J. Math. Anal. Appl. 516 (2022) 126477

Contents lists available at ScienceDirect

Journal of Mathematical Analysis and Applications

www.elsevier.com/locate/jmaa

Regular Articles

Diffusive host-pathogen model revisited: Nonlocal infections, incubation period and spatial heterogeneity

Hongying Shu [a,*], Zongwei Ma [b], Hao Wang [c]

[a] School of Mathematics and Statistics, Shaanxi Normal University, Xi'an, 710062, China
[b] College of Data Science, Jiaxing University, Jiaxing, 314001, China
[c] Department of Mathematical and Statistical Sciences, University of Alberta, Edmonton, AB T6G 2G1, Canada

ARTICLE INFO

Article history:
Received 8 May 2022
Available online 5 July 2022
Submitted by J.J. Nieto

Keywords:
Host-pathogen model
Diffusion
Nonlocal infections
Incubation period
Spatial heterogeneity
Basic reproduction number

ABSTRACT

We formulate and analyze a general diffusive host-pathogen model with an incubation period and nonlocal infections in a spatially heterogeneous environment. The model system is partially degenerate and the solution map is not compact. We first prove that the solutions of the model exist globally and are ultimately bounded. Next, we define the basic reproduction number R_0 as the spectral radius of the sum of two next generation operators corresponding to direct and indirect infection modes, and prove that R_0 is decreasing with respect to the incubation period and the diffusion coefficient of infectious hosts under some conditions. Finally, we demonstrate that the model system possesses a global attractor, and explore the global dynamics of the system. Especially, we show that the infection-free steady state is globally asymptotically stable if $R_0 \leq 1$. On the other hand, if $R_0 > 1$, then the infection will persist and the model system admits at least one positive steady state. For spatial homogeneous system, global asymptotic stability of the positive steady state is proved via Lyapunov functional technique. Numerical simulation is conducted to explore singular perturbation phenomenon when the diffusion coefficients approach zero. We observe that the diffusion will not only spread the infection to the low-risk region, but it may also increase the infection level in the high-risk region.

1. Introduction

To understand the dynamics of the host-pathogen interaction, Anderson and May [2] proposed and investigated a nonlinear system of ordinary differential equations, where a class representing the population of infectious pathogen particles was introduced. This model system was then revised by Dwyer [8] to include density dependent mortality and spatial diffusion of the host population. Moreover, the consumption of the

* Corresponding author.
E-mail address: hshu@snnu.edu.cn (H. Shu).

https://doi.org/10.1016/j.jmaa.2022.126477
0022-247X/

pathogen by the hosts was ignored for simplicity. Dwyer's work was further generalized in [35] to incorporate with spatial heterogeneity in model parameters such as the carrying capacity for the host, the transmission rate, and the shedding rate. It is also noted that in Dwyer's model the habitat was assumed to be unbounded in a one dimensional space, while the domain in the model of [35] was bounded in a finite dimensional space.

Only one transmission path was assumed in the aforementioned models. However, it is more biologically realistic to incorporate both direct and indirect transmission mechanisms in the model. For instance, the *Vibrio cholerae* bacteria can spread Cholera through direct human-to-human infection via faecal-oral route and indirect environment-to-human transmission from polluted aquatic reservoir [21,22]. The direct transmission is rare and can be ignored in the areas where good hygiene is maintained. But in many developing countries such as Rwanda, Zimbabwe, and Haiti, where Cholera outbreaks occurred and caused serious public health crisis [7,12,18], the direct human-to-human infection contributed a significant number of cases. It is thus important to consider transmissions of pathogens both between the hosts and through the environment [23]. As we shall see later in our analysis, ignoring one of the two infection routes will cause the problem of underestimating the basic reproduction number of infection and the seriousness of the pathogen transmission.

Recently, some spatial homogeneous models were proposed and developed to consider both direct and indirect transmission routes; see, for instance, [3,9,14,16,22,23,32,33]. To better understand the spatial pattern of host-pathogen dynamics, one should also introduce spatial heterogeneity into the model. It has been shown in [22,34] that the (local) basic reproduction numbers are different in 10 different regions in Zimbabwe and Haiti. Reaction-diffusion equations were used to investigate traveling waves, asymptotic spreading speed, spatiotemporal dynamics, and bifurcation dynamics of host-pathogen models [6,8,35,37].

Many pathogens undergo a latent/incubation period within the host before becoming infectious [2]. To incorporate the incubation period in our model, we shall make use of the stage structure of the infected host. Let $i(x,t,a)$ be the density of infected hosts at location x time t with infection age a. We consider the following age-structure equation,

$$\left(\frac{\partial}{\partial t}+\frac{\partial}{\partial a}\right) i(x,t,a) = -\mu(x,a)i(x,t,a) + \nabla\cdot\left(d(x,a)\nabla i(x,t,a)\right),$$

for $x \in \Omega,\ t > 0,\ a > 0$, where $\Omega \subset \mathbb{R}^n$ is a bounded spatial habitat with a smooth boundary $\partial\Omega$, $\nabla\cdot(d(x,a)\nabla i(x,t,a))$ describes the divergence of $d(x,a)\nabla i(x,t,a)$ with $d(x,a)$ being the diffusion rate of infected hosts with infection age a, and $\mu(x,a)$ is the death rate of infected hosts with infection age a. Let τ be a cutoff age for the incubation period of the infected hosts, and denote by $u_{2,I}(x,t)$ and $u_2(x,t)$, respectively, the densities of inactively and actively infected hosts; namely,

$$u_{2,I}(x,t) = \int_0^\tau i(x,t,a)da, \quad u_2(x,t) = \int_\tau^\infty i(x,t,a)da.$$

Denote $u_1(x,t)$ and $u_3(x,t)$ as the density of susceptible hosts and pathogen particles at location x time t, respectively. We assume they satisfy the following differential equations.

$$\begin{aligned}
\frac{\partial u_1}{\partial t} &= \nabla\cdot(d_1(x)\nabla u_1) + n(x,u_1) - f(x,u_1,u_2) - g(x,u_1,u_3),\\
\frac{\partial u_3}{\partial t} &= k(x)u_2 - \mu_3(x)u_3,
\end{aligned}$$

for $x \in \Omega,\ t > 0$, where $\nabla\cdot(d_1(x)\nabla u_1)$ represents the divergence of $d_1(x)\nabla u_1$ with $d_1(x)$ being the diffusion rate of susceptible hosts, $n(x,u_1)$ is the intrinsic growth function of susceptible hosts, which couples the recruitment (or influx) and the natural death, $f(x,u_1(x,t),u_2(x,t))$ and $g(x,u_1(x,t),u_3(x,t))$ are the direct and indirect nonlinear transmission functions, respectively, $k(x)$ and $\mu_3(x)$ are the reproduction rate by actively infected hosts and the death rate of the pathogen particles, respectively. The inflow of infected hosts comes from the nonlinear transmissions:

$$i(x,t,0) = f(x,u_1(x,t),u_2(x,t)) + g(x,u_1(x,t),u_3(x,t)).$$

It is natural to assume that $i(x,0,\infty) = 0$. Now, we assume that the diffusion rate and mortality rate are piecewisely defined as

$$d(x,a) = \begin{cases} d_{2,I}(x), & x \in \Omega,\ a \le \tau, \\ d_2(x), & x \in \Omega,\ a > \tau, \end{cases} \qquad \mu(x,a) = \begin{cases} \mu_{2,I}(x), & x \in \Omega,\ a \le \tau, \\ \mu_2(x), & x \in \Omega,\ a > \tau. \end{cases}$$

An integration along the characteristic lines leads to the following equation for the actively infected hosts.

$$\begin{aligned} \frac{\partial u_2(x,t)}{\partial t} =&\ \nabla \cdot (d_2(x)\nabla u_2(x,t)) - \mu_2(x)u_2(x,t) \\ &+ \int_\Omega K(x,y,\tau)\left(\beta_1(y)u_1(y,t-\tau)u_3(y,t-\tau) + \beta_2(y)u_1(y,t-\tau)u_2(y,t-\tau)\right) dy, \end{aligned}$$

where $K(x,y,t)$ is the kernel function for the solution operator (i.e., C_0 semigroups) $T_{2,I}(t)$ generated by the differential operator $\nabla \cdot (d_{2,I}\nabla) - \mu_{2,I}$ with no-flux boundary condition on Ω. To consider a more general kernel function $K(x,y,\tau)$, we make the following assumptions:

(H$_1$) For any $\tau \ge 0$, $\int_\Omega K(x,y,\tau)dy$ is continuous in $x \in \bar{\Omega}$, $\int_\Omega K(x,y,\tau)dx$ is continuous in $y \in \bar{\Omega}$, and $\int_\Omega K(x,y,\tau)\psi(y)dy > 0$ for any $x \in \bar{\Omega}$ and $\psi \in C(\bar{\Omega},\mathbb{R}_+)$ with $\psi \not\equiv 0$. Moreover, there exists $\alpha(\tau) > 0$ such that

$$\int_\Omega v(x)\left[\int_\Omega K(x,y,\tau)w(y)dy\right]dx \le \alpha(\tau)\int_\Omega [v^2(x) + w^2(x)]dx \text{ for any } v, w \in C(\bar{\Omega}).$$

It is obvious that both the heat kernel and the delta kernel satisfy this condition. For convenience, we introduce the following operator: for $x \in \Omega$ and $t > 0$,

$$(\chi(\tau)\psi)(x) = \int_\Omega K(x,y,\tau)\psi(y)dy \quad \text{for any} \quad \psi \in C(\bar{\Omega}).$$

For simplicity, we denote $u_{i,-\tau}(x,t) = u_i(x,t-\tau)$ for $i = 1,2,3$. Motivated by the above derivation, we propose a general diffusive host-pathogen model with an incubation period and two nonlocal infection modes in a spatially heterogeneous environment:

$$\begin{aligned} \frac{\partial u_1}{\partial t} &= \nabla \cdot (d_1(x)\nabla u_1) + n(x,u_1) - f(x,u_1,u_2) - g(x,u_1,u_3), \\ \frac{\partial u_2}{\partial t} &= \nabla \cdot (d_2(x)\nabla u_2) + \chi(\tau)f(\cdot,u_{1,-\tau},u_{2,-\tau}) + \chi(\tau)g(\cdot,u_{1,-\tau},u_{3,-\tau}) - \mu_2(x)u_2, \\ \frac{\partial u_3}{\partial t} &= k(x)u_2 - \mu_3(x)u_3, \end{aligned} \tag{1.1}$$

for $x \in \Omega, t > 0$, with nonnegative initial conditions and homogeneous Neumann boundary conditions

$$\nabla u_i \cdot \nu = 0, \quad i = 1, 2, \ x \in \partial\Omega, \ t > 0,$$

where ν is the unit outward normal to $\partial\Omega$. Throughout this paper, we assume that $d_1(x), d_2(x),\ k(x)$, $\mu_2(x), \mu_3(x)$ are positive and continuous functions on $\bar{\Omega}$. We further make the following biologically motivated assumptions:

($\mathbf{H}_2$) $n(x, u_1) \in C^{0,1}(\bar{\Omega} \times \mathbb{R}_+)$ and $\partial_{u_1} n(x, u_1) \leq 0$ for all $x \in \Omega$ and $u_1 \geq 0$; for each $x \in \bar{\Omega}$, there exists a unique $\bar{u}_1(x) > 0$ in $C(\bar{\Omega}, \mathbb{R})$ such that $n(x, \bar{u}_1(x)) = 0$.

($\mathbf{H}_3$) $f(x, u_1, u_2), g(x, u_1, u_3) \in C^{0,1,2}(\bar{\Omega} \times \mathbb{R}_+ \times \mathbb{R}_+)$, which are strictly increasing with respect to u_i and concave down with respect to the third variable for all $x \in \Omega$ and $u_i \geq 0$ $(i = 1, 2, 3)$; $f(x, v, w) = 0$ (resp. $g(x, v, w) = 0$) if and only if $vw = 0$.

