > (z\bar{a}_1 + wk_1)(v_2 + \bar{a}_2)\bar{a}_1. \tag{2.4.1}$$

Claim: (2.4.1) implies $\mathcal{P}\dot{\mathcal{P}} - 2\dot{\mathcal{Q}} < 0$. In fact, we have

$$\begin{aligned}
-\mathcal{P}\dot{\mathcal{P}}v_1^2 &= (x(1+\bar{a}_1/v_1) + yk_1/v_1 + zk_2/v_2 + w(1+\bar{a}_2/v_2))(x\bar{a}_1 + yk_1) \\
&> (x + zk_2/v_2 + w(1+\bar{a}_2/v_2))(x\bar{a}_1 + yk_1) \\
&= ((xv_2 + zk_2) + w(v_2+\bar{a}_2))(\bar{a}_1k_1 + yk_1^2/x)x/(k_1v_2) \\
&> ((yv_2 + wk_2)k_1^2 + (xv_2 + zk_2)\bar{a}_1k_1 - wk_2k_1^2 + w(v_2+\bar{a}_2)\bar{a}_1k_1)x/(k_1v_2) \\
&> ((z\bar{a}_1 + wk_1)(v_2+\bar{a}_2)\bar{a}_1 - wk_2k_1^2 + w(v_2+\bar{a}_2)\bar{a}_1k_1)x/(k_1v_2) \quad \text{by (2.4.1)} \\
&> (2w(v_2+\bar{a}_2)\bar{a}_1k_1 - wk_2k_1^2)x/(k_1v_2) = (2xw\bar{a}_1(v_2+\bar{a}_2) - xwk_1k_2)/v_2 \\
&> 2(xw - yz)(\bar{a}_1(v_2+\bar{a}_2) - k_1k_2)/v_2 = -2\dot{\mathcal{Q}}v_1^2.
\end{aligned}$$

The proof is complete by substituting $\bar{a}_1 = a_1 + k_1$ and $\bar{a}_2 = a_2 + k_2$ into (2.4.1). □

Remark 2.11. The biological interpretation of the inequality in Proposition 2.10 is not easy. However, if the emigration rate $k_1 = 0$, then the inequality always fails and $\rho(A)$ is consistently increasing in v_1. So, the decreasing phenomenon is due to the emigration of the corresponding exposed class and the fact that 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 et al. [39], see also Allen et al. [3]). Note that only A_{11} contains φ_{ij}^E and only A_{33} contains φ_{ij}^I. We know $\rho(M) = \rho(A^E A_{11}^{-1}) = \rho(A^I A_{33}^{-1})$, 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 2.12. *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

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

which is equivalent to

$$(x(a_1 + k_1) + yk_1 + zk_2 + w(a_2 + k_2))(x + y) - 2(xw - yz)a_2 \leq 0 \tag{2.4.2}$$

or

$$(xk_2 + y(a_2 + k_2))((x + y)a_1 - (z + w)a_2)(xw - yz) < 0. \tag{2.4.3}$$

Since $xk_2 + y(a_2 + k_2) > 0$ and $xw > yz$, (2.4.3) is reduced to $(x + y)a_1 < (z + w)a_2$. It is easy to verify that (2.4.2) implies (2.4.3). 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 2.13. The conclusion in Proposition 2.12 still holds if $e, h, a_1, a_2 > 0$, $f, g, k_1, k_2 \geq 0$, $eh > fg$, 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 2.14. 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 non-increasing 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 2.15. *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 notations as in Proposition 2.12 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

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

which is equivalent to

$$(x(a_1+k) + yk + zk + w(a_2+k))(x+y+z+w) \leq 2(xw - yz)(a_1 + a_2) \quad (2.4.4)$$

or

$$-((x+z)a_1 - (y+w)a_2)((x+y)a_1 - (z+w)a_2)(xw - yz) < 0. \quad (2.4.5)$$

Since $xw > yz$, the solutions to (2.4.5) 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 (2.4.4) implies (2.4.5). The proof is complete. □

Remark 2.16. 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 non-increasing 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 multi-patch 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 non-monotone dependence can occur. We will investigate these situations by presenting some examples in the

next section.

2.5 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 et al. [15] and the references therein.

Example 2.17. 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 (2.2.1) 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 yields 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 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

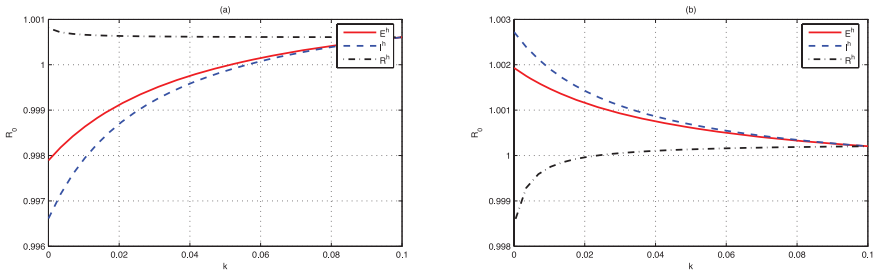

Figure 2.2: *The basic reproduction number $\mathcal{R}_0$ in terms of k. (a) $\mathcal{R}_0 = 1.0006$ as $k = 0.1$, the optimal strategy for reducing $\mathcal{R}_0$ to be less than 1 is to restrict the travel of infectious humans. (b) $\mathcal{R}_0 = 1.0002$ as $k = 0.1$, the optimal strategy for reducing $\mathcal{R}_0$ to be less than 1 is to restrict the travel of recovered humans.*

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 Fig 2.2(a). The monotonicity of the curves is predicted by Proposition 2.15. Since $\mathcal{R}_0 = 1.0006 > 1$ as $k = 0.1$, the disease is endemic in both patches by Theorem 2.8. 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 Fig 2.2(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 2.18. For model (2.2.1), 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.

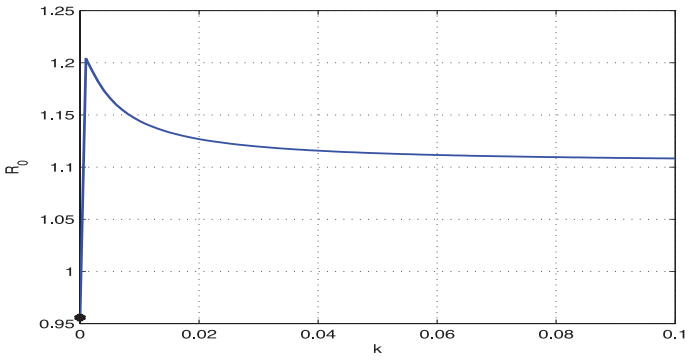

Figure 2.3: *$\mathcal{R}_0$ as a function of $k = \varphi_{12}^S$ with $\mathcal{R}_0^{(1)} = \mathcal{R}_0^{(2)} = 0.9557$. The disease dies out in each isolated patch, but it becomes endemic in both patches even when there is small human movement.*

Case 1: $\mathcal{R}_0^{(1)} < 1$ and $\mathcal{R}_0^{(2)} < 1$, but $\mathcal{R}_0 > 1$. For $i = 1, 2$, suppose $\lambda_i^h = 5.5 \times 10^{-5}$, $\mu_i^h = 8.8 \times 10^{-6}$, $\rho_i^h = 2.0 \times 10^{-7}$, $\lambda_i^v = 0.13$, $\mu_i^v = 0.033$, $\rho_i^v = 4.0 \times 10^{-5}$, $\nu_i^h = 0.1$, $\nu_i^v = 0.083$, $r_i^h = 2.1 \times 10^{-3}$, $\alpha_i^h = 4.8 \times 10^{-3}$, $\gamma_i^h = 1.8 \times 10^{-5}$, $\beta_i^h = 2.7 \times 10^{-3}$, $a_i^v = 0.14$, $c_i^{vh} = 0.11$, $c_i^{hv} = 0.08$, $d_i^{hv} = 0.008$. 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 Fig 2.3. In particular, we have $\mathcal{R}_0^{(1)} = \mathcal{R}_0^{(2)} = 0.9557$ and the disease can die out in each isolated patches (see Fig 2.4(a)). When humans move between these two patches, even for very small travel rate ($k > 10^{-5}$), $\mathcal{R}_0$ exceeds 1 and the disease becomes endemic in both patches (see Fig 2.4(b)) which is coincident with Theorem 2.8.

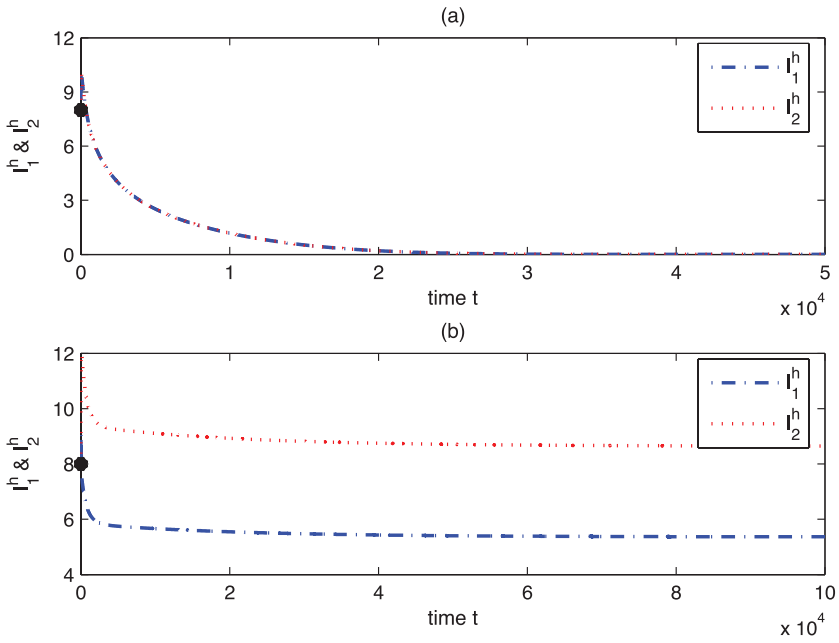

Figure 2.4: *Numerical solutions of system (2.2.1) with (a) $k = 0$ (no human movement) and (b) $k = 0.06$ (the corresponding $\mathcal{R}_0 = 1.1116$), respectively. In both situations, the initial conditions are $S_i^h(0) = 187, E_i^h(0) = 3, I_i^h(0) = 8, R_i^h(0) = 9, S_i^v(0) = 2310, E_i^v(0) = 10, I_i^v(0) = 4$ 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.*

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. 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 Fig 2.5. Suitable human movement may result in the extinction of the disease in both patches, even though the disease persists in each isolated patch (see Fig 2.6).

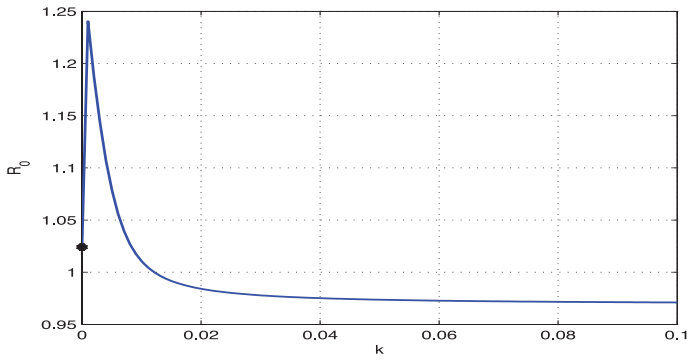

Figure 2.5: $\mathcal{R}_0$ *in terms of* $k = \varphi_{12}^S$ *with* $\mathcal{R}_0^{(1)} = \mathcal{R}_0^{(2)} = 1.0240$. *The disease persists in each isolated patch, but it becomes extinct in both patches when there is suitable human movement.*

In studying how travel affects the spatial spread of certain disease, Hsieh et al. [39] 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 disease becoming endemic. 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

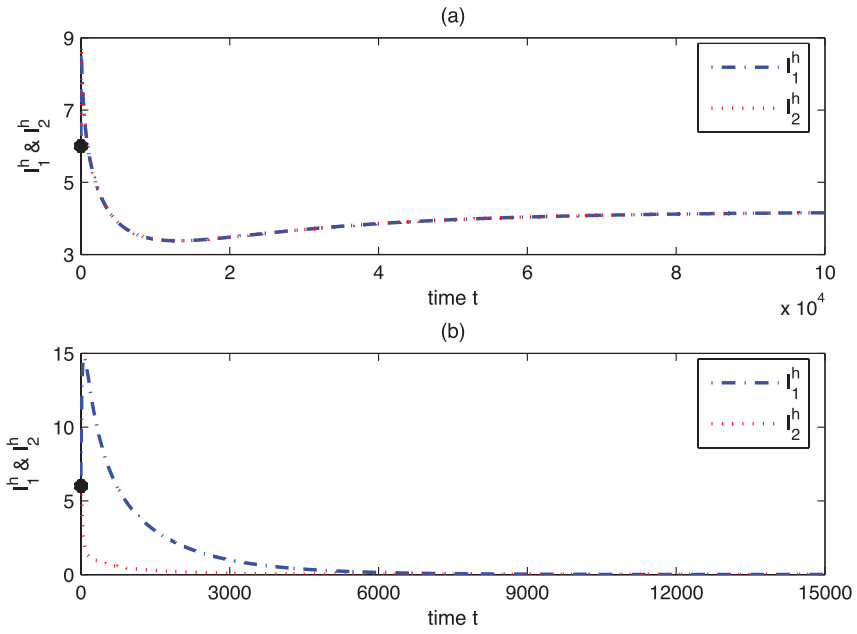

Figure 2.6: *Numerical solutions of system (2.2.1) with (a) $k = 0$ (no human movement) and (b) $k = 0.06$ (the corresponding $\mathcal{R}_0 = 0.9727$), respectively. In both situations, the initial conditions are $S_i^h(0) = 221, E_i^h(0) = 3, I_i^h(0) = 6, R_i^h(0) = 4, S_i^v(0) = 2150, E_i^v(0) = 8, I_i^v(0) = 7$ 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.*

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, 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. [16] 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 one. This dilution of the overall prevalence could lessen the severity of the disease so that it becomes minor in both patches.

