Infectious Disease Modelling 9 (2024) 931–962

Contents lists available at ScienceDirect

Infectious Disease Modelling

journal homepage: www.keaipublishing.com/idm

Analysis of a diffusive two-strain malaria model with the carrying capacity of the environment for mosquitoes ☆

Jinliang Wang [a], Wenjing Wu [a], Yuming Chen [b,*]

[a] Engineering Research Center of Agricultural Microbiology Technology, Ministry of Education & Heilongjiang Provincial Key Laboratory of Ecological Restoration and Resource Utilization for Cold Region & School of Mathematical Science, Heilongjiang University, Harbin, 150080, PR China

[b] Department of Mathematics, Wilfrid Laurier University, Waterloo, Ontario, N2L 3C5, Canada

A R T I C L E I N F O

Article history:
Received 26 January 2024
Received in revised form 6 March 2024
Accepted 6 May 2024
Handling Editor: Dr. Jianhong Wu

2000 MSC:
92D30
35K57
35B40

Keywords:
Threshold dynamics
Two-strain malaria model
Competition and coexistence
Reproduction number

A B S T R A C T

We propose a malaria model involving the sensitive and resistant strains, which is described by reaction-diffusion equations. The model reflects the scenario that the vector and host populations disperse with distinct diffusion rates, susceptible individuals or vectors cannot be infected by both strains simultaneously, and the vector population satisfies the logistic growth. Our main purpose is to get a threshold type result on the model, especially the interaction effect of the two strains in the presence of spatial structure. To solve this issue, the basic reproduction number (BRN) $\Re_0^i$ and invasion reproduction number (IRN) $\widehat{\Re}_0^i$ of each strain ($i = 1$ and 2 are for the sensitive and resistant strains, respectively) are defined. Furthermore, we investigate the influence of the diffusion rates of populations and vectors on BRNs and IRNs.

1. Introduction

Malaria, a mosquito-borne epidemic arising from parasites of the genus plasmodium, still remains a fatal epidemic. Its primary reservoirs are female anopheles mosquitoes. The malaria transmission generally involves a transmission cycle between humans and female mosquitoes (Forouzannia & Gumel, 2014), that is, infected mosquitoes can transmit malaria to susceptible individuals through effective bites and susceptible mosquitoes can get infection from infected individuals by biting. Plasmodium vivax leads to approximately 80% of malaria infections (Titus, 1990) and Plasmodium falciparum is the most lethal. Once humans get infections from infected mosquitoes, some typical symptoms such as chills, fever, sweating will occur. If patients can not receive timely treatment, malaria will cause serious complications even death. In 2019, as reported in

☆ This research was partially supported by the National Natural Science Foundation of China (Nos. 12071115, 11871179), the Heilongjiang Natural Science Funds for Distinguished Young Scholar (No. JQ2023A005), and Heilongjiang Provincial Key Laboratory of the Theory and Computation of Complex Systems (JW); and NSERC of Canada (No. RGPIN-2019-05892) (YC).

* Corresponding author. Department of Mathematics, Wilfrid Laurier University, Waterloo, ON, N2L 3C5, Canada.
E-mail addresses: jinliangwang@hlju.edu.cn (J. Wang), 2190980@s.hlju.edu.cn (W. Wu), ychen@wlu.ca (Y. Chen).

Peer review under responsibility of KeAi Communications Co., Ltd.

https://doi.org/10.1016/j.idm.2024.05.001

(World Health Organization, 2019), there were approximately 228 million cases all over the world. Nowadays, malaria is still prevalent in Africa, Asia and South America, which brings negative influences on the public health and local economies.

Mathematical models on malaria spread have received a lot of attention in recent years as investigation of such models can give us better understanding of the mechanisms of malaria transmission and also provide guidance or suggestions on malaria control. Since the study of (Macdonald, 1957) and (Ross, 1911), mathematical models on malaria spread have been extensively studied by many researchers, which incorporate various factors in malaria transmission. A typical factor is spatial heterogeneity in disease transmission. Indeed, spatial transmission of diseases subject to differences in social, cultural, economic, demographic, and geographical factors may in turn give rise to the spatial patterns of diseases (Hagenaars et al., 2004). In recent years, more and more malaria transmission models have been established to investigate the spatial spread of malaria in the forms of reaction-diffusion equations. In a recent work (Ge et al., 2015), Ge et al. argued that the movement of mosquitoes and individuals affects the geographic spread of malaria. Considering spatial heterogeneity, one often adopts space-dependent functions instead of constants for parameters. On the other hand, the authors in (Lou & Zhao, 2011) extended Macdonald's malaria model (Macdonald, 1957) to a nonlocal reaction-diffusion model by introducing the extrinsic incubation period (EIP). They explored the threshold dynamics and investigated the impact of spatial heterogeneity on malaria spread numerically. Chamchod et al. (Chamchod & Britton, 2011) proposed a vector-bias malaria model involving the incubation time, diffusion term and chemotaxis term. They studied the phenomenon of transcritical bifurcation in a critical case where the incubation time and diffusion term are ignored. They also performed numerical simulations on results of the wave speed to verify the result on the minimum wave speed from qualitative analysis when the diffusion term and chemotaxis term are included. It is confirmed that a large incubation time can reduce the prevalence of malaria. Further, Xu and Zhao (Xu & Zhao, 2013) investigated the threshold-type result of a vector-bias malaria model with diffusion term in a homogeneous case. Some conditions on the global attractivity of the positive steady state (PSS) are also obtained in a heterogeneous case. Subsequently, Bai et al. (Bai et al., 2018) extended theories proposed in (Chamchod & Britton, 2011), (Lou & Zhao, 2011) and (Wang & Zhao, 2017) to a model involving seasonality, spatial heterogeneity, vector-bias, and EIP. They concluded that spatial heterogeneity remarkably increases the epidemic burden and EIP would be helpful in controlling malaria transmission.

It is highlighted in (Laxminarayan et al., 2016) that the high use of antimalarial drugs has accelerated the evolution of resistance to some plasmodium parasites during the treatment of malaria, which directly threatens the fight against malaria. The drug resistance of Chloroquine (which was frequently used to control malaria in the 1950's) was found in Southeast Asia and South America and spread to every country in the following decades (Talisuna et al., 2004). Generally speaking, antimalarial drugs will eliminate drug-sensitive parasites in hosts. But drug-resistant parasites survive and reproduce due to the high use and long term treatment (Esteva et al., 2009). Sulfadoxine-pyrimethamine, as an alternative to Chloroquine, has also been proved to have the phenomenon with the decline of efficacy. Recently, Artemisinin combination therapies are widely used in the treatment for malaria. However, drug-resistance remains inevitable and brings difficulties in malaria control (see, for example (Bushman et al., 2018; Tumwiine et al., 2014),). Further, Forouzannia and Gumel (Forouzannia & Gumel, 2015) assessed the effect of antimalaria drugs on malaria control by an age-structured model. Very recently, Shi and Zhao (Shi & Zhao, 2021) explored a diffusive two-strain (sensitive and resistant strain) malaria model, where the following biological factors in malaria transmission are taken into account:

(i) **The total human population stabilizes at $\overline{H}(x)$.** Let t and x be the time and space variables, respectively. Assume that the total population lives in a bounded spatial habitat Ω with a smooth boundary $\partial\Omega$. The total population $H := H(t,x)$ is divided into susceptible individuals $H_u := H_u(t,x)$, individuals infected by the sensitive strain $I_1 := I_1(t,x)$ and individuals infected by the resistant strain $I_2 := I_2(t,x)$, that is, $H = H_u + I_1 + I_2$. Further, H satisfies the following equation,

$$\begin{cases} \dfrac{\partial H}{\partial t} = D_h \Delta H + b_h H - \gamma H, & (t,x) \in (0,\infty) \times \Omega, \\ \dfrac{\partial H}{\partial n} = 0, & (t,x) \in (0,\infty) \times \partial\Omega, \end{cases} \tag{1.1}$$

where $D_h > 0$ is the diffusion rate of the population, b_h and γ are the recruitment rate and mortality rate of the population, respectively. Here $\frac{\partial}{\partial n}$ represents the normal derivative along n on $\partial\Omega$. As in (Bai et al., 2018), the total population $H(t, x)$ is assumed to be $\overline{H}(x)$, i.e., $H(t,x) \equiv \overline{H}(x)$ for $(t, x) \in [0, \infty) \times \Omega$.

(ii) **The total of female adult mosquitoes remains constant.** The total density of female adult mosquitoes $M := M(t,x)$ is divided into susceptible individuals $S_v := S_v(t, x)$, mosquitoes infected by the sensitive strain $I_{v1} := I_{v1}(t, x)$ and individuals infected by the resistant strain $I_{v2} := I_{v2}(t, x)$, that is, $M = S_v + I_{v1} + I_{v2}$. M is assumed to be governed by the following system:

$$\begin{cases} \dfrac{\partial M}{\partial t} = D_v \Delta M + \Lambda - \eta M, & (t,x) \in (0,\infty) \times \Omega, \\ \dfrac{\partial M}{\partial n} = 0, & (t,x) \in (0,\infty) \times \partial\Omega, \end{cases}$$

where Λ and η are the recruitment rate and mortality rate of female adult mosquitoes, respectively. $D_v > 0$ stands for the diffusion rate of all mosquitoes. According to the results in (Magal et al., 2018), (Cantrell & Cosner, 2003),

$$\lim_{t\to\infty} M(t,x) = \overline{M} := \frac{\Lambda}{\eta}. \tag{1.2}$$

(iii) **Vector-bias mechanism.** In view of the works (Chamchod & Britton, 2011) and (Bai et al., 2018), vector-bias mechanism was introduced to characterize the distinct attractiveness of host population to mosquitoes. Infectious humans exhibit greater attractiveness to female adult mosquitoes than susceptible humans. The constant p (respectively, l) is used for the probability when a vector randomly bites a susceptible (respectively, infectious) host.

We use $i = 1$ and 2 to differentiate the sensitive and resistant strains, respectively. The basic reproduction number (BRN) $\Re_0^i$ and the invasion reproduction number (IRN) $\widehat{\Re}_0^i$ of the i strain are defined in (Shi & Zhao, 2021) as the threshold values to investigate the competition and coexistence phenomena, that is, (i) if $\Re_0^1 < 1$ and $\Re_0^2 < 1$, then malaria vanishes; (ii) if $\Re_0^1 > 1$, $\widehat{\Re}_0^1 < 1$, $\Re_0^2 > 1$, $\widehat{\Re}_0^2 > 1$, then malaria with $i = 1$ strain becomes extinct and malaria with $i = 2$ strain becomes epidemic; (iii) if $\Re_0^1 > 1$, $\widehat{\Re}_0^1 > 1$, $\Re_0^2 > 1$, $\widehat{\Re}_0^2 < 1$, then malaria with $i = 1$ strain becomes epidemic and malaria with $i = 2$ strain becomes extinct; (iv) if $\Re_0^1 > 1$, $\widehat{\Re}_0^1 > 1$, $\Re_0^2 > 1$, $\widehat{\Re}_0^2 > 1$, then both strains coexist. Further, numerical simulations are performed to investigate the impact of the vector-bias mechanism on epidemic spread.

This work intends to investigate the competition and coexistence phenomena in a diffusive two-strain (sensitive and resistant strain) malaria model arising from high use of antimalarial drugs. Based on the two-strain malaria transmission model proposed in (Shi & Zhao, 2021), we shall borrow the idea used in (Magal et al., 2018) to modify (1.1), i.e., the density for susceptible populations stabilizes at the spatial location rather than the density for the total population stabilizes at the spatial location as in (Lou & Zhao, 2011) and (Bai et al., 2018). Considering that the total number of mosquitoes is affected by the maximum environmental capacity, we modify the linear growth rate of mosquitoes (Shi & Zhao, 2021) with a logistic growth. To make things not too complicated (as competition and coexistence phenomena between the two strains have already made the problem very challenging), we adopt the mass action for the interaction between humans and mosquitoes. Furthermore, our analysis gives the influences of diffusion coefficients and shows the competition and coexistence of the two strains while keeping the spatial heterogeneity (with all nonconstant coefficients except the diffusion rates of humans and mosquitoes) in hosts and vectors.

In the next section, we introduce the diffusive two-strain malaria model in a heterogeneous environment. We rigorously analyze the well-posedness in Section 3, which includes the existence and uniqueness of classical solutions, the ultimate boundedness of solutions, and the existence of a global attractor. In Section 4, we first explore the subsystems of single strains. The local basic reproduction number (LBRN) $\Re_0^i(x)$ and the BRN $\Re_0^i$ of each strain ($i = 1$, 2) are introduced and the relationships between $\Re_0^i(x)$ and $\Re_0^i$ are established. The local invasion reproduction number (LIRN) $\widehat{\Re}_0^i(x)$ and IRN $\widehat{\Re}_0^i$ ($i = 1, 2$) are analyzed in the same way. Furthermore, we identify the asymptotic consequences of BRNs and IRNs when the diffusion coefficients of hosts and vectors tend to infinity or zero. In Section 5, we study the threshold dynamics determined by BRNs and IRNs. The stabilities of the disease-free steady state (DFSS) and the boundary steady state (BSS), results of uniform persistence, and the existence of a PSS are all addressed. Finally, we end the paper with a brief discussion.

2. The model

Based on the malaria models in (Shi & Zhao, 2021), (Fitzgibbon et al., 2017), (Magal et al., 2018), and (Magal et al., 2019), we propose a diffusive two-strain malaria transmission model. As it is well-known, malaria, zika virus, and dengue fever are all highly dangerous vector-borne infectious diseases. Thus they can be modeled with a similar mathematical framework. We mentioned that (Fitzgibbon et al., 2017) highlighted the effect of susceptible hosts stabilizing at spatial location in zika epidemic. Indeed, approximately 395 per hundred thousand residents of Rio de Janeiro were infected with zika during eight and a half months, which means that infected residents are less than 1% of the total population (Villela et al., 2016). It is thus of interest to analyze the effect of this factor on the transmission of malaria. Subsequently, Magal et al. (Magal et al., 2018) revisited the model in (Fitzgibbon et al., 2017) to investigate the threshold dynamics according to BRN $\Re_0$ (obtained via the next generation operator method). Their results also revealed the relationship between $\Re_0 - 1$ and the principal eigenvalue of the corresponding eigenvalue problem. Generally speaking, it is difficult to visualize $\Re_0$ for reaction-diffusion systems with multiple infective compartments. Inspired by the dynamics of the associated ordinary differential equation model, but with LBRN, Magal et al. (Magal et al., 2019) further explored the relationship between BRN and LBRN and investigated the asymptotic consequences of BRN and LBRN when the diffusion coefficients of hosts and vectors tend to infinity or zero.

Inspired by the above works, we shall adopt the two-strain malaria model in (Shi & Zhao, 2021) based on the following assumptions.

(i) During a relatively short-time epidemic, susceptible humans are not affected. Let $H_u(x)\in C(\overline{\Omega},\mathbb{R})$ be the stabilized susceptible humans at location x, which is a continuous positive function on $\overline{\Omega}$. Suppose that each susceptible individual or vector cannot be infected by both strains simultaneously. We use

$$c_i(x)H_u(x)I_{vi}(t,x),\ \ i=1,2,$$

to represent the flux of newly infected humans with the i strain, where $c_i(x)\in C(\overline{\Omega},\mathbb{R}_+)$ denotes the transmission rate that an infected mosquito of the i strain bites a susceptible individual. Similarly, we use

$$\alpha_i(x)S_v(t,x)I_i(t,x),\ \ i=1,2,$$

to represent the flux of newly infected mosquitoes with the i strain, where $\alpha_i(x)\in C(\overline{\Omega},\mathbb{R}_+)$ denotes the transmission rate that a susceptible mosquito bites an infected individual.

(ii) The total number of vectors is affected by the environmental carrying capacity in the sense that $M=S_v+I_{v1}+I_{v2}$ obeys a logistic type growth, that is,

$$\begin{cases} \dfrac{\partial M}{\partial t}=D_v\Delta M+\beta(x)M-\mu(x)M^2, & (t,x)\in(0,\infty)\times\Omega,\\ \dfrac{\partial M}{\partial n}=0, & (t,x)\in(0,\infty)\times\partial\Omega,\\ M(0,x)=M_0(x)\in C(\overline{\Omega};\mathbb{R}_+), \end{cases} \tag{2.1}$$

where $\beta(x)$ denotes the breeding rate of mosquitoes and $\mu(x):=\frac{\beta(x)}{K(x)}$ with $K(x)$ denoting the environmental carrying capacity at location x. According to the analysis in (Cantrell & Cosner, 2003), it is obvious that for any positive initial data $M_0(x)\in C(\overline{\Omega},\mathbb{R})$, M satisfies

$$\lim_{t\to\infty}\|M-\overline{M}(x)\|_\infty=0 \quad \text{for } (t,x)\in(0,\infty)\times\overline{\Omega}, \tag{2.2}$$

where $\overline{M}(x)$ is the unique positive solution of

$$\begin{cases} -D_v\Delta\omega(x)=\beta(x)\omega(x)-\mu(x)\omega^2(x), & x\in\Omega,\\ \dfrac{\partial\omega(x)}{\partial n}=0, & x\in\partial\Omega. \end{cases} \tag{2.3}$$

By incorporating the above assumptions, the model studied in this paper is

$$\begin{cases} \dfrac{\partial I_1}{\partial t}=D_h\Delta I_1-\gamma_1(x)I_1+c_1(x)H_u(x)I_{v1},\\ \dfrac{\partial I_2}{\partial t}=D_h\Delta I_2-\gamma_2(x)I_2+c_2(x)H_u(x)I_{v2},\\ \dfrac{\partial S_v}{\partial t}=D_v\Delta S_v-\alpha_1(x)S_vI_1-\alpha_2(x)S_vI_2+\beta(x)M-\mu(x)MS_v,\\ \dfrac{\partial I_{v1}}{\partial t}=D_v\Delta I_{v1}+\alpha_1(x)S_vI_1-\mu(x)MI_{v1},\\ \dfrac{\partial I_{v2}}{\partial t}=D_v\Delta I_{v2}+\alpha_2(x)S_vI_2-\mu(x)MI_{v2} \end{cases} \tag{2.4}$$

for $(t,x)\in(0,\infty)\times\Omega$, associated with

$$\frac{\partial \mathcal{W}_1}{\partial n} = 0,\ \mathcal{W}_1 = I_1, I_2, S_v, I_{v1}, I_{v2},\ (t,x)\in(0,\infty)\times\partial\Omega. \tag{2.5}$$

We further impose the following initial data on (2.4),

$$(I_1(0,\cdot),\ I_2(0,\cdot),\ S_v(0,\cdot),\ I_{v1}(0,\cdot),\ I_{v2}(0,\cdot)) = (I_1^0,\ I_2^0,\ S_v^0,\ I_{v1}^0,\ I_{v2}^0). \tag{2.6}$$

3. Well-posedness

This section mainly establishes the well-posedness of system (2.4) with (2.5) and (2.6). Let $\mathbb{X} := C(\overline{\Omega}, \mathbb{R}^5)$ be the Banach space of all continuous functions from $\overline{\Omega}$ to $\mathbb{R}^5$ equipped with the supremum norm $\|\cdot\|_{\mathbb{X}}$ and $\mathbb{X}^+ := C(\overline{\Omega}, \mathbb{R}_+^5)$ be the positive cone of $\mathbb{X}$. For convenience, we let $\mathbb{Y} := C(\overline{\Omega}, \mathbb{R})$ and $\mathbb{Y}^+ := C(\overline{\Omega}, \mathbb{R}_+)$. The supremum norm on $\mathbb{Y}$ is denoted as $\|\cdot|_{\mathbb{Y}}$.

Following the standard arguments in [27, Section 7.1 and Corollary 7.2.3], we denote respectively $T_i(t),\ i = 1,2,3 :\ \mathbb{Y}\to\mathbb{Y}$ the compact and strongly positive evolution operators associated with

$$\frac{\partial I_1}{\partial t} = D_h\Delta I_1 - \gamma_1(x)I_1 := A_1 I_1, \quad (t,x)\in(0,\infty)\times\Omega,$$
$$\frac{\partial I_2}{\partial t} = D_h\Delta I_2 - \gamma_2(x)I_2 := A_2 I_2, \quad (t,x)\in(0,\infty)\times\Omega,$$

and

$$\frac{\partial S_v}{\partial t} = D_v\Delta S_v := A_3 S_v, \quad (t,x)\in(0,\infty)\times\Omega$$

subject to (2.5). Furthermore, $T(t) = \mathrm{diag}\{T_1(t), T_2(t), T_3(t), T_3(t), T_3(t)\} :\ \mathbb{X}\to\mathbb{X},\ t\geq 0$, generated by the operator $\mathcal{A} = \mathrm{diag}\{A_1, A_2, A_3, A_3, A_3\}$, is a strongly continuous semigroup. Here $\mathcal{A}$ is defined on $D(\mathcal{A}) = D(A_1)\times D(A_2)\times D(A_3)\times D(A_3)\times D(A_3)$, where

$$D(A_i) := \left\{\theta\in C(\overline{\Omega}) : \lim_{t\to 0^+}\frac{(T_i(t)-\mathbb{I}_d)\theta}{t}\ \text{exists},\ i = 1,2,3\right\}$$

with $\mathbb{I}_d$ denoting the identity operator.