Throughout this paper, we assume that ($\mathbf{H}_1$), ($\mathbf{H}_2$) and ($\mathbf{H}_3$) are satisfied. The motivation of this paper is to investigate the joint impacts of nonlocal infections, incubation period and spatial heterogeneity on the dynamics of diffusive host-pathogen models. As we shall see, the global dynamics is determined by a threshold parameter called the basic reproduction number, which is defined as the spectral radius of the sum of two next generation operators corresponding to direct and indirect infection modes. Under certain conditions, we will also prove that this threshold parameter is decreasing with respect to the incubation period and the diffusion coefficient of infectious hosts. We will further conduct numerical simulation to explore singular perturbation phenomenon when the diffusion coefficients approach zero. Moreover, we will show that the diffusion will not only spread the infection to the low-risk region, but it may also increase the infection level in the high-risk region.

The rest of this paper is organized as follows. In Section 2, we obtain some preliminary results on the well-posedness of our model system, including uniqueness, global existence, and ultimately uniform boundedness of the solution. In Section 3, we define the basic reproduction number R_0 by using the next generation operator, and explore its properties as the dispersal rate varies from zero to infinity. In Sections 4, we prove a dichotomy result that the infection-free steady state is globally stable when $R_0 \leq 1$ while the model is uniformly persistent and possesses a positive steady state when $R_0 > 1$. In Section 5, we consider the special case when the system is spatial homogeneous and prove that the positive steady state is unique, homogeneous, and globally asymptotically stable. In Sections 6, we conduct numerical simulations to verify the theoretical results on monotonicity of basic reproduction number and to illustrate the singular perturbation phenomenon of steady state solutions when the diffusion rates approach zero. In Section 7, a brief summary is provided to conclude the paper.

2. Well-posedness and basic dynamics

Denote by $\mathbb{X} := C(\bar{\Omega}, \mathbb{R}^3)$ the Banach space of continuous functions on $\bar{\Omega}$ with the supremum norm $\|\cdot\|_{\mathbb{X}}$. For $\tau \geq 0$, let $\mathcal{C}_\tau := C([-\tau, 0], \mathbb{X})$ be the Banach space of continuous maps from $[-\tau, 0]$ to $\mathbb{X}$ with the norm $\|\phi\| := \max_{\theta \in [-\tau, 0]} \|\phi(\theta)\|_{\mathbb{X}}$ for any $\phi \in \mathcal{C}_\tau$. The nonnegative cones of $\mathbb{X}$ and $\mathcal{C}_\tau$ are denoted by $\mathbb{X}^+ = C(\bar{\Omega}, \mathbb{R}^3_+)$ and $\mathcal{C}_\tau^+ := C([-\tau, 0], \mathbb{X}^+)$, respectively. It is obvious that $(\mathbb{X}, \mathbb{X}^+)$ and $(\mathcal{C}_\tau, \mathcal{C}_\tau^+)$ are strongly ordered spaces [29]. Given a continuous function $u(x, t) : \Omega \times [-\tau, \infty) \to \mathbb{X}$, we define $u_t \in \mathcal{C}_\tau$ as $u_t(\theta) = u(\cdot, t + \theta)$ for any $\theta \in [-\tau, 0]$. Let $T_1(t)$ and $T_2(t)$ be the C_0 semigroups generated by the second-order differential operators $\nabla \cdot (d_1 \nabla)$ and $\nabla \cdot (d_2 \nabla) - \mu_2(\cdot)$, respectively, with homogeneous Neumann boundary conditions. It then follows from [29, Corollary 7.2.3] that $T_i(t)$ is compact and strongly positive for all $t > 0$ and $i = 1, 2$. Moreover, $T(t) := (T_1(t), T_2(t), T_3(t))$ is a C_0 semigroup on $\mathbb{X}$ with an infinitesimal generator A [26], where $T_3(t)\varphi_3 = e^{-\mu_3(\cdot)t}\varphi_3$. We define $\hat{u}(t) = u(\cdot, t + \cdot) \in \mathcal{C}_\tau^+$ for $t \geq 0$. Then system (1.1) can be written as an abstract differential equation

$$[\hat{u}'(t)](\cdot,\theta) = \begin{cases} \frac{\partial[\hat{u}(t)]}{\partial\theta}(\cdot,\theta), & \theta \in [-\tau, 0), \\ A\{[\hat{u}(t)](\cdot,0)\} + F(\hat{u}(t)), & \theta = 0, \end{cases}$$

where the nonlinear operator $F = (F_1, F_2, F_3) : \mathcal{C}_\tau^+ \to \mathbb{X}$ is defined by

$$F(\varphi)(x) := \begin{pmatrix} n(x, \varphi_1(x,0)) - f(x, \varphi_1(x,0), \varphi_2(x,0)) - g(x, \varphi_1(x,0), \varphi_3(x,0)) \\ [\chi(\tau) f(\cdot, \varphi_1(\cdot,-\tau), \varphi_2(\cdot,-\tau))](x) + [\chi(\tau) g(\cdot, \varphi_1(\cdot,-\tau), \varphi_3(\cdot,-\tau))](x), \\ k(x)\varphi_2(x,0) \end{pmatrix}$$

for any $\varphi = (\varphi_1, \varphi_2, \varphi_3) \in \mathcal{C}_\tau^+$. Given $\varphi \in \mathcal{C}_\tau^+$, it is obvious that $F(\varphi) \in \mathbb{X}$. Moreover, there exists $c > 0$ such that $f(x, \varphi_1(x,0), \varphi_2(x,0)) + g(x, \varphi_1(x,0), \varphi_3(x,0)) \le c\varphi_1(x,0)$ for all $x \in \bar{\Omega}$. Hence, $\varphi(x,0) + \varepsilon F(\varphi)(x) \ge (\varphi_1(x,0)(1-\varepsilon c), \varphi_2(x,0), \varphi_3(x,0))^T$ for $x \in \Omega$. If $\varepsilon \in (0, 1/c)$, then $\varphi(\cdot,0) + \varepsilon F(\varphi) \in \mathbb{X}^+$. Especially,

$$\lim_{\varepsilon \to 0^+} \frac{1}{\varepsilon} \mathrm{dist}(\varphi(\cdot,0) + \varepsilon F(\varphi), \mathbb{X}^+) = 0.$$

Thus, by using [20, Corollary 4] or [29, Theorem 7.3.1], we establish the existence of a unique solution to system (1.1). Since the nonlinear operator $F = (F_1, F_2, F_3)$ is mixed quasimontone [25], the nonnegativity of solutions can be easily obtained by using the comparison principle. To summarize, we obtain the following lemma on the existence, uniqueness, and nonnegativity of solutions to system (1.1).

Lemma 2.1. *For every initial condition $\varphi \in \mathcal{C}_\tau^+$, system (1.1) with homogeneous Neumann boundary conditions has a unique solution $u(\cdot,t,\varphi) = (u_1(\cdot,t,\varphi), u_2(\cdot,t,\varphi), u_3(\cdot,t,\varphi))$ on a maximal interval of existence $[0, t_{\max})$ for $u(\cdot,0,\varphi) = \varphi$, and if $t_{\max} < \infty$, then $\limsup_{t \to t_{\max}^-} \|u(\cdot,t)\|_{\mathbb{X}} = \infty$. Moreover, $u(x,t) \ge 0$ for all $t \in [-\tau, t_{\max})$.*

We are now in the position to address that $t_{max} = \infty$ by proving the boundedness of solutions for system (1.1). First, we recall the following lemma in [28].

Lemma 2.2. *Let $n(x, u_1)$ satisfy ($\boldsymbol{H}_2$). For any positive and continuous diffusion coefficient $d_1(x)$, the reaction-diffusion equation*

$$\frac{\partial w(x,t)}{\partial t} = \nabla \cdot (d_1(x) \nabla w(x,t)) + n(x, w(x,t)), \; x \in \Omega, \; t > 0 \tag{2.1}$$

with the homogeneous Neumann boundary condition admits a unique and strictly positive steady state $w^*(x)$, which is globally asymptotically stable in $C(\bar{\Omega}, \mathbb{R}_+)$. Moreover, if $d(x) = d$ and $n(x,w) = n(w)$ are independent of x, then $\bar{u}_1(x) = \bar{u}_1$ is also independent of x and $w^*(x) \equiv \bar{u}_1$, where $\bar{u}_1$ is defined in ($\boldsymbol{H}_2$).

Theorem 2.3. *For every initial condition $\varphi \in \mathcal{C}_\tau^+$, system (1.1) has a unique global solution $u(x,t) = (u_1(x,t), u_2(x,t), u_3(x,t)) \ge 0$ for $t \ge 0$, and all solutions are ultimately bounded in $\mathcal{C}_\tau^+$ with the ultimate bound independent of initial conditions.*

Proof. For any initial condition $\varphi \in \mathcal{C}_\tau^+$, the first equation of (1.1) yields $\partial u_1(x,t)/\partial t \le \nabla \cdot (d_1(x) \nabla u_1) + n(x, u_1(x,t))$. It follows from the comparison principle and Lemma 2.2 that $u_1(x,t) \le w(x,t)$ for all $t \in [0, \tau_{\max})$, where $w(x,t)$ is the solution of (2.1) with initial condition $w(x,0) = \varphi_1(x,0)$. Since $w(x,t) \to w^*(x)$ as $t \to \infty$, we have

$$\limsup_{t \to \infty} u_1(x,t) \le w^*(x) \;\; \text{uniformly for} \;\; x \in \bar{\Omega}. \tag{2.2}$$

Recalling the definitions of $T_i(t)$ $(i = 2, 3)$ from the beginning of Section 2 for the last two equations of (1.1), we have

$$u_2(x,t) = T_2(t)\varphi_2(\cdot,0) + \int_0^t T_2(t-s)\chi(\tau)[f(\cdot,u_{1,-\tau},u_{2,-\tau}) + g(\cdot,u_{1,-\tau},u_{3,-\tau})]ds$$

$$= T_2(t)\varphi_2(\cdot,0) + \int_{-\tau}^{t-\tau} T_2(t-\tau-s)\chi(\tau)[f(\cdot,u_1(\cdot,s),u_2(\cdot,s)) + g(\cdot,u_1(\cdot,s),u_3(\cdot,s))]ds,$$

$$u_3(x,t) = T_3(t)\varphi_3(\cdot,0) + \int_0^t T_3(t-s)ku_2(\cdot,s)ds.$$

Let $-\lambda_2 < 0$ be the principal eigenvalue of $\nabla\cdot(d_2\nabla) - \mu_2$ with the homogeneous Neumann boundary condition, and denote $\lambda_3 = \min\{\min_{x\in\bar\Omega}\mu_3(x), \lambda_2/2\} > 0$. We obtain $\|T_2(t)\| \le e^{-\lambda_2 t}$ and $\|T_3(t)\| \le e^{-\lambda_3 t}$. By $(\mathbf{H}_1)$ and continuity of $[\chi(\tau)1](x) = \int_\Omega K(x,y,\tau)dy$ in $\bar\Omega$, there exists $m_1 > 0$ such that

$$\chi(\tau)\left(f(\cdot,u_1(\cdot,s),u_2(\cdot,s)) + g(\cdot,u_1(\cdot,s),u_3(\cdot,s))\right) \le m_1\left(\|u_2(\cdot,s)\| + \|u_3(\cdot,s)\|\right)$$

for all $s \in [-\tau, t_{max})$. Consequently,

$$\begin{aligned}\|u_2(\cdot,t)\| &\le e^{-\lambda_2 t}\|\varphi_2\| + m_1\int_0^{t-\tau} e^{-\lambda_2(t-s)}\left(\|u_2(\cdot,s)\| + \|u_3(\cdot,s)\|\right)ds,\\ \|u_3(\cdot,t)\| &\le e^{-\lambda_3 t}\|\varphi_3\| + \bar k\int_0^t e^{-\lambda_3(t-s)}\|u_2(\cdot,s)\|ds,\end{aligned} \tag{2.3}$$

where $\bar k = \max_{x\in\bar\Omega} k(x)$. Substituting the second inequality into the first one gives

$$\|u_2(\cdot,t)\| \le C_1 + C_2\int_0^{t-\tau}\|u_2(\cdot,s)\|ds \le C_1 + C_2\int_0^t \|u_2(\cdot,s)\|ds \quad \text{for any} \quad t\in(0,t_{max}).$$

Thus, Gronwall's inequality implies that $\|u_2(\cdot,t)\| \le C_1 e^{C_2 t}$ for $t \in [0, t_{max})$. This together with the second inequality in (2.3) yields

$$\|u_3(\cdot,t)\| \le \|\varphi_3\| + \frac{\bar k C_1}{C_2}e^{C_2 t} \quad \text{for} \quad t\in[0,t_{max}).$$

By Lemma 2.1, $t_{max} = \infty$ and the solution $u(x,t)$ exists globally.