Example 2.19. Assume all parameters are as in Case 1 of Example 2.18 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. 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 (2.3.3), 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 Fig 2.7 shows how $\mathcal{R}_0$ varies with k from 0 to 0.10.

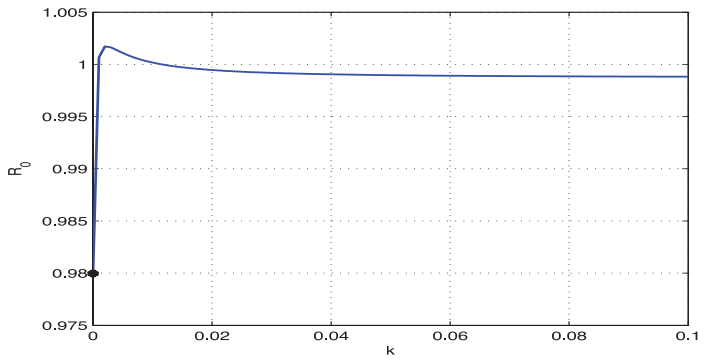

Figure 2.7: *Relationship between* $\mathcal{R}_0$ *and* $k = \varphi_{12}^E = \varphi_{12}^I = \varphi_{12}^R = \varphi_{21}^E = \varphi_{21}^I = \varphi_{21}^R$. *The disease dies out when the exposed, infectious and recovered human travel rate is small or large, it persists otherwise.*

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 to the disease becoming 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 feedback. 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.

2.6 Discussion

Malaria is one of the world's most common infectious diseases and it 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 chapter, taking the transmission heterogeneity into account, we proposed a multi-patch 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 monotonically 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 for the disease spread. The first example explores the role of different exposed, infectious and recovered classes in the disease propagation. The second one 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. Non-monotonicity of $\mathcal{R}_0$ in the exposed, infectious and recovered human travel rate which is 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 symptomatic individuals, 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 [87]). Accordingly, a full understanding of movement is important in designing effective anti-malaria measures.

There is still much work to do with our model. First of all, 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 $n = 2$), consequently, it is also difficult to give a formula for $\mathcal{R}_0$. Even if we obtained such a formula, it may be too complicated to use it directly. Unlike models in Salmani and van den Driessche [76] and Hsieh et al. [39], here we cannot use a comparison theorem for the vector-host model using their methods. Secondly, the existence, uniqueness and stability of the endemic equilibrium is in general unclear. Thirdly, 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 ODE 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. [59], Smith et al. [78]). The impact of climate change can be investigated by assuming that 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.

Chapter 3

A Periodic Ross-Macdonald Model in a Patchy Environment

3.1 Background

Malaria, a widely prevalent vector-borne disease in tropical and subtropical areas, is caused by a parasite that is transmitted to humans and many other animals by the *Anopheles* mosquito. Once infected, people may experience a variety of symptoms, ranging from absent or very mild symptoms to severe complications and even death. It is one of the most deadly infectious diseases that causes major economic loss due to illness and death in humans.

The so-called Ross-Macdonald model is the earliest and also simplest mathematical model of malaria transmission between human and mosquito populations. It was initially proposed by Ross in 1911 [74] and later extended by Macdonald in 1950s [54–56]. The modeling framework is now widely used for malaria and some other mosquito-borne diseases. It captures the essential features of malaria transmission process, but ignores many factors of real-world ecology and epidemiology (see Ruan et al. [75]).

One omission in the classical Ross-Macdonald model is the temporal heterogeneity

in the number of both populations and the human feeding rate of mosquitoes. In many nations like Niger, seasonal human migration has a long history, and destinations and reasons vary by community and ethnic group. It is a common sense that there are more mosquitoes in the summer and fewer in the winter. The biological activity and geographic distribution of malaria parasite and its vector are greatly influenced by climatic factors such as rainfall, temperature and humidity. These influences can be investigated by assuming some parameters to be time dependent. In recent years, epidemic models with seasonal fluctuation have been proposed and explored by many researchers. We refer to [10, 11, 49, 99, 100] and references therein for more studies in this topic. Periodicity mainly lies in contact rate, birth or death rate, vaccination rate, etc. Another omission is the spatial movements of hosts. The migration of humans can influence disease spread in a complicated way [28]. To get a better understanding of disease dynamics, it is necessary to incorporate periodic variations and population dispersal into epidemic models. These two concerns are considered in [52] via a periodic reaction-diffusion-advection model. We shall formulate a periodic epidemiological model in a patchy environment and establish the threshold dynamics of the model in Section 2 and Section 3, respectively. The last section gives some numerical simulations and a brief discussion of our main results.

3.2 Model Formulation

Most mosquitoes can only travel a couple of kilometers throughout their lifetime (Costantini et al. [17] and Midega et al. [61]), so we assume no movement for vector populations (see Auger et al. [8]). For simplicity, the human vital dynamics are

ignored and the population model for vectors is the same as that studied in Smith et al. [79]. Following the classical Ross-Macdonald model, we divide the adult female mosquito and human populations into two classes in each patch: susceptible and infectious. The total number of patches is p. We assume that the total populations of humans and mosquitoes at time t in patch i are $H_i(t)$ and $V_i(t)$, respectively. Let $h_i(t)$ and $v_i(t)$ denote the numbers of infectious humans and infectious mosquitoes in patch i, respectively. The interactions between humans and mosquitoes in patch i can be described by the following periodic system with non-negative initial conditions:

$$\frac{dH_i}{dt} = \sum_{j=1}^{p} m_{ij}(t)H_j, \quad 1 \le i \le p, \tag{3.2.1a}$$

$$\frac{dV_i}{dt} = \epsilon_i(t) - d_i(t)V_i, \quad 1 \le i \le p \tag{3.2.1b}$$

$$\frac{dh_i}{dt} = a_i(t)b_i\frac{H_i(t) - h_i}{H_i(t)}v_i - r_i h_i + \sum_{j=1}^{p} m_{ij}(t)h_j, \quad 1 \le i \le p, \tag{3.2.1c}$$

$$\frac{dv_i}{dt} = a_i(t)c_i\frac{h_i}{H_i(t)}(V_i(t) - v_i) - d_i(t)v_i, \quad 1 \le i \le p, \tag{3.2.1d}$$

where

$\epsilon_i(t) > 0$	is mosquito birth rate;
$d_i(t) > 0$	is mortality rate of mosquitoes;
$a_i(t) > 0$	is human feeding rate;
$b_i > 0$	is transmission probability from infectious mosquitoes to susceptible humans;
$c_i > 0$	is transmission probability from infectious humans to susceptible mosquitoes;

$1/r_i > 0$ is human infectious period;

$m_{ij}(t) \geq 0$ is the human immigration rate from patch j to patch i for $i \neq j$;

$-m_{ii}(t) \geq 0$ is the human emigration rate in patch i.

All time-dependent parameters in system (3.2.1) are continuous and periodic functions with the same period $\omega = 365$ days. We assume that there is no death or birth during travel, so the emigration rate of humans in patch i, $-m_{ii}(t) \geq 0$, satisfies

$$\sum_{j=1}^{p} m_{ji}(t) = 0 \quad \text{for } i = 1, \ldots, p \quad \text{and} \quad t \in [0, \omega].$$

Unless otherwise indicated, the travel rate matrix $(m_{ij}(t))_{p\times p}$ is assumed to be irreducible for any fixed $t \in [0, \omega]$. The notation H will mean $(H_1, \ldots, H_p)$, with similar notations for other vectors. The following theorem indicates that model (3.2.1) is mathematically and epidemiologically well-posed.

Theorem 3.1. *For any initial value z in*

$$\Gamma = \{(H, V, h, v) \in \mathbb{R}_+^{4p} : h_i \leq H_i, v_i \leq V_i, i = 1, \ldots, p\},$$

system (3.2.1) *has a unique nonnegative bounded solution through z for all $t \geq 0$.*

Proof. Let $G(t, z)$ be the vector field described by (3.2.1) with $z(t) \in \Gamma$. Then $G(t, z)$ is continuous and Lipschitzian in z on each compact subset of $\mathbb{R}^1 \times \Gamma$. Clearly, $G_k(t, z) \geq 0$ whenever $z \geq 0$ and $z_k = 0$, $k = 1, \ldots, 4p$. It follows from Theorem 5.2.1 in [80] that there exists a unique nonnegative solution for system (3.2.1) through $z \in \Gamma$ in its maximal interval of existence. The total numbers of hosts and vectors,

$N^h(t) = \sum_{i=1}^{p} H_i(t)$ and $N^v(t) = \sum_{i=1}^{p} V_i(t)$, satisfy

$$\frac{dN^h(t)}{dt} = \sum_{i=1}^{p}\sum_{j=1}^{p} m_{ij}(t)H_j = \sum_{i=1}^{p}\sum_{j=1}^{p} m_{ji}(t)H_i = 0$$

and

$$\frac{dN^v(t)}{dt} = \sum_{i=1}^{p}(\epsilon_i(t) - d_i(t)V_i(t)) \leq \epsilon - dN^v(t),$$

respectively, where $\epsilon = \max_{0\leq t\leq\omega}\left(\sum_{i=1}^{p}\epsilon_i(t)\right)$ and $d = \min_{0\leq t\leq\omega}\left(\min_{1\leq i\leq p} d_i(t)\right)$ are positive constants. Thus $N^h(t) \equiv N^h(0)$. The comparison principle (see Theorem B.1 in Smith and Waltman [83]) implies that $N^v(t)$ is ultimately bounded. Hence every solution of (3.2.1) exists globally. □

3.3 Mathematical analysis

In this section, we first show the existence of a unique disease-free periodic solution and then evaluate the basic reproduction number for the periodic system. By using theory of monotone dynamical systems, we establish its global dynamics. The following result is analogous to Lemma 1 in Cosner et al. [16] for the autonomous case.

Lemma 3.2. *The human migration model* (3.2.1a) *with* $H_i(0) \geq 0$ *for* $i = 1, \ldots, p$ *and* $N^h(0) > 0$ *has a unique positive* ω*-periodic solution* $H^*(t) \equiv (H_1^*(t), \ldots, H_p^*(t))$*, which is globally asymptotically stable. The mosquito growth model* (3.2.1b) *with* $V_i(0) \geq 0$ *for* $i = 1, \ldots, p$ *has a unique positive* ω*-periodic solution* $V^*(t) \equiv (V_1^*(t), \ldots, V_p^*(t))$*, which is globally asymptotically stable.*

Proof. Since the travel rate matrix $(m_{ij}(t))_{p\times p}$ is continuous, cooperative, irreducible and ω-periodic and it also satisfies $e(m_{ij}(t))_{p\times p} \equiv 0$ with $e = (1, \ldots, 1)_{1\times p}$, it follows from Theorem 1 in Aronsson and Kellogg [7] that there is a unique positive ω-periodic solution $H^*(t)$ such that $\sum_{i=1}^{p} H_i^*(t) = N^h(0)$. Moreover, any solution $H(t)$ of (3.2.1a) satisfying $\sum_{i=1}^{p} H_i(t) = N^h(0)$ approaches $H^*(t)$ exponentially as $t \to \infty$.

The i-th equation of (3.2.1b) has a unique positive periodic solution

$$V_i^*(t) = e^{-\int_0^t d_i(s)ds}\Big(V_i(0) + \int_0^t e^{\int_0^s d_i(\tau)d\tau}\epsilon_i(s)ds\Big) \text{ with } V_i^*(0) = \frac{\int_0^\omega e^{\int_0^s d_i(\tau)d\tau}\epsilon_i(s)ds}{e^{\int_0^\omega d_i(s)ds} - 1},$$

which is globally asymptotically stable. □

Remark 3.3. We can relax the positivity assumption on $\epsilon_i(t)$ to $\bar{\epsilon}_i > 0$ where $\bar{\epsilon}_i = \frac{1}{\omega}\int_0^\omega \epsilon_i(t)dt$ is the average value of $\epsilon_i(t)$. See Lemma 2.1 in Zhang and Teng [101] for results on a general nonautonomous system of the form $dV_i/dt = \epsilon_i(t) - d_i(t)V_i$.

The above result guarantees that system (3.2.1) admits a unique disease-free periodic solution

$$E_0(t) = (H_1^*(t), \ldots, H_p^*(t), V_1^*(t), \ldots, V_p^*(t), 0, \ldots, 0, 0, \ldots, 0).$$

Biologically, both human and mosquito populations in each patch are seasonally forced due to seasonal human migration and periodic changing in the birth rate of mosquitoes, respectively. Now we consider the asymptotically periodic system for

malaria transmission

$$\begin{aligned}\frac{dh_i}{dt} &= a_i(t)b_i\frac{H_i^*(t)-h_i}{H_i^*(t)}v_i - r_ih_i + \sum_{j=1}^{p} m_{ij}(t)h_j, \quad 1 \le i \le p,\\ \frac{dv_i}{dt} &= a_i(t)c_i\frac{h_i}{H_i^*(t)}(V_i^*(t)-v_i) - d_i(t)v_i, \quad 1 \le i \le p.\end{aligned} \tag{3.3.1}$$

In what follows, we use the definition of Bacaër and Guernaoui [10] (see also Bacaër [9]) and the general calculation method in Wang and Zhao [95] to evaluate the basic reproduction number $\mathcal{R}_0$ for system (3.3.1). Then we analyze the threshold dynamics of system (3.3.1). Finally we study global dynamics for the whole system (3.2.1) by applying the theory of internally chain transitive sets (Hirsch et al. [36]).