For simplicity of notations, we denote

$$\mathbb{X}_H := \{\phi = (\phi_1,\phi_2,\phi_3,\phi_4,\phi_5)\in\mathbb{X}^+ : 0\leq M_1(t,x) \triangleq \phi_3+\phi_4+\phi_5\leq \overline{M}(x),\ (t,x)\in[0,\infty)\times\overline{\Omega}\}.$$

Moreover, we define $\mathcal{F} = (\mathcal{F}_1, \mathcal{F}_2, \mathcal{F}_3, \mathcal{F}_4, \mathcal{F}_5) : \mathbb{X}_H\to\mathbb{X}$ by

$$\begin{cases} \mathcal{F}_1(\phi)(x) = c_1(x)H_u(x)\phi_4(0,x), \\ \mathcal{F}_2(\phi)(x) = c_2(x)H_u(x)\phi_5(0,x), \\ \mathcal{F}_3(\phi)(x) = -\alpha_1(x)\phi_3(0,x)\phi_1(t,x) - \alpha_2(x)\phi_3(0,x)\phi_2(0,x) + \beta(x)M_1(0,x) \\ -\mu(x)M_1(0,x)\phi_3(0,x), \\ \mathcal{F}_4(\phi)(x) = \alpha_1(x)\phi_3(0,x)\phi_1(0,x) - \mu(x)M_1(0,x)\phi_4(0,x), \\ \mathcal{F}_5(\phi)(x) = \alpha_2(x)\phi_3(0,x)\phi_2(0,x) - \mu(x)M_1(0,x)\phi_5(0,x) \end{cases} \tag{3.1}$$

for $\phi = (\phi_1,\phi_2,\phi_3,\phi_4,\phi_5)\in\mathbb{X}_H$ and $x\in\overline{\Omega}$. By letting $u(t) = (I_1(t,\cdot), I_2(t,\cdot), S_v(t,\cdot), I_{v1}(t,\cdot), I_{v2}(t,\cdot))\in\mathbb{X}_H,\ t>0$ and

$$\phi_0 := (\phi_1(0,\cdot), \phi_2(0,\cdot), \phi_3(0,\cdot), \phi_4(0,\cdot), \phi_5(0,\cdot)) = (I_1^0, I_2^0, S_v^0, I_{v1}^0, I_{v2}^0)\in\mathbb{X}_H,$$

we can rewrite (2.4) as

$$\begin{cases} \dfrac{du(t)}{dt} = \mathcal{A}u(t) + \mathcal{F}(u(t)),\ t>0, \\ u(0) = \phi_0\in\mathbb{X}_H. \end{cases} \tag{3.2}$$

Lemma 3.1. *For any $\phi_0\in\mathbb{X}_H$ and $T_{\max}\leq\infty$, system (2.4)-(2.5) admits a unique solution $u(t,\cdot,\phi_0)$, on $[0, T_{\max})$ with $u(0,\cdot) = \phi_0$. Moreover, $u(t,\cdot,\phi_0)$ is a classical solution.*

Proof. By appealing to [23, Corollary 4] and [40, Corollary 8.1.3], we know that a mild solution with $\phi_0\in\mathbb{X}_H$ can be viewed as a continuous solution of

$$\begin{cases} u(t) = T(t)\phi_0 + \int_0^t T(t-s)\mathcal{F}(u(s))ds, \ t>0, \\ u(0) = \phi_0 \in \mathbb{X}_H, \end{cases}$$

where $\mathcal{F}$ is locally Lipschitz continuous. Moreover, for all $(t,\phi)\in[0,\infty)\times\mathbb{X}_H$ and positive k, one can easily check that

$$\phi(0,x) + k\mathcal{F}(\phi)(x) \geq \begin{pmatrix} \phi_1(0,x) \\ \phi_2(0,x) \\ \phi_3(0,x)[1-k\mathcal{M}(\overline{\alpha}_1+\overline{\alpha}_2+3\overline{\mu})] \\ \phi_4(0,x)[1-3k\overline{\mu}\mathcal{M}] \\ \phi_5(0,x)[1-3k\overline{\mu}\mathcal{M}] \end{pmatrix},$$

where $\overline{f} = \max_{x\in\overline{\Omega}} f(x)$ for $f = \alpha_1$, α_2, μ, and $\mathcal{M} = \max_{x\in\overline{\Omega}}\overline{M}(x)$. Moreover,

$$\overline{M}(x) - [\phi_3(0,x) + k\mathcal{F}_3(\phi)(x)] \geq \overline{M}(x) - \phi_3(0,x) - k\beta(x)M_1(0,x).$$

Similarly, we get

$$\overline{M}(x) - [\phi_4(0,x) + k\mathcal{F}_4(\phi)(x)] \geq \overline{M}(x) - \phi_4(0,x) - k\alpha_1(x)\phi_3(0,x)\phi_1(0,x)$$

and

$$\overline{M}(x) - [\phi_5(0,x) + k\mathcal{F}_5(\phi)(x)] \geq \overline{M}(x) - \phi_5(0,x) - k\alpha_2(x)\phi_3(0,x)\phi_2(0,x).$$

As a result, for $(t,\phi)\in\mathbb{R}_+\times\mathbb{X}_H$, we can obtain that

$$\lim_{k\to 0+}\frac{1}{k}\mathrm{dist}(\phi(0,x) + k\mathcal{F}(\phi)(x), \mathbb{Y}^+\times\mathbb{Y}^+\times\mathbb{X}_H\times\mathbb{X}_H\times\mathbb{X}_H) = 0.$$

Thus, by [27, Theorem 3.1], for $0 < T_{\max} \leq \infty$, a unique classical solution $u(t, x)$ exists on $[0, T_{\max})$. □

The following result directly follows from [27, Corollary 7.3.2].

Theorem 3.2. *For $\phi_0\in\mathbb{X}_H$ system (2.4) with (2.5) and (2.6) possesses a unique global classical solution $u(t, \cdot)$, $t\geq 0$, with $u(0, \cdot) = \phi_0$. Furthermore, $u(t, \cdot)$, $t\geq 0$, is ultimately bounded.*

Proof. Recall that (2.1) has a unique global classical solution $M(t, x)$ and

$$\lim_{t\to\infty}\|M(t,x) - \overline{M}(x)\|_\infty = 0.$$

By the comparison principle and arguments in (Smith, 1995), $\max_{t\geq 0}\|M(t,\cdot)\|_{\mathbb{Y}} < N_1$ for some $N_1 > 0$. More precisely, there exist $t_0 > 0$ and $a > 0$ such that $M(t, x) \leq N_1 + a$ for $(t, x) \in (t_0, \infty)\times\Omega$, which in turn implies that

$$S_v(t,x),\ I_{v1}(t,x),\ I_{v2}(t,x) < N_1 + a \qquad \text{for } (t,x)\in(t_0,\infty)\times\Omega.$$

By the comparison principle and the first two equations of system (2.4), we know that $(I_1, I_2) \leq (\overline{h}_1, \overline{h}_2)$ on $[t_0,\infty)\times\overline{\Omega}$, where $(\overline{h}_1, \overline{h}_2)$ is the solution of

$$\begin{cases} \dfrac{\partial\overline{h}_1}{\partial t} = D_h\Delta\overline{h}_1 - \gamma_1(x)\overline{h}_1 + c_1(x)H_u(x)(N_1+a), & (t,x)\in(t_0,\infty)\times\Omega, \\ \dfrac{\partial\overline{h}_2}{\partial t} = D_h\Delta\overline{h}_2 - \gamma_2(x)\overline{h}_2 + c_2(x)H_u(x)(N_1+a), & (t,x)\in(t_0,\infty)\times\Omega, \\ \dfrac{\partial\mathcal{W}_2}{\partial n} = 0,\ \mathcal{W}_2 = \overline{h}_1, \overline{h}_2, & (t,x)\in(t_0,\infty)\times\partial\Omega, \\ \overline{h}_1(t_0,x) = I_1(t_0,x), \overline{h}_2(t_0,x) = I_2(t_0,x),\ x\in\Omega. \end{cases}$$

Obviously, $(\overline{h}_1, \overline{h}_2)\to(\widehat{h}_1, \widehat{h}_2)$ uniformly on $\overline{\Omega}$ as $t \to \infty$, where $(\widehat{h}_1, \widehat{h}_2)$ is the unique solution of

$$\begin{cases} -D_h\Delta\omega_1(x) = -\gamma_1(x)\omega_1(x) + c_1(x)H_u(x)(N_1+a), & x\in\Omega, \\ -D_h\Delta\omega_2(x) = -\gamma_2(x)\omega_2(x) + c_2(x)H_u(x)(N_1+a), & \\ & x\in\Omega, \\ \dfrac{\partial\mathcal{W}_3(x)}{\partial n} = 0,\ \mathcal{W}_3(x) = \omega_1(x), \omega_2(x), & x\in\partial\Omega. \end{cases}$$

Therefore, there exist $t_1 > t_0$ and N_2, $N_3 > 0$ such that $I_1(t,x) \le \overline{h}_1(x) < N_2 + a$ and $I_2(t,x) \le \overline{h}_2(x) < N_3 + a$ for $(t,\ x) \in (t_1, \infty) \times \Omega$. Hence, by taking $G = \max\{N_1 + a,\ N_2 + a,\ N_3 + a\}$, we have

$$0 \le I_1(t,x),\ I_2(t,x),\ S_v(t,x),\ I_{v1}(t,x),\ I_{v2}(t,x) \le G \text{ for } (t,x)\in(t_1,\infty)\times\Omega. \tag{3.3}$$

This proves Theorem 3.2. □

Motivated by [22, Theorem 2.9], the following result can be obtained directly.

Lemma 3.3. *System* (2.4) *with* (2.5) *and* (2.6) *admits a continuous semiflow* $\Phi(t)_{t\ge 0} : \mathbb{X}_H \to \mathbb{X}_H$ *with* $\Phi(t)\phi_0 := u(t,\ \phi_0)$, $t \ge 0$, *for each* $\phi_0 \in \mathbb{X}_H$. *Furthermore,* $\Phi(t)$ *admits a compact attractor in* $\mathbb{X}_H$.

The following result provides the strict positivity of solutions to system (2.4).

Lemma 3.4. *For* $\phi_0 \in \mathbb{X}_H$, *let* $u(t,\ \cdot,\ \phi_0)$ *be the solution of* (2.4). *Suppose that there exists* $t_2 \ge 0$ *such that* $I_1(t_2,\ \cdot,\ \phi_0) + I_{v1}(t_2,\ \cdot,\ \phi_0) > 0$, $I_2(t_2,\ \cdot,\ \phi_0) + I_{v2}(t_2,\ \cdot,\ \phi_0) > 0$, *and* $M(t_2,\ \cdot,\ \phi_0) > 0$. *Then*

$$\mathcal{W}(t,x,\phi_0) > 0 \qquad \text{for } (t,x)\in(t_2,\infty)\times\Omega,$$

where $\mathcal{W} = I_1,\ I_2,\ S_v,\ I_{v1},\ I_{v2}$.

Proof. First, we suppose that $I_{v1}(t_2,\ \cdot,\ \phi_0) + I_{v2}(t_2,\ \cdot,\ \phi_0) = 0$. Then $I_1(t_2,\ \cdot,\ \phi_0) \ne 0$, $I_2(t_2,\ \cdot,\ \phi_0) \ne 0$, and $S_v(t_2,\ \cdot,\ \phi_0) \ne 0$. By the first three equations of (2.4), we have

$$\begin{cases} \dfrac{\partial I_1}{\partial t} \ge D_h\Delta I_1 - \gamma_1(x)I_1, \\ \dfrac{\partial I_2}{\partial t} \ge D_h\Delta I_2 - \gamma_2(x)I_2, \\ \dfrac{\partial S_v}{\partial t} \ge D_v\Delta S_v + S_v(-\alpha_1(x)I_1 - \alpha_2(x)I_2 + \beta(x) - \mu(x)M) \end{cases} \tag{3.4}$$

for $(t,\ x) \in (t_2,\ \infty) \times \Omega$. Due to the fact that $I_1(t_2,\ \cdot,\ \phi_0) \ne 0$, $I_2(t_2,\ \cdot,\ \phi_0) \ne 0$, and $S_v(t_2,\ \cdot,\ \phi_0) \ne 0$, we can use the maximum principle to obtain

$$I_1(t,x) > 0, I_2(t,x) > 0,\ \text{and } S_v(t,x) > 0 \text{ for } (t,x)\in(t_2,\infty)\times\overline{\Omega}.$$

Furthermore, it follows from the fourth and fifth equations of (2.4)-(2.5) that

$$\begin{cases} \dfrac{\partial I_{v1}}{\partial t} > D_v\Delta I_{v1} - \mu(x)MI_{v1}, \\ \dfrac{\partial I_{v2}}{\partial t} > D_v\Delta I_{v2} - \mu(x)MI_{v2} \end{cases} \tag{3.5}$$

for $(t,\ x) \in (t_2,\ \infty) \times \Omega$. Again, by the maximum principle,

$$I_{v1}(t,x) > 0 \text{ and } I_{v2}(t,x) > 0 \text{ for } (t,x)\in(t_2,\infty)\times\overline{\Omega}.$$

Now, suppose that $I_{v1}(t_2,\ \cdot,\ \phi_0) + I_{v2}(t_2,\ \cdot,\ \phi_0) \ne 0$. We distinguish three cases to finish the proof.

Case 1: $I_{v1}(t_2,\ \cdot,\ \phi_0) \ne 0$ and $I_{v2}(t_2,\ \cdot,\ \phi_0) = 0$. Then $I_2(t_2,\ \cdot,\ \phi_0) \ne 0$. By the first equation of (2.4), we have the first inequality of (3.4). Further from the comparison principle and the fact that $H_u(x)$ is nontrivial, we know that the inequality is strict for some $x\in\overline{\Omega}$, which means $I_1(t,\ x) > 0$ for $(t,x)\in(t_2,\infty)\times\overline{\Omega}$. Similarly, we get directly from the second equation of (2.4), the second inequality of (3.4), and the maximum principle that $I_2(t,\ x) > 0$ for $(t,x)\in(t_2,\infty)\times\overline{\Omega}$ as $I_2(t_2,\ \cdot,\ \phi_0) \ne 0$. Notice that

$$\begin{cases} \dfrac{\partial I_{v1}}{\partial t} \ge D_v\Delta I_{v1} - \mu(x)MI_{v1}, \\ \dfrac{\partial I_{v2}}{\partial t} \ge D_v\Delta I_{v2} - \mu(x)MI_{v2} \end{cases} \tag{3.6}$$

for $(t,\ x) \in (t_2,\ \infty) \times \Omega$. It follows immediately from the maximum principle that

$$I_{v1}(t,x) > 0 \text{ and } I_{v2}(t,x) > 0 \text{ for } (t,x) \in (t_2,\infty) \times \overline{\Omega}.$$

By the S_v-equation of (2.4), we have

$$\frac{\partial S_v}{\partial t} > D_v \Delta S_v + S_v(-\alpha_1(x)I_1 - \alpha_2(x)I_2 + \beta(x) - \mu(x)M) \qquad \text{for } (t,x) \in (t_2,\infty) \times \Omega, \tag{3.7}$$

which implies

$$S_v(t,x) > 0 \text{ for } (t,x) \in (t_2,\infty) \times \overline{\Omega}.$$

Case 2: $I_{v1}(t_2,\cdot,\phi_0) = 0$ and $I_{v2}(t_2,\cdot,\phi_0) \neq 0$. Then $I_1(t_2,\cdot,\phi_0) \neq 0$. Consequently,

$$W(t,x,\phi_0) > 0 \text{ for } (t,x) \in (t_2,\infty) \times \Omega,$$

where $W = I_1, I_2, S_v, I_{v1}, I_{v2}$. Clearly, the remaining proof is similar to that for case 1.

Case 3: $I_{v1}(t_2,\cdot,\phi_0) \neq 0$ and $I_{v2}(t_2,\cdot,\phi_0) \neq 0$. By the first two equations of (2.4), we see that the first two inequalities of (3.4) hold and each is strict for some $x \in \overline{\Omega}$. Then from the comparison principle, we get

$$I_1(t,x) > 0 \text{ and } I_2(t,x) > 0 \text{ for } (t,x) \in (t_2,\infty) \times \overline{\Omega}.$$

By the fourth and the fifth equations of (2.4), we know that (3.6) is valid. Again it follows from the maximum principle that

$$I_{v1}(t,x) > 0 \text{ and } I_{v2}(t,x) > 0 \text{ for } (t,x) \in (t_2,\infty) \times \overline{\Omega}.$$

Finally, it yields from the third equation of (2.4) and (3.7) that

$$S_v(t,x) > 0 \text{ for } (t,x) \in (t_2,\infty) \times \overline{\Omega}.$$

This completes the proof. □

4. The reproduction numbers

This section is devoted to defining the BRNs and IRNs for our model. Generally speaking, the epidemic and extinction of malaria according to reproduction numbers provide important implications to the exploration of the complicated impacts of spatial heterogeneity on disease transmission. For the method used here, we refer to (Diekmann et al., 1990; Liang et al., 2017; Magal et al., 2019; Thieme, 2009; Wang & Zhao, 2012) and references therein.

4.1. Basic reproduction numbers

We first define the BRNs by considering two subsystems, which contain only the sensitive strain and the resistant strain, respectively. The subsystem that only contains the sensitive strain is

$$\begin{cases} \dfrac{\partial I_1}{\partial t} = D_h \Delta I_1 - \gamma_1(x)I_1 + c_1(x)H_u(x)I_{v1}, \\ \dfrac{\partial S_v}{\partial t} = D_v \Delta S_v - \alpha_1(x)S_vI_1 + \beta(x)(S_v + I_{v1}) - \mu(x)(S_v + I_{v1})S_v, \\ \dfrac{\partial I_{v1}}{\partial t} = D_v \Delta I_{v1} + \alpha_1(x)S_vI_1 - \mu(x)(S_v + I_{v1})I_{v1} \end{cases} \tag{4.1}$$

for $(t, x) \in (0, \infty) \times \Omega$, associated with

$$\frac{\partial \mathcal{W}_4}{\partial n} = 0, \ \mathcal{W}_4 = I_1, S_v, I_{v1}, \ (t,x) \in (0,\infty) \times \partial\Omega; \tag{4.2}$$

while the subsystem that only contains the resistant strain is

$$\begin{cases} \dfrac{\partial I_2}{\partial t} = D_h \Delta I_2 - \gamma_2(x) I_2 + c_2(x) H_u(x) I_{v2}, \\ \dfrac{\partial S_v}{\partial t} = D_v \Delta S_v - \alpha_2(x) S_v I_2 + \beta(x)(S_v + I_{v2}) - \mu(x)(S_v + I_{v2}) S_v, \\ \dfrac{\partial I_{v2}}{\partial t} = D_v \Delta I_{v2} + \alpha_2(x) S_v I_2 - \mu(x)(S_v + I_{v2}) I_{v2} \end{cases} \tag{4.3}$$

for $(t, x) \in (0, \infty) \times \Omega$, associated with

$$\frac{\partial \mathcal{W}_5}{\partial n} = 0, \ \mathcal{W}_5 = I_2, S_v, I_{v2}, \ (t, x) \in (0, \infty) \times \partial\Omega. \tag{4.4}$$

Obviously, by (2.2), the DFSSs and the PSS of system (4.1) are

$$E_0^1 = (0,0,0), \ E_1^1 = (0, \overline{M}(x), 0) \text{ and } E_E^1 = (I_1^*(x), S_v^*(x), I_{v1}^*(x))$$

while those of system (4.3) are

$$E_0^2 = (0,0,0), \ E_1^2 = (0, \overline{M}(x), 0) \text{ and } E_E^2 = (\widetilde{I}_2(x), \widetilde{S}_v(x), \widetilde{I}_{v2}(x)).$$

Each steady state of system (4.1) and system (4.3) can be viewed as a BSS of system (2.4), which allows us to give the steady states of system (2.4) as follows.

(i) DFSSs of system (2.4):

$$E_0 = (0,0,0,0,0) \text{ and } E_1 = (0,0,\overline{M}(x),0,0);$$

(ii) BSSs of system (2.4):

$$E_\partial^1 = (I_1^*(x), 0, S_v^*(x), I_{v1}^*(x), 0) \text{ and } E_\partial^2 = (0, \widetilde{I}_2(x), \widetilde{S}_v(x), 0, \widetilde{I}_{v2}(x));$$

(iii) PSS of system (2.4):

$$EE = (\mathring{I}_1(x), \mathring{I}_2(x), \mathring{S}_v(x), \mathring{I}_{v1}(x), \mathring{I}_{v2}(x)).$$

Here E_∂^1 is called the sensitive strain steady state as the I_2- and I_{v2}-components are zero. Similarly, E_∂^2 is called the resistant strain steady state.