Next, we will prove that the solution is ultimately bounded by a constant independent of the initial condition. From the above argument, we have $\limsup_{t\to\infty} u_1(x,t) \le w^*(x)$. Especially, there exist $t_1 > 0$ and $M_1 > 0$ such that $u_1(x,t) \le M_1$ for all $x \in \Omega$ and $t \ge t_1$. By $(\mathbf{H}_3)$, there exists $m_2 > 0$ such that

$$f(x,u_1,u_2) + g(x,u_1,u_3) \le m_2(u_2+u_3),\ x\in\Omega,\ t\ge t_1. \tag{2.4}$$

To find the ultimate bound of $\|u_2(\cdot,t)\|_1$ and $\|u_3(\cdot,t)\|_1$, we denote $c_1 = \max_{y\in\bar\Omega} \int_\Omega K(x,y,\tau)dx$ and $\underline{\mu_2} = \min_{x\in\bar\Omega} \mu_2(x) > 0$. Here, c_1 is finite because $\int_\Omega K(x,y,\tau)dx$ is continuous for $y \in \bar\Omega$. By integrating the reaction-diffusion equations for u_1 and u_2, we obtain

$$\begin{aligned}
&\frac{\partial}{\partial t}\int_\Omega u_1 dx = \int_\Omega n(x,u_1(x,t))dx - \int_\Omega [f(x,u_1(x,t),u_2(x,t)) + g(x,u_1(x,t),u_3(x,t))]dx,\\
&\frac{\partial}{\partial t}\int_\Omega u_2 dx \le c_1 \int_\Omega [f(x,u_1(x,t-\tau),u_2(x,t-\tau))\\
&\qquad\qquad + g(x,u_1(x,t-\tau),u_3(x,t-\tau))]dx - \underline{\mu_2}\int_\Omega u_2 dx.
\end{aligned}$$

It then follows from $u_1(t-\tau) \le M_1$ and monotonicity of n in the second variable that

$$c_1\frac{\partial}{\partial t}\int_\Omega u_1(x,t-\tau)dx + \frac{\partial}{\partial t}\int_\Omega u_2(x,t)dx \le c_2 - \underline{\mu_2}[c_1\int_\Omega u_1(x,t-\tau)dx + \int_\Omega u_2(x,t)dx],$$

where $c_2 = \underline{\mu_2}c_1M_1|\Omega| + c_1\int_\Omega n(x,0)dx$. By comparison principle, $\limsup_{t\to\infty}\int_\Omega u_2(x,t)dx \le c_2/\underline{\mu_2}$. Especially, there exist $t_2 > t_1$ and $M_2 > 0$ such that $\|u_2(\cdot,t)\|_1 \le M_2$ for $t \ge t_2$. Similarly, we denote $\underline{\mu_3} = \min_{x\in\bar\Omega}\mu_3(x) > 0$ and obtain

$$\frac{\partial}{\partial t}\int_\Omega u_3 dx \le \bar{k}M_2 - \underline{\mu_3}\int_\Omega u_3 dx \quad \text{for} \quad t \ge t_2.$$

By comparison principle, there exist $t_3 > t_2$ and $M_3 > 0$ such that $\|u_3(\cdot,t)\|_1 \le M_3$ for $t \ge t_3$.

For $t > t_3$, we shall estimate $\|u_2(\cdot,t)\|_2$ and $\|u_3(\cdot,t)\|_2$. First, we multiply the equation for u_2 (resp. u_3) by u_2 (resp. u_3) and integrate on Ω. It follows from (2.4) and ($\mathbf{H}_3$) that

$$\begin{aligned}
&\frac{1}{2}\frac{\partial}{\partial t}\int_\Omega u_2^2 dx \le -\underline{d_2}\int_\Omega |\nabla u_2|^2dx + m_2\alpha(\tau)[\int_\Omega (2u_2^2(x,t) + u_2^2(x,t-\tau) + u_3^2(x,t-\tau))dx],\\
&\frac{1}{2}\frac{\partial}{\partial t}\int_\Omega u_3^2 dx \le \overline{k}\int_\Omega u_2u_3 dx - \underline{\mu_3}\int_\Omega u_3^2 dx,
\end{aligned}$$

where $\underline{d_2} = \min_{x\in\bar\Omega} d_2(x) > 0$. Adding the above two inequalities, and applying Young's inequality:

$$u_2u_3 \le \frac{\underline{\mu_3}}{4\overline{k}}u_3^2 + \frac{\overline{k}}{\underline{\mu_3}}u_2^2,$$

we have

$$\begin{aligned}
\frac{1}{2}\frac{\partial}{\partial t}\int_\Omega (u_2^2+u_3^2)dx \le &-\underline{d_2}\int_\Omega |\nabla u_2|^2dx + (2m_2\alpha(\tau) + \frac{\overline{k}^2}{\underline{\mu_3}})\int_\Omega u_2^2 dx\\
&+ m_2\alpha(\tau)[\int_\Omega (u_2^2(x,t-\tau) + u_3^2(x,t-\tau))dx] - \frac{3}{4}\underline{\mu_3}\int_\Omega u_3^2dx.
\end{aligned}$$

The Gagliardo-Nirenberg interpolation inequality guarantees the existence of $c > 0$ such that

$$\|w\|_2^2 \le \varepsilon \|\nabla w\|_2^2 + c\varepsilon^{-n/2} \|w\|_1^2$$

for any $w \in W^{1,2}(\Omega)$ and small $\varepsilon > 0$. Consequently, we obtain

$$\begin{aligned}\frac{1}{2}\frac{\partial}{\partial t}\int_\Omega (u_2^2 + u_3^2)dx \le & C_1 + C_2[\int_\Omega (u_2^2(x, t-\tau) + u_3^2(x, t-\tau))dx] \\ & - (C_2 + C_3)[\int_\Omega (u_2^2(x,t) + u_3^2(x,t))dx],\end{aligned}$$

for some generic positive constants C_1, C_2, C_3. A simple application of comparison principle gives $\limsup_{t\to\infty}[\int_\Omega (u_2^2(x,t) + u_3^2(x,t))dx] \le C_1/C_3$. Especially, there exist $t_4 > t_3$ and $M_4 > 0$ such that $\|u_2(\cdot,t)\|_2^2 + \|u_3(\cdot,t)\|_2^2 \le M_4$ for all $t \ge t_4$.

Denote $L_p = \limsup_{t\to\infty}(\|u_2(\cdot,t)\|_p^p + \|u_3(\cdot,t)\|_p^p)$. By using a similar argument as in the estimation of L_2, we obtain $L_{2p} \le Cp^{n/2}(L_p + 1)^2$, where C is a constant independent of p and initial condition φ. By a simple induction and limiting argument, we have $\limsup_{t\to\infty} u_i(x,t) \le M$ for all $x \in \Omega$ and $i = 1, 2, 3$, where M is a constant independent of the initial condition. This completes the proof. □

We now state the positivity of solutions of (1.1) and the persistence of $u_1(x,t)$.

Proposition 2.4. *Let $u(x,t) = (u_1(x,t), u_2(x,t), u_3(x,t))$ be the solution of system (1.1) with initial condition $\phi \in \mathcal{C}_\tau^+$.*

(i) We have $u_1(x,t) > 0$ for all $t > 0$ and $x \in \Omega$. Moreover, there exists a positive constant m_0 independent of ϕ such that $\liminf_{t\to\infty} u_1(x,t) \ge m_0$ uniformly for $x \in \bar{\Omega}$.

(ii) If there exists some $t_0 \ge 0$ such that either $u_2(\cdot,t_0) \not\equiv 0$ or $u_3(\cdot,t_0) \not\equiv 0$, then $u_i(x,t) > 0$ for all $i = 2, 3$, $t \ge t_0 + \tau$ and $x \in \Omega$.

Proof. (i) From the first equation of (1.1), it is easily seen that $u_1(x,t) > 0$ for $t > 0$ and $x \in \Omega$ by using the strong maximum principle [27]. From Theorem 2.3, it follows that there exist $t_1 > 0$ and $M > 0$ such that $u_i(x,t) < M$ for all $t > t_1$, $i = 1, 2, 3$ and $x \in \Omega$. Then the first equation of (1.1) and ($\mathbf{H}_3$) imply that, there exists some constant $c_0 > 0$ such that

$$\frac{\partial u_1(x,t)}{\partial t} \ge \nabla \cdot (d_1(x)\nabla u_1(x,t)) + n(x, u_1(x,t)) - c_0 u_1(x,t)$$

for all $t \ge t_1$. By Lemma 2.2 and comparison principle it follows that $u_1(x,t)$ is ultimately bounded below by the unique and strictly positive steady state $\bar{w}^*(x)$ of (2.1). Denote $m_0 = \min_{x\in\bar{\Omega}} \bar{w}^*(x) > 0$. Then $\limsup_{t\to\infty} u_1(x,t) \ge m_0$ for all $x \in \Omega$.

(ii) From the third equation of (1.1), we have

$$u_3(x,t) = e^{-\mu_3(x)(t-t_0)}u_3(x,t_0) + \int_{t_0}^{t} e^{-\mu_3(x)(t-s)}k(x)u_2(x,s)ds,$$

which, together with the assumptions that $u_2(\cdot,t_0) \not\equiv 0$ or $u_3(\cdot,t_0) \not\equiv 0$, implies that $u_3(\cdot,t) \not\equiv 0$ for any $t > t_0$ and sufficiently close to t_0. Then the strong maximum principle implies that $u_3(x,t) > 0$ for all $t > t_0$

and $x \in \Omega$. Similarly, we apply strong maximum principle to the equation for u_2 and obtain $u_2(x,t) > 0$ for all $t > t_0 + \tau$ and $x \in \Omega$. $\square$

3. Basic reproduction number

Note from Lemma 2.2 that (2.1) has a unique and strictly positive steady state $w^*(x)$. Thus, system (1.1) has a unique infection-free steady state $(w^*(x), 0, 0)$. For simplicity, we denote

$$\beta_d(x) = \frac{\partial f(x, w^*(x), 0)}{\partial u_2},\ \ \beta_i(x) = \frac{\partial g(x, w^*(x), 0)}{\partial u_3}, \tag{3.1}$$

where $\beta_d(x)$ and $\beta_i(x)$ are the direct and indirect transmission rates. Linearizing system (1.1) at $(w^*(x), 0, 0)$ gives a single equation for $u_1(x,t)$ and the following cooperative system for $(u_2(x,t), u_3(x,t))$:

$$\begin{aligned} \tfrac{\partial u_2}{\partial t} &= \nabla \cdot (d_2(x)\nabla u_2) + \chi(\tau)\beta_d(x)u_{2,-\tau} + \chi(\tau)\beta_i(x)u_{3,-\tau} - \mu_2(x)u_2, \\ \tfrac{\partial u_3}{\partial t} &= k(x)u_2 - \mu_3(x)u_3, \end{aligned} \tag{3.2}$$

for $x \in \Omega$ and $t > 0$, with the homogeneous Neumann boundary conditions. Now, we introduce two linear operators:

$$F = \begin{pmatrix} \chi(\tau) \circ \beta_d(\cdot) & \chi(\tau) \circ \beta_i(\cdot) \\ 0 & 0 \end{pmatrix},\ \ B = \begin{pmatrix} \nabla \cdot (d_2 \nabla) - \mu_2(\cdot) & 0 \\ k(\cdot) & -\mu_3(\cdot) \end{pmatrix},$$

and define the basic reproduction number R_0 as the spectral radius of $-FB^{-1}$; namely, $R_0 = r(-FB^{-1})$. Since B is resolvent-positive with $s(B) < 0$, where $s(B) = \sup\{\mathrm{Re}\lambda,\ \lambda \in \sigma(B)\}$ is the spectral bound of B, F is positive and $F + B$ is also resolvent-positive. It follows from [31, Theorem 3.5] that $R_0 - 1$ has the same sign as $s(F + B)$.