Let $x = (h_1, \ldots, h_p, v_1, \ldots, v_p)$ be the vector of all infectious class variables. The linearization of system (3.3.1) at the disease-free equilibrium $P_0 = (0, \ldots, 0, 0, \ldots, 0)$ is

$$\frac{dx}{dt} = (F(t) - V(t))x, \tag{3.3.2}$$

where

$$F(t) = \begin{bmatrix} 0 & \mathcal{A} \\ \mathcal{B} & 0 \end{bmatrix} \text{ and } V(t) = \begin{bmatrix} \mathcal{C} & 0 \\ 0 & \mathcal{D} \end{bmatrix}.$$

Here $\mathcal{A} = (\delta_{ij}a_i(t)b_i)_{p\times p}$, $\mathcal{B} = (\delta_{ij}a_i(t)c_iV_i^*(t)/H_i^*(t))_{p\times p}$, $\mathcal{C} = (\delta_{ij}r_i - m_{ij}(t))_{p\times p}$, $\mathcal{D} = (\delta_{ij}d_i(t))_{p\times p}$ and δ_{ij} denotes the Kronecker delta function (i.e. 1 when $i = j$ and 0 elsewhere).

Let $Y(t,s), t \ge s$, be the evolution operator of the linear ω-periodic system

$$\frac{dy}{dt} = -V(t)y.$$

That is, for each $s \in \mathbb{R}^1$, the $2p \times 2p$ matrix $Y(t,s)$ satisfies

$$\frac{dY(t,s)}{dt} = -V(t)Y(t,s),\ \forall t \geq s,\ Y(s,s) = I_{2p},$$

where I_{2p} is the $2p \times 2p$ identity matrix.

Let C_ω be the ordered Banach space of all ω-periodic functions from $\mathbb{R}^1$ to $\mathbb{R}^{2p}$ equipped with the maximum norm. We define a linear operator $L : C_\omega \to C_\omega$ by

$$(L\phi)(t) = \int_{-\infty}^{t} Y(t,s)F(s)\phi(s)ds = \int_{0}^{\infty} Y(t,t-a)F(t-a)\phi(t-a)da,\ \forall t \in \mathbb{R}^1,\ \phi \in C_\omega.$$

The basic reproduction number of the periodic system (3.3.1) is then defined as $\mathcal{R}_0 := \rho(L)$, the spectral radius of L. Let $W(t,\lambda)$ be the monodromy matrix (see [33]) of the homogeneous linear ω-periodic system

$$\frac{dw}{dt} = \Big(-V(t) + \frac{F(t)}{\lambda}\Big)w, t \in \mathbb{R}^1 \tag{3.3.3}$$

with parameter $\lambda \in (0,\infty)$. That is, $W(t,\lambda)$ is a nonsingular matrix associated with a fundamental solution matrix $\mathbb{W}_\lambda(t)$ of system (3.3.3) through the relation $\mathbb{W}_\lambda(t+\omega) = \mathbb{W}_\lambda(t)W(t,\lambda)$.

It is easy to verify that conditions (A1)-(A7) in Wang and Zhao [95] are satisfied. The following two lemmas will be used in numerical computation of the basic reproduction number $\mathcal{R}_0$.

Lemma 3.4 (Wang and Zhao [95], Theorem 2.1)**.** *The following statements are valid:*

(i) *If $\rho(W(\omega,\lambda)) = 1$ has a positive solution λ_0, then λ_0 is an eigenvalue of L and hence $\mathcal{R}_0 > 0$.*

(ii) *If* $\mathcal{R}_0 > 0$, *then* $\lambda = \mathcal{R}_0$ *is the unique solution of* $\rho(W(\omega, \lambda)) = 1$.

(iii) $\mathcal{R}_0 = 0$ *if and only if* $\rho(W(\omega, \lambda)) < 1$ *for all* $\lambda > 0$.

Lemma 3.5 (Wang and Zhao [95], Theorem 2.2)**.** *Let* $\Phi_{F-V}(t)$ *and* $\rho(\Phi_{F-V}(\omega))$ *be the monodromy matrix of system* (3.3.2) *and the spectral radius of* $\Phi_{F-V}(\omega)$. *The following statements are valid:*

(i) $\mathcal{R}_0 = 1$ *if and only if* $\rho(\Phi_{F-V}(\omega)) = 1$.

(ii) $\mathcal{R}_0 > 1$ *if and only if* $\rho(\Phi_{F-V}(\omega)) > 1$.

(iii) $\mathcal{R}_0 < 1$ *if and only if* $\rho(\Phi_{F-V}(\omega)) < 1$.

Thus, the disease-free equilibrium P_0 *is locally asymptotically stable if* $\mathcal{R}_0 < 1$ *and unstable if* $\mathcal{R}_0 > 1$.

According to Lemma 3.4(ii), we see that the basic reproduction number for (3.3.1) is proportional to the biting rate, that is, $\tilde{\mathcal{R}}_0 = k\mathcal{R}_0$ if $\tilde{\beta}_i(t) = k\beta_i(t)$ for $k > 0$ and $1 \leq i \leq p$ (see Lou and Zhao [51] or Liu and Zhao [49]). Lou and Zhao [52] presented a global qualitative analysis for system (3.3.1) with a single patch. We will show that the system with multiple patches does not exhibit more complicated dynamics.

Lemma 3.6. *Let* $\mathbb{D}_t = \{(h, v); 0 \leq h \leq H^*(t), 0 \leq v \leq V^*(t)\}$. *For each* $x(0) = (h(0), v(0)) \in \mathbb{R}^{2p}_+$, *system* (3.3.1) *admits a unique solution* $x(t) = (h(t), v(t)) \in \mathbb{R}^{2p}_+$ *through* $x(0)$ *for all* $t \geq 0$. *Moreover,* $x(t) \in \mathbb{D}_t$, $\forall t \geq 0$, *provided that* $x(0) \in \mathbb{D}_0$.

Proof. Let $K(t, x)$ denote the vector field described by (3.3.1). Since $K(t, x)$ is continuous and locally Lipschitizan in x in any bounded set. By Theorem 5.2.1 in Smith [80]

and Theorem 3.1, system (3.3.1) has a unique solution through $x(0) \in \mathbb{R}^{2p}_+$ which exists globally. To prove the second statement, we introduce an auxiliary system

$$\begin{aligned} \frac{dh_i}{dt} &= a_i(t)b_i\frac{H_i^*(t)-h_i}{H_i^*(t)}v_i + \sum_{j=1}^{p} m_{ij}(t)h_j, \quad 1 \le i \le p, \\ \frac{dv_i}{dt} &= a_i(t)c_i\frac{h_i}{H_i^*(t)}(V_i^*(t)-v_i), \quad 1 \le i \le p. \end{aligned} \tag{3.3.4}$$

and let $\tilde{K}(t,x)$ be defined by the right hand side of (3.3.4). Clearly, $K(t,x) \le \tilde{K}(t,x)$ for all $(t,x) \in \mathbb{R}^1 \times \mathbb{D}_0$. Note that $(H^*(t), V^*(t))$ is the unique solution of (3.3.4) through $(H^*(0), V^*(0))$. It follows from Theorem 5.1.1 in Smith [80] that $x(t) = (h(t), v(t)) \le (H^*(t), V^*(t))$ holds for all $t \ge 0$ whenever $x(0) \in \mathbb{D}_0$. □

Theorem 3.7. *For system* (3.3.1)*, it admits a unique positive ω-periodic solution which is globally asymptotically stable with initial values in $\mathbb{D}_0\backslash\{0\}$ if $\mathcal{R}_0 > 1$ and the disease-free equilibrium P_0 is globally asymptotically stable in $\mathbb{D}_0$ if $\mathcal{R}_0 \le 1$.*

Proof. To show the global asymptotic stability of $E_0(t)$ or P^0, it suffices to verify that $K(t,x) : \mathbb{R}^1_+ \times \mathbb{D}_0 \to \mathbb{R}^{2p}$ satisfies (A1)-(A3) in Theorem 3.1.2 in Zhao [103].

For every $x = (h,v) \ge 0$ with $h_i = 0$ or $v_i = 0$, $t \in \mathbb{R}^1_+$, we have

$$K_i(t,x) = a_i(t)b_iv_i + \sum_{1\le j\le p, j\ne i} m_{ij}(t)h_j \ge 0 \text{ or } K_{p+i}(t,x) = a_i(t)c_i\frac{h_i}{H_i^*(t)}V_i^*(t) \ge 0,$$

$1 \le i \le p$. So (A1) is satisfied.

By Lemma 3.6 and the irreducibility of $(m_{ij}(t))_{p\times p}$, we know that $(\partial K_i/\partial x_j)_{2p\times 2p}$ is cooperative for $t \ge 0$ and $x \in \mathbb{D}_0$, and is irreducible for $t \ge 0$ and $x \in \text{Int}\mathbb{D}_0$, the interior of $\mathbb{D}_0$. Thus, the semiflow generated by (3.3.1) is monotone in $\mathbb{D}_0$ and is strongly monotone in $\text{Int}\mathbb{D}_0$.

For each $t \geq 0$, $i = 1, \ldots, p$, there hold

$$K_i(t, \alpha x) = a_i(t) b_i \frac{H_i^*(t) - \alpha h_i}{H_i^*(t)} \alpha v_i - r_i \alpha h_i + \sum_{j=1}^{p} m_{ij}(t) \alpha h_j$$
$$> \alpha \Big(a_i(t) b_i \frac{H_i^*(t) - h_i}{H_i^*(t)} v_i - r_i h_i + \sum_{j=1}^{p} m_{ij}(t) h_j \Big) = \alpha K_i(t, x)$$

and

$$K_{p+i}(t, \alpha x) = a_i(t) c_i \frac{\alpha h_i}{H_i^*(t)} (V_i^*(t) - \alpha v_i) - d_i(t) \alpha v_i$$
$$> \alpha \Big(a_i(t) c_i \frac{h_i}{H_i^*(t)} (V_i^*(t) - v_i) - d_i(t) v_i \Big) = \alpha K_{p+i}(t, x),$$

for each $x \gg 0, \alpha \in (0, 1)$. That is $K(t, \cdot)$ is strictly subhomogeneous on $\mathbb{R}_+^{2p}$.

Moreover, $K(t, 0) \equiv 0$ and all solutions are ultimately bounded. Therefore, by Theorem 3.1.2 in Zhao [103] or Theorem 2.3.4 in Zhao [103] as applied to the Poincaré map associated with (3.3.1), the proof is complete. □

Using the theory of internally chain transitive sets (Hirsch et al. [36] or Zhao [103]), as argued in Lou and Zhao [53], we find that the disease either dies out or persists at a periodic attractor. The proof is omitted here.

Theorem 3.8. *For system* (3.2.1)*, if* $\mathcal{R}_0 > 1$ *then there is a unique positive* ω*-periodic solution which is globally asymptotically stable; if* $\mathcal{R}_0 \leq 1$ *then the disease-free periodic solution* $E_0(t)$ *is globally asymptotically stable.*

3.4 Simulations and Discussions

In this section, we provide some numerical simulations for the two-patch case to support our analytical conclusions.

Choose parameter values as follows: the first patch has $b_1 = 0.1, r_1 = 0.009, c_1 = 0.3$; $\epsilon_1(t) = 2.5 - 1.3\cos(\frac{2\pi}{365}t), d_1(t) = 0.08 + 0.04\cos(\frac{2\pi}{365}t), a_1(t) = 0.25 - 0.09\cos(\frac{2\pi}{365}t)$; the second patch has $b_2 = 0.1, r_2 = 0.007, c_2 = 0.3$; $\epsilon_2(t) = 1.8 - 1.2\cos(\frac{2\pi}{365}t), d_2(t) = 0.05 + 0.03\sin(\frac{2\pi}{365}t), a_2(t) = 0.15 - 0.06\cos(\frac{2\pi}{365}t)$; and the migration rates are $m_{12}(t) = 0.003 + 0.001\cos(\frac{2\pi}{365}t), m_{21}(t) = 0.004 + 0.002\sin(\frac{2\pi}{365}t)$. Then Lemma 3.4 implies that $\mathcal{R}_0 \approx 0.943 < 1$ and the disease-free periodic solution is globally asymptotically stable (see Figure 3.1).

With the same parameter values and initial data except that the mosquito biting rates $a_1(t) = 1.2(0.25 - 0.09\cos(\frac{2\pi}{365}t))$ and $a_2(t) = 1.2(0.15 - 0.06\cos(\frac{2\pi}{365}t))$, we obtain $\mathcal{R}_0 = 1.13 > 1$ by Lemma 3.4 or the linearity of $\mathcal{R}_0$ in the biting rates. Every solution with infectives initially present approaches a positive periodic solution (see Figure 3.2).

The respective average basic reproduction numbers $\bar{\mathcal{R}}_0$ (see Zhang et al. [100] and references therein), are $0.589 < 1$ and $0.706 < 1$ corresponding to the two cases shown above. Thus, the autonomous Ross-Macdonald model may underestimate or overestimate disease severity.