We first define BRNs for subsystems (4.1) and (4.3), denoted by $\Re_0^1$ and $\Re_0^2$, respectively. Let $\mathbb{E} := C(\overline{\Omega}, \mathbb{R}^3)$ and its positive cone is denoted by $\mathbb{E}^+ := C(\overline{\Omega}, \mathbb{R}_+^3)$. Let

$$\mathbb{E}_H := \{(I_1, S_v, I_{v1})^T \in \mathbb{E}^+ : \ 0 \le S_v(x) + I_{v1}(x) \le \overline{M}(x) \text{ for } x \in \overline{\Omega}\}.$$

A simple calculation shows that the DFSS E_0^1 of subsystem (4.1) is always unstable. Linearize (4.1) around E_1^1 and consider only the infectious compartments to get

$$\begin{cases} \dfrac{\partial I_1}{\partial t} = D_h \Delta I_1 - \gamma_1(x) I_1 + c_1(x) H_u(x) I_{v1}, \\ \dfrac{\partial I_{v1}}{\partial t} = D_v \Delta I_{v1} + \alpha_1(x)\overline{M}(x) I_1 - \mu(x)\overline{M}(x) I_{v1} \end{cases} \tag{4.5}$$

for $(t, x) \in (0, \infty) \times \Omega$, and

$$\frac{\partial \mathcal{W}_6}{\partial n} = 0,\ \ \mathcal{W}_6 = I_1, I_{v1},\ \ (t,x) \in (0,\infty) \times \partial\Omega.$$

Let $\mathbb{W} := C(\overline{\Omega}, \mathbb{R}^2)$. We define the operator $F_1 : \mathbb{W} \to \mathbb{W}$ by

$$F_1(\overline{v}) = \begin{pmatrix} 0 & 0 \\ \alpha_1(x)\overline{M}(x) & 0 \end{pmatrix} \begin{pmatrix} \overline{v}_1(x) \\ \overline{v}_2(x) \end{pmatrix} \qquad \text{for } \overline{v} = (\overline{v}_1, \overline{v}_2)^T \in \mathbb{W}. \tag{4.6}$$

Denote by $\Psi(t) = \mathrm{diag}(T_1(t), T_3(t))$ the evolution operators of the system

$$\frac{d\overline{v}}{dt} = V_1 \overline{v} \triangleq D\Delta\overline{v} - W_1 \overline{v}, \tag{4.7}$$

where

$$\begin{aligned} D(V_1) &= \left\{ \left(h_1, h_2 \right) \in \bigcap_{p \geq 1} W^{2,p}(\overline{\Omega}, \mathbb{R}^2) : \frac{\partial h_1}{\partial n} = \frac{\partial h_2}{\partial n} = 0 \text{ on } \partial\Omega \text{ and } V_1(h_1, h_2) \in \mathbb{W} \right\}, \\ D &= \mathrm{diag}(D_h, D_v), \\ -W_1 &= \begin{pmatrix} -\gamma_1(x) & c_1(x) H_u(x) \\ 0 & -\mu(x)\overline{M}(x) \end{pmatrix}. \end{aligned}$$

In view of [31, Theorem 3.12], V_1 is resolvent positive and $\Psi(t)\mathbb{E}^+ \subset \mathbb{E}^+$ for each $t > 0$.

Following the standard procedure, at $t = 0$, we assume that $\overline{v}_0 = (\overline{v}_1^0, \overline{v}_2^0)^T = (I_1^0, I_{v1}^0)^T$ is the spatial distribution of infectious hosts and vectors with the sensitive strain near E_1^1. Hence, as time evolves, $\Psi(t)\overline{v}_0(x) = (T_1(t)\overline{v}_1^0(x), T_3(t)\overline{v}_2^0(x))$ stands for the distribution of remaining infective hosts and vectors. The distribution of total infective vectors can be calculated by

$$\int_0^\infty \alpha_1(x)\overline{M}(x)(T_1(t)\overline{v}_1^0)(x)dt.$$

As a result, the following continuous and positive operator on $\mathbb{Y}$ defined by

$$L_1(\overline{v}_0)(x) := \int_0^\infty F_1 \Psi(t)\overline{v}_0(x)dt = F_1 \int_0^\infty \Psi(t)\overline{v}_0(x)dt$$

is called the next generation operator. We define the spectral radius of L_1 as the BRN for subsystem (4.1), i.e.,

$$\Re_0^1 := r(L_1). \tag{4.8}$$

The BRN $\Re_0^2$ for subsystem (4.3) can be obtained in the same way. Consequently, the BRN of system (2.4) is defined by

$$\Re_0 = \max\{\Re_0^1, \Re_0^2\}. \tag{4.9}$$

The following observation indicates the relationship between $\Re_0^1$ and the principal eigenvalue of an associated linear elliptic eigenvalue problem.

Lemma 4.1. *Let $\Re_0^1$ be defined by (4.8). Considering*

$$\begin{cases} -D\Delta\varphi + W_1\varphi = \kappa F_1 \varphi, & x \in \Omega, \\ \dfrac{\partial \varphi_i}{\partial n} = 0,\ \ i = 1, 2, & x \in \partial\Omega, \end{cases} \tag{4.10}$$

we have the following statements.

(i) Problem (4.10) admits a unique principal eigenvalue $\kappa_0 > 0$. Futhermore, κ_0 has a strictly positive eigenvector $(\varphi_1^*(x), \varphi_2^*(x))$.
(ii) $\Re_0^1 = \frac{1}{\kappa_0}$.

Proof. We first prove (i). Let (κ, φ) be an eigenvalue pair of problem (4.10) with $\varphi = (\varphi_1, \varphi_2)$, that is,

$$\begin{cases} -D_h\Delta\varphi_1 + \gamma_1(x)\varphi_1 = c_1(x)H_u(x)\varphi_2, & x\in\Omega, \\ -D_v\Delta\varphi_2 + \mu(x)\overline{M}(x)\varphi_2 = \kappa\alpha_1(x)\overline{M}(x)\varphi_1, & x\in\Omega. \end{cases}$$

Recall that $T_1(t)$, $t > 0$, is strongly positive and compact. Let $\widehat{T}_3(t) : \mathbb{Y} \to \mathbb{Y}$ be the strictly positive and compact semigroup generated by the operator $\widehat{A}_3 := D_v\Delta - \mu(x)\overline{M}(x)$. Due to [31, Theorem 3.12], for $\varphi \in \mathbb{Y}$, we have

$$\begin{cases} (\kappa\mathbb{I}_d - A_1)^{-1}\varphi = \int_0^\infty e^{-\kappa t}T_1(t)\varphi dt, & \kappa > s(A_1), \\ (\kappa\mathbb{I}_d - \widehat{A}_3)^{-1}\varphi = \int_0^\infty e^{-\kappa t}\widehat{T}_3(t)\varphi dt, & \kappa > s(\widehat{A}_3). \end{cases} \tag{4.11}$$

Here $s(\overline{A}) = \sup\{\mathrm{Re}\lambda : \lambda \in \sigma(\overline{A})\}$ denotes the spectral bound of $\overline{A}$, where $\sigma(\overline{A})$ denotes the spectral set of $\overline{A}$. Due to

$$s(A_1) = \max_{x\in\overline{\Omega}}\{-\gamma_1(x)\} < 0 \text{ and } s(\widehat{A}_3) = \max_{x\in\overline{\Omega}}\{-\mu(x)\overline{M}(x)\} < 0,$$

taking $\kappa = 0$ in (4.11) leads to

$$-A_1^{-1}\varphi = \int_0^\infty T_1(t)\varphi dt \text{ and } -\widehat{A}_3^{-1}\varphi = \int_0^\infty \widehat{T}_3(t)\varphi dt \quad \text{for } \varphi \in \mathbb{Y}.$$

It follows that the operators $-A_1^{-1}$ and $-\widehat{A}_3^{-1}$ are compact and strongly positive. We rewrite system (4.10) as

$$\begin{cases} -A_1\varphi_1(x) = c_1(x)H_u(x)\varphi_2(x), & x\in\Omega, \\ -\widehat{A}_3\varphi_2(x) = \kappa\alpha_1(x)\overline{M}(x)\varphi_1(x), & x\in\Omega, \end{cases}$$

which allows us to obtain that $\varphi_1(x) = -c_1(x)H_u(x)A_1^{-1}\varphi_2(x)$ and $(\kappa, \varphi_2(x))$ satisfies

$$\frac{1}{\kappa}\widetilde{\varphi} = \alpha_1(x)\overline{M}(x)c_1(x)H_u(x)A_1^{-1}\widehat{A}_3^{-1}\widetilde{\varphi}. \tag{4.12}$$

Note that $\alpha_1(x)\overline{M}(x)c_1(x)H_u(x) > 0$ for $x\in\overline{\Omega}$. Thus the operator $\alpha_1(x)\overline{M}(x)c_1(x)H_u(x)A_1^{-1}\widehat{A}_3^{-1}$ is strongly positive and compact on $\mathbb{Y}$. This combined with the Krein-Rutman Theorem implies that system (4.12) admits a unique principal eigenvalue $\kappa_0 > 0$, corresponding to which, $\varphi_2^*(x) \gg 0$ in $\mathbb{Y}$. Let $\varphi_1^*(x) = -c_1(x)H_u(x)A_1^{-1}\varphi_2^*(x)$. Then $\varphi_1^*(x) \gg 0$. This proves (i).

The assertion (ii) can be easily obtained according to [37, Theorem 3.2]. This completes the proof. □

It is noted that subsystem (4.5) is cooperative and irreducible. We substitute the solution $(e^{\lambda_1 t}\psi_1(x), e^{\lambda_1 t}\psi_2(x))$ into (4.5) to obtain

$$\begin{cases} \lambda_1\psi_1(x) = D_h\Delta\psi_1(x) + c_1(x)H_u(x)\psi_2(x) - \gamma_1(x)\psi_1(x), & x\in\Omega, \\ \lambda_1\psi_2(x) = D_v\Delta\psi_2(x) + \alpha_1(x)\overline{M}(x)\psi_1(x) - \mu(x)\overline{M}\psi_2(x), & x\in\Omega, \\ \dfrac{\partial\mathcal{W}_7(x)}{\partial n} = 0, \ \mathcal{W}_7(x) = \psi_1(x), \psi_2(x), & x\in\partial\Omega. \end{cases} \tag{4.13}$$

Similarly, for $(I_2, I_{v2}) = (e^{\lambda_2 t}\psi_3(x), e^{\lambda_2 t}\psi_4(x))$, we get

$$\begin{cases} \lambda_2\psi_3(x) = D_h\Delta\psi_3(x) + c_2(x)H_u(x)\psi_4(x) - \gamma_2(x)\psi_3(x), & x\in\Omega, \\ \lambda_2\psi_4(x) = D_v\Delta\psi_4(x) + \alpha_2(x)\overline{M}(x)\psi_3(x) - \mu(x)\overline{M}(x)\psi_4(x), & x\in\Omega, \\ \dfrac{\partial\mathcal{W}_8(x)}{\partial n} = 0,\ \mathcal{W}_8(x) = \psi_3(x), \psi_4(x), & x\in\partial\Omega. \end{cases} \tag{4.14}$$

The following result comes from [31, Theorem 3.5], which reveals that $\Re_0^1 - 1$ (respectively, $\Re_0^2 - 1$) has the same sign as the principal eigenvalue of (4.13) (respectively, (4.14)).

Lemma 4.2. *Let F_1 and V_1 be defined in (4.6) and (4.7), respectively. Define*

$$F_2 := \begin{pmatrix} 0 & 0 \\ \alpha_2(x)\overline{M}(x) & 0 \end{pmatrix} \text{ and } V_2 := \begin{pmatrix} D_h\Delta - \gamma_2(x) & c_2(x)H_u(x) \\ 0 & D_v\Delta - \mu(x)\overline{M}(x) \end{pmatrix},\ x\in\Omega.$$

Then $\Re_0^i - 1$ has the same sign as $\lambda_i^*(\overline{M}) = s(F_i + V_i)$, $i = 1, 2$.

4.2. The relationship between $\Re_0^i$ and $\Re_0^i(x)$

When the diffusion terms in subsystem (4.1) are ignored, we arrive at the following ODE system with respect to a specific location x,

$$\begin{cases} \dfrac{dI_1}{\partial t} = -\gamma_1(x)I_1 + c_1(x)H_u(x)I_{v1}, \\ \dfrac{dS_v}{\partial t} = -\alpha_1(x)S_vI_1 + \beta(x)(S_v + I_{v1}) - \mu(x)(S_v + I_{v1})S_v, \\ \dfrac{dI_{v1}}{\partial t} = \alpha_1(x)S_vI_1 - \mu(x)(S_v + I_{v1})I_{v1}. \end{cases} \tag{4.15}$$

At a specific location x, we define

$$\Re_0^1(x) = \Re_1^1(x)\Re_2^1(x), \tag{4.16}$$

where

$$\Re_1^1(x) = \frac{c_1(x)H_u(x)}{\gamma_1(x)} \text{ and } \Re_2^1(x) = \frac{\alpha_1(x)}{\mu(x)}.$$

Here $\Re_1^1(x)$ (respectively, $\Re_2^1(x)$) measures the impact of one infected mosquito (respectively, infectious human) on susceptible humans (respectively, susceptible mosquitoes) for the sensitive strain. Note that $\Re_0^i(x)$ is a multiplication operator, termed as the LBRN for the sensitive strain (when $i = 1$) and resistant strain (when $i = 2$). This subsection is devoted to studying the relationship between $\Re_0^i$ and $\Re_0^i(x)$. The main idea comes from (Magal et al., 2019).

By (4.8), the BRN $\Re_0^1$ for (4.1) is defined as

$$\Re_0^1 = r(-F_1V_1^{-1}).$$

Following the approach developed in [21, Theorem 3.1], we get

$$\Re_0^1 = r(L_1^1\Re_1^1(x)L_2^1\Re_2^1(x)) \tag{4.17}$$

with

$$L_1^1 = (\gamma_1(x) - D_h\Delta)^{-1}\gamma_1(x) \text{ and } L_2^1 = (\mu(x)\overline{M}(x) - D_v\Delta)^{-1}\mu(x)\overline{M}(x).$$

Similarly, we get

$$\Re_0^2(x) = \Re_1^2(x)\Re_2^2(x), \tag{4.18}$$

where

$$\mathfrak{R}_1^2(x) = \frac{c_2(x)H_u(x)}{\gamma_2(x)} \text{ and } \mathfrak{R}_2^2(x) = \frac{\alpha_2(x)}{\mu(x)}.$$

Further,

$$\mathfrak{R}_0^2 = r(L_1^2\mathfrak{R}_1^2(x)L_2^2\mathfrak{R}_2^2(x)) \tag{4.19}$$

with

$$L_1^2 = (\gamma_2(x) - D_h\Delta)^{-1}\gamma_2(x) \text{ and } L_2^2 = (\mu(x)\overline{M}(x) - D_v\Delta)^{-1}\mu(x)\overline{M}(x).$$

From [21, Theorem 3.6], we directly obtain the following result.

Lemma 4.3. *If* $\mathfrak{R}_0^i(x) > 1$ $(i = 1, 2)$ (*respectively*, $\mathfrak{R}_0^i(x) < 1$) *for* $x \in \overline{\Omega}$, *then* $\mathfrak{R}_0^i > 1$ (*respectively*, $\mathfrak{R}_0^i < 1$).

The main contribution of (Magal et al., 2019) is the characterization of the limit behavior of $\mathfrak{R}_0^i$ $(i = 1, 2)$ as the diffusion rates approach infinity or zero. The following first main result of this subsection in the case where the diffusion rates approach infinity can be viewed as a direct consequence of [21, Theorem 3.6 and Remark 4.8]. Thus the proof is omitted here.

Lemma 4.4. *Let* $\mathfrak{R}_0^1$ *and* $\mathfrak{R}_0^2$ *be defined by* (4.17) and (4.19), *respectively. Then the following statements are valid.*

(i) For $i = 1, 2$, $\lim\limits_{D_h\to\infty}\lim\limits_{D_v\to\infty}\mathfrak{R}_0^i = \lim\limits_{D_v\to\infty}\lim\limits_{D_h\to\infty}\mathfrak{R}_0^i = \overline{\mathfrak{R}}_1^i\overline{\mathfrak{R}}_2^i$.
(ii) For $i = 1, 2$, $\lim\limits_{(D_h,\, D_v)\to(\infty,\, \infty)}\mathfrak{R}_0^i = \overline{\mathfrak{R}}_1^i\overline{\mathfrak{R}}_2^i$.

Here

$$\overline{\mathfrak{R}}_1^i := \frac{\int_\Omega \gamma_i(x)\mathfrak{R}_1^i(x)dx}{\int_\Omega \gamma_i(x)dx} = \frac{\int_\Omega c_i(x)H_u(x)dx}{\int_\Omega \gamma_i(x)dx}$$

and

$$\overline{\mathfrak{R}}_2^i := \frac{\int_\Omega \mu(x)\mathfrak{R}_2^i(x)dx}{\int_\Omega \mu(x)dx} = \frac{\int_\Omega \alpha_i(x)dx}{\int_\Omega \mu(x)dx}.$$

The next main result of this subsection in the case where diffusion rates approach zero can be viewed as a direct consequence of [21, Theorem 4.10 and Theorem 4.11]. Again, we omit the proof.

Lemma 4.5. *Let* $\mathfrak{R}_0^1$ *and* $\mathfrak{R}_0^2$ *be defined by* (4.17) and (4.19), *respectively*.

(i) For $i = 1, 2$, $\lim\limits_{D_h\to 0}\lim\limits_{D_v\to 0}\mathfrak{R}_0^i = \lim\limits_{D_v\to 0}\lim\limits_{D_h\to 0}\mathfrak{R}_0^i = \max\{\mathfrak{R}_0^i(x)\}$.
(ii) For $i = 1, 2$, $\lim\limits_{(D_h,\, D_v)\to(0,\, 0)}\mathfrak{R}_0^i = \max\{\mathfrak{R}_0^i(x)\}$.

Here $\mathfrak{R}_0^1(x)$ and $\mathfrak{R}_0^2(x)$ are defined by (4.16) and (4.18), respectively.

Lemma 4.4 and Lemma 4.5 demonstrate the effect of large or small diffusion rates on $\mathfrak{R}_0^i$ $(i = 1, 2)$ for a single-strain system.

4.3. Invasion reproduction numbers

Recall that for $i = 1, 2$, E_∂^i is the BSS of system (2.4), where the non-zero infected components are $I_1^*(x)$ and $I_{v1}^*(x)$ when $i = 1$ while they are $\widetilde{I}_2(x)$ and $\widetilde{I}_{v2}(x)$ when $i = 2$. In this subsection, we define the IRNs for the two strains, denoted by $\widehat{\mathfrak{R}}_0^i$ $(i = 1, 2)$. Here the IRN means the average number of secondary infections by introducing one infective into a susceptible component for one strain, but with the presence of the other strain.

Note that the PSS E_E^2 of system (4.3) satisfies

$$\begin{cases} 0 = D_h\Delta\widetilde{I}_2(x) - \gamma_2(x)\widetilde{I}_2(x) + c_2(x)H_u(x)\widetilde{I}_{v2}(x), & x\in\Omega, \\ 0 = D_v\Delta\widetilde{S}_v(x) - \alpha_2(x)\widetilde{S}_v(x)\widetilde{I}_2(x) + \beta(x)(\widetilde{S}_v(x) + \widetilde{I}_{v2}(x)) \\ -\mu(x)(\widetilde{S}_v(x) + \widetilde{I}_{v2}(x))\widetilde{S}_v(x), & x\in\Omega, \\ 0 = D_v\Delta\widetilde{I}_{v2}(x) + \alpha_2(x)\widetilde{S}_v(x)\widetilde{I}_2(x) - \mu(x)(\widetilde{S}_v(x) + \widetilde{I}_{v2}(x))\widetilde{I}_{v2}(x), & x\in\Omega, \\ \dfrac{\partial\mathcal{W}_9(x)}{\partial n} = 0,\ \mathcal{W}_9(x) = \widetilde{I}_2(x), \widetilde{S}_v(x), \widetilde{I}_{v2}(x), & x\in\partial\Omega. \end{cases} \tag{4.20}$$

By letting

$$I_1 = \omega_1,\ I_2 = \widetilde{I}_2 + \omega_2,\ S_v = \widetilde{S}_v + \omega_3, I_{v1} = \omega_4 \text{ and } I_{v2} = \widetilde{I}_{v2} + \omega_5, \tag{4.21}$$

we linearize system (2.4) around E_∂^2 and consider only infective components ω_1 and ω_4 to obtain

$$\begin{cases} \dfrac{\partial\omega_1}{\partial t} = D_h\Delta\omega_1 - \gamma_1(x)\omega_1 + c_1(x)H_u(x)\omega_4, & (t,x)\in(0,\infty)\times\Omega, \\ \dfrac{\partial\omega_4}{\partial t} = D_v\Delta\omega_4 - \mu(x)(\widetilde{S}_v(x) + \widetilde{I}_{v2}(x))\omega_4 + \alpha_1(x)\widetilde{S}_v(x)\omega_1, & (t,x)\in(0,\infty)\times\Omega, \\ \dfrac{\partial\mathcal{W}_{10}}{\partial n} = 0,\ \mathcal{W}_{10} = \omega_1, \omega_4, & (t,x)\in(0,\infty)\times\partial\Omega, \end{cases}$$

whose associated eigenvalue problem containing ω_1 and ω_4 reads as

$$\begin{cases} \lambda\widehat{\omega}_1(x) = D_h\Delta\widehat{\omega}_1(x) - \gamma_1(x)\widehat{\omega}_1(x) + c_1(x)H_u(x)\widehat{\omega}_4(x), & x\in\Omega, \\ \lambda\widehat{\omega}_4(x) = D_v\Delta\widehat{\omega}_4(x) - \mu(x)(\widetilde{S}_v(x) + \widetilde{I}_{v2}(x))\widehat{\omega}_4(x) + \alpha_1(x)\widetilde{S}_v(x)\widehat{\omega}_1(x), & x\in\Omega, \\ \dfrac{\partial\mathcal{W}_{11}(x)}{\partial n} = 0,\ \mathcal{W}_{11}(x) = \widehat{\omega}_1(x), \widehat{\omega}_4(x), & x\in\partial\Omega. \end{cases} \tag{4.22}$$

As in (Magal et al., 2019; Thieme, 2009; Wang & Zhao, 2012), the IRN $\widehat{\Re}_0^1$ of the sensitive strain for (2.4) is defined as

$$\widehat{\Re}_0^1 = r(-\widehat{F}_1\widehat{V}_1^{-1}), \tag{4.23}$$

where $\widehat{V}_1 : D(\widehat{V}_1)\subset\mathbb{W}\to\mathbb{W}$ and $\widehat{F_1} : \mathbb{W}\to\mathbb{W}$ are linear operators defined respectively by

$$\widehat{V}_1\overline{v} = \begin{pmatrix} D_h\Delta - \gamma_1(x) & c_1(x)H_u(x) \\ 0 & D_v\Delta - \mu(x)(\widetilde{S}_v(x) + \widetilde{I}_{v2}(x)) \end{pmatrix}\overline{v}$$

and

$$\widehat{F}_1\overline{v} = \begin{pmatrix} 0 & 0 \\ \alpha_1(x)\widetilde{S}_v(x) & 0 \end{pmatrix}\overline{v}$$

with $D(\widehat{V}_1) = D(V_1)$. The following lemma can be obtained in a similar way as Lemma 4.2.