Let $\widehat{T}(t)$ be the solution semigroup of the linear system (3.2) with the infinitesimal generator denoted by $\widehat{A}$. Let $\omega(\widehat{T}) := \ln r(\widehat{T}(t))/t$ be the growth bound of $\widehat{T}$. It is well known (see [10, Chapter IV]) that $\omega(\widehat{T}) = \max\{s(\widehat{A}), \omega_e(\widehat{T})\}$, where $\omega_e(\widehat{T}) = (\ln r_e(\widehat{T}(t)))/t$ is the essential growth bound and r_e denotes the essential spectral radius. According to [17, Section 4], $s(\widehat{A})$ has the same sign as $s(F + B)$, which has the same sign as $R_0 - 1$. We have the following results.

Theorem 3.1. *(i) If $R_0 \geq 1$, then $s(\widehat{A}) \geq 0$ is the principal eigenvalue of $\widehat{A}$ with a strongly positive eigenfunction.*
(ii) If $R_0 \leq 1$, then there exists a constant $M_a > 0$ such that $\|\widehat{T}(t)\| \leq M_a$.
(iii) If $R_0 < 1$, then $\omega(\widehat{T}) < 0$.

Proof. We decompose $\widehat{T}(t) = \widehat{T}_2(t) + \widehat{T}_3(t)$, where

$$\widehat{T}_2(t)\hat{\phi} = \left(u_2(\cdot, t, \hat{\phi}), \int_0^t e^{-\mu_3(\cdot)(t-s)} k(\cdot) u_2(\cdot, s, \hat{\phi}) ds \right)$$

and $\widehat{T}_3(t)\hat{\phi} = (0, e^{-\mu_3(\cdot)t}\phi_3)$, for any continuous and nonnegative initial value $\hat{\phi} := (\phi_2, \phi_3)$. Since $\widehat{T}_2(t)$ is compact, we have

$$r_e(\widehat{T}(t)) = r_e(\widehat{T}_2(t) + \widehat{T}_3(t)) = r_e(\widehat{T}_3(t)) \leq e^{-\underline{\mu_3} t},$$

which implies that the essential growth bound $\omega_e(\widehat{T}) \leq -\underline{\mu_3} < 0$.

(i) If $R_0 \geq 1$, then $s(\widehat{A}) \geq 0$ and the spectral radius $r(\widehat{T}(t)) = e^{s(\widehat{A})t} \geq 1 > r_e(\widehat{T}(t))$. By generalized Krein-Rutman Theorem [24], $e^{s(\widehat{A})t}$ is the principal eigenvalue of $\widehat{T}(t)$ with a positive eigenfunction. Consequently, $s(\widehat{A})$ is the principal eigenvalue of $\widehat{A}$ with the same eigenfunction.

(ii) If $R_0 \leq 1$, then $s(\widehat{A}) \leq 0$ and $\omega(\widehat{T}) \leq 0$. Especially, there exists a constant $M_a > 0$ such that $\|\widehat{T}(t)\| \leq M_a$.

(iii) If $R_0 < 1$, then $s(\widehat{A}) < 0$ and $\omega(\widehat{T}) < 0$. $\square$

To derive an equivalent formula and biologically relevant expression of R_0, we first calculate that

$$-B^{-1} = \begin{pmatrix} (\mu_2 - \nabla \cdot (d_2 \nabla))^{-1} & 0 \\ \mu_3^{-1} k(\mu_2 - \nabla \cdot (d_2 \nabla))^{-1} & \mu_3^{-1} \end{pmatrix}.$$

Consequently, we have

$$-FB^{-1} = \begin{pmatrix} \chi(\tau) \circ \beta_d(\mu_2 - \nabla \cdot (d_2\nabla))^{-1} + \chi(\tau) \circ \beta_i \mu_3^{-1} k(\mu_2 - \nabla \cdot (d_2\nabla))^{-1} & \chi(\tau) \circ \beta_i \mu_3^{-1} \\ 0 & 0 \end{pmatrix},$$

which implies

$$R_0 = r(-FB^{-1}) = r\left(A_d + A_i\right), \tag{3.3}$$

where

$$A_d = \chi(\tau) \circ \beta_d(\mu_2 - \nabla \cdot (d_2\nabla))^{-1}, \quad A_i = \chi(\tau) \circ \beta_i \mu_3^{-1} k(\mu_2 - \nabla \cdot (d_2\nabla))^{-1}$$

are the next generation operators for direct and indirect transmission, respectively.

If the kernel function $K(x, y, \tau)$ is a constant multiplication of delta function such that $(\chi(\tau) \circ \psi)(x) = \rho(\tau)\psi(x)$, we have a variational formula for the basic reproduction number

$$R_0 = r(A_d + A_i) = \sup_{\psi \in H^1(\Omega), \psi \neq 0} \frac{\int_\Omega \rho(\tau) \left(\beta_d(x) + \beta_i(x)\mu_3^{-1}(x)k(x)\right) \psi^2(x) dx}{\int_\Omega \left(d_2(x)|\nabla\psi(x)|^2 + \mu_2(x)\psi^2(x)\right) dx}. \tag{3.4}$$

Note that the basic reproduction number for the direct transmission without indirect transmission is

$$R_0^d = r(A_d) = \sup_{\psi \in H^1(\Omega), \psi \neq 0} \frac{\int_\Omega \rho(\tau)\beta_d(x)\psi^2(x) dx}{\int_\Omega \left(d_2(x)|\nabla\psi(x)|^2 + \mu_2(x)\psi^2(x)\right) dx}.$$

On the other hand, in the absence of direct transmission, the basic reproduction number for indirect transmission is given by

$$R_0^i = r(A_i) = \sup_{\psi \in H^1(\Omega), \psi \neq 0} \frac{\int_\Omega \rho(\tau)\beta_i(x)\mu_3^{-1}(x)k(x)\psi^2(x) dx}{\int_\Omega \left(d_2(x)|\nabla\psi(x)|^2 + \mu_2(x)\psi^2(x)\right) dx}.$$

Clearly, $R_0 \leq R_0^d + R_0^i$. To analyze the property of the basic reproduction number R_0, we further assume that d_2 is a constant function on $\bar{\Omega}$. By Krein-Rutman theorem, R_0 is the principal eigenvalue of $A_d + A_i$ with a positive eigenfunction, denoted by $\xi(x)$; namely,

$$\begin{aligned} &\rho(\tau)\beta_d(\mu_2 - \nabla \cdot (d_2\nabla))^{-1}\xi + \rho(\tau)\beta_i(x)\frac{k(x)}{\mu_3(x)}(\mu_2 - \nabla \cdot (d_2\nabla))^{-1}\xi = R_0\xi, \quad x \in \Omega, \\ &\nabla\xi(x) \cdot \nu = 0, \ x \in \partial\Omega, \end{aligned}$$

which can be rewritten as

$$\begin{aligned} &d_2\Delta\xi - \mu_2\xi + \frac{\rho(\tau)\beta_d + \rho(\tau)\beta_i\mu_3^{-1}k}{R_0}\xi = 0, \quad x \in \Omega, \\ &\nabla\xi(x)\cdot\nu = 0, \ x \in \partial\Omega. \end{aligned} \tag{3.5}$$

We obtain the following result.

Theorem 3.2. *Assume that $(\chi(\tau)\circ\psi)(x) = \rho(\tau)\psi(x)$ and d_2 is independent of x. Then R_0 is a monotone decreasing function of d_2 and τ. Moreover, we have*

$$\begin{aligned} &R_0 \to \overline{R}_0 := \max_{x\in\bar{\Omega}}\left\{\frac{\rho(\tau)\beta_d(x)}{\mu_2(x)} + \frac{\rho(\tau)\beta_i(x)k(x)}{\mu_2(x)\mu_3(x)}\right\} \quad as \quad d_2 \to 0, \\ &R_0 \to \underline{R}_0 := \frac{\int_\Omega \left(\rho(\tau)\beta_d(x) + \rho(\tau)\beta_i(x)\mu_3^{-1}(x)k(x)\right)dx}{\int_\Omega \mu_2(x)dx} \quad as \quad d_2 \to \infty. \end{aligned}$$

Proof. (i) We observe that R_0 is a decreasing function of d_2 and τ. We claim that $R_0 \le \overline{R}_0$ for all $d_2 > 0$; otherwise, $-\mu_2 + \rho(\tau)(\beta_d + \beta_i\mu_3^{-1}k)/R_0 < 0$ for some $d_2 > 0$, and consequently, the principal eigenvalue of $d_2\Delta - \mu_2 + \rho(\tau)(\beta_d + \beta_i\mu_3^{-1}k)/R_0$ is negative, which contradicts (3.5). Thus, $\lim_{d_2\to 0} R_0 \le \overline{R}_0$. To show that the equality holds, we assume to the contrary that there exists $\epsilon > 0$ such that $R_0 < \overline{R}_0 - \epsilon$ for all positive d_2. By continuity, there exist $x_0 \in \Omega$, $\delta > 0$ and $\epsilon_0 > 0$ such that

$$-\mu_2 + \frac{\rho(\tau)\beta_d + \rho(\tau)\beta_i\mu_3^{-1}k}{R_0} > \epsilon_0 \ \text{ for all } \ x \in B_\delta(x_0).$$

This together with (3.5) implies that $-\Delta\xi > \epsilon_0\xi/d_2$ for $x \in B_\delta(x_0)$. Denote $\psi_+(x) = \xi(x)/\min_{x\in B_\delta(x_0)}\xi(x)$. Then we have $-\Delta\psi_+(x) > \epsilon_0\psi_+(x)/d_2$ and $\psi_+(x) \ge 1$ in $B_\delta(x_0)$. Let $\eta > 0$ be the principal eigenvalue of $-\Delta$ on $B_\delta(x_0)$ with Neumann boundary condition and $\psi_-(x)$ the corresponding eigenfunction such that $\psi_-(x) \le 1$ on $B_\delta(x_0)$. Then, we obtain $-\Delta\psi_-(x) = \eta\psi_-(x) < \epsilon_0\psi_-(x)/d_2$ for all $d_2 < \epsilon_0/\eta$. Thus, $\psi_+(x)$ and $\psi_-(x)$ are the super- and sub-solutions of $-\Delta\varphi = \epsilon_0\varphi/d_2$ with Neumann boundary condition. Hence, ϵ_0/d_2 is an eigenvalue of $-\Delta$ on $B_\delta(x_0)$ with Neumann boundary condition, which contradicts the fact that $\epsilon_0/d_2 > \eta$ and η is the principal eigenvalue. Therefore, $R_0 \to \overline{R}_0$ as $d_2 \to 0$.

(ii) Note from (3.4) that $R_0 \ge \underline{R}_0$ for all $d_2 > 0$. Hence, $\lim_{d_2\to\infty} R_0 \ge \underline{R}_0$. As $d_2 \to \infty$, the normalized eigenfunction ξ converges to a positive constant function by elliptic regularity [11]. Integrating (3.5) and then passing to the limit $d_2 \to \infty$ imply $R_0 \to \underline{R}_0$. This completes the proof. □

A direct application of the above theorem is the following classification of infection environment.

Corollary 3.3. *Assume that $(\chi(\tau)\circ\psi)(x) = \rho(\tau)\psi(x)$ and d_2 is independent of x. $\beta_d(x), \beta_i(x)$ are defined in* (3.1).

(i) If $\rho(\tau)\beta_d(x)/\mu_2(x) + \rho(\tau)\beta_i(x)k(x)/(\mu_2(x)\mu_3(x)) \le 1$ for all $x \in \Omega$, then $R_0 < 1$ for all $d_2 > 0$ and Ω is an infection-free environment.

(ii) If $\int_\Omega(\rho(\tau)\beta_d(x) + \rho(\tau)\beta_i(x)\mu_3^{-1}(x)k(x))dx \ge \int_\Omega \mu_2(x)dx$, then $R_0 > 1$ for all $d_2 > 0$ and Ω is a favorable environment for infection.