In this project, we have developed a compartmental model to address seasonal variations of malaria transmission among different regions by incorporating seasonal human movement and periodic changing in mosquito ecology. We then define the basic reproduction number and establish the global dynamics of the model. Our result gives a possible explanation to the fact that malaria cases show seasonal peaks

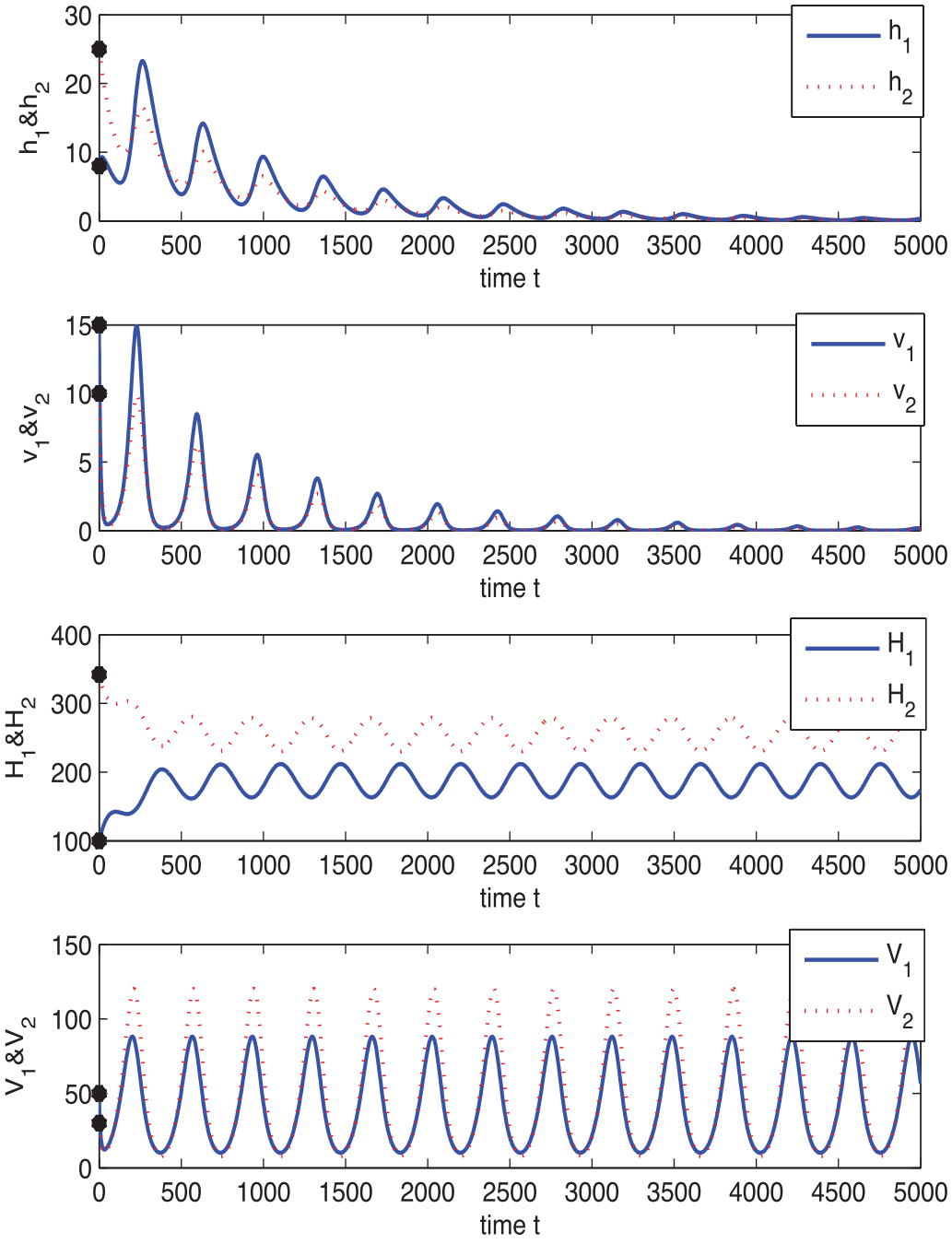

Figure 3.1: *Numerical solution of system* (3.2.1) *with* $a_1(t) = 0.25 - 0.09\cos(\frac{2\pi}{365}t)$ *and* $a_2(t) = 0.15 - 0.06\cos(\frac{2\pi}{365}t)$. *We use the following initial conditions:* $H_1(0) = 100, V_1(0) = 50, h_1(0) = 8, v_1(0) = 15$ *and* $H_2(0) = 342, V_2(0) = 30, h_2(0) = 25, v_2(0) = 10$. *Since* $\mathcal{R}_0 < 1$, *the disease dies out in both patches.*

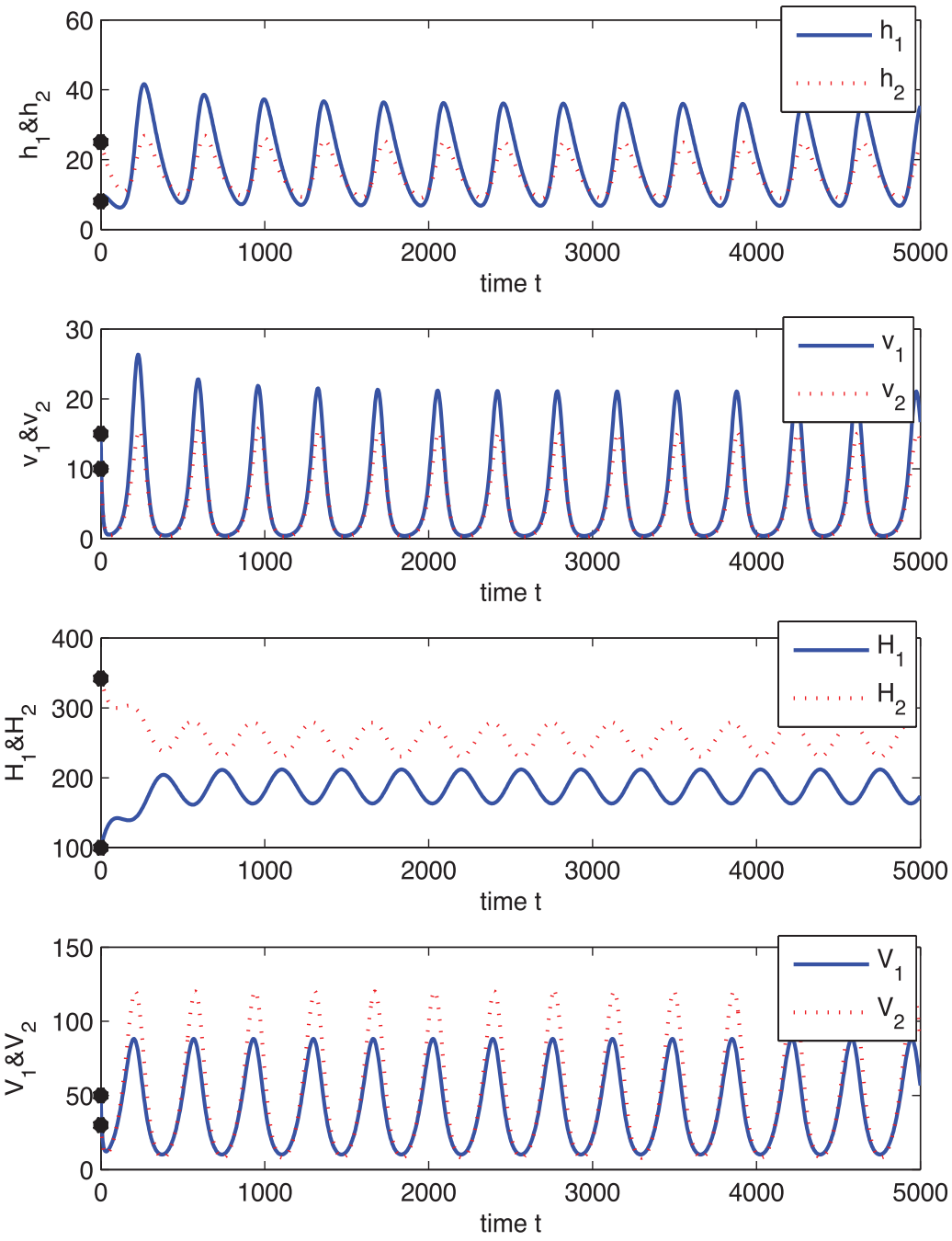

Figure 3.2: *Numerical solution of system* (3.2.1) *with* $a_1(t) = 1.2(0.25 - 0.09\cos(\frac{2\pi}{365}t))$ *and* $a_2(t) = 1.2(0.15 - 0.06\cos(\frac{2\pi}{365}t))$. *We use the following initial conditions:* $H_1(0) = 100, V_1(0) = 50, h_1(0) = 8, v_1(0) = 15$ *and* $H_2(0) = 342, V_2(0) = 30, h_2(0) = 25, v_2(0) = 10$. *Since* $\mathcal{R}_0 > 1$, *the disease persists in both patches.*

in most endemic areas [72]. The numerical example shows that autonomous malaria models can underestimate or overestimate the infection risk.

It is interesting to assess the impacts of climate change on the emerging and reemerging of mosquito-borne diseases, especially malaria. It is believed that global warming would cause climate change. Climatic factors such as rainfall, temperature, humidity and wind speed affect the biological activity and geographic distribution of parasites and their vectors.

The current and potential future impact of climate change on human health has attracted considerable attention in recent years. Many of the early studies (see Ostfeld [69] and the references cited therein) claimed that recent and future trends in climate warming were likely to increase the severity and global distribution of vector-borne diseases, while there is still substantial debate about the link between climate change and the spread of infectious diseases [46]. The controversy is partially due to the fact that although there is massive work using empirical-statistical models to explore the relationship between climatic factors and the distribution and prevalence of vector-borne diseases, there are very few studies incorporating climatic factors into mathematical models to describe disease transmission.

The research that comes closest to what we want to do has been conducted by Parham and Michael in [70], where they used a system of delay differential equations to model malaria transmission under varying climatic and environmental conditions. Model parameters are assume to be temperature-dependent or rainfall-dependent or both. Due to the complexity of the model, mathematical analysis was impossible and only numerical simulations were carried out. We would like to expand our model to a mathematically tractable climate-based model in the future.

Chapter 4

Modeling the Spatial Spread of Rift Valley Fever in Egypt

4.1 Background

Rift Valley fever (RVF) is a viral zoonosis of domestic animals (such as cattle, sheep, camels and goats) and humans caused by the RVF virus (RVFV), a member of the genus *Phlebovirus* in the Bunyaviridae family. Initially identified in the Rift Valley of Kenya in 1931, outbreaks of RVF have been reported in sub-Saharan Africa, Egypt, Saudi Arabia and Yemen. These result in significant economic losses due to high mortality and abortion in livestock. The virus is spread primarily by the bite of an infected female mosquito, typically the *Aedes* or *Culex* genera. The *Aedes* mosquitoes can only transmit the disease to hosts, while the *Culex* mosquitoes can also transmit the disease vertically (mother-to-offspring). Humans can get RVF through the bites of infected mosquitoes or direct/indirect contact with the blood or organs of infected animals, but they cannot transmit it. To date, two types of vaccines are available for veterinary use [41], but there is no licensed vaccine for humans.

Mathematical models have become an important tool in identifying disease transmission process, assessing infection risk and prevalence, and in optimizing control

strategies. However, so far little has been done to model and analyze the RVF transmission dynamics [57]. Gaff et al. [26] proposed a compartment model explored the mechanisms of RVFV circulation including *Aedes* and *Culex* mosquitoes and livestock population, in which each adult mosquito population is divided into classes containing susceptible, exposed and infectious individuals and the livestock population is classified as susceptible, exposed, infectious and recovered. To account for vertical transmission in *Aedes* mosquiotes, compartments for uninfected and infected eggs are also included. Meanwhile, only uninfected eggs are included for *Culex* mosquitoes. They derived the basic reproduction number to assess the stability of the disease-free equilibrium and performed sensitivity analysis to determine the most significant model parameters to disease transmission. In [62], Mpheshe et al. modified the model in Gaff et al. [26] to reduce egg classes of mosquitoes, include human population and exclude vertical transmission in mosquitoes. They gave conditions for the stability of the disease-free equilibrium and persistence of the disease. Sensitivity indices of the basic reproduction number and the endemic equilibrium were evaluated to study the relative importance of different factors responsible for RVF transmission and prevalence. It is believed that RVFV is introduced to a disease-free area by insects carried by wind and animal movements through trade [57]. Xue et al. [97] presented a network-based metapopulation model incorporating *Aedes* and *Culex* mosquitoes, livestock and human populations. They tested the model with data from an outbreak of RVF in South Africa and analyzed the sensitivity of the model to its parameters. Recently, Chamchod et al. [13] proposed a simple but innovative model to investigate the emergence of RVF outbreaks, and epizootic and enzootic cycles of RVFV. Many aspects of their investigation have not been addressed in previous modeling studies. For example, they considered the effect of vaccination on the transmission dynam-

ics of RVFV. However, these models either do not include spatial effects or are too complicated to perform rigorous mathematical analysis.

The main purpose of this chapter is to propose a mathematically tractable model with spatial dynamics. In the next section, we develop a three-patch epidemic model to describe the spatial spread of RVF in Egypt. In Section 3, the basic reproduction number for each patch is calculated and the threshold dynamics of the model will be established. Moreover, the existence and stability of the endemic equilibrium are discussed. In Section 4, we simulate an interesting scenario showing possible explanation to the observed phenomenon in Egypt. A brief discussion is given in Section 5.

4.2 The Model

The first outbreak of RVF in Egypt occurred in the Nile Valley and Delta in 1977 [37]. This was the first RVF outbreak recorded outside traditionally affected areas in sub-Saharan Africa. Due to a combination of a lack of experience in dealing with RVF patients and insufficient public health programs, the outbreak caused at least thousands of human infections and hundreds of human deaths [62]. Since then, Egypt has been experiencing continued RVF outbreaks among domestic animals which indicates that the RVFV has become enzootic in Egypt. The imported animals from Sudan and African Horn were usually not vaccinated against RVFV. Travel time from north-central Sudan, where RVF was epizootic, to livestock markets in southern Egypt (Aswan Province), was less than 5 days, approximating the incubation period of RVFV in sheep [1, 25]. So it is hypothesized that the recurrence of epizootic is

mainly caused by the continuous importation of infected animals from Sudan and failure of the locally applied RVF vaccination program [43].