Lemma 4.6. *Let $\widehat{\Re}_0^1$ be defined by (4.23). The following two statements hold.*

(i) $\widehat{\Re}_0^1 - 1$ has the same sign as $\widehat{\lambda}_1$, where $\widehat{\lambda}_1$ is the principal eigenvalue of (4.22).
(ii) $\widehat{\Re}_0^2 - 1$ has the same sign as $\widehat{\lambda}_2$, where $\widehat{\Re}_0^2$ is the IRN of the resistant strain for (2.4) and $\widehat{\lambda}_2$ is the principal eigenvalue of

$$\begin{cases} \lambda\widehat{\omega}_2(x) = D_h\Delta\widehat{\omega}_2(x) - \gamma_2(x)\widehat{\omega}_2(x) + c_2(x)H_u(x)\widehat{\omega}_5(x), & x\in\Omega, \\ \lambda\widehat{\omega}_5(x) = D_v\Delta\widehat{\omega}_5(x) - \mu(x)(S_v^*(x) + I_{v1}^*(x))\widehat{\omega}_5(x) + \alpha_2(x)S_v^*(x)\widehat{\omega}_2(x), & x\in\Omega, \\ \dfrac{\partial\mathcal{W}_{12}(x)}{\partial n} = 0,\ \mathcal{W}_{12}(x) = \widehat{\omega}_2(x), \widehat{\omega}_5(x), & x\in\partial\Omega. \end{cases} \tag{4.24}$$

4.4. The relationship between $\widehat{\Re}_0^i$ and $\widehat{\Re}_0^i(x)$

As for $\Re_0^i$ $(i=1,2)$, $\widehat{\Re}_0^i(i=1,2)$ is also difficult to visualize. We thus turn our attention to the relationship between $\widehat{\Re}_0^i$ and $\widehat{\Re}_0^i(x)$ with the help of (Magal et al., 2019), where $\widehat{\Re}_0^i(x)$ is the LIRN for the i strain and is defined below.

We first consider the sensitive strain. In this case, $(I_2,S_v,I_{v2})\to(\widetilde{I}_2(x),\widetilde{S}_v(x),\widetilde{I}_{v2}(x))$. We consider the following system with no diffusion terms and containing only the infective compartments for the sensitive strain,

$$\begin{cases} \dfrac{dI_1}{\partial t} = -\gamma_1(x)I_1 + c_1(x)H_u(x)I_{v1}, \\ \dfrac{dI_{v1}}{\partial t} = \alpha_1(x)\widetilde{S}_v(x)I_1 - \mu(x)(\widetilde{S}_v(x) + I_{v1} + \widetilde{I}_{v2}(x))I_{v1}. \end{cases} \tag{4.25}$$

Then

$$\widehat{\Re}_0^1(x) = \widehat{\Re}_1^1(x)\widehat{\Re}_2^1(x), \tag{4.26}$$

where

$$\widehat{\Re}_1^1(x) = \frac{c_1(x)H_u(x)}{\gamma_1(x)} \text{ and } \widehat{\Re}_2^1(x) = \frac{\alpha_1(x)\widetilde{S}_v(x)}{\mu(x)(\widetilde{S}_v(x)+\widetilde{I}_{v2}(x))}.$$

Following the approach in [21, Theorem 3.1], we directly have

$$\widehat{\Re}_0^1 = r(\widehat{L}_1^1\widehat{\Re}_1^1(x)\widehat{L}_2^1\widehat{\Re}_2^1(x)) \tag{4.27}$$

with

$$\widehat{L}_1^1 = (\gamma_1(x) - D_h\Delta)^{-1}\gamma_1(x)$$

and

$$\widehat{L}_2^1 = (\mu(x)(\widetilde{S}_v(x)+\widetilde{I}_{v2}(x)) - D_v\Delta)^{-1}\mu(x)(\widetilde{S}_v(x)+\widetilde{I}_{v2}(x)).$$

Similarly, for the resistant strain,

$$\widehat{\Re}_0^2(x) = \widehat{\Re}_1^2(x)\widehat{\Re}_2^2(x), \tag{4.28}$$

where

$$\widehat{\Re}_1^2(x) = \frac{c_2(x)H_u(x)}{\gamma_2(x)} \text{ and } \widehat{\Re}_2^2(x) = \frac{\alpha_2(x)S_v^*(x)}{\mu(x)(S_v^*(x)+I_{v2}^*(x))}.$$

Furthermore,

$$\widehat{\Re}_0^2 = r(\widehat{L}_1^2\widehat{\Re}_1^2(x)\widehat{L}_2^2\widehat{\Re}_2^2(x)) \tag{4.29}$$

with

$$\widehat{L}_1^2 = (\gamma_2(x) - D_h\Delta)^{-1}\gamma_2(x)$$

and

$$\widehat{L}_2^2 = (\mu(x)(S_v^*(x)+I_{v2}^*(x)) - D_v\Delta)^{-1}\mu(x)(S_v^*(x)+I_{v2}^*(x)).$$

From (4.26) and (4.28), compared with (4.16) and (4.18), respectively, we know that $\widehat{\Re}_0^i(x) < \Re_0^i(x)$ $(i=1,2)$ (see also (Zhao et al., 2020) and (Tuncer & Martcheva, 2012)).

The following result is a direct consequence of [21, Theorem 3.6].

Lemma 4.7. *For $i=1,2$, if $\widehat{\Re}_0^i(x) > 1$ (respectively, $\widehat{\Re}_0^i(x) < 1$) for $x\in\overline{\Omega}$, then $\widehat{\Re}_0^i > 1$ (respectively, $\widehat{\Re}_0^i < 1$).*

In the following, we investigate the limiting behaviors of $\widehat{\Re}_0^i$ $(i=1,2)$ when the diffusion rates approach infinity or zero. According to [15, Proposition 2.5],

$$\lim_{D_v\to 0}(\widetilde{S}_v(x),\widetilde{I}_{v2}(x))\to(\widetilde{S}_v^0(x),\widetilde{I}_{v2}^0(x)),\ \lim_{D_v\to\infty}(\widetilde{S}_v(x),\widetilde{I}_{v2}(x))\to(\widetilde{S}_v^\infty,\widetilde{I}_{v2}^\infty)$$

and

$$\lim_{D_v\to 0}(S_v^*(x),I_{v1}^*(x))\to(S_v^{*0}(x),I_{v1}^{*0}(x)),\ \lim_{D_v\to\infty}(S_v^*(x),I_{v1}^*(x))\to(S_v^{*\infty},I_{v1}^{*\infty}),$$

where $\widetilde{S}_v^0(x),\widetilde{I}_{v2}^0(x),S_v^{*0}(x),I_{v1}^{*0}(x)\in C(\overline{\Omega},\mathbb{R})$ are positive functions of position x while $\widetilde{S}_v^\infty,\widetilde{I}_{v2}^\infty,S_v^{*\infty},I_{v1}^{*\infty}$ are positive constants. The following two result are counterparts of Lemma 4.4 and Lemma 4.5, respectively.

Lemma 4.8. *Let $\widehat{\Re}_0^1$ and $\widehat{\Re}_0^2$ be defined by (4.27) and (4.29), respectively. Denote $\widehat{\Re}_{2,\infty}^1(x)=\lim_{D_v\to\infty}\widehat{\Re}_2^1(x)=\frac{\alpha_1(x)\widetilde{S}_v^\infty}{\mu(x)(\widetilde{S}_v^\infty+\widetilde{I}_{v2}^\infty)}$ and $\widehat{\Re}_{2,\infty}^2(x)=\lim_{D_v\to\infty}\widehat{\Re}_2^2(x)=\frac{\alpha_2(x)S_v^{*\infty}}{\mu(x)(S_v^{*\infty}+I_{v1}^{*\infty})}$. Then the following two statements hold.*

(i) $\lim_{D_h\to\infty}\lim_{D_v\to\infty}\widehat{\Re}_0^1=\lim_{D_v\to\infty}\lim_{D_h\to\infty}\widehat{\Re}_0^1=\widetilde{\Re}_1^1\widetilde{\Re}_2^1$ and $\lim_{(D_h,D_v)\to(\infty,\infty)}\widehat{\Re}_0^1=\widetilde{\Re}_1^1\widetilde{\Re}_2^1$, where

$$\widetilde{\Re}_1^1:=\frac{\int_\Omega\gamma_1(x)\widehat{\Re}_1^1(x)dx}{\int_\Omega\gamma_1(x)dx}=\frac{\int_\Omega c_1(x)H_u(x)dx}{\int_\Omega\gamma_1(x)dx}$$

and

$$\widetilde{\Re}_2^1:=\frac{\int_\Omega\mu(x)\widehat{\Re}_{2,\infty}^1(x)dx}{\int_\Omega\mu(x)dx}=\frac{\widetilde{S}_v^\infty}{(\widetilde{S}_v^\infty+\widetilde{I}_{v2}^\infty)}\frac{\int_\Omega\alpha_1(x)dx}{\int_\Omega\mu(x)dx}.$$

(ii) $\lim_{D_h\to\infty}\lim_{D_v\to\infty}\widehat{\Re}_0^2=\lim_{D_v\to\infty}\lim_{D_h\to\infty}\widehat{\Re}_0^2=\widetilde{\Re}_1^2\widetilde{\Re}_2^2$ and $\lim_{(D_h,D_v)\to(\infty,\infty)}\widehat{\Re}_0^2=\widetilde{\Re}_1^2\widetilde{\Re}_2^2$, where

$$\widetilde{\Re}_1^2:=\frac{\int_\Omega\gamma_2(x)\widehat{\Re}_1^2(x)dx}{\int_\Omega\gamma_2(x)dx}=\frac{\int_\Omega c_2(x)H_u(x)dx}{\int_\Omega\gamma_2(x)dx}$$

and

$$\widetilde{\Re}_2^2:=\frac{\int_\Omega\mu(x)\widehat{\Re}_{2,\infty}^2(x)dx}{\int_\Omega\mu(x)dx}=\frac{S_v^{*\infty}}{(S_v^{*\infty}+I_{v1}^{*\infty})}\frac{\int_\Omega\alpha_2(x)dx}{\int_\Omega\mu(x)dx}.$$

Lemma 4.9. *Let $\widehat{\Re}_0^1$ and $\widehat{\Re}_0^2$ be defined by (4.27) and (4.29), respectively. Then the following two statements are true.*

(i) For $i=1,2$, $\lim_{D_h\to 0}\lim_{D_v\to 0}\widehat{\Re}_0^i=\lim_{D_v\to 0}\lim_{D_h\to 0}\widehat{\Re}_0^i=\max\{\widehat{\Re}_0^i(x)\}$.
(ii) For $i=1,2$, $\lim_{(D_h,\ D_v)\to(0,\ 0)}\widehat{\Re}_0^i=\max\{\widehat{\Re}_0^i(x)\}$.

Here $\widehat{\Re}_0^1(x)$ and $\widehat{\Re}_0^2(x)$ are defined by (4.26) and (4.28), respectively.

5. Threshold dynamics

In this section, we study the threshold dynamics of system (2.4) in terms of $\Re_0^i$ and $\widehat{\Re}_0^i$ $(i=1, 2)$. These results will characterize the competition and coexistence phenomena between the sensitive strain and the resistant strain.

By the standard result in [20, Theorem 2.4 and Theorem 3.12], we first give the following lemma on the global dynamics of subsystems (4.1) and (4.3).

Lemma 5.1. *For $i=1, 2$,*

(i) *if $\Re_0^i<1$ then E_1^i is globally asymptomatically stable;*
(ii) *if $\Re_0^i>1$ then E_1^i is unstable and subsystem for the strain i possesses a positive global asymptotic stable steady state E_E^i.*

Recall that E_∂^i $(i=1, 2)$ is the BSS of system (2.4). In what follows, combining with the BRN $\Re_0^i$ and the IRN $\widehat{\Re}_0^i$, we determine the invasion behaviors by investigating the stability of the BSS E_∂^i.

5.1. The stability of E_0 and E_1

Obviously, E_0 is always unstable. We linearize (2.4) around E_1 and then only consider equations for I_1, I_2, I_{v1} and I_{v2} to obtain

$$\begin{cases} \dfrac{\partial I_1}{\partial t}=D_h\Delta I_1-\gamma_1(x)I_1+c_1(x)H_u(x)I_{v1}, & (t,x)\in(0,\infty)\times\Omega,\\ \dfrac{\partial I_2}{\partial t}=D_h\Delta I_2-\gamma_2(x)I_2+c_2(x)H_u(x)I_{v2}, & (t,x)\in(0,\infty)\times\Omega,\\ \dfrac{\partial I_{v1}}{\partial t}=D_v\Delta I_{v1}+\alpha_1(x)\overline{M}(x)I_1-\mu(x)\overline{M}(x)I_{v1}, & (t,x)\in(0,\infty)\times\Omega,\\ \dfrac{\partial I_{v2}}{\partial t}=D_v\Delta I_{v2}+\alpha_2(x)\overline{M}(x)I_2-\mu(x)\overline{M}(x)I_{v2}, & (t,x)\in(0,\infty)\times\Omega,\\ \dfrac{\partial \mathcal{W}_{13}}{\partial n}=0,\ \mathcal{W}_{13}=I_1,I_2,I_{v1},I_{v2}, & (t,x)\in(0,\infty)\times\partial\Omega. \end{cases} \tag{5.1}$$

Substituting $(I_1, I_2, I_{v1}, I_{v2})=e^{\lambda t}(\psi_1(x), \psi_2(x), \psi_3(x), \psi_4(x))$ into (5.1), we get

$$\begin{cases} \lambda\psi_1=D_h\Delta\psi_1+c_1(x)H_u(x)\psi_3-\gamma_1(x)\psi_1, & x\in\Omega,\\ \lambda\psi_2=D_h\Delta\psi_2+c_2(x)H_u(x)\psi_4-\gamma_2(x)\psi_2, & x\in\Omega,\\ \lambda\psi_3=D_v\Delta\psi_3+\alpha_1\overline{M}(x)\psi_1-\mu(x)\overline{M}(x)\psi_3, & x\in\Omega,\\ \lambda\psi_4=D_v\Delta\psi_4+\alpha_2\overline{M}(x)\psi_2-\mu(x)\overline{M}(x)\psi_4, & x\in\Omega,\\ \dfrac{\partial \mathcal{W}_{14}}{\partial n}=0,\ \mathcal{W}_{14}=\psi_1,\psi_2,\psi_3,\psi_4, & x\in\partial\Omega. \end{cases} \tag{5.2}$$

Due to the fact that the eigenpairs of (4.13) and (4.14) satisfy (5.2) in the form of

$$(\lambda,\psi_1(x),0,\psi_2(x),0) \text{ or } (\lambda,0,\psi_3(x),0,\psi_4(x))$$

and Lemma 4.2, we know that E_1 is stable if $\Re_0^1<1$ and $\Re_0^2<1$, that is, if $\Re_0<1$. In fact, it is also globally stable from the result below.

Theorem 5.2. *If $\Re_0^1<1$ and $\Re_0^2<1$, then E_1 is globally attractive, that is,*

$$\lim_{t\to\infty}\|(I_1,I_2,S_v,I_{v1},I_{v2})-E_1\|_{\mathbb{X}}=0. \tag{5.3}$$

Proof. By Lemma 4.2, we know that $\lambda_1^*(\overline{M})<0$ as $\Re_0^1<1$. Hence there is a small enough number $\epsilon_1>0$ such that $\lambda_1^{\epsilon_1}(\overline{M})<0$. Due to $M(0,\cdot)\neq 0$ and (2.2), $M(t,\cdot)\to\overline{M}(\cdot)$ uniformly on $\overline{\Omega}$ as $t\to\infty$. Therefore, there exists a $t_3>0$ such that $\overline{M}(x)-\epsilon_1<M(t,x)<\overline{M}(x)+\epsilon_1$ for $(t,x)\in(t_3,\infty)\times\overline{\Omega}$. Then

$$\begin{cases} \dfrac{\partial I_1}{\partial t} = D_h \Delta I_1 - \gamma_1(x) I_1 + c_1(x) H_u(x) I_{v1}, & (t,x) \in (t_3,\infty)\times\Omega, \\ \dfrac{\partial I_{v1}}{\partial t} \le D_v \Delta I_{v1} + \alpha_1(x)(\overline{M}(x)+\epsilon_1) I_1 - \mu(x)(\overline{M}(x)-\epsilon_1) I_{v1}, & (t,x)\in(t_3,\infty)\times\Omega, \\ \dfrac{\partial \mathcal{W}_{15}}{\partial n} = 0, & \mathcal{W}_{15} = I_1, I_{v1}, (t,x)\in(t_3,\infty)\times\partial\Omega. \end{cases}$$

Denote the positive eigenvector corresponding to $\lambda_1^{\epsilon_1}(\overline{M})$ by $\overline{\psi} = (\psi_1^{\epsilon_1}, \psi_2^{\epsilon_1})$. By the continuity of $\lambda_1^{\epsilon_1}(\overline{M})$, we have $\lim_{\epsilon_1\to 0}\lambda_1^{\epsilon_1}(\overline{M}) = \lambda_1^*(\overline{M}) < 0$ when $\Re_0^1 < 1$. Moreover, let $\xi_1 > 0$ such that $(I_1^0, I_{v1}^0) \le \xi_1(\psi_1^{\epsilon_1}, \psi_2^{\epsilon_1})$. Then $\xi_1 e^{\lambda_1^{\epsilon_1}(t-t_3)}\overline{\psi}$ is the solution of

$$\begin{cases} \dfrac{\partial I_1}{\partial t} = D_h \Delta I_1 - \gamma_1(x) I_1 + c_1(x) H_u(x) I_{v1}, & (t,x) \in (t_3,\infty)\times\Omega, \\ \dfrac{\partial I_{v1}}{\partial t} = D_v \Delta I_{v1} + \alpha_1(x)(\overline{M}(x)+\epsilon_1) I_1 - \mu(x)(\overline{M}(x)-\epsilon_1) I_{v1}, & (t,x)\in(t_3,\infty)\times\Omega, \\ \dfrac{\partial \mathcal{W}_{15}}{\partial n} = 0, & \mathcal{W}_{15} = I_1, I_{v1}, (t,x)\in(t_3,\infty)\times\partial\Omega. \end{cases}$$

According to the comparison principle, we get

$$(I_1, I_{v1}) \le \xi_1 e^{\lambda_1^{\epsilon_1}(t-t_3)}(\psi_1^{\epsilon_1}, \psi_2^{\epsilon_1}) \quad \text{for } (t,x)\in(t_3,\infty)\times\overline{\Omega}.$$

Hence

$$\lim_{t\to\infty} I_1(t,x) = 0 \text{ and } \lim_{t\to\infty} I_{v1}(t,x) = 0 \quad \text{for } x\in\overline{\Omega}.$$

Similarly, when $\Re_0^2 < 1$, we can obtain

$$\lim_{t\to\infty} I_2(t,x) = 0 \text{ and } \lim_{t\to\infty} I_{v2}(t,x) = 0 \quad \text{for } x\in\overline{\Omega}.$$

These together with (2.2) imply that $S_v(t,x)\to\overline{M}(x)$ for all $x\in\overline{\Omega}$ as $t\to\infty$. Thus the proof is completed. □

5.2. Uniform persistence

We first give a result on non-coexistence, that is, under suitable conditions, one strain can be uniformly persistent while the other one vanishes.