(iii) If $\int_\Omega(\rho(\tau)\beta_d(x) + \rho(\tau)\beta_i(x)\mu_3^{-1}(x)k(x))dx < \int_\Omega \mu_2(x)dx$ and $\rho(\tau)\beta_d(x)/\mu_2(x) + \rho(\tau)\beta_i(x)k(x)/(\mu_2(x)\mu_3(x)) > 1$ for some $x \in \Omega$, then there exists $d_2^* > 0$ such that $R_0 \le 1$ if $d_2 \ge d_2^*$ and $R_0 > 1$ if $d_2 < d_2^*$.

4. Global dynamics of the system

4.1. Global attractor

Define the continuous semiflow $\{\Phi(t)\}_{t\geq 0} : \mathcal{C}_\tau^+ \to \mathcal{C}_\tau^+$ of system (1.1) by

$$\Phi(t)\phi := u(\cdot, t+\cdot, \phi), \quad t \geq 0.$$

Note that the semiflow $\Phi(t)$ of system (1.1) is not compact because the third equation has no diffusion term. However, we will show that $\Phi(t)$ is a κ-contraction. First, recall Kuratowski measure of the noncompactness [13] defined by:

$$\kappa(B) := \inf\{d \geq 0 : B \text{ has a finite cover of diameter less than } d\}$$

for any bounded $B \subseteq \mathcal{C}_\tau^+$. We set $\kappa(B) = \infty$ whenever B is unbounded. Obviously, B is precompact if and only if $\kappa(B) = 0$. Next, we decompose $\Phi(t) = \Phi_1(t) + \Phi_2(t)$, where

$$(\Phi_1(t)u_0)(x,\theta) = \left(u_1(x, t+\theta, u_0), u_2(x, t+\theta, u_0), \int_0^{t+\theta} e^{-\mu_3(x)(t+\theta-s)} k(x) u_2(x, s; u_0) ds \right),$$

$$(\Phi_2(t)u_0)(x,\theta) = (0, 0, e^{-\mu_3(x)(t+\theta)} u_{30}(0)),$$

for $x \in \Omega$, $\theta \in [-\tau, 0]$, $t \geq \tau$, and any initial data $u_0 = (u_{10}, u_{20}, u_{30}) \in \mathcal{C}_\tau^+$. Similar as in [38, Lemma 2.5], we can show that $\Phi_1(t)$ is compact for $t > \tau$. Let $B \subseteq \mathcal{C}_\tau^+$ be a bounded set. Then we have $\kappa(\Phi_1(t)B) = 0$ for any $t > 0$. Consequently,

$$\kappa(\Phi(t)B) \leq \kappa(\Phi_1(t)B) + \kappa(\Phi_2(t)B) = \kappa(\Phi_2(t)B) \leq e^{-\underline{\mu_3} t} \kappa(B)$$

for $t > 0$, which proves that $\Phi(t)$ is a κ-contraction. This implies that $\Phi(t)$ is asymptotically smooth. Note from Theorem 2.3 that $\Phi(t)$ is point dissipative. By [13, Theorem 2.4.6], we have the following result.

Theorem 4.1. *System (1.1) admits a connected global attractor in $\mathcal{C}_\tau^+$.*

4.2. Persistence of infection and existence of positive steady states

Let R_0 be defined in (3.3). If $R_0 > 1$, we apply the permanence theorem in [30, Theorem 3] to obtain persistence of infection. Denote

$$\mathbb{Z}_0 := \{\phi = (\phi_1, \phi_2, \phi_3) \in \mathcal{C}_\tau^+ : \ \phi_2(\cdot, 0) \not\equiv 0 \text{ and } \phi_3(\cdot, 0) \not\equiv 0\}$$

and

$$\partial\mathbb{Z}_0 := \mathcal{C}_\tau^+ \backslash \mathbb{Z}_0 = \{\phi = (\phi_1, \phi_2, \phi_3) \in \mathcal{C}_\tau^+ : \ \phi_2(\cdot, 0) \equiv 0 \text{ or } \phi_3(\cdot, 0) \equiv 0\}.$$

Obviously, $\mathbb{Z}_0 \cap \partial\mathbb{Z}_0 = \emptyset$, $\mathcal{C}_\tau^+ = \mathbb{Z}_0 \cup \partial\mathbb{Z}_0$, $\mathbb{Z}_0$ is open and dense in $\mathcal{C}_\tau^+$, and $\Phi(t)\partial\mathbb{Z}_0 \subseteq \partial\mathbb{Z}_0$. It then follows from Proposition 2.4(ii) and the maximum principle that $\Phi(t)\mathbb{Z}_0 \subseteq \mathbb{Z}_0$, that is, $\mathbb{Z}_0$ is positively invariant with respect to $\Phi(t)$. Let M_∂ be the largest positively invariant set of $\Phi(t)$ in $\partial\mathbb{Z}_0$, i.e.

$$M_\partial := \{\phi \in \partial\mathbb{Z}_0 : \Phi(t)\phi \in \partial\mathbb{Z}_0 \ \text{ for any } \ t \geq 0\}.$$

By the strong maximum principle, for any $\phi \in M_\partial$, we have $u_i(\cdot, t, \phi) \equiv 0$ with $i = 2, 3$ for all $t \geq 0$. Thus, we obtain

$$M_\partial = \{\phi = (\phi_1, \phi_2, \phi_3) \in \mathcal{C}_\tau^+ : \ \phi_2(\cdot, 0) \equiv 0 \text{ and } \phi_3(\cdot, 0) \equiv 0\}.$$

This together with Lemma 2.2 implies that $\lim_{t\to\infty} u_1(x, t, \phi) = w^*(x)$ for any $\phi \in M_\partial$. Hence, $\omega(\phi) = \{(w^*(x), 0, 0)\}$ for all $\phi \in M_\partial$, where $\omega(\phi)$ is the omega limit set of the orbit $\gamma^+(\phi) := \bigcup_{t\geq 0} \{\Phi(t)\phi\}$. We now define a continuous function $d : \mathcal{C}_\tau^+ \to [0, \infty)$ by

$$d(\phi) = \min\{\phi_i(x, 0) : x \in \bar{\Omega}, i = 2, 3\} \ \text{ for any } \ \phi \in \mathcal{C}_\tau^+.$$

It is obvious that $d(\Phi(t)\phi) > 0$ for all $t > 0$ and every $\phi \in d^{-1}(0, \infty) \cup (\mathbb{Z}_0 \cap d^{-1}(0))$. Thus, $d(x)$ is a generalized distance function for the semiflow $\Phi(t)$; see [30, Theorem 3].

We next verify that the stable manifold of $(w^*(x), 0, 0)$ does not intersect $d^{-1}(0, \infty)$ if $R_0 > 1$. Suppose to the contrary that $\Phi(t)\tilde{\phi} = (u_1(\cdot, t, \tilde{\phi}), u_2(\cdot, t, \tilde{\phi}), u_3(\cdot, t, \tilde{\phi})) \to (w^*(x), 0, 0)$ for some $\tilde{\phi} \in d^{-1}(0, \infty)$. For any small $\delta > 0$, there exists $\tilde{t} > 0$ such that

$$f(x, u_1, u_2) > (\beta_d - \delta)u_2, \quad g(x, u_1, u_3) > (\beta_i - \delta)u_3,$$

for all $t \geq \tilde{t} - \tau$ and $x \in \Omega$. Similarly to the proof of Theorem 3.1(i), we can show that the eigenvalue problem

$$\begin{aligned}
\frac{\partial \varphi_2(x,t)}{\partial t} &= \nabla \cdot (d_2(x)\nabla\varphi_2) + \chi(\tau)(\beta_d - \delta)\varphi_{2,-\tau} + \chi(\tau)(\beta_i - \delta)\varphi_{3,-\tau} - \mu_2(x)\varphi_2, \\
\frac{\partial \varphi_3(x,t)}{\partial t} &= k(x)\varphi_2(x,t) - \mu_3(x)\varphi_3(x,t),
\end{aligned}$$

with Neumann boundary condition has a principal eigenvalue λ_δ with a strongly positive eigenfunction $(\varphi_2^\delta, \varphi_3^\delta)$. Since $R_0 > 1$, it follows from Theorem 3.1 that $\lambda_0 = s(\widehat{A}) > 0$. By continuity of λ_δ in δ, we can choose $\delta > 0$ small enough such that $\lambda_\delta > 0$. On the other hand, for $t \geq \tilde{t}$, we have

$$\begin{aligned}
\frac{\partial u_2(x,t)}{\partial t} &> \nabla \cdot (d_2(x)\nabla u_2) + \chi(\tau)(\beta_d - \delta)u_{2,-\tau} + \chi(\tau)(\beta_i - \delta)u_{3,-\tau} - \mu_2(x)u_2, \\
\frac{\partial u_3(x,t)}{\partial t} &= k(x)u_2(x,t) - \mu_3(x)u_3(x,t).
\end{aligned}$$

Since $u_i(x, t, \widetilde{\phi}) > 0$ for all $x \in \bar{\Omega}, t > 0, i = 2, 3$, we can choose $\varepsilon > 0$ sufficiently small such that $(u_2(\cdot, t, \widetilde{\phi}), u_3(\cdot, t, \widetilde{\phi})) \geq \varepsilon(\varphi_2^\delta, \varphi_3^\delta)$ for all $t \in [\tilde{t} - \tau, \tilde{t}]$. By the comparison principle we obtain

$$(u_2(\cdot, t, \widetilde{\phi}), u_3(\cdot, t, \widetilde{\phi})) \geq \varepsilon e^{\lambda_\delta(t - \widetilde{t})}(\varphi_2^\delta, \varphi_3^\delta) \ \text{ for all } \ t > \widetilde{t},$$

a contradiction. It then follows from Proposition 2.4(i) and the abstract persistence theory in [30, Theorem 3] that $\Phi(t)$ is uniformly persistent. Moreover, by [19, Theorem 4.7], $\Phi(t)$ possesses at least one positive steady state $(u_1^*(x), u_2^*(x), u_3^*(x))$, which we refer to as a pathogen persistent steady state. We summarize the above results in the following theorem.

Theorem 4.2. *If $R_0 > 1$, then there exists $\eta > 0$ such that for any $\phi = (\phi_1, \phi_2, \phi_3) \in \mathcal{C}_\tau^+$ with $\phi_2 \not\equiv 0$ or $\phi_3 \not\equiv 0$, we have*

$$\liminf_{t\to\infty} u_i(x, t, \phi) \geq \eta \ (i = 1, 2, 3) \ \ \textit{uniformly for all} \ \ x \in \bar{\Omega}.$$

Moreover, system (1.1) admits at least one positive steady state $(u_1^*(x), u_2^*(x), u_3^*(x))$.

4.3. Global stability of the infection-free steady state when $R_0 \le 1$

It follows from [36, Theorem 3.1] that the infection-free steady state $(w^*(x), 0, 0)$ is locally asymptotically stable when $R_0 < 1$. To establish the global asymptotic stability of the infection-free steady state when $R_0 < 1$, we need the following result.

Theorem 4.3. *Assume that* $R_0 < 1$. *Then the infection-free steady state* $(w^*(x), 0, 0)$ *of* (1.1) *is globally attractive.*

Proof. By (2.2), for any $\delta > 0$, there exists $t_0 > 0$ such that $0 \le u_1 \le w^* + \delta$ for all $t > t_0$. For any $\varepsilon_0 > 0$, in view of ($\mathbf{H}_3$), we can choose δ sufficiently small such that

$$f(x, u_1, u_2) < (\beta_d + \varepsilon_0)u_2, \quad g(x, u_1, u_3) < (\beta_i + \varepsilon_0)u_3,$$

for any $0 \le u_1 \le w^* + \delta$, $u_2 > 0$, $u_3 > 0$ and $x \in \Omega$. Let $T_0(t)$ be the solution semigroup of the linear system

$$\begin{aligned} \frac{\partial u_2(x,t)}{\partial t} &= \nabla \cdot (d_2(x)\nabla u_2) + \chi(\tau)(\beta_d + \varepsilon_0)u_{2,-\tau} + \chi(\tau)(\beta_i + \varepsilon_0)u_{3,-\tau} - \mu_2(x)u_2, \\ \frac{\partial u_3(x,t)}{\partial t} &= k(x)u_2(x,t) - \mu_3(x)u_3(x,t), \end{aligned} \tag{4.1}$$

with the homogeneous Neumann boundary conditions. Since $R_0 < 1$, it follows from Theorem 3.1(iii) that the growth bound $\omega(\widehat{T}) < 0$. By choosing ε_0 sufficiently small, we have $\omega(T_0) < 0$ and any solution of the above linear system converges to $(0, 0)$. Let $(\hat{u}_2(x,t), \hat{u}_3(x,t))$ be the solution of the problem (4.1) for $t > t_0$ with the initial conditions $(\hat{u}_2(x,t), \hat{u}_3(x,t)) = (u_2(x,t), u_3(x,t))$ for $x \in \Omega$ and $t \in [t_0 - \tau, t_0]$. By the comparison principle, we have $(u_2(x,t), u_3(x,t)) \le (\hat{u}_2(x,t), \hat{u}_3(x,t)) \to (0, 0)$ as $t \to \infty$ uniformly for $x \in \bar{\Omega}$. This together with Lemma 2.2 implies that $u_1(x,t) \to w^*(x)$ as $t \to \infty$ uniformly for $x \in \bar{\Omega}$. The proof is completed. □

The critical case $R_0 = 1$ requires a special treatment.