Egypt is an arid country with most of the population concentrated along the Nile, in the Delta and near the Suez Canal. The imported animals enter southern Egypt from northern Sudan, are moved up the Nile, and then consumed at these population centres. Vertical transmission of RVF has not been demonstrated to occur in Egypt [60]. For simplicity, we restrict our focus on the disease transmission between domestic animals and mosquitoes. To capture the idea that more mosquitoes lead to more transmission, it seems most natural to use mass-action transmission terms. The movement timescale of animals is relatively short, so we assume that there is no host reproduction during the journey. Therefore, the density of hosts is determined by movement, mortality, and the rate at which they are introduced, which could be set to depend on demand. We assume that there is no movement for vector population because of their limited mobility. Assume also that the mosquito population satisfies the logistic growth to maintain an equilibrium vector population. For epidemiology, we use a simple SIRS model for hosts and an SI model for vectors.

Based on the above assumptions, we propose a three-patch model with animals movement from patch 1 to patch 2 and then from patch 2 to patch 3:

$$\begin{cases} \dfrac{dS_1}{dt} = r - \alpha_1 S_1 V_1 - \mu S_1 + \zeta R_1 - cS_1, \\ \dfrac{dI_1}{dt} = \alpha_1 S_1 V_1 - (\mu + \gamma + \delta) I_1 - cI_1, \\ \dfrac{dR_1}{dt} = \gamma I_1 - (\mu + \zeta) R_1 - cR_1, \\ \dfrac{dU_1}{dt} = \xi_1 (U_1 + V_1) - \dfrac{\xi_1 - \nu_1}{M_1} (U_1 + V_1)^2 - \nu_1 U_1 - \beta_1 I_1 U_1, \\ \dfrac{dV_1}{dt} = -\nu_1 V_1 + \beta_1 I_1 U_1, \end{cases} \tag{4.2.1a}$$

Table 4.1: *The state variables in model* (4.2.1) *and their descriptions*

Symbol	Description
S_i	Number of susceptible animals in patch i at time t
I_i	Number of infectious animals in patch i at time t
R_i	Number of recovered animals in patch i at time t
U_i	Number of susceptible mosquitoes in patch i at time t
V_i	Number of infectious mosquitoes in patch i at time t

$$\begin{cases} \dfrac{dS_2}{dt} = cS_1 - \alpha_2 S_2 V_2 - \mu S_2 + \zeta R_2 - cS_2, \\ \dfrac{dI_2}{dt} = cI_1 + \alpha_2 S_2 V_2 - (\mu + \gamma + \delta) I_2 - cI_2, \\ \dfrac{dR_2}{dt} = cR_1 + \gamma I_2 - (\mu + \zeta) R_2 - cR_2, \\ \dfrac{dU_2}{dt} = \xi_2 (U_2 + V_2) - \dfrac{\xi_2 - \nu_2}{M_2} (U_2 + V_2)^2 - \nu_2 U_2 - \beta_2 I_2 U_2, \\ \dfrac{dV_2}{dt} = -\nu_2 V_2 + \beta_2 I_2 U_2, \end{cases} \tag{4.2.1b}$$

$$\begin{cases} \dfrac{dS_3}{dt} = cS_2 - \alpha_3 S_3 V_3 - \mu S_3 + \zeta R_3 - cS_3, \\ \dfrac{dI_3}{dt} = cI_2 + \alpha_3 S_3 V_3 - (\mu + \gamma + \delta) I_3 - cI_3, \\ \dfrac{dR_3}{dt} = cR_2 + \gamma I_3 - (\mu + \zeta) R_3 - cR_3, \\ \dfrac{dU_3}{dt} = \xi_3 (U_3 + V_3) - \dfrac{\xi_3 - \nu_3}{M_3} (U_3 + V_3)^2 - \nu_3 U_3 - \beta_3 I_3 U_3, \\ \dfrac{dV_3}{dt} = -\nu_3 V_3 + \beta_3 I_3 U_3. \end{cases} \tag{4.2.1c}$$

The state variables and parameters used in model (4.2.1) and their descriptions are presented in Table 4.1 and Table 4.2, respectively.

The total number of mosquitoes in patch i at time t, denoted by $N_i^v(t)$, satisfies

$$\frac{dN_i^v}{dt} = (\xi_i - \nu_i) N_i^v - \frac{\xi_i - \nu_i}{M_i} (N_i^v)^2, i = 1, 2, 3,$$

Table 4.2: *The parameters in model* (4.2.1) *and their descriptions*

Symbol	Description
r	Recruitment rate of animals
c	Movement rate of animals
μ	Natural death rate for animals
δ	Disease-induced death rate for animals
γ	Recovery rate for animals
ζ	Rate of loss of immunity for animals
ξ_i	Growth rate of mosquitoes in patch i
ν_i	Natural death rate for mosquitoes in patch i
M_i	Carrying capacity for mosquitoes in patch i
α_i	Transmission rate from vector to host in patch i
β_i	Transmission rate from host to vector in patch i

and it converges to M_i as $t \to \infty$ for any positive initial value. Therefore, we may consider the following reduced system

$$\begin{cases} \dfrac{dS_1}{dt} = r - \alpha_1 S_1 V_1 - \mu S_1 + \zeta R_1 - cS_1, \\ \dfrac{dI_1}{dt} = \alpha_1 S_1 V_1 - (\mu + \gamma + \delta) I_1 - cI_1, \\ \dfrac{dR_1}{dt} = \gamma I_1 - (\mu + \zeta) R_1 - cR_1, \\ \dfrac{dV_1}{dt} = -\nu_1 V_1 + \beta_1 I_1 (M_1 - V_1), \end{cases} \tag{4.2.2a}$$

$$\begin{cases} \dfrac{dS_2}{dt} = cS_1 - \alpha_2 S_2 V_2 - \mu S_2 + \zeta R_2 - cS_2, \\ \dfrac{dI_2}{dt} = cI_1 + \alpha_2 S_2 V_2 - (\mu + \gamma + \delta) I_2 - cI_2, \\ \dfrac{dR_2}{dt} = cR_1 + \gamma I_2 - (\mu + \zeta) R_2 - cR_2, \\ \dfrac{dV_2}{dt} = -\nu_2 V_2 + \beta_2 I_2 (M_2 - V_2), \end{cases} \tag{4.2.2b}$$

$$\begin{cases} \dfrac{dS_3}{dt} = cS_2 - \alpha_3 S_3 V_3 - \mu S_3 + \zeta R_3 - cS_3, \\ \dfrac{dI_3}{dt} = cI_2 + \alpha_3 S_3 V_3 - (\mu + \gamma + \delta) I_3 - cI_3, \\ \dfrac{dR_3}{dt} = cR_2 + \gamma I_3 - (\mu + \zeta) R_3 - cR_3, \\ \dfrac{dV_3}{dt} = -\nu_3 V_3 + \beta_3 I_3 (M_3 - V_3). \end{cases} \tag{4.2.2c}$$

Theorem 4.1. *All forward solutions in* $\mathbb{R}^{12}_+$ *of* (4.2.2) *eventually enter into* $\Omega = \Omega_1 \times \Omega_2 \times \Omega_3$, *where* $\Omega_i = \{(S_i, I_i, R_i, V_i) \in \mathbb{R}^4_+ : S_i + I_i + R_i \leq \dfrac{rc^{i-1}}{(\mu + c)^i}, V_i \leq M_i\}, i = 1, 2, 3,$ *and* Ω *is positively invariant for* (4.2.2).

Proof. Let $N_i^h(t)$ be the total number of host population in patch i at time t. Then we have

$$\frac{dN_1^h}{dt} = r - (\mu + c)N_1^h - \delta I_1 \leq r - (\mu + c)N_1^h$$

and

$$\frac{dN_i^h}{dt} = cN_{i-1}^h - (\mu + c)N_i^h - \delta I_i \leq cN_{i-1}^h - (\mu + c)N_i^h, \ i = 2, 3.$$

By a simple comparison theorem [82], the proof is complete. □

4.3 Mathematical Analysis

It is easy to see that (4.2.2) has a unique disease-free equilibrium

$$\begin{aligned} E^0 &= (S_1^0, I_1^0, R_1^0, V_1^0, S_2^0, I_2^0, R_2^0, V_2^0, S_3^0, I_3^0, R_3^0, V_3^0) \\ &= (\frac{r}{\mu + c}, 0, 0, 0, \frac{rc}{(\mu + c)^2}, 0, 0, 0, \frac{rc^2}{(\mu + c)^3}, 0, 0, 0). \end{aligned}$$

System (4.2.2) is in a block-triangular form, the dynamics of patch 1 are independent of patch 2 and patch 3 while the dynamics of patch 2 are independent of patch 3.

4.3.1 The First Patch

Obviously, $E_1^0 = (S_1^0, 0, 0, 0)$ is the unique disease-free equilibrium of subsystem (4.2.2a). To calculate the basic reproduction number corresponding to (4.2.2a), we order the infected state variables by (I_1, R_1, V_1). Following the method and notations of van den Driessche and Watmough [90], the linearization of (4.2.2a) at E_1^0 gives

$$F = \begin{bmatrix} 0 & 0 & \alpha_1 S_1^0 \\ 0 & 0 & 0 \\ \beta_1 M_1 & 0 & 0 \end{bmatrix} \text{ and } V = \begin{bmatrix} \mu+\gamma+\delta+c & 0 & 0 \\ -\gamma & \mu+\zeta+c & 0 \\ 0 & 0 & \nu_1 \end{bmatrix}.$$

Direct calculation yields

$$V^{-1} = \begin{bmatrix} (\mu+\gamma+\delta+c)^{-1} & 0 & 0 \\ \gamma(\mu+\gamma+\delta+c)^{-1}(\mu+\zeta+c)^{-1} & (\mu+\zeta+c)^{-1} & 0 \\ 0 & 0 & \nu_1^{-1} \end{bmatrix}$$

and the basic reproduction number for the first patch equals

$$\mathcal{R}_{10} = \rho(FV^{-1}) = \sqrt{\frac{\alpha_1 S_1^0}{\nu_1} \cdot \frac{\beta_1 M_1}{\mu+\gamma+\delta+c}} = \sqrt{\frac{\alpha_1 r}{(\mu+c)\nu_1} \cdot \frac{\beta_1 M_1}{\mu+\gamma+\delta+c}},$$

which depends on all parameters except ζ, the rate of loss of immunity for animals. $(\mathcal{R}_{10})^2$ is proportional to S_1^0 and M_1, so more mosquitoes and more animals lead to more disease transmission.

Theorem 4.2. *The disease-free equilibrium E_1^0 of* (4.2.2a) *is globally asymptotically stable in Ω_1 if $\mathcal{R}_{10} \leq 1$ and unstable if $\mathcal{R}_{10} > 1$.*

Proof. It is easy to show the local stability of E_1^0 by verifying (A1)-(A5) in van den

Drissche and Watmough [90].

Consider a Lyapunov function $L_1 = \nu_1(\mu + c)I_1 + \alpha_1 r V_1$ on Ω_1. Then

$$\begin{aligned}
L_1' &= \nu_1(\mu + c)I_1' + \alpha_1 r V_1' \\
&= \nu_1(\mu + c)\alpha_1 S_1 V_1 - \nu_1(\mu + c)(\mu + \gamma + \delta + c)I_1 - \alpha_1 r \nu_1 V_1 + \alpha_1 r \beta_1 I_1(M_1 - V_1) \\
&= [\nu_1(\mu + c)\alpha_1 S_1 - \alpha_1 r \nu_1]V_1 + [\alpha_1 r \beta_1(M_1 - V_1) - \nu_1(\mu + c)(\mu + \gamma + \delta + c)]I_1 \\
&= \nu_1(\mu + c)\alpha_1(S_1 - S_1^0)V_1 + [\alpha_1 r \beta_1(M_1 - V_1) - \nu_1(\mu + c)(\mu + \gamma + \delta + c)]I_1 \\
&\leq [\alpha_1 r \beta_1(M_1 - V_1) - \nu_1(\mu + c)(\mu + \gamma + \delta + c)]I_1 \quad \text{in} \quad \Omega_1 \\
&\leq [\alpha_1 r \beta_1 M_1 - \nu_1(\mu + c)(\mu + \gamma + \delta + c)]I_1 \\
&= [(\mathcal{R}_{10}^2 - 1)\nu_1(\mu + c)(\mu + \gamma + \delta + c)]I_1 \\
&\leq 0 \quad \text{if} \quad \mathcal{R}_{10} \leq 1.
\end{aligned}$$

The largest compact invariant set, denoted by Γ_1, in $\{(S_1, I_1, R_1, U_1, V_1) \in \Omega_1 : L_1' = 0\}$ is the singleton $\{E_1^0\}$.

Case 1: $\mathcal{R}_{10} < 1$**.** Preceding calculation shows that $I_1 \equiv 0$. So

$$\frac{dV_1}{dt} = -\nu_1 V_1 \text{ and } \frac{dR_1}{dt} = -(\mu + \zeta + c)R_1.$$

Backward continuation of a compact invariant set indicates that $V_1 = 0$ and $R_1 = 0$. Thus

$$\frac{dS_1}{dt} = r - (\mu + c)S_1.$$

This means that $S_1 = S_1^0$ and hence $\Gamma_1 = \{E_1^0\}$.

Case 2: $\mathcal{R}_{10} = 1$**.** Preceding calculation gives either $V_1 \equiv 0$ or $I_1 \equiv 0$. The latter can be proceeded as before. Suppose $V_1 \equiv 0$, then $\dfrac{dV_1}{dt} = \beta_1 I_1 M_1 \equiv 0$ implies $I_1 = 0$.