Theorem 5.3. *Assume that, for $i, j = 1, 2$ with $i \ne j$, we have $\Re_0^i > 1 > \Re_0^j$. Then there exists $\varsigma_i > 0$ such that*

$$\lim\nolimits_{t\to\infty} I_j(t,x,\phi_0) = 0,\ \lim\nolimits_{t\to\infty} I_{vj}(t,x,\phi_0) = 0$$

and

$$\liminf_{t\to\infty}\ I_i(t,x,\phi_0) \ge \varsigma_i,\ \liminf_{t\to\infty} I_{vi}(t,x,\phi_0) \ge \varsigma_i$$

for $x\in\overline{\Omega}$, where $u(t,\cdot,\phi_0) = (I_1(t,\cdot,\phi_0), I_2(t,\cdot,\phi_0), S_v I_2(t,\cdot,\phi_0), I_{v1} I_2(t,\cdot,\phi_0), I_{v2} I_2(t,\cdot,\phi_0))$ is any solution of (2.4) through ϕ_0 with $I_i^0(x) + I_{vi}^0(x) > 0$ and $S_v^0(x) + I_{vi}^0(x) > 0$ for $x\in\overline{\Omega}$.

Proof. By virtue of $\Re_0^j < 1$ and (i) of Lemma 5.1, we know that

$$\lim\nolimits_{t\to\infty} I_j(t,\cdot,\phi_0) = 0 \text{ and } \lim\nolimits_{t\to\infty} I_{vj}(t,\cdot,\phi) = 0.$$

Arguing similarly as for [20, Lemma 3.11], we see that there exists $\varsigma_i > 0$ such that $\liminf_{t\to\infty} I_i(t,\cdot,\phi_0) \ge \varsigma_i$ and $\liminf_{t\to\infty} I_{vi}(t,\cdot,\phi_0) \ge \varsigma_i$. □

We now investigate the stability of E_∂^i $(i = 1, 2)$ of (2.4) in terms of IRN $\widehat{\Re}_0^i$ $(i = 1, 2)$. Firstly, we linearize (2.4) around E_∂^2 and consider the associated eigenvalue problem,

$$
\begin{cases}
\lambda\psi_1 = D_h\Delta\psi_1 - \gamma_1(x)\psi_1 + c_1(x)H_u(x)\psi_3, & x\in\Omega,\\
\lambda\psi_2 = D_h\Delta\psi_2 - \gamma_2(x)\psi_2 + c_2(x)H_u(x)\psi_4, & x\in\Omega,\\
\lambda\psi_5 = D_v\Delta\psi_5 - \alpha_1(x)\widetilde{S}_v(x)\psi_1 - \alpha_2(x)\widetilde{S}_v(x)\psi_2 - \alpha_2(x)\widetilde{I}_2(x)\psi_5 & \\
+\beta(x)(\psi_5+\psi_3+\psi_4) - \mu(x)(2\widetilde{S}_v(x)+\widetilde{I}_{v2}(x))\psi_5 - \mu(x)\widetilde{S}_v(x)(\psi_3+\psi_4), & \\
 & x\in\Omega,\\
\lambda\psi_3 = D_v\Delta\psi_3 - \mu(x)(\widetilde{S}_v(x)+\widetilde{I}_{v2}(x))\psi_3 + \alpha_1(x)\widetilde{S}_v(x)\psi_1, & x\in\Omega,\\
\lambda\psi_4 = D_v\Delta\psi_4 + \alpha_2(x)\widetilde{S}_v(x)\psi_2 + \alpha_2(x)\widetilde{I}_2(x)\psi_5 & \\
-\mu(x)\widetilde{I}_{v2}(x)(\psi_5+\psi_3+2\psi_4) - \mu(x)\widetilde{S}_v(x)\psi_4, & \\
 & x\in\Omega,\\
\dfrac{\partial\mathcal{W}_{16}}{\partial n} = 0,\ \mathcal{W}_{16} = \psi_1,\psi_2,\psi_5,\psi_3,\psi_4, & x\in\partial\Omega.
\end{cases}
\tag{5.4}
$$

Note that the first and second equations of (5.4) are decoupled from the others. Let λ be an eigenvalue of (5.4). Then it satisfies

$$
\begin{cases}
\lambda\psi_1 = D_h\Delta\psi_1 - \gamma_1(x)\psi_1 + c_1(x)H_u(x)\psi_3, & x\in\Omega,\\
\lambda\psi_3 = D_v\Delta\psi_3 - \mu(x)(\widetilde{S}_v(x)+\widetilde{I}_{v2}(x))\psi_3 + \alpha_1(x)\widetilde{S}_v(x)\psi_1, & x\in\Omega,\\
\dfrac{\partial\mathcal{W}_{17}}{\partial n} = 0,\ \mathcal{W}_{17} = \psi_1,\psi_3, & x\in\partial\Omega,
\end{cases}
\tag{5.5}
$$

or

$$
\begin{cases}
\lambda\psi_2 = D_h\Delta\psi_2 - \gamma_2(x)\psi_2 + c_2(x)H_u(x)\psi_4, & x\in\Omega,\\
\lambda\psi_5 = D_v\Delta\psi_5 - \alpha_2(x)\widetilde{S}_v(x)\psi_2 - \alpha_2(x)\widetilde{I}_2(x)\psi_5 & \\
+\beta(x)(\psi_5+\psi_4) - \mu(x)(2\widetilde{S}_v(x)+\widetilde{I}_{v2}(x))\psi_5 - \mu(x)\widetilde{S}_v(x)\psi_4, & \\
 & x\in\Omega,\\
\lambda\psi_4 = D_v\Delta\psi_4 + \alpha_2(x)\widetilde{S}_v(x)\psi_2 + \alpha_2(x)\widetilde{I}_2(x)\psi_5 & \\
-\mu(x)\widetilde{I}_{v2}(x)(\psi_5+2\psi_4) - \mu(x)\widetilde{S}_v(x)\psi_4, & \\
 & x\in\Omega,\\
\dfrac{\partial\mathcal{W}_{18}}{\partial n} = 0,\ \mathcal{W}_{18} = \psi_2,\psi_5,\psi_4, & x\in\partial\Omega.
\end{cases}
\tag{5.6}
$$

Due to the stability of the associated E_E^2 [20, Theorem 3.12], we know that the principal eigenvalue of (5.6) is negative. Furthermore, problem (5.5) is cooperative, which implies that (5.5) admits a principal eigenvalue $\widehat{\lambda}_1$ with a positive eigenvector $(\overline{\psi}_1(x),\overline{\psi}_3(x))$ according to (Lam & Lou, 2016). We conclude from this and (i) of Lemma 4.6 that $\widehat{\lambda}_1<0$ if $\widehat{\Re}_0^1<1$ while $\widehat{\lambda}_1>0$ if $\widehat{\Re}_0^1>1$. Similarly, by (ii) of Lemma 4.6, we know that $\widehat{\lambda}_2<0$ if $\widehat{\Re}_0^2<1$ while $\widehat{\lambda}_2>0$ if $\widehat{\Re}_0^2>1$. Hence we immediately have the following result.

Lemma 5.4. *Let $\Re_0^1$, $\Re_0^2$, $\widehat{\Re}_0^1$, and $\widehat{\Re}_0^2$ be defined by (4.17), (4.19), (4.27), and (4.29), respectively.*

(i) If $\Re_0^2>1$, then E_∂^2 is locally asymptotically stable when $\widehat{\Re}_0^1<1$ while it is unstable when $\widehat{\Re}_0^1>1$.
(ii) If $\Re_0^1>1$, then E_∂^1 is locally asymptotically stable when $\widehat{\Re}_0^2<1$ while it is unstable when $\widehat{\Re}_0^2>1$.

We next confirm that E_0, E_1, E_∂^1, and E_∂^2 are uniform weak repellers with respect to solutions of (2.4) under the condition that $\Re_0^1>1$ and $\Re_0^2>1$. Recall that $\Phi(t):\mathbb{X}_H\to\mathbb{X}_H$ is the continuous solution semiflow of (2.4). We define

$$\mathbb{X}_{H0} := \{\phi\in\mathbb{X}_H : \phi_1(t,\cdot)+\phi_4(t,\cdot)>0 \text{ and } \phi_2(t,\cdot)+\phi_5(t,\cdot)>0 \text{ and } M_1(t,\cdot)>0\}$$

and

$$\partial\mathbb{X}_{H0} := \{\phi \in \mathbb{X}_H : \phi_1(t,\cdot) + \phi_4(t,\cdot) = 0 \text{ or } \phi_2(t,\cdot) + \phi_5(t,\cdot) = 0 \text{ or } M_1(t,\cdot) = 0\}.$$

Then $\mathbb{X}_H = \mathbb{X}_{H0} \cup \partial\mathbb{X}_{H0}$ and the boundary $\partial\mathbb{X}_{H0} = \mathbb{X}_H - \mathbb{X}_{H0}$ is closed in $\mathbb{X}_H$.

Lemma 5.5. *Suppose that* $\mathfrak{R}_0^1 > 1$, $\mathfrak{R}_0^2 > 1$, $\widehat{\mathfrak{R}}_0^1 > 1$, *and* $\widehat{\mathfrak{R}}_0^2 > 1$. *Then* E_1, E_0, E_∂^1, *and* E_∂^2 *are uniform weak repellers for* $\Phi(t)$, *that is, for* $U \in \{E_1, E_0, E_\partial^1, E_\partial^2\}$, *there is* $\delta > 0$ (*may depend on* U) *such that*

$$\limsup_{t\to\infty} \|\Phi(t)\phi_0 - U\|_{\mathbb{X}} \geq \delta \qquad \text{for } \phi_0 \in \mathbb{X}_{H0}. \tag{5.7}$$

Proof. We first prove the result for the case where $U = E_1$. Assume, for the contrary, that for any $\varepsilon_2 > 0$ there exists a solution of (2.4) such that

$$\limsup_{t\to\infty} \|\Phi(t)\phi_0 - E_1\|_{\mathbb{X}} < \varepsilon_2. \tag{5.8}$$

Then for some $t_4 > 0$ we have

$$\overline{M}(x) - \varepsilon_2 < S_v < \overline{M}(x) + \varepsilon_2 \text{ and } 0 < I_1,\ I_2,\ I_{v1}, I_{v2} < \varepsilon_2 \qquad \text{for } (t,x) \in (t_4,\infty) \times \overline{\Omega}.$$

Due to

$$\begin{cases} \dfrac{\partial I_1}{\partial t} = D_h \Delta I_1 - \gamma_1(x) I_1 + c_1(x) H_u(x) I_{v1}, & (t,x) \in (t_4,\infty) \times \Omega, \\ \dfrac{\partial I_{v1}}{\partial t} \geq D_v \Delta I_{v1} + \alpha_1(x)(\overline{M}(x) - \varepsilon_2) I_1 - \mu(x)(\overline{M}(x) + 3\varepsilon_2) I_{v1}, & (t,x) \in (t_4,\infty) \times \Omega, \\ \dfrac{\partial \mathcal{W}_{19}}{\partial n} = 0, & \mathcal{W}_{19} = I_1, I_{v1}, (t,x) \in (t_4,\infty) \times \partial\Omega, \end{cases}$$

when $\mathfrak{R}_0^1 > 1$, Lemma 4.2 implies that $\lambda_1^*(\overline{M}) > 0$, where $\lambda_1^*(\overline{M})$ is the principal eigenvalue of (4.5). Form Lemma 3.4, one has $I_1(t_4, x) > 0$ and $I_{v1}(t_4, x) > 0$ for all $x \in \overline{\Omega}$. In view of $\lim_{\varepsilon_2 \to 0} \widetilde{\lambda}_1^{\varepsilon_2} = \lambda_1^*(\overline{M}) > 0$, there exists $\varepsilon_2 > 0$ such that the principal eigenvalue $\widetilde{\lambda}_1^{\varepsilon_2} > 0$ and it has a positive eigenfunction $\overline{\varphi}^{\varepsilon_2} = (\varphi_1^{\varepsilon_2}, \varphi_2^{\varepsilon_2})$. Choose $C_{E_1} > 0$ small enough such that $(I_1(t_4,x),\ I_{v1}(t_4,x)) \geq C_{E_1}(\varphi_1^{\varepsilon_2},\ \varphi_2^{\varepsilon_2})$ for all $x \in \overline{\Omega}$. Obviously, $C_{E_1} e^{\widetilde{\lambda}_1^{\varepsilon_2}(t-t_4)} \overline{\varphi}^{\varepsilon_2}$ is a solution of

$$\begin{cases} \dfrac{\partial I_1}{\partial t} = D_h \Delta I_1 - \gamma_1(x) I_1 + c_1(x) H_u(x) I_{v1}, & (t,x) \in (t_4,\infty) \times \Omega, \\ \dfrac{\partial I_{v1}}{\partial t} = D_v \Delta I_{v1} + \alpha_1(x)(\overline{M}(x) - \varepsilon_2) I_1 - \mu(x)(\overline{M}(x) + 3\varepsilon_2) I_{v1}, & (t,x) \in (t_4,\infty) \times \Omega, \\ \dfrac{\partial \mathcal{W}_{19}}{\partial n} = 0, & \mathcal{W}_{19} = I_1, I_{v1}, (t,x) \in (t_4,\infty) \times \partial\Omega. \end{cases}$$

It follows from the comparison principle that

$$(I_1, I_{v1}) \geq C_{E_1} e^{\widetilde{\lambda}_1^{\varepsilon_2}(t-t_4)} (\varphi_1^{\varepsilon_2}, \varphi_2^{\varepsilon_2}) \qquad \text{for } (t,x) \in (t_4,\infty) \times \overline{\Omega}.$$

Since $\widetilde{\lambda}_1^{\varepsilon_2} > 0$ when $\mathfrak{R}_0^1 > 1$, this implies that

$$\lim_{t\to\infty} I_1(t,x) = \infty,\ \lim_{t\to\infty} I_{v1}(t,x) = \infty \text{ uniformly for } x \in \overline{\Omega}. \tag{5.9}$$

Similarly, if $\mathfrak{R}_0^2 > 1$, then

$$\lim_{t\to\infty} I_2(t,x) = \infty,\ \lim_{t\to\infty} I_{v2}(t,x) = \infty \text{ uniformly for } x \in \overline{\Omega}. \tag{5.10}$$

These results contradict with the boundedness of $(I_1, I_2, I_{v1}, I_{v2})$. This proves the result in the case where $U = E_1$.

Secondly, we prove the result in the case where $U = E_0$. If (5.7) does not hold, then for any $\epsilon_3 > 0$ there is a solution of (2.4) satisfies

$$\limsup_{t\to\infty}\|\Phi(t)\phi_0 - E_0\|_{\mathbb{X}} < \epsilon_3 \tag{5.11}$$

and hence there is $t_5 > 0$ such that

$$S_v(t,\cdot),\ I_{v1}(t,\cdot),\ I_{v2}(t,\cdot) < \epsilon_3 \qquad \text{for } (t,x)\in(t_5,\infty)\times\overline{\Omega}.$$

However, from (2.2), we have $M(t,x)\to\overline{M}(x)$ uniformly on $\overline{\Omega}$ as $t\to\infty$, a contradiction. This proves the result in the case where $U = E_0$.

Thirdly, we consider the case where $U = E^1_\partial$. Since $\widehat{\Re}^2_0 > 1$, we know that $\widehat{\lambda}_2 > 0$ by Lemma 4.6. Due to the continuity of $\widehat{\lambda}_2$, we can find a small enough ϵ_4 such that $\widehat{\lambda}^{\epsilon_4}_2 > 0$. We show that (5.7) holds with $\delta = \epsilon_4$ by contradictory arguments. Otherwise, there is a solution of (2.4) satisfying

$$\limsup_{t\to\infty}\|\Phi(t)\phi_0 - E^1_\partial\|_{\mathbb{X}} < \epsilon_4. \tag{5.12}$$

It follows that, for some $t_6 > 0$,

$$I^*_1(x) - \epsilon_4 < I_1(t,x) < I^*_1(x) + \epsilon_4,\ 0 < I_2(t,x) < \epsilon_4,\ S^*_v(x) - \epsilon_4 < S_v(t,x) < S^*_v(x) + \epsilon_4,$$

$$I^*_{v1}(x) - \epsilon_4 < I_{v1}(t,x) < I^*_{v1}(x) + \epsilon_4 \text{ and } 0 < I_{v2}(t,x) < \epsilon_4 \qquad \text{for } (t,x)\in(t_6,\infty)\times\overline{\Omega},$$

which lead to

$$\begin{cases} \dfrac{\partial I_2}{\partial t} = D_h\Delta I_2 - \gamma_2(x)I_2 + c_2(x)H_u(x)I_{v2}, & (t,x)\in(t_6,\infty)\times\Omega,\\ \dfrac{\partial I_{v2}}{\partial t} \ge D_v\Delta I_{v2} + \alpha_2(x)(S^*_v(x) - \epsilon_4)I_2 - \mu(x)(S^*_v(x) + I^*_{v1}(x) + 3\epsilon_4)I_{v2}, & (t,x)\in(t_6,\infty)\times\Omega,\\ \dfrac{\partial \mathcal{W}_{20}}{\partial n} = 0,\ \mathcal{W}_{20}(t,x) = I_2, I_{v2}, & (t,x)\in(t_6,\infty)\times\partial\Omega. \end{cases}$$

Denote by $\widehat{\varphi}^{\epsilon_4} = (\varphi^{\epsilon_4}_1, \varphi^{\epsilon_4}_2)$ the eigenfunction corresponding to $\widehat{\lambda}^{\epsilon_4}_2$. Choose $C_{E^1_\partial} > 0$ small enough such that

$$(I_2(t_6,x),\ I_{v2}(t_6,x)) \ge C_{E^1_\partial}(\varphi^{\epsilon_4}_1, \varphi^{\epsilon_4}_2).$$

By the comparison principle, we have

$$(I_2,\ I_{v2}) \ge C_{E^1_\partial}(\varphi^{\epsilon_4}_1, \varphi^{\epsilon_4}_2)e^{\widehat{\lambda}^{\epsilon_4}_2(t-t_6)} \qquad \text{for } t > t_6.$$

Clearly,

$$\lim_{t\to\infty}(I_2, I_{v2}) = (\infty,\infty),$$

which contradicts with the boundedness of (I_2, I_{v2}). Thus the result holds in the case where $U = E^1_\partial$. Similarly, we can show that the result holds in the case where $U = E^1_\partial$.

This completes the proof. □

With the above preparation, we are ready to show the persistence.

Theorem 5.6. *Suppose that $\Re^1_0 > 1$, $\Re^2_0 > 1$, $\widehat{\Re}^1_0 > 1$, and $\widehat{\Re}^2_0 > 1$. Then there is a $\delta^* > 0$ such that, for any $\phi_0\in\mathbb{X}_{H0}$,*

$$\liminf_{t\to\infty}\mathcal{W}(t,x) \ge \delta^*, \tag{5.13}$$

where $\mathcal{W} = I_1, I_2, S_v, I_{v1}, I_{v2}$. Furthermore, system (2.4) has at least one PSS in $\mathbb{X}_{H0}$.

Proof. We complete the proof in the following four steps.

Step 1. For $\phi_0\in\mathbb{X}_{H0}$, show $\Phi(t)\phi_0\in\mathbb{X}_{H0}$ for $t > 0$, that is, $\mathbb{X}_{H0}$ is invariant under $\Phi(t)$.

The proof has been given in the proof of Lemma 3.4.

Step 2. For any $\phi_0 \in \partial\mathbb{X}_{H0}$, prove that $\Phi(t)\phi_0 \in \partial\mathbb{X}_{H0}$ for $t \geq 0$ (that is, $\partial\mathbb{X}_{H0}$ is invariant under $\Phi(t)$) and $\omega(\phi_0)$ is either $\{E_1\}$ or $\{E_\partial^1\}$ or $\{E_\partial^2\}$ or $\{E_0\}$, where $\omega(\phi_0)$ is the ω-limit set of ϕ_0.

If $\phi_0 \in \partial\mathbb{X}_{H0}$, then $I_1^0 + I_{v1}^0 = 0$ or $I_2^0(x) + I_{v2}^0 = 0$ or $S_v^0 + I_{v1}^0 + I_{v2}^0 = 0$. We distinguish four cases to finish the discussion for this step.

Case 1: $I_1^0 + I_{v1}^0 = 0$, $I_2^0 + I_{v2}^0 = 0$, and $S_v^0 \neq 0$. It then follows from the equations on I_1, I_2, I_{v1}, I_{v2} of (2.4) that

$$I_1(t,\cdot) = I_{v1}(t,\cdot) = I_2(t,\cdot) = I_{v2}(t,\cdot) = 0 \quad \text{for } t \geq 0,$$

which means that $\Phi(t)\phi_0 \in \partial\mathbb{X}_{H0}$ for $t \geq 0$. As the equation on S_v of (2.4) satisfies (2.1), we have from (2.2) that $S_v(t,x) \to \overline{M}(x)$ uniformly on $\overline{\Omega}$ as $t \to \infty$. This tells us that $\omega(\phi_0) = \{E_1\}$.