Theorem 4.4. *If* $R_0 = 1$, *then the infection-free steady state* $(w^*(x), 0, 0)$ *of* (1.1) *is globally asymptotically stable.*

Proof. First, we prove that the infection-free steady state $(w^*(x), 0, 0)$ is locally asymptotically stable. Let $\delta > 0$ be an arbitrary small number and $u(x,t)$ be the solution with initial condition in the δ neighborhood of the infection-free steady state:

$$\max_{\theta \in [-\tau, 0]} [\|u_1(\cdot, \theta) - w^*(x)\| + \|u_2(\cdot, \theta)\| + \|u_3(\cdot, \theta)\|] < \delta.$$

By the comparison principle, there exists $M_1 > 0$ such that $u_1(x,t) < M_1$ for all $x \in \Omega$ and $t \ge -\tau$. Since $\omega(x,t) = u_1(x,t) - w^*(x)$ satisfies

$$\frac{\partial \omega}{\partial t} \le \nabla \cdot (d_1(x)\nabla\omega(x,t)) - \underline{\mu}_1\omega,$$

where $\underline{\mu}_1$ is the minimum of $-\frac{\partial n(x,u_1)}{\partial u_1}$ for $x \in \bar{\Omega}$ and $0 \le u_1 \le M_1$, we obtain

$$u_1(x,t) - w^*(x) = \omega(x,t) \le \widetilde{M}\delta e^{-\lambda_1 t},$$

where $-\lambda_1 < 0$ is the principal eigenvalue of the differential operator $\nabla\cdot(d_1(\cdot)\nabla) - \underline{\mu}_1$ with the homogeneous Neumann boundary condition, and $\widetilde{M} > 0$ is a constant that depends on the semigroup generated by such operator.

Recall that $\widehat{T}(t)$ is the solution semigroup of the linear system (3.2) with the infinitesimal generator denoted by $\widehat{A}$. Moreover, since $R_0 = 1$, we have from Theorem 3.1(ii) that $\|\widehat{T}(t)\| \le M_a$ for some $M_a > 0$. Denote

$$q = \chi(\tau)(f(x,u_1,u_2) - \beta_d u_2 + g(x,u_1,u_3) - \beta_i u_3).$$

We have

$$\begin{pmatrix} u_2(\cdot,t) \\ u_3(\cdot,t) \end{pmatrix} = \widehat{T}(t)\begin{pmatrix} u_2(\cdot,0) \\ u_3(\cdot,0) \end{pmatrix} + \int_0^t \widehat{T}(t-s)\begin{pmatrix} q(\cdot,s-\tau) \\ 0 \end{pmatrix} ds.$$

On account of $(\mathbf{H}_3)$ and $u_1(x,t) - w^*(x) \le \widetilde{M}\delta e^{-\lambda_1 t}$, we obtain

$$q \le \widetilde{M}\delta e^{-\lambda_1 t}(\overline{f}u_2 + \overline{g}u_3),$$

where

$$\bar{f} = \max_{0\le u_1\le M_1}\left|\frac{\partial^2 f(u_1,0)}{\partial u_1\partial u_2}\right|, \quad \bar{g} = \max_{0\le u_1\le M_1}\left|\frac{\partial^2 g(u_1,0)}{\partial u_1\partial u_3}\right|.$$

Denote

$$E(t) = \max\left\{\max_{x\in\bar{\Omega}} u_2(x,t), \max_{x\in\bar{\Omega}} u_3(x,t)\right\}.$$

It follows that $E(\theta) \le \delta$ for all $\theta \in [-\tau, 0]$ and

$$E(t) \le \delta M_a + \delta M_a(\bar{f} + \bar{g})\widetilde{M}\int_0^t e^{-\lambda_1(s-\tau)}E(s-\tau)ds.$$

By Gronwall's inequality, we obtain $E(t) = O(\delta)$. It remains to prove $w^* - u_1(\cdot,t) = O(\delta)$ as $\delta \to 0$. By $(\mathbf{H}_3)$, we have

$$f(x,u_1,u_2) \le \frac{\partial f(x,M_1,0)}{\partial u_2}u_2 = O(\delta), \quad g(x,u_1,u_3) \le \frac{\partial g(x,M_1,0)}{\partial u_3}u_3 = O(\delta).$$

Thus, it follows from the above inequalities and the first equation of (1.1) that

$$\frac{\partial[w^*(x) - u_1(x,t)]}{\partial t} \le \nabla\cdot(d_1(x)\nabla[w^*(x) - u_1(x,t)]) - \underline{\mu}_1[w^*(x) - u_1(x,t)] + Q\delta,$$

where $Q > 0$ is a large constant. By the comparison principle, $w^*(x) - u_1(x,t) \le Q\delta/\underline{\mu}_1$. Therefore, $\|u_1(\cdot,t) - w^*(\cdot)\| + \|u_2(\cdot,t)\| + \|u_3(\cdot,t)\| = O(\delta)$ as $\delta \to 0$, which implies the local asymptotic stability of $(w^*(x), 0, 0)$.

Next, we prove the global attractivity of $(w^*(x), 0, 0)$ in the positively invariant set $D := \{\phi = (\phi_1, \phi_2, \phi_3) \in \mathcal{C}_\tau^+ : \phi_1 \leq w^*\}$. Let $u = (u_1, u_2, u_3)$ be the solution of (1.1) with the initial data $\phi = (\phi_1, \phi_2, \phi_3) \in D$. If $\phi_2 \equiv 0$ and $\phi_3 \equiv 0$, it follows from Lemma 2.2 that $(u_1, u_2, u_3) \to (w^*(x), 0, 0)$. Now, we assume that $\phi_2 \not\equiv 0$ or $\phi_3 \not\equiv 0$. Proposition 2.4 implies that $u_i > 0$ for all $t > \tau$. Since $R_0 = 1$, 0 is the principal eigenvalue of $F + B$ with a positive eigenfunction; namely, there exists $(\varphi, \psi) > 0$ such that

$$\begin{aligned}
0 &= \nabla \cdot [d_2(x)\varphi(x)] - \mu_2(x)\varphi(x) + \chi(\tau)[\beta_d(x)\varphi(x) + \beta_i(x)\psi(x)], \\
0 &= k(x)\varphi(x) - \mu_3(x)\psi(x).
\end{aligned}$$

We introduce

$$c(t; u) = \max\left\{ \max_{x\in\bar{\Omega},\theta\in[-\tau,0]} \frac{u_2(x, t+\theta)}{\varphi(x)}, \max_{x\in\bar{\Omega},\theta\in[-\tau,0]} \frac{u_3(x, t+\theta)}{\psi(x)} \right\}.$$

Since $u_1 \leq w^*$, we obtain from $(\mathbf{H}_3)$ that $f(x, u_1, u_2) < \beta_d u_2$ and $g(x, u_1, u_3) < \beta_i u_3$ for all $x \in \Omega$. Consequently, we have

$$\begin{aligned}
\frac{\partial u_2(x,t)}{\partial t} &< \nabla \cdot (d_2(x)\nabla u_2(x,t)) - \mu_2(x)u_2(x,t) + \chi(\tau)[\beta_d u_2(\cdot, t-\tau) + \beta_i u_3(\cdot, t-\tau)](x), \\
\frac{\partial u_3(x,t)}{\partial t} &= k(x)u_2(x,t) - \mu_3(x)u_3(x,t).
\end{aligned}$$

By the strong maximum principle, $u_2(x,t) < c(t_1; u)\varphi(x)$ and $u_3(x,t) < c(t_1; u)\psi(x)$ for all $t > t_1 > \tau$. Thus, $c(t; \phi_0)$ is strictly decreasing and $c^* := \lim_{t\to\infty} c(t; \phi_0) \geq 0$ exists. We claim that $c^* = 0$. Otherwise, there exist $t_k \to \infty$ such that $\Phi_{t+t_k}(\phi) \to U = (U_1, U_2, U_3) \in D$ and either U_2 or U_3 is not a zero function. By a similar argument as above, we can define $c(t, U)$ and show that $c(t, U)$ is strictly decreasing. However, $c(t, U) = \lim_{k\to\infty} c(t + t_k, u) = c^*$, a contradiction. So, we have $c^* = 0$. Especially, $u_2(x,t) \to 0$ and $u_3(x,t) \to 0$ as $t \to 0$. Since the limiting system when $u_2 \equiv 0$ and $u_3 \equiv 0$ has a unique globally attractive steady state w^*, it follows from [31, Theorem 4.1] that $(w^*(x), 0, 0)$ is globally attractive in D.

Finally, given any $\phi \in \mathcal{C}_\tau^+$, the comparison principle shows that the omega limit set $\omega(\phi) \subset D$. This together with [39, Theorem 1.2.1] implies that $(w^*(x), 0, 0)$ is globally attractive in $\mathcal{C}_\tau^+$. The proof is completed. □

5. Spatially homogeneous case

For the spatially heterogeneous case, we obtain persistence of infection and existence of at least one positive infection steady state if $R_0 > 1$. To achieve uniqueness and global asymptotic stability of the positive infection steady state, we require that the model parameters are spatially homogeneous; namely, we assume that d_1, d_2, μ_2, μ_3 and k are constants, and $n(x, u_1) = n(u_1)$ is independent of x. It is readily seen that β_d and β_i are constants, and $w^*(x) = \bar{u}_1$, where $\bar{u}_1$ is the unique positive solution of $n(u_1) = 0$. Assume further that $\chi(\tau)$ is a constant multiplication of delta function: $(\chi(\tau) \circ \psi)(x) = \rho(\tau)\psi(x)$. It then follows from (3.3) and Theorem 3.2 that

$$R_0 = \overline{R}_0 = \underline{R}_0 = \frac{\rho(\tau)\beta_d}{\mu_2} + \frac{\rho(\tau)\beta_i k}{\mu_2\mu_3} \tag{5.1}$$

is independent of the diffusion coefficient d_2. First, we shall establish the existence of a positive homogeneous steady state, which satisfies the algebraic system

$$n(u_1) = f(u_1, u_2) + g(u_1, u_3) = \frac{\mu_2}{\rho(\tau)} u_2 = \frac{\mu_2\mu_3}{k\rho(\tau)} u_3.$$

Eliminating u_2 and u_3, we obtain

$$G(u_1) := f(u_1, \frac{\rho(\tau)}{\mu_2} n(u_1)) + g(u_1, \frac{\rho(\tau)k}{\mu_2\mu_3} n(u_1)) - n(u_1) = 0.$$

Obviously, $G(0) = -n(0) < 0$ and $G(\bar{u}_1) = 0$. Moreover, it is easy to calculate that $G'(\bar{u}_1) = (R_0 - 1)n'(\bar{u}_1) < 0$. Hence, there exists $u_1^* \in (0, \bar{u}_1)$ such that $G(u_1^*) = 0$. Consequently,

$$u_2^* = \frac{\rho(\tau)}{\mu_2} n(u_1^*) > 0, \quad u_3^* = \frac{\rho(\tau)k}{\mu_2\mu_3} n(u_1^*) > 0.$$