Once again this can proceed as before.

By LaSalle's Invariance Principle [47], E_1^0 is globally asymptotically stable in Ω_1. □

Theorem 4.3. *If $\mathcal{R}_{10} > 1$, then system* (4.2.2a) *has a unique endemic equilibrium, denoted by $E_1^* = (S_1^*, I_1^*, R_1^*, V_1^*)$, which is locally asymptotically stable. Moreover, the disease is uniformly persistent in Ω_1^0, the interior of Ω_1, i.e., there is a constant $\epsilon > 0$ such that any solution of* (4.2.2a) *starting at a point of Ω_1^0 satisfies*

$$\liminf_{t\to\infty}(I_1(t), R_1(t), V_1(t)) > (\epsilon, \epsilon, \epsilon).$$

Proof. If $E_1^* = (S_1^*, I_1^*, R_1^*, V_1^*)$ is a positive equilibrium of (4.2.2a), then it satisfies the following system of algebraic equations

$$\begin{aligned} r - \alpha_1 S_1 V_1 - \mu S_1 + \zeta R_1 - cS_1 &= 0, \\ \alpha_1 S_1 V_1 - (\mu + \gamma + \delta) I_1 - cI_1 &= 0, \\ \gamma I_1 - (\mu + \zeta) R_1 - cR_1 &= 0, \\ -\nu_1 V_1 + \beta_1 I_1 (M_1 - V_1) &= 0. \end{aligned} \tag{4.3.1}$$

Solving S_1, R_1 and V_1 in terms of I_1 from the last three equations of (4.3.1), that is,

$$S_1 = \frac{(\mu+\gamma+\delta+c)(\nu_1+\beta_1 I_1)}{\alpha_1\beta_1 M_1},\ R_1 = \frac{\gamma I_1}{\mu+\zeta+c},\ V_1 = \frac{\beta_1 I_1 M_1}{\nu_1+\beta_1 I_1},$$

and substituting them into the first equation, we obtain

$$r - (\mu+\gamma+\delta+c)I_1 - (\mu+c)\frac{\mu+\gamma+\delta+c}{\alpha_1\beta_1 M_1}(\beta_1 I_1 + \nu_1) + \zeta\frac{\gamma}{\mu+\zeta+c}I_1 = 0,$$

which can be simplified to a linear equation

$$\Big[(\mu+\gamma+\delta+c)+(\mu+c)\frac{\mu+\gamma+\delta+c}{\alpha_1 M_1}-\frac{\zeta\gamma}{\mu+\zeta+c}\Big]I_1+\Big[(\mu+c)\frac{\mu+\gamma+\delta+c}{\alpha_1\beta_1 M_1}\nu_1-r\Big]=0.$$

The coefficient of I_1 is always positive and the constant part is negative if and only if $\mathcal{R}_{10}>1$. Hence, system (4.2.2a) has a unique endemic equilibrium if and only if $\mathcal{R}_{10}>1$.

Next we study the local stability of E_1^* by using the Routh-Hurwitz criterion. The Jacobian matrix of system (4.2.2a) at the endemic equilibrium E_1^* is

$$J(S_1^*,I_1^*,R_1^*,V_1^*)=\begin{pmatrix} -\alpha_1 V_1^*-\rho & 0 & \zeta & -\alpha_1 S_1^* \\ \alpha_1 V_1^* & -(\rho+\gamma+\delta) & 0 & \alpha_1 S_1^* \\ 0 & \gamma & -(\rho+\zeta) & 0 \\ 0 & \beta_1(M_1-V_1^*) & 0 & -\nu_1-\beta_1 I_1^* \end{pmatrix},$$

where $\rho=\mu+c$ and the corresponding characteristic equation is

$$P_1(\lambda)=(\lambda+\rho+\zeta)(\lambda^3+b_2\lambda^2+b_1\lambda+b_0)-\zeta\alpha_1 V_1^*\gamma(\lambda+\nu_1+\beta_1 I_1^*)=0,$$

where

$$b_2=\alpha_1 V_1^*+2\rho+\gamma+\delta+\nu_1+\beta_1 I_1^*>0,$$
$$b_1=(\alpha_1 V_1^*+\rho)(\rho+\gamma+\delta)+(\alpha_1 V_1^*+2\rho+\gamma+\delta)(\nu_1+\beta_1 I_1^*)-\alpha_1\beta_1 S_1^*(M_1-V_1^*),$$
$$b_0=(\alpha_1 V_1^*+\rho)(\rho+\gamma+\delta)(\nu_1+\beta_1 I_1^*)-\alpha_1\beta_1 S_1^*\rho(M_1-V_1^*).$$

It follows from the second and fourth equations of (4.3.1) that

$$(\rho+\gamma+\delta)\nu_1 = \alpha_1\beta_1 S_1^*(M_1 - V_1^*)$$

and hence

$$b_1 = (\alpha_1 V_1^* + \rho)(\rho+\gamma+\delta+\nu_1) + (\alpha_1 V_1^* + 2\rho + \gamma + \delta)\beta_1 I_1^* > 0,$$
$$b_0 = (\rho+\gamma+\delta)(\alpha_1\nu_1 V_1^* + \alpha_1\beta_1 V_1^* I_1^* + \rho\beta_1 I_1^*) > 0 \text{ and } b_1 b_2 > b_0.$$

Then

$$P_1(\lambda) = \lambda^4 + c_3\lambda^3 + c_2\lambda^2 + c_1\lambda + c_0 = 0,$$

where

$$c_3 = \rho + \zeta + b_2 > 0, c_2 = (\rho+\zeta)b_2 + b_1 > 0,$$

$$c_1 = (\rho+\zeta)b_1 + b_0 - \zeta\alpha_1 V_1^*\gamma = \rho b_1 + b_0 + \zeta(b_1 - \alpha_1 V_1^*\gamma) > 0,$$

$$c_0 = (\rho+\zeta)b_0 - \zeta\alpha_1 V_1^*\gamma(\nu_1 + \beta_1 I_1^*) = \rho b_0 + \zeta(b_0 - \alpha_1 V_1^*\gamma(\nu_1 + \beta_1 I_1^*)) > 0.$$

Now it suffices to show that $c_1c_2c_3 > c_1^2 + c_3^2c_0$. In fact

$$\begin{aligned}
&c_1c_2c_3 - c_1^2 - c_3^2c_0 = c_1(c_2c_3 - c_1) - c_3^2c_0 \\
=&c_1[c_3(\rho+\zeta)b_2 + (b_1b_2 - b_0) + \zeta\alpha_1 V_1^*\gamma] - c_3^2c_0 \\
>&c_1c_3(\rho+\zeta)b_2 - c_3^2c_0 = c_3[c_1(\rho+\zeta)b_2 - c_3c_0] \\
=&c_3[(\rho+\zeta)^2(b_1b_2 - b_0) - \zeta\alpha_1 V_1^*\gamma((\rho+\zeta)b_2 - (\rho+\zeta+b_2)(\nu_1 + \beta_1 I_1^*))] \\
>&c_3[(\rho+\zeta)\zeta(b_1b_2 - b_0) - \zeta\alpha_1 V_1^*\gamma(\rho+\zeta)b_2] \\
=&c_3(\rho+\zeta)\zeta(b_1b_2 - b_0 - \alpha_1 V_1^*\gamma b_2) > 0.
\end{aligned}$$

Thus, the Routh-Hurwitz criterion implies that all eigenvalues of the characteristic equation have negative real parts. Hence, the endemic equilibrium is locally asymptotically stable.

Finally, the uniform persistence of system (4.2.2a) in Ω_1^0 can be proved by applying Theorem 4.6 in Thieme [88]. We omit the proof here, since it is similar to that of Theorem 2.5 in Gao and Ruan [27]. □

Remark 4.4. It is worth to mention that Yang et al. [98] studied a similar vector-host epidemic model with an SIR structure for the host population and without disease-induced host deaths. They used the method of the second additive compound matrix (see [48] and references therein) to establish the global stability of the endemic equilibrium when it exists. Unfortunately, we cannot use that approach to establish the global result because of the higher complexity in our model.

4.3.2 The Second Patch

By a simple comparison theorem, we conclude that the disease is uniformly persistent in Ω^0 if it is uniformly persistent in Ω_1^0. Namely, the disease will persist in all three patches if $\mathcal{R}_{10} > 1$. Indeed, it follows from Theorem 4.3 that for any fixed initial data we have

$$\frac{dI_2}{dt} \geq c\epsilon - (\mu + \gamma + \delta + c)I_2$$

for t large enough. So $\liminf_{t\to\infty} I_2(t) \geq c\epsilon/(\mu + \gamma + \delta + c)$. Similarly, we can find positive lower limits for all other variables. If the disease dies out in patch 1, i.e., $\mathcal{R}_{10} \leq 1$, each solution of (4.2.2a) with nonnegative initial data converges to E_1^0 and

the limiting system of (4.2.2b) is

$$\begin{aligned}
\frac{dS_2}{dt} &= cS_1^0 - \alpha_2 S_2 V_2 - \mu S_2 + \zeta R_2 - cS_2, \\
\frac{dI_2}{dt} &= \alpha_2 S_2 V_2 - (\mu + \gamma + \delta) I_2 - cI_2, \\
\frac{dR_2}{dt} &= \gamma I_2 - (\mu + \zeta) R_2 - cR_2, \\
\frac{dV_2}{dt} &= -\nu_2 V_2 + \beta_2 I_2 (M_2 - V_2).
\end{aligned} \tag{4.3.2}$$

Comparing (4.3.2) with (4.2.2a), we immediately find that (4.3.2) possesses a unique disease-free equilibrium $E_2^0 = (S_2^0, I_2^0, R_2^0, V_2^0) = (cS_1^0/(\mu + c), 0, 0, 0) = (rc/(\mu + c)^2, 0, 0, 0)$ and obtain the basic reproduction number of patch 2 as

$$\mathcal{R}_{20} = \sqrt{\frac{\alpha_2 S_2^0}{\nu_2} \cdot \frac{\beta_2 M_2}{\mu + \gamma + \delta + c}} = \sqrt{\frac{\alpha_2 rc}{(\mu + c)^2 \nu_2} \cdot \frac{\beta_2 M_2}{\mu + \gamma + \delta + c}}.$$

If $\mathcal{R}_{10} \leq 1$ and $\mathcal{R}_{20} \leq 1$, then the disease goes extinct in the first two patches; if $\mathcal{R}_{10} \leq 1$ and $\mathcal{R}_{20} > 1$, then the disease dies out in the first patch but persists in the last two patches.

4.3.3 The Third Patch

Similarly, if $\mathcal{R}_{10} \leq 1$ and $\mathcal{R}_{20} \leq 1$, we obtain a limiting system of (4.2.2c) as follows:

$$\begin{aligned}
\frac{dS_3}{dt} &= cS_2^0 - \alpha_3 S_3 V_3 - \mu S_3 + \zeta R_3 - cS_3, \\
\frac{dI_3}{dt} &= \alpha_3 S_3 V_3 - (\mu + \gamma + \delta) I_3 - cI_3, \\
\frac{dR_3}{dt} &= \gamma I_3 - (\mu + \zeta) R_3 - cR_3, \\
\frac{dV_3}{dt} &= -\nu_3 V_3 + \beta_3 I_3 U_3,
\end{aligned} \tag{4.3.3}$$

System (4.3.3) has a unique disease-free equilibrium $E_3^0 = (S_3^0, I_3^0, R_3^0, V_3^0) = (cS_2^0/(\mu + c), 0, 0, 0) = (rc^2/(\mu+c)^3, 0, 0, 0)$ and the basic reproduction number of patch 3 is given by

$$\mathcal{R}_{30} = \sqrt{\frac{\alpha_3 S_3^0}{\nu_3} \cdot \frac{\beta_3 M_3}{\mu + \gamma + \delta + c}} = \sqrt{\frac{\alpha_3 r c^2}{(\mu + c)^3 \nu_3} \cdot \frac{\beta_3 M_3}{\mu + \gamma + \delta + c}}.$$

If $\mathcal{R}_{10} \leq 1$, $\mathcal{R}_{20} \leq 1$ and $\mathcal{R}_{30} \leq 1$, then the disease goes extinct in all three patches; if $\mathcal{R}_{10} \leq 1$, $\mathcal{R}_{20} \leq 1$ and $\mathcal{R}_{30} > 1$, then the disease dies out in the first two patches, but persists in the third patch. So we have the following result:

Theorem 4.5. *For the full model* (4.2.2)*, if* $\mathcal{R}_{10} > 1$*, the disease persists in all three patches; if* $\mathcal{R}_{10} \leq 1$ *and* $\mathcal{R}_{20} > 1$*, the disease dies out in the first patch but persists in the remaining two patches; if* $\mathcal{R}_{10} \leq 1$*,* $\mathcal{R}_{20} \leq 1$ *and* $\mathcal{R}_{30} > 1$*, the disease dies out in the first two patches, but persists in the last patch; if* $\mathcal{R}_{10} \leq 1$*,* $\mathcal{R}_{20} \leq 1$ *and* $\mathcal{R}_{30} \leq 1$*, the disease dies out in all three patches and* E^0 *is globally asymptotically stable.*

Theorem 4.6. *System* (4.2.2) *has a unique endemic equilibrium, denoted* $E^* = (S_1^*, I_1^*, R_1^*, V_1^*, S_2^*, I_2^*, R_2^*, V_2^*, S_3^*, I_3^*, R_3^*, V_3^*)$*, if and only if* $\mathcal{R}_{10} > 1$ *and it is locally asymptotically stable when it exists.*