Case 2: $I_1^0 + I_{v1}^0 \neq 0$, $I_2^0 + I_{v2}^0 = 0$, and $S_v^0 \neq 0$. It then follows from the equations on I_2 and I_{v2} of (2.4) that $I_2(t,\cdot) = I_{v2}(t,\cdot) = 0$ for $t \geq 0$ and hence $\Phi(t)\phi_0 \in \partial\mathbb{X}_{H0}$ for $t \geq 0$. Note that either (i) $I_1^0 \neq 0$ and $I_{v1}^0 = 0$; or (ii) $I_1^0 = 0$ and $I_{v1}^0 \neq 0$; or(iii) $I_1^0 \neq 0$ and $I_{v1}^0 \neq 0$. In either case, due to the maximum principle, we have

$$I_1(t,x) > 0,\ I_{v1}(t,x) > 0 \text{ and } S_v(t,x) > 0 \qquad \text{for } (t,x) \in (0,\infty) \times \overline{\Omega}.$$

Then by Theorem 5.3, $\omega(\phi_0) = \{E_\partial^1\}$.

Case 3: $I_1^0 + I_{v1}^0 = 0$, $I_2^0 + I_{v2}^0 \neq 0$, and $S_v^0 \neq 0$. It then follows from the equations of I_1 and I_{v1} of (2.4) that $I_1(t,\cdot) = I_{v1}(t,\cdot) = 0$ for all $t \geq 0$, which also implies that $\Phi(t)\phi_0 \in \partial\mathbb{X}_{H0}$ for $t \geq 0$. Similar arguments as those in case 2 yield $\omega(\phi_0) = \{E_\partial^2\}$.
Case 4: $S_v^0 + I_{v1}^0 + I_{v2}^0 = 0$. It then follows from the equations on S_v, I_{v1}, and I_{v2} of (2.4) that $S_v(t,\cdot) = I_{v1}(t,\cdot) = I_{v2}(t,\cdot) = 0$ for all $t \geq 0$ and hence $\Phi(t)\phi_0 \in \partial\mathbb{X}_{H0}$ for $t \geq 0$. Then the equation on I_1 of (2.4) becomes

$$\frac{\partial I_1}{\partial t} = D_h \Delta I_1 - \gamma_1(x) I_1 \quad \text{with } \frac{\partial I_1}{\partial n} = 0,$$

which implies that $I_1(t,\cdot) \to 0$ uniformly on $\overline{\Omega}$ as $t \to \infty$. Similarly, we have $I_2(t,\cdot) \to 0$ uniformly on Ω as $t \to \infty$. As a result, $\omega(\phi_0) = \{E_0\}$.

Denote by Φ_∂ the restriction of $\Phi(t)$ on $\partial\mathbb{X}_{H0}$. Result in Step 2 implies that Φ_∂ has a global compact attractor B_∂ and

$$\widetilde{B}_\partial := \cup_{\phi_0 \in B_\partial} \omega(\phi_0) = \{E_0,\ E_1,\ E_\partial^1,\ E_\partial^2\}.$$

Step 3. Show that $\widetilde{B}_\partial$ has an acyclic covering $\mathbb{Q} = \{E_1\} \cup \{E_\partial^1\} \cup \{E_\partial^2\} \cup \{E_0\}$.

It is suffices to show that

$$\{E_\partial^1\} \nrightarrow \{E_1\},\ \{E_\partial^2\} \nrightarrow \{E_1\},\ \{E_0\} \nrightarrow \{E_1\},$$

$$\{E_\partial^1\} \nrightarrow \{E_0\},\ \{E_\partial^2\} \nrightarrow \{E_0\} \text{ and } \{E_\partial^1\} \nrightarrow \{E_\partial^2\},$$

i.e.,

$$\begin{aligned} &W^u(E_\partial^1) \cap W^s(E_1) = \emptyset,\ W^u(E_\partial^2) \cap W^s(E_1) = \emptyset,\ W^u(E_0) \cap W^s(E_1) = \emptyset, \\ &W^u(E_\partial^1) \cap W^s(E_0) = \emptyset,\ W^u(E_\partial^2) \cap W^s(E_0) = \emptyset \text{ and } W^u(E_\partial^1) \cap W^s(E_\partial^2) = \emptyset, \end{aligned}$$

where $W^u(\varkappa)$ and $W^s(\varkappa)$ are the unstable and stable manifold of $\varkappa$, respectively. In what follows, we only verify $W^u(E_\partial^1) \cap W^s(E_1) = \emptyset$ as the others can be dealt with similarity.

For any $\phi_0 \in W^s(E_1)$, denote by $(I_1, I_2, S_v, I_{v1}, I_{v2})$ the complete orbit of ϕ_0. It follows that $I_1^0(\cdot) = I_{v1}^0(\cdot) = 0$ and further $I_1(t,\cdot) = I_{v1}(t,\cdot) = 0$ for $t \in (-\infty, \infty)$. Therefore, $I_1 \not\to I_1^*(x)$ and $I_{v1} \not\to I_{v1}^*(x)$ as $t \to -\infty$, a contradiction with $\phi_0 \in W^u(E_\partial^1)$. Consequently, there exists an acyclic covering $\mathbb{Q}$ for $\widetilde{B}_\partial$.

Step 4. Prove that $W^s(E_1) \cap \mathbb{X}_{H0} = \emptyset$, $W^s(E_\partial^1) \cap \mathbb{X}_{H0} = \emptyset$, $W^s(E_\partial^2) \cap \mathbb{X}_{H0} = \emptyset$, and $W^s(E_0) \cap \mathbb{X}_{H0} = \emptyset$.

Set

$$M_\partial := \{\phi_0 \in \partial\mathbb{X}_{H0} : \Phi(t)\phi_0 \in \partial\mathbb{X}_{H0} \text{ for } t > 0\}.$$

Clearly, in M_∂, there are only four steady states E_1, E_∂^1, E_∂^2 and E_0. By Lemma 5.5, they are isolated invariants of $\Phi(t)$ in $\mathbb{X}_{H0}$. The result follows immediately.

With the help of [43, Theorem 1.3.1 and Remark 1.3.1], $\Phi(t)$ is uniformly persistent in regard to $(\mathbb{X}_{H0}, \partial\mathbb{X}_{H0})$. Further, $\Phi(t)$ is point dissipative (see Theorem 3.2). According to [22, Theorem 3.7 and Remark 3.10], $\Phi(t)$ has a global attractor $\widehat{A}$ in $\mathbb{X}_{H0}$. Furthermore, for $\phi_0 \in \widehat{A}$, we have

$$\phi_1(0,\cdot) > 0,\ \phi_2(0,\cdot) > 0,\ \phi_4(0,\cdot) > 0 \text{ and } \phi_5(0,\cdot) > 0.$$

By a similar argument as that in (Shi & Zhao, 2021), we define a continuous function $m(\cdot) : \mathbb{X}_{H0} \to \mathbb{R}_+$ by:

$$m(\phi_0) := \min\left\{\min_{x\in\overline{\Omega}}\phi_1(0,x),\ \min_{x\in\overline{\Omega}}\phi_2(0,x),\ \min_{x\in\overline{\Omega}}\phi_4(0,x),\ \min_{x\in\overline{\Omega}}\phi_5(0,x)\right\} \qquad \text{for } \phi_0 \in \mathbb{X}_{H0}.$$

Then $m(\cdot)$ is a generalized distance function for $\Phi(t)$ (Smith & Zhao, 2001). Therefore, with the help of Lemma 3.4 and [13, Theorem 4.1], (5.13) holds. Moreover, system (2.4) has at least one PSS in $\mathbb{X}_{H0}$ due to [22, Theorem 4.7]. □

5.3. The limiting problem

This subsection analyzes the limiting system associated with system (2.4). Note that $M(t,\cdot) \to \overline{M}(x)$ as $t \to \infty$ if $S_v^0 + I_{v1}^0 + I_{v2}^0 \neq 0$ (see (2.2)). Inspired by (Magal et al., 2018) and (Zhao, 2012), we consider the following limiting system:

$$\begin{cases} \dfrac{\partial I_1}{\partial t} = D_h\Delta I_1 - \gamma_1(x)I_1 + c_1(x)H_u(x)I_{v1}, \\ \dfrac{\partial I_2}{\partial t} = D_h\Delta I_2 - \gamma_2(x)I_2 + c_2(x)H_u(x)I_{v2}, \\ \dfrac{\partial I_{v1}}{\partial t} = D_v\Delta I_{v1} + \alpha_1(x)\Theta(t,x)I_1 - \mu(x)\overline{M}(x)I_{v1}, \\ \dfrac{\partial I_{v2}}{\partial t} = D_v\Delta I_{v2} + \alpha_2(x)\Theta(t,x)I_2 - \mu(x)\overline{M}(x)I_{v2} \end{cases} \tag{5.14}$$

for $(t,x) \in (0,\infty) \times \Omega$, associated with

$$\begin{cases} \dfrac{\partial \mathcal{W}_{21}}{\partial n} = 0,\ \mathcal{W}_{21} = I_1, I_2, I_{v1}, I_{v2},\ (t,x) \in (0,\infty) \times \partial\Omega, \\ (I_1(0,x), I_2(0,x), I_{v1}(0,x), I_{v2}(0,x)) = \widetilde{\phi} = (I_1^0, I_2^0, I_{v1}^0, I_{v2}^0),\ x \in \Omega, \end{cases} \tag{5.15}$$

where $\Theta(t,x) = (\overline{M}(x) - I_{v1} - I_{v2})^+ = \max\{\overline{M}(x) - I_{v1} - I_{v2}, 0\}$. The steady states of (5.14)-(5.15) satisfies

$$\begin{cases} -D_h\Delta I_1(x) = -\gamma_1(x)I_1(x) + c_1(x)H_u(x)I_{v1}(x), & x\in\Omega, \\ -D_h\Delta I_2(x) = -\gamma_2(x)I_2(x) + c_2(x)H_u(x)I_{v2}(x), & x\in\Omega, \\ -D_v\Delta I_{v1}(x) = \alpha_1(x)\widetilde{\Theta}(x)I_1(x) - \mu(x)\overline{M}(x)I_{v1}(x), & x\in\Omega, \\ -D_v\Delta I_{v2}(x) = \alpha_2(x)\widetilde{\Theta}(x)I_2(x) - \mu(x)\overline{M}(x)I_{v2}(x), & x\in\Omega, \\ \dfrac{\partial \mathcal{W}_{22}(x)}{\partial n} = 0,\ \mathcal{W}_{22}(x) = I_1(x), I_2(x), I_{v1}(x), I_{v2}(x), & x\in\partial\Omega, \end{cases} \tag{5.16}$$

where $\widetilde{\Theta}(x) = (\overline{M}(x) - I_{v1}(x) - I_{v2}(x))^+ = \max\{\overline{M}(x) - I_{v1}(x) - I_{v2}(x), 0\}$. We define

$$\overline{\mathbb{H}} := \{\widetilde{\phi} \in C(\overline{\Omega}, \mathbb{R}^4_+) : I_1^0(x) + I_{v1}^0(x) \neq 0,\ I_2^0(x) + I_{v2}^0(x) \neq 0\}. \tag{5.17}$$

In what follows, we prove that the PSS of (5.14) is globally attractive in $\overline{\mathbb{H}}$ whenever it exists. Before going into details, we utilize the theory developed by (Amann, 1976) and (Zhao, 2017) to confirm that the PSS of (5.14) is unique if it exists.

Lemma 5.7. *If $\mathring{U}(x) = (\mathring{I}_1(x),\ \mathring{I}_2(x),\ \mathring{I}_{v1}(x),\ \mathring{I}_{v2}(x))$ is a nontrivial nonnegative steady state of (5.14)-(5.15) with $\mathring{I}_i(x) + \mathring{I}_{vi}(x) \neq 0$, $i = 1, 2$, then*

(i) $\mathring{I}_1(x),\ \mathring{I}_2(x),\ \mathring{I}_{v1}(x),\ \mathring{I}_{v2}(x) > 0$ *for all* $x\in\overline{\Omega}$;
(ii) $\mathring{I}_{v1}(x_0) + \mathring{I}_{v2}(x_0) < \overline{M}(x_0)$ *for some* $x_0\in\overline{\Omega}$.

Proof. We first prove (i). From the equations on I_1 and I_2 of (5.16), one has

$$(\gamma_i(x) - D_h\Delta)\mathring{I}_i(x) = c_i(x)H_u(x)\mathring{I}_{vi}(x) \quad \text{for } i = 1, 2.$$

Since $\mathring{U}(x)$ is nontrivial and $\mathring{I}_i(x) + \mathring{I}_{vi}(x) \neq 0$, we know that $\mathring{I}_i(x) \neq 0$ and $\mathring{I}_{vi}(x) \neq 0$ for $i = 1, 2$. An application of the maximum principle gives

$$\mathring{I}_1(x),\ \mathring{I}_2(x),\ \mathring{I}_{v1}(x),\ \mathring{I}_{v2}(x) > 0 \qquad \text{for } x\in\overline{\Omega}.$$

We next prove (ii). If $\mathring{I}_{v1}(x) + \mathring{I}_{v2}(x) \geq \overline{M}(x)$ for all $x\in\overline{\Omega}$, then from the equations on I_{v1} and I_{v2} of (5.16) we obtain that

$$-D_v\Delta\mathring{I}_{vi}(x) = \alpha_i(x)\widetilde{\Theta}(x)\mathring{I}_i(x) - \mu(x)\overline{M}(x)\mathring{I}_{vi}(x) = -\mu(x)\overline{M}(x)\mathring{I}_{vi}(x)$$

for $x\in\overline{\Omega}$, $i = 1, 2$. This implies that $\mathring{I}_{vi}(x) = 0$, $i = 1, 2$, which is a contradiction. □

Lemma 5.7 tells us that every nontrivial nonnegative steady state $\mathring{U}(x)$ is strictly positive if it exists and $\mathring{I}_i(x) + \mathring{I}_{vi}(x) \neq 0$, $i = 1, 2$. With this in mind, for any $\mathcal{C}_1 > 0$, we define

$$\mathbb{S} = \Big\{(\mathring{I}_{v1}(x),\ \mathring{I}_{v2}(x))^T \in C(\overline{\Omega}; \mathbb{R}^2_+) : \big\|\mathring{I}_{v1}(x) + \mathring{I}_{v2}(x)\big\|_\infty \leq \mathcal{C}_1 \text{ and } \mathring{I}_{v1}(x_0) + \mathring{I}_{v2}(x_0) < \overline{M}(x_0) \text{ for some } x_0\in\overline{\Omega}\Big\}. \tag{5.18}$$

Further, for $\mathcal{C}_2 > 0$ and $\mathcal{C}_3 > 0$, we define $\widehat{\mathcal{F}} : \mathbb{S}\subset C(\overline{\Omega}) \to C(\overline{\Omega})$ by

$$\widehat{\mathcal{F}}((\mathring{I}_{v1}(x),\ \mathring{I}_{v2}(x))^T) = \begin{pmatrix} (\mathcal{C}_2 - D_v\Delta)^{-1}[\alpha_1(x)\widetilde{\Theta}(x)(\gamma_1(x) - D_h\Delta)^{-1}c_1(x)H_u(x)\mathring{I}_{v1}(x) + (\mathcal{C}_2 - \mu(x)\overline{M}(x))\mathring{I}_{v1}(x)] \\ (\mathcal{C}_3 - D_v\Delta)^{-1}[\alpha_2(x)\widetilde{\Theta}(x)(\gamma_2(x) - D_h\Delta)^{-1}c_2(x)H_u(x)\mathring{I}_{v2}(x) + (\mathcal{C}_3 - \mu(x)\overline{M}(x))\mathring{I}_{v2}(x)] \end{pmatrix}$$

for $(\mathring{I}_{v1}(x),\ \mathring{I}_{v2}(x))^T \in \mathbb{S}$.

Lemma 5.8. *Suppose that $\mathring{I}_i(x) + \mathring{I}_{vi}(x) \neq 0$, $i = 1, 2$. Let $\mathring{U}(x)$ be a PSS of (5.16). Then there is $\mathcal{C}_1^* > 0$ such that for all $\mathcal{C}_1 > \mathcal{C}_1^*$, $\mathcal{C}_2 > 0$, and $\mathcal{C}_3 > 0$, $(\mathring{I}_{v1}(x), \mathring{I}_{v2}(x))^T$ is a nontrivial fixed point (NFP) of $\widehat{\mathcal{F}}$.*

Proof. The equations on $\mathring{I}_1$ and $\mathring{I}_2$ of (5.16) give

$$\mathring{I}_1(x) = (\gamma_1(x) - D_h\Delta)^{-1}c_1(x)H_u(x)\mathring{I}_{v1}(x)$$

and

$$\mathring{I}_2(x) = (\gamma_2(x) - D_h\Delta)^{-1}c_2(x)H_u(x)\mathring{I}_{v2}(x),$$

respectively. Combining them with the equations on $\mathring{I}_{v1}$ and $\mathring{I}_{v2}$ of (5.16) gives

$$\begin{pmatrix} -D_v\Delta\mathring{I}_{v1}(x) \\ -D_v\Delta\mathring{I}_{v2}(x) \end{pmatrix} = \begin{pmatrix} \alpha_1(x)\widetilde{\Theta}(x)(\gamma_1(x) - D_h\Delta)^{-1}c_1(x)H_u(x)\mathring{I}_{v1}(x) - \mu(x)\overline{M}(x)\mathring{I}_{v1}(x) \\ \alpha_2(x)\widetilde{\Theta}(x)(\gamma_2(x) - D_h\Delta)^{-1}c_2(x)H_u(x)\mathring{I}_{v2}(x) - \mu(x)\overline{M}(x)\mathring{I}_{v2}(x) \end{pmatrix}.$$

By Lemma 5.7, $(\mathring{I}_{v1}(x), \mathring{I}_{v2}(x))^T$ is a NFP of $\widehat{\mathcal{F}}$ if $\mathcal{C}_1$ is large. □

Lemma 5.9. *For fixed $\mathcal{C}_1 > 0$, there exists $\mathcal{C}_2^* > 0$ such that $\widehat{\mathcal{F}}$ is monotone for all $\mathcal{C}_2$, $\mathcal{C}_3 > \mathcal{C}_2^*$, that is, for $(\mathring{I}^1_{v1}(x), \mathring{I}^1_{v2}(x))^T$, $(\mathring{I}^2_{v1}(x), \mathring{I}^2_{v2}(x))^T \in \mathbb{S}$ with $(\mathring{I}^1_{v1}(x), \mathring{I}^1_{v2}(x))^T \le (\mathring{I}^2_{v1}(x), \mathring{I}^2_{v2}(x))^T$, we have*

$$\widehat{\mathcal{F}}((\mathring{I}^1_{v1}(x), \mathring{I}^1_{v2}(x))^T) \le \widehat{\mathcal{F}}((\mathring{I}^2_{v1}(x), \mathring{I}^2_{v2}(x))^T).$$

Proof. Denote

$$\mathbb{S}_1 = \{(\widetilde{h}_1, \widetilde{h}_2)^T \in C(\overline{\Omega}; \mathbb{R}^2_+) : 0 \le \widetilde{h}_1, \widetilde{h}_2 \le \overline{M}(x) - \mathring{I}_{v1}(x) - \mathring{I}_{v2}(x)\}.$$

It suffices to show $\widehat{\mathcal{F}}((\mathring{I}_{v1}(x), \mathring{I}_{v2}(x))^T) \le \widehat{\mathcal{F}}((\mathring{I}_{v1}(x) + \widetilde{h}_1, \mathring{I}_{v2}(x) + \widetilde{h}_2)^T)$ for any $(\mathring{I}_{v1}(x), \mathring{I}_{v2}(x))^T \in \mathbb{S}$ and $(\widetilde{h}_1, \widetilde{h}_2)^T \in \mathbb{S}_1$. Define

$$[\widehat{\mathcal{F}}]((\mathring{I}_{v1}(x),\ \mathring{I}_{v2}(x))^T) = ([\widehat{\mathcal{F}}]_1, [\widehat{\mathcal{F}}]_2)^T$$

$$= \begin{pmatrix} \alpha_1(x)\widetilde{\Theta}(x)(\gamma_1(x) - D_h\Delta)^{-1}c_1(x)H_u(x)\mathring{I}_{v1}(x) + (\mathcal{C}_2 - \mu(x)\overline{M}(x))\mathring{I}_{v1}(x) \\ \alpha_2(x)\widetilde{\Theta}(x)(\gamma_2(x) - D_h\Delta)^{-1}c_2(x)H_u(x)\mathring{I}_{v2}(x) + (\mathcal{C}_3 - \mu(x)\overline{M}(x))\mathring{I}_{v2}(x) \end{pmatrix}.$$