This proves the existence of a positive homogeneous steady state $u^* = (u_1^*, u_2^*, u_3^*)$. To obtain the global attractivity of this steady state, we need another assumption:

$$f(u_1, u_2) = u_1 f_1(u_2), \quad g(u_1, u_3) = u_1 g_1(u_3). \tag{5.2}$$

Denote $h(z) = z - 1 - \ln z$. Clearly, $h(z) \geq 0$ for $z > 0$, and $h(z) = 0$ if and only if $z = 1$. We introduce the Lyapunov functional

$$\begin{aligned}\mathcal{L}(\phi) := \int_\Omega \Bigg\{ \int_{-\tau}^{0} &\left[u_1^* f_1(u_2^*) h\left(\frac{\phi_1(x,\theta) f_1(\phi_2(x,\theta))}{u_1^* f_1(u_2^*)} \right) + u_1^* g_1(u_3^*) h\left(\frac{\phi_1(x,\theta) g_1(\phi_3(x,\theta))}{u_1^* g_1(u_3^*)} \right) \right] d\theta \\ &+ u_1^* h\left(\frac{\phi_1(x,0)}{u_1^*} \right) + \frac{u_2^*}{\rho(\tau)} h\left(\frac{\phi_2(x,0)}{u_2^*} \right) + \frac{u_1^* g_1(u_3^*)}{\mu_3} h\left(\frac{\phi_3(x,0)}{u_3^*} \right) \Bigg\} dx\end{aligned}$$

for $\phi = (\phi_1, \phi_2, \phi_3) \in \mathcal{C}_\tau^+$. Taking derivative along the solution $u = (u_1, u_2, u_3)$, we obtain

$$\frac{d}{dt}\mathcal{L}(u) = -\int_\Omega \left(\frac{d_1 u_1^*}{u_1^2} |\nabla u_1|^2 + \frac{d_2 u_2^*}{\rho(\tau) u_2^2} |\nabla u_2|^2 \right) dx - \int_\Omega M(x,t) dx,$$

where

$$\begin{aligned} M =& (1 - \frac{u_1^*}{u_1})(n(u_1^*) - n(u_1)) + \frac{u_1^* u_2}{f_1(u_2)} (f_1(u_2) - f_1(u_2^*)) \left(\frac{f_1(u_2^*)}{u_2} - \frac{f_1(u_2)}{u_2} \right) \\ &+ \frac{u_1^* u_3}{g_1(u_3)} (g_1(u_3) - g_1(u_3^*)) \left(\frac{g_1(u_3^*)}{u_3^*} - \frac{g_1(u_3)}{u_3} \right) \\ &+ u_1^* f_1(u_2^*) \left(h(\frac{u_1^*}{u_1}) + h(\frac{u_2 f_1(u_2^*)}{u_2^* f_1(u_2)}) + h(\frac{u_{1,-\tau} u_2^* f_1(u_{2,-\tau})}{u_1^* u_2 f_1(u_2^*)}) \right) \\ &+ u_1^* g_1(u_3^*) \left(h(\frac{u_1^*}{u_1}) + h(\frac{u_2 u_3^*}{u_2^* u_3}) + h(\frac{u_3 g_1(u_3^*)}{u_3^* g_1(u_3)}) + h(\frac{u_{1,-\tau} u_2^* g_1(u_{3,-\tau})}{u_1^* u_2 g_1(u_3^*)}) \right). \end{aligned}$$

It follows from $(\mathbf{H}_2)$-$(\mathbf{H}_3)$ that n', f_1'' and g_1'' are nonpositive functions. Consequently, $M \leq 0$ and $\frac{d}{dt}\mathcal{L} \leq 0$. The largest invariant set on which the equality holds is the singleton $\{u^*\}$. By Lyapunov-LaSalle invariance principle, the homogeneous steady state u^* is globally attractive. Especially, it is the unique positive steady state.

Finally, we will prove that u^* is locally asymptotically stable when $R_0 > 1$. Assume to the contrary that there exists an eigenvalue λ with positive real part for the linearized system of (1.1) about u^*. There exists a nonnegative eigenvalue ξ of $-\Delta$ with the homogeneous Neumann boundary condition on Ω such that the determinant of the following matrix

$$\begin{pmatrix} n'(u_1^*) - f_1(u_2^*) - g_1(u_3^*) - \lambda - d_1\xi & -u_1^* f_1'(u_2^*) & -u_1^* g_1'(u_3^*) \\ \rho_\lambda(\tau)[f_1(u_2^*) + g_1(u_3^*)] & \rho_\lambda(\tau) u_1^* f_1'(u_2^*) - \mu_2 - \lambda - d_2\xi & \rho_\lambda(\tau) u_1^* g_1'(u_3^*) \\ 0 & k & -\mu_3 - \lambda \end{pmatrix}$$

vanishes, where $\rho_\lambda(\tau) := \rho(\tau)e^{-\lambda\tau}$. A simple calculation yields

$$\begin{aligned} &(\lambda + \mu_3)(\lambda + d_2\xi + \mu_2)\left(\lambda + d_1\xi - n'(u_1^*) + f_1(u_2^*) + g_1(u_3^*)\right) \\ =&\rho_\lambda(\tau)(\lambda + d_1\xi - n'(u_1^*))\left(\lambda u_1^* f_1'(u_2^*) + \mu_3 u_1^* f_1'(u_2^*) + k u_1 g_1'(u_3^*)\right), \end{aligned}$$

which can be rewritten as $P_L = P_R$, where

$$\begin{aligned} P_L :=& \frac{\lambda + \mu_3}{\frac{\lambda u_1^* f_1'(u_2^*)}{u_1^* f_1'(u_2^*) + k u_1 g_1'(u_3^*)/\mu_3} + \mu_3} \left(\frac{\lambda + d_2\xi}{\mu_2} + 1\right)\left(\frac{f_1(u_2^*) + g_1(u_3^*)}{\lambda + d_1\xi - n'(u_1^*)} + 1\right), \\ P_R :=& \frac{\rho_\lambda(\tau)}{\mu_2}\left(u_1^* f_1'(u_2^*) + \frac{k u_1^* g_1'(u_3^*)}{\mu_3}\right). \end{aligned}$$

It is obvious that $|P_L| > 1$. On the other hand, since $f_1'(u_2^*) \le f_1(u_2^*)/u_2^*$ and $g_1'(u_3^*) \le g_1(u_3^*)/u_3^*$, we have

$$|P_R| \le \frac{\rho(\tau)}{\mu_2}\left[\frac{u_1^* f_1(u_2^*)}{u_2^*} + \frac{k u_1^* g_1(u_3^*)}{\mu_3 u_3^*}\right] = 1.$$

This leads to a contradiction. To summarize, we have the following theorem.

Theorem 5.1. *Assume that $(\chi(\tau) \circ \psi)(x) = \rho(\tau)\psi(x)$ and the model parameters are spatial homogeneous. Let R_0, f and g be given as in (5.1) and (5.2), respectively. If $R_0 > 1$, then model (1.1) possesses a unique positive steady state which is homogeneous and globally asymptotically stable.*

6. Numerical simulations

In this section, we perform numerical simulations to verify our theoretical results and to illustrate singular perturbation phenomenon when the diffusion coefficients tend to zero. For simplicity, we assume that the domain is an interval $[0, 1]$ with the length of unit kilometer, and the time unit is one day. Based on [14,22], we introduce spatial heterogeneity to the model system by choosing

$$k(x) = 24 - 12x, \quad \mu_2(x) = 0.24 + 0.24x, \quad \mu_3(x) = 2.4 + 2.4x.$$

Moreover, we assume that $n(x, u_1) = 10 - 0.02u_1 + 0.03u_1(1 - u_1/1500)$, $f(x, u_1, u_2) = 0.00012u_1u_2$ and $g(x, u_1, u_3) = 0.000024u_1u_3$ are spatial homogeneous functions. As shown in Theorem 3.2, the basic reproduction number R_0 is decreasing in both d_2 and τ when we choose the delta kernel $[\chi(\tau)\psi](x) = e^{-0.02\tau}\psi(x)$, see Fig. 1. If we choose the following nonlocal kernel function

$$[\chi(\tau)\psi](x) = \frac{e^{-0.02\tau}\int_\Omega e^{-(x-y)^2}\psi(y)dy}{\int_\Omega e^{-(x-y)^2}dy}. \tag{6.1}$$

It is also observed that R_0 is decreasing in both d_2 and τ, see Fig. 1. We then numerically find out that the nonlocal infection cannot change the monotonicity of the basic reproduction number with respect to d_2 and τ.

Next, we choose the delta kernel $[\chi(\tau)\psi](x) = e^{-0.02\tau}\psi(x)$, and define the local basic reproduction number of infection

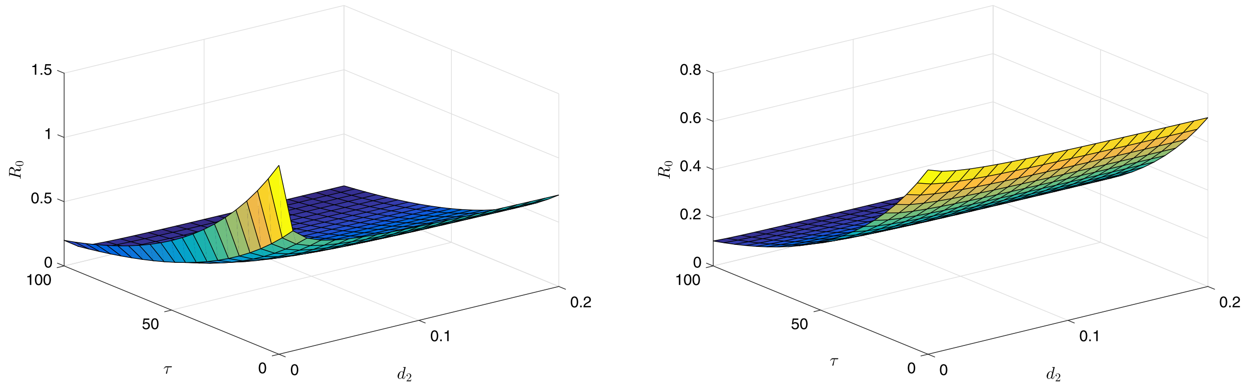

Fig. 1. The basic reproduction number R_0 is a decreasing function of the diffusion coefficient d_2 and the delay τ. Left: $[\chi(\tau)\psi](x) = e^{-0.02\tau}\psi(x)$. Right: $[\chi(\tau)\psi](x)$ is defined in (6.1).

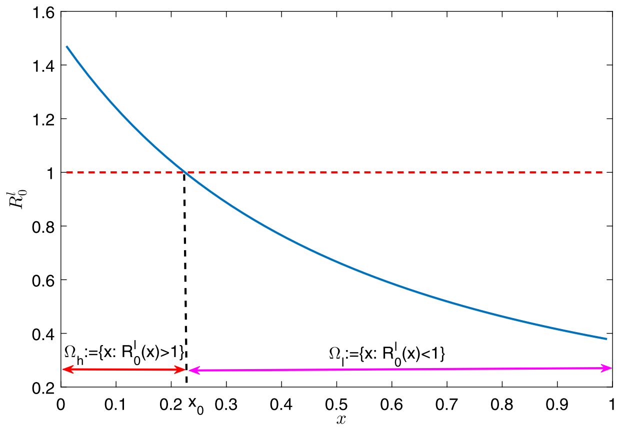

Fig. 2. The local basic reproduction number R_0^l.

$$R_0^l(x) = \frac{e^{-0.02\tau}\beta_d(x)}{\mu_2(x)} + \frac{e^{-0.02\tau}\beta_i(x)k(x)}{\mu_2(x)\mu_3(x)},$$

where $\beta_d(x)$ and $\beta_i(x)$ are defined in (3.1). Following the ideas in [1], we divide the whole domain into a high-risk region $\Omega_h := \{x \in \Omega : R_0^l(x) > 1\}$ and a low-risk region $\Omega_l := \{x \in \Omega : R_0^l(x) < 1\}$. For simplicity, we also set $\tau = 0$. Numerical calculation shows that $R_0^l(x) \leq 1$ when $x \geq x_0 \approx 0.22$ and $R_0^l(x) > 1$ when $x < x_0$, see Fig. 2.