Proof. The necessity is a straightforward consequence of Theorem 4.2. To prove the existence and uniqueness of an endemic equilibrium as $\mathcal{R}_{10} > 1$, it suffices to show that the system

$$\begin{aligned}
\frac{dS_i}{dt} &= cS_{i-1}^* - \alpha_i S_i V_i - \mu S_i + \zeta R_i - cS_i, \\
\frac{dI_i}{dt} &= cI_{i-1}^* + \alpha_i S_i V_i - (\mu + \gamma + \delta) I_i - cI_i, \\
\frac{dR_i}{dt} &= cR_{i-1}^* + \gamma I_i - (\mu + \zeta) R_i - cR_i, \\
\frac{dV_i}{dt} &= -\nu_i V_i + \beta_i I_i (M_i - V_i),
\end{aligned} \tag{4.3.4}$$

has a unique positive equilibrium for $i = 2, 3$. To compute the constant solution of (4.3.4), we set its right hand side be zero and direct calculations yield

$$cS^*_{i-1}+cI^*_{i-1}+\zeta\frac{cR^*_{i-1}+\gamma I_i}{\mu+\zeta+c} = (\mu+\gamma+\delta+c)I_i+(\mu+c)\frac{(\mu+\gamma+\delta+c)I_i - cI^*_{i-1}}{\alpha_i}\cdot\frac{\beta_i I_i+\nu_i}{\beta_i M_i I_i},$$

which can be reduced to a quadratic equation

$$f(I_i) \equiv a_2 I_i^2 + a_1 I_i + a_0 = 0, \tag{4.3.5}$$

where $a_2 = -\Big(1+\frac{\mu+c}{\alpha_i M_i}\Big)(\mu+\gamma+\delta+c)+\zeta\frac{\gamma}{\mu+\zeta+c} < 0$, $a_1 = cS^*_{i-1}+cI^*_{i-1} - \frac{\mu+c}{\alpha_i\beta_i M_i}((\mu+\gamma+\delta+c)\nu_i - cI^*_{i-1}\beta_i)+\zeta\frac{cR^*_{i-1}}{\mu+\zeta+c}$ and $a_0 = \frac{\mu+c}{\alpha_i\beta_i M_i}cI^*_{i-1}\nu_i > 0$.

Thus, (4.3.5) has exactly one positive root, I_i^*. To check the positivity of other variables, we need to verify that $I_i^* > cI^*_{i-1}/(\mu+\gamma+\delta+c)$, or equivalently, $f(cI^*_{i-1}/(\mu+\gamma+\delta+c)) > 0$. In fact, $f(cI^*_{i-1}/(\mu+\gamma+\delta+c))$ equals

$$\frac{\zeta\gamma c^2(I^*_{i-1})^2}{(\mu+\zeta+c)(\mu+\gamma+\delta+c)^2}+\frac{c^2S^*_{i-1}I^*_{i-1}}{\mu+\gamma+\delta+c}+\frac{\zeta c^2R^*_{i-1}I^*_{i-1}}{(\mu+\zeta+c)(\mu+\gamma+\delta+c)} > 0.$$

The local stability of the endemic equilibrium $(S_i^*, I_i^*, R_i^*, V_i^*)$ of system (4.3.4) can be proved in a way similar to that of E_1^* in Theorem 4.3. □

4.3.4 Model with Restriction

Research in RVF indicates that an infection leads to a durable, probably life-long, immunity in animals [71]. Meanwhile, the immunity period is relatively longer than the duration of movement. We may assume that ζ equals zero and use an SIR model for the host population. In this case, since R_i does not appear in other equations of

(4.2.2), system (4.2.2) can be reduced to

$$\begin{cases} \dfrac{dS_1}{dt} = r - \alpha_1 S_1 V_1 - \mu S_1 - cS_1, \\ \dfrac{dI_1}{dt} = \alpha_1 S_1 V_1 - (\mu + \gamma + \delta) I_1 - cI_1, \\ \dfrac{dV_1}{dt} = -\nu_1 V_1 + \beta_1 I_1 (M_1 - V_1), \end{cases} \tag{4.3.6a}$$

$$\begin{cases} \dfrac{dS_2}{dt} = cS_1 - \alpha_2 S_2 V_2 - \mu S_2 - cS_2, \\ \dfrac{dI_2}{dt} = cI_1 + \alpha_2 S_2 V_2 - (\mu + \gamma + \delta) I_2 - cI_2, \\ \dfrac{dV_2}{dt} = -\nu_2 V_2 + \beta_2 I_2 (M_2 - V_2), \end{cases} \tag{4.3.6b}$$

$$\begin{cases} \dfrac{dS_3}{dt} = cS_2 - \alpha_3 S_3 V_3 - \mu S_3 - cS_3, \\ \dfrac{dI_3}{dt} = cI_2 + \alpha_3 S_3 V_3 - (\mu + \gamma + \delta) I_3 - cI_3, \\ \dfrac{dV_3}{dt} = -\nu_3 V_3 + \beta_3 I_3 (M_3 - V_3). \end{cases} \tag{4.3.6c}$$

The following result can be proved in a way similar to that of Theorem 4.3 in Yang et al. [98]. Consequently, the disease dynamics of (4.3.6) are completely determined by the basic reproduction numbers $\mathcal{R}_{i0}$ for $i = 1, 2, 3$.

Theorem 4.7. *For system* (4.3.6), *if* $\mathcal{R}_{10} > 1$, *then the disease persists at an endemic equilibrium level in all three patches ; if* $\mathcal{R}_{10} \leq 1$ *and* $\mathcal{R}_{20} > 1$, *then the disease dies out in the first patch but persists at an endemic equilibrium level in the remaining two patches; if* $\mathcal{R}_{10} \leq 1$, $\mathcal{R}_{20} \leq 1$ *and* $\mathcal{R}_{30} > 1$, *then the disease dies out in the first two patches but persists at an endemic equilibrium level in the last patch; if* $\mathcal{R}_{10} \leq 1$, $\mathcal{R}_{20} \leq 1$ *and* $\mathcal{R}_{30} \leq 1$, *then the disease dies out in all three patches.*

4.3.5 The Relation Between $\mathcal{R}_0$ and Model Parameters

It follows from Theorem 4.5 that the disease dies out in all patches if and only if $\mathcal{R}_{i0} \leq 1$ for $i = 1, 2, 3$. In other words, to eliminate the disease from the whole system, all three threshold parameters $\mathcal{R}_{10}, \mathcal{R}_{20}$ and $\mathcal{R}_{30}$ must be reduced to be less than 1. To do so, we should study how the basic reproduction numbers vary with the model parameters which can help us design highly efficient control strategies. Recall that

$$\mathcal{R}_{i0}^2 = \frac{\alpha_i r c^{i-1}}{(\mu + c)^i \nu_i} \cdot \frac{\beta_i M_i}{\mu + \gamma + \delta + c}, i = 1, 2, 3.$$

Obviously, $\mathcal{R}_{i0}$ is strictly increasing in α_i, β_i, M_i or r, and strictly decreasing in ν_i, μ, γ or δ. An increase in the movement rate, c, will decrease $\mathcal{R}_{10}$. The dependence of $\mathcal{R}_{i0}$ on c becomes more complicated if $i > 1$, since c appears in both the numerator and denominator of the formula for $\mathcal{R}_{i0}^2$.

Proposition 4.8. *For $i > 1$, there exists some c_i^* such that the basic reproduction number $\mathcal{R}_{i0}$ is strictly increasing in c if $c \in (0, c_i^*)$ and strictly decreasing if $c \in (c_i^*, \infty)$. Furthermore, $(i-1)\mu/2 < c_i^* < (i-1)\mu$.*

Proof. Let $g_i(c)$ be the partial derivative of $\mathcal{R}_{i0}^2$ with respect to c. Then

$$\begin{aligned}
g_i(c) &= \frac{\alpha_i r \beta_i M_i}{\nu_i} \cdot \frac{\partial}{\partial c}\Big(\frac{c^{i-1}}{(\mu + c)^i(\mu + \gamma + \delta + c)}\Big) \\
&= \frac{\alpha_i r \beta_i M_i}{\nu_i} \cdot c^{i-2} \cdot \frac{(i-1)(\mu + c)(\mu + \gamma + \delta + c) - ci(\mu + \gamma + \delta + c) - c(\mu + c)}{(\mu + c)^{i+1}(\mu + \gamma + \delta + c)^2} \\
&= \frac{\alpha_i r \beta_i M_i}{\nu_i} \cdot c^{i-2} \cdot \frac{i\mu(\mu + \gamma + \delta + c) - (\mu + c)(\mu + \gamma + \delta + c) - c(\mu + c)}{(\mu + c)^{i+1}(\mu + \gamma + \delta + c)^2} \\
&= \frac{\alpha_i r \beta_i M_i}{\nu_i} \cdot c^{i-2} \cdot \frac{-2c^2 - (\gamma + \delta + (3-i)\mu)c + (i-1)\mu(\mu + \gamma + \delta)}{(\mu + c)^{i+1}(\mu + \gamma + \delta + c)^2}
\end{aligned}$$

and the sign of $g_i(c)$ is the same as that of

$$h_i(c) = -2c^2 - (\gamma + \delta + (3-i)\mu)c + (i-1)\mu(\mu + \gamma + \delta).$$

Since $h_i(0) = (i-1)\mu(\mu+\gamma+\delta) > 0$, the equation $h_i(c) = 0$ has exactly one positive root, denoted by c_i^*, satisfying $h_i(c) > 0$ if $c \in (0, c_i^*)$ and $h_i(c) < 0$ if $c \in (c_i^*, \infty)$. Note that

$$\begin{aligned} h_i(k\mu) =& -2k^2\mu^2 - (\gamma + \delta + (3-i)\mu)k\mu + (i-1)\mu(\mu+\gamma+\delta) \\ =& [-2k^2 - (3-i)k + (i-1)]\mu^2 - [(\gamma+\delta)k - (i-1)(\gamma+\delta)]\mu \\ =& (k+1)(-2k+i-1)\mu^2 + (i-k-1)(\gamma+\delta)\mu \quad \text{for } k > 0. \end{aligned}$$

In particular, we have

$$h_i((i-1)\mu) = -i(i-1)\mu^2 < 0 \text{ and } h_i((i-1)\mu/2) = (i-1)(\gamma+\delta)\mu/2 > 0,\ i > 1,$$

which implies $c_i^* \in ((i-1)\mu/2, (i-1)\mu)$. □

Remark 4.9. The duration of movement, $1/c$, is about a few weeks or months, while the life span of an animal, $1/\mu$, could be a couple of years or even longer. Namely, the timescale of the movement is very short relative to the host population dynamic timescale. So generally speaking, $\mathcal{R}_{i0}$ is decreasing in c and shortening the duration of host movement could reduce the possibility of a disease spread.

4.4 Numerical Simulations

In this section, we conduct numerical simulations to confirm our analytical results. The model uses a daily time step and some of the parameter values are chosen from the data in Gaff et al. [26] and the references therein.

Firstly, we explore the relation between $\mathcal{R}_{i0}$ and the travel rate c. We use the following set of parameter values: $r = 30, \mu = 1.2 \times 10^{-3}, \delta = 0.1, \gamma = 0.4, \zeta = 5 \times 10^{-3}, M_1 = 80, M_2 = 1000, M_3 = 100, \nu_i = 0.06, \alpha_i = 0.002$ and $\beta_i = 0.002$ for $i = 1, 2, 3$. Figure 4.1 shows how the basic reproduction number varies as a function of the livestock movement rate c, in the range $c \in [0, 0.5]$. As predicted by Proposition 4.8, the curve of $\mathcal{R}_{10}$ is constantly decreasing, and the curves of $\mathcal{R}_{20}$ and $\mathcal{R}_{30}$ are increasing for small c and then decreasing.

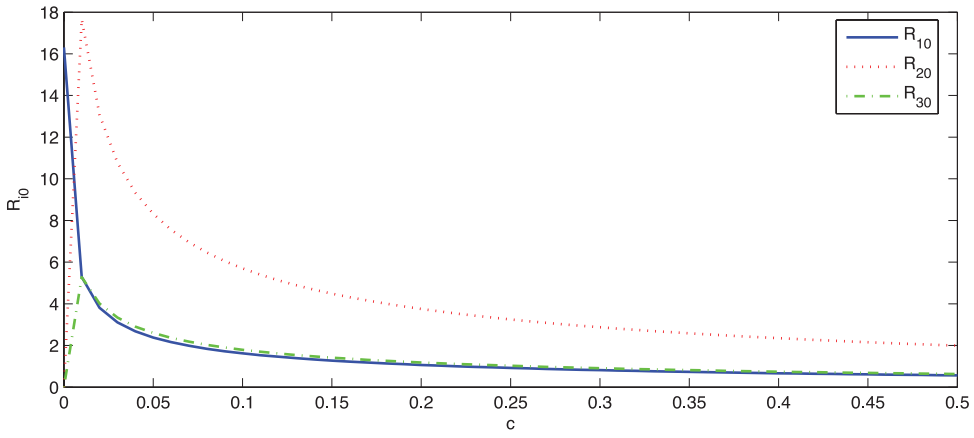

Figure 4.1: *The curves of the basic reproduction number of patch i, $\mathcal{R}_{i0}$, versus c.*

Now we fix c at 0.3 and the respective basic reproduction numbers are $\mathcal{R}_{10} = 0.8143 < 1, \mathcal{R}_{20} = 2.8731 > 1$ and $\mathcal{R}_{30} = 0.9067 < 1$. To consider a hypothetical disease invasion scenario, we set the initial data of patches 2 and 3 to zero such that there is no infected animals or mosquitoes in patches 2 and 3 at the beginning

of travel. The disease dies out in patch 1, but persists in patches 2 and 3, which is coincident with Theorem 4.5 (see Figures 4.2 and 4.3). This may represent an interesting phenomenon regarding the role that animal movement plays in the spatial spread of RVF from Sudan to Egypt. Though the disease is introduced to patch 2 from patch 1, it goes extinct in its origin because of lower mosquito density in patch 1. Patch 2 (the Nile) has high mosquito population density and the disease will reach an endemic level once it appears. Patch 3 cannot sustain a disease alone, but this becomes possible because of continuous immigration of infectious animals from patch 2.