A direct calculation gives

$$[\widehat{\mathcal{F}}]((\mathring{I}_{v1}(x) + \widetilde{h}_1, \mathring{I}_{v2}(x) + \widetilde{h}_2)^T) - [\widehat{\mathcal{F}}]((\mathring{I}_{v1}(x), \mathring{I}_{v2}(x))^T)$$
$$\ge$$
$$\begin{pmatrix} \alpha_1(x)(\widetilde{\Theta}_{\widetilde{h}_1}(x) - \widetilde{\Theta}(x))(\gamma_1(x) - D_h\Delta)^{-1}c_1(x)H_u(x)\mathring{I}_{v1}(x) + (\mathcal{C}_2 - \mu(x)\overline{M}(x))\widetilde{h}_1 \\ \alpha_2(x)(\widetilde{\Theta}_{\widetilde{h}_2}(x) - \widetilde{\Theta}(x))(\gamma_2(x) - D_h\Delta)^{-1}c_2(x)H_u(x)\mathring{I}_{v2}(x) + (\mathcal{C}_3 - \mu(x)\overline{M}(x))\widetilde{h}_2 \end{pmatrix}$$
$$\ge$$
$$\begin{pmatrix} \widetilde{h}_1[-\alpha_1(x)(\gamma_1(x) - D_h\Delta)^{-1}c_1(x)H_u(x)\mathring{I}_{v1}(x) + \mathcal{C}_2 - \mu(x)\overline{M}(x)] \\ \widetilde{h}_2[-\alpha_2(x)(\gamma_2(x) - D_h\Delta)^{-1}c_2(x)H_u(x)\mathring{I}_{v2}(x) + \mathcal{C}_3 - \mu(x)\overline{M}(x)] \end{pmatrix},$$

where $\widetilde{\Theta}_{\widetilde{h}_1}(x) = (\overline{M}(x) - \mathring{I}_{v1}(x) - \mathring{I}_{v2}(x) - \widetilde{h}_1)^+$ and $\widetilde{\Theta}_{\widetilde{h}_2}(x) = (\overline{M}(x) - \mathring{I}_{v1}(x) - \mathring{I}_{v2}(x) - \widetilde{h}_2)^+$. Here we have used the inequalities

$$|\widetilde{\Theta}_{\widetilde{h}_1}(x) - \widetilde{\Theta}(x)| \le \widetilde{h}_1 \text{ and } |\widetilde{\Theta}_{\widetilde{h}_2}(x) - \widetilde{\Theta}(x)| \le \widetilde{h}_2.$$

With the help of the elliptic estimate, we note that the following set

$$\left\{ \begin{pmatrix} (\gamma_1(x) - D_h\Delta)^{-1}c_1(x)H_u(x)\mathring{I}_{v1}(x) \\ (\gamma_2(x) - D_h\Delta)^{-1}c_2(x)H_u(x)\mathring{I}_{v2}(x) \end{pmatrix},\ (\mathring{I}_{v1}(x),\ \mathring{I}_{v2}(x))^T \in \mathbb{S} \right\}$$

is bounded, which implies that

$$[\widehat{\mathcal{F}}]((\mathring{I}_{v1}(x) + \widetilde{h}_1, \mathring{I}_{v2}(x) + \widetilde{h}_2)^T) - [\widehat{\mathcal{F}}]((\mathring{I}_{v1}(x), \mathring{I}_{v2}(x))^T) \ge 0$$

if $\mathcal{C}_2$ and $\mathcal{C}_3$ are large. Hence

$$\widehat{\mathcal{F}}((\mathring{I}_{v1}(x)+\widetilde{h}_1,\mathring{I}_{v2}(x)+\widetilde{h}_2)^T)-\widehat{\mathcal{F}}((\mathring{I}_{v1}(x),\mathring{I}_{v2}(x))^T)\geq 0,$$

i.e., $\widehat{\mathcal{F}}$ is monotone if $\mathcal{C}_2$ and $\mathcal{C}_3$ are large. □

In the coming discussion, for ϕ, $\varphi\in C(\overline{\Omega},\mathbb{R})$, we say $\phi\ll\varphi$ if $\phi(x)<\varphi(x)$ for $x\in\overline{\Omega}$.

Lemma 5.10. *For any* $\tau\in(0,\ 1)$ *and* $(\mathring{I}_{v1}(x),\ \mathring{I}_{v2}(x))^T\in\mathbb{S}$ *with* $(\mathring{I}_{v1}(x),\ \mathring{I}_{v2}(x))^T\gg 0$, *we have* $\tau\widehat{\mathcal{F}}((\mathring{I}^1_{v1}(x),\mathring{I}^1_{v2}(x))^T)\ll\widehat{\mathcal{F}}((\tau\mathring{I}^1_{v1}(x),\tau\mathring{I}^1_{v2}(x))^T)$.

Proof. From the definition of $\mathbb{S}$, we know that $\mathring{I}_{v1}(x_0)+\mathring{I}_{v2}(x_0)<\overline{M}(x_0)$ for some $x_0\in\overline{\Omega}$. Then

$$(\overline{M}(x_0)-\mathring{I}_{v1}(x_0)-\mathring{I}_{v2}(x_0))^+<(\overline{M}(x_0)-\tau\mathring{I}_{v1}(x_0)-\tau\mathring{I}_{v2}(x_0))^+$$

and

$$(\overline{M}(x)-\mathring{I}_{v1}(x)-\mathring{I}_{v2}(x))^+\leq(\overline{M}(x)-\tau\mathring{I}_{v1}(x)-\tau\mathring{I}_{v2}(x))^+$$

for $x\in\overline{\Omega}$. Hence

$$\tau[\widehat{\mathcal{F}}]((\mathring{I}^1_{v1}(x_0),\mathring{I}^1_{v2}(x_0))^T)<[\widehat{\mathcal{F}}]((\tau\mathring{I}^1_{v1}(x_0),\tau\mathring{I}^1_{v2}(x_0))^T)\text{ and }\tau[\widehat{\mathcal{F}}]((\mathring{I}^1_{v1}(x),\mathring{I}^1_{v2}(x))^T)\leq[\widehat{\mathcal{F}}]((\tau\mathring{I}^1_{v1}(x),\tau\mathring{I}^1_{v2}(x))^T).$$

Recall that

$$\widehat{\mathcal{F}}=((\mathcal{C}_2-D_v\Delta)^{-1}[\widehat{\mathcal{F}}]_1,(\mathcal{C}_3-D_v\Delta)^{-1}[\widehat{\mathcal{F}}]_2)^T.$$

By the strong positivity of $(\mathcal{C}_2-D_v\Delta)^{-1}$ and $(\mathcal{C}_3-D_v\Delta)^{-1}$, the assertion follows. □

Lemma 5.11. *The PSS of (5.14), if exists, is unique.*

Proof. If $(I^1_1(x),I^1_2(x),I^1_{v1}(x),I^1_{v2}(x))$ and $(I^2_1(x),I^2_2(x),I^2_{v1}(x),I^2_{v2}(x))$ are two distinct PSSs. Then $(I^1_{v1}(x),I^1_{v2}(x))\neq(I^2_{v1}(x),I^2_{v2}(x))$ by the first and second equations of (5.16). Assume that $(I^1_{v1}(x),I^1_{v2}(x))>(I^2_{v1}(x),I^2_{v2}(x))$ and define

$$\tau=\max\{\widetilde{\tau}\geq 0:\widetilde{\tau}(I^1_{v1}(x),I^1_{v2}(x))^T\leq(I^2_{v1}(x),I^2_{v2}(x))^T\}.$$

It follows that $\tau\in(0,1)$,

$$\tau(I^1_{v1}(x),I^1_{v2}(x))^T\leq(I^2_{v1}(x),I^2_{v2}(x))^T$$

and

$$\tau(I^1_{v1}(x_0),I^1_{v2}(x_0))^T=(I^2_{v1}(x_0),I^2_{v2}(x_0))^T$$

for some $x_0\in\overline{\Omega}$. We can choose $\mathcal{C}_1$, $\mathcal{C}_2$ and $\mathcal{C}_3$ such that $(I^1_{v1}(x),I^1_{v2}(x))^T$ and $(I^2_{v1}(x),I^2_{v2}(x))^T$ are NFPs of $\widehat{\mathcal{F}}$, i.e.

$$\widehat{\mathcal{F}}((I^1_{v1}(x),I^1_{v2}(x))^T)=(I^1_{v1}(x),I^1_{v2}(x))^T$$

and

$$\widehat{\mathcal{F}}((I^2_{v1}(x),I^2_{v2}(x))^T)=(I^2_{v1}(x),I^2_{v2}(x))^T.$$

On the other hand, by Lemma 5.9 and Lemma 5.10, we have

$$\begin{aligned}
&\tau(I_{v1}^1(x), I_{v2}^1(x))^T \\
&= \tau\widehat{\mathcal{F}}((I_{v1}^1(x), I_{v2}^1(x))^T) \\
&\lll \\
&\widehat{\mathcal{F}}(\tau(I_{v1}^1(x), I_{v2}^1(x))^T) \\
&\ll \\
&\widehat{\mathcal{F}}((I_{v1}^2(x), I_{v2}^2(x))^T) = (I_{v1}^2(x), I_{v2}^2(x))^T,
\end{aligned}$$

that is, $\tau(I_{v1}^1(x), I_{v2}^1(x))^T \ll (I_{v1}^2(x), I_{v2}^2(x))^T$, which contradicts with

$$\tau(I_{v1}^1(x_0), I_{v2}^1(x_0))^T = (I_{v1}^2(x_0), I_{v2}^2(x_0))^T.$$

This completes the proof. □

Denote by $\widetilde{\Psi}(t) : C(\overline{\Omega}, \mathbb{R}^4) \to C(\overline{\Omega}, \mathbb{R}^4)$ the semiflow generated by (5.14). Recall that system (5.14) is cooperative. By the standard theory developed in (Smith, 1995), we know that $\widetilde{\Psi}(t)$ is monotone.

Lemma 5.12. *Let $\overline{\mathbb{H}}$ be defined by (5.17). For any $\widetilde{\phi} \in \overline{\mathbb{H}}$, the solution of (5.14) satisfies*

$$I_1 > 0,\ I_2 > 0,\ I_{v1} > 0 \text{ and } I_{v2} > 0 \quad \text{for } (t, x) \in (0, \infty) \times \overline{\Omega}.$$

Proof. Since $\widetilde{\Psi}(t)$ is monotone, by the comparison principle, we directly have

$$I_1 \geq 0,\ I_2 \geq 0,\ I_{v1} \geq 0 \text{ and } I_{v2} \geq 0 \quad \text{for } (t, x) \in [0, \infty) \times \overline{\Omega}.$$

Under the condition $\widetilde{\phi} \in \overline{\mathbb{H}}$, that is, $I_1^0(x) + I_{v1}^0(x) \neq 0$ and $I_2^0(x) + I_{v2}^0(x) \neq 0$, we distinguish the following four cases to finish the proof.

Case 1. $I_{v1}^0(x) \neq 0$ and $I_{v2}^0(x) \neq 0$.

Notice that

$$\begin{cases}
\dfrac{\partial I_{v1}}{\partial t} \geq D_v \Delta I_{v1} - \mu(x)\overline{M}(x) I_{v1}, & (t, x) \in (0, \infty) \times \Omega, \\
\dfrac{\partial I_{v2}}{\partial t} \geq D_v \Delta I_{v2} - \mu(x)\overline{M}(x) I_{v2}, & (t, x) \in (0, \infty) \times \Omega, \\
\dfrac{\partial \mathcal{W}_{22}}{\partial n} = 0,\ \mathcal{W}_{22} = I_{v1}, I_{v2}, & (t, x) \in (0, \infty) \times \partial\Omega.
\end{cases} \tag{5.19}$$

By the comparison principle,

$$I_{v1} > 0 \text{ and } I_{v2} > 0 \qquad \text{for } (t, x) \in (0, \infty) \times \overline{\Omega}.$$

Then, by the first two equations of (5.14), together with the first two inequalities of (3.4) and the fact that $H_u(x)$ is nontrivial, we have

$$I_1 > 0 \text{ and } I_2 > 0 \qquad \text{for } (t, x) \in (0, \infty) \times \overline{\Omega}.$$

Case 2. $I_{v1}^0(x) \neq 0$ and $I_{v2}^0(x) = 0$.

In this case, we have $I_2^0(x) \neq 0$. By the third equation of (5.14), we have the first inequality of (5.19). Again from the comparison principle, we get

$$I_{v1}(t, x) > 0 \qquad \text{for } (t, x) \in (0, \infty) \times \overline{\Omega}.$$

Then, similarly as in case 1, we have

$$I_1(t,x)>0 \text{ and } I_2(t,x)>0 \qquad \text{for } (t,x)\in(0,\infty)\times\overline{\Omega}.$$

Due to (5.18) and the continuity of $I_{v2}(t,x)$ and $I_{v2}(0,x)=0$, we obtain $\Theta(t,x)>0$ for $(t,x)\in(0,t_7]\times\overline{\Omega}$ for some $t_7>0$. Then by the comparison principle and

$$\frac{\partial I_{v2}}{\partial t}>D_v\Delta I_{v2}-\mu(x)\overline{M}(x)I_{v2},\,(t,x)\in(0,t_7]\times\overline{\Omega}, \tag{5.20}$$

we get $I_{v2}(t,x)>0$ for $(t,x)\in(0,t_7]\times\overline{\Omega}$. Finally, by the second inequality of (5.19), we have $I_{v2}(t,x)>0$ for $(t,x)\in(0,\infty)\times\overline{\Omega}$.

Case 3. $I^0_{v1}(x)=0$ and $I^0_{v2}(x)\neq0$.

In this case, we have $I^0_1(x)\neq0$. Similar to case 2, we have

$$I_1(t,x)>0,\ I_2(t,x)>0,\ I_{v1}(t,x)>0 \text{ and } I_{v2}(t,x)>0 \qquad \text{for } (t,x)\in(0,\infty)\times\overline{\Omega}.$$

Case 4. $I^0_{v1}(x)+I^0_{v2}(x)=0$.

In this case, $I^0_1(x)\neq0$ and $I^0_2(x)\neq0$. By the first two equations of (5.14), together with the first two inequalities of (3.4) and the fact that $H_u(x)$ is nontrivial, we have

$$I_1(t,x)>0 \text{ and } I_2(t,x)>0 \qquad \text{for } (0,x)\in(t,\infty)\times\overline{\Omega}.$$

By the continuity of $I_{v1}(t,x)$, $I_{v2}(t,x)$, and $I_{v1}(0,x)=I_{v2}(0,x)=0$ for $x\in\overline{\Omega}$, we obtain $\Theta(t,x)>0$ for $(t,x)\in(0,t_8]\times\overline{\Omega}$ for some $t_8>0$. Then by

$$\frac{\partial I_{v1}}{\partial t}>D_v\Delta I_{v1}-\mu(x)\overline{M}(x)I_{v2},\,(t,x)\in(0,t_8]\times\overline{\Omega}, \tag{5.21}$$

(5.20), and the comparison principle, we have $I_{v1}(t,x)>0$, $I_{v2}(t,x)>0$ for $(t,x)\in(0,t_8]\times\overline{\Omega}$. Finally, by (5.19), we have

$$I_{v1}(t,x)>0 \text{ and } I_{v2}(t,x)>0 \qquad \text{for } (t,x)\in(0,\infty)\times\overline{\Omega}.$$

In conclusion, we have completed the proof. □

Lemma 5.13. *Let $\overline{\mathbb{H}}$ be defined by (5.17). For any $\widetilde{\phi}\in\overline{\mathbb{H}}$, the solution of (5.14) satisfies*

$$0\le I_1(t,x),\ I_2(t,x),\ I_{v1}(t,x),\ I_{v2}(t,x)\le\mathbb{B} \qquad \text{for } (t,x)\in(0,\infty)\times\Omega,$$

where $\mathbb{B}$ is large enough.

Proof. Let $\mathbb{B}_1=\max\{\left\|\overline{M}(x)\right\|_{\mathbb{Y}}+1,\left\|I^0_{v1}(x)\right\|_{\mathbb{Y}}+1,\ \left\|I^0_{v2}(x)\right\|_{\mathbb{Y}}+1\}$. The third and fourth equations of (5.14) together with the comparison principle give

$$I_{v1}(t,x)\le\mathbb{B}_1 \text{ and } I_{v2}(t,x)\le\mathbb{B}_1 \qquad \text{for } (t,x)\in(0,\infty)\times\overline{\Omega}.$$

Then by the first two equations of (5.14), for $i=1,2$, we have

$$\begin{cases}\dfrac{\partial I_i}{\partial t}\le D_h\Delta I_i-\gamma_i(x)I_i+c_i(x)H_u(x)\mathbb{B}_1, & (t,x)\in(0,\infty)\times\Omega,\\[2mm] \dfrac{\partial I_i}{\partial n}=0, & (t,x)\in(0,\infty)\times\partial\Omega.\end{cases}$$

So $I_i(t,x)$ is a lower solution of

$$\begin{cases} \dfrac{\partial \upsilon}{\partial t} = D_h \Delta \upsilon - \gamma_i(x)\upsilon + c_i(x) H_u(x) \mathbb{B}_1, & (t,x) \in (0,\infty) \times \Omega, \\ \dfrac{\partial \upsilon}{\partial n} = 0, & (t,x) \in (0,\infty) \times \partial\Omega, \\ \varsigma(0,x) = I_i^0(x), & x \in \Omega. \end{cases}$$

Let $\mathbb{B}_2 = \max\{(\|c_i(x)\|_{\mathbb{Y}} + 1)(\|H_u(x)\|_{\mathbb{Y}} + 1)\mathbb{B}_1 / \underline{\gamma_i}, \left\| I_i^0(x) \right\|_{\mathbb{Y}} + 1\}$, where $\underline{\gamma_i} = \min\{\gamma_i(x) : x \in \overline{\Omega}\}$. Then we have $0 \le \upsilon(t,x) \le \mathbb{B}_2$ for $(t,x) \in (0,\infty) \times \overline{\Omega}$. Again from the comparison principle, $0 \le I_i \le \upsilon \le \mathbb{B}_2$. Consequently, we have got the desired result by letting $\mathbb{B} = \max\{\mathbb{B}_1, \mathbb{B}_2\}$. □

Lemma 5.14. *Assume that $\mathring{U}(x) = (\mathring{I}_1(x),\ \mathring{I}_2(x),\ \mathring{I}_{v1}(x),\ \mathring{I}_{v2}(x))$ is a PSS of (5.14). Then $\mathring{U}(x)$ is globally asymptomatically stable.*

Proof. With the help of [43, Lemma 2.2.1], in the following, we show that for each $\widetilde{\phi} \in \overline{\mathbb{H}}$,

$$\lim_{t \to \infty} I_i(t, \cdot) = \mathring{I}_i(\cdot) \text{ and } \lim_{t \to \infty} I_{vi}(t, \cdot) = \mathring{I}_{vi}(\cdot),\ i = 1, 2.$$

By Lemma 5.12, we have $I_1(t,x) > 0$ $I_2 > 0(t,x)$, $I_{v1}(t,x) > 0$, and $I_{v2}(t,x) > 0$ for $(t,x) \in (0,\infty) \times \overline{\Omega}$, which allow us to assume that $I_1^0(x) > 0$, $I_2^0(x) > 0$, $I_{v1}^0(x) > 0$, and $I_{v2}^0(x) > 0$ for $x \in \overline{\Omega}$. Choose ϵ_6 small enough and let

$$\underline{U} = (\underline{I}_1,\ \underline{I}_2,\ \underline{I}_{v1},\ \underline{I}_{v2}) = (\epsilon_6 \mathring{I}_1(x),\ \epsilon_6 \mathring{I}_2(x),\ \epsilon_6 \mathring{I}_{v1}(x),\ \epsilon_6 \mathring{I}_{v2}(x))$$

which satisfies

$$\begin{cases} -D_h \Delta \underline{I}_1(x) = -\gamma_1(x) \underline{I}_1(x) + c_1(x) H_u(x) \underline{I}_{v1}(x), & x \in \Omega, \\ -D_h \Delta \underline{I}_2(x) = -\gamma_2(x) \underline{I}_2(x) + c_2(x) H_u(x) \underline{I}_{v2}(x), & \\ x \in \Omega, & \\ -D_v \Delta \underline{I}_{v1}(x) \le \alpha_1(x)(\overline{M}(x) - \underline{I}_{v1}(x) - \underline{I}_{v2}(x))^+ \underline{I}_1(x) - \mu(x) \overline{M}(x) \underline{I}_{v1}(x), & \\ x \in \Omega, & \\ -D_v \Delta \underline{I}_{v2}(x) \le \alpha_2(x)(\overline{M}(x) - \underline{I}_{v1}(x) - \underline{I}_{v2}(x))^+ \underline{I}_2(x) - \mu(x) \overline{M}(x) \underline{I}_{v2}(x), & \\ & x \in \Omega, \\ \dfrac{\partial \mathcal{W}_{23}(x)}{\partial n} = 0,\ \mathcal{W}_{23}(x) = \underline{I}_1(x), \underline{I}_2(x), \underline{I}_{v1}(x), \underline{I}_{v2}(x), & x \in \partial\Omega, \\ \underline{I}_1(x) \le I_1^0,\ \underline{I}_2(x) \le I_2^0,\ \underline{I}_{v1}(x) \le I_{v1}^0,\ \underline{I}_{v2}(x) \le I_{v2}^0, & x \in \Omega. \end{cases} \tag{5.22}$$

Recall that $\widetilde{\Phi}(t)\underline{U}(t,x)$ is monotone increasing in t and converges to a PSS of (5.14) (see [27, Corollary 7.3.6]). As $\mathring{U}(x)$ is the unique PSS of (5.14), it follows that

$$\widetilde{\Psi}(t)\underline{U}(x) \to \mathring{U}(x) \text{ as } t \to \infty.$$

Similarly, for sufficiently large number $\overline{G}$, we define

$$\overline{U} = (\overline{I}_1,\ \overline{I}_2,\ \overline{I}_{v1},\ \overline{I}_{v2}) = (\overline{G}\mathring{I}_1(x),\ \overline{G}\mathring{I}_2(x),\ \overline{G}\mathring{I}_{v1}(x),\ \overline{G}\mathring{I}_{v2}(x))$$

and then $\widetilde{\Psi}(t)\overline{U}(t,x) \to \mathring{U}(x)$ as $t \to \infty$. By the definitions of $\underline{U}$ and $\overline{U}$, we get

$$\underline{U}(t,x) \le \widetilde{\phi} \le \overline{U}(t,x).$$

As $\widetilde{\Psi}(t)$ is monotone, we directly have

$$\widetilde{\Psi}(t)\underline{U}(t,x) \le \widetilde{\Psi}(t)\widetilde{\phi} \le \widetilde{\Psi}(t)\overline{U}(t,x),\ t \ge 0.$$

Clearly, $\widetilde{\Psi}(t)\widetilde{\phi} \to \mathring{U}(x)$ as $t \to \infty$. This completes the proof. □

5.4. Global dynamics of EE

As stated in Theorem 5.6, if $\Re_0^1 > 1$, $\Re_0^2 > 1$, $\widehat{\Re}_0^1 > 1$, and $\widehat{\Re}_0^2 > 1$, then system (2.4) has at least a PSS, denoted by EE. From (2.2), we know that $\mathring{S}_v + \mathring{I}_{v1} + \mathring{I}_{v2} = \overline{M}$. Hence $\mathring{U}$ is the unique PPS of (5.14), which in turn implies that EE is the unique PSS of (2.4).