Now, we set $d_1 = 0.02$ and $d_2 = 0.002$, and compute the steady state solution via finite difference and Newton's method. It is noted from Fig. 3 that the steady state of actively infected hosts distributions $u_2(x)$ for diffusion-free system is zero in the low-risk region, and the infection will persist only in the high-risk region. However, the diffusion enables the infection to propagate through the whole domain. Moreover, it may also increase the infection level in the high-risk region. This agrees with the phenomenon observed in [28].

To further understand the singular perturbation of steady state solution when the diffusion coefficients approach zero, we choose small diffusion coefficients $d_1 = d_2 = 0.000002$, and compare the steady state solution with that for the diffusion-free system. Note from Fig. 4 that the steady state solutions for small diffusion system and diffusion-free system are close to each other except near the high-risk boundary or the interface of high-risk and low-risk regions. To investigate the boundary and internal layers, we compare the gradients of steady state solutions (i.e., $u_2'(x)$) for both systems. We observe that a boundary layer occurs near the high-risk boundary (i.e., $x = 0$), where the steady state solution for the diffusion-free system

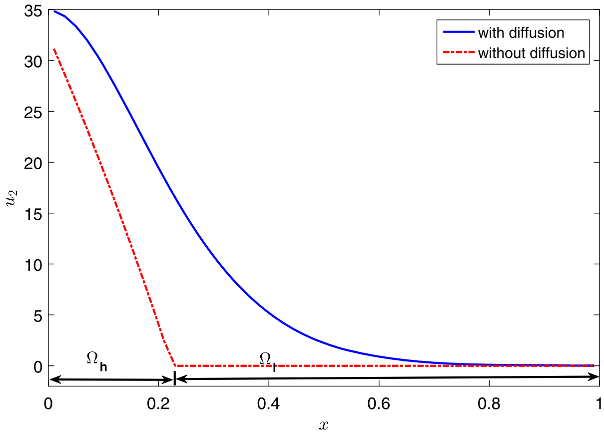

Fig. 3. Comparison of steady states of actively infected hosts distributions $u_2(x)$ for diffusion-free system (solid curve) and diffusion system (dashed curve).

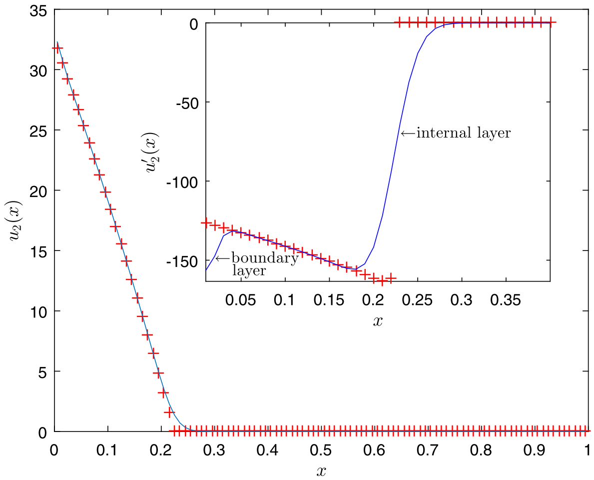

Fig. 4. The profiles of steady states $u_2(x)$ and their gradients $u_2'(x)$ of actively infected hosts distributions for diffusion-free system (plus signs) and low diffusion system (solid curves), respectively.

does not satisfy the homogeneous Neumann boundary condition. Moreover, the gradient of the steady state solution for the diffusion-free system is not continuous near the interface of high-risk and low-risk regions, which induces an internal boundary layer.

7. Conclusion

As a summary, we have proposed a general diffusive host-pathogen model with an incubation period and nonlocal infections in a spatially heterogeneous environment. Energy estimate and interpolation inequality are used to obtain the global existence and well-posedness of the system. We define the basic reproduction number R_0 in terms of the next generation operators for both direct and indirect infection modes. Analytical properties of R_0 and biological interpretations are also provided. We further prove that R_0 is the threshold parameter for the global dynamics of the model. If $R_0 \leq 1$, then the infection-free steady state is globally asymptotically stable. If $R_0 > 1$, then the infection is uniformly persistent and there exists at least one positive steady state. For the special case of spatial homogeneous system, there is a unique positive steady state, which is homogeneous and globally asymptotically stable. We use numerical simulations to illustrate the theoretical results on the monotonicity of R_0 in the diffusion coefficient of actively infected hosts and the incubation period. We also observe that the diffusion will spread the infection to the low-risk region and increase the infection level in the high-risk region. When the diffusion coefficients approach zero, the homogeneous Neumann boundary conditions will induce a boundary layer near the high-risk boundary. Moreover, an internal layer may occur near the interface of high-risk and low-risk regions. Finally, we mention that a possible future research work is to incorporate the models with fractional derivatives; see [4,5,15].

Acknowledgments

We would like to express our gratitude to the anonymous referees for their constructive comments and suggestions. H. Shu is partially supported by the National Natural Science Foundation of China (No. 11971285), and the Fundamental Research Funds for the Central Universities (No. GK202201002). H. Wang is partially supported by the Natural Sciences and Engineering Research Council of Canada (Discovery Grant RGPIN-2020-03911 and Accelerator Grant RGPAS-2020-00090).

References

[1] L.J.S. Allen, B.M. Bolker, Y. Lou, A.L. Nevai, Asymptotic profiles of the steady states for an SIS epidemic reaction-diffusion model, Discrete Contin. Dyn. Syst. 21 (2008) 1–20.
[2] R.M. Anderson, R.M. May, The population dynamics of microparasites and their invertebrate hosts, Philos. Trans. R. Soc. Lond. B, Biol. Sci. 291 (1981) 451–524.
[3] J.R. Andrews, S. Basu, Transmission dynamics and control of cholera in Haiti: an epidemic model, Lancet 377 (2011) 1248–1255.
[4] D. Baleanu, M.H. Abadi, A. Jajarmi, K.Z. Vahid, J.J. Nieto, A new comparative study on the general fractional model of COVID-19 with isolation and quarantine effects, Alex. Eng. J. 61 (2022) 4779–4791.
[5] D. Baleanu, F.A. Ghassabzade, J.J. Nietoe, A. Jajarmi, On a new and generalized fractional model for a real cholera outbreak, Alex. Eng. J. 61 (2022) 9175–9186.
[6] E. Bertuzzo, R. Casagrandi, M. Gatto, I. Rodriguez-Iturbe, A. Rinaldo, On spatially explicit models of cholera epidemics, J. R. Soc. Interface 7 (2010) 321–333.
[7] S.F. Dowell, J.W. Tappero, T.R. Frieden, Public health in Haiti − challenges and progress, N. Engl. J. Med. 364 (2011) 300–301.
[8] G. Dwyer, Density dependence and spatial structure in the dynamics of insect pathogens, Am. Nat. 143 (1994) 533–562.
[9] M.C. Eisenberg, Z. Shuai, J.H. Tien, P. van den Driessche, A cholera model in a patchy environment with water and human movement, Math. Biosci. 246 (2013) 105–112.
[10] K.-J. Engel, R. Nagel, One-Parameter Semigroups for Linear Evolution Equations, Graduate Texts in Mathematics, vol. 194, Springer-Verlag, New York, 2000.
[11] I.D. Gilbarg, N.S. Trudinger, Elliptic Partial Differential Equations of Second Order, Springer, Berlin, 1983.
[12] Goma Epidemiology Group, Public health impact of Rwandan refugee crisis: what happened in Goma, Zaire, in July, 1994?, Lancet 345 (1995) 339–344.
[13] J.K. Hale, Asymptotic Behavior of Dissipative Systems, American Mathematical Society, Providence, 1988.
[14] D.M. Hartley, J.G. Morris Jr., D.L. Smith, Hyperinfectivity: a critical element in the ability of V. cholerae to cause epidemics?, PLoS Med. 3 (2006) 63–69.
[15] A. Jajarmi, D. Baleanu, K.Z. Vahid, S. Mobayen, A general fractional formulation and tracking control for immunogenic tumor dynamics, Math. Methods Appl. Sci. 45 (2022) 667–680.
[16] R.I. Joh, H. Wang, H. Weiss, J.S. Weitz, Dynamics of indirectly transmitted infectious diseases with immunological threshold, Bull. Math. Biol. 71 (2009) 845–862.
[17] W. Kerscher, R. Nagel, Asymptotic behavior of one-parameter semigroups of positive operators, Acta Appl. Math. 2 (1984) 297–309.
[18] R. Koenig, Public health: International groups battle cholera in Zimbabwe, Science 323 (2009) 860–861.
[19] P. Magal, X.-Q. Zhao, Global attractors and steady states for uniformly persistent dynamical systems, SIAM J. Math. Anal. 37 (2005) 251–275.
[20] R. Martin Jr., H.L. Smith, Abstract functional differential equations and reaction-diffusion systems, Trans. Am. Math. Soc. 321 (1990) 1–44.
[21] C. Miller, R. Feachem, B. Drasar, Cholera epidemiology in developed and developing countries: new thoughts on transmission, seasonality, and control, Lancet 1 (1985) 261–263.
[22] Z. Mukandavire, S. Liao, J. Wang, H. Gaff, D.L. Smith, J.G. Morris, Estimating the reproductive numbers for the 2008-2009 cholera outbreaks in Zimbabwe, Proc. Natl. Acad. Sci. USA 108 (2011) 8767–8772.
[23] E.J. Nelson, J.B. Harris, J.G. Morris, S.B. Calderwood, A. Camilli, Cholera transmission: the host, pathogen and bacteriophage dynamics, Nat. Rev. Microbiol. 7 (2009) 693–702.
[24] R.D. Nussbaum, Eigenvectors of Nonlinear Positive Operator and the Linear Krein-Rutman Theorem, Fixed Point Theory, Lecture Notes in Mathematics, vol. 886, Springer, Berlin, 1981, pp. 309–331.

[25] C.V. Pao, Nonlinear Parabolic and Elliptic Equations, Plenum, New York, 1992.
[26] A. Pazy, Semigroups of Linear Operators and Application to Partial Differential Equations, Springer, Berlin, 1983.
[27] M.H. Protter, H.F. Weinberger, Maximum Principles in Differential Equations, Springer-Verlag, New York, 1984.
[28] H. Shu, Z. Ma, X.-S. Wang, Threshold dynamics of a nonlocal and delayed cholera model in a spatially heterogeneous environment, J. Math. Biol. 83 (2021) 41–73.
[29] H.L. Smith, Monotone Dynamical Systems: an Introduction to the Theory of Competitive and Cooperative Systems, American Mathematical Society, Providence, 1995.
[30] H.L. Smith, X.-Q. Zhao, Robust persistence for semidynamical systems, Nonlinear Anal. 47 (2001) 6169–6179.
[31] H.R. Thieme, Spectral bound and reproduction number for infinite-dimensional population structure and time heterogeneity, SIAM J. Appl. Math. 70 (2009) 188–211.
[32] J.P. Tian, J. Wang, Global stability for cholera epidemic models, Math. Biosci. 232 (2011) 31–41.
[33] J.H. Tien, D.J.D. Earn, Multiple transmission pathways and disease dynamics in a waterborne pathogen model, Bull. Math. Biol. 72 (2010) 1506–1533.
[34] A.R. Tuite, J.H. Tien, M.C. Eisenberg, D.J.D. Earn, J. Ma, D.N. Fisman, Cholera epidemic in Haiti, 2010: using a transmission model to explain spatial spread of disease and identify optimal control interventions, Ann. Intern. Med. 154 (2011) 293–302.
[35] F.B. Wang, J. Shi, X. Zou, Dynamics of a host-pathogen system on a bounded spatial domain, Commun. Pure Appl. Anal. 14 (2015) 2535–2560.
[36] W. Wang, X.-Q. Zhao, Basic reproduction numbers for reaction-diffusion epidemic models, SIAM J. Appl. Dyn. Syst. 11 (2012) 1652–1673.
[37] X. Wang, X.-Q. Zhao, J. Wang, A cholera epidemic model in a spatiotemporally heterogeneous environment, J. Math. Anal. Appl. 468 (2018) 893–912.
[38] Y. Wu, X. Zou, Dynamics and profiles of a diffusive host-pathogen system with distinct dispersal rates, J. Differ. Equ. 264 (2018) 4989–5024.
[39] X.-Q. Zhao, Dynamical Systems in Population Biology, second edition, CMS Books in Mathematics, Springer, 2017.