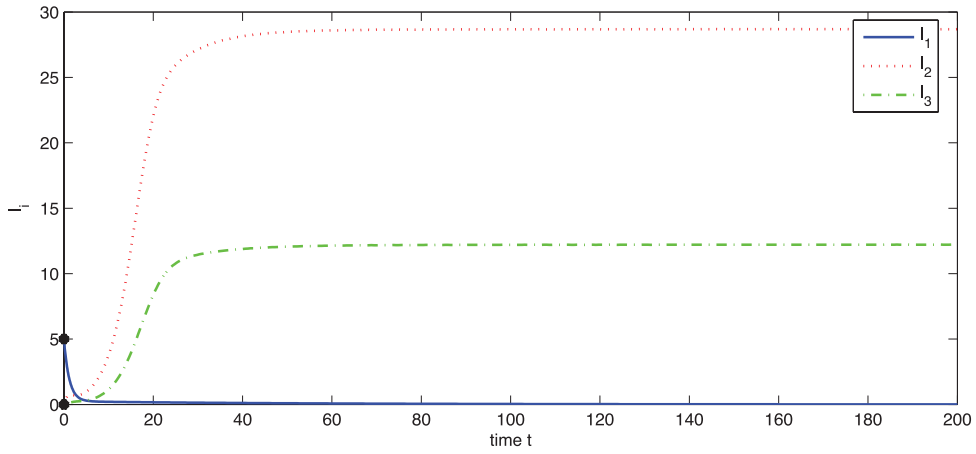

Figure 4.2: *Numerical simulations of system* (4.2.2a) *showing* I_i *vs* t. *Initial conditions:* $S_1(0) = 100, I_1(0) = 5, R_1(0) = 0, V_1(0) = 0$ *and* $S_2(0) = I_2(0) = R_2(0) = V_2(0) = S_3(0) = I_3(0) = R_3(0) = V_3(0) = 0$. $\mathcal{R}_{10} < 1, \mathcal{R}_{20} > 1$ *and* $\mathcal{R}_{30} > 1$.

4.5 Discussion

In this chapter, we have formulated a simple epidemic patch model aimed at capturing a scenario where animals are imported into Egypt from the south and taken north

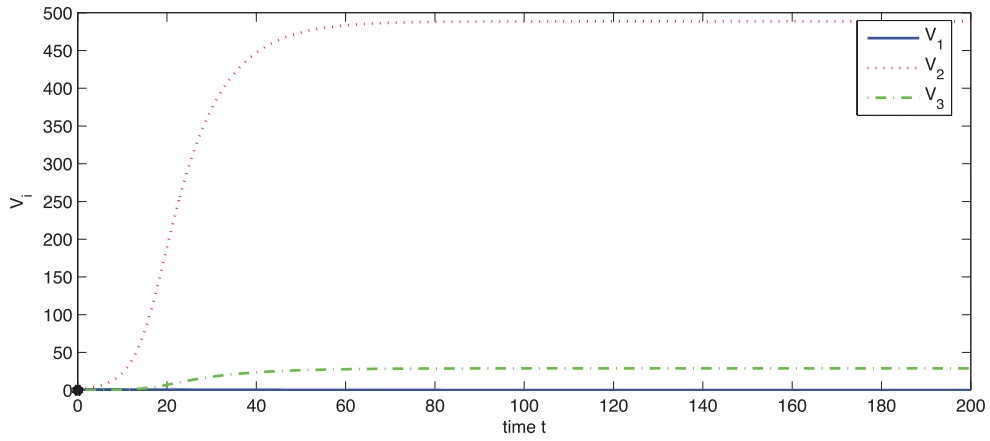

Figure 4.3: *Numerical simulations of system* (4.2.2a) *showing* V_i *vs* t*. Initial conditions:* $S_1(0) = 100, I_1(0) = 5, R_1(0) = 0, V_1(0) = 0$ *and* $S_2(0) = I_2(0) = R_2(0) = V_2(0) = S_3(0) = I_3(0) = R_3(0) = V_3(0) = 0$*.* $\mathcal{R}_{10} < 1, \mathcal{R}_{20} > 1$ *and* $\mathcal{R}_{30} > 1$*.*

along the Nile for human consumption, with the risk of a RVF outbreak if some of them are infected. A similar model might apply to Saudi Arabia and Yemen based on some descriptions [2]. We have evaluated the basic reproduction number for each patch and established the threshold dynamics of the model. It is suggested that a small amount of imported infectious animals from Sudan could result in an outbreak of RVF in Egypt. Increasing the recruitment rate of animals, c, or the carrying capacity of mosquitoes, M_i, will increase the basic reproduction number, $\mathcal{R}_{i0}$. So the likelihood of a RVF outbreak is higher when both r and M_i are large. The rate r at which animals are fed in might be determined by demand, which would be large during Muslim festival periods. For example, millions of animals are slaughtered as each religious Muslim has traditionally to slaughter one animal during the celebration of Eid al-Adha (also known as the Feast of Sacrifice). The date of Eid al-Adha varies from year to year and more attention should be paid to the transmission of RVFV when the rainy season (more mosquitoes) corresponds to the time of the occurrence

of festivals [2].

We may assume that some animals starting the journey are recovered. It might be that way even if no sick animals are starting the journey, since recovered ones could be healthy. If this happens, the subsystem (4.2.2a) will become

$$\begin{cases} \dfrac{dS_1}{dt} = r - \alpha_1 S_1 V_1 - \mu S_1 + \zeta R_1 - cS_1, \\ \dfrac{dI_1}{dt} = \alpha_1 S_1 V_1 - (\mu + \gamma + \delta) I_1 - cI_1, \\ \dfrac{dR_1}{dt} = r_R + \gamma I_1 - (\mu + \zeta) R_1 - cR_1, \\ \dfrac{dV_1}{dt} = -\nu_1 V_1 + \beta_1 I_1 (M_1 - V_1), \end{cases} \tag{4.5.1}$$

where r_R is a constant recruitment of recovered individuals into patch 1. Let $\tilde{R}_1 = R_1 - r_R/(\mu + \zeta + c)$ and $\tilde{r} = r + \zeta r_R/(\mu + \zeta + c)$. Then (4.5.1) can be written as

$$\begin{cases} \dfrac{dS_1}{dt} = \tilde{r} - \alpha_1 S_1 V_1 - \mu S_1 - cS_1, \\ \dfrac{dI_1}{dt} = \alpha_1 S_1 V_1 - (\mu + \gamma + \delta) I_1 - cI_1, \\ \dfrac{d\tilde{R}_1}{dt} = \gamma I_1 - (\mu + \zeta) \tilde{R}_1 - c\tilde{R}_1, \\ \dfrac{dV_1}{dt} = -\nu_1 V_1 + \beta_1 I_1 (M_1 - V_1), \end{cases} \tag{4.5.2}$$

which is qualitatively equivalent to (4.2.2a). Therefore, all of the aforementioned results still hold for system (4.5.2) or (4.5.1) and its associated new full system.

The work presented in this chapter enables us to gain useful insights into the spread of RVF among different regions. However, there are a number of other aspects we have not done in this study. Can we simplify our SIRS model to an SI/SIR model for hosts? Do we need more detailed epidemiological models, for example SEIR for

hosts, SEI for vectors? We may want to think about extending the model to a larger and more realistic patch network, for example if we want to study how changing the network affects disease spread, but we would need to know at least something qualitative about movement patterns of herds to set the movement coefficients. Seasonal effects on mosquito population and time-dependence of animal importation may also be incorporated. Data for disease, vector and animal migration need to be collected so that we can testify the validity of our model.

Chapter 5

Conclusions and Future Work

In this chapter, we summarize the main conclusions in this thesis and then discuss various research directions that we plan to study in the future.

5.1 Conclusions

Emerging and reemerging infectious diseases are viewed as a major threat to public health and global economies. Each year, about one third of human deaths throughout the world is from an communicable disease, such as AIDS/HIV, TB and malaria. The current situation may become even worse with the appearance of multidrug-resistant strains, new viruses, the climate change and urbanization. In particular, modern transportation facilitates the spread of infectious diseases. For example, SARS was first reported in China in February 2003. Due to global travel, the illness rapidly spread to more than two dozen countries in North America, South America, Europe, and Asia before it was contained. Multi-patch epidemic models have been developed to study the effects of population dispersal on the spatial spread of infectious disease in the past thirty years. These studies could play an important role in the prevention and control of infectious diseases.

It has been observed that media coverage can affect the spread and control of

infectious diseases. During outbreaks of serious infectious diseases, public media has massive reports on the number of infections and deaths per day, the locations where these happen, the symptoms of the disease, the proper protections to decrease the possibility of being infected, etc. People follow the reports and thus choose to protect themselves by reducing their social activities and direct contact with others, especially with those high-risk groups, which could therefore lead to a reduction of effective contacts between susceptible individuals and infectious individuals. In Chapter 1, we proposed an SIS (susceptible-infectious-susceptible) patch model in which the transmission coefficient is a nonincreasing function of the number of the infectious individuals.

We derived the basic reproduction number $\mathcal{R}_0$ and found that it is a threshold parameter between the extinction and the uniform persistence of the disease. Namely, the disease-free equilibrium is globally asymptotically stable if $\mathcal{R}_0 \leq 1$, and the disease is uniformly persistent if $\mathcal{R}_0 > 1$. Since the basic reproduction number of the model is between the minimum and maximum of the respective basic reproduction numbers in isolation. The disease persists or dies out in each isolated patch then remains persistent or extinct, respectively, when human movement occurs. In the case where there is no disease-induced death and susceptible and infectious individuals have identical travel rates, there exists a globally asymptotically stable endemic equilibrium if $\mathcal{R}_0 > 1$. The results indicate that the media coverage has no influence on the dynamics of disease transmission. However, the final infected size in each patch can be reduced with more media coverage when the disease persists.

In chapter 2, a multi-patch malaria model was formulated to address the spatial heterogeneity of vectors and hosts. An explicit formula for the basic reproduction number $\mathcal{R}_0$ was derived and we found that the disease-free equilibrium is locally

asymptotically stable if $\mathcal{R}_0 < 1$ and unstable if $\mathcal{R}_0 > 1$. A sufficient condition for the existence of an endemic equilibrium when $\mathcal{R}_0 > 1$ was obtained. For the two-patch submodel, we studied how the dispersal of individuals, in particular of the exposed and infectious individuals, contributes to the spread of diseases from one region to another. 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.

In Chapter 3, based on the classical Ross-Macdonald model, we developed a periodic malaria model in a patchy environment to include the effects of seasonal variation and population dispersal in disease transmission. Following the recipe of Wang and Zhao [95], we defined the basic reproduction number $\mathcal{R}_0$. By the theory of monotone dynamical systems and internally chain transitive sets, we established the global dynamics of the system, i.e., the disease dies out if $\mathcal{R}_0 \leq 1$ and persists at a periodic attractor if $\mathcal{R}_0 > 1$. This is coincident with the observation that malaria cases show seasonal fluctuations in most endemic areas.

Rift Valley fever (RVF) is a viral zoonosis of domestic animals (such as cattle, sheep, camels and goats) and humans caused by the RVF virus. It was first identified in Kenya in 1931 and later spread to Africa, Indian Ocean states and the Arabian Peninsula. The disease causes major losses in the livestock industry. It is believed that RVF in Egypt is mainly caused by the continuous importation of infected animals from Sudan. The imported animals enter southern Egypt from northern Sudan, are moved up the Nile, and then consumed at the feast. In Chapter 4, we proposed a three-patch model to study the spatial spread of RVF in Egypt, with animals movement from patch 1 to patch 2 and then from patch 2 to patch 3. The basic

reproduction number for each patch was introduced and then the threshold dynamics of the model was established. We performed numerical simulations to investigate an interesting scenario showing possible explanation to the observed phenomenon in Egypt.

In summary, we proposed several epidemic patch models to study the effects of human movement on the spatial spread of infectious diseases. The analytical and numerical results suggest that the migration of humans can influence disease spread in a complicated way and to control or eliminate an infectious disease we need global and regional strategies.

5.2 Future Work

The present work enables us to gain valuable insights into the spread of infectious disease among different regions. However, there are a number of other aspects we have not considered in this study.

In Chapter 1, the uniqueness and stability of the endemic equilibrium is unclear even for two-patch case. Can the model exhibit more complicated dynamical behaviors like Hopf bifurcation? In Chapter 2, we are interested in the global stability of the disease-free equilibrium when $\mathcal{R}_0 < 1$. Also, the existence, uniqueness and stability of the endemic equilibrium is in general unclear. In Chapter 4, the global stability of the endemic equilibrium is unknown when there is recovered individual enters into susceptible compartment.

To determine the relative importance of model parameters in disease transmission and prevalence, we would like to carry out systematic sensitivity analysis and calculate

the sensitivity indices of the basic reproduction number and the endemic equilibrium. This can improve the efficiency of disease intervention strategies. It is also interesting to test these epidemic models with real data.

In addition, many additional features should be included to the models studied here to increase realism. For example, it is more reasonable to use time-dependent variables to incorporate the climatic and environmental impact. The latent period or infectious period is short for some disease, so individuals could change their disease status during travel. Different age groups may have different susceptibility, survival capacities and behaviors in response to disease transmission. We leave all these for future consideration.

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