In what follows, we study the global attractivity of EE. The method used here is the theory of asymptotically autonomous semiflows developed in [30, Theorem 4.1].

Theorem 5.15. *Suppose that $\Re_0^1 > 1$, $\Re_0^2 > 1$, $\widehat{\Re}_0^1 > 1$, and $\widehat{\Re}_0^2 > 1$. Then the EE of (2.4) is globally attractive, that is, for any $(I_1^0, I_2^0, S_v^0, I_{v1}^0, I_{v2}^0) \in \mathbb{X}_{H0}$, the solution of (2.4) satisfies*

$$\lim_{t\to\infty} \|u(t,\cdot) - (\mathring{I}_1, \mathring{I}_2, \mathring{S}_v, \mathring{I}_{v1}, \mathring{I}_{v2})\|_{\mathbb{X}} = 0$$

uniformly on $\overline{\Omega}$, where $u(t,x) = (I_1(t,x), I_2(t,x), S_v(t,x), I_{v1}(t,x), I_{v2}(t,x))$ for $(t,x) \in (0,\infty)\times\Omega$.

Proof. We only need to pay attention to the infection compartments of (2.4), which satisfy

$$\begin{cases} \dfrac{\partial I_1}{\partial t} = D_h \Delta I_1 - \gamma_1(x) I_1 + c_1(x) H_u(x) I_{v1}, \\ \dfrac{\partial I_2}{\partial t} = D_h \Delta I_2 - \gamma_2(x) I_2 + c_2(x) H_u(x) I_{v2}, \\ \dfrac{\partial I_{v1}}{\partial t} = D_v \Delta I_{v1} + \alpha_1(x)\Theta(t,x) I_1 + \mathfrak{g}_1(t,x) - \mu(x)\overline{M}(x) I_{v1}, \\ \dfrac{\partial I_{v2}}{\partial t} = D_v \Delta I_{v2} + \alpha_2(x)\Theta(t,x) I_2 + \mathfrak{g}_2(t,x) - \mu(x)\overline{M}(x) I_{v2} \end{cases} \tag{5.23}$$

for $(t,x) \in (0,\infty)\times\Omega$, associated with

$$\begin{cases} \dfrac{\partial \mathcal{W}_{24}}{\partial n} = 0, \ \mathcal{W}_{24} = I_1, I_2, I_{v1}, I_{v2}, \ (t,x) \in (0,\infty)\times\partial\Omega \\ (I_1(0,x), I_2(0,x), I_{v1}(0,x), I_{v2}(0,x)) = (I_1^0(x), I_2^0(x), I_{v1}^0(x), I_{v2}^0(x)), \ x \in \Omega, \end{cases} \tag{5.24}$$

where

$$\mathfrak{g}_i(t,x) = \alpha_i(x)(S_v(t,x) - \Theta(t,x)) I_i(t,x) - \mu(x)(M - \overline{M}(x)) I_{vi}(t,x), \ i = 1,2.$$

It follows from

$$|S_v(t,x) - \Theta(t,x)| \le |M(x) - \overline{M}(x)|$$

that $\mathfrak{g}_i(t,x) \to 0$ uniformly on $\overline{\Omega}$ as $t \to \infty$, $i = 1, 2$. According to the theory developed in [24, Proposition 1.1], system (5.23) is asymptomatically autonomous with the limiting system (5.14). From Theorem 5.6, the ω-limit set of (5.23) is contained in $\overline{\mathbb{H}}$ defined by (5.17). Further from Lemma 5.14 and the definition of $\overline{\mathbb{H}}$, we know that $\overline{\mathbb{H}}$ is the stable set of $\mathring{U}(x)$. An application of the result of asymptomatically autonomous semiflows in [30, Theorem 4.1] gives that

$$(I_1(t,\cdot), I_2(t,\cdot), I_{v1}(t,\cdot), I_{v2}(t,\cdot)) \to \mathring{U} \text{ as } t \to \infty.$$

Further, from $S_v(t,\cdot) + I_{v1}(t,\cdot) + I_{v2}(t,\cdot) \to \overline{M}$ and $\mathring{S}_v + \mathring{I}_{v1} + \mathring{I}_{v2} = \overline{M}$, we have $S_v(t,\cdot) \to \mathring{S}_v$ as $t \to \infty$. This completes the proof. □

6. Conclusion

This paper concentrated on the threshold dynamics of a diffusive malaria model with the sensitive and resistant strains. Taking into account the heterogeneous environment, the vector population growing with a logistic term and the susceptible hosts at space x remaining at $H_u(x)$, we have formulated and analyzed the model to explore the competition and coexistence phenomena between the two strains.

Mathematically, we first investigated the well-posedness of system (2.4). According to the theory developed in (Smith, 1995), we confirmed the existence and uniqueness of classical solutions for system (2.4) on $[0, T_{\max})$ with $0 < T_{\max} \le \infty$. We then proved the ultimate boundedness of the unique global solution, which is verified by using the comparison principle (see Theorem 3.2). Further, thanks to [27, Theorem 2.1 and Theorem 7.3.1] and [22, Theorem 2.9], the existence of a global attractor is ensured (see Lemma 3.3). Based on the maximum principle, we proved the strict positivity of solutions (see Lemma 3.4).

Due to the complexity of the model (the spatial heterogeneity and two-strain structure), we first analyzed the associated single-strain subsystems (4.1) and (4.3). Subsystem (4.1) with the sensitive strain possesses three steady states: DFSSs E_0^1 and E_1^1 and PSS E_E^1; while subsystem (4.3) for the resistant strain possesses three steady states: DFSSs E_0^2 and E_1^2 and PSS E_E^2. The DFSSs and the PSSs of subsystem (4.1) and (4.3) can be viewed as DFSSs and the BSSs of system (2.4), respectively. That is, model (2.4) has five steady states: DFSSs E_0 and E_1, BSSs E_∂^1 and E_∂^2, and the PSS EE.

By the approach developed in (Diekmann et al., 1990; Liang et al., 2017; Magal et al., 2019; Thieme, 2009; Wang & Zhao, 2012), we introduced the BRN $\Re_0^i$ of each strain ($i=1, 2$) for system (2.4) by using the next generation operator. Then we defined the BRN $\Re_0$ of system (2.4) as the maximum of $\Re_0^1$ and $\Re_0^2$ (see (4.9)). We also built up the relationship between $\Re_0^i - 1$ ($i=1, 2$) and the principal eigenvalue of the associated eigenvalue problem (see Lemma 4.2). The main difficulty we overcame is to characterize the BRN of the diffusive malaria model with multiple diffusive infection compartments. With this in mind, we established the connection between the BRN $\Re_0^i$ ($i=1, 2$) and the LBRN $\Re_0^i(x)$ ($i=1, 2$). By appealing to the approach developed in (Magal et al., 2019), we defined the BRN as the spectral radius of a product of LBRN and the strongly positive compact linear operators with spectral radius one (see (4.17) and (4.19)). As described in Lemma 4.3, $\Re_0^i > 1$ when $\Re_0^i(x) > 1$ for all $x \in \overline{\Omega}$, and $\Re_0^i < 1$ when $\Re_0^i(x) < 1$ for all $x \in \overline{\Omega}$. We further investigated the effect of large or small diffusion rates on $\Re_0^i$ ($i=1, 2$) for a single-strain system (see Lemma 4.4 and Lemma 4.5).

We also investigated the competition and exclusion phenomena between the sensitive and resistant strains. To this end, the IRN $\widehat{\Re}_0^i$ of each strain ($i=1, 2$) for system (2.4) is depicted rigorously (see (4.27) and (4.29)). In these circumstances, we aimed to investigate the possibility of the coexistence of the sensitive and resistant strains. We also established the relationship between $\widehat{\Re}_0^i - 1$ ($i=1, 2$) and the principal eigenvalue of the corresponding eigenvalue problem (see Lemma 4.6). With the BRN $\Re_0^i$ ($i=1, 2$) and the IRN $\widehat{\Re}_0^i$ ($i=1, 2$), we carried out the stability analysis of the steady states to understand the interaction between the sensitive and resistant strains. Using the results obtained in (Magal et al., 2018), the threshold dynamics about single-strain models are clearly characterized: The malaria with strain i becomes extinct in the case where $\Re_0^i < 1$ ($i=1, 2$), E_1^i is globally asymptotically stable (see (i) of Lemma 5.1); The malaria with strain i becomes epidemic in the case where $\Re_0^i > 1$ ($i=1, 2$), E_E^i is a unique PSS (see (ii) of Lemma 5.1). As to our model (2.4), we obtained the following results:

(i) E_0 is always unstable. If $\Re_0^1 < 1$ and $\Re_0^2 < 1$, E_1 is globally attractive (see Theorem 5.2), which biologically means that malaria becomes extinct.
(ii) If $\Re_0^i > 1 > \Re_0^j$ ($i, j = 1, 2$ with $i \neq j$), E_∂^i is globally attractive (see Theorem 5.3), which biologically means that malaria with strain i becomes epidemic, while the malaria with strain j becomes extinct (see Theorem 5.3). Combined with the linearized system and the associated eigenvalue problem, we studied the stability of E_∂^i ($i=1, 2$) when another strain invades: malaria with strain j will not invade in the case where $\widehat{\Re}_0^j < 1$ and the strain j becomes established in the case where $\widehat{\Re}_0^j > 1$ for $j=1, 2$ and $i \neq j$, both of which are based on the condition that the i strain becomes endemic (see Lemma 5.4).
(iii) $E_0, E_1, E_\partial^1, E_\partial^2$ are uniform weak repellers in the case where $\Re_0^1 > 1$, $\Re_0^2 > 1$, $\widehat{\Re}_0^1 > 1$ and $\widehat{\Re}_0^2 > 1$, which are proved with by way of contradiction (see Lemma 5.5). The existence of a PSS EE for system (2.4) is also confirmed in Theorem 5.6.

However, it is not easy to get the global dynamics of EE. With the total density of female adult mosquitoes $M(t, x)$ satisfying (2.1), it is natural to consider the dynamics of (2.4) dominated by the corresponding limiting system (5.14). By confirming the existence and uniqueness of the PSS of the limiting system (5.14), we have verified the positivity of solutions to (5.14) (see Lemma 5.7), the well-posedness of NFP by defining an explicitly function $\widehat{\mathcal{F}}_i$ (see Lemma 5.8), the monotonicity of $\widehat{\mathcal{F}}_i$ (see Lemma 5.9), and the sublinear property for $\widehat{\mathcal{F}}_i$ (see Lemma 5.10). As a result, the PSS of the limiting system is unique if it exists (see Lemma 5.11).

Applying the comparison principle for cooperative systems, we proved the positivity (see Lemma 5.12) and boundedness of solutions of the limiting system (see Lemma 5.13), and then obtained the global stability of PSS with the theory of monotone dynamical systems (see Lemma 5.14). Finally, with the help of the theory of asymptotically autonomous semiflows (Thieme, 1992), we confirmed that system (5.23) is asymptomatically autonomous with the limiting system (5.14) and the ω-limit set of (5.23) is contained in the stable set of $\mathring{U}(x)$. We obtained the global asymptotic stability of EE (see Theorem 5.15).

With regard to biological meanings, we analyzed the relationship between the two strains in terms of $\Re_0^i$ and $\widehat{\Re}_0^i$, and then we summarized four phenomena of competition of the sensitive strain and the resistant strain, i.e., if $\Re_0^1 < 1$ and $\Re_0^2 < 1$, then malaria epidemic vanishes; if $\Re_0^1 > 1$, $\widehat{\Re}_0^1 < 1$, $\Re_0^2 > 1$, $\widehat{\Re}_0^2 > 1$, then malaria with the sensitive strain becomes extinct and malaria with the resistant strain becomes epidemic; if $\Re_0^1 > 1$, $\widehat{\Re}_0^1 > 1$, $\Re_0^2 > 1$, $\widehat{\Re}_0^2 < 1$, then malaria with the sensitive strain becomes epidemic and malaria with the resistant strain becomes extinct; if $\Re_0^1 > 1$, $\widehat{\Re}_0^1 > 1$, $\Re_0^2 > 1$, $\widehat{\Re}_0^2 > 1$, then the two strains become epidemic and prevalent in the habitat. Recently, Wang et al. (Wang et al., 2023) considered the spreading speeds and traveling wave solutions for a diffusive vector-borne disease model, we leave these problems for our model in a future study.

CRediT authorship contribution statement

Jinliang Wang: Writing – review & editing, Supervision, Methodology, Funding acquisition, Conceptualization. **Wenjing Wu:** Writing – original draft, Methodology. **Yuming Chen:** Writing – review & editing, Supervision, Methodology, Funding acquisition, Conceptualization.

References

Amann, H. (1976). Fixed point equations and nonlinear eigenvalue problems in ordered banach spaces. *SIAM Review, 18*(4), 620–709.
Bai, Z., Peng, R., & Zhao, X.-Q. (2018). A reaction-diffusion malaria model with seasonality and incubation period. *Journal of Mathematical Biology, 77*(1), 201–228.
Bushman, M., Antia, R., Udhayakumar, V., et al. (2018). Within-host competition can delay evolution of drug resistance in malaria. *PLoS Biology, 16*(8), Article e2005712.
Cantrell, R. S., & Cosner, C. (2003). *Spatial ecology via reaction-diffusion equations*. Chichester: Wiley.
Chamchod, F., & Britton, N. F. (2011). Analysis of a vector-bias model on malaria transmission. *Bulletin of Mathematical Biology, 73*, 639–657.
Diekmann, O., Heesterbeek, J. A. P., & Metz, J. A. J. (1990). On the definition and the computation of the basic reproduction ratio R_0 in models for infectious diseases in heterogeneous populations. *Journal of Mathematical Biology, 28*(4), 365–382.
Esteva, L., Gumel, A. B., & Vargas-De-León, C. (2009). Qualitative study of transmission dynamics of drug-resistant malaria. *Mathematical and Computer Modelling, 50*(3–4), 611–630.
Fitzgibbon, W. E., Morgan, J. J., & Webb, G. (2017). An outbreak vector-host epidemic model with spatial structure, the 2015-2016 Zika outbreak in Rio De Janeiro. *Theoretical Biology and Medical Modelling, 14*(1), 7.
Forouzannia, F., & Gumel, A. (2014). Mathematical analysis of an age-structured model for malaria transmission dynamics. *Mathematical Biosciences, 247*, 80–94.
Forouzannia, F., & Gumel, A. (2015). Dynamics of an age-structured two-strain model for malaria transmission. *Applied Mathematics and Computation, 250*, 860–886.
Ge, J., Kim, K. I., Lin, Z., et al. (2015). A SIS reaction-diffusion-advection model in a low-risk and high-risk domain. *Journal of Differential Equations, 259*(10), 5486–5509.
Hagenaars, T. J., Donnelly, C. A., & Ferguson, N. M. (2004). Spatial heterogeneity and the persistence of infectious diseases. *Journal of Theoretical Biology, 229*(3), 349–359.
Lam, K. Y., & Lou, Y. (2016). Asymptotic behavior of the principal eigenvalue for cooperative elliptic systems and applications. *Journal of Dynamics and Differential Equations, 28*, 29–48.
Laxminarayan, R., Matsoso, P., Pant, S., et al. (2016). Access to effective antimicrobials, a worldwide challenge. *Lancet, 387*(10014), 168–175.
Liang, X., Zhang, L., & Zhao, X.-Q. (2017). Basic reproduction ratios for periodic abstract functional differential equations (with application to a spatial model for lyme disease). *Journal of Dynamics and Differential Equations, 31*, 1247–1278.
Lou, Y., & Zhao, X.-Q. (2011). A reaction-diffusion malaria model with incubation period in the vector population. *Journal of Mathematical Biology, 62*(4), 543–568.
Macdonald, G. (1957). *The epidemiology and control of malaria*. London: Oxford University Press.
Magal, P., Webb, G., & Wu, Y. (2018). On a vector-host epidemic model with spatial structure. *Nonlinearity, 31*, 5589–5614.
Magal, P., Webb, G., & Wu, Y. (2019). On the basic reproduction number of reaction-diffusion epidemic models. *SIAM Journal on Applied Mathematics, 79*(1), 284–304.
Ross, R. (1911). *The prevention of malaria*. London: John Murray.
Shi, Y., & Zhao, H. (2021). Analysis of a two-strain malaria transmission model with spatial heterogeneity and vector-bias. *Journal of Mathematical Biology, 82*, 24.
Smith, H. L. (1995). *Monotone dynamical systems: An introduction to the theory of competitive and cooperative systems*. Providence: American Mathematical Society.
Smith, H. L., & Zhao, X.-Q. (2001). Robust persistence for semidynamical systems. *Nonlinear Analysis: Theory, Methods & Applications, 47*(9), 6169–6179.
Talisuna, A. O., Bloland, P., & D'Alessandro, U. (2004). History, dynamics, and public health importance of malaria parasite resistance. *Clinical Microbiology Reviews, 17*(1), 235–254.
Thieme, H. R. (1992). Convergence results and Poincare-Bendixson trichotomy for asymptotically autonomous differential equations. *Journal of Mathematical Biology, 30*, 755–763.
Thieme, H. R. (2009). Spectral bound and reproduction number for infinite-dimensional population structure and time heterogeneity. *SIAM Journal on Applied Mathematics, 70*(1), 188–211.
Titus, J. G. (1990). Strategies for adapting to the greenhouse effect. *Journal of the American Planning Association, 56*, 311–323.
Tumwiine, J., Hove-Musekwa, D. S., & Nyabadza, F. (2014). A mathematical model for the transmission and spread of drug sensitive and resistant malaria strains within a human population. *International Scholarly Research Notices, 4*, 1–12.
Tuncer, N., & Martcheva, M. (2012). Analytical and numerical approaches to coexistence of strains in a two-strain SIS model with diffusion. *Journal of Biological Dynamics, 6*(2), 406–439.
Villela, D. A. M., Bastos, L. S., de Carvalho, L. M., et al. (2016). Zika in rio de janeiro: Assessment of basic reproduction number and comparison with dengue outbreaks. *Epidemiology and Infection, 145*(8), 1649–1657.
Wang, X., Lin, G., & Ruan, S. (2023). Spreading speeds and traveling wave solutions of diffusive vector-borne disease models without monotonicity. *P. Roy. Soc. Edinb. A., 153*(1), 137–166.
Wang, W., & Zhao, X.-Q. (2012). Basic reproduction numbers for reaction-diffusion epidemic models. *SIAM Journal on Applied Dynamical Systems, 11*(4), 1652–1673.
Wang, X., & Zhao, X.-Q. (2017). A periodic vector-bias malaria model with incubation period. *SIAM Journal on Applied Mathematics, 77*(1), 181–201.
World Health Organization. (2019). *World malaria report 2019*. Geneva: World Health Organization.
Xu, Z., & Zhao, X.-Q. (2013). A vector-bias malaria model with incubation period and diffusion. *Discrete and Continuous Dynamical Systems - Series B, 17*(7), 2615–2634.
Zhao, X.-Q. (2012). Global dynamics of a reaction and diffusion model for Lyme disease. *Journal of Mathematical Biology, 65*, 787–808.
Zhao, X.-Q. (2017). *Dynamical systems in population biology*. Springer.
Zhao, L., Wang, Z.-C., & Ruan, S. (2020). Dynamics of a time-periodic two-strain SIS epidemic model with diffusion and latent period. *Nonlinear Analysis: Real World Applications, 51*, Article 102966.